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Evolution of Mother-to-Child HIV-1 Transmission Rate in Mali from 2009 to 2018

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Abstract

Despite enormous efforts to achieve the goal of eliminating mother-to-child transmission of HIV-1, it remains a major challenge for many countries in sub-Saharan Africa, particularly Mali. Our objective is to assess changes in the rate of mother-to-child transmission of HIV-1. We conducted a cross-sectional study between January 1, 2009 to December 31, 2018 (10 years) of early diagnosis activity in newborns and children born to HIV-1-positive mothers at the National Institute for Public Health (INSP). The samples came from health and referral centers in mali. All samples were received at the Laboratory of Molecular Biology at the INSP. Proviral DNA extraction was performed from a blood spot sample with a Roche DNA kit, Cobas AmpliPrep/Cobas TaqMan HIV-1 qualitative Test, V2.0 (Roche Molecular System, Inc, USA) following the company procedures. Molecular diagnosis was performed using the same kits using an algorithm of three identical PCRs. The Epi Info version 7 software was used for data analysis with a significance threshold of 5%. A total of 10,714 samples of infants and children born to HIV-positive mothers were analyzed by PCR. Ninety-six percent of mothers were on ARV prophylaxis (AZT + 3TC + NVP and AZT + NVP) and 60% of newborns received the same ARV prophylaxis. Of these children, 956 tested positive with an overall transmission rate of 8.92%, varying between 7.27% in 2009 and 08.01% in 2018. This rate was relatively low among children receiving prophylaxis at 2.04% and remained high for children who received breastfeeding at 5.62%. However, the transmission rate remains low for those who have benefited from mixed and artificial breastfeeding at 1.58% and 1.27% respectively. A

significant proportion of children remained infected by their mothers during pregnancy, childbirth or breastfeeding. This study shows the importance of early diagnosis of HIV in children using molecular technology.

Keywords

Early Diagnosis, Mothers-to-Child, Newborns, PCR, DNA, HIV-1

1. Introduction

For several decades, the fight against the human immunodeficiency virus (HIV) has remained a public health issue [1]. An HIV-infected woman could transmit the virus to her child during pregnancy, labour, delivery or breastfeeding [1] [2]. The main route of mother-to-child transmission of HIV remains vertical [1]. In 2021, United Nations programs on HIV/AIDS (UNAIDS) have estimated that 1.7 million children (0 - 14 years) were living with HIV [3]. It has been described that the HIV transmission rate during childbirth is 15% to 30% and 20% to 45% for breastfed children, in the absence of surgery [1] [4] [5]. In 2021, it was noted that at the global level, efforts are still needed, in particular to reduce breast-feeding-related mother-to-child HIV-1 transmission [6]. However, in developed countries, the risk of mother-to-child transmission of HIV-1 has been reduced to less than 1% because of the widespread of antiretroviral therapy among pregnant women and children exposed to HIV and the routine use of breastfeeding [7]. This transmission was 2.27% in 2017 in Taiwan and highly variable in Africa, with 12.7% in 2013 in the DRC and 7.8% in Cameroon in 2011 [1] [8] [9]. In Mali, this transmission was variable, with 9.14% in 2017 and 6.96% in 2021 [10] [11]. The vertical transmission appears to be very high in resource-limited countries, making the prevention of mother-to-child transmission of HIV (PMTCT) a priority of the HIV/AIDS program. Literature shows that the evolution of the rate of mother-to-child transmission of HIV1 in sub-Saharan Africa is highly variable and decreased by 48% between 2009 and 2014 [12]. PMTCT is one of the priority interventions of the HIV/AIDS program and countries' strategy for an effective response to AIDS. The PMTCT, started in 2001 in Mali with only one site, today there has been significant progress in the field of prevention. In 2011, there were 338 PMTCTT prevention sites, evidence that the increase in PMTCT sites has undoubtedly increased the number of pregnant women screened and the number of women receiving ARVs. Despite these efforts in the prevention of mother-to-child transmission, there are still shortcomings in the number of children screened to HIV-positive mothers for the determination of the transmission rate. To our knowledge, very few studies on the evolution of the mother-to-child transmission rate of HIV-1 have been conducted in Mali to date. The objective of this study is to assess the 10-year change in the rate of mother-to-child transmission of HIV.

