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HIV-Exposed Children: Determinants of Early Diagnosis and Survival in the Kongo Central Province, Democratic Republic of the Congo

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Abstract: Introduction. Successful prevention of mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) requires early diagnosis, consistent access to antiretroviral therapy (ART), and regular health care during and after pregnancy. This study assessed the determinants of early HIV diagnosis by children born to HIV-positive (HIV+) mothers in the Kongo Central Province, Democratic Republic of the Congo (DRC). Methodology. Data from 230 HIV+ mothers screened under the PMTCT program between July 2015 and December 2017 were extracted from the databases of 31 Health Zones (HZ) of Kongo Central province. Data detailing laboratory and anthropometric findings, morbidity, and mortality were collected from each exposed child. The determinants of inaccessibility to early diagnosis were identified using logistic regression. Results. The mothers' mean age was 32.4 years, and 90.9% were on ART; 68.8% of children were older than 12 months at diagnosis. Diagnosis during the first 6 months of the child's life was critical. Malnutrition was found in almost 90% of the children. Determinants of non-access to an early diagnosis were mothers who attained a primary education level and did not disclose their HIV status. Conclusion. All possible interventions should be considered to prevent mother-to-child HIV transmission. To ensure a child's survival to their first birthday, early diagnosis should be performed soon after birth to an HIV+ mother and ART should be initiated.

Keywords: HIV-exposed Infants, Determinant, Diagnosis, Survival

1. Introduction

The goal of conquering the HIV epidemic has become more attainable in the last 15 years, making it possible to achieve the United Nations (UN) General Assembly's 2016 ambition to eliminate HIV/AIDS by 2030; UN member countries endorsed this goal as part of the Sustainable Development Goals endorsed by the Joint United Nations Program on HIV and AIDS (UNAIDS) and the World Health Organization (WHO). This call to mobilize nations and implement WHO recommendations will help countries with limited resources to reach the 2030 goal.

The number of people living with HIV (PLWHIV) under antiretroviral therapy (ART) has increased by approximately one third, from 15 million in 2015 to 17 million, an increase of 2 million compared to the target set by the United Nations General Assembly in 2011 [1]. ART remains the only effective treatment to prevent new infections and deaths and

improve the economic burden of this disease [2]. The UN's 90/90/90 goal would screen 90% of PLWHIV, give ART to 90%, and achieve a suppressed viral load in 90%; by the end of 2015, overall coverage had improved to 43%. The increased coverage was most noticeable in the 21 affected priority countries including the Democratic Republic of Congo (DRC) [2]. The worldwide elimination of mother-to-child transmission of HIV is an ambitious goal. Despite significant progress toward this goal over the past decade, most of the 220,000 new pediatric HIV infections in 2014 were attributed to vertical transmission [1].

Although there has been overall progress in achieving WHO recommendations, HIV-exposed children still have limited accessibility to diagnosis and treatment [2]. Late diagnosis of pediatric HIV infections and persistence of vertical transmission continue to be a major challenge despite the introduction of the prevention of mother-to-child transmission (PMTCT) program. In 2014, the WHO estimated that only 50% of all HIV-exposed infants accessed early infant diagnosis (EID) services within 2 months of age, [3] far below the 80% EID coverage recommended by the WHO [4].

These statistics suggest pregnant women and children have limited accessibility to EID in resource-limited settings [5]. Successful PMTCT requires early HIV diagnosis, consistent access to ART, and regular care during and after pregnancy [6]. However, the accessibility of children to diagnosis and antiretroviral (ARVs) remains limited in many countries, including the DRC [7-10], because of socio-cultural barriers described in previous studies: emotional violence, mother's fear of disclosing HIV status to the male partner, fear of societal stigma, and lack of technical facilities in hospitals. The diagnostic technique using a dried blood spot test requires sophisticated equipment, which results in children with HIV / AIDS dying before their first birthdays or not tested until they are at an advanced stage of the disease [11-17].

This study assesses the accessibility of HIV-exposed children to EID and treatment and determines the main deterrents preventing access to care.

2. Methods

2.1. Research Strategy and Data Sources Techniques

Data from the PMTCT program between July 2015 and December 2017 were searched, and data from 230 HIV-positive (HIV+) mothers were extracted from the databases of 31 Health Zones (HZ) of Kongo Central Province. HIV+ mother living in HZ were identified and given to local sub-recipients of the 2015–2017 grant to identify health facilities reporting new cases of HIV+ women from PMTCT services.

