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Outcomes of Newborns Exposed to Human Immunodeficiency Virus/Viral Hepatitis B Co-Infection Attended at a Referral Hospital in Abidjan

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Abstract

Introduction: Infection with hepatitis B virus (HBV) and human immunodeficiency virus (HIV) is a public health problem worldwide, particularly in sub-Saharan Africa. The aim of the study was to determine the seroprevalence of HIV/HBV co-infection in pregnant women and to determine the outcomes of exposed newborns. **Methods:** This was a prospective longitudinal descriptive study conducted from October 2016 to March 2019 (18 months) among HIV/HBV co-infected pregnant women and their newborns in the pediatrics department of Cocody University Hospital. **Results:** Of a total of 7210 parturients, 31 were co-infected with HIV/HBV, representing a frequency of 0.4%. The mean age of the mothers was 30 years. They were not immunized against HBV (100%). The HBV viral load was more than 106 IU/L in 32.3% of them and HIV status was discovered in the delivery room in 39% of cases. Newborns were premature (51.9%) and low birth weight was noted in 22% of cases. All newborns were immunized against hepatitis B before the 12th hour of life and received ARV prophylaxis before the 72nd hour. The outcome showed a mortality rate of 29%, and for alive infants, HIV serology was negative at 18 months of life and all of them were immunized against HBV. **Conclusion:** Early well-managed care leads to preventing mother-to-child transmission of these two diseases. However, further action needs to be taken in terms of prevention.

Keywords

Hepatitis B Virus, HIV, Co-Infection, Newborn, Antenatal Transmission,

Abidjan

1. Introduction

Infection by hepatitis B virus (HBV) and human immunodeficiency virus (HIV) each represent a major public health problem worldwide, particularly in sub-Saharan Africa. By 2023, UNAIDS estimated that 40.4 million people would have died from HIV-related illnesses since the start of the epidemic, and 39 million would be living with HIV. The African region accounts for more than two-thirds of all people living with HIV, *i.e.*, some 25.4 million people and 1.7 million children, 70% of them in sub-Saharan Africa. Nearly 630,000 people died of HIV-related causes, and 1.3 million were newly infected with HIV. According to the estimation, 7.7 million deaths will be added to the heavy toll of HIV infection if nothing is done in the next 10 years [1]. Similarly, in 2022, the World Health Organization (WHO) estimates that some 254 million people will be living with chronic hepatitis B, six times the number infected with HIV. HBV-related mortality is estimated at 1.1 million, and there are 1.2 million new infections [2].

Mother-to-child transmission is the main mode of HBV and HIV infection in children. The prevalence of these infections among pregnant women was particularly high in resource-poor settings (HIV: 2.9% [0.8% - 6.1%]; HBV: 4.9% [3.8% - 6.1%] [3]. When contamination with hepatitis B virus occurs in the neonatal period, the risk of chronicity and its consequences (liver cirrhosis, hepatocellular carcinoma) is higher [4].

In cases of HBV/HIV co-infection, HBV-related morbidity and mortality are significantly increased. In fact, HIV infection accelerates the transition to chronicity and progressive complications of hepatitis B. In addition, the risk of mortality is increased 17-fold compared with patients infected with HBV alone [5] [6]. Early administration of antiretroviral combinations during pregnancy is effective and has reduced the rate of mother-to-child transmission of HIV to less than 5% [7] [8].

Peripartum antiviral prophylaxis plus infant immunoprophylaxis is promising for interrupting HBV MTCT [9]. Furthermore, the risk of MTCT is dramatically reduced by timely neonatal HBV vaccination and the administration of hepatitis B immunoglobulin after birth in high-risk infants [10]. Immunoprophylaxis remains difficult to access and expensive in our context. According to the WHO, administration of hepatitis B vaccine within 24 hours of birth, followed by at least two additional doses, prevents peri-natal hepatitis B virus infection and confers immunity against hepatitis B [11].

