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# Nearly half of HIV-positive children attending public health facilities are suffering from chronic under-nutrition in conflict-affected zones of Southern Ethiopia

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**Background:** In combination with HIV infection, malnutrition is a complicated medical condition with high morbidity and mortality rates in affected children due to a variety of socioeconomic and medical etiological variables. To combat this, information from a range of contexts is required, but there is little evidence, particularly about the nutritional status of under 15 living with HIV in impoverished communities such as conflict affected areas. Therefore, in this study the magnitude and related factors of stunting among under 15 children antiretroviral therapy at public health facilities was assessed.

**Methods:** An institution-based cross-sectional study was conducted among under 15 children living with HIV in conflict-affected zones of Southern Ethiopia. After providing written informed consent to study participants, data were collected using an interviewer-administered questionnaire and anthropometric measurements. Bivariable and multivariable logistic regression models were used to identify factors associated with nutritional status, using SPSS Version 25.

**Results:** Of the 401 participants, 197 (49.1%, 95% CI: 0.44, 0.54) had height-forage z-score  $\leq$ -2. In the multivariable analysis, larger household size (AOR = 1.58, 95% CI: 1.04–2.40), dietary diversity (AOR = 1.78; 95% CI: 1.07–2.96) and having a history of recurrent diarrhea (AOR = 1.96; 95% CI: 1.07–3.59) were significantly associated with chronic under nutrition.

**Conclusions:** The prevalence found in this study was high when compared with the stunting target set in SDG, which states to end all forms of malnutrition In order to mitigate the negative health effects of diarrhea during HIV therapy, extra attention needs to be paid to facilitate timely detection and on-going monitoring. Nutrition programs in conflict-affected areas need to consider households with larger family sizes and/or routinely having fewer food groups.

#### KEYWORDS

chronic malnutrition, antiretroviral, pediatrics, HIV/AIDS, conflict, Southern Ethiopia

# Background

Stunting is low height for age which is an indicator of chronic under-nutrition (1). Globally, chronic undernutrition affects both adults and children and is a worldwide public health concern (2). Thus, 22% of children under 5 years of age in 2019 and 23% of school-age children (5–14 years) in 2020 were stunted (3, 4). Similarly, the prevalence of stunting in the Sub-Saharan Africa (SSA) region was 32.3% (5). In Ethiopia, stunting also remains as high as 49.7% which calls for continued adequate investment in nutrition (6). Stunting significantly increased the risk of childhood morbidity and mortality (7, 8). Further, stunted children also have a higher risk of being overweight or obese later in life, putting them at risk of chronic disease in adulthood (7, 9). More than 35% of child mortality (10), 11% of the world's disease burden (11), and abnormalities including cognitive decline, chronic diseases, and growth failure are all caused by under nutrition (10).

Acquired immune deficiency syndrome (AIDS), is a disease caused by a retrovirus, the human immunodeficiency virus (HIV), which attacks and impairs the body's natural defense system against disease and infections (12). About two-thirds of the 38.4 million people living with HIV (PLWH), 45% of the 1.5 million new cases, and 43% of the 650,000 AIDS-related mortality recorded worldwide in 2021 were from SSA (13). When HIV/AIDS and malnutrition coexist in the same individual, they can be fatal combos that feed off one another. Malnutrition increases susceptibility to infection by causing immune dysfunction in manifold ways. Weakened immune function can increase HIV replication and hasten the development of HIV illness into AIDS (14). When people with HIV/AIDS are not receiving treatment, they are more likely to become malnourished (15), which raises their risk of dying when antiretroviral medication (ART) is started (14). Furthermore, people with untreated or advanced HIV/AIDS often have weakened immune systems, which leaves them vulnerable to a range of opportunistic infections (16).

Despite Ethiopia being the oldest sovereign state on the African continent, conflict has become the norm (17). The political unrest and instability that invariably accompanies leadership changes instill a sense of uneasiness in citizens. It wouldn't be an overstatement to suggest that war and conflict have characterized Ethiopia's history (18). Renewing hostilities in most regions, including Southern Ethiopia, between non-state armed groups and regional security forces over resource competitiveness and land disputes have resulted in violent confrontations that have forced people out of their homes in recent years (19). Conflict halts farming and destroys people's livelihoods, thereby diminishing households' and communities' capacity to cope with the basic root causes of chronic malnutrition (20, 21). Interruptedly conflict may block food aid from reaching populations at risk of malnutrition (22, 23).

