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ORIGINAL ARTICLE

Prevalence and Identification of Serum Markers Associated with Vertical Transmission of Hepatitis B in Pregnant Women in Yaounde, Cameroon

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ABSTRACT

Objective: To determine the prevalence of Hepatitis B Virus (HBV) infection in pregnant women and identify markers associated with vertical transmission of HBV.

Methods: Prospective and cross-sectional study over 10 months on 298 pregnant women attending antenatal clinics in the Cité Verte and Efoulan District hospitals in Cameroon. A dry tube blood collection was performed on all pregnant women and babies born to HBsAg-positive mothers. Serum from the women was used to test for HBsAg through immunochromatography and then confirmed by ELISA. The test for HBeAg, HBeAb and HBcAb and dosage of transaminases were performed on the serum of HBsAg-positive women. Only HBsAg was tested in babies within 24 hours after birth.

Results: HBsAg was present in 23 (7.7%) mothers while 275 (92.3%) tested negative. Due to loss to follow-up, we assessed vertical transmission in 20 babies born to20 mothers. In all, eight babies tested HBsAg-positive; six mothers tested positive with HBeAg; 10 mothers with HBeAb and two were simultaneously infected with HBV and HIV.

Conclusion and Global Health Implications: HBeAg and increase in liver transaminases were serum markers associated with the vertical transmission of HBV while HBeAb and anti-HIV therapy were protective markers. There is need to systematically screen all pregnant women for hepatitis B, follow up those that are positive, and administer a dose of gammaglobulin anti-HBs to their children to reduce the risks of chronic hepatitis and hepatocellular carcinoma (CHC) and curb mortality and morbidity due to viral hepatitis B.

Keywords: Hepatitis B Virus • Serum Markers • Vertical Transmission • Cell Hepatocellular Carcinoma • Cameroon

1. Background and Introduction

Hepatitis is an inflammatory and necrotic liver disease.[1] Six viruses cause hepatitis A, B, C, D, E and G which can all result in acute hepatitis. Only viruses B, C and D lead to chronic hepatitis that can degenerate to cirrhosis and hepatocellular carcinoma cell; they result in about a million deaths each year.[2] Hepatitis B is the most frequent of hepatitis infections and mainly affects the young.[3] The World Health Organization (WHO) estimates that nearly 30% of the world populations are carriers of serological markers of the hepatitis B virus (HBV), among whom 350 million are carriers of the chronic HBs antigen (HBsAg). In many countries, there is no HBV mother to child transmission prevention program (MCTPP). The age of infection onset plays a very important role in carriage.

Children born to mothers with active hepatitis B are under high infection risk in early childhood and become chronic carriers.[1] Later, some of these children are exposed to high risk of death from cirrhosis or hepatocellular carcinoma in adulthood. In Africa, chronic hepatitis B virus has become one of the major causes of cancerous deaths.[4] Cameroon is an area of high endemicity for HBV infection, with an estimated prevalence between 8% and 20% of the population and a high incidence of hepatocellular carcinoma.[5] A prior study from 'Centre Pasteur' of Cameroon (CPC) reported a prevalence of 26.11% among women of reproductive age.[6] Another study from International Research Centre (CIRCB) reported a prevalence of 19% with molecular biology techniques and 12% with serology techniques.[7] Most infections occur during the perinatal period and infancy, an age at which a symptomatic acute hepatitis B is unlikely to occur but at which the risk of developing a chronic infection remains high.[8] Pregnancy is therefore a most appropriate period to screen for this disease. Indeed, if the mother is a carrier of HBsAg, the risk of transmission to the child in the perinatal period is high. The objective of our study, therefore, was to determine the prevalence of Hepatitis B Virus (HBV) infection in pregnant women and identify markers associated with vertical transmission of HBV.

