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Challenges in implementing digital health in public health settings in low and middle income countries

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Challenges in implementing digital health in public health settings in low and middle income countries

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Editorial: Challenges in implementing digital health in public health settings in low and middle income countries

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digital health, COVID-19, challenge, mHealth, healthcare

Editorial on the Research Topic
Challenges in implementing digital health in public health settings in low and middle income countries

Healthcare challenges in low- and middle-income (LMICs) have been the focus of many digital initiatives that have aimed to ensure consistent implementation of these services. During the COVID-19 pandemic, several lockdowns were imposed globally by government authorities to contain the spread of the virus. This triggered a rapid effort to integrate digital technologies into the existing health systems of LMICs (1). Digital services have the potential to improve access and care coordination across health facilities by overcoming the conventional obstacles and weaknesses of traditional systems. To promote better adoption of digital health tools the challenges need to be understood and strategies to overcome barriers must be evaluated. Hence the aim of this Research Topic was to identify specific organizational and related barriers in implementing digital health in public health settings in LMICs and further explore facilitators for successful implementation of digital technologies.

During the pandemic, many countries have been developing mHealth apps to identify prevalent symptoms, self-assessment, contact tracing and disseminating information. This helped to minimize exposure avoiding physical interaction between patients and health workers. Sujarwoto et al., systematically reviewed COVID-19 related mHealth apps in Indonesia and found the main uses were disseminating information, self-risk assessment, providing an online community forum and teleconsultation. They highlighted the challenges related to data security, privacy, integration and infrastructure. Tjiptoatmadja and Alfian, assessed awareness, perception, and willingness to use telepharmacy services and reported that over half of the study participants, had heard about telepharmacy and the majority of them had a positive perception and were willing to use telepharmacy services.

Lee et al. focused upon developing sustainable genomics surveillance programs in LMICs through adoption of a target operating model in a stepwise manner. The authors discussed the various barriers faced by such programs e.g., resource limitations, workforce strain, unreliable supply chains and lack of enduring champions, which exacerbate implementation and sustainability challenges. In other work, Iyamu et al. (2), discussed various technical (fragmented and unsustainable systems, lack of clear standards, and unreliability of available

data, infrastructure gaps, and workforce capacity gaps) and non-technical challenges (ethics, policy and governance, health equity, resource gaps, and quality of evidence) in the development of digital public health interventions.

One of the challenges of implementation of digital health in LMICs is cost. A detailed protocol on determining the costs of a large mHealth job aid for health and nutrition in India is discussed by Shukla and Kapur, through a behavior change communication tool known as ICDS-CAS (Integrated Child Development Services-Common Application Software). This research used the Activity Based Costing—Ingredients (ABC-I) method approach with aims to break down the program into a sum of mutually exclusive and exhaustive activities. A brief review by Yogesh and Karthikeyan, discussed the future trends and directions in health informatics, noting that there are no proven design blueprints for a comprehensive infrastructure. The authors also report that big data is playing an important role in health informatics, where a large amount of data related to healthcare is generated.

A report of two case studies from India by Senjam and Primo, focused upon the challenges and enablers for smartphone use by persons with vision loss during the COVID-19 pandemic. The most important enabling factors found were the presence of a screen reader, data connection of the mobile and the ability to assess multiple languages. Conversely, frequent challenges included poor battery backup, frequent unwanted ads or pop-ups unreadable by a screen reader, and slow or unresponsive screen readers. In a study from Nepal, Sankhi et al. (3) interviewed blind teenagers about the challenges experienced when using smartphones as assistive devices. Lack of training in using the devices was an issue and screen-readers' limitations in correctly pronouncing the local language are highlighted.

In another study on eye health in Pakistan Khan A. A. et al., had the goal of increasing eye health program coverage and effectiveness by using various strategies including digital data monitoring and visualization. The authors show that modifications of the program based on ongoing review of data and evidence can improve the program, specifically attendance to hospital appointments. The continued monitoring of gender imbalances in program data is another advantage of the system. Burton et al. (4), Mercer et al. (5), and Ramke et al. (6), argue that in order to tackle Sustainable Development Goal (SDG) 5—Gender Equality—it is important to monitor how a program is reaching each gender, and take necessary measures to make it easier for all patients to access assessment and treatment.

In a review of literature on AI approaches for promoting maternal and neonatal health in low resource settings by, Khan M. et al., pointed out to unreliable data collection and explainability in AI is a major roadblock to its widespread adoption of, of AI/ML algorithms,.

Another research article by Chai et al., demonstrated the use of a 5G-based robot-assisted remote ultrasound system (MGIUS-R3; Wisonic Medical Technology Co., Ltd., Shenzhen, China) that was used for the tele-examination for patients with disabilities at a remote care center. The same patients were examined by two independent sonographers using 5G-based robot-assisted remote ultrasound. The authors concluded that the use of a 5G-based robot-assisted remote ultrasound system is feasible in patients with disabilities at a remote care center and results in similar diagnostic efficacy to traditional bedside ultrasound, the gold standard. A similar article by Lim et al., evaluated the reliability and accuracy of 2D photogrammetry, as compared to direct measurement (gold standard). The authors discuss that three facial dimensions cannot be measured reliably and accurately using the 2D photogrammetry method because of poor inter-rater reliability of 2D photogrammetry.

In another study on remote monitoring Jain et al., reported the success of monitoring and holistic care of healthcare workers affected with mild COVID-19 and residing under home isolation through the use of digital technology. Healthcare workers faced additional challenges when compared to the general population besides a greater risk of becoming infected, harboring a higher virological burden, and a potentially more serious illness, they have additional work-related and psychosocial stressors.

Taken together, this collection of articles highlight the need to test the validity and reliability of digital health tools to streamline their function and design them according to the needs of programs in low income countries in order to minimize implementation challenges. Policymakers must consider usefulness, usability, integration, and infrastructure issues to improve their digital health functions. For full-scale sustainability, financing for all aspects of digital health solutions needs to be integrated into routine health budgets and the budgeting processes.

Author contributions

MD wrote the editorial. All authors co-edited the Research Topic, contributed to the editorial editing, and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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ORIGINAL RESEARCH
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Reliability and Accuracy of 2D Photogrammetry: A Comparison With Direct Measurement

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Objective: Facial anthropometric data is important for the design of respirators. Two-dimensional (2D) photogrammetry has replaced direct anthropometric method, but the reliability and accuracy of 2D photogrammetry has not been quantified. This study aimed to assess inter-rater reliability of 2D photogrammetry and to examine the reliability and accuracy of 2D photogrammetry with direct measurement.

Design: A cross-sectional study.

Setting: Malaysia.

Participants: A subset of 96 participants aged 18 and above.

Primary and secondary outcomes: Ten facial dimensions were measured using direct measurement and 2D photogrammetry. An assessment of inter-rater reliability was performed using intra-class correlation (ICC) of the 2D images. In addition, ICC and Bland-Altman analyses were used to assess the reliability and agreement of 2D photogrammetry with direct measurement.

Results: Except for head breadth and bigonial breadth, which were also found to have low inter-rater reliability, there was no significant difference in the inter-rater mean value of the 2D photogrammetry. The mean measurements derived from direct measurement and 2D photogrammetry were mostly similar. However, statistical differences were noted for two facial dimensions, i.e., bizygomatic breadth and bigonial breadth, and clinically the magnitude of difference was also significant. There were no statistical differences in respect to the remaining eight facial dimensions, where the smallest mean difference was 0.3 mm and biggest mean difference was 1.0 mm. The ICC showed head breadth had poor reliability, whilst Bland-Altman analyses showed seven out of 10 facial dimensions using 2D photogrammetry were accurate, as compared to direct measurement.

Conclusion: Only certain facial measurements can be reliably and accurately measured using 2D photogrammetry, thus it is important to conduct a reliability and validation study before the use of any measurement methods in anthropometric studies. The results of this study also suggest that 2D photogrammetry can be used to supplement direct measurement for certain facial dimensions.

Keywords: 2D photogrammetry, direct measurement, accuracy, facial anthropometric measurements, reliability

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BACKGROUND

Craniometry is a specific component of anthropometry that focuses on the measurement of the anatomical size of the head and face of living subjects. It is widely applied in orthodontic and reconstructive surgery, forensics, and the design of helmets, masks, eyeglasses and respirators (1). Numerous local anthropometric studies have been undertaken to achieve various objectives for the different needs of a range of target groups such as preschool children (2), young adults (3) and older persons (4), and such studies include some that have focused on the facial anthropometry of the Malaysian population (5–10). Many of these studies highlight the importance of incorporating ergonomic principles into design to ensure end-products fit with the body conditions and sizes of the target users.

Several methods can be used to measure facial soft tissues. These include manual anthropometry (11, 12) and two-dimensional (2D) (5, 10, 13–16) and 3-dimensional (3D) (8, 17, 18) imaging techniques. Manual anthropometry takes direct measurements from the subject using sliding and spreading callipers, flexible measuring tapes and protractors. The main advantages of this method are that it is non-invasive and low cost. However, despite being considered the gold standard for facial measurement, it has some disadvantages; for example, it is time consuming and it depends on the participant's compliance for reliable results. Furthermore, it is investigator dependent, meaning that there is a possibility that the investigator may apply too much pressure on the equipment during measurement, which may distort soft tissue and introduce measurement errors.

Nowadays, 2D and 3D measurement techniques are commonly used to measure human anthropometric characteristics. The 2D imaging technique provides a snapshot of an object, thus it requires the participant's cooperation during image acquisition. Despite evidence to show that the 3D imaging technique is more accurate (19, 20), the 2D option is still preferred because it is cheap, non-invasive, less time consuming and can be conducted on the ground, as in population surveys.

A number of studies have compared the performance of different anthropometry methods (19, 21–25). For example, one study that investigated the difference in human skull measurements by comparing conventional cephalometric radiographs against 3D measurements on 3D models found that measurements of the same skull can differ significantly (21). Likewise, another study also noted significant differences in facial dimensions when using 2D and 3D imaging techniques, and concluded that the two facial anthropometry methods cannot be equivalently used (22). Conversely, other studies that compared 3D with 2D (19, 23, 24) and 3D with direct measurement (19, 25, 26) found that the methods produced comparable results in terms of identifying facial soft-tissue landmarks.

Although 2D images have been used widely for facial tissue analysis (5, 10), evidence demonstrating the accuracy of 2D photogrammetry in measuring facial dimensions is lacking and that which does exist shows contradicting results. While some studies have shown that different anthropometry methods can be used interchangeably (19, 24, 27), other studies have revealed otherwise (21, 22). Nevertheless, studies that have examined the reliability and agreement of 2D photogrammetry in measuring facial dimensions, as compared to the gold standard manual method are still limited (19, 20, 28). Thus, this study aimed to determine the inter-rater reliability of 2D photogrammetry in measuring facial anthropometry, as well as the reliability and agreement of 2D photogrammetry, as compared to direct measurement. The significance of this validation study is that it will be used for a future population nationwide study to help us to develop own bivariate and Principal Component Analysis (PCA) panels, which is critical for the development of respirator.

Abbreviations: 95%CI, 95% Confidence Interval; 2D, 2-Dimensional; 3D, 3-Dimensional; ICC, Intraclass correlation; NHMS, National Health and Morbidity Survey; NIOSH, National Institute for Occupational Safety and Health; PCA, Principal Component Analysis; SD, Standard deviation; SE, Standard error.

METHODOLOGY

Study Design

A cross-sectional study was conducted among a subset of participants aged 18 and above who were involved in the National Health and Morbidity Survey (NHMS) Malaysia 2020. NHMS 2020 was a national population-based survey aimed at determining seroprevalence of COVID-19, hepatitis B and C in Malaysia. Representative samples were selected randomly from 2000 living quarters in selected Enumeration Blocks (EBs) using a two stage stratified sampling from the Department of Statistics, Malaysia (29). All household members who consented and fit the inclusion criteria were recruited into the survey. For this validation study, a subset of 96 respondents was conveniently selected from one district (Banting, Selangor) in West Malaysia and one district (Tawau, Sabah) from East Malaysia. Participants with a history of previous facial surgery, dental or facial deformity, and those with a beard or moustache were excluded from participating.

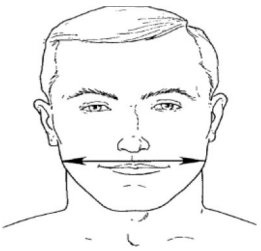
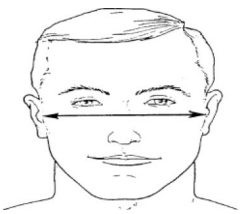
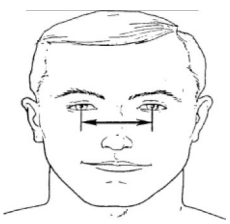
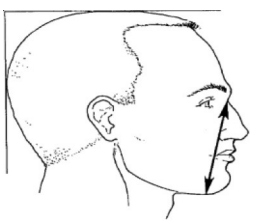
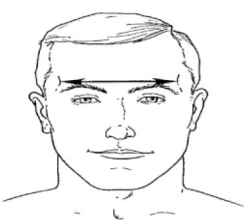
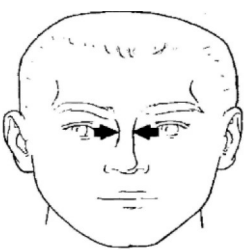
Data Collection

The 10 facial dimensions listed in **Table 1** were measured because they are critical for the development of respirators (30). A measurer's manual was created prior to the field investigation. The measurer was trained until the measurement errors were less than what was allowed. Usually, the allowable error margin was set at 2 mm for all the dimensions measured (28, 31). Prior to image acquisition, direct measurements were taken.

Direct Measurement Procedure

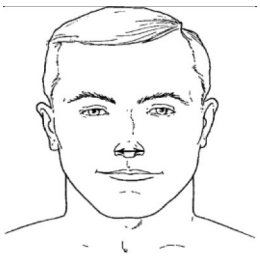
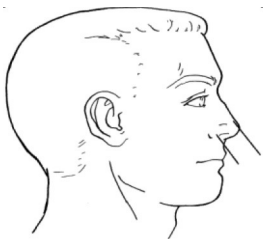
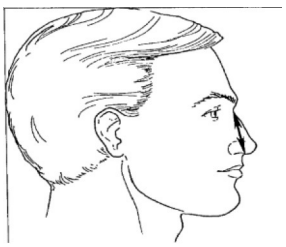
The 10 selected morphological points were located by inspection and/or palpation in accordance with the 1988 Anthropometric Survey of the US Army Personnel Project (31). Spreading callipers were used to measure head breadth, zygomatic breadth and bigonial breadth, whereas sliding callipers were used for the remaining seven facial dimensions. During the measurement process, the investigators endeavoured to ensure that the participants were relaxed and seated with a natural head position and relaxed lips.

TABLE 1 | Description, definition, and diagram of measurements (30).

Dimension	Description	Diagram
1. Bigonial breadth	Distance between the right and left gonion	
2. Bizygomatic breadth	Maximum horizontal breadth of the face	
3. Head breadth	Maximum horizontal breadth of the head	
4. Interpupillary distance	Distance between the centre of pupil	
5. Menton-sellion length	Distance between the menton and the sellion	
6. Minimum frontal breadth	Distance between the right and left frontotemporal	
7. Nasal root breadth	Horizontal breadth of nose at the sellion	

(Continued)

TABLE 1 | Continued

Dimension	Description	Diagram
8. Nose breadth	Distance between the right and left alare	
9. Nose protrusion	Distance between the pronasale and the subnasale	
10. Subnasale-sellion length	Distance between the subnasale and the sellion	

Photographic Set-Up

The participants' images were captured using a 20.0-megapixel digital camera (Canon IXUS 190, Tokyo, Japan) positioned on a tripod (Manfrotto MKCOMPACTLT-BK, Cassola, Italy) at a fixed distance of 1.0 metre. The tripod maintained the stability and correct height of the camera according to each participant's height. Participants were requested to wear a surgical cap to remove hair strands from their face and ears when needed. The frontal bony landmarks on their face were labelled with stickers. Before image capture, the participants were asked to look straight ahead holding their head in a neutral position without flexing or extending the neck, and to not smile or frown. Also, the head was kept in a posture so that the optical axis of the camera lens would pass through the Frankfurt plane of the head (32).

For each participant, one anterior and one lateral photo were taken. A blue screen was used as the background in order to create sufficient contrast with the colour of the skin. The camera height was adjusted based on the height of the subject's ear from the floor. For calibration purposes, a metric-scale ruler was placed above the forehead of the subject for the image taken from the anterior view (**Supplementary e-Figure 1**). On the other hand, the ruler was placed perpendicular to the nose of the subject for the image taken from the lateral view (**Supplementary e-Figure 2**). Each image was checked immediately after it was obtained to ensure absence of acquisition errors such as imaging artefacts, blurring, absence of surface data, poor orientation, closed eyes, and lack of neutral facial expression. Images with the incorrect characteristics were discarded, and new images were obtained to ensure that they met the established requirements.

All images were captured in JPEG format and were transferred to a computer after each day of shooting. The anthropometric dimensions were calculated using the software package Digimizer version 5.4.4. This software is very useful for analysing images as it is very flexible and simple to use. Its capabilities include providing the user with the ability to set contrast and brightness, change background images, change images to grayscale mode, measure angles, determine the centre of the segment and reduce image noise (33).

Inter-Rater Reliability of 2D Photogrammetry

For the inter-rater reliability assessment, the measurements made by the first observer were compared with those carried out by the second observer on the same photo images at a minimum of a 3-week interval, with no landmarks saved after the first measurement.

Statistical Analysis

The analyses were conducted using SPSS version 26 and MedCalc version 19.8. Normal distribution of the data was evaluated using the Shapiro-Wilk test. The results showed that none of the variables violated the normality distribution. To evaluate the inter-rater measurement reproducibility of 2D images, a different

TABLE 2 | Summary of anthropometric statistics between observers of the 2D photogrammetry and inter-rater reliability coefficient of 2D photogrammetry.

Dimensions	Observer A Mean ± SD	Observer B Mean ± SD	Mean differences ± SD	95% CI of mean differences	*P*-value	ICC	95% CI
1. Bizygomatic breadth*	140.2 ± 11.9	141.0 ± 9.8	0.8 ± 12.4	−3.1 to 1.5	0.468	0.66	0.50 to 0.76
2. Minimum frontal breadth	98.9 ± 9.1	99.0 ± 9.1	0.1 ± 1.5	−0.4 to 0.2	0.719	0.99	0.99 to 0.99
3. Bigonial breadth†	118.9 ± 13.0	126.9 ± 11.58	8.1 ± 12.4	−10.6 to −5.6	<0.005	0.16	−0.25 to 0.44
4. Menton-sellion length	115.8 ± 9.2	115.9 ± 9.3	0.1 ± 2.1	−0.5 to −0.4	0.776	0.99	0.98 to 0.99
5. Interpupillary distance	64.4 ± 3.8	64.6 ± 3.9	0.1 ± 1.1	−0.4 to −0.1	0.248	0.98	0.97 to 0.99
6. Head breadth†	149.3 ± 18.3	160.6 ± 9.7	11.2 ± 19.5	−15.2 to −0.7	<0.005	0.03	−0.46 to 0.35
7. Nose protrusion	17.1 ± 2.3	17.1 ± 2.2	0.1 ± 1.1	−0.2 to 0.2	0.865	0.94	0.91 to 0.96
8. Nose breadth	42.2 ± 3.5	42.3 ± 3.6	0.1 ± 1.1	−0.3 to 0.1	0.343	0.98	0.97 to 0.99
9. Nasal root breadth	18.9 ± 2.7	18.5 ± 2.3	0.4 ± 1.8	−0.1 to 0.7	0.060	0.85	0.78 to 0.91
10. Subnasal-sellion length	47.3 ± 4.6	47.5 ± 4.6	0.2 ± 2.0	−0.6 to 0.2	0.411	0.95	0.93 to 0.98

**Moderate reliability with wide CI.*
† Low reliability with wide CI.
CI, confidence interval; ICC, intraclass correlation; SD, standard deviation.

observer took measurements using the same method as the first observer, and results were evaluated using paired sample *t*-test and intra-class correlation (ICC) coefficient. Next, paired sample *t*-test and ICC were also conducted to determine the mean differences and reliability between direct measurement and the average of 2D photogrammetry methods.

ICC provides information on the ability to differentiate variations between participants and measurement. The ICC was defined as the ratio of variance among participants (participant variability) over the total variance (participant variability, observer variability and measurement variability). The ICC value ranges between 0 (no reliability) and one (perfect reliability). In line with prior research, in this study < 0.4 indicates poor reliability, 0.4–0.75 indicates moderate reliability, and ≥ 0.75 indicates excellent reliability (34).

The degree of agreement between the two methods was further evaluated using Bland-Altman analysis, where the difference between the measurements was plotted against the average of the two measurements. The plot generates three horizontal reference lines that are superimposed on a scatterplot: one line represents the average difference between the measurements, and the upper and lower lines mark the two-standard deviation (±2 SD) from the mean differences. In a Bland-Altman analysis, two criteria need to be met to establish that the two measurement methods are comparable. First, the mean differences should be small and close to 0. Second, the SD of this difference should be small (35). However, there are no guidelines on how narrow the limit of agreement needs to be before the two methods can be considered interchangeable.

For all the statistical analyses, the methods were considered to be in good agreement and interchangeable at an arbitrary value of 2 mm between two observers and two methods (28). The statistical significance level was set as $p < 0.005$ for all statistical analysis.

Patient and Public Involvement

The study participants were not involved in the development of this study. The results of the study were not shared with the participants.

RESULTS

A total of 96 participants participated in this study, of whom 51 (53.1%) were female. The mean age of the participants was 43.3 ± 16.9 years old and they were predominantly of Malay ethnicity (60, 62.5%).

A reproducibility assessment was conducted to determine the mean differences and the level of reliability of 2D photogrammetry between two observers. The mean values between the two observers for the abovementioned 10 facial dimensions revealed no significant difference, except for bigonial breadth (8.1 mm) and head breadth (11.2 mm) (**Table 2**). The inter-rater ICC scores for the eight facial dimensions of 2D photogrammetry varied from 0.66 (95% CI 0.50–0.76) for bizygomatic breadth to 0.99 (95 % CI 0.98–0.99) for minimum frontal breadth, except for bigonial breadth (ICC: 0.16, 95 % CI: −0.25 to 0.44) and head breadth (ICC: 0.03, 95% CI: −0.46 to 0.35).

The mean differences between the direct and the 2D photogrammetry measurements were within 2.0 mm, except for bizygomatic breadth and bigonial breadth (**Table 3**). The largest mean differences were observed in bigonial breadth (9.3 mm), followed by bizygomatic breadth (3.3 mm). The smallest mean difference between the two methods was found in nose protrusion (0.4 mm) and nose breadth (0.4 mm).

The reliability of using 2D photogrammetry and direct measurement for all measured dimensions varied from ICC = 0.81 (nose protrusion) to 0.99 (subnasal sellion length), except for head breadth [ICC: 0.36, 95% confidence interval (CI): 0.05–0.58] (**Table 4**). The highest ICC score was noted for subnasal sellion length (ICC: 0.99, 95% CI: 0.98–0.99), followed by menton sellion length (ICC: 0.98, 95% CI: 0.97–0.99) and minimum frontal breadth (ICC: 0.98, 95% CI: 0.97–0.99).

Supplementary e-Figure 3a to **Supplementary e-Figure 3j** show the level of agreements between direct measurement and 2D photogrammetry for 10 facial dimensions according to Bland-Altman plots (**Supplementary e-Figure 3**). The Y axis displayed the mean difference between two methods, whereas the X axis showed the mean of two different method. Ninety-five percentage

TABLE 3 | Summary of anthropometric statistics between direct measurement and 2D photogrammetry.

Dimensions	Direct measurement Mean ± SD	2D photogrammetry Mean ± SD	Mean differences ± SD	95% CI of mean differences	*P*-value
1. Bizygomatic breadth	137.3 ±9.6	140.6 ±9.3	3.3 ±5.5	2.2 to 4.4	<0.005
2. Minimum frontal breadth	98.4 ±9.8	99.0 ±9.0	0.6 ±2.9	0.02 to 1.2	0.040
3. Bigonial breadth	113.5 ±10.4	122.8 ±11.1	9.3 ±5.3	8.3 to 10.4	<0.005
4. Menton-sellion length	116.0 ±10.8	115.8 ±9.2	1.0 ±6.4	−2.3 to 0.3	0.124
5. Interpupillary distance	64.5 ±3.8	63.9 ±4.2	0.7 ±2.4	0.1 to 1.1	0.012
6. Head breadth	154.6 ±7.8	154.9 ±10.9	0.3 ±9.9	1.7 to 2.4	0.733
7. Nose protrusion	16.7 ±2.6	17.1 ±2.2	0.4 ±2.1	0.1 to 0.9	0.049
8. Nose breadth	42.6 ±3.8	42.2 ±3.5	0.4 ±2.3	−0.1 to 0.9	0.078
9. Nasal root breadth	18.2 ±3.6	18.7 ±2.4	0.5 ±2.3	0.1 to 1.0	0.028
10. Subnasal-sellion length	47.7 ±4.9	47.4 ±4.5	0.3 ±1.3	−0.5 to −0.1	0.044

CI, confidence interval; SD, standard deviation.

CI of limit of agreement was chosen to demonstrate the error bars for both the upper and lower limit of agreement. Seven facial dimensions showed a high degree of agreement between the two methods, i.e., minimum frontal breadth, subnasal sellion length, menton sellion length, interpupillary distance, nose protrusion, nose breadth and nasal root breadth. Poor agreement with a wide 95% CI was found for bigonial breadth (mean = 9.4, 95% CI: −0.9 to 19.6), bizygomatic breadth (mean = 3.3, 95% CI: −7.5 to 14.2) and head breadth (mean = 0.3, 95% CI: −19.0 to 19.7).

TABLE 4 | Reliability coefficient between direct measurement and 2D photogrammetry.

Dimensions	ICC	95% CI
1. Bizygomatic breadth	0.84	0.76–0.90
2. Minimum frontal breadth	0.98	0.97–0.99
3. Bigonial breadth	0.91	0.86–0.94
4. Menton-sellion length	0.98	0.97–0.99
5. Interpupillary distance	0.90	0.92–0.97
6. Head breadth*	0.36	0.05–0.58
7. Nose protrusion	0.81	0.72–0.88
8. Nose breadth	0.92	0.88–0.95
9. Nasal root breadth	0.83	0.75–0.90
10. Subnasal-sellion length	0.99	0.98–0.99

**Low reliability with wide CI.*
CI, confidence interval; ICC, intraclass correlation.

DISCUSSION

This study evaluated the reliability and accuracy of 2D photogrammetry, as compared to direct measurement which has been accepted as the gold standard. Our study showed that three facial dimensions, i.e., bigonial breadth, bizygomatic breadth, and head breadth, cannot be measured reliably and accurately using the 2D photogrammetry method. This was because, there were poor inter-rater reliability of 2D photogrammetry as well as between two different measurement methods for bigonial breadth and head breadth. There was also significant difference in the mean values between the two methods for bizygomatic breadth and bigonial breadth. Thus, only seven out of 10 facial dimensions can be measured reliably and accurately using 2D photogrammetry. The main reason for inaccurate head breadth may be the demography of respondents in this study. In Malaysia, the predominant religion is Islam and most female Muslims wear the hijab as a demonstration of their faith following the requirements of their religion. However, even without the hijab, the head breadth cannot be measured accurately because of varying hair thickness. Because of the limitations of 2D photogrammetry, it is also quite impossible to view zygomatic and gonial landmarks from the anterior view in 2D photogrammetry, even after marking the bony landmarks with stickers. The remaining seven dimensions showed no difference in terms of mean value and had a high level of agreement according to the ICC analysis.

The 2D photogrammetric method has been used widely by international (13–16) and local studies (5, 10). However, studies that compare 2D photogrammetry with direct measurement are scarce and have some limitations (19, 20, 28). There is also a lack of consensus among the existing studies. One study showed that 2D photogrammetry is not as accurate as the direct and 3D measurement methods for certain facial dimensions (19), while the two other studies showed that 2D photogrammetry is comparable to direct measurement (20, 28). Moreover, previous studies have mainly focused on oral maxillofacial dimensions, in contrast to our study, and none of the studies assessed the reliability and agreement of 2D photogrammetry with direct measurement simultaneously (20, 28). Furthermore, appropriate data analysis should be employed to confirm that tested and validated tools are both reliable and accurate.

Hence, the validation of the 10 facial dimensions considered in our study will be an important step in our future research, which aims to produce an anthropometric database of Malaysian head and facial measurements. The same 10 facial dimensions were used by the United States National Institute for Occupational Safety and Health in 2003 on 3997 civilian workers and by the

Chinese government in 2008 on 3000 Chinese civilian workers to develop respirator fit test panels (30, 36). Respirator fit test panels provide an objective measurement for selecting representative human test samples based on their facial dimensions for use in research, testing, certification and most importantly for respirator development.

Likewise, the 10 critical facial dimensions measured in our study can be used to develop two respirator fit test panels, i.e., a bivariate panel using face length and face width and a PCA panel using all 10 facial dimensions. The bivariate panel is simpler to use than the PCA panel. However, the inclusion of the eight additional facial measurements allows the PCA panel to apply better criteria to exclude the use of extreme face sizes. These 10 dimensions have been found to be associated with respirator fit and leakage and can predict the remaining face dimensions well (1). Moreover, the study in the United States showed that respirators designed to fit PCA panel are expected to accommodate more than 95% of current US civilian workers (30).

We acknowledge that our study has some limitations. First, direct measurements were only measured by one observer, thus reliability of this method cannot be calculated, as compared to the 2D photogrammetry measurements. However, we believe that the measurement errors in the direct measurement procedure were minimal in view of training that was conducted prior to the validation part of the study. Even though the facial dimensions were not measured using the 3D photogrammetry method, which has been found to be more accurate, direct measurement or 2D photogrammetry are more feasible for a nationwide population survey, especially in low- and middle-income countries. However, the disadvantages of the 2D technique include measurement errors due to subjective analysis, magnification errors, parallax, variation in lighting, and variation in head orientation.

On the other hand, the novelty of our work lies in the robust validation analysis that we undertook to validate the results generated by 2D photogrammetry against the gold standard of direct measurement. In addition to comparing the mean values of these two methods, we also used ICC and Bland-Altman Limit of Agreement analysis. The Bland-Altman Limit of Agreement and the ICC are the most popular methods to investigate statistical agreement and to assess the reliability of medical instruments, respectively (37). Agreement and reliability parameters are equally important in determining the quality of the applied method and these two parameters have not been assessed together in previous validation studies (19, 20). It is important to note that a method with good reliability will not be useful if it is not in good agreement with and vice versa. The other strength of our study lies in the reporting of the CI value when using the limits of agreement approach, as this means that the data can be generalised to a larger population. Moreover, the advantage of using the Bland-Altman approach is that it can reveal both systematic errors (bias) and random errors (limit of agreement) (38).

CONCLUSION

This study reveals that only seven out of 10 facial measurements can be measured reliably and accurately using 2D photogrammetry, thus it is important that a validation and reliability study is conducted before the use of any measurement methods in anthropometric studies. The results of this study also suggest that, given its practical benefits of being inexpensive, non-invasive, operator dependent and less time consuming, 2D photogrammetry can be used to supplement direct measurement for facial dimensions. Our future study, which will take place during the COVID-19 pandemic, will use a combination of direct measurement and 2D photogrammetry to create an anthropometric database of Malaysian head and facial measurements from over 3,000 participants. The use of 2D photogrammetry can also help to reduce exposure between observers and participants. The findings also indicate the important role that 2D photogrammetry can play in assessing certain facial morphologies in countries that have limited 3D scanner resources. Lastly, future studies to compare and validate the output of 2D photogrammetry against direct measurement in respect of other facial dimensions are also warranted to ensure that more of the dimensions can be measured in this way and it will be both accurate and reliable.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Materials**, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Medical Research and Ethics Committee (NMRR-20-1217-55489). The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

The study conception was by YL and RS. YL and RS designed the study. YL collected the data. YL, AA, and RS conducted the statistical analysis and interpreted the results. YL and AA drafted the manuscript. All authors have read and approved the final version of the submitted manuscript.

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SUPPLEMENTARY MATERIAL

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An Implementation Strategy to Develop Sustainable Surveillance Activities Through Adoption of a Target Operating Model

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The increasing threat of emerging and re-emerging pathogens calls for a shared vision toward developing and maintaining global surveillance mechanisms to enable rapid characterization of pathogens, a foundational requirement for effective outbreak response. Efforts establishing new surveillance programs in low- and middle-income countries (LMICs) have repeatedly led to siloed systems that prove unsustainable or ineffective due to narrowly focused approaches, competing priorities, or lack of resourcing. Barriers inherent to LMICs, such as resource limitations, workforce strain, unreliable supply chains, and lack of enduring champions exacerbate implementation and sustainability challenges. In order to improve adoption and endurance of new surveillance programs, more effective design and implementation of programs is needed to adequately reflect stakeholder needs and simultaneously support population-level disease monitoring and clinical decision-making across a range of chronic and acute health issues. At the heart of this cross-sectorial integration between clinical care and public health initiatives are emerging technologies and data modalities, including sequencing data. In this prospective, we propose an implementation strategy for genomics-based surveillance initiatives in LMICs founded on the use of a target operating model. Adoption of a target operating model for the design and implementation of genomic surveillance programs will ensure programs are agile, relevant, and unified across diverse stakeholder communities, thereby increasing their overall impact and sustainability.

Keywords: surveillance, public health, capacity building, low-middle-income countries, pathogen genomics, data architecture

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INTRODUCTION

The emergence of the COVID-19 pandemic has clearly demonstrated the importance of an expansive and dynamic global health surveillance network; however, as outlined in the 2021 Global Health Security Index, no country has adequate preparedness and control measures to prevent and respond to emerging infectious diseases and surveillance mechanisms proved insufficent to meet the public and global health demands (1, 2). Public health surveillance systems, such as the WHO's Global Influenza Surveillance and Response System, have proven the value of pre-existing health surveillance infrastructure that can pivot to address emerging needs during health crises

(3, 4). Despite decades of progress, these surveillance programs have proven insufficiently scalable or far-reaching to meet the demands of the pandemic (5).

Advanced sequencing techniques have proven invaluable in our collective efforts to detect SARS-CoV-2 and characterize its evolution throughout the pandemic (6, 7). While there has been rapid innovation in sequencing technologies and data analytics that enable high-throughput and cost-effective pathogen discovery and detection (8, 9), the full impact of these advances in infectious disease surveillance has yet to be realized. Prior to the COVID-19 pandemic, only 39% of low-income countries had contributed influenza virus genome sequences to public databases, in comparison to 78% of upper-middle and high-income countries, indicating a significant gap in operational genomics-based surveillance capacity (10). Across Africa, nearly three quarters of the roughly 200 available sequencers are located in just five countries, the vast majority of which are situated in privately owned genomic sequencing institutions (11, 12). For LMICs that do have pathogen genomics capacity, these efforts are often siloed (i.e., operating within a single sector and/or for a specific disease), with data analysis and interpretation performed outside the host country or even the continent (13). Health surveillance systems are inherently complex, and implementation programs for pathogen genomics in LMICs are confronted with additional roadblocks such as sparse infrastructure and limited resources (14–16). Efforts to expand these capabilities during the pandemic have faced compounding challenges, competing with other resource-intensive priorities in medical and laboratory settings which require a steady flow of supplies (17, 18).

Promising initiatives aim to dramatically improve genomic surveillance capacity. USAID has invested over one billion dollars in capacity development in LMICs (19), and implementation partners such as National Institutes of Health (NIH) Fogarty International Center continue to strengthen capacity in partner nations (20). A noteworthy recent example is the Africa Pathogen Genomics Initiative. This $100 million four-year collaboration between the Africa Centers for Disease Control and Prevention (CDC) Institute of Pathogen Genomics, US CDC, Bill & Melinda Gates Foundation, and industry leaders, aims to create an integrated pan-African disease surveillance and laboratory network, including a major genomic surveillance capability, to bolster public health responses to infectious disease (11, 12). These promising efforts provide strong models for multi-national collaboration and capacity development; however, such extraordinary investment cannot be expected at a global scale, and, once established, these systems must be self-sustaining and enduring to be effective in bolstering national and global preparedness.

There is clear acknowledgment by the global health community of the need to build surveillance systems that are no longer reactionary to individual outbreak events, but are flexible and sustainable, serving as ready resources in future infectious disease outbreaks. These objectives require re-envisioning how surveillance programs are designed and implemented, maximizing opportunities for long-term impact while minimizing requirements for ongoing investment. Critical factors for consideration include feasibility of epidemiological and genomic data integration into large-scale systems, relevance to decision-makers from the individual to national level, modular technologies enabling pathogen-agnostic detection, and cost-effective workflows to ensure resource requirements are matched to local and national contexts. To meet these challenges, the design of surveillance programs must be carefully evaluated and prioritized, particularly in LMICs where resources and infrastructure are constrained.

The framing of this problem space in the corporate world, described as optimizing resource investment to achieve strategic priorities, is traditionally defined as a target operating model (TOM). This approach relies on development of a roadmap to formulate and execute strategic objectives to reach a desired end state. A TOM also provides stakeholders a high order visualization and a shared understanding of the organizational components that comprise the operational workflow and how they unite to support desired objectives. This vantage allows for a shared mission and promotes consistency, critical in building a unified genomic surveillance system given the numerous stakeholders and range of needs to be supported by the workflow. Systems engineering best practices also provide means to model and deconstruct complex systems which are inherent in the operationalization of genomic surveillance, facilitating the identification of gaps in the TOM. Here, we propose a TOM for the design, development, and implementation of enduring genomic surveillance programs in LMICs.

A TARGET OPERATING MODEL FOR IMPLEMENTATION OF GENOMICS-BASED SURVEILLANCE PROGRAMS

Genomic sequencing is a powerful tool for detection and routine surveillance of emerging pathogens. It can provide absolute discriminatory power of viral pathogens during an outbreak by identifying single-point mutations or genes associated with increased virulence and pathogenicity in bacterial genomes. One of the most valuable features of sequencing is culture-free identification of pathogens, decreasing bias and time-to-answer. Real-time sequencing for the purpose of pathogen diagnostics provides critical epidemiological data to understand pathogen transmission, commonly referred to as genomic epidemiology (21). Broadly, the genomic surveillance workflow can be segmented into five distinct modules: sampling, testing, bioinformatics, analysis, and response (**Figure 1**). The success of a genomic surveillance program requires that necessary data are generated at the appropriate scale and can be interpreted within a relevant timeframe to support decision making; for example, early detection of an emerging infectious disease requires active sequencing capacity at sufficient scale in high vulnerability areas, while diagnostic sequencing requires actionable results in as close to real-time as possible (22).

A clear mechanism to define genomic surveillance objectives, develop an implementation strategy to reach them, and evaluate program success has been lacking. The TOM described here is a tool to define an implementation strategy for genomic

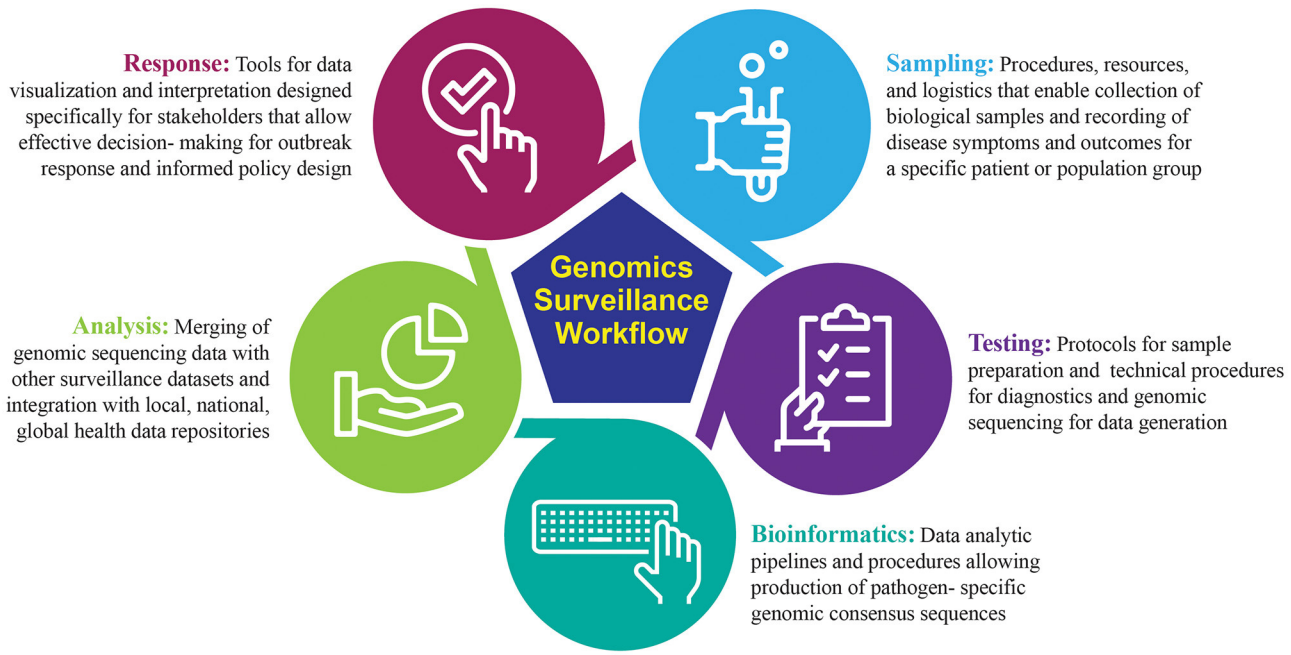

FIGURE 1 | Overview of end-to-end genomics-based surveillance workflow.

surveillance, fit to both stakeholder objectives and end-user needs. Each element of the TOM captures critical information to inform strategy development and outlines key considerations to achieve programmatic objectives (**Figure 2**).

Prioritized Sampling Detection

The first element of the TOM specifies objectives of the genomic surveillance program, including the desired pathogen(s) for detection and the catchment area parameters for establishing a genomic surveillance workflow. This element incorporates anthropological information describing the local population and their environment. Baseline data, such as age distribution and common underlying health conditions, contextualizes downstream epidemiologic analyses. Pathogen-specific information that describes current and historical trends for endemic diseases helps guide the prioritization of pathogens. Effort should be made to acknowledge local practices that increase risk of exposure to emerging infectious disease, such as the presence of live markets or burial customs, as these can be particularly relevant when designing surveillance strategies within a given region. This information can be gathered through a combination of literature reviews, interviews with those who have local expertise, and in partnership with local government.

Compiling this broad scope of data provides essential information to define the target population and catchment area parameters for high-priority pathogens. Together, this information permits further prioritization of surveillance activities and their required technologies. Passive and scalable methods such as satellite imagery of habitat destruction, analyses of regional climate fluctuation, or dynamics of human and animal migration could all provide additional information to further refine an ideal region for surveillance.

Capacity Needs Determination

The information collected to prioritize sampling is then used as the basis to determine optimal capacity and associated resource costs over the entire genomic surveillance workflow. Calculations to define optimal capacity needs should be guided by historical data, providing estimates of required sampling throughput to achieve the stated objectives. While there are tools that can assist in generating these estimates (23), there is a considerable need to develop tools specifically designed for genomic surveillance programs. Information gathered in TOM element one, such as historical trends and priority pathogens, will be essential in framing these calculations, ideally yielding a cost analysis for implementation and operational phases, including materials, equipment, infrastructure, and labor costs to achieve the desired objectives.

This analysis will further refine the scope and design of the program by assessing feasibility given financial constraints. It is critical to ensure that any planned surveillance programs are sustainable. For example, it may not be feasible to build a program to survey both blood-born and respiratory pathogens as the sampling and downstream processing requirements are different, which can substantially increase costs. However, coupled with the product of element one, this analysis will support further prioritization of objectives and will provide a roadmap for future expansion.

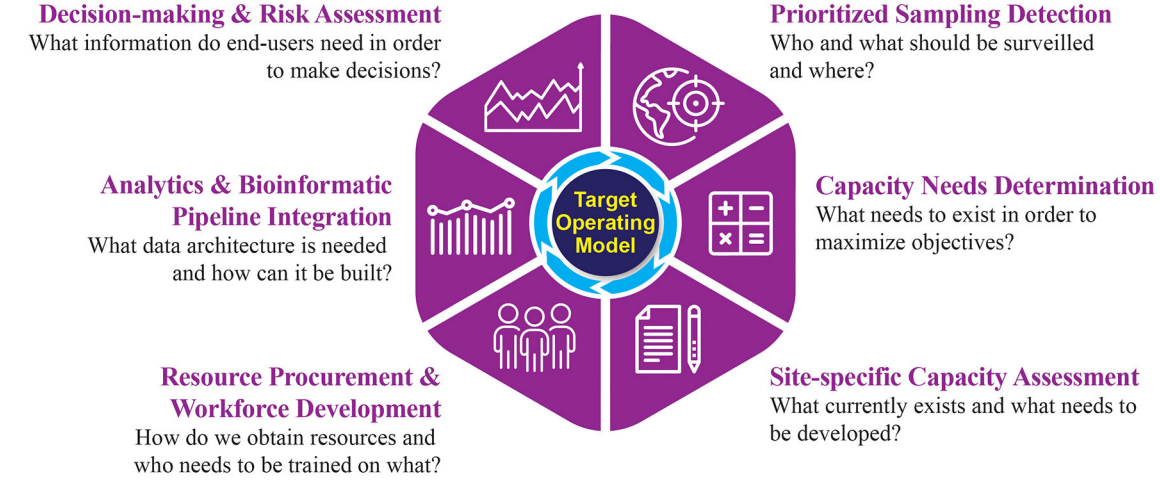

FIGURE 2 | A target operating model for the implementation of genomics-driven surveillance activities.

Site-Specific Capacity Assessment

Once calculations have been completed to determine the optimal needs for deploying a genomic surveillance workflow, the third element outlines an onsite detailed assessment of current capacity. Assessments should be conducted across stakeholders and alongside the local workforce to ensure every module that comprises the genomic sequencing workflow is scrutinized. This includes a detailed analysis of medical and laboratory capabilities as well as biosafety infrastructure, sample transport, record keeping, and data storage. Multiple tools are available to evaluate established surveillance systems to improve efficiency in data generation; however, the majority of these focus on laboratory performance and data quality while undervaluing operational considerations (24, 25). Future efforts should develop readiness and requirement assessment tools specific for the full genomic surveillance workflow.