Maintaining optimal nutrition is still a significant difficulty for children living with HIV; factors that contribute to this problem include insufficient dietary intake, side effects of antiretroviral therapy (ART), and HIV infection itself (24). Although there have been some studies assessing the nutritional status of children living with HIV in Ethiopia, they have focused on either the general nutritional status or acute malnutrition but none specifically exploring chronic malnutrition in conflict-affected settings (25–29). Although chronic malnutrition remains a major public health problem and a major cause of morbidity and mortality in HIV-positive children, there is a deficit of studies assessing the nutritional status and associated factors in HIV-positive children in conflict-affected zones of Southern Ethiopia.

The current study, therefore, aimed to assess determinants of chronic malnutrition among children receiving antiretroviral therapy (ART) in health facilities of conflict-affected zones of Southern Ethiopia. The findings from this study may be helpful for public health authorities and other stakeholders to rethink the current health and nutritional strategies and programs for this vulnerable population group. The study findings may also be important for parents, caretakers and children in familiarizing the factors associated with stunting, and ways of redress.

# Methodology

### Study area, period, and design

From 9th June to 29th July 2022 a health facility-based crosssectional study was conducted in Amaro, Burji, Derashe, Ale, and Konso zones, in Southern Ethiopia. These areas were respectively 357, 546, 550, and 522 km from south of Addis Ababa, the capital of Ethiopia.

Based on the latest population projection of the Central Statistics Agency of Ethiopia, the population of the study area was projected to be 3,157,673 (with 473 597 urban (15%) and 2,684,076 rural (85%) residents) (30). This area is one of inter-communal conflict-affected Ethiopian zones (31). In this study area, there are 21 health facilities delivering ART services during the study period.

## Study population

All under 15, HIV-positive children receiving ART in health facilities of conflict-affected zones of South Ethiopia regional State were the study population.

## Inclusion and exclusion criteria

All HIV-infected children who had ART follow-up in randomly selected health facilities of conflict-affected zones were included. Children with incomplete baseline medical information had physical malformation (kyphosis and lordosis) and/or were seriously ill were excluded from the study.

#### Sample size determination

Our target sample size was 419. This sample size was determined using a formula for single population proportion by

Abbreviations: AIDS, Acquired Immune Deficiency Syndrome; AOR, Adjusted Odds Ratio; COR, Crude Odds Ratios; CI, Confidence Interval; GDP, Gross Domestic Product; ART, Antiretroviral Therapy; HIV, Human Immunodeficiency Virus; OI, Opportunistic Infection; PLWH, People Living With HIV; SDG, Sustainable Developmental Goal; SPSS, Statistical Package for Social science; WHO, World Health Organization.

considering a 45.2% proportion (p) of chronic malnutrition; 5% margin of error; 10% non-response rate; and 95% confidence intervals (CI) (32). The same approach was used by similar studies (32, 33). The study was conducted at eight selected healthcare facilities. Initially, a sampling frame was prepared using the patient's medical registration number from each health facility's ART registration log. Following that, the total sample size was distributed proportionally to each facility. The study participants were then picked from each of the identified healthcare facilities using a computer-generated basic random sampling procedure.

#### Variables

#### Outcome variable

The outcome variable was stunting among HIV- positive children on ART in conflict-affected zones of Southern Ethiopia. Stunting was defined as a child having either a height for age Z-score below -2 standard deviation (SD) of the median value of WHO standard (33). Data were collected by using standard procedures.

#### Independent variables

These included socio-demographic and clinical-related variables. Socio-demographic variables such as age, sex and residence of the child, age of mother, educational status of household head, marital status of household head, occupation of household head, household family size, dietary diversity, main source of family food, and counseling on child nutrition, were considered. In addition, several *clinical-related variables* were considered; Immunodeficiency status (CD4 count), viral load, WHO clinical stage, exposure to prophylaxis, opportunistic infections, recurrent diarrhea, oropharengeal disease, adherence to ART, duration on ART, anemia history, and history of tuberculosis.

### **Operational definitions**

*HIV-Positive Children*: Children aged <15 years with confirmed HIV infection (27).