Each recruiting facility identified a mother–child pair who were HIV-positive. Based on antenatal consultation records, the mother–child pair was seen in the area where they lived. For reasons of confidentiality, the providers in charge of screening and monitoring the subjects were the only ones able to access information from the ANC and laboratory registers and obtain the informed consent of each HIV+ woman.

2.2. Method of Data Collection

The data were collected using a pre-tested, standard questionnaire. Once selected from the register, we located the mother and child and obtained informed consent, and stated that they had the right to withdraw from the study at any time. Sociodemographic data were collected for both mother and child, including age, marital status, education level, use or no-use of ARV, ARV start date, and anthropometric variables (ages of mother and child, child's birth weight, and date of death if the child had died).

2.3. Method of Data Analysis

The data were collected using Excel 2010 and analyzed with SPSS software version 22. Tables or graphs were used, as appropriate, for the presentation of the results. Continuous quantitative variables with Gaussian distribution were presented as mean±standard deviation and extremes. Kolmogorov-Smirnov test and Levine's test were used to assess the assumption of normal distribution and homogeneity of the data between the two groups (access to care and non-access to care). The qualitative variables were described as absolute and relative frequency (%). The proportions and averages were compared using chi-square and Student's t-tests, respectively.

A Kaplan–Meier estimate described the survival of children between the start of care and death (complete data) and the end of the study (censored data). A log-rank test was used to compare survival curves, and logistic regression was used to search independent determinants for non-access to the children's diagnoses using the backward method step-by-step upward, calculated odds ratios (OR) and their intervals. A 95% confidence interval (CI) was used to estimate the association between independent variables and non-access to diagnosis. A value of $p < 0.05$ was considered the statistical significance level.

2.4. Reliability and Validity

2.4.1. Reliability

The reliability of the study was ensured respectively by a pre-tested standard questionnaire and the training of the interviewers to ensure the correct use of the information collection tool.

2.4.2. Validity

Validity was ensured internally through a random selection of HIV+ pregnant women and their children and externally by the representability ensured by a random selection of the sample in relation to all the HZs and PMTCT sites in Kongo Central.

2.4.3. BIAS

(i) Selection Bias

Selection bias results from subject selection and follow-up

and influences the composition of the sample. In this study, selection bias was reduced by using probability sampling that gives each participant equal chances of being selected.

(ii) Nonresponse Bias

Potential participants who are not found or do not answer certain questions can bias a study because they could have provided different risks or characteristics about the disease. Their nonresponse may be related to their state of health (illness, death) or their interest/disinterest in the study. Efforts were made to find the participants selected for the study.

3. Ethical Consideration

This study was conducted under international standards for research on humans. Before data collection, the protocol was submitted to the Ethics Committee of the Protestant University in Congo (Ref: CEUPC00042) for approval; at the provincial level, authorization was obtained from the Provincial Coordination of the PNLS Kongo Central.

4. Results

The general characteristics of the mothers/guardians in the study are summarized in Table 1. The average age of the mothers was 32.4±6.5 years (range: 16–45), with the highest percentage (51.3%) between 26 and 35 years. The women's marital status was dominated by married and common-law unions (40.9% and 29.1%, respectively).

Table 1. *General characteristics of mothers of children.*

	N=230	**%**
Age		
Mean±SD, Range	32 (4±6.5)	(16–45)
16–25	34	14.8
26–35	118	51.3
36–45	78	33.9
Marital Status		
Married	94	40.9
Cohabitation	67	29.1
Single	42	18.3
Divorced	15	6.5
Widowed	12	5.2
Educational level		
Elementary	123	53.5
High school	100	43.5
University	7	3.0
ARV		
No	21	9.1
Yes	209	90.9
Start of ARV before pregnancy	82	35.7
Start of ARV during pregnancy	127	55.2
Regimen		
AZT + 3TC + NVP	96	41.7
AZT + 3TC + EFV	14	6.1
TDF + 3TC + EFV	67	29.1
NVP alone	3	1.3
AZT alone (prophylaxis)	29	12.6
Last CD4 before delivery		
Available	5	2.2
Unavailable	225	97.8
Last VC before delivery		
Available	1	0.4
Unavailable	299	99.6

Abbreviations: ARV, antiretrovirals; AZT, 4.2 zidovudine; EFV, efavirenz; NVP, nevirapine; TDF, Tenofovir; 3TC, lamivudine.