Capacity assessments should also include neighboring regions to identify opportunities for collaboration and resource sharing. This process is often overlooked in surveillance program development, leading to siloed systems that would benefit from an information exchange but are not interoperable. There may be no need to build out every component of the genomic sequencing workflow locally if collaboration is available. For example, in development of a new program, it may be more cost-efficient while maintaining time requirements to leverage existing cold-chain delivery mechanisms that allow for rapid delivery of the locally collected samples to a neighboring locale for diagnostics or sequencing capabilities. The outcome of this TOM element is a streamlined workflow facilitating inclusive sampling of the defined population, rapid diagnosis and sample delivery, efficient genomic sequencing, swift downstream analysis, and delivery of results.

Resource Procurement and Workforce Development

This element defines procurement and training processes required to implement the workflow. Resource and staffing limitations must be addressed for initiatives to be successful and achieve desired outcomes. As assessed in TOM element two, there are costs associated with implementation and operations. These costs manifest not just monetarily, but also in areas such as time needed to transport samples and obtain reagents, staff onboarding, and continued availability of information technology and electrical infrastructure (26).

The local workforce needs to be trained and empowered to sustain local capability. Building out local expertise is crucial, but the breadth of required knowledge across biology, bioinformatics, and information technology is much too broad for a single individual. Hiring and cross-training staff to fill one or more required domains is often necessary to facilitate implementation of a workflow, and twinning partnerships may facilitate external support, particularly for nascent programs (27). Ongoing training and outreach are required to ensure a skilled labor pool and continuous independent operation.

Equipment, infrastructure, software, reagents, and other assets need to be procured to facilitate ready adoption; selections should prioritize usability and accessibility of training. These capabilities should either be tailored to available expertise or incorporate training to be not only administered during the implementation process but also continually available during operation. Technologies and processes that require highly specialized expertise or are incongruent with existing workflows and priorities will be abandoned in favor of older, more familiar methods. Data architectures must be planned with appropriate data storage, internet connectivity, processing power, and bandwidth in mind at all incorporated sites to allow timely, near-autonomous transport of data and information. Considerations

should include not only hardware and software, but also a critical awareness of their geographic locations, facilities, and proximity to reliable utilities to avoid the implementation of a brittle capacity (28).

Analytics and Bioinformatics Pipeline Integration

Once the means to develop or obtain assets are resolved, data architectures must be leveraged to enable connectivity of data systems and enable data analysis to support the goals of the workflow. A central site needs to be identified and all data pipelines must terminate there. Pipelines should be established such that they are resilient and fault-tolerant to internet and power outages. Data standards must be evaluated to achieve the delicate balance of sufficient structure to ensure high quality data without hindering or preventing data reporting and submission. Establishing consistent data formats across sites enables reliable processing and quality checking of data standards compliance. Where possible, the minimum amount of data to support analyses should be transferred to meet timeliness objectives and overcome bandwidth and storage limitations. Data pipelines should incorporate a transformation step that directly integrates the data with an existing surveillance system or produces a visual artifact.

Mechanisms by which sequence data or its metadata will be transported to a central surveillance system and corresponding repositories needs to be determined. A plethora of software tools and libraries exist which enable processing of sequence data. More importantly, workflow management capabilities that facilitate modular development and integration of analytic pipelines have recently become more widely available (29). Selecting analytic pipelines that both reduce complexity of implementation and lower required technical expertise for execution and interpretation is critical.

Decision-Making and Risk Assessment

The final element aims to isolate the information required by end users to enable them to make specific decisions and implement critical response measures. Using artifacts produced in the previous TOM element, analysts can begin to interpret the data. It is imperative to decide how epidemiological and genomic data are integrated and presented for end-user consumption; however, the specific approach will vary based on the program objectives. Just as data fidelity and timeliness is important to the end-user, so is the ability to convey information in a readily interpretable manner. For example, a geographical categorization of data is appropriate to evaluate the prevalence of pathogens stratified by variants across regions, while a network graph indicates transmission chains by utilizing case and genomic data. Determining the correct visualization for the right audience such that there is little ambiguity is critical. Inclusion of techniques such as statistical anomaly detection and forecasting should be considered but care must be taken to ensure that outputs of these elements are overlaid and communicated appropriately. Regardless of the method used, information outputs should be easily configurable, interpretable, and shareable to ease the analytic burden on end-users and place an emphasis on making decisions.

DISCUSSION

The importance of genomics-based surveillance has been clearly demonstrated in diverse contexts, including characterizing pathogen transmission routes, contact tracing, vaccine design, and more. The COVID-19 pandemic has reinforced the need for genomic surveillance and integration of both genomic and epidemiological data to support stronger decision making in response to emerging infectious disease. Additionally, uniting genomic surveillance in human and animal populations can provide predictive indicators of potential or emerging outbreaks. As such, genomic surveillance represents a critical capability in preparedness and response.

To fully realize the promise of genomic surveillance, several key requirements must be met. First, genomic surveillance data must be meaningfully integrated with traditional health surveillance data for clinical characterization of an emerging pathogen. Second, sufficient sampling coverage and throughput is necessary to adequately support research and an informed public health response. Third, genomic surveillance infrastructure must be present and operational, featuring sufficient flexibility to support broad-spectrum pathogen surveillance in order to be relevant in emerging outbreak scenarios. Finally, genomic surveillance initiatives must be sustainable, providing sufficient value to local and national decision makers to justify the investment required for continuing operation, maintenance, and improvement.

The genomics-based surveillance TOM presented here provides an in-depth framework for development of an implementation strategy for new genomic surveillance programs. While relevant in both high-income and LMIC contexts, we have focused on an implementation scenario in LMICs given observed challenges in sustainability of similar programs. Additionally, the increased burden of infectious disease on LMICs and frequently insufficient infrastructure and allocation of resources for preparedness and response capabilities mandates deeply cost-effective surveillance strategies. As such, the TOM provides a mechanism to ensure surveillance objectives established by a given LMIC are clearly presented and upheld in the development of an implementation strategy. Use of the TOM to evaluate and adapt or refine an existing genomic surveillance program will also ensure minimal investments achieve the greatest possible impact.

The TOM provides a flexible framework upon which specific priorities for sampling and capacity development can be defined based on a combinatorial evaluation of surveillance priorities, available resources, and stakeholder needs. This operational model can be used to drive development and refinement of surveillance programs through top-down planning and allows gap identification within any given surveillance workflow. Integrating interdisciplinary models to support TOM assessments will provide a rich quantitative basis for prioritization of resource allocation in development or adaptation of genomic surveillance programs. As new

global health capabilities are developed and refined, the TOM is understood to be an evolving product, providing a reflection of both global and national health priorities and continually strengthened by advances in knowledge surrounding health and infectious disease. As technical and analytic resources are identified, a common resource repository, including trainings and lessons learned regarding genomic surveillance implementation, can be developed. Further adaptation of the TOM to broader health surveillance objectives (e.g., pathogen emergence, livestock surveillance, and more) should be explored as well.

We have presented here a target operating model for the establishment of a genomic surveillance program for infectious disease in LMICs; however, we recognize additional needs in the sustainment of newly developed capacity in COVID-19 response in high-income countries as well. The logic and decision framework underlying the LMIC TOM instantiation is easily translated to highly-resourced settings. Application of the TOM to assess genomic surveillance program performance and opportunities for refinement or realignment against national surveillance priorities for any nation should be built into existing program reviews to ensure our health surveillance capabilities remain strong and vibrant to protect all nations from the next emerging health crisis.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

NL wrote the majority of the manuscript. NL and MS contributed equally to the concept described in the manuscript. JD, MS, and SL contributed to the content of the manuscript. All authors approved the final version of the manuscript.

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Health Informatics: Engaging Modern Healthcare Units: A Brief Overview

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In the current scenario, with a large amount of unstructured data, Health Informatics is gaining traction, allowing Healthcare Units to leverage and make meaningful insights for doctors and decision-makers with relevant information to scale operations and predict the future view of treatments *via* Information Systems Communication. Now, around the world, massive amounts of data are being collected and analyzed for better patient diagnosis and treatment, improving public health systems and assisting government agencies in designing and implementing public health policies, instilling confidence in future generations who want to use better public health systems. This article provides an overview of the HL7 FHIR Architecture, including the workflow state, linkages, and various informatics approaches used in healthcare units. The article discusses future trends and directions in Health Informatics for successful application to provide public health safety. With the advancement of technology, healthcare units face new issues that must be addressed with appropriate adoption policies and standards.

Keywords: health informatics, public health, information systems, health policy, public health systems

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1. INTRODUCTION

Machine Learning is the fastest-growing topic in computer science today, and Health Informatics (HI) is the most difficult problem to solve (1, 2).

Emerging economies are increasing their investments in healthcare, which makes sense and encourages health professionals to adopt sound frameworks and regulatory standards, as well as health IT, to improve the quality and efficacy of care (3). In this expanding field, new age occupations can be established. This new field has the potential to be a lucrative career path in the future. With a clear flow of information across many medical subsystems, adoption of electronic health record systems (EHRs) will improve the health care system going forward (4).

Big Data is frequently employed in the field of health informatics, as new data is constantly pouring into the system, requiring analysis and interpretation in order to make rational decisions (5, 6).

A bigger impact can be accomplished in healthcare has ushered in a new era for healthcare companies to improve decision-making through the comprehensive integration of data from a range of sources, allowing for much faster and more effective decision-making (7). Within and outside of the medical business, computational health informatics is an emerging study field (7–9).

In recent years, the healthcare industry has seen a rapid growth in medical and healthcare data, which can be used to improve facilities and public health care utilization and implementation by modern healthcare units using novel treatment and diagnosis methodologies, which gives citizens confidence in using the best public healthcare services available and aids governments in developing better healthcare policies (10).

Computerized systems for analysis and diagnosis were first adopted by health professionals. More recent technology are making it easier for people to make better decisions (11, 12).

Health Informatics' promise to improve public health activities would be fully realized if information science and technology were applied (13).

In a complex social and economic environment, the issue is thus how to increase the quality of offered healthcare services while lowering prices. Information and communication technologies (ICT) have been shown to help healthcare systems increase productivity, which has resulted in significant cost savings in operations and service delivery. For administrative and healthcare objectives, ICTs have already proven to be quite effective. New prospects for new medical equipment and systems are opening up as ICTs become smaller, quicker, wireless, and remotely controlled.

The Internet and the web have recently brought up new possibilities for increasing the response time of health-care services while also lowering costs. It is clear that we are in the early stages of a new era that will fundamentally alter the way healthcare services are provided. This will help us acquire the public's trust in using high-quality healthcare services.

New e-Health services and technology should be researched, developed, promoted, and disseminated with significant effort. With the present pandemic (COVID-19) sweeping the globe, increasing ICT use has demonstrated that healthcare will become more contactless in the future, with fresh means of treating patients and providing healthcare services emerging. This is a popular yet difficult research subject since it necessitates interdisciplinary competence (14).

The major purpose of Health Informatics is to increase our understanding of medicine and medical practice by using real-world medical data. In the subject of healthcare, health informatics is a blend of information science and computer science (15).

Big data in healthcare is intimidating not only because to its sheer magnitude, but also due to the variety of data types and the pace with which it must be managed. To gain people' trust and give quality healthcare services, all health service providers are now putting in extra effort to use the most up-to-date technologies to provide health services and advanced treatments.

Various requirements drive innovation in this industry, such as finding appropriate accommodation with standardization and coordinating the acquisition and implementation of newer healthcare systems and services on a national/international level.

With the present COVID-19 scenario, investments in this sector are gaining steam with new age healthcare units in many nations, and growing economies such as India and China will play a vital part in providing good and quality healthcare services in the future.

As a result, New Age Healthcare Units and Systems will play a critical role in dramatically lowering costs, making Public Healthcare Systems more dependable and instilling citizens' confidence in using inexpensive healthcare.

2. RELATED WORK

Big data is a term used to describe a significant volume of data that is collected and stored today and has outgrown standard data management and analysis solutions. Solutions like Hadoop and Spark, according to Roger Fyre and Mark McKenney, have arisen to solve some of the big data concerns (16).

Researchers have used Hadoop to implement a variety of parallel processing algorithms to efficiently handle geographical data (17, 18). Multistage map and reduce algorithms, which generate on-demand indexes and retain persistent indexes, are examples of these techniques (19).

Much of the current work on predictive analytics, particularly in clinical contexts, is aimed at improving health and financial outcomes, which will aid in making better decisions (20). Data mining, which is defined as the processing and modeling of huge amounts of medical/health data to identify previously unknown patterns or associations, is one of the most important machine learning approaches (21, 22).

Data collection for diseases such as cancer and neurological disorders in order to improve disease prognosis (23, 24). Cancer detection and diagnosis, as well as other health-related issues, have been made possible because to these breakthroughs. Here, prominent research in the topic of health monitoring and informatics is discussed, which can be used to verify future research (25).

Machine Learning is crucial in the testing and development of various models that take into account clinical and other important medical characteristics for decision-making.Medical imaging, which incorporates capabilities such as image segmentation, image registration, annotation, and database retrieval, is one of the most famous examples of newer medical technologies that can be utilized for decision making in the future. For all of this, updated ML/DL models for speedier decision-making can be constructed (26).

Machine learning/data science researchers are in high demand for developing algorithms that adapt to changing data. Deep Learning (DL) is now being used to solve more difficult problems in the healthcare/informatics arena (26, 27).

Holzinger et al. (28) discussed many approaches to developing an explainable model for the medical domain were examined. Prediction explanations can be useful in a variety of situations, including teaching, learning, research, and even court. The demand for interpretable and explainable models is growing in the medical field. They need to be able to re-enact the decision-making and knowledge extraction processes. In their article, Ribeiro et al. (29) discussed how machine learning models are black boxes. Understanding the reasons for predictions can help to build trust. It can be used to assess model performance and construct better, more accurate, and correct models by providing insights into the model. Ribeiro et al. (29) propose the LIME algorithm for explaining predictions of any model. This article by Bahdanau et al. (30) deals with neural machine translation, but the model proposed can be used in a variety of other applications.

3. INTRODUCTION TO HL7 FHIR ARCHITECTURE

In the last two decades, electronic health records (EHR) have been widely implemented in the United States to improve health-care quality, increase patient happiness, and reduce health-care costs (31–33). As growing countries such as India, China, and Bangladesh experiment with innovative ways to establish EHR systems, it will significantly aid in the development of effective public health systems.

FHIR's basic idea was to create a set of resources and then create HTTP-based REST application programming interfaces (APIs) to access and use these resources. FHIR uses components called resources to access and perform operations on patient's health data at the granular level. This feature distinguishes FHIR from all other standards because it was not present in any earlier version of HL7 (v2, v3) or the HL7 clinical document architecture (CDA).

The fundamental building blocks of FHIR are the so-called resources, which are generic definitions of common health care categories (for example, patient, observation, practitioner, device, condition). For data interchange and resource serialization, FHIR employs JavaScript object syntax and XML structures. FHIR not only supports RESTful resource exchange but also manages and documents an interoperability paradigm.

FHIR has grown in popularity and is being increasingly used by the health care industry since its inception. In 2018, six major technology companies, including Microsoft, IBM, Amazon, and Google, vowed to remove barriers to health care interoperability and signed a statement mentioning FHIR as an emerging standard for the interchange of health data. With incorporation of Substitutable Medical Applications Reusable Technologies (SMART), a platform for inter operable applications (34), FHIR can be expected to attract even more attraction in digital health in the future.

The use of FHIR for medical data transmission has the potential to deliver benefits in a wide range of disciplines, including mobile health apps, electronic health records (EHRs), precision medicine, wearable devices, big data analytics, and clinical decision support.

The primary goal of FHIR is to reduce implementation complexity while maintaining information integrity. Furthermore, this new standard integrates the benefits of existing HL7 standards (v2, v3, and CDA) and is projected to overcome their drawbacks. FHIR enables developers to create standardized browser applications that allow users to access clinical data from any health care system, regardless of the operating systems and devices used. **Figure 1** represents the general architecture of FHIR (35).

3.1. FHIR for Patient Access to Medical Records

FHIR, or Fast Healthcare Interoperability Resources, is an HL7 standard for electronically transferring healthcare information. The CMS Interoperability and Patient Access final regulation, announced in 2020, mandates all CMS-regulated payers to use FHIR version 4. Unlike earlier releases, the fourth iteration is backward compatible, ensuring that software suppliers' solutions will not become obsolete when a new FHIR version is released.

The FHIR (pronounced "fire") standard defines a collection of HTTP-based RESTful APIs that allow healthcare platforms to exchange and share data in XML or JSON format. FHIR offers mobile apps, which users can obtain from the Apple App Store or Google Play in order to access their medical records and claims data.

FHIR's basic exchangeable data piece is known as a resource. Each resource is formatted similarly and contains roughly the same amount of data. It offers information about patient demographics, diagnosis, prescriptions, allergies, care plans, family history, claims, and so on, depending on the kind. They span the complete healthcare workflow and can be used independently or as part of a larger document.

Each resource is given a unique ID, and many parties—health systems, insurers, patients, or software developers—can access the underlying data element using an API. **Figure 2** represents the data layers and resources of FHIR (35).

3.2. FHIR Resource

A resource is the smallest discrete concept that can be independently maintained and is the lowest feasible unit of a transaction (36). As a result, a resource is a known identity that provides useful data. Each resource has distinct bounds and differs from all others. A resource should be provided in sufficient depth to specify and enable the process's medical data interchange. The FHIR community has specified over 150 resources till date, according to the most recent FHIR version (R4) (37).

There are five key categories in which these resources can be found: (1) Administrative: location, organization, device, patient, and group; (2) Clinical: CarePan, diagnostics, medication, allergy, and family history; (3) Financial: billing, payment, and support; (4) Infrastructure: conformance, document, and message profile; and (5) Workflow: encounter, scheduling, and order.

FHIR is fast gaining popularity due to its dynamic properties. FHIR is projected to quickly become a symbol for clinical data interchange in the health-care industry.

3.3. Workflow Description

Workflow is a critical component of healthcare; orders, care regimens, and referrals drive the majority of activity in in-patient settings, as well as a significant amount of activity in community care. FHIR (Fast Health Interoperability Resources) is concerned with workflow when it is necessary to share information about workflow state or relationships, when it is necessary to coordinate or drive the execution of workflow across systems, and when it is necessary to specify permissible actions, dependencies, and behavior requirements.

3.4. Workflow State and Relationships

FHIR does not have to be used for workflow execution. Orders, care plans, test findings, hospital admissions, claim payments, and other documents can all be exchanged utilizing FHIR resources without the need for an FHIR transaction to solicit

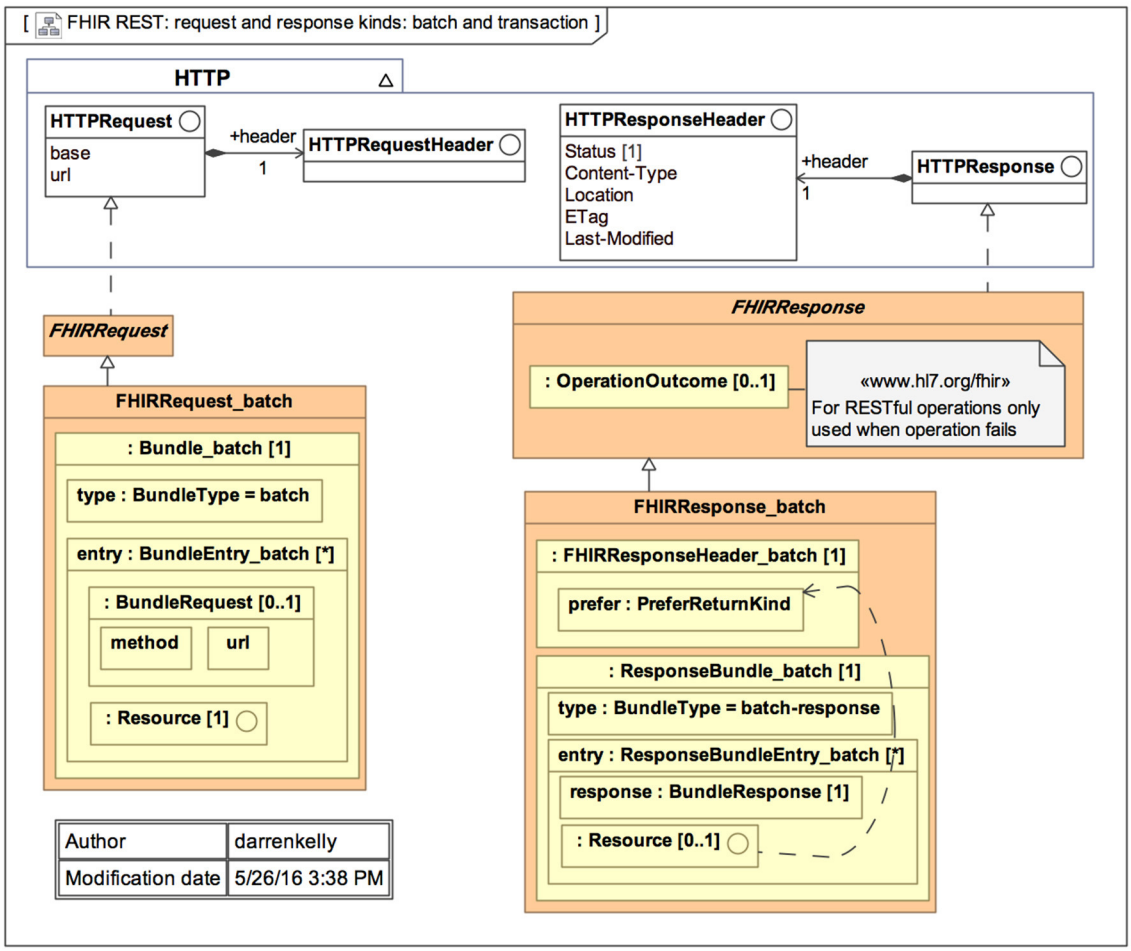

FIGURE 1 | General architecture of the Fast Health Interoperability Resources (FHIR) standard (35).

fulfillment of those orders or request payment of those claims. Because it necessitates a greater level of standardization, interoperable support for workflow execution is a more advanced FHIR activity. Interoperable workflow execution necessitates the standardization of processes, roles, and activities across multiple systems, rather than just the data to be exchanged.

Even if FHIR is not used for workflow execution, there is still a requirement to standardize workflow data elements: how does an event or a result point to the order that allowed it? How are parent and child steps tied together? How does a care plan know which protocol it is following?

FHIR distinguishes three types of resources engaged in activities: requests, events, and definitions. Each of these categories is associated with a "pattern." Resources in that category are encouraged to follow their specific pattern. These patterns provide conventional elements that are common to the majority of resources in each category. Work groups are anticipated to align with common domain behavior and requirements as more authoritative than "desired" architectural patterns, therefore strict conformance is not necessary. When a pattern capability is assessed to be "not common, but nonetheless relevant" for a given resource, it may be supplied through extensions rather than core parts. **Figure 3** represents the work flow relations of FHIR Standard (38).

4. OVERVIEW OF HEALTH INFORMATICS

Health informatics involves more than merely automating routine tasks. With contemporary technology developments in machine learning and deep learning, it is possible to redesign systems using methodologies that were previously impossible or not even considered (26).

Such a study is computationally expensive and can now be handled by the latest IBM POWER9 processors with GPU capabilities, which was previously impossible because the data was not available in electronic form and the number of possible symptoms/incident patterns was too big to manage. Early detection of patterns that can assist anticipate what kind of treatment or diagnosis can be offered to such patients has improved dramatically (39).

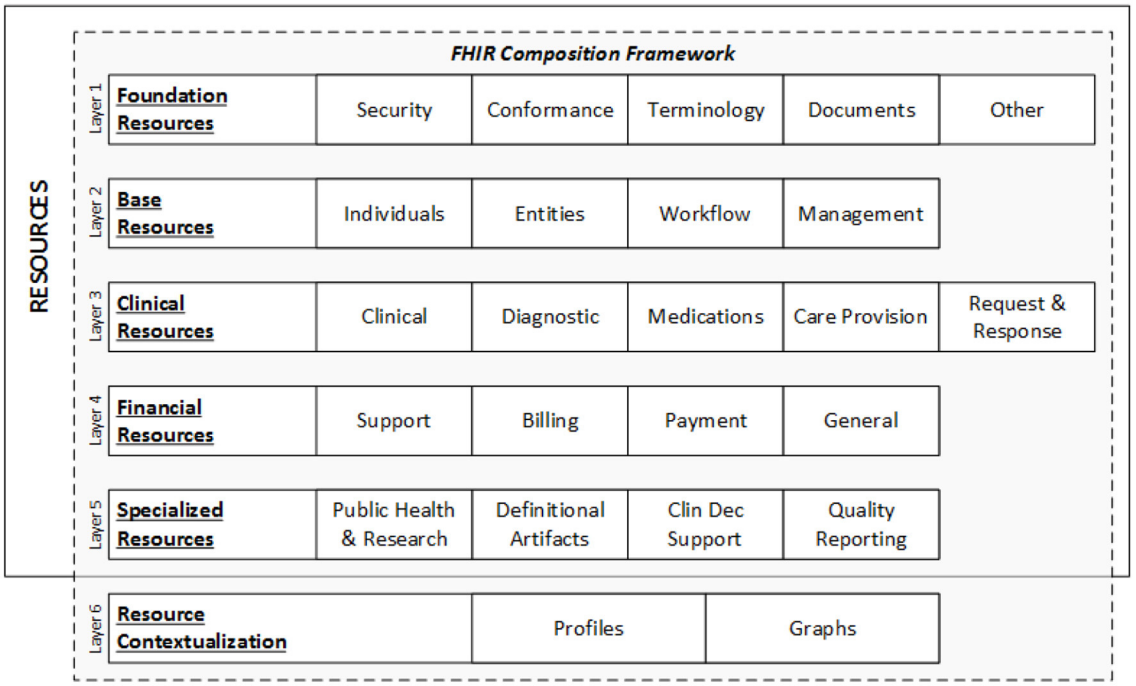

FIGURE 2 | FHIR data layers and resources (35).

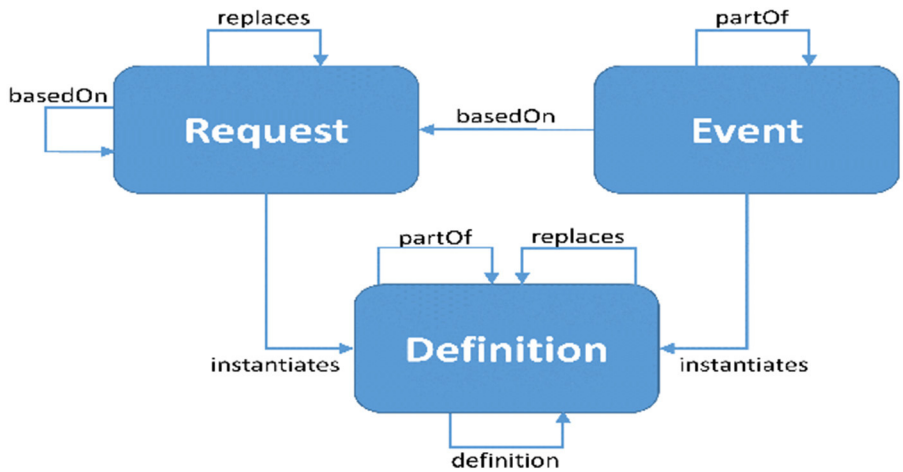

FIGURE 3 | Work flow relations Fast Health Interoperability Resources (FHIR) standard (38).

In the future, modern healthcare units will make use of such a framework for successful treatment delivery for society as a whole, making effective use of data obtained from such systems by extracting insights that assist decision makers such as doctors, hospital owners, and health policymakers.

In terms of vital signs, an example of classification in healthcare informatics is clearly handled (40, 41). The prediction of a patient's breathing rate obtained from sensors is an example of regression (42). In the future, Bayesian Inference will be used to make better predictions in the domain of health informatics.

Some of the most pressing future difficulties in healthcare informatics will be addressed by developing systems based on the principles listed below, which are not commonly employed in this sector:

- Multi-task Learning
  Traditional machine learning frameworks consider only one learner attempting to solve a single task. However, in many applications, there are multiple tasks that label the same data instances differently. When the tasks are related, the information learned from each task can be used to improve learning of other tasks. Learning relevant tasks concurrently, rather than learning each task independently, is thus advantageous. Multi-task learning makes use of the intrinsic relationships between multiple tasks to improve generalization performance. It benefits all tasks by leveraging task relatedness and shared information across relevant tasks (43).
- Transfer Learning
  Traditional machine learning technology has had a lot of success and has been used in a lot of practical applications, but it still has certain limits in some real-world settings. Machine learning works best when there are a lot of labeled training cases with the same distribution as the test data. In many cases, however, gathering sufficient training data is costly, time-consuming, or even impossible. Semi-supervised learning can help to alleviate this difficulty by removing the requirement for large amounts of labeled data. A semisupervised approach typically requires a small amount of labeled data and a large amount of unlabeled data to improve learning accuracy. However, in many cases, unlabeled instances are difficult to collect, making the resulting traditional models unsatisfactory (44).
- Multi-agent-Hybrid Systems
  Multi-agent systems are networks of interconnected autonomous agents in which the behavior of neighboring agents influences the dynamics of each agent.Because of the increasing importance of multi-agent systems, there is a growing interest in coordination control to ensure consensus, flocking, containment, formation, rendezvous, and so on. To better understand multi-agent coordination, a variety of dynamic models of agents have been developed over the last two decades. Furthermore, many mathematical methods are used in the analysis and control of multi-agent systems. For more information, see survey article (45) and the references therein (46).
- Representation Learning
  Patient-specific data such as vital signs, medications, laboratory measures, observations, clinical notes, fluid balance, procedure codes, diagnostic codes, and so on are all included in modern EHR systems. Clinicians originally employed the codes and their hierarchies, as well as their associated ontologies, for internal administrative and invoicing functions. Recent deep learning algorithms, on the other hand, have attempted to project discrete codes into vector space, identify intrinsic commonalities between medical concepts, more accurately depict patients' health, and perform more precise predicting tasks. Word embedding and unsupervised learning have been used to examine medical concepts and patient representations in general (47).

Health informatics has a number of long-term benefits in terms of research and healthcare delivery that can be used to create a sustainable ecosystem. ICTs aid in the enrichment of relevant data for analysis and decision-making by health professionals. Following the pandemic (COVID-19), new age healthcare units will arise, with increased investment and research spending making public healthcare more accessible. As a result, solutions are required to manage the massive amounts of data created by medical equipment and healthcare systems, allowing for effective storage and retrieval in real-time data analysis and decision-making.

4.1. Informatics Approaches

To make electronic health data more easily usable for research, recent publications have identified the need for effective adoption and use of standards, essential data and research services, clear and consistent policies regarding data access and use, and transparent and effective governance structures (48, 49).

To achieve data quality criteria, electronic health data utilized in research frequently require standardized ontologies, additional contextual information, field transformations, and missing or contradictory data to be handled (50). For research-related data or functions, such as cohort identification and repeated extracts of source data over time, system development is frequently required (49). Organizations with expertise utilizing and enhancing their health IT infrastructure for research have shared their lessons learned in these areas, adding value to organizations with similar goals but less experience or resources (51).

For example, when preparing data for research use, organizations must understand the clinical context and structure of electronic health data, just as they do for other data uses such as decision support or population health. Individual researchers and data analysts can be relieved of their load by informatics support that spans research and operational usage of data. It is vital to evaluate and develop informatics tools and approaches by establishing processes that allow for coordinated governance and decisions informed by research users.

Investing in infrastructure to enable the use of electronic health data for research has also been shown to be beneficial to researchers by providing them with the necessary tools and expertise, to patients by providing clinical trial participation opportunities, to clinicians by enabling more rapid translation of research into practice, and to population health analysts by facilitating patient cohort views. In order to reduce project-specific IT costs, using health IT to assist research necessitates greater flexibility, increasing use of standards, and reusable ways for getting, preparing, and evaluating data (52).

Any use of operational data in research necessitates the establishment of a privacy and security framework, as well as data governance monitoring. Two initiatives, Informatics for Integrating Biology and the Bedside (i2b2) and Observational Health Data Sciences and Informatics (OHDSI), have developed informatics tools and approaches that allow researchers to

query organizational participants and support transformation or analytics of relevant data to facilitate research (53, 54).

Specifically, i2b2 has standardized data models and distributed computational tools that enable for the anonymous identification of potential genomic study participants at the institution level. OHDSI also employs a single data model, which incorporates information such as health economics and health systems. The methodologies utilized in these programmes demonstrate the kind of functionality that may be required in health IT systems to better support research, as well as the types of concerns with the quality of electronic health data that regularly arise.

5. STATUS QUO IN HEALTH INFORMATICS: AN INDIAN PERSPECTIVE

5.1. Health Care Delivery Systems

Despite having a solid telecommunication infrastructure, the existing systems are based on manual record keeping. The value of medical informatics in healthcare delivery has yet to be recognized by policymakers (55).

In countries such as India, health informatics is a new and emerging discipline. Its future prospects are very bright, thanks to the development of excellent infrastructure here. However, in order to implement a robust framework, this necessitates a multidisciplinary interaction with various stakeholders.

Information systems development could be another area where research is being conducted to improve the way data flows from various sources such as devices and medical equipment, allowing doctors and decision makers to make rational decisions on critical cases or equipment purchases in the future.

Digitizing all medical data also aids in the creation of a structure for patient-related data in a hospital that can be easily retrieved and searched. Finally, the development of some kind of electronic health record can be accomplished through the development of information systems (56).

5.2. Applications of Health Informatics

Health Informatics in India can become cost effective and ensure proper service delivery, which aids in beneficiary behavior change through the use of ICTs (57). We can create novel applications that can be used effectively by utilizing local talent and effective use of ICT in remote parts of India (58). Various governance issues can be addressed in the future with certain checks and balances in the data collection and analysis process (59). The following are some of the areas where health informatics can be used:

1. Epidemiological disease prediction
2. Disaster management
3. Awareness in Healthcare Processes
4. Healthcare in Remote areas
5. Electronic Health Records and its linkages with health systems
6. Health Statistics
7. Education and Training
8. Development of Decision Support Systems (DSS)
9. Public Health Research
10. Visualization tools for doctors
11. Recommendation Systems for Health Informatics
12. Precision Drug Prediction.

The potential of this emerging area has far-reaching benefits over a long period of time, and new and novel solutions can be built using various machine/deep learning models. There is a lot of work to be done in this area where we can use cutting-edge technology to aid/assist in the development of robust products and frameworks for public health policy (60–63).

5.3. Future Trends and Directions in Health Informatics

These are a few of the current trends in the field of Health Informatics that can be used to develop sustainable products, services, and health-related policies for effective implementation across the country and internationally. A few of them are listed below, and many more trends may emerge in the near future as a result of discussions with multiple stakeholders.

1. Data standards and Interoperability
2. Processes to transform medical/clinical data
3. Toolkits and Pipelines: Data Management
4. Standardized Reporting Methodologies
5. Appropriate Use of Informatics Expertise.

More trends may emerge in the future, taking into account the most recent technological advancements. Because health informatics is a new and emerging field, more research challenges may emerge, bringing forth newer perspectives in the future. To solve more difficult problems in this area, future researchers will prefer machine/deep learning methods/models (26). There are numerous other research directions being pursued in relation to various aspects of health care data such as quality, veracity, privacy, and timeliness. The following are some of the most notable data characteristics of healthcare data (9, 64):

1. **Complexity and Noise:** Because healthcare data is multisource and multimodal, it has a high level of complexity and noise. Furthermore, there are issues with impurity and missing values in high-volume data. It is difficult to deal with all of these issues, both in terms of scale and accuracy, despite the fact that a number of methods have been developed to improve data accuracy and usability (65). Because the quality of data dictates the quality of information, which in turn affects decision-making, it is vital to develop efficient big data cleansing ways to improve data quality in order to make effective and correct decisions (66).
2. **Heterogeneity:** Traditional healthcare data is frequently fragmented with multiple forms due to a lack of standardization. As a result, it is both reasonable and important to investigate and adopt universal data standards. However, due to the complexity of developing universal data standards, it is a difficult undertaking. Not only is healthcare data diverse, but there are numerous technical challenges to integrating that data for specific purposes (67). Even with standardized data formats, the multi modal character of data makes efficient fusion difficult (68), necessitating

the development of advanced analytics that cope with vast amounts of multi modal data. The integration and synthesis of multi source and multi modal healthcare data on a larger scale would be a significant issue.

3. **Longitudinal Analysis:** Longitudinal data is the collection of repeated measurements of participant outcomes and possibly treatments or exposures (69), which means that "the outcome variable is repeatedly measured on the same individual on multiple occasions (70)." In recent decades, longitudinal data analysis, particularly statistical longitudinal data analysis, has gotten a lot of attention. Longitudinal studies are used to characterize normal growth and aging, as well as to evaluate the effectiveness of risk factors and therapies. It is extremely important in epidemiology, clinical research, and therapeutic evaluation. With big data analytic tools, it is possible to perform longitudinal care analysis across patients and diagnoses to identify the optimal care options.
4. **Scale:** Healthcare data is continuously expanding in quantity and scope (68). The fact that data volume is growing faster than processing power is a significant challenge in managing vast amounts of data. Several fundamental adjustments are occurring to handle this enormous transition (71). First, in recent years, CPU technology has increasingly turned its focus to parallel data processing within nodes and the packing of numerous sockets. Second, the shift to cloud computing allows for information sharing and the consolidation of multiple workloads into large-scale clusters. Third, the transformation of the traditional I/O subsystem from Hard Disk Drives (HDDs) to Solid-State Drives (SSDs), as well as other storage technologies, is reforming data processing system design and operation.
5. **Real Time:** The velocity of big data in health informatics reflects not only the rate of data collecting and processing, but also the timeliness of replies. There are various instances that call for a quick choice. For example, it would be immensely desirable to monitor and analyse a person's health condition in real time or near real time in order to predict potential disease. It would also be critical to raise the alert for a potential influenza outbreak by examining public health statistics. Although real-time analytic applications are still in their infancy in the big data era, they represent the strongest trend and most promising direction in health informatics' future (72).
6. **Privacy:** Data privacy is another major worry for future big data analytics in healthcare informatics (73). Although strong laws control more formalized EHR data, extra attention should be taken and standards should be enforced to regularize the use and dissemination of personal and sensitive information obtained from diverse sources. In addition to data privacy, there are a number of other challenges, like as data protection, data security, data safety, and the protection of doctors from liability resulting from manipulated data, that necessitate the use of specialized big data analytics to address these complicated constraints (73, 74).
7. **Visualization:** The visualization of healthcare data is crucial for exploratory or discovery analytics, which aim to investigate and discover elements that are hidden or encrypted in the data (75). Effective visualization tools will enable clinicians and physicians to explore data without the need for IT assistance (72).
8. **Multidisciplinary and Human-Computer Interaction:** Big data in health informatics is expected to be a multidisciplinary job requiring ongoing contributions from multiple topic experts (76). They include, but are not limited to, engineering scientists who provide basic big data infrastructure to collect, store, share, and manage big data; computer science data scientists who provide solutions for processing and analyzing high-volume, high-velocity healthcare data using a variety of data mining and machine-learning techniques; and clinicians and physicians from the medical domain who provide professional healthcare data analysis, personalized care, and make recommendations. Computer algorithms can struggle to find patterns and interpret results at times; consequently, it is a desirable feature for an advanced big data analysis system to be able to enable input from numerous human specialists, exchange of viewpoints, and collaborative exploration of outcomes. Furthermore, in the health sector, we sometimes do not have massive data: we are confronted with a small number of datasets or unusual events, where, for example, machine-learning algorithms suffer from insufficient training samples. In such circumstances, we require more than just automatic machine learning; we also require a person in the loop. In other words, interactive Machine Learning (iML) or "human in the loop" techniques can be used in health informatics when automatic machine-learning algorithms cannot handle rare occurrences on their own and a human expert is required to interact in the learning process (77).The interplay between computer algorithms and human specialists has the potential to improve the learning process.

6. CHALLENGES IN HEALTH INFORMATICS

There are numerous challenges in this area, particularly in a country like India, where a large population is denied affordable healthcare, which can serve as a starting point for developing and implementing robust health informatics applications, products, and Research and Development investments. The start-up/venture costs, people, and equipment are very high, and it is a niche sector in which many people are hesitant to venture into such a space/sector that can be leveraged making very good business sense (78).

To improve the way health services are delivered and implemented to the public, a multidisciplinary approach involving various sectors/stakeholders is required. These informatics systems can be used for a variety of purposes. Medical/healthcare data will be more structured and democratized by competent authorities.

The advancement of EHRs and web-based health monitoring systems will aid in rational decision making and policy framework implementation (11). There may be numerous bottlenecks in the development of ICT systems for Health Informatics (59, 79).

The majority of stakeholders are unconvinced about the benefits of Internet technologies in health care and are unfamiliar with how to use such new technology (80). Concerns about security and privacy may arise as robust healthcare systems are developed in the future (11).

Proper techniques are essential to ensure patient data confidentiality, and system security may become a concern when data policy standardization increases.

Many new challenges can be encountered while developing novel and innovative ways to promote public health through the use of information technology (IT) and other computing technological advances such as Cloud Computing, Data Visualization, and Medical Informatics. Future research is required because the healthcare/informatics domain is still in its early stages, where more difficult problems can be solved and newer products and services can be spawned as a business venture. Deep Learning in Health Informatics has its own set of challenges (26).

Despite significant investments in information technology, patient safety and productivity have not improved. Preventable medical errors are the third leading cause of death in the United States, after heart disease and cancer, killing over 400,000 people each year. These blunders cost the United States over one trillion dollars per year. To combat this disease, the federal government has mandated that the healthcare industry transition to electronic health records (EHRs) and use these records to improve patient processes and outcomes (i.e., meaningful use). Emerging economies have to allocate and give incentives to healthcare units/organizations to promote the use of EHRs.

The following are the main gaps and challenges to an effective pandemic response in health information management and health informatics:

1. A lack of standards for information exchange between providers and PHAs (Public Health Authorities)
2. Issues with data collection and data quality, particularly in terms of completeness and timeliness
3. Governance, Public Policies, and Regulations.

The latter included a lack of procedures to support efficient data sharing, contact tracking, and data governance, as well as providers' concerns about privacy regulations, which resulted in insufficient data sharing.

Governance and public policy hurdles stem from chronic underfunding of public health infrastructure, as well as a lack of adequate investments in resources (particularly qualified employees) and facilities. A key difficulty was also recognized as a lack of international coordination. Many overlapping and interrelated legal, ethical, scientific, technical, technological, health equality, and privacy elements influenced how health information was managed or mismanaged during the COVID-19 global pandemic. Other long-standing systemic difficulties in health information management will need to be addressed in order to operationalize many of the data and information system recommendations (81).

The financial investment required to design, execute, and sustain e-health programmes is a key difficulty in health informatics, and Anderson cited a lack of financial backing and high initial expenses as hurdles to implementing ICT in health care (82). While health informaticians and information professionals may see future benefits from investments in ICTs, health professionals and managers may be skeptical, especially if they are satisfied with current methods of working and wish to maintain the status quo, and may see such initiatives as diverting financial resources away from under-resourced clinical care (83).

Resistance to the establishment of ICT systems by health professionals and managers can lead to further issues once the systems are in place, and the restricted adoption of health informatics applications has meant that their potential is not always achieved. Decision support systems, for example, may be ignored or overridden, and evidence-based information may have limited applicability for an individual patient. Clinicians make life-changing judgments or act in life-threatening situations, and if they don't comprehend the reasons behind computer-based decision support systems, they won't trust them or use them effectively (84).

This highlights the importance of not only involving physicians and healthcare professionals in the construction of systems and the interpretation of outcomes, but also of providing adequate explanation and information at the point of care for healthcare practitioners to trust the systems (84).

As previously stated, identifying the types of information that clinicians require, as well as the methods by which they access and utilize information, is critical in ensuring that developments not only meet the needs of the users, but are also perceived to be valuable, so that health professionals and other users will want to maximize their potential. Addressing healthcare professionals', patients', and the public's concerns about data security, as well as threats to patient privacy and confidentiality, will be critical in developing online access to patient records (85). Greater security measures integrated into system design will help boost system confidence, however the chance of third parties getting access to sensitive patient-identifiable data remains a danger (82).

Another challenge that can stall the creation and execution of health informatics efforts is quality. The real and perceived quality of data entered into systems and then used for health care is vital not only for assuring system use, but also for the safety and well-being of patients. If data is not input, or is not entered correctly, the buildup of missing or low quality data discourages others from using the system and creates additional suspicion and skepticism about future advancements. The importance of accurate and correct data will grow as lifelong electronic records are established (84), both prospectively as individuals are born and retrospectively using data acquired over an existing person's lifetime to date.

As previously noted, the earlier development of small-scale information systems within individual departments or hospitals resulted in system incompatibility and difficulties communicating or transferring data when larger-scale systems were later built. One approach to addressing this issue is to increase interoperability and employ known electronic record architectures in the creation of new systems. In addition, the lack of data standards in health presents additional challenges for moving and sharing data between systems (82). Attempts to address these issues include the creation of

information-management standards such as Digital Imaging and Communications in Medicine (DICOM), Health Level Seven (HL7), and terminologies and coding systems [e.g., the International Classification of Diseases (ICD), Read coding, and Snomed] to standardize the ways in which medical conditions and diseases are represented in computer-based systems and to attempt to codify the natural language used by medical staff.

The International Classification of Diseases (ICD) was created to provide a standard method of classifying medical diagnoses for epidemiology and health-care purposes; initially, it only included causes of death, but more recent versions have included causes of morbidity, and it is now in its eleventh version (86). There are numerous challenges, and many new problems can be solved using cutting-edge technologies such as ML/DL and cloud computing (26, 87–92).

6.1. Health Data Standards Challenges and Possible Solutions to Them

Clearly, data standards are not lacking in the healthcare industry. SDOs (standard development organization) have created a plethora of them to address nearly every facet of communication between diverse health systems.

However, the simple fact that they exist and are available does not address all of the issues surrounding interoperability. We'll go over some of the more difficult standards issues, as well as potential solutions.

