



Availability of the Yellow Fever Vaccine in Primary Health Care Services in Brazil

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Objectives: To analyze the availability of the Yellow Fever (YF) vaccine at Primary Health Care (PHC) services located in areas with vaccine recommendation in Brazil between two different periods.

Methods: Secondary data from the Program for Improving Access and Quality in PHC. with 13,666 services in 2013-14, and 19,125 in 2017-18, were used. A structured questionnaire was used for the data collection. Pearson's chi-square and thematic cartographic maps were used to analyze the frequency of the YF vaccine, and Poisson regression with robust variances was used to analyze the associated factors.

Results: The overall frequency of PHC facilities with YF vaccine always available increased from 87.0% (CI 95%; 86.4-87.5) in 2013-14 to 89.7% (CI 95%; 89.2-90.1) in 2017-18. Facilities located in the South, Southeast, Midwest and Northern regions and in non-state capitals, as well as centers that had adequate facilities for vaccination actions, as well as an adey -50quate cold chain network, showed a greater prevalence of YF vaccine always available.

Conclusion: The frequency of a steady supply of YF vaccine available at PHC facilities, located in Areas with Routine Vaccination Recommendations, increased between 2013-14 and 2017-18. Geographical and structural characteristics related to vaccine actions at PHC facilities influenced access. The effective supply chain networks for the YF vaccine, together with adequate services at PHC facilities are essential to ensuring that the YF vaccine is always available.

Keywords: vaccines, yellow fever vaccine, yellow fever, primary health care, cross-sectional study, health services accessibility

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INTRODUCTION

Despite the importance of epidemiological control of the Yellow Fever (YF), many countries have reported shortages of vaccine for up to three or more years during the last decade (1) and others have constantly faced situations of insufficient stock, even while experiencing disease outbreaks (2-4). Considering that such a vaccine is highly effective and that a single dose provides immunity throughout life, the inadequate availability of vaccines, in the face of demand, may be one of the answers to the persistence of the problem that poses risks to global health (2, 5).

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In addition to the shortcomings in the supply of the vaccines, recognized in many countries, problems with continued access can affect the day-to-day of the health services that should consistently offer it as part of the immunization program supply chain. In this regard, the lack of vaccines, when individuals seek them out, has been repeatedly identified as one of the main causes of missed opportunities in vaccination (6, 7).

There are no studies that analyze the continued availability of the YF vaccine in Brazilian Primary Health Care (PHC) services. Additionally, there is still no evidence that the expansion of the Areas with Routine Vaccination Recommendations (ARVR) (8), beginning in 2001, in Brazil, has been accompanied by an adequate supply of vaccine in these services. On the another hand, there is evidence that geographical and structural characteristics of the services can influence the continued availability of vaccines at PHC facilities (5, 7, 9, 10).

The expansion of ARVR was intensified simultaneously with the emergence of an YF outbreak in Brazil from 2016 to 2017 (8). This outbreak may have contributed to the availability of the YF vaccine at PHC facilities. In fact, the acquisition of YF vaccine was expanded in response to the outbreak by the Brazilian Minister of Health in 2016. However, the distribution of this vaccine to the PHC facilities did not occur equally, resulting in shortages of this vaccine throughout metropolitan regions (11).

Considering this context and the recommendations for assessing the distribution of YF vaccines (3), the objective of this study was to analyze the availability of the YF vaccine at PHC facilities located in ARVR in Brazil, between the periods 2013-14 and 2017-18.

METHODS

This was a study that used secondary data from a cross-sectional survey applied to the professionals responsible for the PHC facilities that participated in the second and third cycles of the Program for Improving Access and Quality in Primary Health Care (PIAQ-PHC). The PIAQ-PHC is a financial incentive program of the Brazilian Ministry of Health that aims to improve access and quality of PHC in the context of the National Health System (Sistema Único de Saúde - SUS)

These evaluation cycles were conducted by the Ministry of Health in partnership with 41 research institutions under the leadership of the Oswaldo Cruz Foundation (12). Data collection was conducted in 2013-14 (second cycle) and in 2017-18 (third cycle), using a structured questionnaire. On-site guided inspections and verification of records was also done in order to certify the information contained in the questionnaire. About one thousand trained interviewers took part in data collection using electronic devices (tablets). The questionnaire responses were automatically sent to a central server, and the evaluation of data consistency was performed under the coordination of the Department of Primary Care of the Ministry of Health. The data resulting from these two processes are available at https://aps. saude.gov.br/ape/pmaq.