2. Methodology

Data entry and analysis were carried out using Epi Info software, version 7 with a significance threshold α equal to 5%.

The study took place in Bamako at the laboratory of Molecular Biology, INSP. This was a descriptive cross-sectional study over a period of 10 years from January 1th 2009 to December 31, 2018. It focused on newborns and children (less than 6 weeks of age to 104 weeks or less) born to HIV-1 positive mothers in the health districts of five regions of Mali (Kayes, Koulikoro, Sikasso, Ségou, Mopti) and the District of Bamako. At baseline, a detailed medical history of treatment for each HIV-1 positive mother and a blood sample from her newborn were taken. Blood samples were collected on blotting paper (confetti) from newborns and children included in the study. Newborns and children born to HIV-2 positive mothers were not included in the study. For HIV infection diagnostics in newborns and children born to HIV-1 positive mother, we performed whole blood dried on blotting paper (confetti and proviral DNA was extracted from confetti according to the extraction protocol of the Roches Cobas AmpliPrep/Cobas TaqMan48 HIV-1 qualitative Test, V2.0 (Roche Molecular System, Inc., 1080 US Highway 202 South Switzerland /Roche Molecular System, Inc, USA) and Abbott molecular qualitative kits (Abbott mSample Preparation System DNA (4 × 4 Preps), Madison, WI 53711 USA) and on the Cobas AmpliPrep (Roche, Switzerland) and Abbott m2000sp automate (Abbot Molecular Inc., Des Pleines, IL 60018 USA). The amplification was performed on COBAS Taqman48 (Roche Diagnostics Ltd., Rotkreuz, Switzerland) and m2000rt (Abbot Molecular Inc., Des Pleines, IL 60018 USA) respectively from Roche molecular and Abbott molecular laboratories.

The interpretation of the diagnosis was made according to an algorithm of three identical PCRs: 1st PCR on all confetti, 2nd PCR on the positives of the 1st PCR and the cases of confirmation request and the 3rd PCR to confirm the cases of possible discrepancies on the results of the first two PCRs. Data entry and analysis were carried out using the Epi Info software, version 7 with a significance threshold α equal to 5%.

Ethical considerations

Participation in this study was voluntary, free and anonymous. It was conditional on obtaining verbal and signed consent. The protocol has been approved by the Institutional Ethics Committee of the National Institute for Public Health (INRSP) under number 06/2016/CE-INRSP.

3. Results

From 2009 to 2018, a total of 10714 newborns and children born to HIV-1-positive mothers under the age of 18 months were included in the study. There was no significant difference between the two sexes p = 0.76 (Table 1), the age of our children born to HIV-1 positive mothers included was categorized in week intervals and according to the achievement of the different PCRs.

Table 1. Social demographic characteristics of children according to completion of PCRs and according to age.

Variables	Number of children					
Sex	Number			Percentage		
Male	5373			50.15		
Feminine	5341			49.85		
	Sex, p-value = 0.76					
Age PCR1	Number			Percentage		
≤6	1726			16.11		
>6	8988			83.89		
Age group	**PCR 1**		**PCR 2**		**PCR 3**	
	Sex		**Sex**		**Sex**	
	Male	Feminine	Male	Feminine	Male	Feminine
≤6	856 (49.59%)	870 (50.40%)	3 (50%)	3 (50%)	0	0
[7 - 12]	2135 (50%)	2135 (50%)	245 (49.80%)	247 (50.20%)	3 (37.5%)	5 (72.5%)
[13 - 24]	687 (50.70%)	668 (49.30%)	372 (48.90%)	389 (51.12%)	12 (70.59%)	5 (29.41%)
[25 - 48]	749 (50.13%)	745 (49.87%)	324 (50.55%)	317 (49.45%)	16 (61.54%)	10 (38.46%)
[49 - 72]	486 (52.15%)	446 (47.85%)	67 (41.36%)	95 (58.64%)	7 (33.33%)	14 (66.67%)
[73 - 104]	2 (50%)	2 (50%)	3 (50%)	3 (50%)	7 (41.18%)	10 (58.82%)
NP*	458 (49.10%)	475 (50.90%)	497 (49.35%)	510 (50.65%)	770 (48.37%)	822 (51.63%)
[PCR age]*	-		7639		9033	
Total	5373 (50.15%)	5341 (49.85%)	1511 (49.14%)	1564 (50.86%)	815 (48.48%)	866 (51.52%)
Sites	Number			Percentage		
Bamako	7760			72.43		
Kayes	295			2.75		
Koulikoro	514			4.80		
Sikasso	1256			11.72		
Segou	776			7.24		
Mopti	113			1.05		

[PCR age]*: PCR age not performed; There is not a big gender gap in different age groups.