2. Methods

This was a prospective, cross-sectional study carried out over a period of 10 months in two health districts of the town of Yaounde, namely, the district hospitals of Cité Verte and Efoulan in Cameroon. These hospitals are located in the outskirts of the city of Yaounde and are frequented by cosmopolitan populations, coming from urban, semi-urban and rural areas. The target population consisted of pregnant women under antenatal consultation in these health districts as well as the babies delivered by these mothers. We obtained ethical clearance No. 2014/12/532/EC/CNERSH/SP from the National Ethics Committee of Research on Human Health. We collected our samples through convenient sampling technique. Standard questionnaires were given (on explanation and consent of recipient) to pregnant women who came to these hospitals for childbirth. The questionnaires which were intended to collect demographic and clinical data were completed by the women after they had been delivered. A dry tube blood collection was performed on all pregnant women and babies born to HBsAg-positive mothers. Serum from the women was used to search for HBsAg through immunochromatography (HexagoneHBsAg Test) and then confirmed by ELISA (Monolisa AgHBsPlus Test). The search for HBeAg, HBeAb and HBcAb through the VIKIAR rapid test and dosage of transaminases were performed on the serum of HBsAg-positive women. Only HBsAg was tested in babies within 24 hours after birth. Biological analyses were carried out at the Laboratory of Epidemiology of the Institute of Medical Research and Medicinal Plants Studies (IMPM). A descriptive analysis was done on the study population and the relative risk and rating ratio of association measures used. The results were analyzed with EPI Info (7.0) with statistical significance fixed at <0.05 for all tests.

3. Results

3.1. Characteristics of mothers

Three of the 298 mothers left the hospital within 24 hours after delivery. The mean age of the mothers was 26.3 years, ranging from 15 and 42 years. About 73% were less than 30 years old; 63.1% had secondary school education; 38.60% were resident

in semi-urban areas; 63.1% were multiparous; 30.2% were housewives; while a majority, 186 (62.4%) were single mothers.

In total, 23 (7.7%) of the women were carriers of HBV markers. Of the mothers who tested positive for HBV markers, 6 (26.1%) were carriers of HBsAg and HBeAg concurrently; all of the mothers 23 (7.7%) HBsAg-positive mothers were carriers of AcHBc; and 23 (7.7%) of the women were HIV1 positive. Antibodies to HIV alone were present in 20 women (6.7%); 3 (1%) were co-infected with HBV/HIV and were on ARV therapy. Very few 4 (1.3%) women were vaccinated but none of the vaccinated women were infected with HBV (Table 1).

3.2. Characteristics of newborns and mother-to-child HBV transmission rate

In total, 20 infants born to mothers who were positive for viral hepatitis B were included in the study. They were all less than 24 hours old; 17 (85%) of these infants were born through vaginal delivery; 8 (40%) were positive for HBsAg. Of these 8 infants, 7 (87.5%) were born through vaginal delivery and 1 (12.5) was delivered through caesarean sections. Six (75%) of the 8 infants born with HBsAg were also positive for HBeAg. Of the 14 infants born to HBsAg-positive mothers and who were negative for HBeAg, 12 (85.70%) were HBsAg-negative as compared to 2 (14.3%) positive. The 3 newborns born to mothers co-infected with HBV/HIV who were on ARV treatment were HBsAg negative. Ten of the 20 infants born to HBV-infected mothers were carriers of HBe antibodies and all tested negative for hepatitis B.

3.3. Risk factors for infection of mothers and infants by HBV

Associations between mothers' ages, education, occupation, marital status, blood transfusion or surgical history, and presence of HBV markers were not statistically significant ($p = 0.21$-0.88), contrary to the vaccinated cases ($p = 0.0024$) (Table 2).

Nostatistically significant risk of antenatal infection with HBV was associated with the delivery channel, low birth weight or sex of the baby at birth ($p \geq 0.44$). The risks of HBsAg in infants were statistically significant in those born to HBsAg and HBeAg infected mothers. In contrast, the presence of AcHBe in HBsAg-positive mothers appears to significantlyprotect the infants. Being on ARV therapy for mothers with HBV and HIV co-infection was protective for infants.

4. Discussion

Viral hepatitis B is a major public health problem in our community. Our country is among the most affected by the infection given that it is situated in a high endemicity zone.[9] This high endemicity is sustained by an intense vertical transmission (mother-to-child). The woman is therefore the center of this transmission process. We investigated the seroprevalence and factors associated with HBV infection in a rural, semi-rural and urban area of Yaounde city in Cameroon. The information from this study may contribute to improving knowledge on HBV infection epidemiology in pregnant women, and may be used to inform local and national antenatal HBV screening and infant immunization policies.