The original data totaled 24,499 PHC services evaluated in 2013-14 and 30,346, in 2017-18. In this study, was considered: services located in the ARVR that offered vaccinations regularly. Applying these criteria, 13,666 PHC facilities from the second cycle and 19,125 from the third were studied, corresponding to approximately 45.0% and 78.0% of the total Brazilian PHC facilities, respectively. The exclusion of services did not represent losses for this study. We selected all vaccination services that should mandatorily offer the YF vaccine in municipalities that adhered to the Program.

The dependent variable was "YF vaccine always available" (Yes/No), which means that when a person seeks the service to receive the vaccine, the vaccine is always available. The independent variables, chosen on the basis of previous studies and for theoretical reasons (7, 9, 13), were geographical (municipalities, capitals [Yes/No], the 26 Brazilian States and the Federal District Capital and the country's five Regions [North, Northeast, South, Southeast, and Midwest]); the adequacy of the PHC facility services for vaccination actions (Yes/No) and adequate cold chain network (Yes/No). "Adequate facilities for vaccination actions" were defined as a PHC facility with adequate capacity specifically for this purpose. "Adequate cold chain network" was assumed when the PHC facility had a vaccination room exclusively for vaccination actions, exclusive refrigerators and thermal vaccine boxes for vaccines.

The analyses were performed using the Statistical Package for Social Sciences (SPSS) software, version 20.0. Initially, the geographical characteristics and those related to the facilities and functioning of the PHC services were analyzed, considering absolute and relative frequencies, according to the periods. Next, the frequency of "YF vaccine always available" was analyzed, for both periods, according to the independent variables, considering the 95% confidence intervals (CI) and Pearson's chi-square test. Additionally, the frequency of "YF vaccine always available" in the municipalities were analyzed using Choropleth Thematic maps. The frequency was calculated considering the number of PHC facilities responding "Yes" to "YF vaccine always available" over the number of services studied multiplied by 100. Poisson regression models were used to analyze possible differences in the availability of the vaccine between the periods 2013-14 and 2017-18. In the complete model (model 2), using a multivariate Poisson regression with robust variances, the analyze was controlled by geographic variables and those related to the structure and functioning of the services, considering those with p-value <0.05 in Pearson's chi-square. For these models, the prevalence ratios were estimated, with their respective 95%CI, using the Wald test. The level of statistical significance was set at 5% (p <0.05) for all analyzes.

RESULTS

Data from 32,791 PHC facilities assessments, from both periods and distributed across country, was included in this study. The largest number of services evaluated was in the Northeast region and the smallest was in the Northern region. The states of Minas

Gerais and Bahia had the largest number of facilities included, ranging from 13.9 to 15.2%. The facilities located in the state capitals represented just under 7% of the total. The vast majority had adequate physical capacities for vaccination actions and an adequate cold chain network (**Table 1**).

The overall frequency of PHC facilities with YF vaccine, always available, was 87.0% (CI 95%; 86.4-87.5) in 2013-14 and 89.7% (CI 95%; 89.2-90.1) in 2017-18. In both study periods, the services located in the Northeast region had the YF vaccine always available with less frequency when compared to those located in the other regions (p<0.001). Also, during both periods, services located in state capitals had YF vaccine always available with less frequency

(p<0.001). A greater frequency of availability was identified at PHC facilities that possessed an adequate physical capacity and an adequate cold chain network for vaccination actions (**Table 2**).

The frequency distribution of the available on demand YF vaccine always available at PHC facilities across the country, during both periods, is presented in **Figure 1**. The maps stand for the spatial differences for the availability of the YF vaccine. In 2017-18, there was a greater proportion of municipalities having dark tones when compared to 2013-14.