Dietary diversity: The number of reported different foods and food groups consumed in an individual over 24 h. This includes food groups consumed outside the home and <4 and greater or equal to 4 food groups are fair/poor and good dietary diversity, respectively (34).

*History of Opportunistic Infections*: child with HIV-related infections other than chronic diarrhea and disease; within the last 6 months before stunting and wasting diagnosis (27).

*History of Oropharengeal Disease*: A child with oral ulcer or candidiasis/oral thrush; within the last 6 months before stunting and wasting diagnosis (27).

*History of recurrent Diarrheal Disease:* A child with diarrheal disease of 30 days or more duration; within the last 6 months before diagnosis (27).

Adherence to ART: This was categorized as Good, Fair and Poor treatment adherence if a child missed  $\leq 2$ ,  $<2\leq 5$ , and >5 medical prescriptions, respectively (35).

#### Data collection procedures

A total of eight research assistants and three supervisors assisted with data collection. They were at least diploma holder health professionals who spoke the local language and had previous experience in data collection. Training about the objectives of the study, the contents of the tool and data collection procedures were given to data collectors and supervisors for 4 days at their respective zonal centers.

Height was measured by using a stadiometer. Sociodemographic data from mother/caregiver of child were collected by face-to-face interviews and clinical characteristics were taken from medical records. At the time of actual data collection, nutritional advice was given to all caregivers. The assigned supervisors and principal investigator closely monitored and supervised the whole data collection process.

## Statistical analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS) Version 25. The anthropometric measurements were converted into Z-scores using WHO Anthro and WHO Anthro++ software version 3.2.2. Frequencies and crosstabulation were used to check for missing values of variables and to describe the study population concerning relevant variables. Moreover, percentages, proportions, and summary statistics were used in summarizing the study population characteristics. Binary logistic regression analysis was conducted to assess the independent association of factors against the outcome variable. Variables with p-values < 0.25 in the bi-variable analysis were entered into the Multivariable Logistic Regression model to control for the effect of confounders and identify significant factors. The adequacy of the model to fit the outcome variable with the predictors was checked using the Hosmer-Lemeshow test for goodness of fit, and the value was 0.39, which was in the good range. In the multivariable analysis, variables with *p*-values < 0.05 were considered statistically significant, and we reported their respective adjusted odds ratios (AOR) with correspondence 95% confidence intervals (CI).

#### Patients and the public involvement

Patients and the public were not involved in the design of the study, the conduct of the study or the dissemination of the findings.

## Results

# Socio-demographic characteristics of study participants

Out of the 419 potential participants approached, 401 agreed and successfully participated in this study with a response rate of 95.7%. Of the total (401) respondents nearly half (50.6%) were rural dwellers, 220 (54.9%) were married, and 209 (52.1%) respondents had five or less family size. Regarding the index child characteristics 212 (52.9%) children were male, and 156 (38.9%) children were  $\leq$ 60 months of age while 129 (32.2%) were 60–120 months of age (Table 1). In addition, 297 (74.1%) households had poor dietary diversity, with the majority (46.1%) of households obtaining their food from aid, 125 (31.17%) buying from the market, and 91 (22.7%) from farming. However, about 151 (37.7%) participants responded that they did not get nutritional counseling.

## **Clinical related characteristics**

Majority of children, 239 (59.6%) were not given prophylaxis and 194 (48.4%) of them had stayed <60 months on ART. Two hundred and forty-seven of children were in WHO clinical stage I and II category, and the rest 152 (37.9%) of them were in clinical stage III and IV. More than half, 219 (54.6%) of children had experienced opportunistic infection (such as oropharengeal disease in 60.3%, chronic diarrhea in 85.8%, and tuberculosis in 38.2% of children; Table 2).

## Prevalence of stunting

Of the 401 HIV positive children in this study, 197 (49.1%, 95% CI = 0.44–0.54) were found to be stunted i.e., HAZ < -2 and 55 (13.7%) were severely stunted; HAZ < -3 (Figure 1). The mean height of the study population was 109.5 cm with standard deviation (SD) =  $\pm 18.8$ .