1. **Medical coding speed and accuracy issues:**
   The manual work required to convert diagnoses, treatments, services, treatment plans, and other concepts into medical codes is undertaken by professionally qualified individuals. Computer-assisted coding systems are now used by coders. However, the translation process's speed and precision are far from flawless. To that aim, high hopes are placed on AI-powered tools capable of identifying proper codes and recommending them for expert evaluation. Currently, such intelligent systems speed up coding, but they cannot completely replace humans and automate the entire process.
2. **Need for mapping between codes:**
   Each code in healthcare serves a specific purpose: SNOMED allows physicians to provide a thorough clinical picture of a patient being treated, whereas ICD-10 presents diagnoses quickly and CPT summarizes services. However, there are times when translation from one code system to another is required. As previously stated, SNOMED cannot be used for billing reasons and must be translated to ICD-10-CT. To overcome mapping issues, standard development groups experiment with various approaches.
3. **Lack of compatibility between old and new standards:**
   To comply with existing interoperability regulations, hospitals must make content described by USCDI available *via* FHIR-based APIs. But, let's face it, the truth is: Most EHR systems were designed with previous standards in mind. Some of them are only capable of importing and exporting HL7 v2 messages. Others rely heavily on C-CDA materials. Neither v2 nor C-CDA are compatible with granular USCDI data elements or FHIR basic interchangeable data blocks—resources. As a result, hospitals will require additional digital technologies and human resources to extract data from legacy formats and convert it into FHIR and USCDI-compliant parts.
4. **No two-way communication between patients and EHRs:**
   The FHIR standard enables patients to access health data through apps of their choice. However, because EHRs only allow read-only access to their systems, this is a one-way street. The software allows users to request information but does not allow them to modify or change it. Many industry experts believe that the next major difficulty for healthcare is a lack of two-way communication between medical apps and EHR systems. And, sooner or later, it will need the development of new data standards (93).

7. CONCLUSION

Research in this fresh domain of health informatics is vital because we need to be aware of the necessary discipline of health informatics where new discoveries can be realized effectively and *via* rigorous testing. There are no proven design blueprints for such a comprehensive infrastructure, and the goal is always shifting due to the nature of real-time data collecting from a variety of sources, such as patient/medical/equipment data. The future of health informatics is to create novel algorithms, models, and an ecosystem that is conducive to health professionals and decision makers.

Some of the advantages that will result from innovation in this new emerging area will be critical, such as:

- Case/Incident related Health Information Standards and Services
- Professionalism among Healthcare Units
- Various Innovative Industrial Processes
- Enhanced National and International Collaboration for Research
- Visualization Tools
- Novel Prediction Models (Machine Learning/Deep Learning/Reinforcement Learning)
- New Products and Services related to Healthcare/Health Informatics Domain
- Storage and Retrieval Mechanisms with Healthcare Related Data
- Curated New/Novel Datasets for Research Community.

Current cutting-edge health informatics research projects aim to discover new condition onset behaviors that are visible in physiological data streams earlier than traditional condition detection in critical care data (94). Cloud computing has attracted a lot of research attention, but only a small portion of the work done so far has addressed performance issues, and only a few of these have used a rigorous analytical approach (95–98).

Big data is also playing an important role in health informatics, where a large amount of data related to healthcare is generated, assisting and assisting doctors and decision makers in making rational decisions regarding patient treatment and diagnosis. Newer computational technologies may emerge that will improve the way healthcare is delivered and implemented

in the future, thereby vastly improving the public healthcare system. Policymakers can propose tried-and-true use cases that can be transformed into a meaningful framework in which all stakeholders can deliberate and decide on the best model for improving the public health care system.

Health informatics is a new field with many stakeholders involved in the design and implementation of sustainable public health systems and policies for the benefit of society as a whole.

AUTHOR CONTRIBUTIONS

MY has written the manuscript with relevant information from the literature regarding the major challenges and gaps that the present Health Informatics system and public health system are undergoing. The manuscript was reviewed and inputs were given by JK to focus on Health Informatics and policy framework. All authors contributed to the article and approved the submitted version.

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COVID-19 Mobile Health Apps: An Overview of Mobile Applications in Indonesia

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Background: Mobile health applications (mHealth apps) have been widely used for various purposes for mitigating the COVID-19 pandemic, such as self-assessment, contact tracing, disseminating information, minimizing exposure, and reducing face-to-face health consultation. The objective of this study is to systematically review COVID-19 related mHealth apps and highlight gaps to inform the development of future mHealth initiatives in Indonesia.

Methods: A systematic search strategy using a PRISMA flowchart was used to identify mHealth apps available in Google Play and Apple Play stores. We searched mHealth apps using certain specific terms related to COVID-19 outbreaks. The inclusion criteria were apps-based smartphone users related to COVID-19 using local language, free of cost, available in the Google Play and Apple Play Stores, and supported by the Indonesian government. We excluded games, apps on infectious diseases unrelated to COVID-19 specifically, and apps with non-Bahasa Indonesia (Indonesian language). The selected mHealth apps were assessed based on two measures: (1) the WHO guidelines on digital health intervention and (2) the four dimensions of the mHealth technology fit framework. In addition, user feedback from experienced and non-experienced users was conducted to evaluate four dimensions of the apps.

Results: A total of 339 mHealth apps were generated from the initial search, remaining seven selected apps that met inclusion criteria. The results highlighted that mHealth apps reviewed had still not been widely used by the general public. The applications were purposed to disseminate information, conduct a self-risk assessment, provide an online community forum, and telemedicine or teleconsultation regarding COVID-19. Data services, including data storage, aggregation, and data exchange, are available in most apps. The rarest function found was contact tracing and assisting health management and health workers, such as the availability of testing facilities, reporting test results, and prescribing medication. The main issues reported were the lack of data security and data privacy protection, integration and infrastructures, usability, and usefulness.

Conclusion: Our study highlighted the necessity to improve mHealth apps' functions related to assisting health workers and the function of digital contact tracing. An effort to increase public awareness regarding the use of mHealth is also necessary to streamline the function of this innovation. Policymakers must consider usefulness, usability, integration, and infrastructure issues to improve their mHealth function.

Keywords: COVID-19, pandemic, public healthcare, mHealth apps, Indonesia COVID-19, Indonesia

INTRODUCTION

Digital technology innovations are known as an enabler of health systems against pandemics. During Ebola and Zika epidemics, mHealth apps have improved access to testing, public awareness, supporting health workers, and contact tracing (1, 2). mHealth apps have also been developed to identify infected areas and contact tracing during the 2003 SARS-CoV-1 outbreak in China (3). In the current novel coronavirus disease (COVID-19) pandemic, many countries have developed mHealth apps to identify prevalent symptoms and infected areas, self-assessment, contact tracing, disseminate information, and minimize exposure and reduce face-to-face interaction between patients and health workers (3, 4).

A considerable amount of literature has been published to examine COVID-19 mHealth (5–15). Most of these studies focused on the goals and approaches of developing the apps quality, and technology advances (5–9). Although there are studies focused on the analysis of the features and functionalities, their evaluation is restricted to the general features of the apps such as usability and ease of use but did not include COVID-19 specific functionalities and features (10, 11). Some of them only discuss the breadth of common mHealth apps and their primary function during COVID-19 (3, 12). mHealth apps used in various countries during the pandemic were classified by the type of technology, targeted users, and function based on patient' needs (13). In addition, the review specifically related to the COVID-19 mHealth apps focused on specific functions, such as contact tracing (15), and only focused on specific populations, such as older people (14). Although prior studies have shown the utility and potential benefits of mHealth apps in preventing the pandemic, translating these ideas and early research into clinical tools on patients' mobile devices have received less attention (14).

Recent evaluation of mHealth apps concerning COVID-19 reported higher adoption of contact tracing systems is essential to lower the number of infections (16). Therefore, the success of a COVID-19 mHealth app depends on the adoption of the population. Nevertheless, low uptake rates were experienced in many countries (16). Many COVID-19 mHealth apps initiatives have not been as successful as originally expected in many countries. In a best-case scenario, Xia and Lee (17) posit that 90–95% of the population must use a contact tracing app to stop the spread of COVID-19 and allow normalcy without physical distancing. However, since March 2019, the apps have only been installed by about 9.3% of people in the 13 most populous countries with government-endorsed apps (18). Australia has reported the highest adoption rate with 21.6%, followed by Turkey with 17.3%, Germany with 14.4%, India with 12.5%, Italy with 7.2%, Peru with 6.8%, and Japan with 5%. The rest of the countries have an implementation rate below 5% (18). This evidence shows a need to understand the utilities and functionalities of COVID-19 mHealth apps and their gaps in a specific country to inform the development of future mHealth initiatives for improving apps uptakes.

Like many other countries, the Indonesian government has launched various mHealth apps for mitigating COVID-19. In April 2020, The Ministry of Communications and Informatics launched mHealth apps for COVID-19 screening called "*PeduliLindungi*", while the Indonesian Social Security Administrator for Health (BPJS) launched their mHealth apps for COVID-19 screening called "Mobile JKN" (19). Some local governments and private organizations have also developed mHealth apps to mitigate the pandemic in their constituencies and organizations (19). Looking at the COVID-19 mitigation in Indonesia was crucial as it has the highest number of cases in the South-East Asia region and reached 1.51 million by 21 February 2022, with the number of fatalities reaching 146,202 deaths on the same date (20). Mitigating COVID-19 has thus become public health priority in Indonesia. With unexpected potential pandemics in the future, the objective of this study is to systematically review the utilities and functionalities of those mHealth apps and highlights their gaps to inform the development of future mHealth initiatives in the country.

METHODS

The mHealth apps reviewed were searched in the Google play store and Apple play store as Indonesians mainly use them. The search was conducted in the third week of August 2021 and updated on 7 November 2021. The inclusion and exclusion criteria were applied based on the PRISMA procedure to collect the data (digital applications) (21). The following inclusion criterion was used to choose the applications accessible in the mentioned stores: (1) apps launched for smartphone users and apps that are related to COVID-19 using *Bahasa Indonesia (Indonesian language)* or local language in Indonesia; (2) apps had to be free of cost and had to be launched and updated during the COVID-19 outbreak for the management of COVID-19 in Indonesia; (3) apps that available in Google Play Store and Apple Play Store, and (4) apps had to be launched and supported by the governments of Indonesia. We excluded games, apps on infectious diseases unrelated to COVID-19 specifically, and apps with non-*Bahasa Indonesia* (Indonesian language). We searched

for the mHealth apps using the term "COVID-19," "corona virus," "epidemic," and "pandemic" within the app title and description.

The functionalities of the COVID-19 apps were reviewed through the selected apps and the literature on epidemic management using digital-related programs (15, 22, 23). We categorized the mHealth apps' functionalities under the categories of the clients (general public), health workers, health system managers, and data services based on WHO recommendations on digital interventions for health system strengthening (24). We collected information about COVID-19 specific functions, the name, and the developer through selected apps then summarized the frequency and percentages of the information obtained from the selected apps. The detailed process of app reviews and results was available at https://figshare.com/s/bde8b7c1082234dd012e.

In addition to the systematic review, we conduct user feedback to understand users' evaluation of four dimensions of the apps: usefulness dimension, usability dimension, integration and infrastructure dimension, and other additional dimensions (25, 26). Each dimension consists of polar questions (a yes-no question) measuring the users' evaluation using the seven selected apps. Before field data collection, the instrument was translated into *Bahasa Indonesia* and had been verified by three academic experts in the field for approval. A pre-test of the survey platform was conducted for pilot testing. We asked five eligible participants to identify any vague or very complicated questions as well as response options. All of them reported that all questions and responses in the questionnaire were clear and easy to understand. The average time to finish all questions was 10–15 min. Validity and reliability tests were applied to the questionnaire. The validity coefficient (correlation coefficients) and the reliability coefficient (Cronbach's alpha) for each dimension were 0.81 and 0.81 for the usefulness dimension, 0.83 and 0.84 for the usability dimension, 0.86 and 0.86 for the integration and infrastructure dimension, and 0.82 and 0.82 for the others dimension. In addition, to estimate the reliability of the entire survey, the Spearman-Brown correction was applied. Kappa values were 0.83 indicates the instrument was statistically reliable.

Users were purposively selected based on their experience using the apps. We classified the users into two groups. Group 1 was users who had prior experience using all seven selected apps after meeting inclusion criteria (49 individuals), whole group 2 was users with no prior experience using those of the seven selected apps (49 individuals). All respondents were educated from high school or higher with IT and medicine background knowledge to ensure they were able to evaluate all of the app evaluation items. We used a non-probability sampling method based on convenience sampling to determine the number of samples in both groups (27). We followed Pett and Salkind who suggest $n > 30$ as the minimum sample size for using a parametric statistical test (28, 29). For group 2, we employed five facilitators to interview 49 participants. Before participants answered the questions, each facilitator asked them to install and use the apps. For group 1, we employed three facilitators to interview 31 users. Each facilitator recorded participant responses using the excel sheet form provided. An independent *t*-test was used to determine if there is a significant difference between the means of the groups.

This study received ethical approval from the Ministry of Education and Culture, University of Brawijaya (Number 123/KEP/UB/2021). Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

RESULTS

Systematic Review

We identified 339 potential COVID-19 apps in Indonesia. Of these, 337 apps used the Indonesian language. **Figure 1** provides the flowcharts of the apps selection procedure.

Of the 339 apps screened, 309 were excluded because they were games or simulators, eighteen apps were also excluded because of their duplication ($n = 16$) and using non-Bahasa ($n = 2$). We also excluded seven apps not specifically related to COVID-19 ($n = 6$) and non-free apps (in-app purchase). The remaining seven apps were analyzed in this study. The reviewed apps ($n = 7$) in **Figure 2** consisted of four apps (57.1%) that were developed by the central government (*PeduliLindungi*, *10 rumah aman*, *Mobile JKN*, and *SiLacak*), and three apps (42.8%) developed by the local government (*Pikobar Jabar, Sawarna Kabupaten Bandung,* and *Papa Sulbar*). By November 2021, the *PeduliLindungi* app was downloaded by 50 million people out of the 273.5 million Indonesian population (18.3% of the Indonesian population), while *Mobile JKN,* which belongs to the BPJS was downloaded by 10 million people (3.65% of the population) (30). Other apps developed by local governments were downloaded by fewer than fifty thousand individuals (1.7% of the total local government population).

Table 1 lists the function of the reviewed COVID-19 apps and their comparison with the WHO recommendation for digital health intervention. Of the seven reviewed apps, six (85.7%) apps (i.e., *PeduliLindungi, 10 Rumah, Mobile JKN, PIKOBAR, Sawarna,* and *Papa Sulbar*) provided a self-risk assessment function that screened users with a set of questions related to their symptoms, occupations, travel history, and contact history. Six (85.7%) apps (i.e., *PeduliLindungi, 10 Rumah, Mobile JKN, PIKOBAR, Sawarna,* and SiLacak) also provided information through chatbots or helplines. Most apps (71.4%) were developed to supply information dissemination regarding preventative measures (i.e., *PeduliLindungi, 10 Rumah, Mobile JKN, PIKOBAR,* and *Papa Sulbar*). Five apps (71.4%) offered online community forums for patients and family members and provided symptom trackers for the users (i.e., *PeduliLindungi, 10 Rumah, Mobile JKN, PIKOBAR,* and *Papa Sulbar*). The function of enrolment to health service and teleconsultation or testing appointments were available in five (71.4%) apps (i.e., *PeduliLindungi, 10 Rumah, Mobile JKN, PIKOBAR,* and *Papa Sulbar*). The reported COVID-19 test results and the prescription/medication management were only available in three (42.9%) apps (i.e., *PeduliLindungi, Mobile JKN*, and *PIKOBAR*). Only the *PeduliLindungi* app, which is sponsored by the Ministry of Information and Communication, offered specific facilities for the high-risk population, such as the availability of

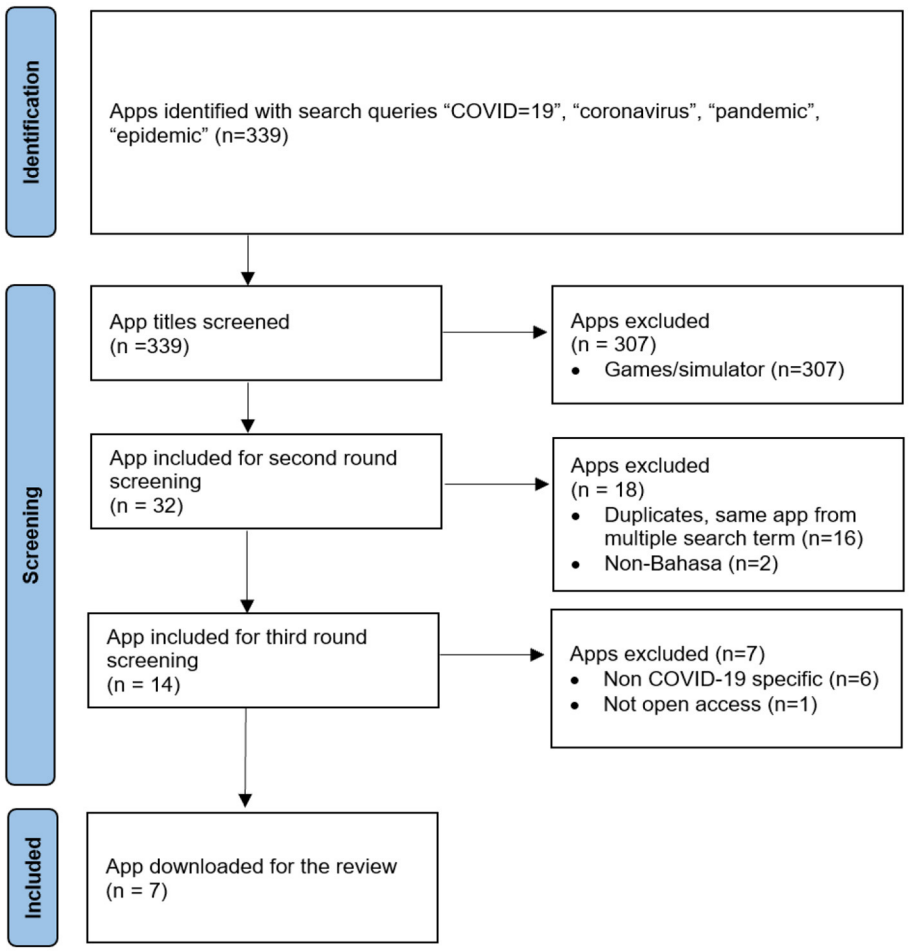

FIGURE 1 | Screening process flowchart.

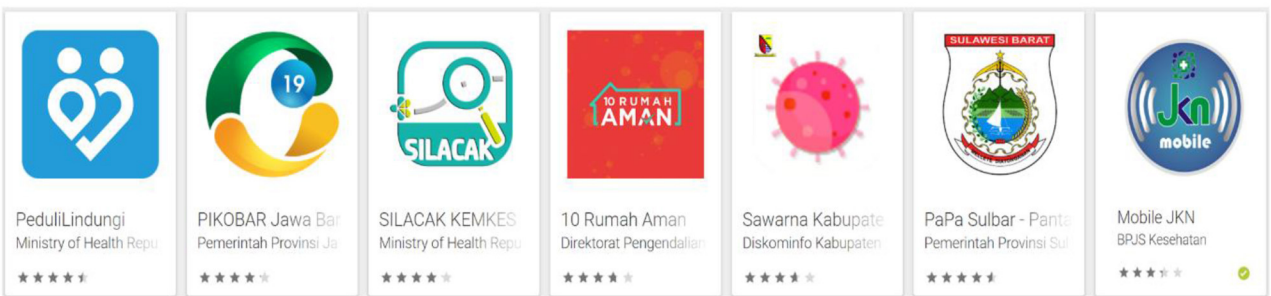

FIGURE 2 | Selected COVID-19 related mHealth apps.

testing services and protective equipment. All apps still did not have facilities for client financial transactions. Most apps (85.7%) provided notifications for confirmed cases and deaths (i.e., *PeduliLindungi, 10 Rumah, Mobile JKN, PIKOBAR, Sawarna,* and *Papa Sulbar*), and four apps (57.1%) provided hotspot identification (i.e., *PeduliLindungi, Mobile JKN, PIKOBAR*, and *Sawarna*). However, only the *PeduliLindungi* app allowed contact tracing. As for data service management, six apps (85.7%) had provided data storage, aggregation, and visualization (i.e., *PeduliLindungi, 10 Rumah, Mobile JKN, PIKOBAR, Sawarna,* and *Papa Sulbar*). Five (71.4%) apps could record the location data or offer Bluetooth handshakes (i.e., *PeduliLindungi, 10 Rumah,*

Mobile JKN, PIKOBAR, and *Sawarna)*. Finally, the location mapping of health facilities was available in four (57.1%) apps (i.e., *PeduliLindungi, Mobile JKN, Sawarna*, and *PIKOBAR*). The detailed information on seven selected apps based on the WHO guidelines on digital health intervention is available at https://figshare.com/s/bde8b7c1082234dd012e.

Users' Feedback

Users' feedback for seven selected apps was drawn from the questionnaire is presented in **Table 2**. Concerning usefulness dimension, participants report 21.4% of apps were able to consistently function from session to session (p-value = 0.91). Participants in both groups reported that 14.3% of apps work as advertised (p-value = 1.00), 14.3% of apps do not become clinically effective for the target population, disease, or disability (p-value = 1.00), and 14.3% of need more than 1 min to derive information they need (p-value = 1.00).

In terms of usability dimension, participants reported that 28.6% of apps are pleasurable and enjoyable to use (p-*value* = 1.00), 14.3% of apps can be used easily (p-*value* = 1.00), 14.3% of apps support the local language, and materials relevant to local culture and ethnicity (p-value = 1.00), 14.3% of apps take into account socioeconomic status and the user's age that support users with lack digital literacy (p-value = 1.00). All apps do not have tools that support disabled users (p-value = 1.00).

With regard to integration and infrastructure dimension, all users reported that all apps contain personal health information and share data with other apps, networks, and medical record systems (p-value = 1.00). Participants reported that 86% of the apps do not work within their user's workflow (p-value = 1.00). All users stated that the apps' data were not encrypted on the device, on transmission, were not anonymized, and did not contain a robust privacy policy to protect users (p-value = 1.00).

Furthermore, 28.6% of the apps could not be used to educate or train patients, families, and/or support staff, did not provide information for clinicians and point of care, and did not provide a differential diagnosis (p-value = 1.00). Only 21.4% of the apps were able to gather history of patients and provide useful information (p-value = 0.91), while 14.3% (p-value = 1.00) gave a comprehensive output.

DISCUSSION

This study aimed to evaluate COVID-19 related mobile apps used in Indonesia and highlight gaps to inform the development of mHealth related COVID-19 initiatives. We found very small investments from central and local governments in mHealth app development to deal with the pandemic crisis. Moreover, the proportion of the mHealth apps available for the population is relatively small, while evidence suggests that at least 70% of the population should have the apps installed for the digital contact tracing efforts to be effective (31). For example, *PeduliLindungi* and *Mobile JKN,* which national agencies developed, were downloaded by <20% of the national population. Prior studies have documented that inadequate Information and Communication Technology (ICT) infrastructure, low internet connectivity, low prescription, user resistance, and mHealth illiteracy are the main barriers to mHealth adoption in Indonesia, which is also commonly found in other developing countries (32–34).

All apps still did not meet the WHO recommendation for digital health information for COVID-19 mitigation (24). Most apps were used to disseminate COVID-related information on preventative strategies in which information provision was also delivered through chatbots or helplines. Despite that, a few apps are used to educate or train patients, families, and support staff. This finding corroborates a previous review of COVID-19 apps in East and South-East Asia and highlights the primary function of COVID-19 mHealth apps in most countries in the region for dissemination purposes (35). While interactive services and targeted client communication are crucial (11), most apps were still not designed for interactive engagement with users. For example, most of them have no user feedback on services and no facilities for client financial transactions. Only one app (*PeduliLindungi*) provides information regarding testing services and equipment for a high-risk population. The user feedback also reported that all apps did not incorporate facilities for disabled people and local language.

Most of the apps were not designed to assist health workers and health system managers. There is no function for health worker decision support, communication, activity planning, scheduling and training, hospital staff/human resources, monitoring, health commodity stock monitoring, and the movement system for health workers using electronic passes. Users also reported that they could not gather comprehensive output about patient history from the apps. These also confirm previous findings in a previous systematic review in East and South-East Asia (35). The review also found that the key feature to suppress coronavirus spread, contact tracing, was unavailable in most apps. Only one app reported contact tracing events. Most of the contact tracing activities have been manually conducted by surveillance officers, and therefore, the results of contact tracing can be directly reported for decision making (36).

Data and information privacy were the biggest issue in all apps. In the apps reviewed, when installing the apps and using the main features, users should input their data such as name, phone number, citizen registration number, email, Bluetooth interaction with other apps users, and real-time location. Data privacy concerns were also reported from user feedback. All users found that data encryption was not designed and anonymized, while the apps collect individuals' privacy preferences and personally identifiable information. The apps also did not include a robust privacy policy addressing personal and confidential information collected, the rationale for collecting information, sharing of information, and user control. These findings support evidence of previous mHealth related COVID-19 investigations in the country that data protection and security are a big concern as most of the apps have low-security protection technology (37, 38). The threat to privacy and personal data was also addressed in prior mHealth related COVID-19 evaluation in East and South-East Asia (11, 35, 39).

Issues of synchronization were also found in all apps. While most apps provided data exchange, storage, and aggregation, the apps did not integrate with each other. Each app had

TABLE 1 | Functionalities of COVID-19 mHealth apps and their comparison with WHO recommendations for digital health interventions ($n = 7$).

WHO recommendations	COVID-19 related functions	Available	Not available
		n (%)	*n* (%)
Clients			
Targeted client communication	Availability of testing services and protective equipment for high-risk population	1 (14.3)	6 (85.7)
Untargeted client communication	Preventive measures and demystification	5 (71.4)	2 (28.6)
Client to client communication	Community forums for patients and family members	5 (71.4)	2 (28.6)
Personal health tracking	Symptom tracker	5 (71.4)	2 (28.6)
	Self-risk assessment	6 (85.7)	1 (14.3)
	Quarantine monitoring	4 (56.1)	3 (42.9)
Citizen based reporting	User feedback on services	3 (42.9)	4 (56.1)
On-demand information services to clients	Information provision through chatbots or helpline	6 (85.7)	1 (14.3)
Client financial transactions	Manage out of pocket payments by service users	0 (0)	7 (100)
Health workers			
Client identification and registration	Enroll users for health services/clinical care	5 (71.4)	2 (28.6)
Client health records	Longitudinal tracking of user's health status	4 (56.1)	3 (42.9)
Health worker decision support	Job-aid for frontline health workers	0 (0)	7 (100%)
Telemedicine	Teleconsultation and testing appointments	5 (71.4)	2 (28.6)
Health worker communication	Provider to provider communication	0 (0)	7 (100)
Referral coordination	Manage referrals between points of service within the health sector	2 (28.6)	5 (71.4)
Health worker activity planning and scheduling	Electronic pass for the movement of the health workers during the lockdown	0 (0)	7 (100%)
Health worker training	Train new and existing healthcare staff	0 (0)	7 (100%)
Prescription and medication management		3 (42.9)	4 (56.1)
Laboratory and diagnostics imaging management	Testing for COVID-19	3 (42.9)	4 (56.1)
Health system managers			
Human resource management	Human resource monitoring for hospital staff	0 (0)	7 (100)
	Participation/volunteer recruitment	2 (28.6)	5 (71.4)
Supply chain management	Monitor stock levels of health commodities	1 (14.3)	6 (85.7)
Public health event notification	Notification of confirmed cases	6 (85.7)	1 (14.3)
	Contact tracing	1 (14.3)	6 (85.7)
	Hotspot identification	4 (56.1)	3 (42.9)
Civil registration and vital statistic	Notification of deaths	6 (85.7)	1 (14.3)
Health financing	Accepting donations from contributors	2 (28.6)	5 (71.4)
Equipment and asset management	Monitor status of beds and ventilators	1 (14.3)	6 (85.7)
Facility management	Priority checklists for facility management	1 (14.3)	6 (85.7)
Data services			
Data collection, management, and use	Data storage, aggregation, and visualization	6 (85.7)	1 (14.3)
	Prediction of future trends of disease	0 (0)	7 (100)
Location mapping	Map location of health facilities	4 (56.1)	3 (42.9)
	Location data recording or Bluetooth handshakes	5 (71.4)	2 (28.6)
Data exchange and interoperability	Data exchange across systems	5 (71.4)	2 (28.6)

been developed with its own function, design, and platform. There is no data integration between central government apps and local government apps. The local government-initiated apps were designed only for people in their jurisdiction and cannot be synched to central government apps. With the characteristics of a fragmented, decentralized health care system in which the government system consists of many tiers of government organization, the current mHealth apps can be detrimental for technology-assisted COVID-19 contact tracing as the technology was unable to monitor the movement of people across jurisdictions. Previous studies suggest that single national contact tracing, which is incorporated with specific contacts information and the local health system, is preferable in such a fragmented decentralized health system (31).

Based on the research, there are several recommendations that mobile app developers can consider to improve their existing COVID-19 apps or create a high-quality COVID-19 mobile app in the future. First, the developers must implement the core data protection principles such as the General Data Protection Regulation (GDPR) to ensure that the app is secure and provide assurance to the users that all shared information is kept confidential. Second, creating an application integration network

TABLE 2 | Comparison of users' feedback for seven selected apps for group 1 and group 2.

Usefulness dimension	Group 1	Group 2	Total	*P*-value
	Yes (%)	Yes (%)	Mean Yes (%)	
Will the app consistently function from session to session?	28.6	14.3	21.4	0.91
Does the app work as advertised?	14.3	14.3	14.3	1.00
Is the app clinically effective with demonstrated improved outcomes for the target population, disease, or disability?	14.3	14.3	14.3	1.00
What time is required for the user to derive some benefit from the app? Yes mean <1 min or vice versa	14.3	14.3	14.3	1.00
Usability dimension	28.6	28.6	28.6	1.00
Is the app pleasurable and enjoyable to use, or does it discourage repeat use?				
Can the user easily-or with minimal training-use and understand the app?	14.3	14.3	14.3	1.00
Does the app work effectively with the user's culture (as defined by factors such as ethnicity and language)?	14.3	14.3	14.3	1.00
Does the app take into account socioeconomic status and the user's age, with potential implications for the user's digital health literacy?	14.3	14.3	14.3	1.00
Is the app usable by those with disabilities (e.g., incorporates screen readers for blind users, close captions for the hard-of-hearing and deaf communities)?	0.0	0.0	0.0	1.00
Integration and infrastructure dimension	100	100	100	1.00
Is the app containing personal health information?				
Does the app share data with other apps, networks, and medical record systems?	100	100	100	1.00
Does the app work within its user's workflow?	14.3	14.3	14.3	1.00
Is the app anonymised?	0.0	0.0	0.0	1.00
Does the app contain a robust privacy policy addressing the type of information collected, rationale for collecting information, sharing of information, and user control?	0.0	0.0	0.0	1.00
Is the app's data encrypted on the device?	0.0	0.0	0.0	1.00
Is the app's data encrypted in transmission?	0.0	0.0	0.0	1.00
Others	28.6	28.6	28.6	1.00
Can the app provide information for either clinician education or point of care?				
Does the app provide a differential diagnosis?	28.6	28.6	28.6	1.00
Can the app be used to educate or train patients, families, and/or support staff?	28.6	14.3	21.4	0.91
Can the app gather history (e.g., from the patients) and provide useful comprehensible output?	14.3	14.3	14.3	1.00

is essential to allow applications to communicate with each other so that work processes can be done more effectively and efficiently. For example, application integration between central and local governments would be very useful to maintain, manage, and keep the apps up to date while alleviating data duplication and redundancy across governments. A collaboration with local health authorities to develop a mHealth app can increase the reliability of the app, which will encourage more users to be engaged in its use. Third, improvement of user interface designs of existing apps is needed. For example, to increase the apps' uptake of the public, the apps should take into account socioeconomic status and the user's age, the local language, and ethnicity as well as those with disabilities. The apps should be made available without requiring any payment in both the Apple App Store and the Google Play Store to make them more accessible to the public. It is also crucial to categorize mobile apps into appropriate categories to enable users to find an app easily and thus improve its user uptake. Fourth, the findings suggested designing an app that can assist health workers and health system managers. For example, they would need to add functions for health worker decision support, contact tracing, notification of confirmed cases, monitoring status of beds and ventilators, priority checklists for facility management, and a telemedicine system. Adoption of mHealth and telemedicine in the current pandemic requires health workers to use videoconferencing, while the medical care system is still managing the outbreak (9, 40). Hence, the application of mHealth has become timely while providing great potential to protect health workers and patients.

CONCLUSION

mHealth apps for COVID-19 in Indonesia are mainly designed for disseminating information, conducting a self-risk assessment, providing an online community forum, and telemedicine or teleconsultation regarding COVID-19. The least function found was contact tracing and assisting health management and health workers, such as availability of testing facilities, reporting test results, and prescribing medication. The main issues were data security and data privacy protection, integration and infrastructures, usability, and usefulness. This study suggests the necessity to improve the usefulness, usability, integration, and

infrastructure of mHealth apps, especially data security and data privacy protection.

The study was limited by the fact that COVID-19 mHealth apps selected were limited to free applications available in the Google Play Store and Apple Play Store. We were unable to review in-app purchases. Another limitation is that we did not include web-based applications. We did not perform a more robust search in publication indexes such as PubMed, Web of Science, and Scopus. New COVID-19 mobile apps may be launched that could not be included in this review. Moreover, our sample was based on convenience sampling which was characterized by insufficient power to identify differences in population subgroups. The potential bias of the sampling technique because under-representation of subgroups in the sample in comparison to the population of interest may occur (41). Future research may address these limitations by including non-free apps and conducting apps review based on a database such as PubMed, Web of Science, and Scopus focusing on technologies, functions, and features of mHealth apps that can be used by medical practitioners, application developers, and governments to collaborate in the process of containing the spread of coronavirus. More importantly, future studies should use probability sampling methods based on a sample of the general population to get a more reliable statistical inference of the population regarding COVID-19 mHealth apps uptake.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

SS, TA, HD, HH, and AM prepared study design. RS, HH, and TA collected data and conduct data analyses. SS and AM wrote the main manuscript text. All authors reviewed the manuscript. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.879695/full#supplementary-material

Supplementary Table 1 | Search strategy.

Supplementary Material | Functionalities of the coronavirus disease-19 apps.

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Knowledge, Perception, and Willingness to Use Telepharmacy Among the General Population in Indonesia

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Introduction: COVID-19 emerged as a pandemic in early 2020. Various steps were taken in an attempt to decrease the spread, which resulted in limited mobility. As people were dissuaded from going out, multiple numbers of digitalized pharmacy services arose to fulfill people's needs for medicine. The objective of this study was to assess knowledge, perception, and willingness to use telepharmacy services and the affecting factors among the general population in Indonesia.

Patients and Methods: A cross-sectional study was conducted with the inclusion criteria of Indonesian citizenship, living in Indonesia, and agreement to participate. Details of demographic characteristics, knowledge and perception of telepharmacy services and willingness to use them were collected using an online questionnaire that was adapted from a previous study. The results were analyzed using a descriptive analysis method. The associations between demographic characteristics and knowledge, perception, and willingness to use telepharmacy services were tested with the Mann–Whitney U Test.

Results: Of 203 participants participated in this study, 51% of them had heard about telepharmacy. Over 98% of the participants had a positive perception of telepharmacy services. The majority of those who had never used it were willing to try telepharmacy services in the future. Age and educational level were significantly associated with knowledge of telepharmacy services. No associations were observed between demographic characteristics and perception and willingness to use telepharmacy services.

Conclusions: General population in Indonesia had a fair knowledge, a positive perception, and were willing to use telepharmacy services. Interventions to increase knowledge of telepharmacy in Indonesia need to target older adults and people who are less educated.

Keywords: telepharmacy, knowledge, willingness, perception, Indonesia

INTRODUCTION

In late December 2019, cases of illness with pneumonia-like symptoms arose in Wuhan, China. By January 2020, the World Health Organization (WHO) concluded that the disease was caused by a novel coronavirus which was later named Sars-COV-2. The WHO announced that the outbreak was a public health emergency of international concern by January 30th, 2020, making it a pandemic (1).

COVID-19 spread quickly in over 210 countries (2). In March 2020, the first case of COVID-19 was detected in Indonesia (3). As the number of cases rapidly increased, the government enforced various measures to control the spread of the virus. The measures included the obligation to wear a mask, self-quarantine when one felt unwell, physical distancing, and later on, the requirement to get vaccinated (4, 5). The Indonesian government has been issuing restrictions on communities' activities since July 2021 and these have been prolonged until the beginning of 2022 (6). The measures resulted in limited mobility and made it difficult for face-to-face pharmacy counseling to take place. Furthermore, medical facilities in Indonesia were overloaded as the cases soared (7).

To overcome this, the Indonesian government issued a policy to implement telemedicine by July 6th, 2021 (4). Telemedicine is defined as health care services that are performed from a distance using technology and include an exchange of information on diagnosis, treatment, and prevention (8). Telepharmacy, as one type of telemedicine, provides remote pharmaceutical services including drug counseling, self-medication, drug monitoring, and evaluation by a qualified pharmacist (9).

Telepharmacy is a tool that can be used to reach underrepresented populations and thereby ensure equitable pharmaceutical services (10). Telepharmacy services in the United Arab Emirates can improve patient access to health care providers, ease the health care burden, and reduce dispensing errors (11). In the Republic of Srpska, Bosnia and Herzegovina, telepharmacy was used most for consulting on chronic disease, followed by consulting about COVID-19, and about acute diseases (12).

A previous study conducted in Jordan including 364 community pharmacists as participants showed that 91% of them agreed that telepharmacy helps patients to get faster medical feedback (13). Another studies reported that most pharmacy students at the University of Tennessee Health Science Center and one University in Jordan were not familiar with telepharmacy but thought that it would be useful to prevent medication error, save time (14) and they showed a positive willingness to use the services (13). The factors affecting people's choice to use telepharmacy in Indonesia are the regulations, the technology used by the patients, and financial status (15). However, evidence about knowledge and perception of telepharmacy and willingness to use it among people in Indonesia remains unclear. This information is important to develop interventions to improve the acceptability of telepharmacy.

The objective of this study is to assess awareness, perception, and willingness to use telepharmacy services and the affecting factors among the general population in Indonesia.

MATERIALS AND METHODS

Study Design and Setting

An observation cross-sectional survey was conducted among the general population in Indonesia. The data were collected from October 7th, 2021 to October 15th, 2021 from participants who met the inclusion criteria: being an Indonesian citizen, currently living in Indonesia, and agreeing to participate. We did not restrict the inclusion criteria based on participants' demographic characteristics such as age or length of residency to capture the

TABLE 1 | Demographic characteristics of the participants ($N = 203$).

	N	Percentage (%)
Age (years)		
<15	3	1.5
16–19	22	10.8
20–30	120	58.8
31–40	28	13.7
41–50	18	8.8
51–60	12	5.9
>60	1	0.5
Gender		
Male	64	31.5
Female	139	68.5
Level of education		
Middle school	5	2.5
High school	81	39.7
Associate's degree	10	4.9
Undergraduate	91	44.6
Master's degree	10	4.9
Doctoral degree	5	2.5
Others	2	1
Province of origin		
Aceh	4	2
Banten	10	4.9
Bengkulu	3	1.5
Central Java	10	4.9
DI Yogyakarta	2	1
DKI Jakarta	8	3.9
East Java	12	5.9
East Kalimantan	1	0.5
Lampung	1	0.5
Maluku	1	0.5
North Sumatera	2	1
Riau	2	1
South Sulawesi	1	0.5
South Sumatera	1	0.5
West Java	143	70.1
West Kalimantan	3	1.5

general population in Indonesia. The Health Research Ethics Committee of Universitas Padjadjaran, Indonesia approved the study protocol (No. 967/UN6.KEP/EC/2021).

Procedure

The participants were randomly approached online through social media (Twitter, Instagram, and Facebook) and groups chat in smartphone applications. Data about knowledge and perception of telepharmacy services and willingness to use them were collected using an online questionnaire (Google Forms) in Indonesian language that was based on a previously published study (16). The questionnaire consisted of four sections: demographic characteristics, knowledge, perception, and willingness to use telepharmacy.

Demographics

This section explores the diversity of the participants using questions on age, gender, level of education, and province of origin.

Knowledge About Telepharmacy Services

Knowledge of telepharmacy was assessed using several questions including, "Do you have a chronic disease?," "Have you ever heard about telepharmacy?," and "Have you ever used a telepharmacy service?"

Perception of Telepharmacy Services

This section is to assess participant's perception of the telepharmacy services to agree or not with some statements including, "There are many telepharmacy services that I can use in Indonesia." "I like using the telepharmacy services," "The telepharmacy service is important to be able to communicate with medical practitioners whenever and wherever," "The telepharmacy service helps to save energy and time," "The telepharmacy service helps to cut service costs," "I am willing to pay for telepharmacy services," and "I will recommend telepharmacy services to my family and friends." The questions' ratings for perception were measured using a five-point Likert-type scale ranging from 1 = strongly disagree to 5 = strongly agree. The perception groups were divided into two which were defined a priori as participants with total score of 1–17 being grouped as having poor perception, whereas participants with total score of 18–35 being grouped as having good perception.

Willingness to Use Telepharmacy Services

The participants who had not used telepharmacy before were assessed about their willingness to use it in the future by asking the question, "If not, are you interested in using telepharmacy?"

Sample Size Calculation

Using the Slovin formula (17, 18) to determine the minimum sample size, a minimum of 100 participants was required to obtain a 95% confidence level and a margin of error of 10% based on the Indonesian total population of 273 million (19).

Data Analysis

Descriptive statistics were used to summarize the participants' characteristics. The normality test was conducted using the Kolmogorov–Smirnov test since the sample size was higher than 50 participants. The associations between demographic characteristics and knowledge, perception, and willingness to use telepharmacy services were tested with the Mann–Whitney U Test since all data were not normally distributed. All statistical analyses were carried out using SPSS software (version 25.0; IBM, Armonk, NY, USA).

RESULTS

Demographic Characteristics

A total of 203 participants participated in this study (response rate 99.5%). The majority of the participants were aged around 20–30 years old ($n = 120$, 58.8%) and female ($n = 139$, 68.6%). Most participants came from West Java ($n = 143$, 70.1%), followed by East Java ($n = 12$, 5.9%), Banten ($n = 10$, 4.9%), and Central Java ($n = 10$, 4.9%) (**Table 1**). Most participants did not report having a chronic disease ($n = 181$, 89.9%).

Knowledge, Perception, and Willingness to Use Telepharmacy Services

For the section on participants' knowledge about telepharmacy, 181 participants (89.6%) had no chronic illness and 104 participants (51%) had heard of telepharmacy (**Table 2**). Most of them ($n = 162$, 79.8%) had never used the telepharmacy services, but 89.9% of them ($n = 160$) were interested in using it (**Table 2**).

Seventy-six participants (37.4%) felt neutral about the statement "there are many different telepharmacy services I can use in Indonesia" (**Table 3**). The second question was only for those who had used telepharmacy services and 68 out of 146 participants (46.6%) felt neutral about the statement on liking to use a telepharmacy service. The third question was about the importance of telepharmacy for communicating with medical practitioners whenever and wherever in which 92 participants (45.3%) agreed. The participants strongly agreed that the telepharmacy service is important in saving time and

TABLE 2 | Knowledge and willingness to use telepharmacy services.

Questions	N (%)	
	Yes	No
Knowledge about telepharmacy services		
Have you ever heard about telepharmacy?	104 (51.0%)	99 (49.0%)
Have you ever used telepharmacy service before?	41 (20.2%)	162 (79.8%)
Willingness to use telepharmacy services		
If not, are you interested in using telepharmacy services?	160 (89.9%)	18 (10.1%)

TABLE 3 | Perception of telepharmacy services.

Statements	Answer (%)				
	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
There are many telepharmacy services that I can use in Indonesia	2 (1%)	25 (12.3%)	76 (37.4%)	69 (34%)	31 (15.3%)
I like using telepharmacy service	3 (2.1%)	6 (4.1%)	68 (46.6%)	47 (32.2%)	22 (15.1%)
Telepharmacy service is important to be able to communicate with medical practitioner whenever and wherever	0 (0%)	1 (0.5%)	25 (12.3%)	92 (45.3%)	85 (41.9%)
Telepharmacy helps to save time and energy	0 (0%)	1 (0.5%)	23 (11.3%)	83 (40.9%)	96 (47.3%)
Telepharmacy helps to reduce service costs	2 (1%)	6 (3%)	49 (24.1%)	60 (29.6%)	86 (42.4%)
I am willing to pay for telepharmacy services	7 (3.4%)	16 (7.9%)	65 (32%)	82 (40.4%)	33 (16.3%)
I will recommend telepharmacy to my friends and family	1 (0.5%)	7 (3.4%)	53 (26.1%)	79 (38.9%)	63 (31%)

energy. Of them, 86 participants (42.4%) also strongly agreed that the telepharmacy service helps in cutting service costs and 82 participants (40.4%) were willing to pay for the service. Lastly, 79 participants (38.9%) were willing to recommend telepharmacy services to their family and friends (**Table 3**).

Factors Associated With Knowledge Perception, and Willingness to Use Telepharmacy Services

Age (p-value = 0.000) and educational level (p-value = 0.031) were significantly associated with knowledge about telepharmacy services (**Table 4**). No association was observed between gender and knowledge of telepharmacy services.

In the perception section, the results were divided into participants who had used telepharmacy services (Group 1) and participants who had never used the telepharmacy services (Group 2). There were no associations between age, gender, educational level and perception about telepharmacy services among these two groups (**Table 4**).

There were no associations observed between age (p-value = 0.589), gender (p-value = 0.664), educational level (p-value = 0.536) and willingness to use the telepharmacy services (**Table 4**).

DISCUSSION

Over half of the 203 participants in our study had heard about telepharmacy services. Most participants had a good perception of the telepharmacy services that were offered. Participants who had never used a telepharmacy service also showed an interest in using it in the future. Age and educational level were significantly associated with knowledge of telepharmacy services. No associations were observed between demographic characteristics and perception and willingness to use telepharmacy services.

This study showed that 51% of the participants had heard about telepharmacy. This number is higher than a study conducted in India (18.9%) (16). Furthermore, 89.9% of the participants who had never used telepharmacy services in our study were willing to use them in the future. This result is in line with a previous finding that telemedicine usage s has been increasing since the pandemic occurred (20). It was supported by the fact that although 89.6% of our participants are healthy, they have heard of telepharmacy before. The reason might be the restrictions that have been implemented in Indonesia; which resulted in people using more online services, such as telepharmacy, to fulfill their daily needs.

TABLE 4 | Association between demographic characteristics and knowledge, perception, and willingness to use telepharmacy.