Two different regression models were considered for the analysis of the availability of the YF vaccine (**Table 3**). The basic model (model 1) considered only the variable "period" (2017-

TABLE 1 | Geographic and structural characteristics of the Primary Health Care facilities studied in 2013-14 and 2017-18, Brazil.

	2013-14 n = 13666		2017-18 n = 19125		Total	
	n	%	N	%	n	%
Regions						
North	1321	(9.67)	1758	(9.19)	3079	(9.39)
Midwest	1532	(11.21)	1702	(8.90)	3234	(9.86)
South	2574	(18.84)	2902	(15.17)	5476	(16.70)
Southeast	3637	(26.61)	5915	(30.93)	9552	(29.13)
Northeast	4602	(33.67)	6848	(35.81)	11450	(34.92)
States		, ,		, ,		, ,
Federal District	21	(0.15)	29	(0.15)	50	(0.15)
Roraima	35	(0.26)	59	(0.31)	94	(0.29)
Paraíba	47	(0.34)	169	(0.88)	216	(0.66)
Amapá	51	(0.37)	54	(0.28)	105	(0.32)
Acre	81	(0.59)	132	(0.69)	213	(0.65)
Espírito Santo	83	(0.61)	262	(1.37)	345	(1.05)
Rondônia	113	(0.83)	110	(0.58)	223	(0.68)
Alagoas	126	(0.92)	342	(1.79)	468	(1.43)
Sergipe	143	(1.05)	150	(0.78)	293	(0.89)
Rio de Janeiro	177	(1.30)	892	(4.66)	1069	(3.26)
Amazônia	222	(1.62)	313	(1.64)	535	(1.63)
Tocantins	226	(1.65)	273	(1.43)	499	(1.52)
Mato Grosso do Sul	298	(2.18)	354	(1.85)	652	(1.99)
Rio Grande do Norte	312	(2.28)	517	(2.70)	829	(2.53)
Pernambuco	374	(2.74)	648	(3.39)	1022	(3.12)
Maranhão	444	(3.25)	1127	(5.89)	1571	(4.79)
Mato Grosso	453	(3.31)	553	(2.89)	1006	(3.07)
Ceará	459	(3.36)	664	(3.47)	1123	(3.42)
Piauí	571	(4.18)	781	(4.08)	1352	(4.12)
Pará	593	(4.34)	817	(4.27)	1410	(4.30)
Santa Catarina	640	(4.68)	705	(3.69)	1345	(4.10)
Goiás	760	(5.56)	766	(4.01)	1526	(4.65)
Rio Grande do Sul	863	(6.31)	1050	(5.49)	1913	(5.83)
São Paulo	1032	(7.55)	2122	(11.10)	3154	(9.62)
Paraná	1071	(7.84)	1147	(6.00)	2218	(6.76)
Bahia	2126	(15.56)	2450	(12.81)	4576	(13.96)
Minas Gerais	2345	(17.16)	2639	(13.80)	4984	(15.20)
Located in state capitals	2040	(17.10)	2000	(10.00)	4004	(10.20)
Yes	907	(6.64)	1377	(7.20)	2284	(6.97)
No	12759	(93.36)	17748	(92.80)	30507	(93.03)
Adequate physical capacity for vaccination actions	12709	(90.00)	17740	(32.00)	30307	(33.03)
Yes	9708	(71.04)	14999	(78.43)	24707	(75.35)
No	3958	(28.96)	4126	(21.57)	8084	(24.65)
Adequate cold chain network	0300	(20.30)	7120	(21.01)	0004	(24.00)
Yes	12110	(88.61)	17968	(93.95)	30078	(91.73)
No	1556	(11.39)	1157	(6.05)	2713	(8.27)
INC	1330	(11.39)	1101	(0.00)	2110	(0.27)

TABLE 2 | Analysis of the of the availability of the Yellow Fever vaccine at Primary Health Care facilities in the second and third cycles of external evaluations of the Program for Improving Access and Quality in Primary Health Care, according to geographic and structural variables related to vaccine actions, Brazil, 2013-2014 (n = 13666) and 2017-2018 (n = 19125).