We believe that the ages of the mothers included in our study were representative of those of the overall population of pregnant women in Cameroon. The rate of HBsAg carriage in mothers (7.70%) was comparable to those reported in other studies in pregnant women in urban areas of Yaounde in Cameroon, such as from studies by Fomulu et al[10] (7.7%) and Kfutwah et al[9] in 2012 (7.85%) but below the 10.2% reported by Noubiap et al. in rural areas in the far north of Cameroon.[11]

Distribution of subjects according to their HBsAg status shows that 23 of the 298 women tested positive, giving a prevalence of 7.7%. This result is close to that of 7.85% obtained in 2012 by Kfutwah[9] which was set as the national prevalence of HBV infection in pregnant women in Cameroon. Given that only 62% of deliveries take place in health centers in the presence of qualified personnel, one would expect that in the absence of any intervention, there would be an increase in the mother-to-child transmission rate of the infection.

Distribution of children according to their HBsAg status shows that vertical transmission is at a rate of 40%. In 2009, the work of Sangaré et al.[12] in Ouagadougou reported a 37.1% rate of HBV vertical

Table 1: Immunological considerations of mothers according to demographic and social characteristics

Variables	Number of mothers	Serology of immunological markers of mothers			
		HBsAg+	HBsAg+/HBeAg+	HBsAg+/HBeAg-	HBsAg -
Total	298 (100%)	23 (7.70%)	6 (26.10%)	17 (73.10%)	275 (92.30%)
Age (yrs)					
<20	32 (10.70)	2 (8.70)	1 (16.70)	1 (5.90)	30 (10.90)
21-30	184 (61.70)	13 (56.50)	4 (66.70)	9 (52.90)	171 (57.40)
31-40	76 (25.50)	7 (30.40)	1 (16.70)	6 (35.30)	69 (25.40)
>40	6 (2.0)	1 (4.30)	0 (00.00)	1 (5.90)	5 (1.80)
Marital status					
Married	105	13	4	9	92
Single	186	9	2	7	177
Divorced	6	1	1	0	5
Widow	1	0	0	0	1
Residence					
Rural	71 (23.80)	3 (13.00)	2	1	68 (24.70)
Semi-urban	115 (38.60)	12 (52.20)	4	8	103 (37.50)
Urban	112 (37.60)	8 (34.80)	0	8	104 (37.80)
Occupation					
Formal sector	50 (16.80)	3 (13.00)	3	0	47 (17.10)
Informal sector	76 (25.50)	5 (21.70)	2	3	71 (25.80)
Housewife	90 (30.20)	11 (47.80)	1	10	79 (28.70)
Student	82 (27.52)	4 (17.40)	0	4	78 (28.40)
Educational level					
Primary	42 (14.10)	4 (17.40)	2	2	38 (13.80)
Secondary	188 (63.1)	15 (65.20)	2	13	173 (62.90)
Higher	68 (22.80)	4 (17.40)	2	2	64 (23.30)
Medical and surgical history					
HepB Vaccine	4 (1.30)	0 (0.00)	0	0	4 (1.60)
Surgery	21 (7.00)	1 (0.30)	0	1	20 (7.30)
Transfusion	7 (2.40)	2 (6.70)	0	2	5 (1.80)
HIV +	23 (7.70)	3 (1.00)	0	3	20 (6.70)
ARV Treatment	20 (6.70)	3 (13.00)	0	3	17 (6.20)
Parity					
Primipara	110 (36.90)	5 (21.70)	2	3	105 (38.20)
Multipara	188 (63.10)	18 (78.30)	4	14	170 (61.80)
Channel of delivery					
Vaginal delivery	/	17	5	12	/
Caesarean section	/	3	1	2	/

transmission. This difference in results may be explained by the fact that the care given to HBsAg-positive women in Burkina Faso may be more effective and efficient.[2]

Distribution of patients according to HBeAg status shows that 30% of HBsAg-positive patients are carriers of HBeAg and 100% of these gave birth to HBsAg-positive childrenthus making HBeAg a serum

Table 2: Prevalence of HBsAg among infants at birth according to mothers' immunological markers