All children have received the 1st PCR, however, among them, those in the age group 6 weeks to 6 months were mostly represented with 68.6% (7351/10714) followed by those from 7 - 12 weeks with 39.9% of the study population (Table 1 and Table 2). The age was not provided for 8.7%, 9.4% and 14.86% of the children for the 1st PCR, 2nd PCR and 3rd PCR respectively. The frequency of children who did not receive the 2nd PCR and 3rd PCR, was 71.3% and 84.3% respectively (Table 2).

It appears that 96.2% of mothers of study population were on antiretroviral prophylaxis (Table 3). The overall rate of HIV positive children was 8.9% in our study population (Table 4). Among them, 5.6% mothers were on prophylaxis, compared to 3.1 whose mothers were not on prophylaxis (Table 4). There was no HIV in children who received Nevirapine from birth (Table 5). However, a relatively low rate of transmission was observed in the group of children who received AZT, AZT/NVP, AZT/3TC/NVP as a prophylactic regimen, respectively, 0.03%, 0.03% and 0.07% (Table 5). The rate of mother-to-child transmission of HIV was higher among children who did not receive prophylaxis and those whose treatment with prophylaxis was unknown respectively 4% and 3% (Table 5). Compared to breastfeeding patterns, the rate of transmission was higher among children on protected breastfeeding (ART) at 5.6% (Table 5). Over the ten years of evaluation, the transmission rate on the year varied from 7% to 10%, this rate reached a relatively high level in 2012 with 10% (Figure 1, Table 6).