	(*p*-value)
Knowledge	
Age	0.000
Gender	0.912
Level of education	0.031
Perception	
Age group 1	0.245
Age group 2	0.634
Gender group 1*	0.669
Gender group 2#	0.663
Level of education group 1*	0.435
Level of education group 2#	0.982
Willingness	
Age	0.589
Gender	0.664
Level of education	0.536

**Group 1: Participants who had used telepharmacy services. #Group 2: Participants who had never used the telepharmacy services.*

Despite the limited knowledge, we observed that 98% of the participants had a positive perception of telepharmacy services. They agreed that telepharmacy would benefit them in terms of cutting time, energy, and cost. They also believed that the service would be beneficial to give them more flexibility because it is performed online. This finding is supported by a previous study that the patients who received telemedicine health care were very satisfied with the service they had received (21). The usage of telemedicine has been proven to enhance the quality of care for patients with diabetes in Saudi Arabia by successfully monitoring and maintaining their blood glucose levels (22).

In this study, we observed that age is significantly associated with knowledge about telepharmacy services in Indonesia. This can be explained by the different amounts of exposure to technology in each group. The younger groups tend to be more familiar with the newer technology, which results in them being more aware of the newer services that have been offered. In another study that was conducted in the United States, older people were not likely to be interested in using telemedicine services due to their lack of belief that the health care purpose can be achieved at a distance (23).

Participants who have higher education in our study seem to be more aware of telepharmacy services. Similarly, this was due to people with higher education being exposed to more technology. They are also more likely to pay more attention to the newest regulations that have been issued by the Indonesian government. This finding is also supported by another study in Egypt that showed highly educated people have more knowledge of telemedicine services (24). We further observed no association between gender and knowledge about telepharmacy services. This may be due to digitalization where everyone has access to the internet regardless of their gender.

No association was observed between gender, age, and educational level with the perception of telepharmacy services in our study might be due to the awareness of participants about the importance of maintaining their health. There was adequate exposure from health promotion programs through social media and counseling to everyone regardless of their age, gender, or educational level. Although no association was observed between age, gender, or level of education and willingness to use telepharmacy services, we observed that most participants are willing to use the services.

Our findings implied that there is still a gap between the knowledge about telepharmacy the participants have within different age and educational level groups. A more thorough approach should have been given to older people and people who are less educated by offline counseling to ensure that people who are not so familiar with technology can get the same exposure. Furthermore, a health promotion program should target the patients' families for supporting older people. The health promotion program can also be conducted in education and health facilities to ensure that everyone knows the newest regulations regarding telepharmacy services.

To our knowledge, this is the first thorough evaluation of knowledge, perception, and willingness to use telepharmacy, as well as factors associated with it, among Indonesian participants. However, some limitations need to be mentioned. Data collection using online questionnaire has several methodological drawbacks: certain populations are less likely to have internet access and to respond to online questionnaire, the lack of a trained interviewer to clarify the information provided can lead to less reliable data, and voluntary participation can result in participants with biases selecting themselves into the sample. We also could not draw causal inferences regarding the temporal associations between age and educational level with knowledge of telepharmacy services. Furthermore, most of the participants in our study were university students and without chronic diseases, thus, possibly not representative of the general population. Therefore, we advise caution in interpreting and extrapolating our results. Future studies should focus on qualitative research to provide a more in-depth understanding of the acceptance of telepharmacy services. Furthermore, a better understanding of the knowledge and perception of telepharmacy services and willingness to use it of different age, location (urban vs. rural) and comorbidity groups over a longer period including all provinces would give a more comprehensive overview of telepharmacy practices in Indonesia. Such findings might support research on how to develop effective interventions and acceptance of telepharmacy practices.

CONCLUSIONS

Of the 203 participants in our study, most of them had a fair knowledge and had positive perceptions about the telepharmacy service. Those who had never used it were also interested in using telepharmacy in the future. Interventions to increase knowledge of telepharmacy in Indonesia need to target older adults and people who are less educated.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Health Research Ethics Committee of Universitas Padjadjaran. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

NT conceived and designed the study, performed the study, analyzed and interpreted the data, and wrote the paper. SA conceived and designed the study and analyzed and interpreted the data. Both authors contributed to the article and approved the submitted version.

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METHODS
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Methods and Lessons From Costing a Large mHealth Intervention at Scale in India

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The use of mobile devices to deliver public health interventions is rapidly increasing, particularly in low resource settings. Despite their proliferation, several mHealth interventions in developing countries fail to reach geographical scale, and long-term sustainability for most remains uncertain. There is a need to cost for such programs, to enable better planning and budgeting and tailor programs as required. Cost estimates can contribute to a more informed debate on resource allocation priorities and help make choices clearer for policymakers. This paper has two main objectives: (1) present a detailed protocol on determining the costs of a large national mHealth job aid and behavior change communication tool known as Integrated Child Development Services - Common Application Software (ICDS-CAS) in India, and (2) to present lessons for policymakers on how to ensure financial planning for scaling mHealth interventions. The study uses the Activity Based Costing—Ingredients (ABC-I) method. The major advantage of the ABC-I method is the clarity it brings to costs for each input and activity, across levels and geographies. It also accounts for indirect costs. There are five key lessons while costing for mHealth programs. First, that there are many activities and ingredients that must be budgeted for and discussed while planning and implementing mHealth programs. Second, the ABC-I method described in this paper provides great clarity on costs, yet its major limitation is the availability of data, which must be mitigated with the careful use of assumptions. Third, mHealth technology life cycles have financial implications which must be accounted for. Fourth, determining cost locations and all sources of funding including non-government sources is crucial. Fifth, since costing estimates are subject to a set of assumptions, a disaggregation of costs allows for scenario-building, which is useful while planning ahead and accounting for program changes. The evidence generated can be used for more informed debate on resource allocation priorities, given competing priorities in low- and middle-income countries.

Keywords: low and middle income countries (LMICs), costing, methods - estimation, planning, budgeting, India, mHealth

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INTRODUCTION

The use of mobile and wireless technologies to support the achievement of health objectives or mHealth interventions has been increasing. They have been heralded as having the ability to transform the delivery of health services (1). In particular, mobile phones have the potential to improve access, knowledge, and healthy behaviors. Several studies have also reported that mHealth

interventions are cost-effective, economically beneficial, or cost saving (2). Further, mHealth has found a degree of acceptability among health workers who use them as well (3). Given the ever-increasing mobile phone usage in Low and Middle Income Countries (LMICs) (4), the use of mobile devices to deliver public health interventions is believed to be effective, particularly in low resource settings (5).

Despite their proliferation, a systematic review of mHealth interventions found that while the low cost of mobile technology enabled their adoption, successful expansion was often hampered by mechanisms for financial sustainability and a lack of data on the cost of programs at scale (2). Consequently, several mHealth interventions in developing countries fail to reach geographical scale (2), and long-term sustainability for most remains uncertain (6). Sustainable financing is fundamental to the capacity of any mHealth project to increase its scale, yet it is often the most difficult part of the process (7), especially without transferring costs to users (8). Part of the problem when it comes to scaling up, for governments, is the lack of data on the cost of programs at scale (2). Shortage of high-quality data allowing assessments of comparative effectiveness and comparative value makes it difficult for governments to select, scale up, and integrate mHealth solutions into existing national systems (9). While several pilot studies have estimated costs of pilot programs, covering countries such as Nepal (10) as well as states in India such as Uttar Pradesh and Bihar (11, 12), there are only limited studies that have estimated what it would cost to scale-up the program (13).

In the absence of quality administrative data and given financial limitations and several competing priorities in LMICs, economic evaluations are an important tool for effective prioritization of resources (14). Where programs do not have the data, resources, time or expertise to conduct a full economic evaluation, partial evaluations (sometimes referred to as "costing studies") may be undertaken to measure the costs of a single program (cost description) (15). When done for costs, they can provide cost amounts, key cost drivers, resource estimates required to sustain and scale an intervention, or to develop more comprehensive economic evaluations (16).

This paper attempts to strengthen the evidence base by presenting a comprehensive, bottom-up methodology on undertaking a cost evaluation of a large-scale national mHealth program. We have applied this method to cost for such an intervention in India, known as the Integrated Child Development Services-Common Application Platform (ICDS-CAS). In September 2020, the program was replaced by another application with similar aims known as *Poshan* Tracker (*Poshan* means nutrition).

Objectives

This study aims to (1) present a detailed protocol on determining the costs of a large national mHealth job aid and behavior change communication tool known as ICDS-CAS in India, and (2) to present lessons for policymakers on how to ensure financial planning for scaling mHealth interventions.

There are two common starting points for any costing study. First, to develop a financial forecast for sustaining and/or expanding program activities; and second, to model the sector-wide implications of scaling up (17). The methods described here solely focus on the former.

What Was ICDS-CAS?

Launched in 2016, the ICDS-CAS program sought to improve service delivery of nutrition programs and had four key features. First, through a smartphone application, it digitized and automated 10 of the 11 service registers that frontline workers (FLWs) - known as Anganwadi Workers (AWWs) are expected to maintain (except the stock register). This information was then aggregated through a web-based dashboard at different sub-national levels including block, district, state, and finally at the national level. Second, since AWWs are meant to conduct regular home visits to pregnant women and lactating mothers, it had a scheduler that helped prioritize home visits. Third, the software also contained counseling videos which could be used as a job aid. Finally, with features such as a photo capture feature and GPS capability, the application helped create channels for monitoring. AWW supervisors known as Lady Supervisors (LSs) had access to real-time data (18). Between 2016–2019, over 6,00,000 out of 1.4 million community workers had been trained under the program, and INR 640 crore (or 9.1 million USD) had been spent overall as per a Right to Information request filed by the authors.

Studies have found that AWWs spend substantial amounts of time on administrative tasks (19). ICDS-CAS was thus envisaged to reduce this burden. Recent evaluations have also shown that mHealth interventions such as ICDS-CAS can support gains in immediate term service delivery outcomes by enabling more age-appropriate home-visits and counseling but require longer term evaluations to improve other outcomes (20).

Yet, the program was not without its challenges. A process evaluation found that impediments to roll-out included state readiness, delays in device procurement and set-up, dashboard readiness, and low data storage space (21). This study builds on the findings from the process evaluation by focusing on the need for appropriate planning by analyzing costs incurred and required for all components over time.

Outlining the Protocol

This research uses the Activity Based Costing - Ingredients (ABC-I) method which has been used in several costing studies (22–24). The activity-based costing approach aims to break down the program into a sum of activities. These activities can be described as "cost centers or Activity Based Cost-Centers (AB-CCs) which should be mutually exclusive and exhaustive". These activities are further broken down into ingredients which are combined to get total costs. The ingredients method requires three pieces of information to derive program costs. (1) list of inputs, (2) the quantities of the inputs used to realize the program, and (3) the cost per unit of an input. In the method described subsequently, these approaches are combined. The output is a detailed cost matrix, which can be used in many ways.

Possible Applications

Resources are typically scarce in LMICs, and any expenditure at scale requires careful prioritization between competing needs.

Cost estimates can contribute to a more informed debate on resource allocation priorities (24), and help make choices clearer for policymakers. Given their disaggregated nature, cost analyses using ABC-I are replicable across programs in other LMICs and can be used by policymakers to plan and budget for new programs, tailor existing programs as they develop, and to determine costs to measure the effectiveness of any program.

The objective of budgeting is estimating existing revenues required and likely expenditures as well as determining future funding needs. As mHealth programs expand across LMICs, every government will have to construct a budget including start-up costs, fixed costs, and variable costs, as well as creating annual or longer-term plans. ABC-I provides a basis for that. Furthermore, since ABC-I aims to disaggregate costs, it can be helpful in creating budgets tailored to a detailed roll-out plan. For example, the program may only be launched in a limited geography or with limited features initially, and gradually expand.

Additionally, as with most government interventions, it is possible that some components of mHealth programs are phased out in the future, or the component-mix and resource-mix requires change. To this end, ABC-I can provide detailed inputs on the minutiae of the program and help visualize these changes easily. For example, this can help in determining the impact of delays or changes in the implementation modalities on total program costs.

Results using the ABC-I method can serve as a toolkit for governments, policymakers, donors, and practitioners. It allows for a comparison with other similar programs that could be rolled out across LMICs in the future.

METHODS

The following five steps were involved in application of the ABC-I approach in this cost evaluation.

Step 1: Developing a Detailed Description of the Intervention

This process involves sequentially listing out all processes and components that go into implementing the program as desired. This includes, but is not limited to, procurement of equipment, hiring staff, training of FLWs, mid-level managers, and officials, and setting up the monitoring and upkeep procedures. This helps in creating a timeline of all activities conducted for the intervention as well. This description helps in grasping the scope of the intervention and narrowing the focus on activities that require the most time, effort, and resources.

Detailed program descriptions can be created based on operational guidelines set by the implementing authority or be co-created with them. Primary documents used should ideally include the operations manual, impact pathways, training, hiring, and other process manuals, etc. Various partners need to be consulted to understand their exact role, if it is unclear from secondary sources.

Step 2: Identify and Isolate Activity Based Cost-Centers (AB-CCs)

The procedure for this step is similar to the previous one and some degree of convergence between these steps is anticipated. The detailed checklist created in step one shall be used to identify *mutually exclusive and exhaustive* AB-CCs to avoid double counting and should be sufficiently detailed, to allow for granular analysis of each element of the intervention. A descriptive report helps identify all possible activities, and to break them down by which stage they are needed – start-up, maintenance, or scale-up. Every AB-CC itself comprises various "ingredients" that come together, and the various inputs needed for each activity. For example, training activities could be described as an AB-CC, broken down into ingredients such as FLW training, training of officials and other personnel. Each ingredient requires various inputs such as space to conduct the training, trainer's remuneration, and so on.

Step 3: List all Ingredients That Go Into an Activity

Every activity must be broken down, as much as possible, into all its elements. This enables the compilation of a cost database, where all inputs and ingredients needed for a given activity are listed in detail. This database specifies the category, ingredient name and description, and a unit of measurement for each (for instance, wages are usually defined as the product of the wage rate per hour).

In this step, vital categories of inputs are delineated—shared vs. non-shared costs, fixed vs. variable costs, and recurrent vs. non-recurrent costs. Capital goods represent a type of fixed and non-recurrent cost which needs to be depreciated over the assets' potential life term. These include vehicles, buildings, etc. Recurrent costs include remuneration for personnel or maintenance costs, which are purchased frequently, often in regular intervals (daily, monthly, or annually). Sometimes for an ingredient, both recurrent and non-recurrent costs exist. For example, while the purchase of a smartphone for the mobile application is a fixed cost it is recurrent every few years because the lifespan of a phone rarely exceeds 2–3 years, whereas the phone servicing and maintenance is a recurrent cost.

This step also entails determining the number of units of each input required for any given activity such as the number of hours of the training agency's time, the number of mobiles and tablets needed, the amount of office space required, and so forth.

The first three steps shall occur simultaneously. Furthermore, they are iterative to an extent whereby new information should be included as and when required.

Step 4: Compiling Unit Costs

For each activity and ingredient, unit costs are to be compiled from various sources including the government program budget and expenditure documents, training guidelines, procurement registers, etc. There can be certain ingredients for which exact unit costs cannot be compiled. For instance, when personnel work across multiple interventions including mHealth programs, the time they spend and therefore the remuneration paid to them

solely for the mHealth program may be unclear. A mitigation strategy for such scenarios is mentioned in the subsection on limitations and mitigation.

Ideally, the cost of any activity should be measured as the total sacrifice made to complete that activity. For this purpose, we may have to use market prices as well as economic costs. It is important to note, however, that market prices may not reflect true economic costs. This is particularly true for inputs that are donated, capital inputs, or have distorted or non-existent markets. For our purpose, the idea is to include time costs, personal costs, and social costs, if any.

To cost for ICDS-CAS, unit costs were obtained from a central Indian state Madhya Pradesh (MP), which was one of the pilot states for the program.

Accounting for Private and Social Costs

Private costs are those borne by individuals. Health interventions can affect the ability of people to work (they may have to spend more or less time away from work, and therefore affect the total resources available to them. The effect of productivity costs and gains should therefore be included in the study (24). This covers values for non-market items. Some major non-market items include travel costs for various functionaries for the repair, maintenance, replacement of phones, submitting data, charging phones, and so on. Functionaries may not be compensated for certain costs; however, these should be included in the cost profile. Social costs entail costs that are not budgeted for, or don't have markets, and are borne by society or social structures. For most programs, such costs are typically negligible.

Step 5: Estimating Total Costs

The total cost of each activity or AB-CC can now be calculated, as well as the total cost of the intervention. We have,

$$Total\ Costs\ \ (TC) = \sum_{1}^{n} AB - CC\ Costs$$

Where n is the total number of AB-CCs.

However, there are several adjustments that must be made when presenting these numbers. First, we need to account for the fact that there is a preference for consumption in the current time period, rather than consumption in any future time period. Therefore, we need to take discounted values for total costs in future years. The WHO recommends a discount rate of 3 per cent, to enable comparisons with other studies (24). In addition, we can use discount rates specific to a country or state as well.

Second, we must index all costs based on inflation rates. That is, we must assess costs in real terms, and not in nominal terms. For example, if the intervention is to be scaled up in 2019, then costs calculated in 2018 must be adjusted for price inflation between 2018 and 2019.

Finally, to account for variability in program design and to test the sensitivity of assumptions, the activity-wise range of costs under different scenarios should be presented.

Why ABC-I?

The advantages of using the ABC-I method are briefly outlined here. First, ABC-I is a method that provides detailed costs for each input and each activity they go into. Since we put each activity and input under a magnifying lens, calculating marginal costs is easier. Marginal costs are often needed to decide when estimating the scaled-up costs of the program. It is necessary to note that marginal costs are not constant with scale, and ABC-I accounts for that.

Secondly, ABC-I allows for clarity in the reporting of both prices and quantities at various levels and in different contexts. This approach allows us to estimate costs for this program in a different setting (replicability), or on a larger scale (scaling up) without any need to re-collect prices and quantities for different scenarios.

Thirdly, ABC-I accounts for indirect costs that cannot be attributed to a particular program alone. ABC allows us to apportion these costs for each input based on a direct tracing of personnel time to services (25). For example, if personnel work across multiple interventions and only devote part of their time to the mHealth intervention in question.

This methodology is proposed as it brings clarity to the costing exercise by using unit costs, taking into account the possibility of double counting, and by allowing to account for indirect costs (social costs, private costs, among others).

RESULTS AND DISCUSSION

Key Outputs

The steps listed above lead to the production of two key outputs. First, the construction of a cost profile. This profile lists out the various costs associated with each activity in a comprehensive and disaggregated manner. A cost profile can list activities based on whether they are start-up costs, maintenance costs, or costs sustained during the scale-up process. We can then visualize the shape of the intervention with greater clarity, with information on which activities and inputs cost the most, require the bulk of maintenance costs, or are the costliest aspects of scaling up. This allows comparisons across activities and can inform discussions on optimizing the intervention.

Second, visualizing scale-up costs. Several mHealth interventions start as pilots but aim to scale-up. While an intervention is scaled up, input quantities, and therefore, costs may not increase in a linear fashion. This is particularly true of fixed costs, such as the physical infrastructure and overhead costs. Excluding certain inputs and costs is relatively straightforward using the ABC-I methodology proposed for this exercise. Simultaneously, it allows us to analyze the costs required to replicate the program in vastly different contexts.

There were several lessons from the application of ABC-I to understand ICDS-CAS costs. They are presented below:

Lesson 1: Each Activity of mHealth Programs Have Several Ingredients Which Need to Be Budgeted for

An application of the method to costing for ICDS-CAS, found that broadly, the intervention could be categorized into 3 broad activities (**Figure 1**):

1. Administrative costs which include all costs related to managing and organizing the implementation of ICDS-CAS.

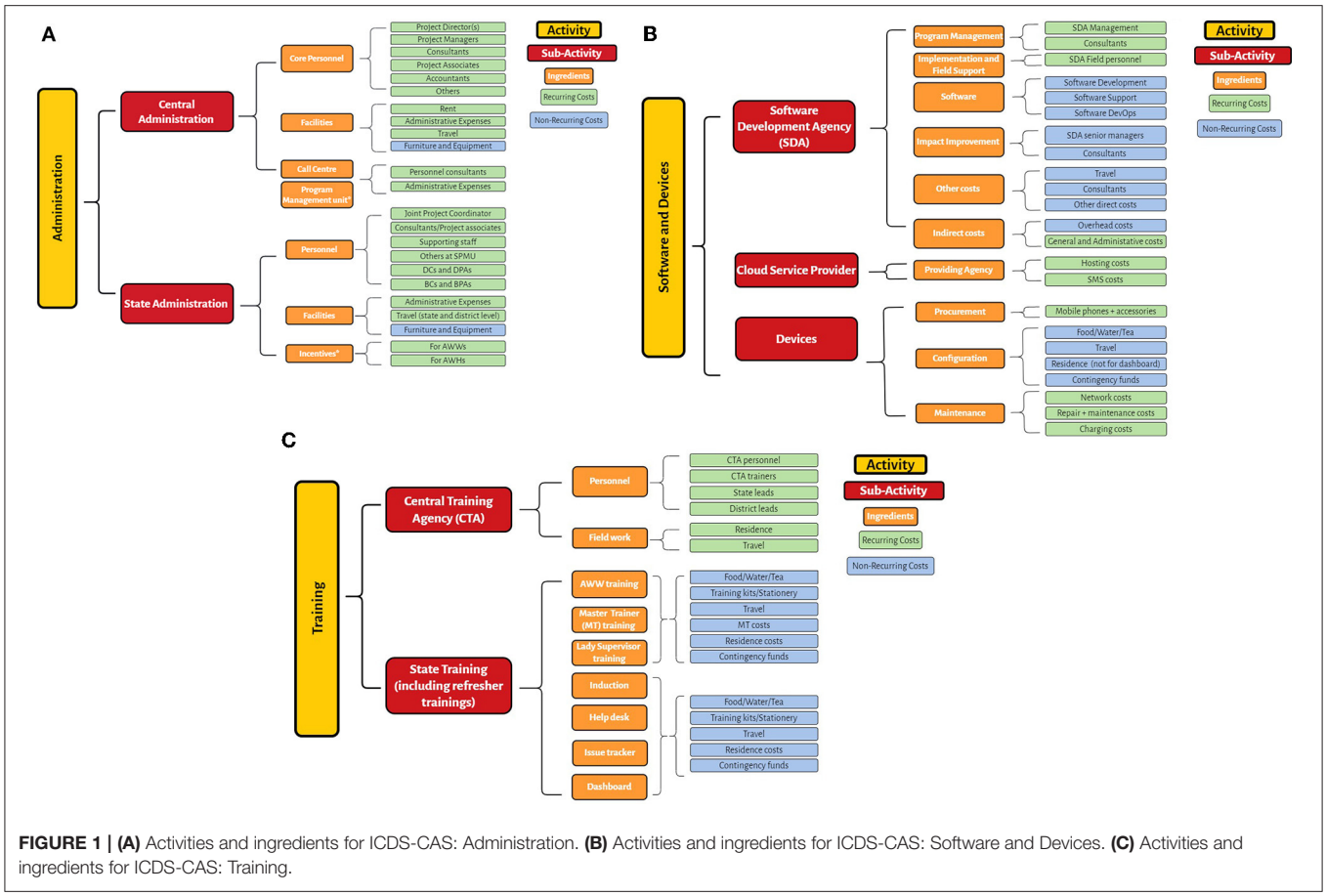

FIGURE 1 | (A) Activities and ingredients for ICDS-CAS: Administration. **(B)** Activities and ingredients for ICDS-CAS: Software and Devices. **(C)** Activities and ingredients for ICDS-CAS: Training.

At both the central and state level, project management units were set up to manage CAS, coordinating CAS implementation across states and districts, known as the Central Program Management Unit (CPMU) and the State Program Management Unit (SPMU). These include both non-recurring costs such as facility costs (furniture and equipment) and recurring costs such as personnel costs, expenses on electricity, stationery, etc. Examples of personnel included District Coordinators (DCs), District Project Assistants (DPAs), Block Coordinators (BCs), Block Project Assistants (BPAs)

2. Software and devices including costs for the software developer, Cloud Service Provider (CSP), and devices. Data collected through mHealth interventions requires huge cloud storage capacity. Simultaneously, device costs include not just the purchase of devices and accessories, but also costs to maintain and repair devices, and monthly usage fees.

   The software component includes all costs incurred on developing the CAS platform incurred primarily by the Software Development Agency (SDA). The ingredients for the software developer include program management, software development, data analytics, impact assessment and improvement, field support, and travel.

3. Training costs include costs for the Training Agency (TA), and related training costs. The two main parts to training costs are designing and implementing the training, and providing the resources (location, food, etc.) for the same.

Each of the major components (administrative costs, software and device costs, and training costs in the case of ICDS-CAS) have several ingredients which need to be budgeted for. Moreover, programs must be augmented with continuous training, supervision and the provision of equipment as well as planning costs over time (26). An example of the cost profile for ICDS-CAS is given in the format below (**Table 1**).

Lesson 2: The Major Limitation of ABC-I Is Data Availability, but It Can Be Mitigated

There are many kinds of data gaps that may exist. First, certain costs may be unavailable. With government programs, several costs might be sensitive, and access may be restricted. It is also possible that figures obtained may be estimates themselves. For instance, while applying the ABC-I method to cost for ICDS-CAS in India, detailed data on cloud storage costs, costs for maintaining the call center, and costs for the program management unit were not available and had to be inputted based on limited information. For pilot programs, it is also hard to predict how large or small certain costs would be if the program scaled up. The lack of cost data has been a challenge while evaluating other mHealth interventions as well (27).

TABLE 1 | An example of assumptions while costing for ICDS-CAS.

Type	Assumption and method
Personnel time costs	Costs for setting up and managing the CPMU are taken from guidelines issued on 26.02.18. Since these costs are for the scheme as a whole and not just for the specific mHealth intervention, we have apportioned 70% of the total CPMU costs to CAS in year 1, 50% in year 2, and 30% in year 3 and thereafter.
	Since states oversee implementation, we assumed that 90% of time of SPMU resources in year 1, 70% in year 2, and 50% in year 3 and thereafter (personnel and office costs).
Absence of Cloud Storage Provider Costs	We calculated average month wise per AWW costs and multiplied that by the number of AWWs in a state. This assumes that cloud storage provider costs scale linearly.
Software Developer	For calculating scale-up costs, centrally incurred costs of software are based on total grant given for software development. Further, additional administrative costs of the software developer were also included.
Life span related assumptions for Devices	We assumed a device has an average life of 3 years.

TABLE 2 | Ratio of Recurring and non-recurring costs across activities.

Activity	Ratio of recurring costs	Ratio of Non-recurring costs
Central Administration	86	14
State Administration	94	6
Administration	94	6
Software Developer	0	100
Cloud service provider	100	0
Devices	20	80
Software and Devices	25	75
Training Agency	0	100
State training	50	50
Training	45	55
Total	41	59

Second, estimating exact annual costs is difficult, given the dynamic evolution of programs. Several programs are rolled out in a phased manner, starting with a pilot. In the absence of information on how the program would evolve in the next, say 5–10 years, costing must be based on current guidelines. Therefore, changes in costing due to economies of scale, technological dividends, or a change in the implementation design if the scale-up is staggered are hard to account for.

Relatedly, as programs are scaled up, costs across geographical settings might not be available in disaggregated form. In a country like India, for instance, every state may eventually have a slightly different implementation model based on their current technological and administrative capacity. This would impact how the intervention is scaled and costed. Finally, assigning costs for personnel working across interventions and programs might be challenging in absence of a detailed time-use study, as mentioned before.

To mitigate some of these limitations, assumptions can play a critical role. These could be assuming proxy values for certain costs, assuming time spent by personnel on the program, more general things such as identifying different sources, and setting discount rates, inflation rates, conversion rates, etc. All these assumptions must be carefully listed out to enable replication and justified as well.

The sensitivity of each assumption should also be tested i.e., how much do costs change with changing assumptions. For instance, how much do total costs vary if we assume that certain personnel spend 50% of their time on the mHealth program instead vs. if this figure were 70%. These assumptions are useful in calculating the range of possible costs under different sets of assumptions and should be used as a guide to a more comprehensive planning and budgeting exercise. An example of some assumptions, used when calculating costs for ICDS-CAS are given below.

A related strategy is to leverage data collected by various studies and surveys which analyze different aspects of programming including time use of personnel. This data can be directly used while inputting unit costs, or indirectly in the form of using it in assumptions to proxy for certain costs.

Lesson 3: mHealth Technology Life Cycles Have Financial Implications

Overall costs of the program are the most important costs to highlight, as well as per FLW costs. Along with this, costs for each component should be noted as well. For example, for ICDS-CAS, 55% of total costs at scale would have been on buying devices. This is then followed by the cost of conducting state level training of AWWs and LSs, at 18%, and state administration at 17% of the total costs incurred.

Any cost description should differentiate between recurring fixed costs, variable costs, and onetime capital costs. As an example, within the AB-CC 'software and devices', cloud storage costs are all recurring costs, while all costs for the software developer are non-recurring.

Overall, for ICDS-CAS, in year 1, non-recurring costs account for 59% of total costs with the bulk being costs for devices (75% of recurring costs) and training (15% of recurring costs) (**Table 2**). Their proportions however decreased significantly in subsequent years. Instead, the proportion of recurring costs related to administrative costs and cloud storage increased. Accounting for these changes is useful to plan resources, particularly for the medium term.

At the same time, for financial sustainability of mHealth interventions, it is important to remember the life cycle of technology. The cyclical nature of fixed costs must therefore be accounted for over time. Over time, costs across programs can also be reduced by avoiding monolithic architecture and investing in interoperability (6).

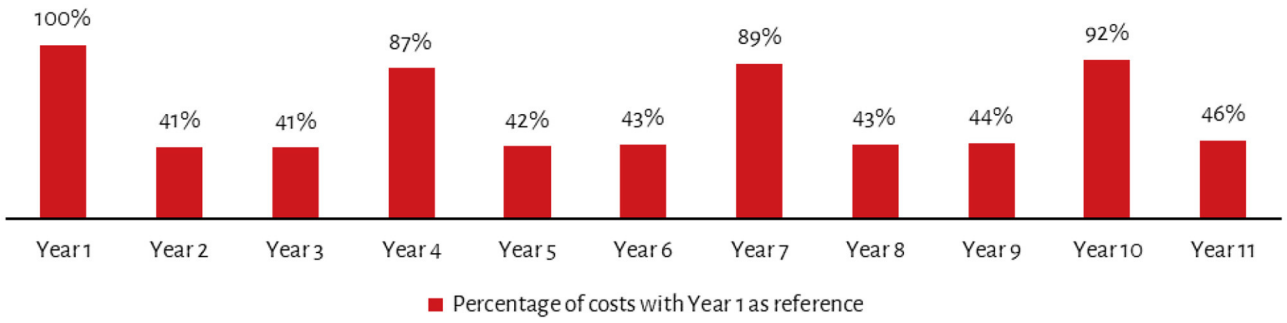

FIGURE 2 | Year-wise costs as a proportion of year 1 costs.

Certain non-recurring costs such as devices and other equipment may need to be replaced every 3–5 years. Extending this analysis over a 10-year period for ICDS-CAS and accounting for inflation and discount future spending in present time, shows a non-linear cost progression. Thus, while year 4, 7 and 10 sees significant spikes in costs due to replacement of devices and other equipment, for the remaining years costs are less than half the costs incurred in year 1 (**Figure 2**). Moreover, following year 1, costs would be highest in year 10 which in addition to replacement of devices, assumes replacement of other furniture and equipment. Similarly, since it is assumed that most training will be conducted in year 1, the training costs in subsequent years pertain only to refresher training and thus decrease from the second year.

Lesson 4: Determine Cost Locations and all Sources of Funding Including Non-government Sources

In the early stage of large mHealth interventions, sources of funding may include non-government ones including donor funding, implementing organizations responsible for training etc. It is thus useful to disaggregate costs based on the source of funding for each component. Paired with plans to spend funds over time, this also ensures that the funds are sourced appropriately, and advance planning can ensure the government has funds coming through for the program. Furthermore, it should attempt to quantify any in-kind contributions they may receive from other organizations, and identify cost-share opportunities (7).

Restrictions on the use of government money may impede implementation by impacting procurement, including the procurement of third-party software and hardware and ongoing maintenance and support from vendors with the necessary skill sets. Continued donor funding can be difficult to sustain but nevertheless provides added flexibility to be responsive to evolving needs on the ground (6).

For ICDS-CAS, costs such as central administration and cloud storage were fully funded by the Union government. For the others, costs were shared between the Union government and states in an 80:20 ratio for large states, 95:5 for hilly states, and 100:0 for UTs, as per scheme cost-sharing norms. In India, based on this fund sharing pattern, a majority (78%) of the total scaled up costs for ICDS-CAS in year 1 was to be funded by the Union government. State governments combined would have to fund 17% of the total costs. The remaining costs for training and software development were to be borne by non-government entities.

Lesson 5: Cost Estimates Are Subject to a Set of Assumptions, Which Allows for Scenario-Building

One of the major challenges of costing studies is the absence of disaggregated financial data (28). To address this challenge, a series of clear assumptions must be used and disclosed to ensure studies can be replicable. Another advantage of using different assumptions is that it allows for scenario building. For example, what would costs be if the program were scaled only to some regions and not the entire country; what would costs be if programmatic norms were different say, regarding training of FLWs; how would costs change with different unit costs; and how would costs vary with the addition of new components. These scenarios provide various paths that the program can take, and can help decision-makers make more informed choices. Some examples are given below, in the context of ICDS-CAS (**Table 3**).

In the absence of information on exact time spent by the CPMU and SPMU staff on ICDS-CAS specifically, assumptions had to be made regarding personnel time, as mentioned above. Administrative costs account for only 17% of total costs and thus changing the assumption did not significantly impact the overall costs.

On the other hand, software and device costs are driven primarily by device costs and the support required for configuration. The purchase price for devices can thus alter costs in a significant way. To the extent that the application doesn't change radically in the future, we can assume that device costs should not rise in the future. In fact, devices have been getting cheaper over time. However, if the application requires a better device for optimal performance, costs may rise. Therefore, total program costs are sensitive to the way the application will be structured in the future, and the way the application is used.

For training, costs vary substantially based on the amount of support to be provided by the TA, whether the training is to be

TABLE 3 | Cost variability as a proportion of expected costs due to changes in assumptions: an example.

	Minimum cost scenario	Expected/presented scenario	Maximum cost scenario
Central Administration			
Assumptions	30% personnel time spent on CAS; All equipment and furniture available; No project management unit (PMU)	70% personnel time spent on CAS; Equipment and furniture purchased as per national guidelines; No project management unit	100% personnel time spent on CAS; Equipment and furniture purchased as per national guidelines; PMU costing information as per key stakeholder(s)
Amount as a proportion of expected costs	42%	100%	761%
State Administration			
Assumptions	50% personnel time spent on CAS, Costs from the pilot state (MP); All equipment and furniture available; No incentives given	90% personnel time spent on CAS, Costs from the pilot state (MP); Equipment and furniture purchased as per MP norms; No incentives given	100% time spent on CAS, Costs as per national guidelines; All equipment and furniture available; Incentives given and all FLWs meet inclusion criteria
Amount as a proportion of expected costs	90%	100%	569%
Software and Devices			
Assumptions	Costs for devices, network, and configuration based actual expenditure in the pilot state (MP); No additional support by TA	Costs for devices, network, and configuration based actual expenditure in the pilot state (MP); No additional support by TA	Device and network costs as per national guidelines; Configuration costs as per actual expenditure in the pilot state (MP); Additional support costs as per TA; additional SDA costs incurred
Amount as a proportion of expected costs	100%	100%	194%
Training			
Assumptions	Initial training: based on norms in the pilot state and costs as per national guidelines; Refresher training: Norms and costs as per national guidelines, non-residential training; No additional TA support	Initial training: based on norms in the pilot state and costs as per national guidelines; Refresher training: based on norms in the pilot state and costs as per national guidelines, residential training for district and block officers; No additional TA support	Initial training: based on norms in the pilot state, residential training for FLWs; Refresher training: Norms and costs as per national guidelines, residential training for all; Continued TA support with 1 person per for 6 months
Amount as a proportion of expected costs	95%	100%	287%
Overall costs			
Total	97%	100%	265%

residential or not, and whether some groups require refresher training. For ICDS-CAS, the main assumption impacting training costs is whether training is residential or not.

CONCLUSION

Mhealth interventions for health and nutrition have been studied at length. There are three primary gaps which have been highlighted which are addressed with the methods and lessons described above. First, is the reporting on program sustainability, scale-up costs, and long-term effects of the intervention (29). Second, all the active ingredients of the intervention are reported in sufficient detail (30). Relatedly, these components should be reassessed before scaling, with an emphasis on effectively responding to government procurement and distribution challenges, which should be costed for. Third, sustainability strategies tend to focus on initial capital investment rather than ongoing recurring costs (31).

Adding to the literature, the study presents the method from the first attempt at costing a large-scale national mHealth intervention in India. In India's context, applicable to other developing countries as well, there are several crucial related lessons related to scaling up. The study highlights five key lessons while costing for mHealth programs. First, that there are many activities and ingredients that must be budgeted for and discussed while planning and implementing mHealth programs. Second, the ABC-I method described in this paper provides great clarity on costs, yet its major limitation is the availability of data. Given that ABC-I aims to be as comprehensive and disaggregated as possible, a large amount of data is required. The lack of data for activities and inputs must be mitigated with the careful use of assumptions. These assumptions should be clearly listed out, and their sensitivity should be tested as well, as an indication of robustness of the costing study. Third, mHealth technology life cycles have financial implications. This includes understanding the life cycle of the technology

used. For example, phones must be replaced every 2–3 years, which must be budgeted for. Fourth, in the early stages of a large mHealth intervention, sources of funding may include non-government sources. Embedding digital health solutions into health systems will require transitioning management and ownership to government partners who will have to bear the additional costs. Fifth, since costing estimates are subject to a set of assumptions, a disaggregation of costs allows for scenario-building, which is useful while planning ahead. Pilot costs are very different from costs at scale, and in fact, the component mix may be completely different, which should be kept in mind. As they say, you may pilot "apples" but have to scale "oranges" (31). At the same time, defining governance structures and roadmaps up front is helpful while scaling and taking decisions over future program pathways (31).

As mHealth programs expand globally, governments and policymakers require a lot of information not just on their effectiveness, but on financial implications as well. For full-scale sustainability, financing for all aspects of digital health solutions needs to be integrated into routine health budgets and the budgeting processes. Gathering and estimating program costs is essential for LMICs, given that resources are typically scarce and there are several competing priorities. Project teams should also keep in mind that drafting a budget should not be a one-off event. Budgets should be revisited regularly since funding, assumptions and activities can all change. Regular reviews will assist project teams to plan appropriately for increasing their scale and managing resources efficiently (7). This entails not just costing and budgeting for the long term. Given that building consensus around the roles of national and state governments, implementing and technical partners and donors has been a challenge, it entails sustaining relationships that navigate the corridors of power between different stakeholders across governments and funding agencies (6, 31).

Exercises such as the costing method described above can be used by policymakers to plan and budget for new programs, tailor existing programs as they develop, and to determine the cost-effectiveness of any program. For India specifically, the government of India has replaced ICDS-CAS with a new mHealth intervention known as *Poshan* Tracker, and similar interventions are being launched globally. With that in mind, we hope that this analysis can help assess the resources necessary to undertake or sustain similar interventions including in low-resource settings.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

AUTHOR CONTRIBUTIONS

AK and RS conceptualized the paper outline. RS conducted the literature review with inputs from AK. RS collected and analyzed the data, while AK reviewed the data analysis. RS wrote the first draft of the manuscript and AK reviewed it and provided feedback, suggestions, and comments. AK also edited significant sections of the manuscript. Both authors contributed to manuscript revision, read, and approved the submitted version.

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CASE REPORT
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Challenges and Enablers for Smartphone Use by Persons With Vision Loss During the COVID-19 Pandemic: A Report of Two Case Studies

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Purpose: Studies have reported that knowledge and skills to operate smartphones among people with profound visual loss are limited especially in low- to middle-income countries as many important functions of smartphones are unknown to them. This report presents smartphone use, its challenges, and enablers in two persons with profound visual impairment while executing their daily routine and instrumental living activities amidst the COVID-19 pandemic.

Case selection and interview: During the lockdown period, we provided tele (vision) rehabilitation service. From the list of the callers, we purposely selected two callers with significant visual impairment, one woman and one man, to allow us to gather rich information related to smartphone use, enablers, and challenges faced during the usage. A semistructured interview was done to obtain insights into the information. The selection criteria were (1) continuous smartphone use independently for more than 5 years; (2) graduation-level education or higher; and (3) no additional disabilities.

Discussion: We found substantial use of smartphones in executing their daily and instrumental daily living activities by these two participants. The extent of the use of mainstream apps for various tasks was almost equivalent to what we observed among sighted persons. The most important enabling factors were the presence of a screen reader "TalkBack" on Android phones and data connection of the mobile, followed by the ability to assess multiple languages using the text-to-speech feature. A supportive environment from peers or family members is important for the beginner. Poor battery backup, frequent unwanted ads or pop-ups while using the phone, not readable contents with a screen reader, e.g., CAPTCHA, and slow or unresponsiveness of the screen reader were frequent challenges faced by them. Both cases reported that around 80% of daily solutions were helped by using a smartphone.

Conclusions: The current advances in accessible technology of smartphones enable an individual with profound visual loss to use them almost equivalently as a sighted person. To reduce the gap in digital inclusion, people with visual impairment should be encouraged to use the smartphone for their daily solutions with attention to proper training.

Keywords: visual impairment, assistive technology, smartphone use, accessible apps, challenges, enablers

INTRODUCTION

Smartphones are not only increasingly ubiquitous in low- to middle-income countries (LMICs) but also have become one of the essential commodities in life for everyone. Earlier, users with visual impairment face substantial challenges in terms of accessing and inclusion in the smartphone environment despite a widespread prevalence of touch screen technology. With the progress in screen readers software technology with audio or tactile feedback, users with visual impairment do not need sighted assistance to be used independently. Today, mobile technologies have grown exponentially over the past few years, including built-in accessible features and third-party accessible applications for people who are visually impaired (1). Such a recent advance in smartphone technology provides a new opportunity to bring various solutions in performing everyday activities for persons with visual disabilities. Evidence shows that the use of smartphones enhances the quality of life of people with visual impairment by improving their autonomy and safety, and encouraging them to interact with the community and society (2, 3). Various studies have reported the use of smartphones among blind users for social media engagement, performing instrumental daily living activities such as shopping, finance management, navigation, educational purposes, and employment (4–6).

As of today, the majority of the evidence on smartphone use among people with visual impairment IS documented primarily from high-income nations as compared to LMICs though few studies reported smartphones use particularly in students with visual impairment (4, 7, 8). Nearly a decade ago, smartphones were associated with a high cost and were considered to be an electronic product for people living in high-income countries. However, the cost of smartphones has decreased over the past few years, the availability of smartphones across LMICs is also growing (9). Access to smartphones, therefore, is not a major issue in these countries. Although smartphone use is documented among people with visual impairment for their daily solutions in LMICs, there is a lack of evidence about how much a smartphone is helpful in terms of executing tasks for independent daily and instrumental daily living activities of a person with profound visual impairment or total blindness. A study in Nepal reported a lack of knowledge and skills to operate the accessible features and apps of smartphones among blind students despite the participants being aware of smartphones and their accessibility features (10). Several studies also reported the inability to fully use the accessible features, and many vital functions of smartphones were undiscovered among blind users (10, 11). Therefore, there is a need for documentation for rich information on comprehensive usage of the smartphone along with various challenges, particularly by people with profound vision impairment or total blindness who have an adequate user experience.

Given the current advance in digital technology, there may be a potential risk that persons with visual disabilities might be left behind without availing of the full use of such accessible technology, especially in LMICs. The inclusion of people with visual disabilities in the digital world is essential for their overall development and quality of life. A smartphone is one of the digital technologies that can support social inclusion, connectedness, and participation in civic life (12, 13). In addition, the smartphone is one of the known assistive technologies (ATs) under the World Health Organization (WHO) Global Cooperation on Assistive Technology that helps to reduce functional difficulties (14). The GATE aims to improve access to AT and its related services as a part of the Universal Health Coverage. Besides, the Sustainable Development Goals focus on the need for social inclusion and participation and pledged that no one should be left behind in all dimensions of life based on disabilities or any other personnel disadvantages or characteristics (15). Therefore, generating evidence on the smartphone's usability among blind users is critically important which will further help not only digital inclusion but also social inclusion and participation in the current digital world. Indeed, studies reported smartphone use for social media engagement actively among blind users which is directly linked to an increase in social inclusion and participation (11, 12, 16).

In addition, to our knowledge, the majority of individuals with visual disabilities in LMICs still depend on a simple basic or feature phone which has limited functionality compared to the current smartphones. Moreover, mobile technology is pragmatic, cost-effective, and universally designed assistive devices, so it is less likely to be a social stigma and make public attention among blind users. Therefore, there is a need to promote the use of smartphones across the population with visual disabilities, especially in LMICs.

The purpose of this case report was to understand the extent of smartphone usage by persons with profound visual impairment to the maximum. It also presents the challenges and enablers of smartphone use by them during the COVID-19 pandemic in Delhi, India. Such a case study will provide a positive impression that will motivate smartphone use among the visually impaired, thereby helping to address the digital inclusion gap of persons with visual disabilities. At the same time, it will also help to assess

whether the visually disabled are one of the potential clients of the current smartphone world.

CASE SELECTION

We run a vision rehabilitation (VR) clinic where patients with low vision and blindness are referred from various ocular subspecialties of the out-patient department of our eye center and from other facilities or organizations. To maintain the continuum of services, we also liaised with many civil or community-based organizations, including schools for the blind in Delhi and National Capital Region. During the COVID-19 emergency period in 2021, we circulated a few telephone hotline numbers to the representatives of these organizations for support of healthcare and rehabilitation services.

The cases were selected purposely from the list of callers who have availed of VR services to date. Graduate-level and above in education, profound visual loss, active users of smartphones for more than 5 years independently, and no other co-disabilities were selection criteria for the cases. The VR staff contacted the participants by telephone and scheduled them for an in-person meeting at the clinic. We aimed to collect rich information on the use of smartphones by persons with total or profound visual loss or not relying on vision functions for smartphone use.

CASE DESCRIPTION

Case 1

The patient, named UK, was a man aged 29 years with total blindness (no light perception in both eyes), diagnosed with phthisis bulbi with glaucoma and has been using a smartphone independently for the last 10 years. He has no other co-disabilities. He completed his post-graduation 2 years ago and currently looking for a suitable job. He understands the English language but cannot speak it fluently. His degree of disability as shown on his certificate was 100%.

Case 2

The patient, named JS, was a woman aged 27 years with profound vision loss with her left eye vision no light perception and finger counting close to the face in the right eye. She was an employee in a private bank. She has been using smartphones independently for more than seven years. She was a case of Stevens–Johnson Syndrome with corneal opacity. She has no other disabilities. She understands the English language but cannot speak fluently. Her degree of disability as shown on her certificate was 90%.