In Côte d'Ivoire, the prevalence of HBV in pregnant women is estimated at 18.2% [12]. With vaccination starting in the sixth week after delivery, the overall rate of mother-to-child transmission of HBV ranges from 4% to 7% [13] [14]. The prevalence of HIV infection in pregnant women is 1.7%, and the perinatal inci-

dence is 10.3% in the absence of any intervention [15].

Despite the scale of HBV infection and its lethal consequences, there is little mobilization and funding for its prevention and management, unlike HIV infection, which is the subject of a well-established prevention of mother-to-child transmission program supported by national and international health donors. Joint management of HBV and HIV infection should significantly improve the prognosis of co-infection in exposed newborns. This would involve ante- and neonatal screening for both conditions, as well as regular clinical and biological follow-up of exposed children until definitive serostatus is obtained.

This study was set up in order to contribute to the improvement of the quality of care for newborns exposed to HBV/IBV co-infection.

2. Method

2.1. Study Site, Type and Period

This was a longitudinal, descriptive cohort study carried out over a 3-year period (October 1, 2016 to March 31, 2019) in the pediatrics department of the teaching hospital of Cocody in Abidjan.

2.2. Study Population

Newborns whose mothers were co-infected with HBV/HIV during the study period were referred to the department of pediatrics of teaching hospital of Cocody for follow-up.

2.3. Inclusion Criteria/Population Size

All newborns whose mothers were co-infected with HVB/HIV, referred to the pediatrics department for follow-up and whose mothers were informed and have given free and written consent to take part in the study were included. Mothers who refused or did not agree to participate in the study were not included.

2.4. Study Procedure

All the mothers who attended the delivery room during the study period and meet the inclusion criteria were screened using Rapid Diagnostic. After the announcement of their positive HIV status, counceling was done and antiretroviral treatment (ART) was initiated and mothers were followed up in the Prevention of Mother-to-Child Transmission unit. Then, the mother was referred to a hepato-gastroenterology specialist for screening and management of HBV infection when a positive status was noticed (hepatitis B serology and viral load.)

Newborns exposed to HBV/HIV co-infection were referred to the pediatric department for management. They received a first dose of hepatitis B vaccine within 12 hours of birth, then at 6 weeks, 10 weeks and 14 weeks according to the Expanded Program of Immunization.

Antiretroviral prophylaxis consisted of nevirapine (0.5 to 1.5 ml daily) and Zidovudine (0.5 to 1.5 ml twice daily) for 6 weeks, according to the national recom-

mendations.

In addition to the postnatal visit, the follow-up schedule included a visit at 6 weeks, 6 months, 12 months and 18 months. At each visit, the child underwent a complete clinical examination, as well as an assessment of feeding, statural and weight development, psychomotor development and immunization.

At the 6-week appointment, early PCR screening was performed and cotrimoxazole treatment was started. From 18 months onwards, children were called for definitive HIV status and to assess seroconversion for hepatitis B (find attached the schedule of monitoring for HIV/HBV—exposed children).

2.5. Data Collection and Analysis

Data were collected, based on a questionnaire and medical folders, using a survey form containing the following parameters

Mothers' characteristics: age, profession, level of education, parity, HBV immunization status, HBV viral load. HIV type, HIV viral load,

For newborns: sex, mode of delivery, gestational age, birth weight, trophicity, vital status, mode of feeding, immunization status, weight and height and psychomotor development, morbid events during follow-up, PCR at 6 weeks of life, HIV serology at 18 months and determination of the following markers: HBsAg, anti-HBsAb, anti-HBcAb.

Data were analyzed using EPI INFO 7 software. Qualitative variables were expressed in terms of percentages (%) and numbers (n); quantitative variables were expressed in terms of means and standard deviations.

2.6. Ethical Considerations

Mothers co-infected with HIV/HBV gave free written consent after receiving information on the study's objectives, the different possibilities for results and management. The results of the tests performed on the children were announced to the mothers.

The data has been treated anonymously and confidentially.