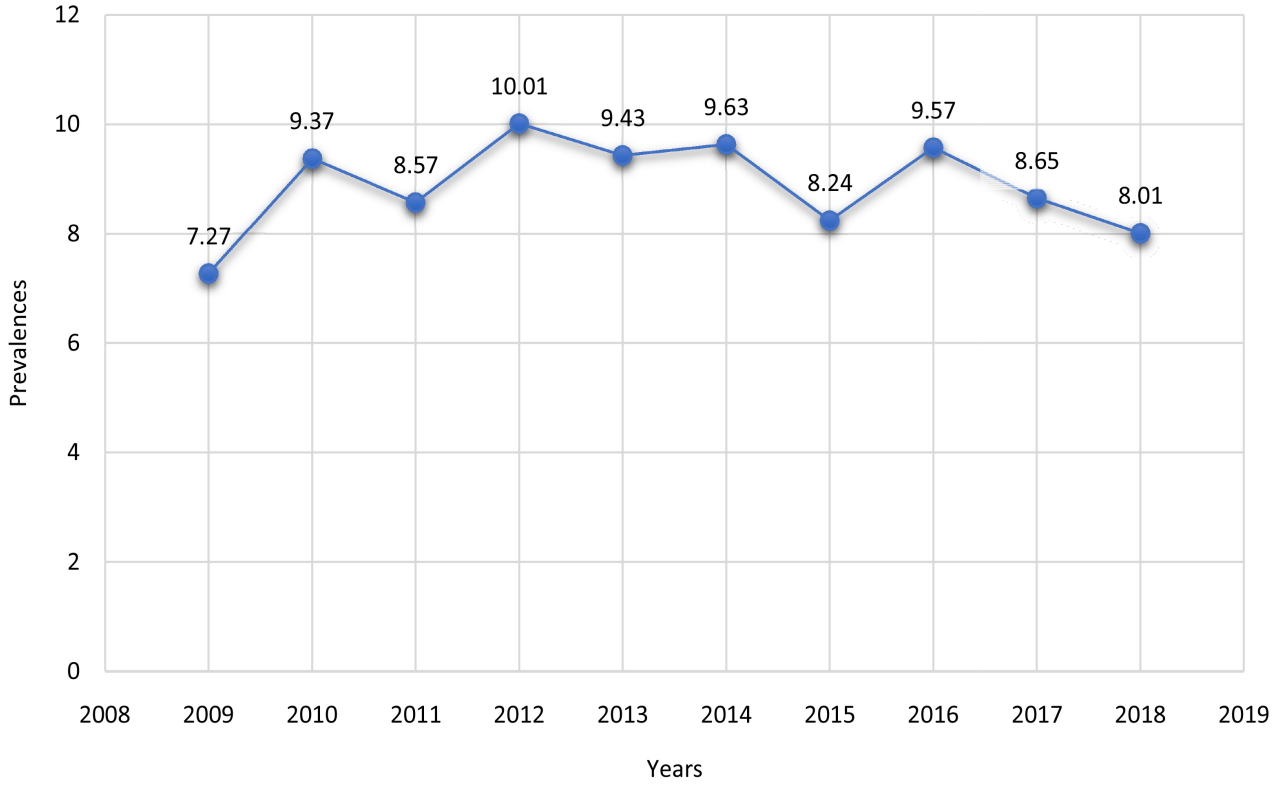

Figure 1. Evolution of HIV transmission in children depending on the year.

Table 2. Number of children according to the completion of PCRs and according to age.

Age of performing PCR in intervals of weeks	Number of children based on PCR carried out		
	PCR 1	PCR 2	PCR 3
	Number	Number	Number
≤6	1726 (16.11%)	6 (0.06%)	0
[7 - 12]	4270 (39.85%)	492 (4.59%)	8 (0.07%)
[13 - 24]	1355 (12.65)	761 (7.10%)	17 (0.16%)
[25 - 48]	1494 (13.94%)	641 (5.98)	26 (0.24%)
[49 - 72]	932 (8.70%)	162 (1.51%)	21 (0.20%)
[73 - 104]	4 (0.04%)	6 (0.06%)	17 (0.16%)
NP*	933 (8.71%)	1007 (9.40%)	1592 (14.86%)
[PCR age] not carried out	-	7639 (71.30%)	9033 (84.31%)
Total	**10714**	**10714**	**10714**

NP*: Not specified.

Table 3. Distribution of mothers according to prophylaxis.

Maternal prophylaxis	Frequency	Percentage
Yes	10,311	96.24%
No	386	3.60%
NP*	17	0.16%
Total	**10,714**	**100**

NP*: Not specified.

Table 4. HIV transmission rates among children according to maternal prophylaxis.

Prophylaxis in mothers	Transmission Rates in Children	
	Negative NOT	Positive NOT
Yes	9706 **(91)**	605 **(5.64)**
No	52 **(0.48)**	334 **(3.12)**
NP*	0 **(0)**	17 **(0.16)**
Total	**9758 (91.08)**	**956 (8.92)**

NP*: Not specified.

Table 5. HIV transmission rates in children according to prophylaxis and type of feeding in the child.

Prophylaxis in children	Transmission rate	
	Negative NOT	Positive NOT
Yes	5484 **(51.19%)**	**194 (1.81%)**

Continued

No	2778 (25.93%)	434 (4.05%)
NP*	1496 (13.96%)	328 (3.06%)
Total	**9758 (91.08%)**	**956 (8.92%)**
Type of Prophylaxis in children		
AZT	10 **(0.09%)**	3 **(0.03%)**
AZT/3TC/NVP	51 **(0.48%)**	7 **(0.07%)**
AZT/NVP	283 **(2.64%)**	3 **(0.03%)**
NPV	8 **(0.07%)**	0 **(0%)**
Yes (prophylactic regimen not specified)	5132 **(47.90%)**	181 **(1.69%)**
No	2778 **(25.93%)**	434 **(4.05%)**
NP*	1496 **(13.96%)**	328 **(3.06%)**
Total	**9758 (91.07%)**	**956 (8.93%)**
Power type		
AAE	2398 **(22.38%)**	136 **(1.27%)**
A. M.	363 **(3.39%)**	169 **(1.58%)**
AMP	6431 **(60.02%)**	602 **(5.62%)**
NP*	566 **(5.28%)**	49 **(0.46%)**
Total	**9758 (91.07%)**	**956 (8.93%)**

NP*: Not specified; AAE*: Artificial Breastfeeding; AM*: Mixed Breastfeeding; AMP*: Protected Breastfeeding; AZT*: Zidovudine; AZT/3TC/NVP*: Zidovudine/Lamivudine/Nevirapine; **NPV***: Nevirapine.