	Yellow Fever vaccine always available							
	2013-14			2017-18				
	n	(%)	(CI 95%)	р	n	(%)	(CI 95%)	р
Brazilian	11886	(87.00)	(86.4-87.5)		17150	(89.70)	(89.2-90.1)	
Regions				< 0.001				< 0.001
Northeast	3484	(75.71)	(74.4-96.4)		5471	(79.89)	(78.9-80.8)	
Southeast	3307	(90.93)	(89.9-91.8)		5656	(95.62)	(95.1-96.1)	
South	2361	(91.72)	(90.6-92.7)		2656	(91.52)	(90.4-92.5)	
North	1259	(95.31)	(94.0-96.4)		1705	(96.99)	(96.0-97.7)	
Midwest	1475	(96.28)	(95.2-97.1)		1662	(97.65)	(96.8-98.3)	
State capital locations				0.002				0.010
Yes	819	(90.30)	(88.1-92.1)		1263	(91.72)	(90.1-93.1)	
No	11067	(86.74)	(86.1-87.3)		15887	(89.51)	(89.1-90.0)	
Adequate physical capacity for vaccination actions				< 0.001				< 0.001
Yes	8612	(88.71)	(88.1-89.3)		13537	(90.25)	(89.8-90.7)	
No	3274	(82.72)	81.5-83.9)		3613	(87.57)	(86.5-88.6)	
Adequate cold chain network				< 0.001				< 0.001
Yes	10724	(88.55)	(88.0-89.1)		16189	(90.10)	(89.7-90.5)	
No	1162	(74.68)	(72.4-76.8)		961	(83.06)	(80.7-85.2)	

n, number of services; p, statistical significance test (chi-square); 95% Cl, Confidence Interval.

18 and 2013-14). In the complete model (model 2) all independent variables were included in the analysis, including the variable "period". Model 1 shows that, in the most recent period, PHC facilities had a greater frequency of YF vaccine always available (PR = 1.027; 95%CI: 1.020-1.035). After adjusting for all independent variables, in model 2, the prevalence ratio for the most recent period dropped from 1.027 to 1.025 but maintained statistical significance (p<0.001). Services located in the South, Southeast, Midwest and North regions and in non-state capitals, as well as an

adequate cold chain network, demonstrated a greater prevalence of YF vaccine always available.

DISCUSSION

The proportion of PHC facilities located in the ARVR with YF vaccine always available increased from 2013-14 to 2017-18. With this result, we can assume that the number of vaccine doses were more sufficient for the population in the second studied

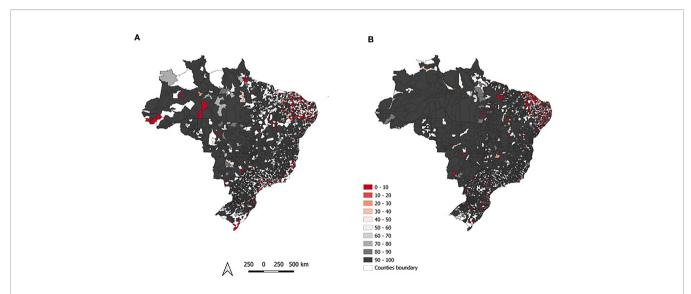


FIGURE 1 | - Geographical distribution of the Yellow Fever vaccine (always available) at primary health care facilities located in Areas with Routine Vaccination Recommendations in Brazil between the periods 2013-14 (A) and 2017-18 (B).

TABLE 3 | Poisson regression analysis for the Yellow Fever vaccine (always available) at primary health care facilities located in Areas with Routine Vaccination Recommendations in Brazil between the periods 2013-14 and 2017-18.