3. Results

3.1. Global Results

During the study period, 7210 mothers were screened, 31 of whom were co-infected with HBV and HIV. The prevalence of HBV/HIV co-infection was 0.4%. We noted 9 deaths, including 4 stillbirths, 3 deaths in the early neonatal period and 2 deaths during follow-up. The mortality rate was 29%. **Figure 1** shows the flow chart.

3.2. Mothers' Characteristics

The mean age of the mothers was 30, ranging from 15 to 44 years. Most of the mothers worked in the informal sector (48.4%), and 61.3% had no formal education. None of the mothers had been vaccinated against HBV. All mothers were

infected with HIV-1. HIV-positive status was known, and 61% of mothers were on ARV treatment prior to delivery. Table 1 describes the characteristics of the mothers.

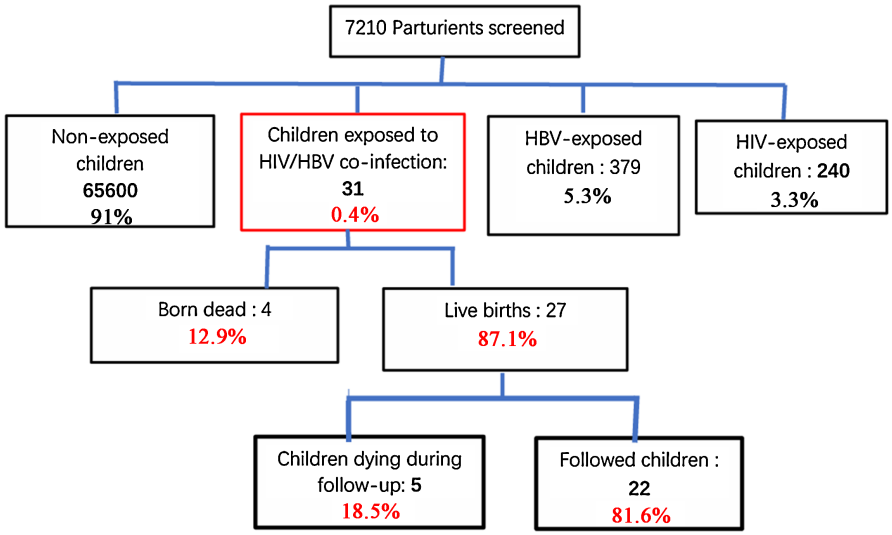

Figure 1. Characteristics of the mothers.

Table 1. Mothers' characteristics.

	Number (n = 31)	Percentage (%)
Age (years)		
[15 - 24]	3	9.7
[25 - 34]	21	67.7
[35 - 44]	7	22.6
Professionnel activity		
Student	2	6.4
Housewives	8	25.8
Informal sector	15	48.4
Employed	6	19.4
Education level		
Never attended school	5	16.1
Primary	14	45.2
Secondary	10	32.3
Superior	2	6.4
Deliveries		
1	12	38.7
2 - 4	12	38.7
>4	7	22.6

Continued

HIV Status		
known on HAART	19	61.3
unknown	12	38.7
HBV Status		
known on therapy	0	0
unknown	31	100

3.3. Characteristics of HIV/HBV-Exposed Newborns

Of the 31 exposed newborns, 51.9% were born prematurely, with a mean gestational age of 35 weeks of amenorrhea ± 2 SA [min 28; max 41]. The sex ratio was 1, and vaginal delivery predominated in 58.1% of cases. These newborns had a mean weight of 2754 g, a mean height of 49.5 cm and a mean head circumference of 32 cm, and 22% of them were hypotrophic. Table 2 shows the characteristics of the newborns.

Table 2. Newborns characteristics

	Number (n = 31)	Percentage (%)
Delivery route		
Vaginal route	18	58.1
Cesarean section	13	41.9
Sex		
Male	15	48.4
Female	16	51.6
Weight (grams)		
>2500	14	45.2
2500-3900	16	51.6
>3900	1	3.2
Gestational Age (weeks)		
<37	16	**51.6**
>37	15	48.4
Trophicity		
Hypotrophic	19	61.3
Normotrophic	12	38.7
APGAR score		
<7	4	12.9
≥7	25	87.1

3.4. Characteristics of Children during Follow-Up

Of the 22 surviving children, 10 were lost to follow-up. Figure 2 shows the distribution of children according to compliance with appointments. Twelve children were followed up to 18 months.