Table 6. Transmission rate according to type of breastfeeding per year.

Year	Type of breastfeeding									
	AAE*		AM*		AMP*		NP*		Total	
	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive
2009	225 (39.89%)	15 (2.66%)	24 (4.26%)	15 (2.66%)	258 (45.74%)	10 (1.77%)	16 (2.84%)	1 (0.18%)	523 (92.73%)	41 (7.27%)
2010	360 (42.20%)	21 (2.46%)	41 (4.81%)	38 (4.45%)	333 (39.04%)	15 (1.76%)	39 (4.57%)	6 (0.70%)	773 (90.62%)	80 (9.37%)
2011	425 (30.36%)	10 (0.71%)	79 (5.64%)	30 (2.14%)	732 (52.29%)	74 (5.28%)	44 (3.14%)	6 (0.43%)	1280 (91.43%)	120 (8.57%)
2012	145 (17.49%)	5 (0.60%)	34 (4.10%)	15 (1.81%)	510 (61.52%)	57 (6.88%)	57 (6.88%)	6 (0.72%)	746 (89.99%)	83 (10.01%)
2013	268 (20.40%)	10 (O.76%)	54 (4.11%)	23 (1.75%)	814 (61.95%)	87 (6.62%)	54 (4.10%)	4 (0.30%)	1190 (90.56%)	124 (9.43%)
2014	170 (16.88%)	8 (0.79%)	35 (3.48%)	17 (1.69%)	651 (64.65%)	68 (6.75%)	54 (5.36%)	4 (0.40%)	910 (90.37%)	97 (9.63%)

Continued

2015	77 (16.28%)	7 (1.48%)	8 (1.69%)	2 (0.42%)	306 (64.69%)	29 (6.13%)	43 (9.09%)	1 (0.21%)	434 (91.75%)	39 (8.24)
2016	187 (16.42%)	13 (1.14%)	16 (1.41%)	10 (0.88%)	754 (66.26%)	79 (6.94%)	72 (6.33%)	7 (0.62%)	1029 (90.42%)	109 (9.58%)
2017	302 (16.65%)	25 (1.38%)	54 (2.98%)	13 (0.72%)	1179 (64.99%)	112 (6.17%)	122 (6.73%)	7 (0.38%)	1657 (91.35%)	157 (8.65%)
2018	239 (18.08%)	22 (1.66%)	18 (1.36)	6 (0.45%)	894 (67.62%)	71 (5.37%)	65 (4.92%)	7 (0.53%)	1216 (91.98%)	106 (8.01%)

AAE*: Exclusive Artificial Breastfeeding, AM*: Mixed Breastfeeding, AMP*: Protected Breastfeeding, NP*: Not specified.

4. Discussion

Almost half of the children in our study were female. This result is similar to the study carried out by Gutema *et al.* and Desta ML. and collaborators in Ethiopia [13] [14]. The 1st PCR test for newborns and children born to HIV-positive mothers is recommended by the HIV testing algorithm in Mali at six weeks old. Thus, all the age groups enrolled in our study have received the 1st PCR, children of 7 - 12 weeks age group were majority with a frequency of 39.9%. This rate is about half of that reported by Anoje *et al.* 2012 in Nigeria, in which more than 70% of infants receive the first PCR after six weeks old [15]. More than half of the children between 6 weeks and 6 months of age in this study had received PCR1 (68.61%), this result is comparable to that of Nguefack and collaborators who found 53.3% of PCR1 performs in children of the same age group [16]. However, the majority of children of our study were older than 6 weeks, which is contrary to those found by Gutema *et al.* in Ethiopia [14]. This delay in carrying out PCR tests in this age group could be explained by the non-compliance with the PCR test by mothers included in PMTCT as well as those outside PMTCT. Ninety-six percent of our study children mothers were on ARV prophylaxis. This rate is higher than those reported in 2015 in Burkina Faso and in 2012 in Nigeria by Soubeiga *et al.* and Anoje *et al.* respectively [15] [17]. This observation is a good sign of progress and commitment of our governments in meeting the requirements for the achievement of the objectives of PMTCT with the aim of reducing the rate of mother-to-child transmission (MTCT). The transmission rate reported by Linguisssi *et al.* in 2012 was 4.8% in Burkina Faso. This rate is relatively lower than that reported during our study which was 5.6% for children and newborns of mothers under prophylaxis [18]. On the other hand, these rates are much higher than those reported by Soubeiga *et al.* in 2015 and Kouanda *et al.* in 2010 in Burkina Faso who did not have MTCT rate, which could be explained by the small sample size of their study following the PMTCT protocol [17] [19]. Over the entire period of our study, the transmission rate was 8.9% and varied from year to year. These differences in values in transmission rates for geographically close populations could be explained by the methodologies used but also by the non-compliance of the mothers of the children in our study.