The largest percentage of women had achieved a primary level of education (53.5%) and were under ARV treatment (90.9%), with most receiving combined treatment of 4.2 zidovudine (AZT) plus lamivudine (3TC) plus Nevirapine (NVP) (41.7%); 35.7% had started ARV before pregnancy and 55.2% during pregnancy.

The general characteristics of the study's child subjects are summarized in Table 2, which indicates that the majority of children were aged between 13–24 months (51.7%); the weight/age ratio shows that 16.2% of children were below -2DS; the height/age ratio was 35.5%; and the weight/height index was 12.6%.

Table 2. *The characteristics of the children.*

	All groups N=230	Female N=120	Male N=110	P value
Age months [n (%)]				0.364
0–12	74 (32.2)	34 (28.3)	40 (36.4)	
13–24	119 (51.7)	67 (55.8)	52 (47,3)	
25–36	37 (16.1)	19 (15.8)	18 (16,4)	
Birth weight	3.06±0.50	3.05±0.49	3.06±0.51	0.920
Height, cm	77.6±10.25	78.2±12.1	76.9±7.7	0.408
Current weight	10.0±1.93	10.0±2.2	9.9±1.63	0.832
Zscore W/A	–0,57±1.45	–0.40±1.53	–0.75±1.30	0.094
Zscore H/A	–1,05±2.74	–0.64±3.04	–1.51±2.29	0.023
Zscore W/H	0.08±1.81	0.09±1.81	0.07±1.81	0.934
W/A [n (%)]				0.474
<−2DS	32 (16.2)	18 (17.3)	14 (14.9)	
−2 ≥ DS ≤+2	161 (81.3)	82 (78.8)	79 (84.0)	
>+2DS	5 (2.5)	4 (3.8)	1 (1.1)	
H/A [n (%)]				0.127
<−2DS	72 (35.5)	32 (29.9)	40 (41.7)	
−2 ≥ DS ≤+2	109 (53.7)	60 (56.1)	49 (51.0)	
>+2DS	22 (10.8)	15 (14.0)	7 (7.3)	
W/H [n (%)]				0.680
<−2DS	24 (12.6)	12 (12.2)	12 (12.9)	
−2 ≥ DS ≤+2	142 (74.3)	71 (72.4)	71 (76.3)	
>+2DS	25 (13.1)	15 (15.3)	10 (10.8)	
W/A [n (%)]				0.226
Malnutrition	37 (18.7)	22 (21.2)	15 (16.0)	
Normal	16 (81.3)	82 (78.8)	79 (84.0)	
H/A [n (%)]				0.282
Malnutrition	94 (46.3)	47 (43.9)	47 (49.0)	
Normal	109 (53.7)	60 (56.1)	49 (51.0)	
W/H [n (%)]				0.413
Malnutrition	49 (24.1)	27 (25.2)	22 (22.9)	
Normal	154 (75.9)	80 (74.8)	74 (77.1)	