Maternal variables	Total number	HBV serology of children	
		HBsAg+	HBsAg-
Immunological markers of the mother			
HBsAg+	20	8	12
HBsAg+/AcHBc+	20	8	12
HBsAg+/HBeAg+	6	6	0
HBsAg+/HBeAg+/AcHBc+	6	6	0
HBsAg+/HBeAg-	14	2	12
HBsAg+/HBeAg+/HIV+	0	0	0
HBsAg+/HBeAg-/HIV+	2	0	2
HBsAg+/HBeAg+/HIV-	6	6	0
HBsAg-/HBeAg-	275	0	275
HBsAg-/HBeAg-/HIV+	20	0	20
HBsAg-/HBeAg-/HIV-	255	0	255
HBsAg+/AcHBe+	10	0	10
Serum transaminases of the mother			
Average GOT (UI)		32.00	18.92
Average GPT (UI)		31.51	15.58

marker associated with the vertical transmission of HBV with anRR = 7 and P <0.05. These results agree with those reported in 2003 by Berges et *al.*[13] which showed that HBeAg was a marker associated with the vertical transmission in 100% of cases in France.

HBcAb was found in all our HBsAg-positive women. This could be explained by the fact that HBcAb is the second marker to appear after HBsAg and persists even after recovery. Distribution of women according to their HBeAb status shows that 50% of HBsAg-positive women were carriers of this antibody. All infants born to these positive-tested women tested negative for HBsAg, making a zero percent vertical transmission. This result is statistically significant (P <0.05) showing HBeAb as a protective marker against the vertical transmission of HBV with an Odds Ratio of 0.00 and a Relative Risk of 0.00. These results are in agreement with those reported by Pascal Berges et al.[13] who reported a 100% protection rate for babies born to HBsAg-positive/HBeAb-positive mothers in France. According to Lok et al.[14] the presence of HBeAb in HBsAg-positive subjects was evidence of the absence of viral replication and made the subject a healthy carrier in most cases.

The distribution of infants according to the HIV status of mothers shows that two mothers (10%) were HIV-positive. This HIV/HBV co-infection had no impact on vertical transmission of HBV. However, the works of Sangaré et al.[12] in Burkina Faso showed that HIV among HBsAg-positive pregnant women was a marker associated with the vertical transmission of HBV. They claim that HIV can influence the natural history of HBV infection by increasing occurrence of chronic HBV infections and rates of HBV replication, but reduce anti-HBs and anti-HBe seroconversion rates. These opposing results could be explained by the fact that our subjects were receiving anti-retroviral treatment. The anti-HIV combination therapy seems to affect the mother-to-child transmission of HBV.

Evaluation of transmission based on markers of liver injury (transaminases GOT/GPT) shows that the average value of GOT among mothers who gave birth to negative-tested children was 18.92 IU/L and an average GPT value of 15.58 IU/L in the same subjects as against 32.00 IU/L and 31.51 IU/L as average respectively of GOT and GPT among those mothers whose children tested positive for HBsAg. These statistically significant results show a more marked elevation of transaminase values among mothers with HBsAg who transmitted it to their babies. These results corroborate the findings of Heathcote and colleagues[15] in Canada which reported that a transaminase value greater than 20 IU/L in an HBsAg-positive woman was an indication of hepatic inflammatory activity in progress. According to this study, this activity correlates with the high viral load resulting from viral replication (presence of HBeAg) and was responsible simultaneously for the vertical transmission of HBV and increase of the risk of developing hepatocellular carcinoma.[15]

5. Conclusion and Global Health Implications

The results obtained showed that mother-to-child transmission of HBV is high in Cameroon and may reflect a high risk of developing chronic infections and hepatocellular carcinomas in young adults. The

chemotherapy of viral hepatitis B by molecules like Lamivudine or Entecavir is inaccessible to majority of the country's population who are also highly affected by the HIV pandemic. Screening for HBV in women and immunization of mothers and children in the first day of life should be a priority of the viral hepatitis B programs in Cameroon. Nevertheless, to our knowledge, only the immunization of children six weeks after birth has been effective since 2005.

Compliance with Ethical Standards

Conflict of Interest: *Authors declare they have no conflicts of interest.* ***Ethical Approval:*** *Study was approved by an Institutional Review Boards. I****nformed Consent:*** *Informed consent was obtained from the study participants.* ***Funding:*** *Authors report no funding.*

Key Messages

- Mother-to-child transmission of viral hepatitis B remains a public health problem in Cameroon as it is in most developing countries;
- There is a demonstrable benefit of Hepatitis B Virus immunization of mothers and newborns' first few day of life in the mitigation of vertical transmission of HBV; and
- Nationwide programs aimed at highlighting the importance of antenatal screening for HBV in women and infants are needed.

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