### Factors associated with stunting

This study examined a relationship between different participant characteristics and stunting. In the bivariable analysis, occupation of household head, dietary diversity, household size, duration on ART, history of aneamia, exposure to prophylaxis, viral load, WHO clinical stage and history of chronic diarrhea showed independent significant association with stunting among HIV positive children. After adjusting for possible confounders in the multivariable analysis, household size (AOR = 1.58; *P*-value = 0.02), dietary diversity (AOR = 1.78; *P*-value = 0.03), and history of chronic diarrhea (AOR = 1.96; *P*-value = 0.03) had statistically significant association with stunting of HIV positive children (Table 3).

Based on the multivariable analysis children from households with family size of five or more members were 1.58 times more likely to be stunted than children from family size of <5 members (AOR = 1.58; 95% CI: 1.04–2.40). Similarly, children who had poor dietary diversity practice were 1.78 times more likely to be stunted than children who had good dietary diversity practice (AOR = 1.78; 95% CI: 1.07–2.96). Moreover, children who had a history of chronic diarrhea were 1.96 times more likely to be stunted than those with no history of chronic diarrhea (AOR = 1.96; 95% CI: 1.07–3.59; Table 3).

# Discussion

The prevalence and associated factors of stunting among HIVinfected children in conflict affected zones of Southern Ethiopia TABLE 1 Socio-demographic characteristics of HIV positive under 15 years of age attending ART clinics of health facilities of conflict-affected areas in South Ethiopia, 2022.

Variable	Category	Frequency, <i>n</i> (%), <i>N</i> = 401
Age of child in months	≤60	156 (38.9)
	>60 to ≤120	129 (32.2)
	120 to 179	116 (28.9)
Sex of child	Male	212 (52.9)
	Female	189 (47.1)
Sex of household head	Male	248 (61.8)
	Female	153 (38.2)
Age of mother	≤20	146 (63.6)
	>20	255 (36.4)
Educational level of	No education	98 (24.4)
household head	Primary	126 (31.4)
	Secondary	95 (23.7)
	Certificate and above	82 (20.5)
Occupation of	Not employed	102 (25.4)
household head	Employed with salary	133 (33.2)
	Casual labor	84 (20.9)
	Small scale trading	82 (20.4)
Residence	Urban	163 (40.6)
	Semi-urban	40 (10.0)
	Rural	198 (49.4)
Marital status	Married	220 (54.9)
	Divorced/separated/widowed	110 (27.4)
	Single	71 (17.7)
Family size	1-4	192 (47.9)
	≥5	209 (52.1)
Source of food for	Farming	91 (22.7)
household	Buying	125 (31.2)
	Aid	185 (46.1)
Exposure to	No	151 (37.7)
nutritional counseling	Yes	250 (62.3)
Dietary diversity	Good	104 (25.9)
	Poor	297 (74.1)

were investigated in this study. Our study showed that nearly half (49.1%) of HIV-positive children were stunted. This prevalence was higher than that reported from other studies in Adama, Amhara region, and a previous study in Southern Ethiopia (32, 33, 36). Researches indicated that children were disproportionately affected in environments where there is conflict (37, 38). Most chronically malnourished people on the planet and three out of every four stunted children live in conflict-affected countries (39). When compared to the sustainable developmental goal (SDG) stunting target, the current study's findings indicate that study participants

Variable	Category	N (%)	
Exposure to prophylaxis	No prophylaxis given	239 (59.6)	
	Prophylaxis given	162 (40.4)	
Duration on ART in month	≤60	194 (48.4)	
	>60	207 (51.6)	
Adherence to ART	Poor	302 (75.3)	
	Good	55 (13.7)	
	Fair	44 (11.0)	
Viral load (the number of HIV	0–999	291 (72.6)	
copies in a milliliter of blood)	≥1,000	110 (27.4)	
CD4 count (in cells/mm <sup>3</sup> ) <sup>a</sup>	<350	146 (61.5)	
	≥350	154 (38.5)	
Who clinical stage <sup>b</sup>	Stage I ∧ Stage II	247 (61.6)	
	Stage III $\wedge$ Stage IV	152 (37.9)	
History of anemia	No	186 (46.4)	
	Yes	215 (53.6)	
History of opportunistic	No	182 (45.4)	
infections	Yes	219 (54.6)	
History of oropharengeal	No	159 (39.7)	
disease	Yes	242 (60.3)	
History of chronic diarrhea	No	57 (14.2)	
	Yes	344 (85.8)	
History of tuberculosis	No	248 (61.8)	
	Yes	153 (38.2)	

TABLE 2 Clinical characteristics of HIV positive under 15 years of age children attending ART clinics of conflict affected zones in South Ethiopia, 2022.