QUESTIONNAIRE AND INTERVIEW

A face-to-face, in-depth interview with the cases was conducted using a semistructured questionnaire to obtain insight into the spectrum of the use of smartphones, enabling factors, and various challenges encountered by the users. The purpose of using the personal interview was to gain significant information of insights and to improve data accuracy.

Section A of the questionnaire consisted of two parts, namely, the domains of smartphone use and the enabling factors for each domain of the usage. Section B consists of additional factors that help to use smartphones consistently. The last Section C part includes challenges faced by cases while using the smartphone. The responses to the last two sections of the questionnaire were ordinal. The questionnaire was developed in consultation with the trainers who provide training, primarily on the use of digital assistive devices for visual impairment. Furthermore, pretesting was done among non-study individuals with similar characteristics. The reason for conducting several pretests was we expected that respondents will have different levels of information and experiences in using a smartphone, whereby, the question developed could capture adequate information on the use of smartphones at the maximum level. One open-ended question was included "How much does your smartphone help in doing daily living activities without support from sighted persons? Rate it in percentages from 0 to 100."

We used the English language for the tool since the interviewer was well-versed in English. The day of the interview was fixed according to the convenience of the cases. The cases were explained about the purpose and the content of the questionnaires before we obtained informed written consent. The response to the entire questionnaire took ∼60 min of participants' time.

The rehabilitation team helped both cases in terms of the issuance of a visual disability certificate from the institute. Case number one was informed about various relevant schemes for his benefits, including job reservation under the Government of India. He was educated about available vocational training facilities in Delhi and National Capital Region that we liaised with our VR clinic and was advised to contact them in the future if he is willing to undergo any vocational training in our networking centers. Besides these, they were provided the orientation and mobility training as per standard guidelines and standard dining techniques and explained the need for the creation of a safe environment, particularly at home and the workplace. They were educated about COVID-19 preventive steps and informed to contact for any medical conditions, including COVID-19-related issues.

DISCUSSION

The present case study aimed to explore comprehensively the use of the smartphone, including challenges, while executing daily and instrumental daily living activities by visually disabled persons who do not rely on vision for use. We believe that the diagnosis of blinding eyes will not impact the study findings. However, we recorded the diagnosis and percentages of visual disability written on the certificate which is issued based on the guidelines given by the Ministry of Social Justice Empowerment, Government of India.

This report shows that not only does the current smartphone technology provide an invaluable asset to everyone but the recent advancement in touchscreen and accessible features and apps means the content has become more accessible to people with visual disabilities. In this case report, we presented two cases with profound visual impairment who have been using smartphones

TABLE 1 | Domains of smartphone use by person with profound visual impairment.

Domains of smartphone use	Available means to use the domain	Case 1	Case 2
Communication	SMS, Voice call, Audio-visual call, email, any other	SMS, Voice calls, Audio-visual, email	SMS, Voice calls, Audio-visual
Health consultation	SMS, Voice call, Audio-visual call, any other	Voice calls	Voice calls
Information on COVID-19	Newspaper, YouTube, News channel, any other	YouTube, News Channel	YouTube, Twitter
Online banking	Mainstream system, special apps	Not used	Not used
Online payment	Mainstream apps, special apps	Google Pay, Phone Pay, Paytm,	Google Pay, Paytm,
Online shopping/Tele shopping	Mainstream apps, special apps	Flip Kart, Amazon prime, Zomato	Flip Kart, Amazon prime, Swiggy, Meesho
Reading print materials	Special apps	Insta reader	Envision AI app
Entertainment	DISH satellite TV, YouTube, Netflix, Amazon prime,	YouTube, Tiktok, Wynk, Hotstar	YouTube, Jio TV
Color identification	Special accessible apps	Eye D pro	Not used
Money identification	Special accessible apps	Mani App, Mani reader	Mani App, KITNA App
Object identification	Special accessible apps	Not used	Not used
Online booking for local travel	Mainstream apps, special apps	OLA, UBER app	OLA, UBER app
Indoor navigation	Special apps	Not used	Not used
Identifying medicine	Special app	Not used	Envision AI
Alarm/reminder	Mainstream system, special apps	Mobile alarm	Mobile alarm
Audio-video conferencing platform	Mainstream system, special apps	Google meet, Zoom	Google meet, Zoom, CISCO
Calculator	Mobile calculator, special apps	Mobile calculator	Mobile calculator
Face recognition	Special apps	Not used	Not used
Social media	Mainstream system, special apps	Facebook, WhatsApp, Instagram, telegram	Facebook, WhatsApp
Photography	Mainstream camera, Special apps	Documents only	Mobile camera,
Data storage and recording	Mainstream system, special apps	Mainstream system	Mainstream system
Taking notes or writing	Mainstream system, special apps	Mainstream system	Mainstream system

for more than 5 years in executing and bringing solutions for their daily activities. This report will provide rich information regarding the extent of smartphone use by persons with severe or total blindness. Besides this, the report may motivate other people with similar visual problems, particularly from LMICs, to adopt smartphones in their daily living lives.

USAGE OF SMARTPHONES

The domain of smartphone usage by two of them is as comprehensive as smartphone use by a sighted person. The extent of smartphone use is quite substantial in bringing solutions and improving other daily living activities. **Table 1** shows the spectrum of smartphone use and means for each usage by the cases. The majority of routine tasks were executed with the help of available mainstream support systems or means, for example, they used SMS (short message services), voice calls, audio-visual calls, and emails for communication with friends and family members. Likewise, YouTube, Hot star, Google Pay, Paytm, Amazon prime, Flip Kart, and Zomato apps were being used for various daily solutions. Furthermore, Facebook, WhatsApp, Instagram, and even Twitter were also used for social media engagement. In addition, participants also used special accessible apps for their daily tasks: Insta Reader, Envision AI accessible app were used for reading print materials, Mani App for currency identification, and Eye D pro for color identification. Furthermore, OLA (Operational Level Agreement) and UBER (Uncorrected Bit Error Rate) apps were mainstream apps that were used for online booking of local travel.

Given smartphone usage, both cases have reported that around 75–80% of their daily living solutions can be executed using their smartphone. Furthermore, both considered smartphones to be an essential asset in their lives.

TABLE 2 | Enabling factors for smartphone use among people with profound visual impairment.

Factors which help smartphone use	Case 1	Case 2
Familiarity of smartphones	Very important (Samsung)	Moderately important (Xiaomi)
Presence of screen reader	Very important (Talkback)	Very important (Talkback)
Availability of third accessible party apps	Very important	Very important
Available Wi-Fi/Data internet at home	Very important	Very important
Power source, including power bank	Less Important	Important
Apps that can read bilingual or multiple languages	Very Important	Important
Basic understanding in English	Important	Moderately Important
Getting help or training on the use of smartphone from others	Important	Very Important
Using headphone	Very Important	Very Important

The responses were recorded in an ordinal scale: 1: very important, 2: moderately important, 3: important, and 4: less important.

TABLE 3 | Challenges faced during the smartphone use.

Challenges	Case 1	Case 2
Unlocking the smartphones	Never	Never
Slow screen reader	Sometimes	Sometimes
Screen reader unresponsiveness	Sometimes	Rarely
Third-party accessible app unresponsive	Rarely	Rarely
Not understanding the voice output or sound	Sometimes	Never
Facing problem with the speaker or loudspeaker	Very often	Never
Unintentional selection of icons	Never	Rarely
Getting lost when using a browser	Very often	Rarely
Unable to locate a specific website for a purpose	Rarely	Sometimes
Facing problems for safe keeping	Never	Sometimes
Feeling difficulty in carrying smartphone	Never	Never
Financial constrained to repair maintained phone	Sometimes	Never
Facing issues for poor battery backup	Sometimes	Sometimes
Not a user friendly	Rarely	Never
Difficult to text entry with aloud voice	Very often	Rarely
Confusion due to verbose from smartphone	Sometimes	Sometimes
Disturbance unwanted add or advertisement when using smartphone	Very often	Very often
Smartphone content not readable with screen reader, e.g., CAPCHA	Very often	Very often

The responses were recorded in an ordinal scale: 1: never, 2: rarely, 3: sometimes, 4: very often, and 5: always.

ENABLERS OF SMARTPHONES USE

The participants reported the most essential enabling factors were the presence of screen reader technology, namely, "TalkBack" of Android phones, and the availability of internet data connection of the mobile (**Table 2**). The participant "UK" quoted that:

"Without the screen reader and internet accessibility, our smartphone is like a log lying in a corner of a house."

Another very important feature is the ability to read multiple languages using the text-to-speech setting of the TalkBack menu. The participant can select a native language, e.g., Hindi, for audio output. This feature is very important because they said many documents, including Hindi, are required to be read in their daily lives. Furthermore, both the cases stated that headphones were one of the very important accessories that help in maintaining their privacy and make less disturbance to a person sitting next to them during travel.

Familiarity with a smartphone is not so important because they said that even if a new one was acquired within 1 or 2 days, they can operate the smartphone comfortably. Finally, both cases underpinned that a supportive environment from peers or family members is important for the initial learning and training of an individual with vision loss.

CHALLENGES WHILE USING SMARTPHONES

In this report, both cases reported a few most frequent challenges faced by two of them while using smartphones (**Table 3**). First, poor battery backup of their smartphone, especially during long-hour travel was difficult. Case 1 (UK) stated since they used many accessible apps with voice output, the battery drained out quickly though it was fully charged. Therefore, both cases reported that they always carry power backup devices, such as Power Bank, during the long-hours travel.

Second, typically the loudspeaker is located at the bottom of the smartphone though a smaller speaker is present at the top of the phone that is used for conversations. Such a location of the loudspeaker causes inconvenience to listen to voice output as shared by case 1. Third, the frequent unwanted ads or pop-ups advertisement while using one app also caused a problem in case 2, but not in case 1 since he said that he used an add guard that prevented unwanted ads while using apps. Fourth, few content or labels in the smartphone are not readable with a screen reader. This causes a great challenge to use certain web pages. For example, both cases said that the CAPTCHA and any image files on the page cannot be read by their screen reader. Furthermore, both reported that certain contents were required to be opened

by using a mouse or touch screen. This creates a lot of challenges when using smartphones for a certain purpose as shared by cases.

Furthermore, both cases shared that the less frequent issues encountered were slow or unresponsiveness of the screen readers, unable to locate a specific webpage, unable to trace or lose a web page in the middle of browsing, and not accepting voice entry using, such as Google assistant.

There is a paucity of studies available on the technological challenges either hardware or software faced by individuals with visual impairment on smartphone use. However, studies from India reported the most common problem encountered by novice users is language comprehension, including pronunciations and occasional shortcomings in the local language support, challenges in setting up and activation for accessibility features, maintaining the accessibility functionality after reboots, and unable to control the speaking speed while working with text-to-speech (17, 18). Several problems such as operating and using basic accessibility features while interacting touchscreen are also reported in a study conducted in a high-income country (19).

Therefore, the current advanced smartphones still have room for improvement in terms of simplifying the activation process, standardization of the operating procedure for a screen reader, and configuring accessibility features rather than having multiple steps to activate it. For example, several participants of a study conducted in Nepal wanted to have a simple shortcut button for the activation of both built-in and accessible features (10). The same study also concluded that people with visual impairment prefer a fixed region instead of browsing the mobile menu system. Finally, a universal and easy solution to operating for all accessible features could potentially be helpful, particularly to individuals with profound visual impairment.

CONCLUSIONS

The present case report provides valuable insights on how much smartphones enable help in executing daily living solutions in persons with a profound visual impairment. This study gives evidence that without relying on a good visual function, smartphones can help in bringing a wide range of everyday solutions to the visually impaired, and can be concluded that such individuals are one of the potential clients of the current smartphone environment. Furthermore, the smartphone is a universally accepted design without having any stigma on the user. It is, therefore, overarching that such assistive devices should be encouraged to be used so that individuals with vision loss can integrate into society and participate at their best level thereby helping in contributing to their potential.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by All India Institute of Medical Sciences, New Delhi. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

SS conceived the need for documentation about smartphone use comprehensively among people with severe visual impairment or total blindness, particularly from low- to middle-income countries, further designed the work overall, and wrote the manuscript. SP commented on the draft and edited it. Both authors approved the draft.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.912460/full#supplementary-material

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Remote Monitoring and Holistic Care of Home-Isolated COVID-19 Positive Healthcare Workers Through Digital Technology During the Omicron (B1.1.529) Wave: A Prospective Cohort Study From India

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Background: Remote monitoring through digital technology offers a promising solution for the diverse medical, psychological and social issues that plague patients with COVID-19 under home-isolation, but remain neglected due to a lack of streamlined medical services for these patients.

Methods: This prospective cohort study determined the feasibility of remote telemonitoring of healthcare workers with mild COVID-19 under home isolation during the Omicron (B1.1.529) wave and characterized their clinico-demographic profile. A holistic monitoring model comprising of mandatory phone calls at the beginning and end of isolation, assisted by home oximetry, predesigned google forms, and opt-in software-based (eSanjeevani OPD) teleconsultation was employed. Factors associated with development of symptomatic disease were also determined.

Results: Out of 100 COVID-19 positive healthcare workers under home-isolation, data for 94 participants was available [median age 27(20–52) years, 56(60%) females]. 93(99%) patients were previously vaccinated for COVID-19 (median time from last dose = 248 days); 34(36%) had a past history of COVID-19. Fever (67%), myalgia (69%), sore throat/dry cough (70%), and running nose (45%) were the most common symptoms. No patient progressed to moderate-severe disease or required care escalation during the remote monitoring period. Most participants reported several additional psychosocial concerns which were adequately addressed. Symptomatic patients had higher BMI (24.1 vs. 21.8kg/m^2, $p = 0.01$) compared to asymptomatic patients. Age, past infection with COVID-19, and time since last vaccine dose were not different between symptomatic and asymptomatic patients.

Conclusion: COVID-19 patients under home isolation have multi-faceted medical and psychosocial issues which can be holistically managed remotely through digital technology.

Keywords: COVID-19, healthcare worker (HCW), digital technology, remote monitoring, cohort

INTRODUCTION

With repeated waves due to newly emerging variants of the novel Severe Acute Respiratory Syndrome-Corona Virus-2 (SARS-CoV-2), the scourge of coronavirus disease 2019 (COVID-19) continues unabated. Two years after being declared a pandemic by the World Health Organization, about 405 million confirmed COVID-19 cases, including ∼6 million deaths have been reported as of 11 February 2022 (1). The vast majority (80-90%) of affected patients have asymptomatic or mild disease and can safely be managed under home-isolation without the need for hospital admission. However, despite a "clinically mild" disease, the physical symptoms may sometimes be very disabling and often remain inadequately addressed due to a lack of streamlined medical services for these patients living under a strict home-isolation. A few of these patients have the potential to progress to moderate-or-severe disease, and this transition needs to be picked up early in order to improve patient outcomes. Additionally, the disease or diagnosis itself is associated with a significant stress, phobia, depression and anxiety which continue to persist as neglected issues (2, 3). Concerns about fitness to re-join work or duty, ending of isolation, requirement (if any) of repeat testing prior to it, effect of the infection on vaccine schedules, and management of household contacts can be a cause of significant botheration to these patients. Thus, dedicated mechanisms need to be put in place for a holistic management of these patients' medical, psychological and social issues. Implementation of home monitoring programs or "virtual hospitals", where patients under home isolation are monitored remotely, offer a promising solution, although the available data are limited and focussed mainly on medical issues and "admission avoidance" (4–12). The mental and psychosocial issues remain largely unaddressed. There is no data on remote monitoring for COVID-19 patients under home-isolation from the Indian subcontinent.

Direct-to-consumer telemedicine also helps to avoid the risk of transmission of COVID-19 to frontline healthcare workers, who are already over-worked and under-staffed due to the infrastructural crises imposed by COVID-19 (7). Healthcare workers affected with COVID-19 face additional challenges when compared to the general population—besides a greater risk of becoming infected, harboring a higher virological burden, and a potentially more serious illness (due to continual exposure), they are prone to have additional work-related and psychosocial stressors (2). Since they form the backbone of healthcare systems which are already working at strained capacities during the COVID-19 pandemic, focussing on their medical and psychosocial needs is of paramount importance.

Finally, although the third wave of the pandemic [epidemiologically linked to the Omicron (B.1.1.529) variant] was deemed to be milder compared to the previous waves (13), the clinico-demographic profile of Indian patients affected during this wave, and the factors associated with development of symptomatic disease remain to be characterized in detail (14).

In an attempt to address these knowledge lacunae, we sought to determine the feasibility of remote telemonitoring and holistic telecare of healthcare workers affected with mild COVID-19 and home-isolated during the third wave of the COVID-19 pandemic, and characterized the clinico-demographic profile of these patients.

METHODS

Study Design, Setting and Participants

This single-center, prospective cohort study was done at the Postgraduate Institute of Medical Education and Research, a tertiary care center in North India. Consecutive healthcare workers who tested positive for COVID-19 [microbiologically confirmed by SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) positivity] between 31 December, 2021 and 28 January, 2022 and were advised home isolation were included after a verbal, informed consent. Those requiring hospital admission for supplemental oxygen or any other reason, those unwilling to give consent to participate in the study, or those whose provided contact details were incorrect, were excluded. A sample size of convenience, with consecutive sampling, was chosen. The study was approved by the Institutional Ethics Committee (INT/IEC/2022/SPL-281) and the principles of the 1964 Helsinki declaration were adhered to.

Study Procedures

Remote monitoring of COVID-19 positive healthcare workers isolating at home was done under the Department of Telemedicine. Affected healthcare workers were assessed telephonically through fixed-line telephones at baseline (date of positivity) and at day 7 [end of isolation period as per the revised National guidelines (15)] regarding clinical symptoms and oximetry readings. Red flag features (if any) were identified, and concerns related to symptoms, treatment, duration of isolation, repeat testing, testing of household contacts, and re-joining of duty were addressed in consultation with the specialist physician (psychosocial concerns were self-reported by the patient). For all included subjects, baseline demographic data including age, gender, body mass index (BMI), cadre (resident, faculty, nursing staff, student, clerical staff, or research staff), comorbidities, and clinical data relevant to COVID-19 [past COVID-19 infection, number of vaccine doses, type of vaccine received (BBV152/Covaxin or AZD1222/ChAdOx1 nCoV-19/Covishield), and time since the last vaccine dose] were recorded through a google form which was circulated through email or WhatsApp (self-administered), or administered telephonically by the research assistant or telemedicine operator. In addition, telephonic helplines and audio-video teleconsultation services through eSanjeevani OPD (a doctor-to-patient telemedicine system deployed nationally by the Ministry of Health and Family Welfare, Government of India for providing teleconsultations under the Ayushman Bharat Digital Mission) were also put in place for use by the affected patients anytime during their period of isolation. The former were direct access, while the latter required access through one-time password protected sign in on the website or smart phone application. Information about these facilities was notified on the institute website, notice boards and individually to affected patients. Symptomatic treatment was advised to all patients; no

antiviral or immunomodulatory therapy was suggested as per the national guidelines, since all patients under home isolation had mild disease (15).

The human resource required for implementation of this model included a team of two medical consultants, a research assistant, a telemedicine operator, and a data entry operator. Phone calls through fixed-line telephones at baseline and day 7 were made by the research assistant and the telemedicine operator, and patients' medical and psychosocial concerns were addressed in consultation with the specialist physician(s). In addition, the medical consultants also went through the completed google forms circulated to the patient for identifying any red flag feature not self-reported by the patient. A psychiatrist was available on-call basis, in case specialist help was required. All staff were already employed and working in the Department of Telemedicine, making the model cost-effective and sustainable. The time taken per consult varied from 5–15 min, depending on the participant's concerns.

Outcomes

The feasibility of remote monitoring and holistic telecare of home-isolated COVID-19 positive healthcare workers through telemedicine was assessed. In addition, the clinico-demographic profile of the affected healthcare workers was characterized, and the factors associated with the development of symptomatic (vs. asymptomatic) COVID-19 were explored.

Virological Testing

Nasopharyngeal and throat swabs were collected in viral transport media, transported in cold chain to designated laboratories in the Department of Virology, and used for viral RNA extraction (QiaAmp Viral RNA isolation kit, Hilden, Germany). The extracted RNA was subjected to real time RT-PCR. Variant analysis was not done. Repeat virological testing to document cure, or mark the end of isolation was not done as per the national guidelines (15).

Statistical Analysis

Data were entered in an excel spreadsheet and analyzed using the Statistical Package for Social Sciences version 26 [SPSS Inc., Chicago, IL]. Normality was tested using the Kolmogorov-Smirnov test. Continuous variables were summarized as mean and standard deviation (normally distributed), or median (range) (non-normal). Categorical variables were assessed as frequencies and proportions. Student's *T*-test or Mann-Whitney U test were used for comparison of means, while proportions were compared using the Chi-square or Fisher's Exact test. All statistical tests were two-sided and a *p*-value cut-off of $\leq$0.05 was used for defining statistical significance.

RESULTS

Out of a total of 100 healthcare workers who were identified to be COVID positive and telephonically contacted, three did not respond, one did not give consent, and the provided contact number was incorrect for two patients. Thus, the data of total 94 participants were included in the final analysis. Apart from the mandatory telephonic contact at baseline and day 7, 32 additional contacts (30 through telephonic helplines and two *via* eSanjeevani OPD) were initiated by the study patients with the remote monitoring team.

TABLE 1 | Baseline demographic and clinical parameters of the included patients.

Parameter	Value (n = 94)
Age, years	27 (20-52)
Female gender	56 (60%)
Body mass index, kg/m^2	23.8 (3.2)
Cadre	
• Faculty	7(7.4%)
• Resident	53(56.4%)
• Nursing staff	14(14.9%)
• Student	9(9.6%)
• Clerical staff	5(5.3%)
• Research staff	6(6.4%)
Comorbidities	
• Diabetes	1(1.1%)
• Hypertension	4(4.3%)
• Kidney disease	1(1.1%)
• Lung disease including bronchial asthma	4(4.2%)
• Thyroid disease	2(2.1%)
Vaccine received	
• BBV152/Covaxin	6(6.4%)
• AZD1222/ChAdOx1 nCoV-19/Covishield	87(92.6%)
• None	1 (1.1%)
Number of vaccine doses received	
• None	1(1.1%)
• One	2(2.1%)
• Two	89(94.7%)
• Three (including booster)	2(2.1%)
Time since last vaccine dose (days)	248 (9-357)
Past history of COVID-19 infection	
• Once	32(34%)
• Twice	2(2.1%)

Demographic Data

The median age of the included participants was 27 (20–52) years. Fifty six (60%) were females. Mean BMI was 23.8 (3.2) kg/m^2. Twelve (13%) patients reported having one or more comorbidities, most commonly hypertension or lung disease (including bronchial asthma). 53 (56%) of the study participants were medical residents at various stages of their residency, 14 (15%) were nursing staff, 9 (10%) were students, while the remaining were faculty, research, or clerical staff (**Table 1**).

Clinical Presentation

Eighty one (86%) participants suffered from mild COVID-19, remaining 13 (14%) were asymptomatic. Fever (67%), myalgia or body aches (69%), sore throat or dry cough (70%), and running nose (45%) were the most common symptoms reported. Gastrointestinal symptoms, anosmia, and retro-orbital pain were

TABLE 2 | Clinical details of the current COVID-19 infection in the included patients.

Parameter	Value ($n = 94$)
Disease severity	
Asymptomatic	13 (14%)
Mild	81 (86%)
Moderate	0
Severe	0
Clinical presentation	
Fever	63 (67%)
Sore throat or cough	66 (70%)
Running nose	42(45%)
Myalgia or bodyaches	65(69%)
Headache	4(4.3%)
Subjective breathing difficulty	4(4.3%)
Diarrhea	1(1.1%)
Nausea or vomiting	1(1.1%)
Loss of appetite	1(1.1%)
Anosmia	1(1.1%)
Retro-orbital pain	1(1.1%)
Oximetric readings	
Pulse rate (per minute)	89 (16)
Oxygen saturation on room air (%)	98 (1)

TABLE 3 | Risk factors for symptomatic COVID-19 in the third wave among healthcare workers.

Parameter	Symptomatic ($n = 81$)	Asymptomatic ($n = 13$)	*p*-value
Age, years	27 (20-52)	25 (22-52)	0.33
Male gender	36 (44%)	2 (15%)	0.067
Body mass index, kg/m^2	24.1 (3.2)	21.8 (2.8)	0.01
Presence of comorbidities	12 (15%)	0	0.21
Time since last vaccine dose, days	237 (9-357)	265 (58-321)	0.35
Past COVID-19 infection	32 (40%)	2 (15%)	0.12

rare and seen in one patient each. Mean pulse rate and oxygen saturation on pulse oximeter were 89 (16) per minute and 98 (1) %, respectively (**Table 2**).

Need for Care Escalation or Hospitalization

No patient progressed to moderate or severe disease, or required care escalation/hospital admission during the period of telemonitoring during home isolation.

Psychosocial Concerns

Most participants had additional concerns related to testing and management of family and household contacts including elderly and children, timing of joining back to duty and whether repeat testing was needed prior to it, effect of the infection on vaccine schedules, etc which were mentally bothering them. These were adequately addressed through our integrated remote monitoring model.

COVID-19 Vaccination and Past Infection With COVID

All patients (except one) were previously vaccinated for COVID-19 using AZD1222 (93%) or BBV152 (7%). Most patients (95%) had completed their two-dose vaccine schedule at the time of being infected with COVID-19, with the median time from the last vaccine dose to acquisition of current COVID-19 being 248 days. Two (2.1%) patients developed COVID-19 even after having received the booster or precautionary third dose; however this was within nine days of immunization with the booster dose. Thirty four (36%) patients had a past history of being infected with COVID-19; two (2%) of these had suffered from COVID-19 twice prior to the current episode (**Table 1**).

Factors Associated With Symptomatic COVID-19

Symptomatic patients in the cohort had higher BMI (24.1 vs. 21.8 kg/m^2, $p = 0.01$) and were more likely to be males (44% vs. 15%, $p = 0.067$) compared to asymptomatic patients (**Table 3**). There was no difference in age between the two groups. Past infection with COVID-19 and time since last vaccine dose were also not different between symptomatic and asymptomatic patients (**Table 3**).

DISCUSSION

This study reports on the success of remote monitoring and holistic care of healthcare workers affected with mild COVID-19 and residing under home isolation through the use of digital technology and characterizes the clinico-demographic profile of these patients infected during the third wave of the pandemic in India caused by the Omicron (B.1.1.529) variant.

The use of virtual care in health management has assumed greater relevance and significance in the current COVID-19 era. The existing healthcare infrastructure and manpower have the potential to be overwhelmed by the huge number of COVID-19 affected patients unless mechanisms for triaging these patients are put in place; since the vast majority of COVID-19 patients have a mild disease, strengthening of virtual care, remote telemonitoring and telecare can help rationalize the scarce healthcare resources. Studies done so far have showed promising results of remote home monitoring for COVID-19 in a pre-hospital as well as post-hospital, step-down setting, with earlier identification of a need for hospitalization or re-admission (in discharged patients), reduction of bed days, and length of hospital stay (4–12). However, most of these studies have included a mix of mild, moderate, or even severe patients in a community setting, and focussed primarily on the medical aspects of a largely "admission avoidance" centric model aimed at reducing the burden on healthcare systems. A significant proportion of suspect (unconfirmed or non-COVID) patients have often been included, compromising the external validity. Our study is different in its focus on providing holistic care for not just medical but also mental and psychosocial needs of patients affected with mild (or even asymptomatic) COVID-19, inclusion of health care workers as the target population rather than the general community as their medical and psychosocial

needs may be different, and inclusion of only microbiologically confirmed COVID-19 cases into the study. Care must be taken to avoid extrapolation of data available from different settings since significant ethno-geographic differences in COVID-19-related clinical behavior exist, which could influence the success (or failure) of implementation of remote telemonitoring models, besides the model characteristics themselves. To the best of our knowledge, this is the first study on remote monitoring of mild COVID-19 patients under home isolation from India. Remote monitoring models till date have variably employed smartphone or web applications, in-house softwares, paper-based monitoring, or phone calls, with or without home oximetry, for the purpose of monitoring. Software or application-based approaches are believed to have a wider reach, while phone call-based approaches are considered more inclusive since they are able to overcome barriers associated with technological availability and technological literacy (7). In this study, we used a comprehensive, synergistic model comprising of mandatory phone calls at the beginning and end of isolation, assisted by google forms, home oximetry, and voluntary (opt-in) web or application-based interactions as and when deemed necessary by the patient. This enabled us to overcome limitations of individual approaches and accommodate wider patient preferences. The use of existing resources and staff at the Department of Telemedicine helped to avoid issues pertaining to reallocation of limited resources or staff, cost-effectiveness and sustainability of the model.

Healthcare workers are indispensable to the functioning of healthcare systems. Clear strategies to manage exposed and infected healthcare workers including risk stratification, appropriate clinical monitoring, easy diagnostic access, decision making about quarantine leave and return to work, and home-isolation vs. hospital quarantine are essential to ensure effective staff management and workplace trust (16). Healthcare workers, especially those directly involved in diagnosing or treating suspected or confirmed COVID-19 patients, live in a constant state of psychological stress due to the fear of contracting and transmitting the virus, repeated exposures, and the unpredictable behavior of the disease. This has been shown to result in a higher prevalence of depression, anxiety, sleep disturbances and post-traumatic stress disorders in this population, often necessitating psychosocial intervention (2). Otherwise also, social isolation has been linked to depression even in a non-COVID setting (17). Through remote monitoring, we could manage the home-isolated health care workers both medically and psychologically. None of the study patients progressed clinically to moderate-severe disease, or required care escalation during the period of remote monitoring. Most participants had additional psychosocial concerns which were mentally bothering them; these were adequately addressed through our integrated remote monitoring model. We could not find any study focussing on, or addressing these non-medical aspects of COVID-19.

Our study cohort had milder symptoms compared to studies on remote monitoring from other parts of the world; one of the reasons contributing to this difference, apart from the ethno-geographic differences, was the timing of conduct of this study during the third wave of the pandemic in India, which was epidemiologically linked to Omicron (B.1.1.529), an inherently milder variant of SARS-CoV-2 (14). The clinical presentation was dominated by fever, sore throat, running nose and myalgia. Anosmia, gastrointestinal symptoms, or breathing difficulty were hardly seen, in contrast to the previous waves of the pandemic caused by other SARS-CoV-2 strains including the delta variant (B.1.617.2) (18). Our study thus provides indirect evidence about the clinico-demographic profile of Indian patients infected with the Omicron (B.1.1.529) variant, although formal variant testing was not done as a part of the study. On comparing mildly symptomatic and asymptomatic patients, a higher BMI (and a trend toward male predilection) was seen in symptomatic patients in our cohort, which is in line with the available literature (19). Counterintuitively, no difference in the presence of comorbidities, time since last vaccine dose, and past COVID infection was noted between symptomatic and asymptomatic patients.

The collected data show that multi-faceted issues of COVID-19 affected healthcare workers under home isolation can be managed remotely using telemedicine. The merits of the study are inclusion of microbiologically confirmed COVID-19 patients (rather than suspect patients), a focus on health care workers as the target population, and employment of a holistic remote monitoring model comprising of mandatory phone calls assisted by home oximetry, administration of a predesigned google form with relevant clinical details, and voluntary, opt-in software-based and/or telephonic consultation. Use of existing resources and staff (by virtue of a separate Department of Telemedicine) avoided issues pertaining to cost-effectiveness and sustainability of the model. The limitations of the study include a relatively small sample size from a single center; a lack of progression to moderate or severe disease was seen, which could be explained by the inherently mild nature of the Omicron (B.1.1.529) variant, small sample size, and inclusion of a fairly young study population with a relatively low prevalence of comorbidities. A formal assessment of the participants' psychological problems was not done. Analysis of factors associated with symptomatic COVID-19 included only limited variables. Inclusion of a control group could have facilitated better inferences regarding effectiveness of remote monitoring and the extent of improvement in patient outcomes. Finally, since the study population comprised of healthcare workers who are better informed about the disease, these findings cannot be directly extrapolated to the general population, although the principles of remote monitoring would still be valid.

CONCLUSION

Integration and deployment of digital technology is important in the management of COVID-19. Diverse medical and psychosocial issues of COVID-19 patients under home isolation can be holistically managed remotely through telemedicine and digital technology. The clinico-demographic profile of healthcare workers infected with mild COVID-19 during the third wave [epidemiologically linked to Omicron (B.1.1.529) variant] has also been reported.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institute Ethics Committee PGIMER Chandigarh INT/IEC/2022/SPL-281. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

SJ and AA planned the study and conducted the study. AB helped in gathering and entering the data. PL helped in providing the healthcare workers data who came COVID positive. AC and MaS helped in preparing final version of manuscript. MeS looked overall performance of the study and also helped in getting the ethical clearance of the study. All authors contributed to the article and approved the submitted version.

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Successful Use of a 5G-Based Robot-Assisted Remote Ultrasound System in a Care Center for Disabled Patients in Rural China

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Background: Disability has become a global population health challenge. Due to difficulties in self-care or independent living, patients with disability mainly live in community-based care centers or institutions for long-term care. Nonetheless, these settings often lack basic medical resources, such as ultrasonography. Thus, remote ultrasonic robot technology for clinical applications across wide regions is imperative. To date, few experiences of remote diagnostic systems in rural care centers have been reported.

Objective: To assess the feasibility of a fifth-generation cellular technology (5G)-based robot-assisted remote ultrasound system in a care center for disabled patients in rural China.

Methods: Patients underwent remote robot-assisted and bedside ultrasound examinations of the liver, gallbladder, spleen, and kidneys. We compared the diagnostic consistency and differences between the two modalities and evaluated the examination duration, image quality, and safety.

Results: Forty-nine patients were included (21 men; mean age: 61.0 ± 19.0 [range: 19–91] years). Thirty-nine and ten had positive and negative results, respectively; 67 lesions were detected. Comparing the methods, 41 and 8 patients had consistent and inconsistent diagnoses, respectively. The McNemar and kappa values were 0.727 and 0.601, respectively. The mean duration of remote and bedside examinations was 12.2 ± 4.5 (range: 5–26) min and 7.5 ± 1.8 (range: 5–13) min ($p < 0.001$), respectively. The median image score for original images on the patient side and transmitted images on the doctor side was 5 points (interquartile range: [IQR]: 4.7–5.0) and 4.7 points (IQR: 4.5–5.0) ($p = 0.176$), respectively. No obvious complications from the examination were reported.

Conclusions: A 5G-based robot-assisted remote ultrasound system is feasible and has comparable diagnostic efficiency to traditional bedside ultrasound. This system may provide a unique solution for basic ultrasound diagnostic services in primary healthcare settings.

Keywords: disability, rural health, 5G network, care center, robot-assisted, ultrasonography

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INTRODUCTION

Disability has become a global population health challenge. According to the World Disability Report, approximately 15% of the global population (1 billion people) has various disabilities, and more than 13% of the population with disabilities (85 million people) being in China (1–3). Due to difficulties in self-care or independent living, these patients mainly live in community-based care centers or institutions for long-term care and rehabilitation, rather than being hospitalized (4–6). Care centers for persons with mental disorders or physical disabilities without access to tertiary healthcare services are frequently the primary sites for long-term care and rehabilitation (7–9). However, these settings often lack healthcare resources, including facilities for basic ultrasound examinations (10–12).

Ultrasound imaging is the most easily adaptable diagnostic imaging technology for establishing rapid and non-invasive diagnoses (13). Nonetheless, owing to the lack of skilled sonographers, conducting a traditional on-site ultrasound examination is difficult in several care centers. At care centers for disabled patients, the staff often include mental health professionals, caregivers, and general practitioners only, and there is difficulty in recruiting sonographers (8, 14, 15). Emergencies often force disabled patients to be transferred to nearby hospitals for diagnostic ultrasound examination, increasing the risk of infections and complications related to transportation (15, 16). Advances in telemedicine provide a unique solution to this problem (17–19). With the progressive development of broadband technologies, robotic arm-assisted ultrasound systems improve access to imaging services and close the health equity gap for radiology practices and health systems (19–22).

Over the past 20 years, advances in human-robot interaction systems, master-slave control scheme, and communication technologies have led to the development of remote ultrasonic robot technology for clinical applications across wide geographical regions (16, 23). Furthermore, the availability of off-site medical expertise has become a reality. The initial application of a fifth-generation cellular technology (5G)-based robot-assisted remote ultrasound system during the coronavirus disease (COVID-19) pandemic has achieved encouraging results (22, 24–26). Duan et al. (26) demonstrated that the diagnostic system has considerable value for application in intensive care units. However, to date, none of 5G-based telerobotic ultrasound systems experiences in rural care centers for disabled patients have been reported.

Therefore, we aimed to assess the feasibility of using a 5G-based robot-assisted remote ultrasound system for patients in a rural care center for persons with disabilities in China and to explore a solution for providing basic ultrasound examinations in centers lacking local ultrasound experts and conventional ultrasound devices.

MATERIALS AND METHODS

Patients

The present study involved patients living in the Yuanshu Disabled Care Center, Deqing County, Huzhou, Zhejiang Province, located 35.9 km from the hospital where the 5G-based tele-ultrasound examinations were remotely performed by experts (tele-doctor) in real time, from March to April 2021. All examinations were performed after obtaining written informed consent from each patient or their family and were approved and were approved by the Human Ethics Review Committee of the Zhejiang Provincial People's Hospital.

The inclusion criteria were as follows:

(1) Clinical indications for acute abdomen, such as vomiting, diarrhea, constipation, or flatulence;
(2) Chronic abdominal distention, discomfort, or abdomen mass;
(3) No abdominal ultrasound performed in the previous year.

The exclusion criteria were as follows:

(1) Refusal or inability to cooperate with the ultrasound examination;
(2) Abdomen covered with dressings.

Instruments

A 5G-based robot-assisted remote ultrasound system (MGIUS-R3; Wisonic Medical Technology Co., Ltd., Shenzhen, China) was used for the tele-examinations. The MGIUS-R3 consists of two parts-namely, the doctor-side and the patient-side subsystems. The two systems are connected *via* a speed, low-latency, and large-bandwidth 5G network with a downlink rate of 930 Mbps and an uplink rate of 132 Mbps. The delay in the examination process was <200 ms. The doctor-side subsystem consists of a robot-control console, real-time image display system, ultrasound control panel, and audiovisual communication system. The robot-control console comprised a robotic ultrasound probe, position sensor, and pressure sensor. The robotic ultrasound probe has a posture sensor and "UP button". The posture sensor managed three degrees of freedoms (DOFs) for rotation, the position sensor managed two DOFs for the movement on the horizontal plane, the "UP button" and pressure sensor managed one DOF for the up and down movement (27). The tele-doctor can manipulate the robot-control console to maneuver a remote robotic arm. The ultrasound parameters including the time gain compensation, focal position, dynamic range, and mechanical index can be adjusted real-time by the tele-doctor *via* the ultrasound control panel. Audiovisual communication system enables synchronous communication between the tele-doctor and on-site assistant or patients. The patient-side subsystem consisted of an ultrasound imaging system, a six-DOF robotic arm, a precise contact force control system, and a audiovisual communication system. The robotic arm (collaborative robot UR5, Universal Robots, Odense, Denmark) was equipped with a convex array probe (frequency: 2.5–5 MHz). Thus, six dimensions of data (three-dimensional rotation, two-dimensional plane and one-dimensional force control) can be collected (22, 26). The robotic arm also contained a high-precision six-dimensional force sensor at the tip to obtain real-time force feedback information when the probe interacted with human soft tissue. The force control and force protection algorithm can ensure the contact force within the set value. For abdomen examination, the vertical protection

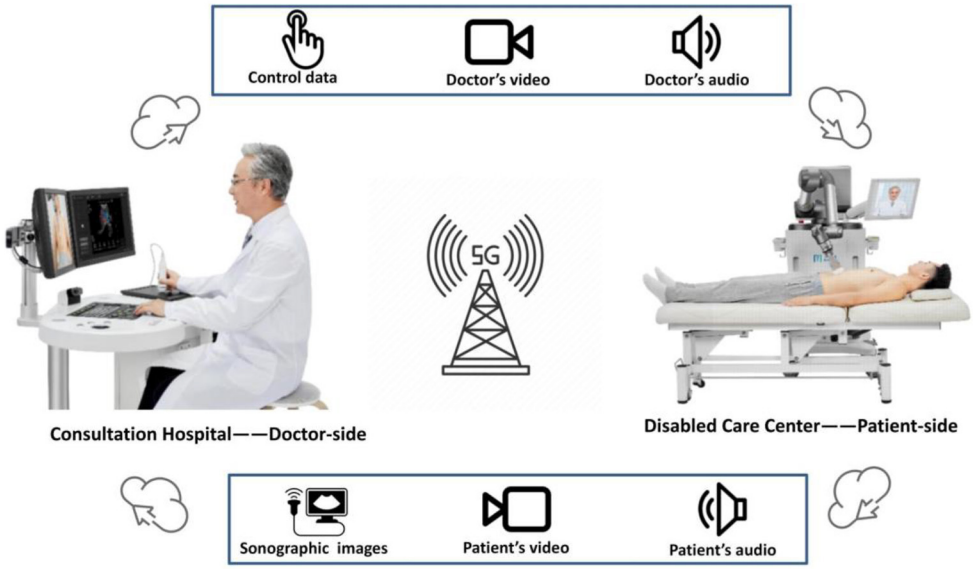

FIGURE 1 | The 5G-based robot-assisted remote ultrasound (MGIUS-R3) comprises two parts: the doctor-side subsystem and the patient-side subsystem. The control data, doctor's operational video, and voice are sent in real time to the patient side through the 5G network. The sonographic images, video of robotic arm manipulation, and patient's audiovisual signal are sent in real time to the doctor side.

force of 3–40 N and the horizontal protection force of 20 N could be set, which could ensure the smooth movement of the probe and output stable ultrasound images and protect the patient (26, 27). The screen interface of ultrasound imaging system (Clover 60; Wisonic Medical Technology) is captured by a video capture card and transferred to the doctor side *via* the Internet; the control signal for the ultrasound main unit is captured through the control panel and sent to the main unit following the control protocol. Camera and voice pickup are also included in each subsystem. Through audio–video transmission technology, remote audio-video communication can also be achieved (**Figure 1**).

In this study, the doctor-side subsystem was located in the Zhejiang Provincial People's Hospital at Hangzhou, and the patient-side subsystem in the Yuanshu Disabled Care Center at Deqing. An expert sonographer remotely operated the robot-control console in the doctor-side subsystem, while the robotic arm of the patient-side subsystem followed the motion instructions transmitted from the doctor side. Then, the real-time sonographic images were sent to the radiologist for evaluation and diagnosis (**Figure 2**).

A portable ultrasonic diagnostic apparatus (Clover 60; Wisonic Medical Technology) was also used for the bedside examinations.

Study Design

The same patients were examined by two independent sonographers using 5G-based robot-assisted remote ultrasound and with standard bedside ultrasound. These sonographers had undergone standardized ultrasound robot manipulation training and had a minimum of 5 years of experience in abdominal ultrasound. Each patient underwent ultrasound examination of the liver, gallbladder, spleen, and kidneys. The ultrasonic findings were classified as positive (a lesion was identified) or negative. If the two examinations were consistent, the results were considered as the final ultrasound diagnosis; otherwise, the patient was re-examined by an on-site senior sonographer (with a minimum of 20 years of abdominal ultrasound experience) to obtain a final diagnosis (**Figure 3**).

Following the completion of 5G-based robot-assisted remote ultrasound examination, the patients were evaluated to determine the presence of complications related to the examination, including pain, skin lesions, swelling, bleeding, and crush injuries.

Additionally, three independent ultrasonography experts were invited to evaluate the original images on the patient side as well as the images transmitted to the doctor side. The quality of images were evaluated using an internationally defined 5-level absolute evaluation scale 5 points: no image quality deterioration, very good; 4 points: visible image quality changes with unhindered viewing, good; 3 points: image quality deterioration that slightly hindered viewing, fair; 2 points: hindered viewing, poor; 1 point: severely hindered viewing, very poor (26).

Data Analysis

Statistical analysis was performed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation for normal distribution or as median and interquartile range (IQR) for skewed distribution. Categorical variables are expressed as percentages

of the total. Paired-sample Student's *t*-test or Mann–Whitney U-test were used to compare the data between the groups. Cohen's kappa consistency test and McNemar's test were used to evaluate the diagnostic differences and consistency between remote and bedside positive diagnoses. The significance level was set at $p < 0.05$. The kappa values were interpreted as follows: <0.20, poor; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, good; and 0.81–1.00, very good (28).

FIGURE 2 | The 5G-based robot-assisted remote ultrasound used for patients in a rural care center for persons with disabilities in China. **(A)** The doctor-side operational scenario in Hangzhou. **(B)** The patient-side operational scenario in Deqing, 35.9 kilometers away from Hangzhou. **(C)** Ultrasound images captured from the patient-side subsystem were sent to the doctor-side subsystem in real time.

RESULTS

Fifty-four patients underwent abdominal ultrasound examinations of the liver, gallbladder, spleen, and kidneys. After the 5G-based robot-assisted remote ultrasound examination, no complications related to the study were found. Five non-diagnosed patients were excluded because of severe intestinal gas interference. A total of 49 patients (21 men and 28 women; mean age 61.0 ± 19.0 [range 19–91] years) were included in the analysis. **Table 1** displays the demographic and clinical characteristics of the included patients. Of these patients, 53.1% (26/49) had various chronic disorders, 63.3% (31/49) had a mental disability, and 38.8% (19/49) had a physical disability.

Among the 49 patients, 39 and 10 had positive negative ultrasound results. As shown in **Table 2,** 41 patients had consistent diagnoses between bedside and remote ultrasound, while eight had inconsistent diagnoses. The inconsistent diagnoses included five positives on bedside ultrasound and negative on the remote one, as well as three with opposite results. The McNemar value associated with the two methods was 0.727, and the kappa value was 0.601($p < 0.001$), indicating that the overall diagnosis results were similar, and there was no significant difference in the diagnosis level between the two methods. **Figure 4** presents a comparison of the results of both ultrasound examinations. Overall, 67 lesions were detected in the 39 positive patients (**Table 3**). The remote ultrasound detected 62 out of 67 lesions (92.5%); the five missed

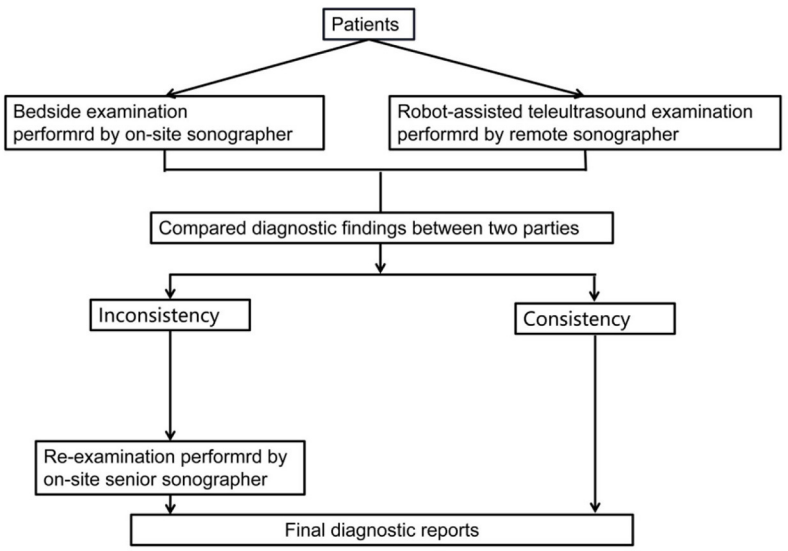

FIGURE 3 | Design of the ultrasound examinations in this study.