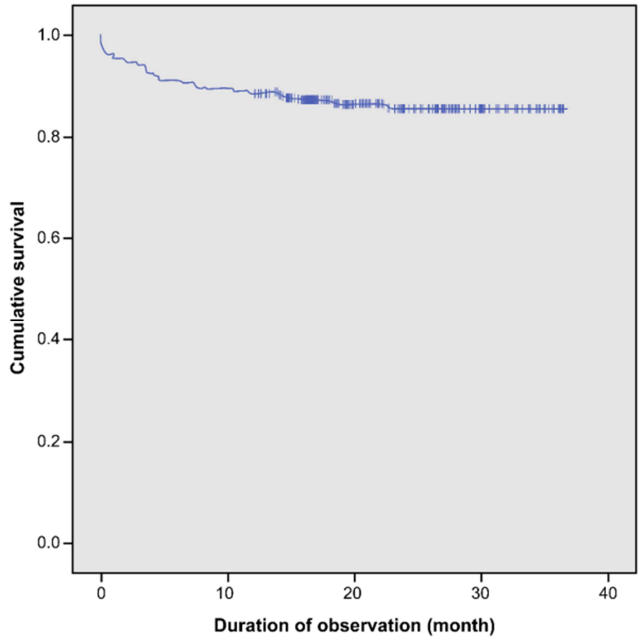

Figure 1. *Overall survival of children.*

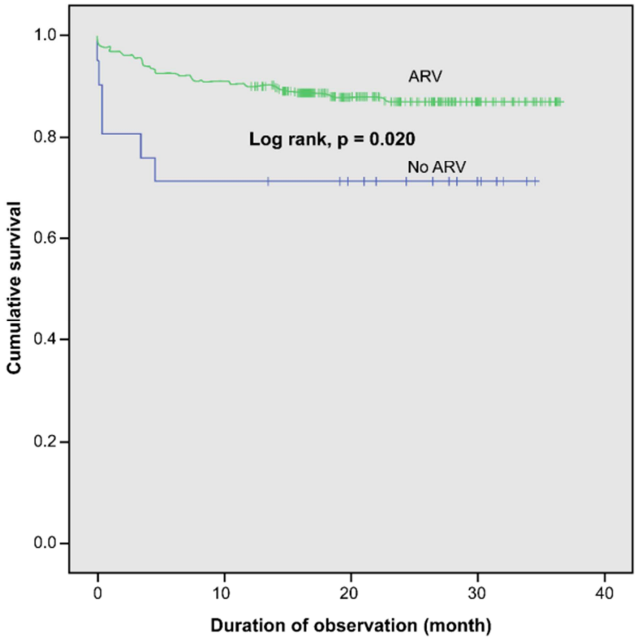

Figure 2. *Child survival by maternal treatment.*

A large percentage of the children were malnourished: 18.7% of children were acutely malnourished; 46.3% were chronically malnourished; and 24.1% were malnourished overall. There was no statistical difference between the prevalence of girls and boys ($p > 0.05$).

There was a statistically significant comparison between the median survival time of HIV-exposed children (Figure 1) who were still alive at the time of the study (20.9 [19.7–22.9] months) and the survival time of HIV-exposed children who had died (3.5 [1.4–6.3] months) ($p < 0.001$). Among all HIV-

exposed children, 13.5% died.

The probability of survival for exposed children who were diagnosed at or before 6 months of age was 90.7%, falling to 88.7% at 12 months, 87% at 18 months, and 86.5% at the peak date, 36 months. It is critical to begin treatment during the first 6 months of life, which is when the highest mortality rate occurs (9.1%).

Figure 2 shows child survival according to maternal treatment and indicates a statistically significant difference between children with ARV-treated mothers, who had a better survival outcome, compared to children whose mothers were not on ARVs (p=0.020).

The most common causes of death for children were anemia (48,4%), respiratory distress (25,8%), neonatal infections (16,1%) and malnutrition (9,7%).

Accessibility to early diagnosis was 67.8%, with girls having a slightly higher frequency than boys, but the difference was not statistically significant (p=0.185). The sampling time for diagnostic access for children was 4 months (2.7–6.1) (range, 0–30 months) (Table 3). Only 30.4% (41 children) had access to the diagnosis within 6 weeks. HIV-exposed children with access to early diagnosis had mothers who were in a common-law marriage or single (p=0.031); were primary school-educated (p=0.020); took ARVs (p=0.018); and had husband or family members informed of their serostatus (p=0.015).