<sup>a</sup>1 missing value. <sup>b</sup>2 missing values.

ART, Antiretroviral therapy; HIV, Human immunodeficiency virus; WHO, World health organization; CD4, Cluster of differentiation 4.

were in worst health status. Ending all forms of malnutrition, including achieving by 2025 the internationally agreed targets on stunting in children under 5 years of age, and addressing the nutritional needs of adolescents was stated (40). Reversing the high prevalence of under-nutrition that has been documented requires stakeholders' joint effort. The implementation of dietary counseling, regular nutritional assessments, and financial and in-kind nutritional support should be reinforced, observed, and assessed.

This study showed that the larger the family size, the higher the likely hood of child stunting. Previous research findings corroborate this conclusion (41–44). As the number of family members in a household increases, the amount of childcare and food consumption will decline, particularly in families where there is not enough food to go around, which exacerbates the nutritional impact and HIV infection process (45–47). The food security of HIV affected households is impaired by a number of factors including the synergy generated by hosting a HIV positive family member (48).



This study has also showed an association of dietary diversity with chronic malnutrition in which children with poor dietary diversity are more likely to be stunted than their counter parts that get good dietary diversity. Consistent finding was reported from previous studies conducted in Hawasa, as well as Amhara regional state public hospitals, Ethiopia (32, 49). The reason could be that an HIV patient who did not receive a variety of foods that are meant to strengthen and/or improve immunity will be immunecompromised due to the infection itself and will be exposed to various other infections, which ultimately lead to the development of a chronic form of stunted malnutrition (50). Furthermore, the poor dietary diversity could be derived by conflict and unrest that disrupt food chain (51), affect people's ability to produce, exchange and access food (52). However, it has been recommended that as HIV-positive individuals have additional energy requirements, particularly children who have more demand to ensure rapid physical growth and development, diversifying their diet is by far an essential part for the care of people living with HIV (53).

Our study revealed that children who had history of chronic diarrhea were about two times likely to be stunted than their counterparts. This finding was in line with reports from different settings of both Ethiopia and overseas (14, 54–56). Diarrhea results in malabsorption of basic macronutrients including carbohydrate (57, 58) and protein (59). Older studies reported that in protein malnutrition, the absorption of dietary vitamin A from the intestinal tract was impaired (60–62). The risk of deficiency of crucial micronutrients for child growth and development like zinc (63), vitamin A (64–66) was enhanced by diarrhea. In addition, conflicts harm medical systems and public health in ways that last much beyond the actual fighting phase, which makes it easier for illnesses like diarrhea to spread (67–69). Therefore, chronic diarrheal history was an indication of previous poor nutrient intake worsened by effects of conflict.

#### Study strengths and limitations

This research allowed accessing a number of variables at the same time by using multicenter study and adequate sample size. Addressing relatively remote health facilities can also be taken TABLE 3 The bivariable and multivariable logistic regression analysis of associated factors of stunting at conflict affected zones of Southern Ethiopia, 2022.

Variable	Crude odds ratio, COR (95% CI)	<i>p</i> -value	Adjusted odds ratio, AOR (95% CI)	p-value
Age of child in months		0.77	N/A	
120 to 179	1			
$6 \text{ to } \leq 60$	1.18 (0.73–1.91)			
>60 to ≤120	1.17 (0.71–1.93)			
Sex of child		0.39	N/A	
Female	1			
Male	1.19 (0.80–1.76)			
Sex of household head		0.91	N/A	
Female	1			
Male	1.02 (0.68–1.53)			
Age of mother		0.40	N/A	
>20	1			
≤20	1.19 (0.79–1.79)			
Educational level of household head		0.68	N/A	
Certificate and above	1			
No education	1.43 (0.80-2.58)			
Primary	1.14 (0.65–1.99)			
Secondary	1.19 (0.66–2.15)			
Occupation of household head		0.12		0.32
Small scale trading	1			
Not employed	0.83 (0.48-1.44)		1.15 (0.62–2.11)	
Employed with salary	1.62 (0.88-3.00)		0.78 (0.44-1.40)	
Casual labor	1.15 (0.64–2.05)		1.32 (0.68–2.53)	
Residence		0.96	N/A	
Urban	1			
Semi-urban	0.94 (0.47-1.88)			
Rural	1.01 (0.51–1.97)			
Marital status		0.59	NA	
Married	1			
Divorced/separated/widowed	1.31 (0.72–2.39)			
Single	1 (0.63–1.58)			
Family size		< 0.01		0.02
≥5	1			
1-4	1.70 (1.15–2.52)		1.58 (1.04-2.40)	
Source of food for household		0.38		
Aid	1			
Farming	1.08 (0.65–1.78)			
Buying	1.37 (0.87–2.17)			
Dietary diversity		< 0.01		0.03
Good	1			