TABLE 1 | Demographic and clinical characteristics of the patients included in this study.

Patient information	*N*
Clinical characteristics	
Age, *y*	
<60	26
60–79	12
≥80	11
Sex	
Male	21
Female	28
Indication of abdominal ultrasonography, number	
Acute abdomen	5
Chronic abdominal distention	11
Chronic abdominal discomfort	13
Abdomen mass	1
Over 1 year since last abdominal ultrasound	19
Primary disease, number	
Alzheimer's disease	9
Organic psychosis	1
Depression	5
Epilepsy	1
Schizophrenia	18
Mental retardation	2
Down's syndrome	1
Subacute degeneration of spinal cord	1
Dysopia	4
Sequelae of cerebral infarction	9
Poliomyelitis	1
Fracture	2
Shoulder-hand syndrome	1
Parkinson-plus syndrome	1
Hypertension	23
Diabetes	11
Chronic kidney diseases	1
Chronic incomplete intestinal obstruction	1

TABLE 2 | Comparison of the results of the 5G robot-assisted remote and bedside ultrasound examinations.

	Bedside ultrasound		Total
	Negative diagnosis	Positive diagnosis	
Remote ultrasound			
Negative diagnosis	10	5	15
Positive diagnosis	3	31	34
Total	13	36	49

lesions (7.5%) were two left kidney stones, one gallstone, one gallbladder polyp, and one liver cyst. The bedside ultrasound detected 64 out of 67 lesions (95.5%); the three missed lesions (4.5%) were one gallstone, one left kidney cyst, and one right kidney cyst.

The mean remote examination time was 12.2 ± 4.5 (range: 5–26) min, whereas the mean bedside time was 7.5 ± 1.8 (range: 5–13) min, with the difference being significant ($p < 0.001$).

Figure 5 shows a comparison of a representative original image at the patient side and a transmitted image at the doctor side.

In the patient-side and doctor-side subsystems, the images with a score of 5 were 72.1 and 68.7%, respectively. The median image scores were 5 points (IQR: 4.7–5.0) and 4.7 points (IQR: 4.5–5.0), respectively ($p = 0.176$), with no significant difference in the image quality.

DISCUSSION

This study compared a 5G-based robot-assisted remote ultrasound with a traditional bedside ultrasound in 49 patients at a care center for persons with disabilities, located 35.9 km away from the main hospital. Overall, 7.5% and 4.5% of the lesions were undiagnosed by remote ultrasound and bedside ultrasound, respectively. The overall diagnostic results were similar between the remote and bedside ultrasound systems, with no significant differences. This study illustrates that a 5G-based robot-assisted remote ultrasound system may be an effective alternative to traditional bedside ultrasound for abdominal lesion evaluation. In this study, the examination time was longer with remote ultrasound than with bedside ultrasound. This may be related to the difficulty of most patients to completely follow the ultrasound operator's remote command to change the position because of movement disorders (e.g., cerebral infarction sequelae) or mental illness (e.g., schizophrenia). However, the use of 5G-based robot-assisted remote ultrasound system in persons with disabilities decreases the total process time, as compared with routine ultrasound. In particular, patients from remote areas take a longer time to arrive at medical facilities and undergo an ultrasound examination (29). This study suggests that the 5G-based robot-assisted remote ultrasound system will hopefully provide patients at rural care centers with the same diagnostic possibilities as those at tertiary hospitals where experts are instantly available.

With respect to safety, all patients successfully completed the 5G-based robot-assisted remote ultrasound examination. No patient was hurt by the sonographic robotic arm or complained of discomfort during or after the 5G-based robot-assisted remote ultrasound examination. The MGIUS-R3 benefits from the following multiple protection measures for ensuring patient safety (22, 25–27): First, when the robotic arm starts moving, the start prompt is displayed on both terminals. Second, an emergency stop button is installed next to the ultrasound probe socket of the robotic arm on the patient's side. Third, the robotic arm has a default speed of 0.675 m/s for the convex array probe, with parameters that can be changed in real time (i.e., the robotic arm stops moving if the set value exceeds the standard). Fourth, the robotic arm has a force sensor that can control the position and contact force on the patient in real time with pressure-limit settings. Overall,

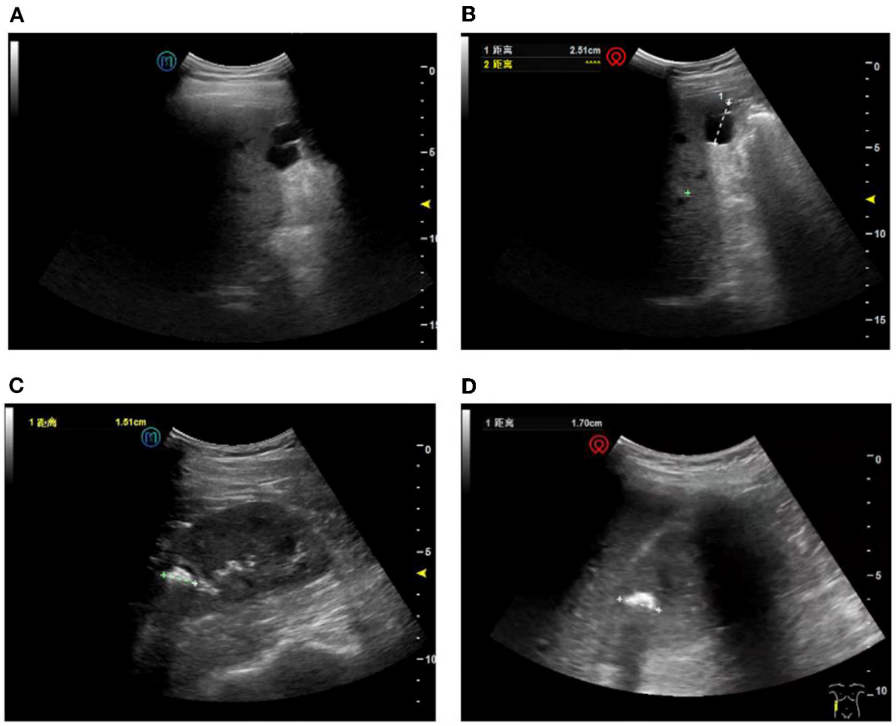

FIGURE 4 | Comparison of the results of the two ultrasound examinations. **(A)** Remote ultrasound image showing a liver cyst. **(B)** Confirmation of the liver cyst using bedside ultrasound. **(C)** Remote ultrasound image showing a right kidney stone. **(D)** Confirmation of the lesion using bedside ultrasound.

TABLE 3 | Comparison between bedside and remote ultrasound examinations.

Positive diagnosis	Number	Inconsistent remote-bedside	Kappa value	*p*-value	Strength of agreement	McNemar value
Liver cyst	7	1	0.911	$p < 0.001$	Very good	1
Fatty liver	14	0	1	$p < 0.001$	Very good	1
Hyperechogenic liver	3	0	1	$p < 0.001$	Very good	1
Enlarged gallbladder	1	0	1	$p < 0.001$	Very good	1
Intrahepatic calcification	2	0	1	$p < 0.001$	Good	1
Hepatic hemangioma	1	0	1	$p < 0.001$	Very good	1
Hepatocellular carcinoma	1	0	1	$p < 0.001$	Very good	1
Gallbladder polyps	2	1	0.657	$P < 0.001$	Good	1
Gallstone	5	2	0.728	$p < 0.001$	Good	1
Left kidney cyst	9	1	0.929	$p < 0.001$	Very good	1
Right kidney cyst	6	1	0.898	$p < 0.001$	Very good	1
Left kidney stone	6	2	0.778	$p < 0.001$	Very good	0.5
Right kidney stone	8	0	1	$p < 0.001$	Very good	1
Enlarged spleen	1	0	1	$p < 0.001$	Very good	1
Spleen calcification	1	0	1	$p < 0.001$	Very good	1

the telerobotic ultrasound system could provide a high degree of safety.

Determining whether or not the ultrasound image quality displayed in the doctor-side subsystem is reliable is crucial (30, 31). Ye et al. (25) investigated the feasibility of a 5G-based robot-assisted remote ultrasound system for the examination of COVID-19 patients, specifically for cardiopulmonary examinations (echocardiography) and evaluation of peripheral lung lesions (lung ultrasound). Ye et al. (25) utilized tele-ultrasound to assess dynamic organs (cardiopulmonary assessment) and revealed that this system is capable of obtaining subtle, complex, and detailed findings. In the current study,

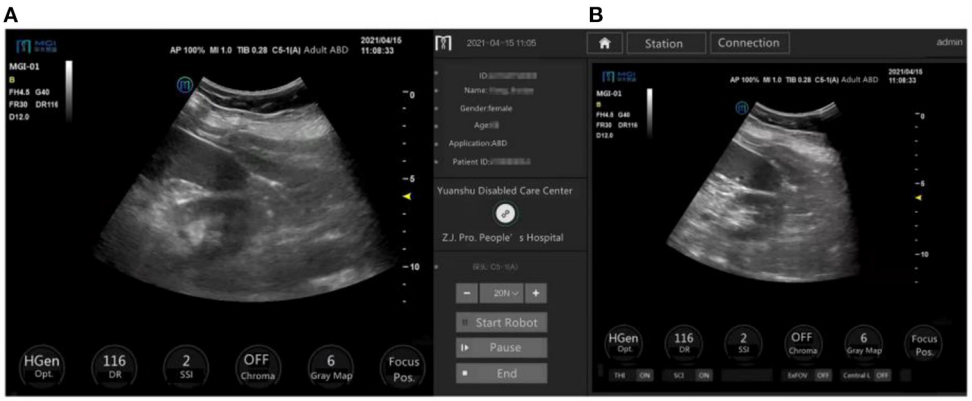

FIGURE 5 | Ultrasound images on the patient side (original images) and doctor side (transmitted images) of the same organs in the same patient. The ultrasound image of the left kidney and the inferior pole of the spleen, displayed on the patient-side, scored 4.3 points on average **(A)**, and on the doctor side scored 4.7 points on average **(B)** according to three independent experts.

we evaluated the received images with respect to gray levels, brightness, and resolution and compared them to original images using a 5-level absolute evaluation scale. Our results indicated that the median scores for the original and transmitted images were comparable (telerobotic ultrasound vs. bedside ultrasound, 5 points [IQR: 4.7–5.0] vs. 4.7 points [IQR: 4.5–5.0]; $p = 0.176$). This finding suggests that there is no perceived degradation in the quality of ultrasound images captured by robot-assisted remote ultrasound systems and that the images can be effectively used for diagnostic purposes.

For the 5G-based robot-assisted remote ultrasound system, it is necessary to ensure high-precision synchronous transmission (32). 5G has the advantages of high speed, greater bandwidth, low latency, and higher reliability (33). In 5G systems, it is thought that 5G download speeds and upload speeds could eventually reach as high as 20 gigabits per second (Gbps) and up to 10 Gbps, respectively (33). The latency is expected to reach a maximum latency of 1 ms with reliability for a packet size of 32 bytes at the user plane (34, 35). The International Telecommunication Union defines three categories of 5G application scenarios—namely, extended mobile broadband, ultra-reliable low-latency communication (URLLC), and massive machine-type communication (33). URLLC can support diverse settings for telemedicine, including telesurgical robots, remote supervision of procedures, integrated intelligent operating rooms, and clinician telepresence (33, 36–39). With network reliability and improvement in latency, realizing the promises of remote ultrasound examination that have been present since the first remote ultrasonic robot system (i.e., the TER system) was reported in 2003 (40). Data streams can more effectively meet the encoding requirements for conveying ultrasound images and videos than the transmission carrying capacity of traditional 4G networks (41). Therefore, no noticeable delay occurred during scanning, and each examination was completed rapidly and almost in real time. In our study, remote experts could fulfill the aims of remote operation and diagnosis. The remote operation and diagnosis were possible due to the 5G network, which provides sufficient transmission speed and reliability in real time across large distances (42, 43).

However, this study has some limitations. First, the 5G-based robot-assisted remote ultrasound system depends on the operator's technical level and requires further improvements. Second, restrictions on patients' examination position and robotic arm's the operating angle occasionally impeded the operator from reaching the regions to be examined. Third, the number of patients enrolled in this study was relatively small, and larger studies are needed in the future.

In conclusion, we demonstrated that the use of a 5G-based robot-assisted remote ultrasound system is feasible in patients with disabilities at a remote care center. Additionally, the 5G-based robot-assisted remote ultrasound system exhibits similar diagnostic efficacy to traditional bedside ultrasound.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because of privacy and ethical restrictions. Requests to access the datasets should be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Human Ethics Review Committee of the Zhejiang Provincial People's Hospital. We followed relevant guidelines to ensure that this study was voluntary and confidential.

AUTHOR CONTRIBUTIONS

C-zP, R-zY, and L-jX designed the study. H-hC, R-zY, C-zP, Z-nX, L-jX, XH, and L-fJ gathered the data. H-hC, R-zY, and L-fX

analyzed the data. H-hC, R-zY, C-zP, L-fX, and XC drafted the manuscript. H-hC, R-zY, C-zP, and L-fX revised the manuscript. All authors read and approved the final manuscript.

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Improving equity, efficiency and adherence to referral in Pakistan's eye health programmes: Pre- and post-pandemic onset

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Background: Over one billion people worldwide live with avoidable blindness or vision impairment. Eye Health Programmes tackle this by providing screening, primary eye care, refractive correction, and referral to hospital eye services. One point where patients can be lost in the treatment journey is adherence to hospital referral.

Context: Peek Vision's software solutions have been used in Pakistan with the goal of increasing eye health programme coverage and effectiveness. This involved collaboration between health system stakeholders, international partners, local community leaders, social organizers and "Lady Health Workers".

Results: From the beginning of the programmes in November 2018, to the end of December 2021, 393,759 people have been screened, 26% of whom (n = 101,236) needed refractive services or secondary eye care, and so were referred onwards to the triage centers or hospital services. Except for a short period affected heavily by COVID-19 pandemic, the programmes reached an increasing number of people over time: screening coverage improved from 774 people per month to over 28,300 people per month. Gathering and discussing data regularly with stakeholders and implementers has enabled continuous improvement to service delivery. The quality of screening and adherence to hospital visits, gender balance differences and waiting time to hospital visits were also improved. Overall attendance to hospital appointments improved in 2020 compared to 2019 from 45% (95% CI: 42–48%) to 78% (95% CI: 76–80%) in women, and from 48% (95% CI: 45–52%) to 70% (95% CI: 68–73%) in men. These patients also accessed treatment more quickly: 30-day hospital referral adherence improved from 12% in 2019 to 66% in 2020. This approach helped to utilize refractive services more efficiently, reducing false

positive referrals to triage from 10.6 to 5.9%. Hospital-based services were also utilized more efficiently, as primary eye care services and refractive services were mainly delivered at the primary healthcare level.

Discussion: Despite various challenges, we demonstrate how data-driven decisions can lead to health programme systems changes, including patient counseling and appointment reminders, which can effectively improve adherence to referral, allowing programmes to better meet their community's needs.

KEYWORDS

digital health, mHealth, referral, attendance, eye health, visual impairment (VI), screening, vision

Introduction

Eye health programmes

Over one billion people worldwide now live with avoidable blindness or visual impairment (VI), the majority in low- and middle-income countries (LMICs) or low-income socioeconomic groups (1). Eye health programmes aim to eliminate avoidable blindness, however their success depends upon effective implementation. Screening is frequently conducted in schools or the community. This step identifies whether the participants have any eye health problems warranting further care. The next steps include provision of primary eye care services and refractive correction, and referral to hospital eye services when needed. In community and school settings, most eye health needs consist of primary eye care and refractive services, which can be met by non-ophthalmologist personnel. The remaining problems which require referral are generally the most severe.

The problem—adherence to referral

Previous studies have shown that community-based screening programmes, when they are delivered with digital solutions, can improve the utilization of eye care (2–4). However, in a model as described above, there are various stages where patients may be missed. They may not attend initial screening, may be lost to follow up at primary eye care/refractive services, may not attend hospital eye services following referral, or may not receive the recommended treatment. This leads to residual unmet need despite an otherwise high volume, effective screening programme. Therefore, when measuring the impact of eye health programmes, it is important to look beyond the number of people screened, as screening of visual impairment does not automatically translate into eye health outcomes (5).

For those with more complex eye care needs, one point in the patient journey where patients can be lost to follow up is adherence to hospital referral: patients failing to attend hospital ophthalmology appointments after a problem is identified. These patients are often those with the most serious ophthalmic problems, so failure at this stage can result in significant morbidity. Those who need hospital eye services require more resources to meet those needs, both from the patients' perspective (e.g., transport and time away from other obligations) (6) and health system perspective (e.g., professional cadre and surgical equipment). Therefore, there can be considerable barriers to attending a hospital appointment. Some previous studies have shown that the adherence to hospital referral after vision screening is low (around 30%) (4) even after provision of education, incentive packages, and subsidiary financial support (7). While these interventions do overcome some socioeconomic and logistic barriers, evidence-based approaches tailored to the local setting are needed to achieve an acceptable level of adherence and to ultimately improve vision (4, 7).

Commitment to hospital referrals is essential if eye health screening programmes are to be well accepted and integrated into existing local eye care systems, and have potential to provide effective outcomes. The inverse of this problem is inappropriate hospital attendance by patients who could have been successfully managed in the community, thereby inefficiently using hospital resources.

Context

Pakistan was one of the earliest countries to adopt a National Eye Health plan, in 1993 (8, 9). However, the country has a substantial VI burden, with an estimated 26 million people living with vision loss in 2020, when near VI and mild distance VI are included (10). Prior to 2018, eye health services in Pakistan were mainly available at secondary care Tehsil Headquarter (THQ) Hospitals, such that the limited ophthalmologist resources were largely spent on simple problems which could be solved in the community.

Since 2018, an international non-governmental organization, CBM: Christian Blind Mission, has partnered with Peek Vision to use their proven public health methodologies supported by software (2, 11–13). These have been started in two areas in Pakistan: Talagang Tehsil in Chakwal district, Punjab province, and Matiari district, Sindh province.

In this paper, we will discuss an example of success in eye health programmes in Pakistan, overcoming the challenges through participatory processes and iterative improvements of the programme.

Methods: Implementation of the programme

Objectives

The objectives of the programme at initiation and during the iteration reviews were to:

- Increase coverage of eye health services
- Increase efficiency by reducing waiting times and workload of the health workforce
- Increase demand of services through community awareness
- Establish eye screening at Basic Health Units
- Integrate Optometrist services at Rural Health Centers connected to Ophthalmologist services at secondary Tehsil Headquarter (THQ) Hospitals
- Help managers to analyse performance, track patients through the services, identify those that are not reached and intervene to reduce barriers, and do so on a regular basis following a participatory process.

Key metrics in the programmes were:

- Number screened
- Number referred to triage
- Adherence to triage referral, i.e., attendance to primary eye care and refractive services
- Number referred to hospital
- Adherence to hospital referral, i.e., attendance to hospital eye services following referral.

The community and school eye health programmes were tailored to local needs and resources, by local teams. Software tools, including smartphone-based vision tests, allowed data to be captured and transmitted digitally. The digital data collection and referral pathways were previously piloted in Kenya and later expanded in several other countries including Pakistan: the rationale and some methodological aspects have been explained in earlier publications (14). This enabled continuous monitoring of the effectiveness of eye health programmes, and a continuous improvement approach. These methods helped to identify hard-to-reach populations and to connect them to life-changing services. Adherence to hospital referral was identified as an area with potential for improvement. This was then targeted by social organizers, who increased community awareness of eye health and vision care. They also contacted patients who had been referred, to provide counseling regarding the importance of attending appointments, and to identify any obstacles to attendance. Allocation of appointments was also altered *via* a patient-initiated fixed appointments functionality, and appointment reminders sent *via* text message. The implementation involved collaboration between health system stakeholders in Pakistan, international partners, and local community health workers such as social organizers and Lady Health Workers (Figure 1).

Timeline—rollout of the programmes

Initially, a situation analysis was carried out in April 2018. This included assessment of health facilities regarding human resources, infrastructure, accessibility, interfacility distances, and internet connectivity. Additionally, a population-based eye health survey using the Rapid Assessment of Avoidable Blindness (RAAB7) methodology, which utilizes Peek software, was conducted in Talagang from November to December 2018, alongside the launch of a Community Eye Health (CEH) programme in Talagang. The RAAB methodology has been described elsewhere (15, 16). The second iteration of this CEH programme was undertaken in September 2019, at the same time as the launch of the School Eye Health programme in the same region. In December 2019, a RAAB survey was undertaken in Matiari. The resulting data were used to design and plan a CEH programme which commenced in Matiari in September 2020. These programmes were led by the College of Ophthalmology and Allied Vision Sciences (COAVS) in Punjab province and the Sindh Institute of Ophthalmology and Visual Sciences (SIOVS) in Sindh province, in partnership with the Brien Holden Vision Institute and district authorities, and sponsored by CBM. 'Lady Health Visitors', optometrists, dispensing opticians, and programme managers were trained to use Peek technology to register and track patients' progress from screening to diagnosis to treatment.

Data sources, data security

RAAB7 and Peek School and Community software for data collection were used within these eye care programmes to monitor effectiveness and provide the data required to track adherence. Data storage, transmission and retrieval was in line with a Data Protection Agreement (DPA) with the local stakeholders, and followed the European Union General Data Protection Regulation (GDPR). Data was discussed regularly

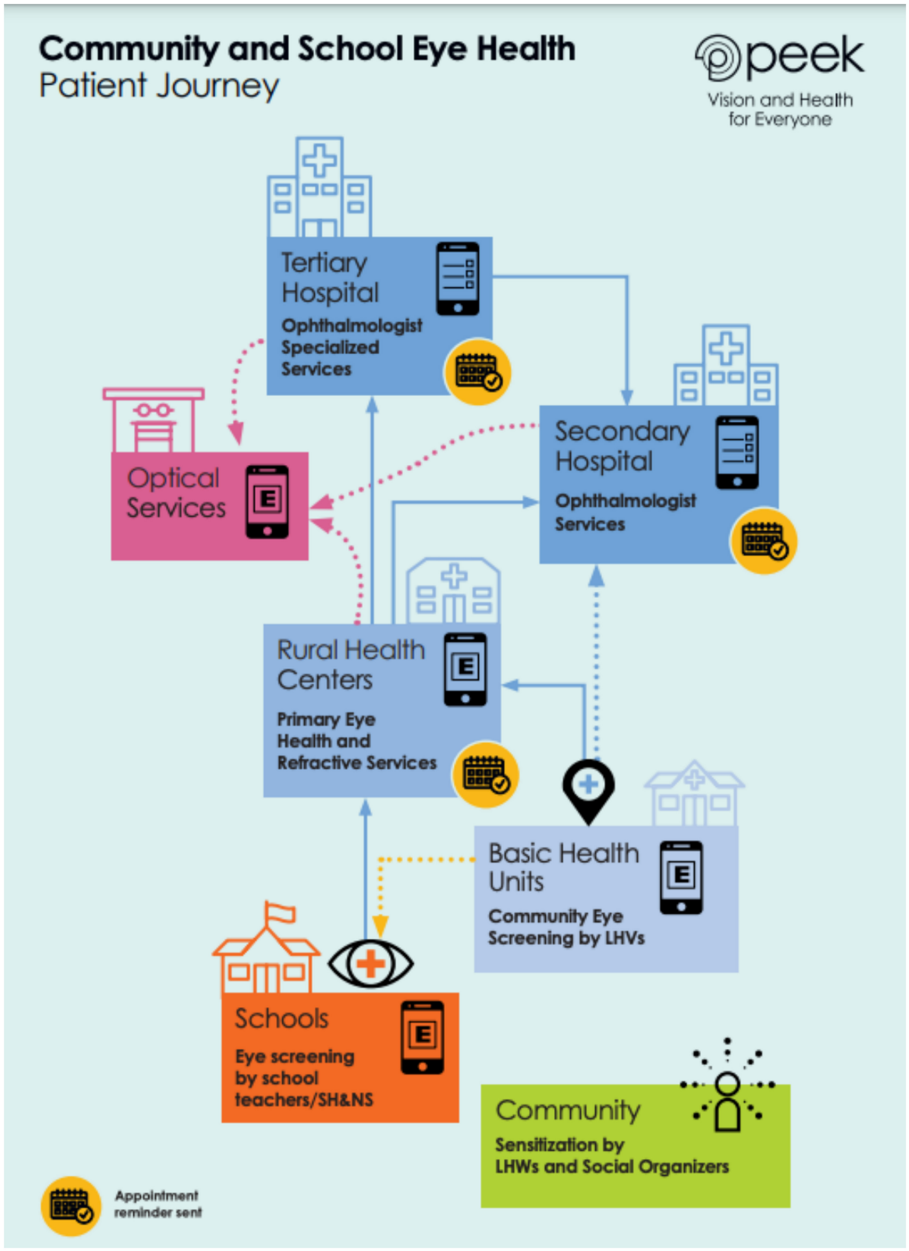

FIGURE 1
The patient journey approach and referral pathway in the Pakistan eye health programmes. LHWs, Lady Health Workers; LHVs, Lady Health Visitors; SH&NS, School Health and Nutrition Supervisors.

with stakeholders and implementers which enabled continuous improvement to service delivery.

Results

Screening coverage

In total, across the Punjab and Sindh Province programmes, the number of health facilities connected in this network increased from 3 in November 2018 (1 community screening Basic Health Unit, 1 triaging Rural Health Center, and 1 secondary eye health hospital) to 111 in 2021. This includes 84 Basic Health Units, 16 Rural Health Centers/City Hospitals, 8 THQ/District Hospitals and 3 specialized Tertiary Eye Hospitals. By the end of 2021, at least 108 Lady Health Visitors have been trained to screen using Peek.

School eye health programmes using Peek technology are being integrated into the CEH programmes in both

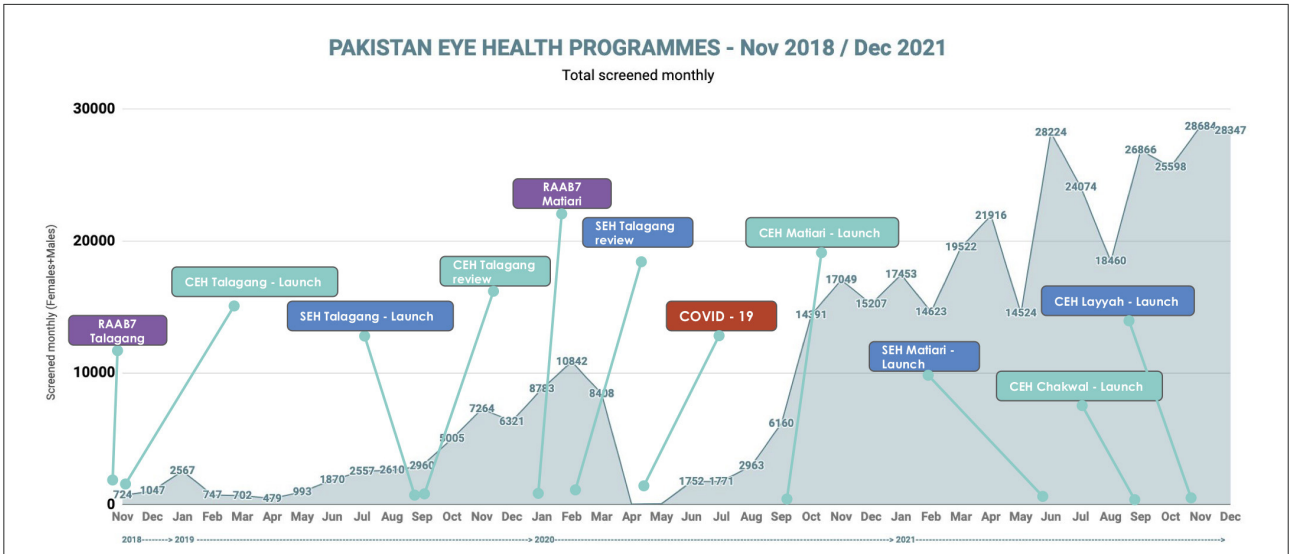

FIGURE 2
Screening volume, from programme initiation in November 2018 to December 2021. CEH, Community Eye Health; SEH, School Eye Health; RAAB7, Rapid Assessment of Avoidable Blindness, version 7 The chronological order of programme activities including RAAB surveys for evaluation of baseline prevalence of visual impairment, the launch of community and school eye health programmes, and iteration reviews for evaluation and monitoring of programmes are shown over time. Additionally, the number of people screened per month in all programmes is represented (blue line).

provinces. The number of schools included within the screening programmes rose from 0 to 1567. This connected primary and secondary schools with their nearest health facilities, with the aim of reaching an estimated 500,000 children in Punjab and Sindh provinces.

From the beginning of the programmes in November 2018, to the end of December 2021, 393,759 people had been screened, approximately 26% of whom (n = 101,236) needed refractive services or ophthalmology visits, and so were referred onwards to the triage centers or hospital services. Except for a short period affected heavily by the COVID-19 pandemic, the programmes reached an increasing number of people over time (Figure 2). Screening coverage improved from 774 people per month to over 28,300 per month. Women participated in screening more than men; however, gender balance in screening improved over time, resulting in the proportion of men accessing vision screening increasing from 18.1% in November 2018 to 33.1% in December 2021. These improvements were seen despite the pandemic.

Programme outcomes: Met and unmet need

Figure 3 shows the details of total recruitment of people in different stages of the programmes. As a longitudinal approach of patient outcomes is important in this figure, we have included data of those who were screened up to the end of September 2021. This is to allow at least a 3-month period for hospital attendance or spectacle dispensation. If someone has not yet reached the hospital, or received spectacles or medication, they were included in the unmet needs column showing that their needs are still waiting to be met. As illustrated in this figure, 337,418 people were screened from the start of the programme to the end of September 2021, 26% of whom were referred for further assessment or treatment. The percentage of true positives following referral to triage (those screened as needing further treatment who did indeed need further treatment) was 92%.

As shown in Figure 3, the majority of people who were referred to an ophthalmologist were referred after the triage stage, however, a small proportion (n = 1,338/10,368, 13%) were directly referred from the screening stage. If we follow recruitment flow from screening, only 0.3% of all those who were screened were referred directly to hospital and ophthalmology visits, and the others (2.6%) who needed ophthalmology visits were referred after triage. In total approximately 3% of the screened population had secondary eye care needs that required hospital visits.

Information about medication was only included from the triage centers where medications for primary eye conditions could be prescribed and dispensed. As shown, 34% of people who were triaged received medical prescriptions. Fifty three perecent of these prescriptions were dispensed on the project site. The remaining 47% may have either collected their medication elsewhere, or not yet had their medication dispensed.

The majority of spectacle prescriptions were provided at triage stage, while some were given following hospital visits.

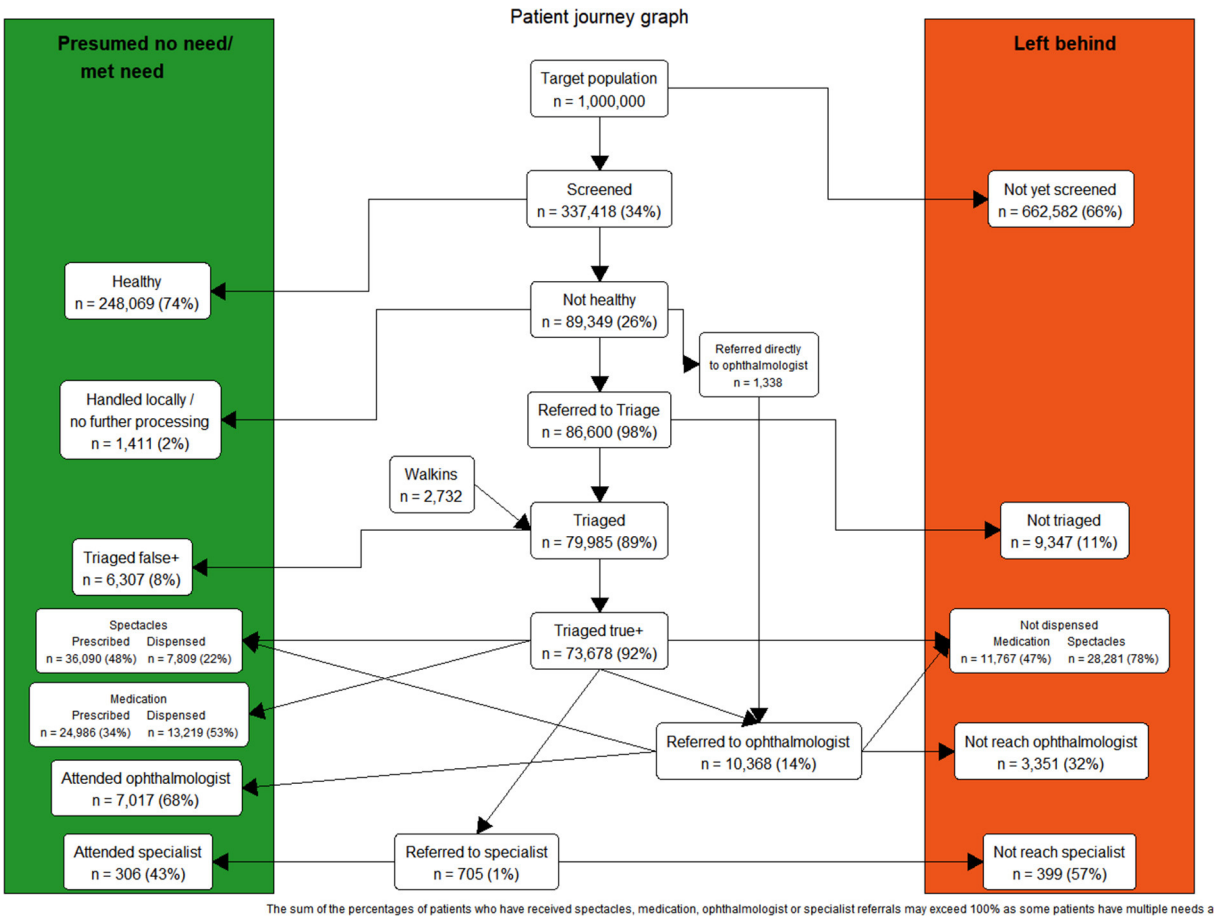

FIGURE 3
Patient Journey Graph: Total recruitment to different stages of community and school eye health programmes in Pakistan, November 2018 to September 2021. This figure shows the total recruitment and patient flow in different stages of the programmes. The programme aimed to reach 1,000,000 people, as defined during its design phase. During this time period, approximately one third of the target population were screened, 26% of whom were referred onwards for further assessment or treatment. 10,368 people were referred for review by an ophthalmologist. If someone has not yet reached hospital following referral, or not received spectacles or medication, they were included in the Left Behind column, showing that their needs are still waiting to be met. Where patients have received service (or have no need of treatment), they are included in the Presumed No Need/Met Need column. Of note, some patients currently have partially met need, e.g., those who have received a spectacle prescription but not yet had spectacles dispensed. In these cases, patients may appear in both columns. Information regarding medication was only gathered from triage centers where medications for primary eye conditions could be prescribed and dispensed.

From data collected thus far, 36,090 persons (48%) were found to have refractive error and received a spectacle prescription. At least 7,809 persons (22%) have received their spectacles from the project sites to date.

Adherence to hospital referral

Figure 4 shows sub-group analysis of adherence to hospital referral in 2019 and 2020, and waiting time to hospital visits. In addition it shows that 30-day hospital referral adherence improved by 5 times from 12% in 2019 to 66% in 2020 (Figure 4A), with a reduction in average waiting time to hospital appointments. Various other factors were shown also to affect adherence to referral. These included location of the programme, with larger improvements in Matiari in Sindh province (Figure 4B). Within each region, adherence varied with distance from the referral center, with lower attendance if not within walking distance of the hospital. In Talagang, early in the programme, >90% adherence to referral was seen amongst patients based within walking distance of the referral center. This is in comparison to 0–30% for those who required transport. There was also lower adherence to referral in younger school children (Figure 4C).

Attendance to hospital appointments was comparable between men and women (Figure 4D) and in both genders

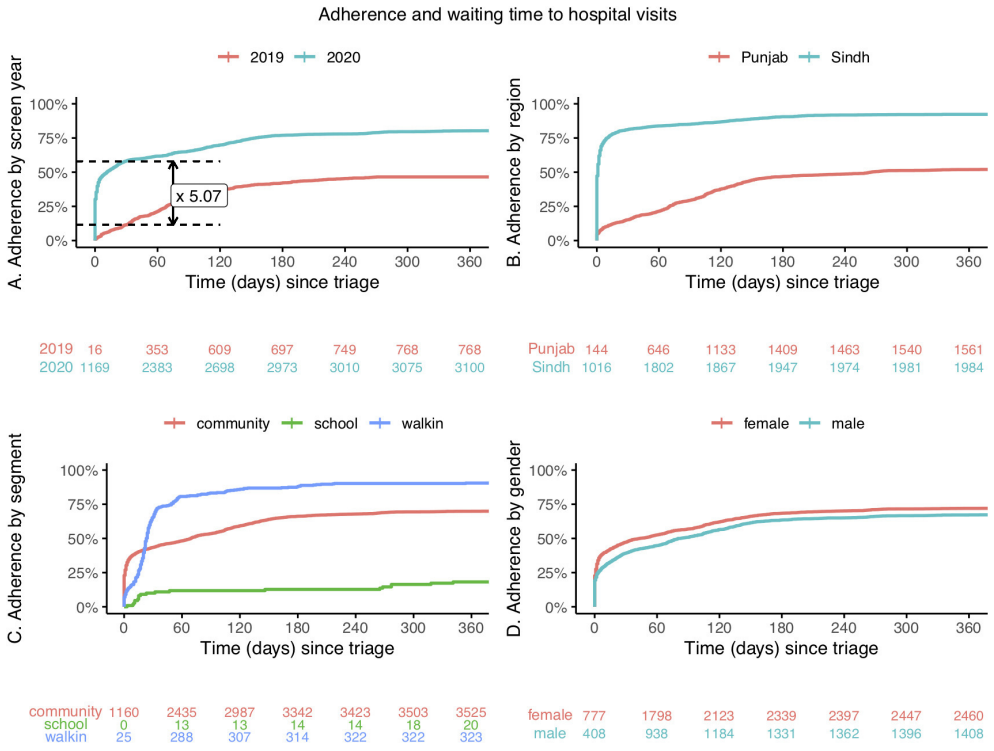

FIGURE 4
Sub-group analysis of cumulative adherence to hospital referral, and waiting time to hospital visit, in 2019 and 2020. **(A)** By screening year. **(B)** By region. **(C)** By source of referral: community screening, school screening, unscreened walk-in patients. **(D)** By gender Red, blue and green numbers below the graphs represent the cumulative number of attendees to hospital eye services following referral from triage.

adherence improved in 2020 compared to 2019: from 45% (95%CI: 42–48%) to 78% (95%CI: 76–80%) in women, and from 48% (95%CI: 45–52%) to 70% (95%CI: 6–73%) in men.

Quality of screening/appropriate referral

As mentioned above, the quantity (number screened) and quality of screening improved during the programme. True and false positives were used as a marking of screening quality, as this information could be collected during the programme. The proportion of false positive referrals from the screening stage to the triage stage was reduced from 10.6% in 2019 and 10.9% in 2020, to 5.9% in 2021. In particular, during the first half of 2021, an audit by location revealed some areas with an especially high rate of false positives, including one THQ hospital receiving 43% false positive referrals from screeners. The location analysis functionality revealed that most cases were referred from a specific facility, allowing the problem to be addressed with re-training. This, combined with increased communication between the Rural Health Center and the referring Basic Health Units, resulted in a reduction of false positive referrals from 86 to 17% at the Rural Health Center in question. In this subregion overall, false positive referrals improved from 43 to 4% by the end of September 2021.

In addition, hospital referrals for patients with refractive errors reduced from 41.2 to 1.2%, while the percentage of hospital patients attending with cataract increased from 6.7 to 50.1% in the first year of programme implementation at the THQ Hospital.

Discussion

Practical implications

Eye health programmes in Pakistan have expanded considerably over the last few years, with significant growth to the network of health facilities and schools. In this community case study, we have shown that modifications of the programme based on ongoing review of data and evidence can increasingly improve the programme, specifically attendance to hospital appointments which is an important step toward eye care utilization. In addition, over time, eye problems that were referred to the hospital included more

complex, secondary care problems, and fewer primary eye care issues. The latter were instead identified and handled in the prehospital stages, reducing pressure on services, and unnecessary travel and potential anxiety for individuals (17). Since 2018 (when the programme started), fewer people are attending THQ hospital services with refractive error, and the proportion attending with cataract increased. Therefore, the implemented screening programme helped to utilize hospital-based services more efficiently, meaning that primary eye care services and refractive services were mainly delivered in the screening and triage levels, maintaining the capacity of hospitals for delivering secondary and tertiary eye care services.

Increasing the proportion of patients who attend hospital eye services following referral will have a range of downstream effects. The number of patients receiving treatment for their more complex disorders will increase, improving treatment coverage, such as Cataract Surgical Coverage. This would be expected to reduce the burden of VI in the region, or at least slow the current increase. The magnitude of this effect would be measurable in future RAAB surveys.

There will be effects not only for the patients, but for the healthcare providers. This significant shift in caseload profile could necessitate changes to the provision of hospital eye services, to ensure hospital ophthalmologists are able to fulfill the new demand.

Strategies used

1. Digital data monitoring and visualization.

In this programme, a digital system was used to constantly monitor patient results and throughput, allowing identification of points at which patients were lost from the care pathway, and the effectiveness of attempts to improve patient retention, *via* iterative review.

2. Establishing and strengthening a referral pathway from community screening to primary and secondary/tertiary eye care.

Screening was undertaken in schools and the community, integrating screening services in Basic Health Units and schools. This was carried out by trained, non-specialist Lady Health Visitors and designated teachers in Sindh, and School Health and Nutrition Supervisors in Punjab. When necessary, patients were then referred directly to existing public health facilities, including optometrist services at Rural Health Centers and ophthalmologists at Tehsil Health Quarter hospitals with the goal of Integrated Person-Centered Eye Care, as recommended by the World Report on Vision (18).

3. Patient counseling and community education.

In this programme, screening was conducted in defined places and the contact information of participants was obtained and stored *via* secured and end-to-end encrypted software. Referral information could then be shared with community members or students' parents *via* text messages, and/or face-to-face interaction with local community health workers, such as social organizers and Lady Health Workers. For patients to attend hospital appointments, the perceived benefit of attending the appointment must outweigh the perceived costs and inconvenience of doing so. The likelihood of this can be increased by patient education regarding the purpose and importance of the appointment (19), and by support with any patient-specific difficulties in attending. Additionally, patient reminders can reduce the number of missed appointments resulting from patients simply forgetting (20), although the effectiveness of this has varied between programmes (21).

Lessons learned

The ease of data management provided by Peek software allowed constant monitoring of the points at which patients were being lost from the treatment pathway. This in turn allowed introduction of relatively simple modifications which could successfully target these dropout points (hospital referral). The modifications as discussed included raising community awareness, patient counseling, and appointment booking and reminders. The significance of distance from hospital was demonstrated, and the addition of fixed appointment functionality led to increased adherence in more distant sites.

Another significant finding was that the gender imbalance seen in patients accessing the programme, with high adherence among women, was the inverse of that which is normally seen, given established gender inequities in access to eye care (18, 22–24). These differences are compounded by reduced access to eye care for women in LMICs, influenced in some regions by reduced control of family finances and freedom to travel alone. These issues lead to significantly lower cataract surgical coverage in women (25, 26). As such, in order to tackle Sustainable Development Goal (SDG) 5—Gender Equality—it is important to monitor how a programme is reaching each gender, and take necessary measures to make it easier for all patients to access assessment and treatment. In this programme, women not only consisted of a noticeably higher proportion of the people who were screened, but also their adherence to the hospital appointments was as high as men. The higher utilization of community based mHealth programmes has been shown previously (4), which shows when programmes are delivered close to the households, gender equity is achievable.

Limitations

For optimal data collection, the RAAB surveys would have been completed prior to initiation of the Community Eye Health programmes. However, data were collected as part of a public health programme rather than a research study, and the intervention was not delayed for this purpose, so RAAB data was collected alongside the community programme.

Components of screening quality beyond true positive rates, including false negatives, could not be measured during these stages of screening and treatment. As more information is collected in future screening and follow up, a more in-depth assessment of screening will be possible.

There was a noticeable difference in adherence to referral between the two areas (Talagang/Chakwal and Matiari). It is important to acknowledge that in combining data from these two programmes, part of the improvement was due to higher adherence in the second programme from the offset. Various possible contributing factors have been suggested for this difference, including the second programme implementing lessons learnt from the first, e.g., optimal workflow with same day triage and referral, raising community awareness, and telephone appointment reminders. Shorter distance to referral site may also contribute to improved adherence in Matiari—most extremely demonstrated in centers where screeners, optometrists and ophthalmologists are all available in the same health facility.

We have reported our observation of the changes to healthcare provision during the pandemic. However, collection of data by the programme did not focus on analysis of the effects of COVID-19. The effect of the pandemic on healthcare seeking behavior and hospital attendance needs more investigation that was beyond the objectives of these programmes.

Contextual factors and generalisability

Peek CEH programmes have been designed to meet community eye health needs. In this paper we have described a successful example of implementation, scale-up and continuation of eye health programmes in different regions of Pakistan. These findings, which are consistent in two different programmes, are promising and in favor of an optimistic approach to eye health for Vision beyond 2020.