Table 3. *General characteristics of the mothers according to diagnosis access.*

	No access to diagnosis N=64 N (%)	**Access to diagnosis N=135 N (%)**	**P value**
Age (years)			0.514
16–25	10 (15.6)	21 (15.6)	
26–35	29 (45.3)	72 (53.3)	
36–45	25 (39.1)	42 (31.1)	
Marital status			0.031
Married	37 (57.8)	50 (37.0)	
Single	7 (10.9)	27 (20.0)	
Divorced	4 (6.3)	5 (3.7)	
Widowed	4 (6.3)	6 (4.4)	
Cohabitation	12 (18.8)	47 (34.8)	
Educational level			0.020
Elementary	30 (46.9)	74 (54.8)	
High school	29 (45.3)	60 (44.4)	
University	5 (7.8)	1 (0.7)	
ARV regimen			0.016
No	7 (10.9)	8 (5.9)	
Yes	57 (89.1)	127 (94.1)	
ARV before pregnancy			0.018
No	38 (66.7)	74 (58.3)	
Yes	19 (33.3)	53 (41.7)	
Sharing of HIV status			0.015
Husband	21 (32.8)	55 (40,7)	
Family member	13 (20.3)	34 (25.2)	
Pastor	3 (4.7)	3 (2.2)	
Husband + Family member + Pastor	1 (1.6)	15 (11.1)	
Other persons	9 (14.1)	10 (7.4)	
No response	17 (26.6)	18 (13.3)	
Gender			0.185
Female	30 (46.9)	74 (54.8)	
Male	34 (53.1)	61 (45.2)	
Age (months)			0.953
0–12	15 (23.4)	33 (24.4)	
13–24	36 (56.3)	78 (57.8)	
25–36	13 (20.3)	24 (17.8)	
Nature of relationship with the caretaker			
Biological mother	62 (96.9)	129 (95.6)	
Biological father	1 (1.6)	3 (2.2)	
Family member	1 (1.6)	3 (2.2)	

In univariate logistic regression analysis, factors such as having a mother who is single, has a low level of education (primary or secondary), has not been given ARVs, and has not disclosed HIV status were the determinants of non-access to the early diagnosis of children (Table 4).

Table 4. *Determinants of inaccessibility to diagnosis.*

	Univariate analysis		Multivariate analysis	
	P value	**OR (95%CI)**	**P value**	**ORa (95%CI)**
Marital status				
Married		1		1
Unmarried	0.018	1.67 (1.04–1.98)	0.059	1.20 (0.99–1.56)
Educational level				
University		1		1
High school	0.024	2.33 (1.38–5.04)	0.092	1.88 (0.73–4.96)
Elementary	0.037	5.35 (1.16–9.65)	0.044	3.80 (1.06–9.51)
ARV taking				
Yes		1		1
No	0.022	1.95 (1.67–5.64)	0.429	1.59 (0.50–5.03)
Disclosure of HIV status				
Yes		1		1
No	0.024	2.35 (1.12–4.95)	0.028	2.36 (1.10–5.08)

After multivariate adjustment, the mother's primary school level education and lack of disclosure of her HIV status were the determinants independently associated with non-access to the diagnosis of exposed children (OR: 3.80, 95% CI: 1.06–9, 51) and (ORa: 2.36, 95% CI: 1.10–5.08).

5. Discussion

The data about mothers given in the Results corroborate other studies in which the average age of mothers/caregivers was 34 years (IQR: 30–38 years), and a majority (95.3%) of the participants were biological mothers; however, others studies found that the majority of participants were single mothers (74.3%), less than 30 years old, and with some high school education. The dominance of biological mothers to caregivers in our study is explained by introducing ARV prophylaxy+, which leads to an improved survival rate of HIV+ mothers. The low education level reflects the early marriages of girls, primarily in rural areas, whose parents give little interest to their education.

Our study showed a high percentage of malnutrition among HIV-exposed children. In most African studies, there is a high prevalence of malnutrition among HIV-infected children at initiation of ART, and the prevalence in our study is low compared with the results obtained by other authors. [18-20] These differences can be explained by sample sizes and the varying prevalence of malnutrition among HIV-infected children in other countries [4, 14, 15]; in our study, we consider only HIV-exposed uninfected and infected children. In addition, it has been shown that HIV infection deteriorates the nutritional status of patients, even when ART is initiated [21].

A previous study confirmed that stunting is more prevalent, and nutritional status deteriorates in children infected with HIV infection [22]. A late diagnosis of HIV infection with its resulting significant immunodeficiency, the duration of the disease, and inadequate nutrition are factors associated with chronic malnutrition. [22-24] Malnutrition and HIV have common biological, immunological, and socioeconomic consequences. These two conditions interact as HIV is often associated with physiological impairments and socioeconomic changes that negatively affect the nutritional status of the HIV-infected persons [25].