(Continued)

#### TABLE 3 (Continued)

Variable	Crude odds ratio, COR (95% CI)	<i>p</i> -value	Adjusted odds ratio, AOR (95% CI)	<i>p</i> -value
Poor	2.30 (1.45-3.64)		1.78 (1.07-2.96)	
Nutrition counseling		0.50	NA	
Yes	1			
No	1.16 (0.77-1.73)			
Exposure to prophylaxis		0.16		0.63
Prophylaxis given	1			
No prophylaxis given	1.34 (0.90-2.00)		1.11 (0.71–1.72)	
Duration on ART in month		< 0.01		0.06
≤60	1			
>60	1.85 (1.24–2.74)		1.46 (0.95–2.24)	
Adherence to ART		0.66		
Good	1			
Poor	1.01 (0.54–1.91)			
Fair	0.77 (0.35-1.72)			
Viral load (the number of HIV copies in a milliliter of blood)		0.24	0.93 (0.56–1.54)	0.78
≥1,000	1			
0-999	1.31 (0.84–2.03)			
CD4 count (in cells/mm <sup>3</sup> )		0.39		0.06
≥350	1			
<350	0.84 (0.56-1.26)		0.66 (0.43-1.02)	
WHO clinical stage		0.07		0.07
Stage I ∧ Stage II	1			
Stage III ^ Stage IV	1.45 (0.96-2.17)		1.49 (0.98–2.27)	
History of anemia		< 0.01		0.08
No	1		1	
Yes	1.70 (1.14-2.53)		1.46 (0.95-2.24)	
History of opportunistic infections		0.86	N/A	
No	1			
Yes	0.97 (0.65–1.43)			
History of oropharengeal disease		0.92	NA	
No	1			
Yes	1.02 (0.68–1.52)			
History of recurrent diarrhea		0.03		0.03
No	1			
Yes	1.93 (1.08–3.43)		<b>1.96</b> (1.07–3.59)	
History of tuberculosis		0.60	NA	
No	1			
Yes	1.11 (0.74–1.67)			

The bolded values indicate significant association in multivariate logistic regression.

as strength. However, during the interpretation of the findings of this study one has to consider the following limitations. Due to the cross-sectional design of the study, it could not establish the possible cause and effect relationship between independent and dependent variables In addition, since data collection was conducted during a rainy season which is usually associated with a surge in common childhood water-borne illness, it was difficult to discover the seasonal variations. Therefore, we recommend future researchers to consider seasonal patterns.

# Conclusions

The current study finding revealed a higher prevalence of chronic malnutrition among HIV-positive children in conflict affected zones of Southern Ethiopia. As compared to the stunting target set in sustainable developmental goal (SDG), which states to end all forms of malnutrition, our finding was in worst status. In order to mitigate the negative health effects of diarrhea in children during HIV therapy, extra attention needs to be paid to facilitate timely detection and on-going monitoring. Nutrition programs in conflict affected areas need to consider households with larger family size and/or routinely having a fewer food groups.

# Data availability statement

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

## **Ethics statement**

Ethical clearance was initially obtained from the Institutional Review Board (IRB) of Wolaita Sodo University, College of Medicine and Health Science with Ref. No: CRCSD105/02/14. The patients/participants [legal guardian/next of kin] provided written informed consent to participate in this study.

## Author contributions

AA: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Software, Supervision, Writing—original draft, Writing—review & editing. JK: Investigation, Methodology, Supervision, Validation, Visualization, Writing—original draft, Writing—review & editing.

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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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