Our study found that the rate of transmission among children and newborns of HIV-1 -positive mothers who were not on prophylaxis was 3.12% overall over the entire study period and varied by year. This rate is lower than that reported by Gueye *et al.* in Senegal in 2019 who found a transmission rate in their study population of 24.2% [20].

For children and newborns whose prophylaxis was not specified for mothers, the transmission rate was 0.16%. However, among children on prophylaxis, the transmission rate was 1.81%, this rate corroborates with that reported by Gueye *et al.* in 2019 in Senegal who found 2.1% for children on treatment, while those who had not been in contact with the drugs recorded a rate of 4.05%, almost three times lower than that reported by Gueye SB *et al.* in 2019 for infants without prophylaxis [20]. The rate of transmission in relation to feeding patterns in our study in children and newborns was 5.62% and 1.58%, respectively, for exclusively breastfed children and those on a mixed diet that combines a mixture of nutrients with breastfeeding. Our results for exclusively breastfed children and newborns were higher than those reported in Burkina Faso in 2015 by Yugbare *et al.*, which were 3.08% [21]. On the other hand, with regard to mixed breastfeeding, the rate reported in Burkina Faso in 2015 by Yugbare *et al.*, which was 5.56%, is higher than ours [21]. In our study, the rate of transmission compared to exclusive and breastfeeding was lowest compared to other infant and newborn feeding methods. These results show that exclusive artificial breastfeeding was more protective against mother-to-child transmission of HIV. During this 10-year evaluation period, we observed a fluctuation in the rate of mother-to-child transmission, which peaked in 2012 followed by a slight decrease. The rate increased from 2009 to peak in 2012 from 7.27% to 10.01% which was followed by slight decreases to 8.01% in 2018. This increase in the rate during the first four years of this study is contrary to several other studies, by Gutema and collaborator in Ethiopia from 2.9% in 2016 to 0.9% in 2020 and by Ghoma Linguissi and collaborator in Burkina Faso from 10.4% in 2006 to 0% in 2015 [14] [18]. However, in 2012, we observed a transmission rate of 10%. This considerable increase in transmission rates during 2012 could be linked to the great instability that has affected our country, which has been plagued by political instability. Our study shows a slight increase in the transmission rate during the years 2013, 2014 and 2016 with rates of 9.4%, 9.6% and 9.6% respectively. These MTCT rates by year are different from those reported by Gueye *et al.*, in 2019 in a study on the efficacy of PMTCT via infant early diagnosis data in Senegal which reported a rate of 14.8% in 2008 and 4.1% in 2015 [20]. This difference in the evolution of MTCT rates over the years in these two countries could be explained by the methodology used for the Senegal study, which assessed the effectiveness of prevention of mother-to-child transmission of HIV-1 through early diagnosis.

5. Conclusion

The positivity rate varies from year to year, but early diagnosis by molecular

tools in assessing the rate of mother-to-child transmission of HIV-1 remains essential. Thus, strengthening prevention capacity, testing, initiation of HIV-1-positive mothers with ARVs and early diagnosis are essential to achieve the goals of eliminating mother-to-child transmission of HIV-1.

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Limitation of the Study

The large sample sizes in the study, covering almost two-thirds of Mali's regions and capital, provide an accurate estimate of the HIV-1 positivity rate among children born to HIV-positive mothers.

However, this study has some limitations, the small sample size of the different regions of the country due to logistical difficulties, the non-completeness of the data on some forms. However, these data cannot be generalized to all regions of Mali.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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