In our study, anemia was the leading cause of death, followed by respiratory infections and malnutrition. The causes are similar to those found in other studies in Africa [26, 27]. Infant mortality is affected by many factors such as geographic and socioeconomic settings, method of feeding, and the mother's HIV status and disease stage. Pooled analyses of data from African studies indicate mortality of HIV-exposed children to be between 39.3 and 49 per 1000 [2, 3]. Mortality of these infants is two to four times higher than children not exposed to HIV in the same region [4, 5], and is even higher for infants of mothers who had advanced HIV disease or who had died [3, 6]. Morbidity is also higher among HIV-exposed infants compared to their unexposed counterparts. In the ZVITAMBO cohort, HIV-exposed, uninfected infants made an average of 30% more sick visits to clinics and had 20% more hospitalizations than unexposed infants [5]. Respiratory and gastrointestinal infections were the main causes of infant morbidity and mortality [6, 7], with malaria also contributing substantially in endemic areas [8].

The children in our study had late access to HIV testing and late HIV diagnoses in older children, which is similar to results in other studies [28, 29]. This implies that access to HIV testing among children at older ages could have been prompted by manifestation of clinical symptoms that required diagnostic testing. Only 30.4% (41 children) had access to the diagnosis within 6 weeks of birth. The data from our study is much lower than that of Feinstein et al., whose study in Kinshasa noted an increase ranging from 28% to 63% between two cohorts [28]. Our study was carried out in a rural area while that of Feinstein et al. was in an urban area, and this shows the disparity between services offered in rural and urban areas.

In a study from the Muheza district in Tanzania, slightly over half of the HIV-exposed children below 5 years of age accessed EID services between 4 and 6 weeks of age. Muheza's EID service is still below the 80% threshold recommended by the WHO [8]; however, coverage for children has increased compared to previously reported data from Tanzania and other countries in sub-Saharan Africa that ranged from 4% to 55% [24, 27, 29-31]. Nevertheless, EID service coverage is considerably lower compared to studies

conducted in Botswana, Burkina Faso, Malawi, Swaziland, and South Africa, which ranged from 58% to 94% [27, 31-33].

Several factors affected access to EID, either individual or health-facility (institutional). At the individual level, barriers to EID included inadequate knowledge about EID services by HIV+ mothers, lower levels of education, lack of paternal support/permission, large-sized household, long distance to health facilities, cost of transportation, and HIV-related stigma. At the health-facility level, unavailability of trained staff, inadequate supplies of laboratory materials, and late return of HIV test results were the main constraining factors.

Older children and those who were HIV-infected had accessed the first HIV test at ≥7 weeks of age. The observed late accessibility to HIV testing and late HIV diagnosis in older children also followed other studies. In univariate logistic regression analysis, the marital status (single), the low education level (primary or secondary), the absence of ARVs provision in PMTCT services to the mother, and the lack of disclosure of HIV status were the determinants to an exposed child not being diagnosed. After multivariate adjustment, a primary school education level of mothers and the lack of HIV status disclosure were the determinants independently associated with non-access to diagnosis of exposed children.

6. Conclusion

Progress in response to the HIV epidemic augurs a better future. With the adoption of the "test and treat" strategy, people living with HIV start treatment at the time of diagnosis, thus prolonging their life expectancy. More people are living with HIV than a decade ago.

For children, early detection in PMTCT remains limited and access to ARVs is not guaranteed. Without treatment, many children will die before their first birthday, or sooner if they have HIV in their mother's womb. The difficult socioeconomic environment and the presence of stigma and discrimination causes these HIV-exposed children to die from mostly preventable diseases: anemia, acute respiratory infections, diarrhea, malaria, and malnutrition.

Children born to HIV+ mothers are more vulnerable compared to unexposed children. Among these HIV-exposed children, those who are HIV-positive are even more vulnerable. Efforts should be directed toward early access to diagnosis for all HIV-exposed children, early access to results for exposed children, and access to health care resources: ARV, nutrition management, cotrimoxazole prophylaxis, and vaccinations. Better monitoring of the mother–child pair is essential and more psychological, social, and economic support should be given to families affected by HIV. These children should be given equal chances of survival as their peers outside Africa, but many children born to HIV+ mothers will lose their lives if they are not given improved access to care.

Limitations of the Study

The retrospective data collection did not ensure that all the information was traced. A prospective collection would have made it possible. A cohort study could obtain more data necessary for the follow-up of these children and to reduce mortality, which remains high among these children.

Conflicts of Interests

The authors declare that they have no competing interests.

Authors' Contribution

LNP supervised the research and led the redaction of the article

MLR made substantial contributions to the research work and in the writing of the manuscript

NNC Supervised collecting data process

All the authors reviewed the final version of the manuscript and gave their consent.

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