Variables	Model 1		Model 2*		
	PR (CI 95%)	P	PR (CI 95%)	Р	
Period					
2013-14	_		_		
2017-18	1.027 (1.020-1.035)	< 0.001	1.025 (1.018-10.33)	< 0.001	
Regions					
Northeast			_		
Southeast			1.163 (1.152-1.174)	< 0.001	
South			1.037 (1.125-1.150)	< 0.001	
North			1.204 (1.192-1.217)	< 0.001	
Midwest			1.204 (1.193-1.216)	< 0.001	
State capital locations					
No			_		
Yes			0.979 (0.967-0.992)	0.001	
Adequate physical capacity for vaccination actions					
No			_		
Yes			1.026 (1.017-1.035)	< 0.001	
Adequate cold chain network					
No			_		
Yes			1.087 (1.069-1.104)	< 0.001	

p, statistically significant test; CI 95%, Confidence Interval; PR, Prevalence Ratio; *Poisson regression with robust variances.

period. Geographical aspects and an adequate cold chain network and an adequate capacity for facilities to engage in vaccination actions influenced YF vaccine availability.

In addition to geographic and structural factors, the increase in the availability of the YF vaccine may have been related to the emergence of an YF outbreak in Brazil, when the acquisition of YF vaccine by Brazilian Minister of Health was expanded (8, 14). The availability of the YF vaccine was greater in non-capital cities, reinforcing that the distribution of this vaccine to the PHC facilities did not occur equally (11).

As reported by other studies, cold chain networks that fail to guarantee safe and uninterrupted conservation and maintenance of immunobiologicals, compromise logistical and operational sustainability of immunization services, resulting in reductions in vaccine stocks (15–17). The lack of inputs and equipment essential for the conservation of immunobiologicals, such as coolers and refrigerators, imposes the first barrier to the availability of the YF vaccine, with risks at compromising vaccination coverage and the formation of grouping of individuals susceptible to the virus (6, 7, 18–21). When infrastructure of the services is inadequate, and large dose losses occur, the population's access to vaccines can be greatly compromised (22, 23).

It should be noted, considering the samples of facilities studied, that the number of PHC facilities in the ARVR increased between the studied periods, reflecting the decision for expansion by the National Immunization Program. However, the frequency of availability of the YF vaccine at PHC facilities increased relatively less than the number of services in the ARVR between the two study periods.

In examining the findings of this study, we conclude that, in addition to expansion of ARVR, it is essential to expand the availability of the YF vaccine in PHC facilities. From a public health standpoint, our findings suggest that the effective supply chain networks for YF vaccine, combined with the adequate capacity of PHC facilities and services, are essential to ensuring their availability in order to achieve universal access to immunoprevention and to improve vaccine coverage indicators.

In view of the last outbreak of YF in Brazil, and the results of our findings, consideration should be directed at the factors related to the physical capacity of PHC facilities and services throughout Brazil targeting actions aimed at maintaining optimal vaccination coverage against the disease. Furthermore, the same factors that are related to YF vaccine availability may also be implicated in the risk of resurgence of other preventable diseases in the country. Studies that consider factors possibly related to vaccine availability at the central levels of distribution and logistics networks are recommended.

As this was a nationwide study, it was possible to assess and compare the availability of YF vaccine at PHC facilities from the five regions of Brazil. However, this study had some intrinsic limitations, including the impossibility of proving causal inferences, since the data were collected over a single moment. Another limitation was related to the lack of evaluation of PHC facilities along remote riverbeds in the Amazon rainforest region.

In 2020, the National Immunization Program in Brazil expanded the recommendation of vaccination against YF to the entire national territory. This expansion occurred in response to a growing number of cases of the disease, which alerted to the reemergence of urban YF in the country. In this sense, structural problems, probably related to regional differences in investments in the health sector, need to be the focus of public policy decision makers.

DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. This data can be found here: https://aps.saude.gov.br/ape/pmaq/ciclo3/.

AUTHOR CONTRIBUTIONS

EV, conceived and designed the analysis, collected the data, wrote the paper, performed the analysis, analysis and interpretation of data, and drafting of manuscript. MH and

TDS, contributed data or analysis tools, wrote the paper, analysis and interpretation of data, and drafting of manuscript. SL, FM, and MB, wrote the paper, analysis and interpretation of data, and drafting of manuscript.

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