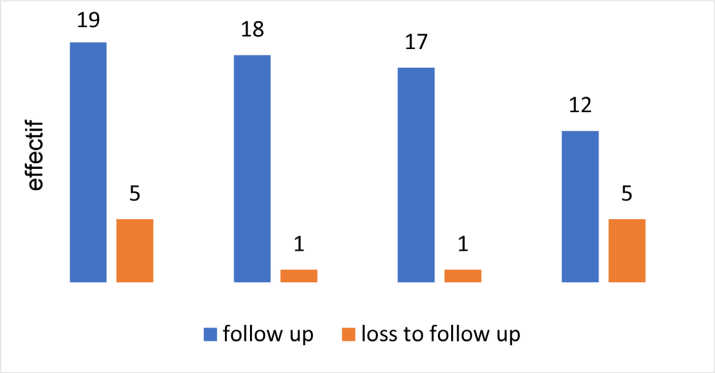

Figure 2. Distribution of children according to compliance with their appointments.

The mothers had practiced exclusive breastfeeding in 53% of cases, followed by well-managed diversification (91.7%). They showed good psychomotor and staturo-weight development. The average weight and height at the end of follow-up were 1108 g and 78.7 cm, respectively. The evolution of the weight curve according to feeding mode is shown below in Figure 3.

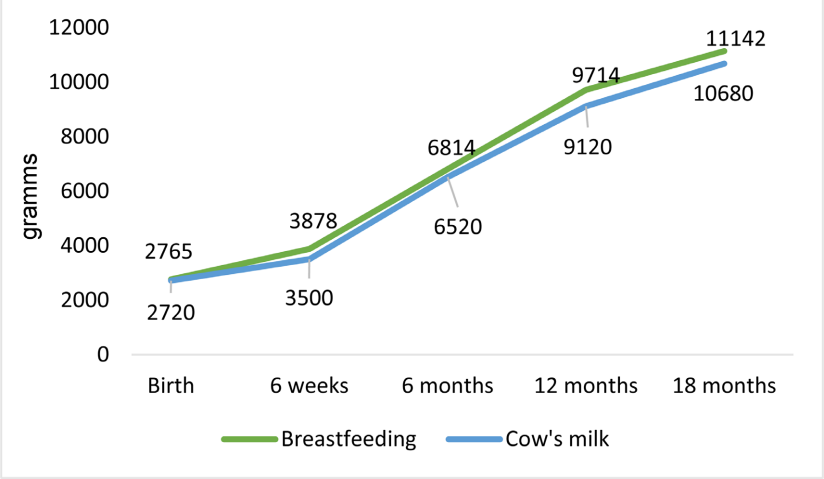

Figure 3. Evolution of weight curve according to type of diet.

Clinical examination was normal in all children, and immunization status was up to date for age. The most frequent diseases observed during follow-up were malaria (83.3%), gastroenteritis (50%) and rhinopharyngitis (66.7%). Initial HIV PCRs were all negative, as was HIV serology at 18 months. Regarding the HBV serological profile, all children were immunized with a sufficient antibody titer (anti-HBs Ac > 10UI). Table 3 describes the HBV serological profile at 18 months of age.

Table 3. HBV serological profile at 18 months of age.

hepatitis B serological profile		Number (n = 12)	Percentage (%)
Post-vaccine immunization	Ag HBs–; Ac anti HBc–; Ac anti HBs+	11	91.7
Cured viral hepatitis B	Ag HBs nég–; Ac anti HBc–; Ac anti HBs+	1	8.3

4. Discussion

The prevalence of HIV/HBV co-infection was 0.4% among parturients. Higher rates were reported by Sangaré in Burkina Faso (1%) [16], Bossali in Congo (2%) [17] and Mutagoma in Rwanda [18] (4.1%). According to the literature, the prevalence of HIV-HBV co-infection varies by region, ranging from less than 2% in developed countries [19] to 20% in HBV-endemic contexts and in resource-limited countries such as Asia and Africa [20] [21].