Previously, it has been shown that using digital capacities enhances the utilization of existing professional eye care resources compared to traditional, paper-based methods: in Kenya, attendance to the ophthalmology services following a school screening programme was significantly higher in the smartphone-based screening group than in paper-based conventional screening (54% vs. 22%) (2). In Iran, mHealth methods (using digital tests and smartphone connectivity capacities) were shown to improve both coverage of screening and adherence to referral compared to conventional means, particularly among people from lower socio-economic groups (4). Part of this effect is due to provision and visualization of real-time eye health and delivery data that enhances targeted resource management and uptake *via* connectivity capacities, and part of it is due to flexibility and mobility of small and cost-effective technology packages that improves reach to more vulnerable groups.

The COVID-19 global pandemic has introduced challenges to health systems all over the world. Simultaneous increased burdens on healthcare services resulting from COVID-19 patients, pressures to reduce inter-personal contact of patients and staff to limit disease transmission, and redistribution of staff, have led to a decrease in patients accessing healthcare, including eye care (27). A systematic review estimated a reduction in healthcare utilization of approximately one third during the pandemic (28). These reductions are thankfully lesser among more severe health conditions. To manage the changes, there has been a surge in the use of remote tele-health and technology-based/mHealth interventions (29, 30). These have included remote appointments (telephone and video call consultations) and virtual appointments in which patients attend a hospital for some tests, and management decisions are made without face-to-face consultations between the patient and doctor. Although tele-healthcare has been most easily implemented in HICs (31), it is perhaps most needed in the LMICs, where 8 out of 10 people with vision loss live, many of whom cannot access the eye care they need (32). In these eye care programmes, while a reduction in attendance was seen in the beginning of the pandemic in 2020, improvements were still achieved overall, exemplifying the potential for successful use of mHealth in a LMIC.

Conclusion

Our experience, particularly in the last three years in Pakistan programmes, shows that mHealth methods are relevant and have the potential to produce good results, even during a pandemic. The data provided highlighted programme-specific areas for improvement, such as adherence to hospital referral, and monitored the success of strategies used to tackle this. In addition, this work emphasized that continuity of eye health programmes is essential to produce better results over time, as programme teams can use ongoing evidence to constantly improve via scalable iterations.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical review and approval was not required for the programme on human participants in accordance with the Local Legislation and Institutional Requirements. Written informed consent from the participants' legal guardian/next of kin was not required to participate in this programme in accordance with the national legislation and the institutional requirements.

Author contributions

AB, AK, KT, ZA, SA, and NB contributed to conception, design, and implementation of the programmes. MK performed data analysis. EW and MK wrote the first draft of the manuscript. SA wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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Conflict of interest

The Peek Vision Foundation (09919543) is a registered charity in England and Wales (1165960) with a wholly owned trading subsidiary, Peek Vision Ltd. (09937174). AB is Chief Excecutive Officer (CEO) of The Peek Vision Foundation and Peek Vision Ltd. SA and NB are employees of Peek Vision Ltd. MK and EW are consultants for Peek Vision Ltd.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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REVIEW
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On AI Approaches for Promoting Maternal and Neonatal Health in Low Resource Settings: A Review

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A significant challenge for hospitals and medical practitioners in low- and middle-income nations is the lack of sufficient health care facilities for timely medical diagnosis of chronic and deadly diseases. Particularly, maternal and neonatal morbidity due to various non-communicable and nutrition related diseases is a serious public health issue that leads to several deaths every year. These diseases affecting either mother or child can be hospital-acquired, contracted during pregnancy or delivery, postpartum and even during child growth and development. Many of these conditions are challenging to detect at their early stages, which puts the patient at risk of developing severe conditions over time. Therefore, there is a need for early screening, detection and diagnosis, which could reduce maternal and neonatal mortality. With the advent of Artificial Intelligence (AI), digital technologies have emerged as practical assistive tools in different healthcare sectors but are still in their nascent stages when applied to maternal and neonatal health. This review article presents an in-depth examination of digital solutions proposed for maternal and neonatal healthcare in low resource settings and discusses the open problems as well as future research directions.

Keywords: maternal health, neonatal health, artificial intelligence, lower and middle income countries, machine learning, deep learning

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1. INTRODUCTION

Child and maternal health are key components of every country's growth. In the early 1990s, world leaders approved eight Millennium Development Goals (MDGs), including improving maternal health and reducing infant mortality by 2015. Between 1990 and 2015, the programme resulted in a decrease in the number of deaths of women and children; the mortality rate of children under the age of five reduced to half since 1990, and maternal mortality decreased by 45% globally. Even with these advancements, over 830 women and 7,400 babies die every day as a result of difficulties during pregnancy, childbirth, and the postnatal period, totaling an estimated 303,000 maternal and 2.87 million newborn deaths per year. An additional 2.6 million newborns lose their lives to stillbirths. A vast majority of these deaths happened in underdeveloped regions with limited resources, such as Africa and Southeast Asia. In 2015, the World Health Organization (WHO) proposed the Sustainable Development Goals (SDGs), a set of 17 objectives to be accomplished by 2030. The third SGD aims to ensure healthy lifestyles for all people on the planet, including a

reduction in maternal mortality to less than 70 deaths per 100,000 live births and neonatal mortality to less than 12 deaths per 1,000 live births (1).

Maternal health is concerned with the health of women throughout gestation, childbirth, and the postpartum period. It is not uncommon for women to experience health problems during pregnancy, however these difficulties can impact their health, baby's growth, or both. Women in good health prior to becoming pregnant can also have difficulties. Despite significant advancements in medicine, a high percentage of women still die during and following pregnancy due to a number of factors, including excessive blood loss, infection, high blood pressure, anemia and heart disease. The following are some of the most prevalent complications during gestation and the postpartum period; however, the list is not exhaustive (1).

1. High Blood Pressure: During pregnancy, often is the case of difficulty in the transportation of blood to various parts of the body due to swollen nerves or the arteries becoming too narrow, which causes high pressure in the arteries. This situation is also known as hypertension (HTN), making it difficult for the blood to reach the placenta and provide necessary nutrition to the fetus. It can result in a fetus with stunted growth and put the mother at an increased risk of premature delivery and preeclampsia.
2. Gestational Diabetes: Diabetes affects people of all ages and genders. It is not an infectious disease but surfaces in an insulin deficit individual. Studies have shown that diabetic women are more likely to experience miscarriage, renal failure, cardiovascular diseases, blindness, and other long-term and deadly illnesses (2). For this reason, it is critical to diagnose diabetes in pregnant women as soon as possible.
3. Infections Acquired during Pregnancy: During pregnancy, the immune system of the woman is at its lowest, and she can be exposed to a number of infections. These infections have the risk of spreading to the fetus as well.
4. Preterm Deliveries: Preterm deliveries can lead the infant to be born with many health issues as the final development of the brain along with the immune system takes place in the final term of the pregnancy.
5. Miscarriage or Loss of Fetus: Miscarriage is the condition in which the pregnancy is lost due to natural causes, and they occur very early in the period of pregnancy, having more than 20% of all pregnancies ending in miscarriages.

Ronsmans et al. (3) highlighted that in the most underdeveloped parts of the world, the risk of a woman dying due to pregnancy abnormalities or childbirth, is about one in six, and about one in 30,000 in developed countries. Such a significant gap between developed and underdeveloped countries has led to a failure to reach the goal of MDGs by the end of 2015. The main causes of having a low maternal mortality ratio are clustered around labor, delivery, and the immediate postpartum period, with obstetric hemorrhage, all of which are underestimated in low resource countries.

While maternal mortality has dropped globally, it remains high in low- and middle-income nations such as India, Pakistan, and Nigeria, where maternal health remains a major public health concern. According to the World Health Organization, in 2017, more than 2,95,000 women died both during pregnancy and childbirth. The majority of these maternal deaths can be prevented if a skilled professional is consulted in a timely manner. Reducing preventable deaths should remain a high priority for the global community.

Child health can be segregated into two parts: perinatal and neonatal. Perinatal health corresponds to health between the 22nd week of pregnancy (or gestation) and the seventh day following birth. The focus on ensuring good perinatal health is to supplement further neonatal development of the baby in the first month of life after birth. Proper care in these periods is essential to build a healthy foundation for the baby, which corresponds to a healthy childhood and adulthood. The neonatal period refers to the first few weeks of the infant after perinatal. These are the most developing weeks of its lifespan, and without access to proper care by healthcare providers such as neonatologists, pediatricians, family physicians, or nurse practitioners, many complications can arise, hampering the health of the baby. Premature birth, intrapartum problems, and infection are the leading causes of neonatal mortality worldwide. Some of the most significant problem statements related to neonatal health focused on by researchers are as follows:

1. Stillbirths: Stillbirth is a condition in which the fetus dies while it is inside the womb.
2. Intrapartum problems: Premature birth, low birth weight infants, fetal growth restriction, antenatal complications (e.g., anemia, eclampsia) and other factors during delivery (e.g., extended labor, umbilical cord prolapse) contribute to the development of neonatal health risks such as cerebral palsy, learning disabilities, and other abnormalities.
3. Infections: Infections affect people of all ages, but they are particularly risky in infants because their immune systems are still developing, and they are thus, more prone to diseases.

The postpartum period is when the mother and kid adjust to one other. During this time, the mother may experience anxiety, annoyance, and melancholy, which, in most circumstances, can lead to depression. Postpartum Depression (PPD) is a severe health issue which impacts not only the mother but the child and the entire family as well. However, it is common for such a disorder to go undiagnosed (4).

Most infant healthcare devices that support neonatal care are designed for high-resource settings and are either inaccessible or ineffective in low-resource settings. As a result, low-resource environments lack the instruments necessary to support high-quality, holistic infant care. There is an immediate need for newborn medical technologies that are cost-efficient, durable, effective, easy to use and maintain, and can run on a variety of power sources (5). Addressing these challenges requires a deep understanding of the kinds of complications that occur during pregnancy and the reasons for these complications. There is a need for further progress in the field of quick detection and treatment of maternal and newborn health issues in low-resource health centers and settings.

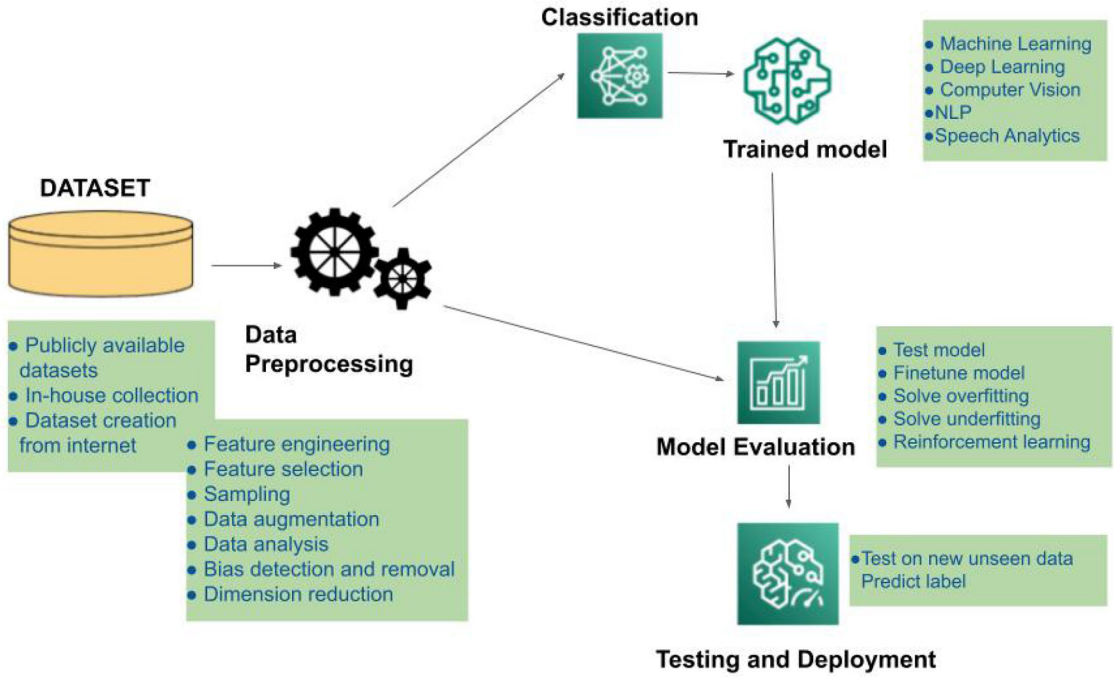

FIGURE 1 | Illustrating different states of an AI based system.

This article examines artificial intelligence-based strategies for developing approaches to improve maternal and neonatal health. Artificial intelligence is an area of computer science that aims to design/develop intelligent machines/models that imitate various aspects of human intellect. These models are capable of performing a variety of tasks, including learning, thinking, and planning, among others. To achieve this, there is a branch of AI called Machine Learning (ML) that consists of a set of tools and techniques for developing such intelligent algorithms. ML includes various methods including supervised (6, 7), unsupervised (8, 9), semi-supervised (10, 11), and reinforcement learning (12, 13).

The simplest approach of Machine learning involves using algorithms to evaluate and analyze the collected data and then applying the outcomes of that interpretation to make judgments and predictions about real-world occurrences. Machine learning, unlike conventional software programmes, analyzes large volumes of data to learn how to efficiently perform certain tasks. **Figure 1** illustrates the roadmap of an AI-based system in terms of data collection and preprocessing methodologies, model construction, training, evaluation, and real-world testing of the developed framework. Based on their individual learning and assessment methodologies, different types of input data can be processed in a variety of ways to provide the appropriate output. ML methods include supervised, semi-supervised, and unsupervised learning. These algorithms are categorized based on whether or not ground truth labels are available at the time of training. These algorithms can deal with small sample size situations (where the amount of data available is limited) by producing robust and dependable models.

AI based technologies have the potential to evaluate health record data, especially for situations where traditional statistical methods are ineffective. The algorithms are even better for large-scale and high-dimensional datasets. As a result, these algorithms may be utilized to tackle challenges including streamlining care pathways, standardizing medical assessment and diagnosis, discovering patient phenotype correlations, and generating predictive models (14).

1.1. Maternal Health Status in Low Resource Settings

Maternal health refers to the well-being of women during various phases, such as during pregnancy (antenatal care), childbirth, and the postpartum period. Taking care of women's health during these periods is crucial in lowering maternal mortality. Direct factors such as significant blood loss, high blood pressure, and obstructed labor or indirect complications such as anemia, depression, and heart disease are the leading causes of maternal death. Maternal mortality refers to the deaths due to pregnancy or while delivering an infant. As per WHO and Elsevier reference module in biomedical sciences, (15), the maternal mortality rate can be measured with the help of the following maternal mortality rate (MMR), which can be defined as the number of maternal deaths in a given time period divided by the number of live births (per 100,000 live births) during the same period:

$$MMR = \frac{number\ of\ maternal\ deaths}{number\ of\ live\ births} \times \frac{1}{100,000}$$

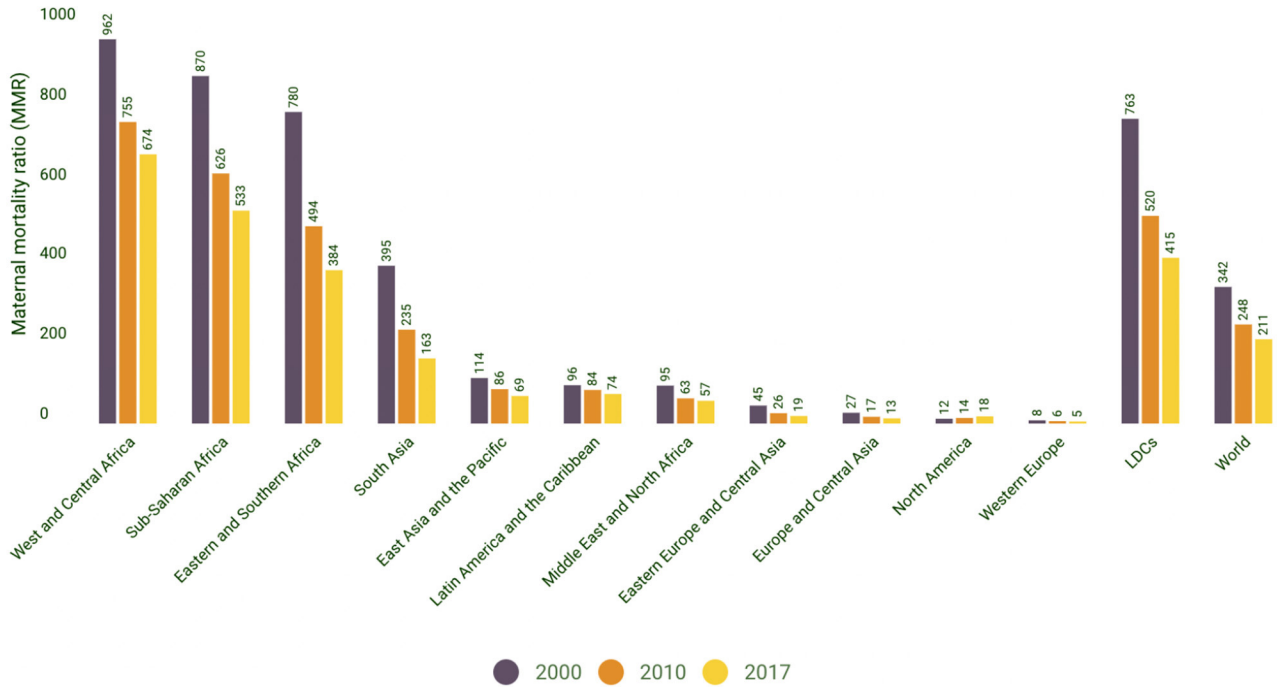

FIGURE 2 | Maternal mortality ratio (MMR) trends by region. Source: World Health Organization, UNICEF, United Nations Population Fund and the World Bank, Trends in Maternal Mortality: 2000–2017 WHO, Geneva, 2019. |UNICEF Data: Monitoring the situation of children and women.

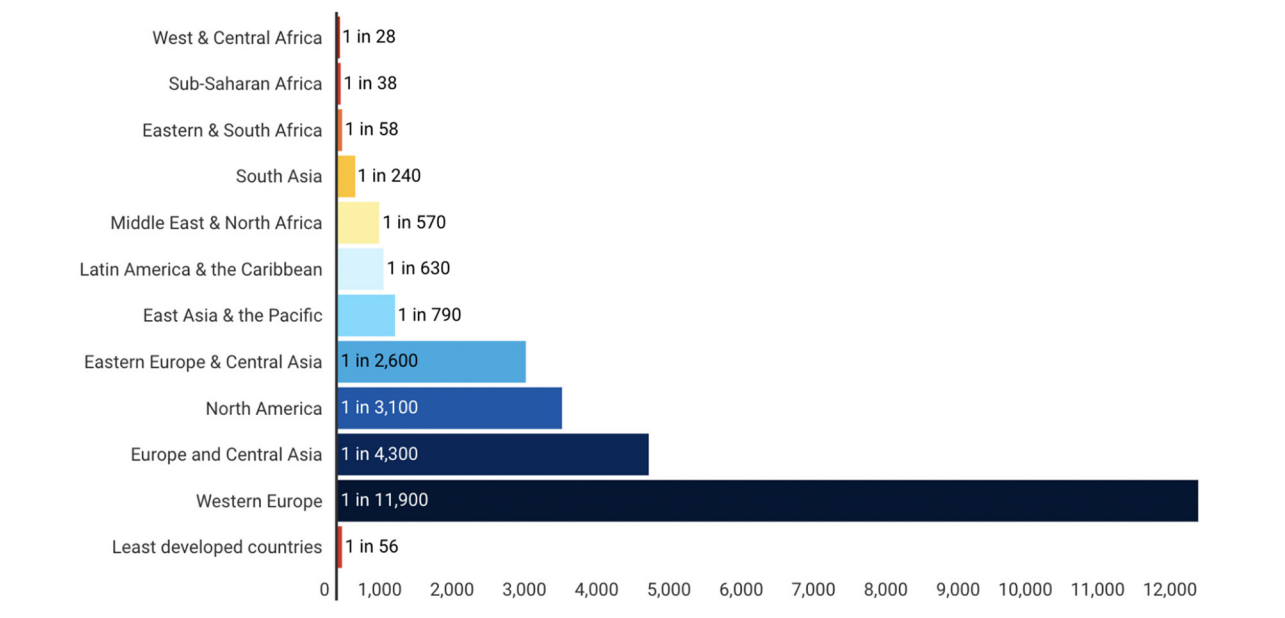

FIGURE 3 | Lifetime risk of maternal death: 1 in X, By region/group. Source: WHO, UNICEF, UNFPA and the World Bank, Trends in Maternal Mortality: 2000 to 2017, WHO, Geneva, 2019. |UNICEF Data: Monitoring the situation of children and women.

Figure 2 Shows the trends in MMRs across different regions in the world, indicating the highest Maternal Mortality ratios in low-income countries compared to very low MMRs in high-incomecountries.

Adult lifetime hazard of maternal mortality is defined as the probability that a 15-year-old female will die as a result of a maternal cause over her lifetime. Similar to trends in MMR, the Lifetime risk of maternal death by region/group as shown

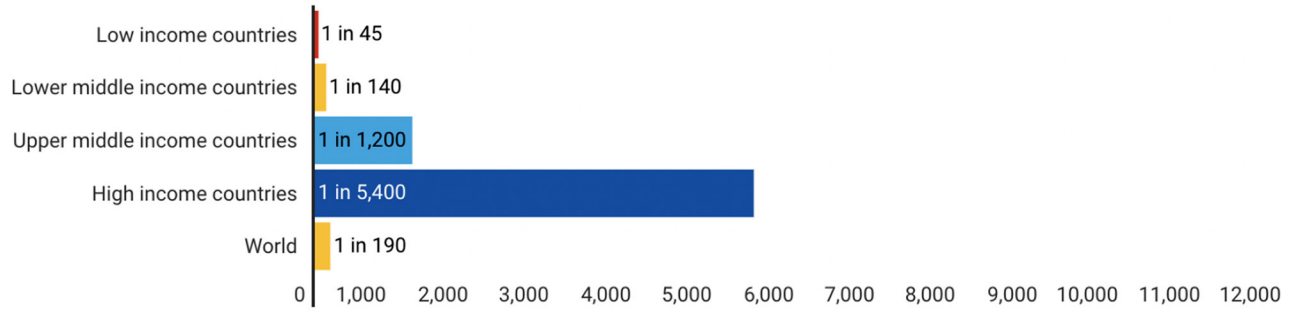

FIGURE 4 | Lifetime risk of maternal death: 1 in X, By income group. Source: WHO, UNICEF, UNFPA and the World Bank, Trends in Maternal Mortality: 2000 to 2017, WHO, Geneva, 2019. |UNICEF Data: Monitoring the situation of children and women.

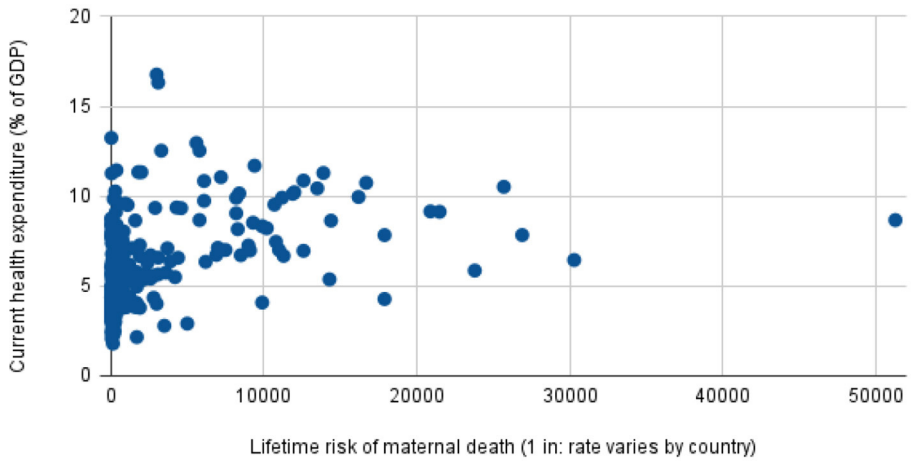

FIGURE 5 | Current health expenditure (% of GDP), by Lifetime risk of maternal death (1 in: rate varies by country) Source: World Bank Data:Current health expenditure (% of GDP), Trends in Maternal Mortality.

in **Figure 3** indicates that women living in countries with low-resource public health countries face a higher risk of maternal death in their lifetime. This is even substantiated by **Figure 4** which further establishes that low and lower-middle-income countries have a significantly high lifetime risk of maternal death. When contrasted with the current health expenditure in health by each country as defined by their GDP, we can although observe in **Figure 5** that countries' health expenditure seems not positively or negatively correlated to the lifetime risk of maternal death.

Special testing during pregnancy is required when there is a higher risk of complications. These are usually started between 32 and 34 weeks of pregnancy; however, they can be done sooner if there are many risk factors present such as (i) high-risk pregnancy where the woman has a pre-existing health condition such as cardiac disease or diabetes, (ii) fetal growth problems, (iii) reduced fetal movement, and post-term delivery. The non-stress test, biophysical profile (Fetal heart rate, breathing movements, body movements, amount of amniotic fluid), fetal movement counts, and a Doppler ultrasound check of the umbilical artery are all used to monitor fetal health.

1.2. Child Health Status in Low Resource Settings

Neonatal health care is necessary for both categories of childbirths, the mature and the premature. A premature baby is a baby born before 37 weeks of pregnancy. However, high infant mortality rates in low-resource settings are caused by a lack of access to and under-utilization of efficient health systems, which is exacerbated by a plethora of variables such as disparities in coverage, scarce human resources and infrastructure, consultation information, and community/public health systems.

Neonatal mortality is frequently used as a metric for a core indicator of neonatal health and well-being and is a significant component of overall under-five mortality, as it is defined as death occurring within the first 28 days of life. UNICEF (16) study demonstrates that a poor nation has a higher neonatal death rate than a developed country. Numerous studies have been conducted in this area to determine the factors that contribute to neonatal mortality, including septicaemia, respiratory distress syndrome, premature births, low birth weight, low APGAR (Appearance, Pulse, Grimace, Activity, and Respiration) scores (a quantitative score to measure

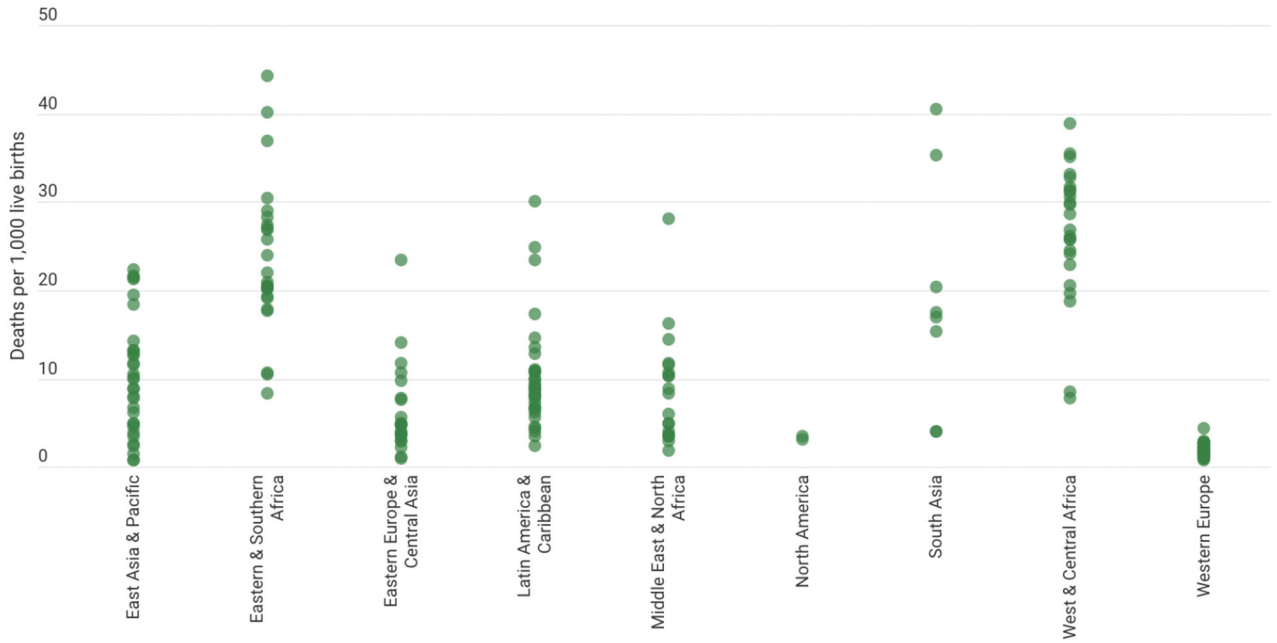

FIGURE 6 | Neonatal mortality rates, by country and region, 2020. Source: United Nations Inter-agency Group for Child Mortality Estimation (UN IGME), 2021|UNICEF Data: Monitoring the situation of children and women.

TABLE 1 | Top 10 countries with the highest number of neonatal deaths, 2020.

Country	Number of newborn deaths in thousands (90% uncertainty interval)
India	490 (425–558)
Nigeria	271 (199–374)
Pakistan	244 (198–298)
Ethiopia	97 (77–123)
Democratic Republic of the Congo	96 (56–163)
China	56 (49–64)
Indonesia	56 (45–70)
Bangladesh	51 (45–57)
Afghanistan	43 (32–55)
United republic of tanzania	43 (30–62)

Source: WHO-Fact Sheets, Neonatal Mortality.

newborn resilience), low socioeconomic status, cesarean section (C-section) delivery, and neonatal age at admission (17). **Figure 6** depicts the disparities in Neonatal Mortality Rates by country and region, highlighting that children born in South Asia and Saharan Africa are most susceptible to illness and mortality in their first month in comparison to any other child born in a high-income, high-resource region/countries. Expanding on the same viewpoint, **Table 1** lists the names of the 10 countries with the highest infant mortality rate, with India having the highest number of newborn deaths in the world.

These statistics indicate an alarming need for interventions to address this issue to alleviate the current status and promote health and nutrition in children, as years later, these would be the driving generation of the country. To overcome these issues, novel and innovative techniques involving the utilization of relevant digital technology are required.

The rest of the article is structured as follows: Section 2 discusses the role of AI in maternal health, including maternal health monitoring, risks of preterm deliveries and miscarriages, gestational diabetes, complications in females with congenital cardiac diseases, gestational anemia, and postpartum depression. Section 3 discusses the role of AI in neonatal health, including pain assessment, sepsis prediction, neonatal jaundice, and machine learning algorithms for tracking malnutrition. Section 4 discusses the path forward, including economic, societal, and technological barriers, and finally, the summary of the article is given in Section 5.

2. ROLE OF AI IN MATERNAL HEALTH

This section reviews the literature on the use of AI to monitor and improve the health of the mother during various phases of pregnancy, childbirth, and postpartum. Timely management of various maternal health issues, including preterm deliveries, miscarriages, gestational diabetes, heart diseases, and postpartum depression, can help in reducing maternal mortality. The main areas of focus for this section are shown in **Figure 7**.

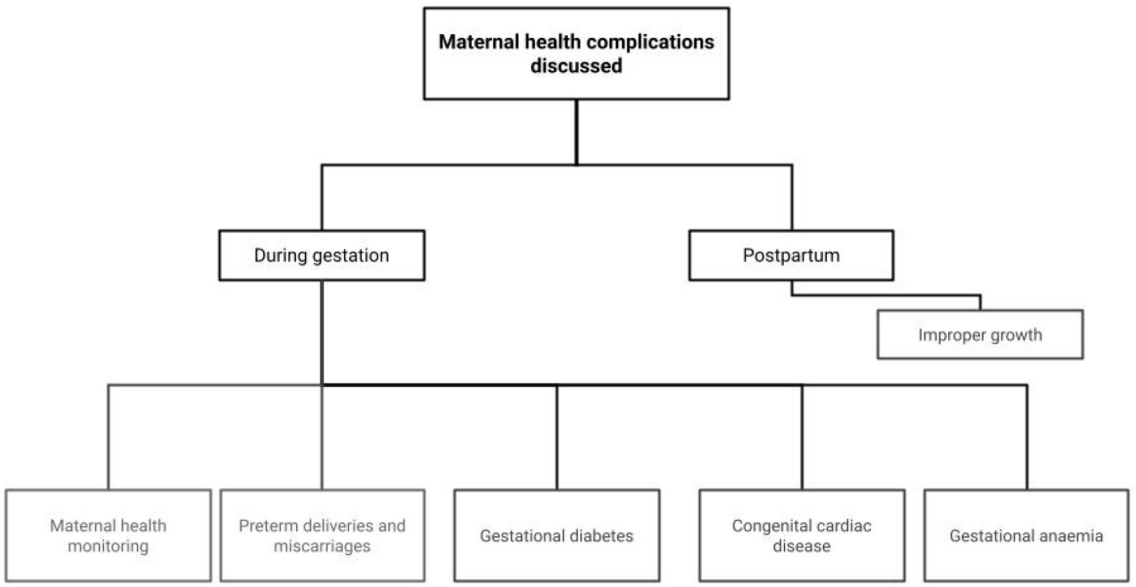

FIGURE 7 | Focus areas on role of AI in complimenting maternal health.

2.1. Maternal Health Monitoring

Maintaining optimum maternal health is vital for the proper growth and development of the fetus. While the mother undergoes several changes during the pregnancy, it is important to monitor maternal health for the signs and symptoms that may indicate a disruption in normal sustenance and functioning of the mother or the fetus. Often during pregnancy, the transportation of blood to all body parts becomes constricted due to swollen nerves or the arteries becoming too narrow, which causes a lot of pressure in the arteries. This situation is also known as hypertension (HTN), which makes it difficult for the blood to reach the placenta and provide necessary nutrition to the fetus. This can cause stunted growth of the fetus and place the mother at greater risk of preterm labor and pre-eclampsia. During pregnancy, the immune system of the woman is also at her lowest, and she is exposed to a number of infections and conditions; and if proper care is not taken, it can even affect the fetus as well. Many of these conditions can be prevented or treated with appropriate pre-pregnancy, prenatal, and postpartum follow-up care (18).

With the widespread adoption of Internet of Things (IoT) technology, building smart IoT devices to support maternal health began to gain traction. **Table 2** summarizes some of these approaches. Li et al. (19) presented an IoT platform with wearable technology, cloud computing, and other innovations. They also explored its usage for surveillance and management techniques for gynecology departments in hospitals and homes. The smart maternal platform promises to reduce medical staff workload, raise overall productivity, make things easier for expectant mothers to see doctors, and enhance obstetrical treatment and follow-ups. The results from the questionnaire were analyzed using SPSS statistical software while the use of wearable IoT devices for women during pregnancy is assessed using the chi-square analysis. The p-value compares the experimental and control groups and comes out to be less than 0.05 showing statistical significance. Tracing a similar path, a machine learning approach for predicting foetal wellbeing is suggested through an e-Health application in work done by Akbulut et al. (20) The suggested model was trained using a dataset collected from 96 expectant mothers. Nine binary classification models were trained, validated, and analyzed to forecast overall foetal health. The Random decision Forest (RF) model had the highest accuracy (89.5%), F1-Score (75%), and AUC (Area under the ROC Curve) (95%). In real-world testing, 87% of the consumers performed well. This estimate is adequate to assess foetal health prior to a doctor's appointment.

2.2. Predicting Risks of Preterm Deliveries and Miscarriages

The gestation period is the time span between conception and birth. Throughout this time, the baby develops and grows inside the mother's womb. Gestational age is a word that is widely used during pregnancy to refer to the stage of pregnancy. It is calculated in weeks, beginning with the first day of the woman's last menstrual cycle and ending with the current date. Pregnancy typically lasts 38–42 weeks.

Premature babies are those born prior to the 37th week of pregnancy. Postmature babies are those born after 42 weeks. Preeclampsia is a condition in which a pregnant woman is in danger of preterm delivery and death. Such deliveries are a major issue in underdeveloped countries, mostly due to a lack of timely professional care and awareness of such practices and complications. Therefore, ML/AI-based systems are required, which can be built with training on the obstetrical data (21).

TABLE 2 | Smart devices and applications based maternal health monitoring.

References	Summary	Key contribution	Dataset used
Li et al. (19)	Building Smart IoT devices to compliment Maternal health.	A novel IoT framework for smart maternity care leveraging wearable devices and essential technologies along with applications, monitoring and administration modes in-home obstetrics departments. Comprehensive review of the challenges and opportunities in the employment of such frameworks as well as their level of acceptance in the current scenario.	Questionnaire dataset from 315 Chinese participants belonging to 27 provinces. No general obstetrics, gynecology, or other general medical histories relating to prenatal treatment were screened out
Akbulut et al. (20)	The authors suggest an e-Health application with a machine learning algorithm for predicting foetal health.	Pregnant women and physicians can get help from an online assistive system and a prediction system. The impact of specific clinical data parameters of pregnant women on foetal health status was statistically connected with the presence of congenital diseases, and advice for future research were provided.	The suggested model was trained on data from 96 pregnant women. The data came from a maternity questionnaire and three clinical examinations at the RadyoEmar radiodiagnostics facility in Istanbul, Turkey.

It has been shown in several studies that AI can be used to detect if there is a chance of getting preeclampsia to a very high degree of certainty. However, the current models are only working at high accuracy for early-onset and not post-onset, which has a higher occurrence rate; therefore, there is a requirement for a prediction model with a low false-positive rate and economically feasible predictors that have a higher sensitivity while maintaining the same specificity as others with low-cost predictors (22).

Miscarriage is the condition in which the pregnancy is lost due to natural causes, and they occur very early in the period of pregnancy, having more than 20% of all pregnancies ending in miscarriages. A miscarriage occurs when a fetus dies naturally before the 20th week of pregnancy. The word "stillbirth" refers to the fetus' death after this period. Although there has been a drastic improvement in prenatal care over the years, however, the reality is stillbirths still happen and often go unexplained. With the advent of AI in healthcare, it is possible to identify nearly half of stillbirths antenatally using a combination of existing pregnancy problems, congenital defects, maternal features, and medical history. When compared to logistic regression (LR), ensemble classifiers provided a slight improvement in prediction (23). The importance of addressing the issue of preterm births lies in the impact of such conditions on the family. Both parents may be affected by a miscarriage, and it is impossible to change the result of the pregnancy. Thus, detecting such conditions is very important yet difficult for a novice health worker and requires extra attention from a trained doctor. Miscarriage may only be dealt with by taking particular precautions and preventing it. However, machine learning-based models have made it easier to detect early signs of miscarriages based on time-lapse images of pre-implantation development (24). Preventing premature delivery and detecting preterm labor certainly have significant health and economic implications. Although most efforts have been focused on reducing the impacts of preterm delivery, researchers have also made efforts to predict the risk of preterm birth in pregnant women using machine learning approaches on specific sample signatures. **Table 3** summarizes the approaches employing AI in predicting the risk of preterm deliveries.

One such diagnostic/prognostic study conducted by Jehan et al. (30) involved using a machine learning model to predict preterm deliveries using the proteomic and metabolomic characterization of blood and urine samples collected from 81 pregnant women belonging to 5 distinct birth cohorts. The study established a link between omics data and the prediction of preterm deliveries, which is crucial for further research into the said area. The study involved the use of plasma samples analyzed for proteins and untargeted RNA profiling, along with urine samples analyzed for metabolites. The Preterm Birth (PTB) characteristic was described as childbirth before the 37th week of pregnancy. Out of the 81 pregnant women, 39 of them had PTBs (48.1%), and 42 of them had term pregnancies (51.9%). Univariate analysis revealed functional biological differences between the five groups. Each biological data set was subjected to a group-adjusted machine learning method, and the findings were subsequently merged into a final integrated framework. When compared to the models developed for each individual biological modality, the integrated model showed more accuracy and area under the receiver operating characteristic curve (AUROC) of 0.83 (95% CI, 0.72-0.91) than the transcriptomics, metabolomics or proteomics model. The main features of PTB were an inflammatory module and a metabolomic module evaluated in urine that was linked to the metabolism of glutamine, glutamate, and valine, as well as the biosynthesis of valine, leucine, and isoleucine. Preterm birth prediction models have traditionally concentrated on early preterm (28–32 weeks) and intermediate to delayed preterm (32–37 weeks). The bulk of newborn deaths is caused by extreme preterm birth (EPB), which occurs before the 28th week of pregnancy. Gao et al. (29) did a study to address the problem statement and found that EPB can be predicted using deep learning techniques that take into account temporal relationships. It was highlighted that individual predictive models could not outperform ensemble models in performance.

Another such work done by Fergus et al. (25) explores the application of Electrohysterography (EHG) techniques to predict preterm deliveries. The study was based on designing a supervised learning model upon an open-source dataset consisting of 300 EHG records of term and preterm

TABLE 3 | Summary of approaches used to predict risk of preterm deliveries.

References	Summary	Key contribution	Dataset used
Fergus et al. (25)	Use of Electrohysterography (the analysis of uterine electrical signals) for diagnosing actual labor and predicting premature birth	Unlike previous works in this domain that focus only on detecting true labor using EHG near the days of delivery, this study uses EHG to even predict term and preterm delivery in early pregnancy	Term-Preterm EHG containing 300 records (38 preterm and 262 term)
Hussain et al. (26)	EHG signals are used to detect preterm births with a novel algorithm	The authors describe a unique dynamic self-organized network immune algorithm for categorizing term and preterm records. The article focuses on boosting sensitivity rates, as forecasting preterm delivery is more crucial than misclassifying a term pregnancy	Term-Preterm EHG
Fergus et al. (27)	Proposed a novel self-organized network immune algorithm that classifies term and preterm records	New electromyography features and feature ranking approaches were used to assess their discriminative powers in detecting term and preterm pregnancies. A comparison of seven different neural networks is performed	Term-Preterm EHG
Despotovic et al. (28)	This study investigates the feasibility of predicting preterm birth from EHG recordings made between the 22nd and 25th week of pregnancy	EHG signals based preterm birth prediction using novel features utilising signal's non-stationarity	Term-Preterm EHG
Gao et al. (29)	Deep learning techniques based Extreme preterm delivery(EPD i.e before the 28th week of pregnancy) prediction	Showed that deep learning algorithms could predict extreme preterm birth (EPB) with the help of temporal relationships in electronic health records (EHRs)	Electronic health records
Jehan et al. (30)	Predicting preterm deliveries using the proteomic and metabolomic characteristics	Established a link between omics data and the prediction of preterm deliveries. Provided a method to predict preterm deliveries in early pregnancy (median gestational age of 13.6 weeks as determined by ultrasonography). PTB prediction accuracy was increased by the use of different omics data sets, implying that PTB is a condition that presents in a variety of biological systems	Blood and urine samples collected from 81 pregnant women. The data was examined from December 2018 to July 2019

deliveries (31). Using the polynomial classifier, the said approach outperforms previous results, with 96% sensitivity, 90% specificity, and a 95% AUC value with an 8% global error. The results obtained were suggestive of the positive potential of EHG signals in classifying term and preterm pregnancies. More future work in more comprehensively collected datasets was suggested in the conclusion of the research work. Similar studies done on the same Physionet dataset (Term-Preterm EHG) by Fergus et al. (27), Hussain et al. (26) and Despotovic et al. (28) individually explore the application of EHG signals combined with additional features which further improved the performance over shorter time length EHG signals of the suggested models.

2.3. Predicting Gestational Diabetes

Diabetes affects people of all ages and genders. It is not an infectious disease but surfaces in an insulin deficit individual. However, it negatively impacts essential organs that it is known as the "mother of all ailments." Diabetes has more significant implications for women due to their shorter lifespan and poor quality of life. As investigated by World Health Organization (WHO) data, several females with diabetes aren't even aware of being diabetic. Even in high-income countries, gestational diabetes tends to impact about 5–7% of pregnancies (32, 33). In India itself, over 5 million women are affected annually by gestational diabetes, and the rate of such incidences has increased over the decade (34). Gestational diabetes also tends to show increased prevalence across specific ethnicities and racial subgroups (35, 36). This condition can be inherited, especially if the mother is diabetic at the time of being pregnant. Diabetic women are more likely to experience miscarriage, renal failure, cardiovascular diseases, blindness, and other long-term and deadly illnesses (2). For this reason, it is critical to diagnose diabetes in pregnant women as soon as possible.

Gestational diabetes affects pregnant women when the pancreas are unable to produce enough insulin. For a decade, it has been one of the top challenges for ML researchers to identify and diagnose diabetes. For the same purpose, many different algorithms have been employed to date to serve the application (37), ranging from classical machine learning (38–41) to deep learning methods (42, 43). Many researchers also came up with custom methods for diabetes prediction (44, 45).

It was thus established that AI could be used in order to detect Gestational diabetes in pregnant women as early as the first trimester. With the help of variables such as age, family history of diabetes in a first-degree relative, multiple pregnancies, previous gestational diabetes history, fasting plasma glucose, HbA1c, triglycerides, and other laboratory indexes during the first trimester can be used to build a neural network-based model for detecting early signs of gestational diabetes. **Table 4** summarizes some of the AI-based approaches for predicting

TABLE 4 | Summary of approaches used to predict risk of gestational diabetes.