Among newborns exposed to HBV/HIV co-infection, 51.6% were born prematurely, 45.2% weighed less than 2500 g and 22.6% were born hypotrophic. Vidya Wave in India [22] found 71% hypo trophic and 16% premature. The mortality rate in this series was 29%. Vidya *et al.* [22] in their study found that all-cause infant mortality at 12 months was higher in the group of children born to HIV/HBV co-infected mothers (9% vs. 4% in the HIV mono-infected group). During follow-up, 1/3 of the children died, 1/3 were lost to follow-up and 1/3 were alive. The loss-of-sight rate was similar to the Sellier Pierre study in France [23] (38% lost to follow-up at 2 years). In contrast, Kouakou *et al* in Côte d'Ivoire [24] and Lawson *et al* in Togo [25] found 100% and 52.2% loss of sight at 12 months respectively. This rate could be explained by insufficient parental income limiting their movements, stigmatization and change of address. At the end of the study, the 12 living children evolved as follows: 33.3% were hospitalized during the neonatal period, 53% fed exclusively on breast milk up to 6 months, and the other half on milk substitute.

Diversification was successfully carried out in 91.3% of cases, according to the protocol recommended in Côte d'Ivoire. In studies carried out in Africa, exclusive breastfeeding for up to 6 months was the most common mode of feeding: 88% according to Kouakou *et al* [24] in Côte d'Ivoire and 62.2% according to Millogo Traoré in Burkina Faso [26]. Weight growth curves were superimposable for all types of feeding. Good psychomotor development, correct immunization status and a normal clinical examination were noted in all cases. Thanks to the optimal follow-up of the PMTCT HIV/AIDS program (ARV prophylaxis, prevention of opportunistic infections, early detection by PCR at 6 weeks and serological tests, AFADS-compliant feeding), all twelve children were HIV-negative at 18 months. Similar results were found by Ilboudo Denise [27] in Burkina Faso and Lasme in Côte d'Ivoire [28].

Regarding the HBV serological profile, post-vaccination immunization was ob-

served in 100% of cases. Despite late screening of mothers for HBsAg, a well-managed vaccination program with one dose at birth resulted in seroconversion of the children and zero MTCT. In the Sellier pierre study in France [23], which assessed the HBV status of children born to women co-infected with HIV/HBV at 2 years of age, mother-to-child transmission was nil. On the other hand, Kouakou [29] in Côte d'Ivoire found 89% seroconversion and 2.2% HBV-infected children, and Ilboudo Denise [27] in Burkina Faso 21.4% HBV-infected children. The factors associated with maternal-fetal transmission are well known. They have high viral load and positive Hbe antigen in mothers. In the absence of immunoglobulin administration, the cost of which remains high in our context, early vaccination against hepatitis B is the best way to prevent HBV infection from mother to child [11].

Study Limitations: The size of the sample was not enough for further statistical analysis. Also, the number of follow-up losses is higher. There is a need for a large scale-study and to set up a policy to reduce the loss of follow-up patients. However, this study's impact is real, showing the basic information on this co-infection HBV/ HIV as prevalence, high rate of death and the difficulty in management. Further studies in this field should be encouraged.

5. Conclusion

HBV/HIV co-infection is responsible for a high rate of prematurity, stillbirths and neonatal mortality in exposed children. However, early and well-managed treatment can limit mother-to-child transmission of these 2 conditions. There is an urgent need to set up a joint program of mass screening for HBsAg and HIV in pregnant women to enable early management of both infections: ARV prophylaxis, vaccination against HBV, early screening of children, and verification of seroconversion. Clinical and biological monitoring of children and psychosocial follow-up of mothers must be integrated into the management of these two conditions, and free of charge.

Conflicts of Interest

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

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