References	Summary	Key Contribution	Dataset used
Debata and Mohapatra (46)	Diabetes diagnosis in pregnant women utilizing a hybridized chaotic-jaya extreme learning machine model	Model achieved a sensitivity of 1 and specificity of 0.9688 which helps to classify both positive and negative classes with exceptional accuracy	Pima Indian diabetes dataset All cases here are females above the age of 21 who are of Pima Indian ancestry. One target variable, Outcome, is included in the datasets. The patient's BMI, insulin level, age, and previous pregnancies are all predictor variables.
Araya et al. (47)	Using machine learning; this study sought to see if there was a link between the maternal thyroid profile and gestational diabetes throughout the first and second trimesters	Found correlation between thyroidal patterns and Gestational Diabetes	Anthropometric and clinical variables of Thirty-nine pregnant women from Concepcion (Chile). The study has analyzed data of subjects from 12 to 28 weeks of pregnancy
Eleftheriades et al. (48)	Prospective cohort analysis to create a predictive machine learning-based model for insulin therapy in GDM women	Demonstrated that we could accurately anticipate the requirement for insulin treatment based on maternal factors such as BMI and the results of an Oral Glucose Tolerance Test (OGTT). Showed insulin therapy is required by 15-30% of women with Gestational Diabetes Mellitus (GDM). Women who are overweight and have a fasting blood glucose of 98 mg/dl or higher need to be closely monitored and exercise more	775 female patients with GDM according to the IADPSG criteria
Liu et al. (49)	Population-based prospective cohort study to construct a gestational diabetes prediction model	Demonstrated that lifestyle adjustments can significantly reduce the risk of gestational diabetes mellitus prior to the 15th week of pregnancy. The XGBoost approach does not necessitate meticulous data cleaning or preparation, such as exception scaling and collinearity	19,331 pregnant Chinese women with gestational age less than 15 weeks

gestational diabetes. For diabetes prediction in pregnant women, Debata and Mohapatra (46) conducted a study. They designed a machine learning model utilizing Chaotic-Jaya (CJaya) algorithm and Extreme Learning Machine (ELM) and trained it on the Pima Indian diabetes dataset. The hybrid approach was named as CJaya-ELM model. The proposed CJaya-ELM model achieved the greatest accuracy of 96.87%, sensitivity of 1, area under the curve (AUC) value of 0.9782 and specificity of 0.9688. The results indicate that the CJaya-ELM model successfully classifies both positive and negative samples from the Pima dataset and outperforms other models such as basic and other modifications ELM, Multi-Layer Perceptron (MLP), CJaya algorithm and Teaching Learning Based Optimization algorithm (TLBO). Another study conducted by Araya et al. (47) used principal component analysis (PCA) on a dataset obtained from 39 pregnant mothers in Concepcion(Chile); the authors found a link between specific thyroidal hormone signatures and Gestational Diabetes. Despite the exploratory nature of these findings and the limited sample size, the correlation is strong enough to predict future behavior. To improve gestational diabetes diagnosis, a multivariate analysis on a larger dataset can be used. Diagnosis of pregnant females with Gestational Diabetes Mellitus (GDM) who need insulin therapy may change their treatment to include more regular monitoring and perhaps preventive services. The goal of a prospective cohort analysis done by Eleftheriades et al. (48) was to create a predictive machine learning-based model for insulin therapy in GDM women. The Classification and Regression Trees (CART) machine learning technique was used to evaluate data from 775 female patients with GDM according to the IADPSG criteria. This basic model demonstrated that we could accurately anticipate the requirement for insulin treatment based on maternal factors such as BMI and the results of an Oral Glucose Tolerance Test (OGTT). Women who are overweight and have an abnormal OGTT initial blood glucose level are more likely to develop gestational diabetes. The prediction model's AUC score for internal and external validation was 0.74 and 0.77, respectively. Another population-based prospective cohort study on a similar subject conducted by Liu et al. (49) intended to construct a prediction model using a dataset collected from 19,331 Chinese women who are pregnant. The risk indicators obtained during registration as pre-pregnancy BMI, maternal age, fasting plasma glucose at the time of registration, and alanine aminotransferase concentration were evaluated and used to build the machine learning model based on the eXtreme Gradient Boosting (XGBoost) approach. Compared with conventional methods like logistic regression, The XGBoost model outperformed the approach in terms of performance with a higher AUR score (0.742 vs. 0.663, $p < 0.001$).

2.4. Predicting Development of Complications in Females Suffering With Congenital Cardiac Disease

Females with congenital cardiac disease are characterized to be at a higher risk of experiencing adverse medical conditions during pregnancy. As a result, Chu et al. (50) conducted a

TABLE 5 | Summary of approaches used to predict risk of complications in women with congenital cardiac disease.

References	Summary	Key contribution	Dataset used
Chu et al. (50)	Two Machine learning-based prenatal risk prediction models were developed for both unfavourable maternal and newborn outcomes, which could help clinicians adapt precise care and treatment in pregnant women with congenital heart defects	Well suited model for prenatal counseling and pregnancy monitoring in low resource settings. The Maternal model has seven high-risk factors: NYHA class, Eisenmenger syndrome, pulmonary hypertension, left ventricular ejection fraction, sinus tachycardia, arterial blood oxygen saturation, and gestation duration. Eisenmenger syndrome, preeclampsia, and arterial blood oxygen saturation were revealed as high-risk indicators in the newborn model	213 patients at Shandong University's Qilu Hospital who gave birth after 28 weeks of pregnancy

TABLE 6 | Summary of approaches used to predict gestational anemia.

References	Summary	Key Contribution	Dataset used
Anggraeni and Fatoni (51)	Early detection of anemia during gestation	Development of a Non-invasive self-diagnostic technique. Use of smartphone camera-based prediction suitable for low-resource settings. More objective detection compared to contemporary visual assessment of anemia	Blood samples and palpebral image of 20 pregnant women between the age of 20–36 years with blood types A, B, AB, and O

retrospective analysis to develop two machine learning-based prediction models for mothers and their children, which could help physicians adapt special care and therapy for expecting women suffering from congenital cardiac diseases. The summary, key contribution and the dataset details of this approach are given in **Table 5**. Such models are particularly well-suited for clinical usage in developing nations, where there is a lack of prenatal counseling and pregnancy monitoring infrastructures. The study included 213 patients falling within the criteria of study who delivered birth after 7 months of pregnancy at Shandong University's Qilu Hospital in China. Univariate and multivariate logistic regression analysis was employed for developing risk prediction algorithms for women and infants. The authors also created two nomogram lists for each patient to forecast the specific risk of complications. The developed models showed high accuracy (76–86% in maternal model and 75% to 80% in neonatal model), implying that they are clinically employable and highlight a substantial correlation between high factors and unfavorable maternal and newborn outcomes.

2.5. Predicting Gestational Anemia

Anemia is related to impaired cognitive and motor development in children and adults, hence affecting the economic growth of countries. Anemia during pregnancy is also connected with unfavorable reproductive outcomes, including preterm birth, low birth weight infants, and diminished iron storage for the newborn, which may result in impaired development. Failure to address anemia may impact the health and quality of life of millions of women, as well as the development and learning of children, and thus, it is important to develop more technologies for timely diagnosis and monitoring of gestational anemia. **Table 6** summarizes some of the approaches that help in predicting gestational anemia.

A study based in Indonesia by Anggraeni and Fatoni (51) explores early detection of anemia during gestation in order to reduce the cases of postpartum hemorrhage. The study aims to build a non-invasive self-care anemia diagnosis system employing a smartphone camera for palpebral color monitoring. The color intensity RGB signals were then quantified with the Colorgrab software (Loomatix) and correlated with the hemoglobin concentration of the specimens, whose standard hemoglobin concentration was determined using the conventional Spectrophotometer method. A high correlation of red color intensity was shown with the help of linear regression. This exploratory investigation could be seen as an early detection method for anemia, as it is claimed to be more objective than the conventional ocular examination.

Ren et al. (52) further highlighted the fact that machine learning methods outperform standard logistic regression models (2018), which extended the use of machine learning to birth outcomes and air quality studies. In two ML-based models, a pregnant mother's exposure to PM10 was recognized as the most potential risk factor for Congenital heart defects. Their models consistently showed that exposure to fine particulate matter raises the chance of congenital cardiac abnormalities in children.

2.6. Predicting Postpartum Depression (PPD) and Anxiety

Various complications of pregnancy also cause women to have anxiety and depression attacks, resulting in a stressful scenario for both the mother and the newborn. Due to a shortage of licensed health practitioners, the mental health system faces a clear capacity restriction. Only three people with mental health concerns have secure access to the system for every ten people (53).

TABLE 7 | Summary of approaches used to predict postpartum depression using machine learning.

References	Summary	Key Contribution	Dataset used
Tortajada et al. (57)	An approach to predict PPD using MLP where the authors have used geometric mean while calculating accuracy	To predict the PPD during the first 32 weeks following childbirthUsed pruning methods to identify the influence of each of the variable on the model performance	Collected data of 1,397 women from 7 Spanish hospitals
Sword et al. (58)	Studied the relationship between mode of delivery and PPD	This study concluded that there is no association between mode of delivery and PPD In addition to common PPD indicators, this work identified more indicators such as unmet learning needs, maternal readmission to hospital, and urinary incontinence.	Collected data of 2,560 women having age >= 16 years from 11 hospitals in Ontario, Canada
Jimenez et al. (59)	An approach to detect the risk of PPD during the first week postpartum by employing socioeconomic, psychiatric, and easy-to-answer questionnaires as variables	This work presents a questionnaire-based clinical decision system to classify the women suffering from PPD This app can be used by both clinicians and the females who had just given birth	Collected data of 1,397 women from 7 Spanish hospitals during an 11-month period
Natarajan et al. (60)	used functional gradient boosting methods to predict PPD using non-clinical data	Identified the features that help in early prediction of PPD ML algorithms have the potential to predict the women suffering from or are at the risk of developing PPD	Facebook groups and Twitter
Fatima et al. (61)	Proposed a generalized approach for the PPD using data from social media text	Studied the relationship of posts (textual features) with the PPD and with general depression This study has limited applicability as the dataset is not complete in terms of not being sure about the participants who took part are actually suffering from PPD	Posts from Reddit
Shin et al. (62)	Studied the effects of nine ML algorithms to predict the PPD	Evaluated various machine learning algorithms and found that RF achieves highest accuracy for the task of predicting PPD Handled the data imbalance problem that makes the models robust	Data from PRAMS (Pregnancy Risk Assessment Monitoring System)
Betts et al. (63)	Proposed an approach to identify the women at risk of postpartum psychiatric admission	Explored how big data can be used with ML algorithms for this task. This can help the clinicians to predict the women at risk of developing PPD	Administrative health data
Zhang et al. (64)	Proposed an approach to detect PPD during pregnancy	Using routinely gathered EHR data, this approach can assist doctors in identifying women who are at risk of developing PPD. This model identifies comorbid indicators such as palpitations, hypertensive disorders vomiting during pregnancy, diarrhea and hypothyroidism which can be associated with PPD	Two electronic health records each containing data of 15,197 and 53,972 women, respectively
Andersson et al. (65)	Evaluated a range of ML methods to predict PPD	Extremely randomized trees were able to achieve a well-balanced specificity (75%) and sensitivity (72%), making the prediction model more robust to be used in addition to clinical method Studied the subgroups with previous depression history (before or during pregnancy) in predicting the PPD	Data is obtained from "Biology, Affect, Stress, Imaging and Cognition (BASIC) cohort study conducted at Uppsala University Hospital, Sweden.

As per the current trends, pregnant women can easily be diagnosed with depression with the help of AI models based on just the voice of the women. According to the study conducted in Borders (54), 87% to 94% of US women report at least one health problem immediate postpartum period, including depression and anxiety, and in the second category (anxiety), the usual response of women is encountered with stress. According to Fisher et al. (55), PPD affects 10-15% of women worldwide, with the number rising to 18% - 25% in low- and middle-income nations. The greater rate is due to the population's cultural and traditional traits (56). There are methods for PPD screening that are accessible; however, they are largely intended for patients who are already having depressive symptoms. Research should focus on developing methods for predicting the risk of developing PPD in people who don't show any signs of depression. To keep moving in this direction, researchers take into consideration a variety of characteristics as well as clinical factors when predicting the risk of developing PPD. **Table 7** summarizes the approaches that employ AI while proposing approaches to predict PPD.

Tortajada et al. (57) devised a method for predicting PPD based on MLP. The authors employed four models and calculated the geometric mean of accuracy to assess model performance. The authors came to the conclusion that the models may predict PPD in the first 32 weeks after childbirth. The model was able to achieve an accuracy of 81%. Fatima et al. (61) conducted a similar study to predict PPD using social media text. The authors showed that Multi-layer Perceptron (MLP) outperformed Support Vector Machine (SVM) and Logistic Regression (LR) in prediction when using

a hold-out validation technique by achieving an accuracy of 81%.

Jimenez et al. (59) have presented a method for predicting PPD during the first week following childbirth. In this study, the authors employed socioeconomic, psychiatric, and easy-to-answer questionnaires as variables. A number of classifiers were used for classification, including Naive Bayes (NB), Linear Regression (LR), Support Vector Machine (SVM) and Artificial Neural Network (ANN), with NB outperforming the others. Furthermore, the authors have created an app that includes a questionnaire that can be completed by patients or physicians who want to keep track of their patients. The approach gives an adequate level of sensitivity and specificity (both close to 0.73), and is also simple to interpret, according to the findings of the experiments.

Zhang et al. (64) have studied the risk of developing PPD among pregnant women. Various features, including the patient's demographic, mental health history, obstetric complications and many more, are used in this work. The authors used a sequential forward selection strategy to find the best set of traits. Grid search was used to identify hyperparameters for the predictors, including Random Forests (RF), Decision Trees (DT), XGBoost, regularized LR, and MLP. The proposed approach achieved an AUC of 0.937 (95% CI 0.912–0.962) and 0.886 (95% CI 0.879–0.893) in the development and validation sets. Experimental analysis demonstrates that this approach can reduce the burden of identifying the risk of PPD.

Natarajan et al. (60) have proposed using functional gradient boosting methods to predict PPD using non-clinical data. The authors have used various classifiers and calculated various performance metrics such as ROC, precision, recall and also metrics to handle class imbalance problems for them. It is reported that the gradient boosting method outperforms the other classifiers and achieved an ROC of 0.952 with a precision of 0.920. Further analysis of the experiments demonstrates that the ML algorithms can accurately predict PPD. Shin et al. (62) have proposed a method for predicting PPD. The authors used nine algorithms, with the best results coming from RF, Adaboost, GBM, and SVM. To resolve the data imbalance and avoid overfitting, the authors used Synthetic Minority Oversampling Technique (SMOTE) and cross-validation. After extensive experimentation with various classifiers, it is found that random forest outperforms the other classifiers and achieved an AUC of 0.884. The authors also concluded that life stress and a history of depression are the two most important factors in predicting PPD. Betts et al. (63) used a gradient-boosting approach that outperformed the LR and elastic net methods. The approach is likely to learn the complex and non-linear relationship within the data, since the experimental results produced an AUC of 0.80 (95% CI = 0.76–0.83).

Andersson et al. (65) looked at a variety of machine learning algorithms for predicting the probability of acquiring PPD. To evaluate the model's performance, the authors used clinical, demographic, and psychometric data. The extremely randomized trees method provides the highest accuracy of 73% and well-balanced sensitivity and specificity of 72 and 75%, respectively. Furthermore, the scientists concluded that depression and mental health difficulties had a major impact on PPD. To verify the relationship between PPD and the mode of delivery, Sword et al. (58) studied the relationship between the risk of getting PPD and the method of delivery. Social support, maternal age, previous pregnancy, and many other factors were considered by the authors. The authors have performed screening after 6 weeks following the hospital discharge. According to the results, there is no link between the mode of delivery and the PPD.

Although the research community is focusing on developing automated approaches to promote AI in maternal health, some limitations still need to be addressed. The proposed approaches should be bias-free (i.e., they should not represent any particular section of the society), ethnicity-agnostic, and explainable. In order to build trust in the AI systems, the end-users should be well aware of the working of the algorithm while making any prediction.

3. ROLE OF AI IN NEONATAL HEALTH

This section examines the research on the use of AI to improve newborn health. Following birth, the baby may develop a variety of health problems that necessitates prompt evaluation and treatment. It aids in lowering the rate of child mortality as well as reducing the severity of the implications if left untreated. Pain assessment, sepsis prediction, jaundice, and malnutrition tracking are just a few of the many health issues that require a timely diagnosis. The subsections that follow go into the role of AI in treating these disorders. The key focus areas of this section are represented in **Figure 8**.

3.1. Pain Assessment in Neonates

Pain is a defensive mechanism that is activated in response to any physical or potential tissue damage (66). The pain assessment can assist the caregiver in getting a greater understanding of the patient's medical state and making an accurate diagnosis. However, this process is difficult for infants because of their lack of communication. Ineffective pain management can result in persistent neuroanatomical and developmental abnormalities, as well as learning difficulties (67, 68). As a result, automated pain assessment systems based on behavioral and other physiological factors are required. Researchers are working on techniques that make use of these features, as seen in **Table 8**.

Zamzami et al. (69) have proposed an approach that uses facial strain to predict neonatal pain. The authors gathered in-house data by recording 10 newborns during painful procedures such as heel lancing. Face detection in newborns is difficult due to occlusion by a hand or pacifier, as well as unpredictable movements; the authors manually identified facial landmarks. The authors used k-nearest neighbors (KNN) and SVM to train for classification and attained an accuracy of 96 and 94%, respectively.

Zamzmi et al. (70) have proposed a multimodal pain assessment approach for neonates that includes both physiological and behavioral pain indicators. The authors also evaluated the unimodal approach by focusing just on facial images. The strain magnitude was measured using optical flow estimation, and the strain was calculated using flow vectors. The

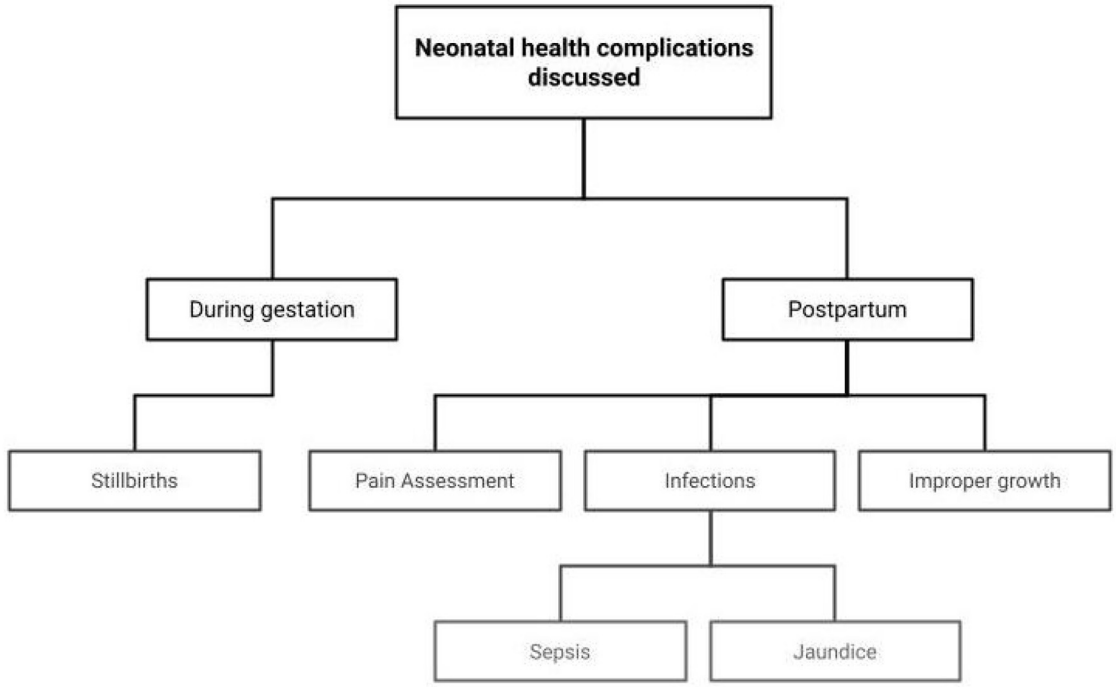

FIGURE 8 | Focus areas on role of AI in supporting Neonatal Health.

results demonstrate that the unimodal system employing facial expression achieved the highest accuracy of 88%. However, while combining various pain indicators, the model achieved an overall accuracy of 95%. To add more features, the authors integrated bodily movements and vital signs such as breathing rate, heart rate, and oxygen saturation level. The authors concluded that facial expression attained the highest accuracy in a unimodal pain assessment method. For the multimodal approach, the authors used majority voting and chose the class with the highest confidence score as the final pain assessment. These results suggest the efficacy of using multiple pain indicators while developing the neonatal pain assessment system.

Zamzmi et al. (72) developed a smart and accessible system employing AI and ubiquitous computing to boost healthcare in rural areas and provide a cost-effective approach for neonatal pain assessment. Using smart sensors, the proposed approach can continually monitor the newborns and report to the caregiver. The authors employed the VGG-Face feature extractor and the ZFace tracker to detect faces in video sequences. For classification, a set of classifiers is trained, including NB, kNN, SVM, and RF.

Zhi et al. (73) presented a method for evaluating neonatal pain using dynamic facial representations. For classification, the authors used dynamic facial texture data and geometric features taken from video sequences. Both feature-level and decision-level fusion techniques were employed by the authors. For each type of facial activity classification, the authors have used SVM and have shown results while combining multiple facial activities using a decision fusion scheme (majority voting).

Zamzmi et al. (74) have evaluated N-CNN, a new CNN architecture for assessing pain in neonates proposed in Zamzmi et al. (81). The authors compared the performance of ResNet50 and VGG16 using facial images. To detect the face, the authors have used the ZFace tracker and geometrical augmentations to increase the size of the data samples. Experiments reveal that the proposed architecture is comparable to the other two deep architectures in performance. In another DL-based study conducted, Salekin et al. (75) presented a method for combining information from the neonates' facial expressions and body movements. The authors additionally use LSTM in the proposed multi-channel network to model temporal information. The proposed approach achieved an accuracy of 92.48% and AUROC of 0.90 on video-level classification.

Infants' face muscles are not well developed, according to clinical investigations, and hence their ability to sustain facial actions is limited. Crying sounds are the most common way for infants to express their pain. Zamzmi et al. (71) have presented an automated multimodal approach for assessing neonatal pain that includes crying sounds. Facial expressions, body motion, and vital signs were also added as input features by the authors. Face features were detected, crying sounds were extracted using Yang's speech recognition approach, body motion features were estimated, and the state of arousal was evaluated using facial expression and body motion. The average accuracy of using crying sounds as pain indicators was 88%, and on combining multiple indicators such as facial expression, body motion, and vital signs, the accuracy was increased to 96.6%. The results of the study are

TABLE 8 | Summary of approaches used to predict neonatal pain using AI.

References	Summary	Key Contribution	Dataset used
Zamzami et al. (69)	This work devises an approach to predict neonatal pain using facial strain by using various machine learning classifiers including SVM and KNN	This system can be helpful both in hospitals and homes by allowing continuous monitoring of the neonate.	Collected data of 10 infants older than 30 gestational weeks during acute and chronic pain.
Zamzmi et al. (70)	A multi-modal neonatal pain assessment system utilizing behavioral and physiological pain indicators is proposed in this work	The authors utilized multiple pain indicators such as facial expression, body movements and the vital signs to design a multimodal system to assess pain in neonates Experiments reveal that combining multiple pain indicators makes the system more robust and accurate	Collected data of 18 infants (having an average gestational age of 36 weeks) during the routine painful procedure at Tampa General Hospital
Zamzmi et al. (71)	An automated multi-modal system is proposed by including facial expressions, body motion and vital signs	Developed a multimodal system including crying sounds in addition to facial expression, body movement and vital signs for assessing neonatal pain. Can act as a non-invasive and fast method of neonatal pain assessment	Collected data of 18 infants (having average gestational age of 36 weeks) during the acute episodic painful procedure
Zamzmi et al. (72)	To propose a cost-effective pain assessment system using smart sensors and ubiquitous computing to resource-restricted areas	This work uses transfer learning for the automatic assessment of pain. Can be helpful for caregivers both at hospitals and in homes	Collected data during painful procedures of 31 neonates having an average gestational age of 36 weeks at Tampa General Hospital
Zhi et al. (73)	The authors proposed a neonatal pain assessment system by utilizing dynamic facial texture and geometric features from video sequences	This work presented an approach for neonatal pain assessment by combining the collected video sequences' geometrical and temporal facial features. The results demonstrate that this method can be helpful in NICU's to monitor the infants for pain continuously.	Collected data from 31 infants during painful procedures such as heel lancing for 5s at NICU at Tampa General Hospital. The average gestational age of the infant was 36.4 weeks
Zamzmi et al. (74)	Evaluated a deep network, N-CNN for neonatal pain assessment	A light-weight CNN is evaluated that helps in the automated assessment of neonatal pain The findings of using N-CNN are promising, demonstrating that it may be used to supplement to the current standard of pain assessment.	Collected data (video, audio and other vital sign readings) of 31 infants both in resting position and during painful procedures at Tampa General Hospital and USF.
Salekin et al. (75)	A multi-channel network is proposed in this work that uses facial expressions and body movements, also incorporated temporal information using LSTM	A system that uses facial expressions and body movements, the visible indicators, can help caregivers assess neonatal pain. There is a strong correlation between assessing pain using face and body features	Collected data of 31 neonates with an average gestational age of 35.9 weeks during heel lancing and immunization
Zamzmi et al. (76)	Proposed a neonatal pain assessment using physiological and behavioral features with various fusion schemes. Also, proposed a neonatal pain dataset, NPAD	This work generates pain scores by fusing multiple pain indicators, and the results demonstrate the feasibility of using this approach which can be helpful to assess pain Introduced a neonatal pain assessment dataset	Collected dataset of 40 neonates during procedural pain and post-operative pain with a mean gestational age of 35.9 weeks
Salekin et al. (77)	Proposed a crying sound based neonatal pain assessment system where the sounds are converted to spectrogram images	Evaluated the N-CNN to assess neonatal pain using crying sounds as a modality The proposed approach analyzed sounds at baseline and during painful procedures and gave promising results, hence acting as an alternative to the current assessment method.	Collected data (video, audio and other vital sign readings) of 31 infants having an average gestational age of 35.9 weeks
Salekin et al. (78)	The authors proposed an approach for assessing post-operative pain in neonates by using bilinear CNN and LSTM	Studied the use of deep learning in estimating the post-operative pain Used LSTM to continuously monitor the temporal changes in neonates for estimating pain intensity	Collected data (visual, vocal and physiological) of 45 neonates at Tampa General Hospital, COPE acute dataset, and post-operative dataset
Ashwini et al. (79)	Proposed an approach by using deep features with SVM for neonatal pain assessment	Studied the use of deep features with a machine learning classifier in designing a model for neonatal cry classification. SVM with RBF kernel gives the best performance for this task.	Collected data of infants aged between 1 and 10 days (from NTU Hospital, Taiwan)
Salekin et al. (80)	A multi-modal approach for neonatal post-operative pain assessment by using spatio-temporal approach is being proposed	Compared the performance of both unimodal and multimodal for this task. The performance gets improved using temporal information	Used USF-MNPAD-I (University of South Florida Multimodal Neonatal Pain Assessment Dataset) consisting of 45 neonates having gestational age ranging from 30 to 41 weeks

promising and could help to enhance the process of measuring neonatal pain.

The authors have presented a comprehensive automatic system that uses the same set of features in another work (76). To generate the pain score, the authors used four fusion schemes: feature-level, decision-level, score-level, and NIPS-based scoring method. The authors have performed experiments using both individual pain indicators and their combination. The highest reported accuracy for the multimodal system was 95.56%.

Salekin et al. (77) did a similar study in which the authors evaluated the N-CNN for measuring pain using crying sounds. The audio signals were converted into spectrogram images by the authors. The authors also compared the performance of the VGG16 and ResNet50 deep architectures. The proposed architecture attained an accuracy of 96.77% and an AUC of 0.94 in experiments. Also, the authors compared their approach with handcrafted features where the results demonstrate that the proposed method outperformed them and achieved an accuracy of 91.20%. The feasibility of employing crying sounds in pain assessment is also demonstrated in this study. Ashwini et al. (79) have reported a strategy in which the authors identified infant crying sounds as hunger, pain, or sleepy using an ML-based classifier. Deep features were extracted and fed to the SVM with different kernels for the classification. Experimental results demonstrate that SVM-RBF achieved the highest accuracy of 88.89% among other variants of kernels in SVM. The authors concluded that using deep features with machine learning classifiers yields good results even with little data samples.

Salekin et al. (78) presented a bilinear CNN with LSTM to assess postoperative pain in newborns. In addition to modeling temporal pain, the authors looked at facial features. The authors used bilinear CNN to extract features relating to distinct pain intensities from both acute and postoperative pain data. The authors achieved an MSE of 3.999 and an MAE of 1.5565. The analysis of the results also demonstrates the feasibility of this framework in assessing newborn postoperative pain. Salekin et al. (80) did a similar study in which the authors presented a multi-modal spatio-temporal technique for assessing postoperative pain in neonates using visual and verbal indicators. The authors have used VGG-NET for feature extraction, followed by classification using Bilinear CNN. Extensive experiments are performed by authors using a single modality and multiple modalities. The authors concluded that the multimodal approach is more reliable and feasible to deploy in a real-world environment.

3.2. Predicting Sepsis in Neonates

Infections affect people of all ages, but they are particularly risky in infants because their immune systems are still developing and, thus, more prone to diseases. Although certain defensive antibodies transfer from the mother to the baby *via* the placenta (the organ that feeds the fetus), the amounts of antibodies in the fetus's bloodstream may not be sufficient to combat an infection. Infections can be acquired by fetuses and neonates either during pregnancy and birth or following birth. A systemic inflammatory response to an infection is defined as sepsis. It is related to the high mortality and morbidity rate. Both adults and children get affected. Early detection can help in reducing mortality and morbidity. For the early detection of sepsis in newborns, the following studies are being done. **Table 9** summarizes the approaches.

Using electronic medical records, Mani et al. (82) presented a non-invasive strategy for late-onset newborn sepsis. The authors used a variety of classifiers, such as NB, SVM, kNN, and others. To deal with missing values, the authors utilized a single imputation strategy, in which a random number is generated for continuous variables based on the mean and standard deviation of the observed values. Imputation for discrete values is done by selecting random values from a set of observed discrete values weighted by their proportion. The results demonstrate that the proposed method outperforms the decision of clinicians in terms of sensitivity and specificity. The authors of Le et al. (83) conducted a similar study in which they employed ensembles of decision trees to predict sepsis in neonates. The results demonstrated that at the time of onset, the algorithm achieved an AUROC of 0.916 for classification between severe sepsis and control pediatric patients and an AUROC of 0.718 at 4h before onset. Their technique outperforms existing sepsis scoring systems, such as pediatric organ failure and inflammatory response scoring systems, according to experimental results. Masino et al. (84) have evaluated the machine learning algorithms for the prediction of neonatal sepsis using electronic health records. The authors have employed 8 machine learning models for classification, out of which 6 models achieved a mean AUROC between 0.80-0.82. Early prediction can help in reducing the need to give antibiotics if found negative for sepsis.

3.3. Predicting Jaundice in Neonates

Jaundice is a common health condition that affects people all over the world. Both adults and children are affected. It results in yellowing of the skin and is generally visible in the eyes and skin. Jaundice in infants is prevalent, especially in babies born before 38 weeks of pregnancy (preterm babies) and some breastfed babies. When a baby's liver isn't developed enough to get rid of bilirubin in the bloodstream, it causes jaundice. A timely diagnosis can lead to a more accurate diagnosis and the avoidance of negative consequences such as neurological disorders. Existing bilirubin level estimation approaches are invasive, requiring blood to be extracted from the patient's body and a diagnostic test to be done. The issue arises when these levels must be monitored on a regular basis.

To help in this direction, the research community is attempting to develop non-invasive, cost-effective solutions. These approaches can assist resource-constrained communities in reducing the requirement for equipment that is scarce and limited in such settings. **Table 10** summarizes the approaches, including the key contribution and the dataset being used. Taylor et al. (85) presented a smartphone-based application for estimating bilirubin levels in newborns. The authors used images taken using smartphones and a calibration card to ensure color consistency. The results demonstrate that the TSB levels and the predicted value have a strong correlation of 0.91. The sensitivity and the specificity of the app were 84.6 and 75.1%, respectively. The results demonstrate that this app can aid in

TABLE 9 | Summary of approaches used to predict neonatal sepsis.

References	Summary	Key Contribution	Dataset used
Mani et al. (82)	Proposed a machine learning approach to predict late-onset neonatal sepsis using electronic medical records	The proposed approach can prove helpful in identifying truly infected neonates and can act as an early warning system. Detected the top three sepsis predictive variables as packed cell volume, chorioamnionitis and respiratory rate.	Collected 299 samples of neonates for late-onset sepsis from the Monroe Carell Jr. Children's Hospital
Le et at. (83)	Proposed an ML-based sepsis prediction system for neonates using machine learning	This system can help in continuous monitoring of EHR data and hence the probability of developing the sepsis in neonates Use of vital signs further improves the model performance	Used de-identified chart data from UCSF where the age of the patients ranges between 2 and 17 years
Masino et al. (84)	Evaluated various ML-based algorithms for the prediction of neonatal sepsis	The authors have studied the feasibility of using machine learning to develop early neonatal sepsis prediction models. Logistic regression can generalize well with other EHR datasets with the same input features and is resilient to overfitting.	Collected data from patients who were hospitalized for at least 48 hrs in the NICU (in CHOP) and also have received at least one sepsis evaluation before 12 months of age

TABLE 10 | Summary of approaches used to predict neonatal jaundice.

References	Summary	Key Contribution	Dataset used
Taylor et al. (85)	A smartphone-based app called BiliCam to estimate the bilirubin levels in neonates is proposed	A technology is proposed based on images to estimate the TSB values in neonates. Can act as a screening device to help identify the neonates that require blood draw. Accurately identifies neonates with high TSB levels	Collected 580 samples of newborns (<7 days old) at 7 sites across United States
Leung et al. (86)	The authors proposed a neonatal jaundice screening method using sclera images	The authors proposed a smartphone-based approach based on two color spaces (RGB and CIE XYZ) that can quantify the yellow color of the sclera. A new grading scale, JECI, is introduced that helps to quantify yellow color and is also device-independent. JECI can be helpful in the screening of jaundice in adults as well.	Collected 87 images of neonates whose age was between 1 day and 28 days (in UCL Hospital)
Aune et al. (87)	A color analysis based solution is proposed to estimate bilirubin levels in neonates using smartphone-captured images	This approach can detect severe jaundice with high sensitivity and also shows that a calibration card can minimize the effect of varying illumination. Limitation: Their dataset mainly contains Caucasian neonates; hence the learnt model may not work well with non-caucasian infants and there was no consensus between sites for data collection.	Collected images of 302 neonates having up to 15 days of age from 2 hospitals (in Norway)
Outlaw et al. (88)	A smartphone-based solution for the screening of jaundice in neonates using sclera and conjunctiva images is proposed	The authors employed ambient-subtracted scleral chromaticity to describe the color of modality to quantify neonatal jaundice, which eliminates the need for color calibration. The results show that linear models based on scleral chromaticity are capable of accurately estimating TSB.	Collected data of 51 neonates (in UCL Hospital) whose gestational age ranges from 35 weeks and 6 days to 1 week and 1 day
Althanian et al. (89)	Proposed a multi-modal approach to detect jaundice in neonates	A predictive model based on a set of modalities such as skin, eye and their combination is proposed to diagnose jaundice in neonates Concluded from results that skin and eye features work best with deep models and traditional machine learning, respectively. The best set of features may not be the best for all classifiers	Collected dataset of 100 neonates (in KKU Hospital in Riyadh) whose average gestational age was 38 weeks and the average age was 1 day

detecting children that need medical attention. Leung et al. (86) proposed to use sclera images to assess neonatal jaundice. The authors used multiple linear regression to find the correlation between pixel values (RGB) of the sclera and the Total Serum Bilirubin (TSB) of the neonates. A comparison of estimated and measured TSB levels is also performed. The results show that $r = 0.75$ and that their method has a sensitivity of 1.00.

Aune et al. (87) performed a similar study in which the authors used color analysis of skin images to assess bilirubin levels. To minimize the effect of ambient illumination, the authors used images with and without a flash of the smartphone. The reported results demonstrate that the sensitivity and specificity of the proposed approach were 100 and 69%, respectively. Furthermore, the authors reported a 0.84 correlation between the estimated value (smartphone) and the TSB and also a correlation of 0.81 between image estimates and TcB, demonstrating the approach's practicality. Outlaw et al. (88) have presented a smartphone-based method for estimating neonatal bilirubin levels. To achieve color consistency, the authors adopted the ambient subtraction method, which eliminated the requirement for any external attachment like a calibration card. The results demonstrate that the proposed method can achieve a sensitivity and specificity of 100 and 61% for infants with TSB above 250μmol/L respectively, and a sensitivity and specificity of 100 and 54% for infants with TSB levels below 250μmol/L.

To propose a multi-modal system and improve the accuracy of the approach, Althanian et al. (89) have proposed to use eye, skin and their combination as the input. The authors have used various image processing techniques like color balancing etc, in this work. The authors have evaluated machine learning algorithms such as MLP, SVM, DT, and RF in addition to deep learning. The results demonstrate the transfer learning approach achieved accuracy and AUC of (86.83%, 81.05%), (79.03%, 69.67%), (79.95%, 71.25%) for skin, eye, and their fused features, respectively, showing that skin features work well with deep models.

3.4. Machine Learning in Tracking Malnutrition

A well-balanced diet is an important component of living a healthy lifestyle. Malnutrition is a global health issue that manifests itself in a variety of ways, including undernutrition, overweight, obesity, and a lack of vitamins and minerals. Malnutrition is directly or indirectly associated to about half of infant mortality in underdeveloped nations, according to Pelletier and Frongillo (90). Malnourished children are more susceptible to infections, weight loss, obesity, and other ailments. Malnutrition can be caused by a variety of causes, including demographic, socioeconomic, health, and physical factors. As a result, the features that constitute malnutrition must be identified. Researchers are concentrating their efforts on creating techniques for predicting malnutrition. In the literature, there are several approaches that employ statistical tools to explain the factors that contribute to malnutrition. The most common methods for predicting the probability of malnutrition in children are linear regression and logistic regression.

Khare et al. (91) studied the relationship between childhood malnutrition and socioeconomic factors. On the identified explanatory features, the authors utilized a logistic regression model. Their research found that machine learning approaches are useful in identifying the most important variables that contribute to malnutrition prediction. Various research studies from different regions also show that AI technologies may be used to predict malnutrition (92–96).

Lingren et al. (97) have provided a method for identifying obese children. On the EHR records, the authors applied rule-based and machine learning techniques. The chi-square approach is used to select features. The approach was also tested utilizing NB. The findings show that their technique has the potential to be employed in clinical trials.

4. CHALLENGES AND PATH FORWARD

4.1. Economic and Social Barriers

Although the maternal mortality rate (MMR) is one of the most critical indicators of a nation's maternal well being, MMR accounts for only a tiny portion of the strain on maternal illnesses, which refers to the medical conditions women face during gestation and the postpartum period. For every female dying from pregnancy-related reasons, another 20 or 30 suffer from underlying medical illnesses, frequently with long-term consequences that impair their ability to function normally (98, 99). These consequences can impact the individual's physical, cognitive, and reproductive health and their ability to perform in specific domains (e.g., intellect, mobility, and socialization), self-image, and cultural-financial standing (99, 100). Maternal mortality and other related issues are expected to be highest in low- and middle-income nations, particularly amongst some of the poorest women families (101). The actual cost of maternal deaths, on the other hand, is unknown. Current estimations and computations are not founded on well-maintained records, techniques etc. Such strategies are ineffective and have low validity in informing initiatives to solve maternal diseases. The lack of a clear definition and standardized identification procedures is one of the main reasons for the challenges in effectively quantifying maternal malaise. Unreliable vital statistics aggravate this issue due to insufficient healthcare information systems (HIS).

Premature birth, low birth weight infants, fetal growth restriction, antenatal complications (e.g., anemia, eclampsia) and other factors during delivery (e.g., extended labor, umbilical cord prolapse) contribute to the development of neonatal health risks such as cerebral palsy, learning disabilities, and other abnormalities. Underskilled caregivers and health workers, such as relatives and midwives, may not be able to recognize and manage intrapartum-related problems in an infant in low resource settings. This reveals a gap between both the commencement and acknowledgment of the problem and seeking appropriate treatment. In the case of intrapartum difficulties, prompt recognition and reaction are critical since even a minor delay in seeking and obtaining adequate healthcare can result in significant impairment to the infant, potentially resulting in life-threatening situations (102).

4.2. Technological Barriers

Even though these technologies are quickly advancing, their clinical use is still in its early stages. A comprehensive validation study is required before clinical clearance for employing AI-based models to assess the applicability of the proposed approach in practical clinical scenarios. Before a model can be implemented in the healthcare area, it is necessary to develop standard validated tools for its use in actual healthcare settings. A few of the technological barriers to wider applicability and acceptance of AI in the clinical scenario are as follows:

- Non-Availability of large scale databases - Whether it is extracting healthcare data, conducting survey-based studies, or studying omics, proteomics, and other data, a majority of existing efforts are laborious and time-consuming. New cutting-edge AI/ML-based technologies are emerging as solutions to the overburdened healthcare paradigm. Their widespread adoption lies in the fact that these technologies are deployable in maternal and neonatal health without requiring too much clinical information about the subjects. However, these technologies need to be trained on information from a large volume of patients to achieve this. This kind of big data collection poses unprecedented issues for storing, handling, transferring, and securing these datasets and ensuring patient privacy.
- Evaluation and validation on a uniformly sampled database which is a true representative of the population - There is also rising concern about the possibility of bias in the AI-based predictions, all of which are contributing to this problem.
- Trustworthiness and explainability of the models - At the moment, the lack of explainability in machine learning prevents the widespread adoption of artificial intelligence. Explainability is especially required in healthcare as here; the medical diagnosis model is accountable for human life. Suppose artificial intelligence (AI) is unable to explain itself in the domain of healthcare. In that case, the risk of making the wrong judgement may outweigh the benefits of precision, rapidity, and judgement efficacy. As a result, the breadth and utility of the system would be significantly restricted. Thus, it is critical that these issues are thoroughly investigated (103).
- Concerns about privacy - AI has often raised concerns in the minds of users regarding their stored data privacy (due to AI requiring big-data to train on) as well as the privacy of the predictions made by AI. For example, the predictive power of AI in healthcare can aid in giving diagnosis to a disease the patient has never disclosed to anyone or didn't even know himself. Here, it's important to store and use this data ethically with proper consent (104).
- Acceptance of AI models and samples integration in daily procedures - The larger community must embrace new tools and drive training, patient participation, and rigorous standard development to enable more methodical collaboration across hospitals. Organizations must contribute to the purposeful and thoughtful creation of medical environment models. Advancements in the machine learning sector will surely assist in shaping future healthcare discoveries if we can achieve this.

4.3. Open Problems for Research

As discussed above, limited access to proper healthcare infrastructure and professionals, along with other societal and economic barriers, put restrictions on providing holistic care to pregnant women and their children in resource-constrained settings. Digital chatbots and support groups can aid in maternal and neonatal health monitoring as well as management (105, 106). One key challenge here lies in handling the cultural diversity of the users pertaining to the language they are comfortable conversing in. Thus, chatbots can be developed to engage the users in follow up questions about their health in their desired language. These conversational healthcare technologies come under the domain of Natural Language Processing (NLP) in AI and help in dispersing basic health information amongst the users.

Explainable Artificial Intelligence (XAI) or Dependable AI (DAI) can be used to give insights into the decision-making process of the AI models. Explainability raises the level of confidence that medical practitioners and AI researchers have in an AI system, leading to more broad adoption of AI in the healthcare field over time. For example, if they explain why someone has been classified as ill or otherwise, we can look inside the programmed thought process of the model. It would change the perception about these models as a "black box" and help in their scalable employment (103). Eventually, XAI can be merged with smart healthcare systems that incorporate the Internet of Things, cloud computing, and artificial intelligence, and which will be particularly applied in the fields of maternal and neonatal health. These intelligent healthcare systems can therefore be utilized for a variety of purposes, including the diagnosis of diseases and the selection of suitable treatment plans (107).

To supplement the lack of data in some crucial small sample size healthcare problems where the large dataset is not available, Few-shot learning or Zero-shot learning can be used to train the AI models. Newer and more efficient few-shot learning frameworks for healthcare are needed to be developed to utilize domain information to reach medical decisions/ predictions. These technologies would be an efficient assistive tool for doctors to handle rare medical conditions and problems that require years of experience (108).

5. SUMMARY

The MDGs stated that one of the primary objectives of world leaders was to improve maternal health and reduce child mortality. In 2015, as part of the 17 Sustainable Development Goals, this objective was expanded to include the reduction of maternal and newborn mortality due to problems during pregnancy and childbirth. Improving maternal and newborn health entails bringing speedy diagnosis and treatment to point-of-care settings in developing nations with limited resources. However, there are currently just a few diagnostic tools and techniques available in point-of-care settings. This is by far the most common cause of maternal and newborn death. The purpose of this study is to examine how artificial intelligence and machine learning are being used to improve currently

developing technologies, revealing critical gaps in development where novel design could boost access to technology and enable rapid diagnosis at the bedside. Issues pertaining to maternal and neonatal health are often not addressed due to a lack of awareness in the social caregivers to recognize the early signs of the impairment. The lack of skilled, professional healthcare workers also devoids proper demographic coverage, and many such health issues go unaddressed or, even worse, unaccounted for. This gives rise to unreliable data collection and, in turn, leads to delays in action to improve health amenities. With the help of AI/ML algorithms, we can address many of these issues; however, the need for explainability in AI is a major roadblock to its widespread adoption. When implementing AI solutions for public health, the ethical concepts of a sense of morality, autonomy, and justice, as well as human rights such as respect, independence, well being, self-determination, fairness, equality, and privacy, must all be taken into account. Once we are able to jump across these hurdles, not only can we reduce the workload of doctors and healthcare workers, we can accumulate reliable data with wide demographic coverage and can see the girth of the problem. This way, we can more efficiently aid in improving maternal and neonatal health, especially in low income and poor resource settings which are otherwise untouched by proper facilities and remedies. Future work on making AI-based techniques explainable would ensure more confidence of health practitioners in this technology and will hopefully help in the large scale adoption of AI in this sector.

AUTHOR CONTRIBUTIONS

MKha and MKhu took the lead in writing the paper. MV, RS, MD, and KS conceptualized the idea and reviewed the paper. All authors contributed to the conception of the idea.

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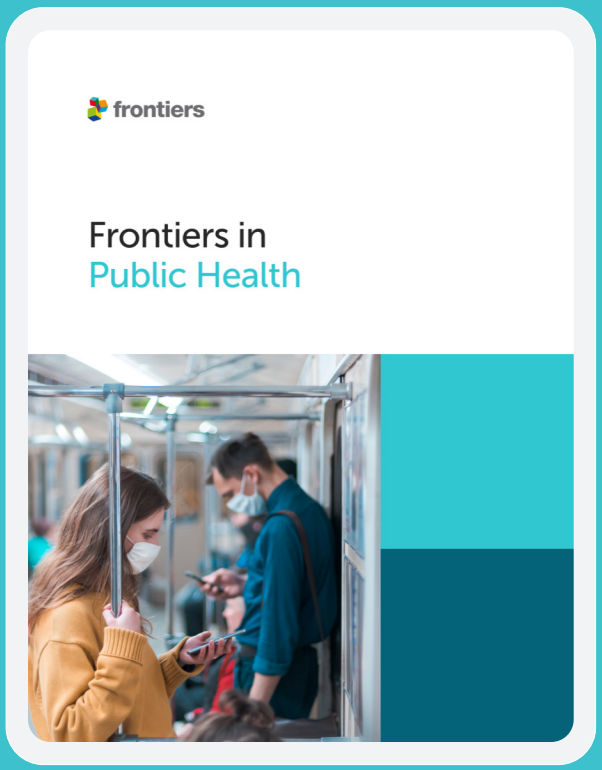

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