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Risks of Viral Hepatitis B Transmission in Mother-to-Infant of Pregnant Women Carriers of Chronic Viral Hepatitis B in Cote d'Ivoire

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Abstract

The aim of this study was to identify the risk factors of mother-to-child transmission of HBV in positive Ag Hbs pregnant women in Cote d'Ivoire. **Methods:** This was a transversal prospective study that took place over a period of 7 months (from February 2016 to August 2016) in 2 university hospital and 2 private clinics. We consecutively recruited 91 pregnant women who were positive for HBs Ag in prenatal consultations. For each pregnant woman record included in the study, we provided Socio-demographic (Age, marital status, education level, social rank, gravidity, parity) and biological data (HBs Ag, Anti-HBc Total Ac, Hbe Ag, Ac anti-Hbe Ac, DNA-VHB, Ac anti-HCV Ac, retroviral serology, transaminases). All of these data were collected using a survey sheet developed for the study. **Results:** The age of our pregnant women HBs positive ranged from 18 years to 44 years with a mean age of 30.10 years. The age group from 20 to 39 years was the most represented with a frequency of 92.31%. Almost of all positive HBs Ag pregnant women was HBe Ag negative, only 3.3% was HBe Ag positive. The viral load above 2000 IU/ml was found in 21 (23.03%) patients. There were 4 co-infected patients, which 3 HBV-HIV and 1 HBV-HCV. Only 19 (20.88%) pregnant HBs Ag positive women were able to bring back the supplementary virological assessment within a period less than one month. **Conclusion:** According to our work the virologic profile of positive HBs Ag in pregnant women in Cote d'Ivoire is characterized by an important viral replication objectified by a high viral load in about 23% pregnant women, a negativity of HBe antigen in 96.6% of them.

Keywords

Côte d'Ivoire, Hepatitis B Virus Surface Antigen Positive, Risk Factors-Mother-to-Child Transmission

1. Introduction

Hepatitis viral B (HVB) is a public health concern by its complications which are cirrhosis and hepatocellular carcinoma (HCC) [1]. According to WHO (World Health Organization), about 2 billion people are put at risk with the hepatitis B and there are about 350 millions of chronic carriers of this virus in the world, 500,000 or 700,000 of them annually die of the consequences of the viral infection [2]. The Sub-Saharan Africa as well as South-East Asia and Southern China, is a high-endemic area with a prevalence in the circa of 8% and 12% for the HBs Ag irrespective of age. [3]. In Cote d'Ivoire, this one goes from 8% to 10% [4] [5]. The infection through the VHB often occurs very early in childhood with a chronic carrying risk of the virus in about 90% of cases [6]. Vertical mother-to-infant transmission is the cause of one third of the chronic infection B [7]. In fact the perinatal transmission seems to prevail in the areas of high prevalence namely some countries of Sub-Saharan Africa [8]. Infants born from mothers carrying Hbs Ag to positive Hbe Ag have got a 90% - 100% chance of being infected in perinatal with a chronic carrying risk in 90% of cases [9]. In Cote d'Ivoire the mother-to-infant transmission rate is about 32.8% [10]. The prevention of mother-to-infant transmission (PMIT) therefore constitutes a particular challenge. This one mainly rests on the serovaccination of the newborns [11], but because of the limited resources in our countries, it is not widely widespread. The antiviral therapy similar to nucleotidic or nucleosidic (lamivudine or tenofovir) in pregnant women carrying the Hbs Ag is another alternative to reduce transmission as certain recent studies have shown with a decrease in the viral load, therefore a transmission reduction [12] [14]. The antiviral therapy was very efficient in reducing the virus transmission of the human immunodeficiency, and the medicine which can be used for pregnant women infected with the VHB is at the same time safe and affordable during pregnancy [13] [15]. In addition, administering of analogous nucleotidic or nucleosidic to viremic women can be more feasible than the regular check-up and administering antiviral B immunoglobulin (BHIG) to the new-born babies, particularly in our areas with very limited resources. The efficient introduction of the antiviral therapy as a method to reduce the virus transmission of hepatitis B (VHB) will require knowing ways of infection and transmission of the VHB as well as risk factors in mother-to-baby.

Several more recent studies [6] have shown that the predictive factors of transmission risk of VHB in mother-to-baby were: the high viral load in the mother during child labour, the carrying of Bhe Ag in mother, the long time during delivery. The objective is to list the risk factors of the mother-to-child transmission of VHB in Hbs Ag positive pregnant women in Cote d'Ivoire.

2. Patients and Methodology

This is about a cross sectional, prospective study which was carried out during a period of seven months (February 2016-August 2016).

Our study was done in collaboration with gastro-enterologists and gyneco-obstreticians from the CHU of Yopougon and Treichville as well as those from the private health centers availing the Social Security System for pregnant women carrying the positive HBs antigen (Hbs Ag). This study has included all the pregnant women who were tested Hbs Ag+ during their prenatal check-up and who gave their oral consent to take part in the so-called study. This study has not included all the pregnant women who were tested Hbs Ag+ and having not completing their biochemical and virologic check-ups or those having not given their consent to participate in the study. A pre-established standard questionnaire was proposed to the pregnant women during their prenatal consultations. This questionnaire is used tocollect socio-demographic data (Age, marital status, education level, social rank, gestity, equality,…), biological (Hbs Ag, Ac anti-HBc totals, Hbe Ag, Ac anti-HBe, DNA-VHB, Ac anti-CVH, retroviral serology, transaminase,…)

The keying up of the data, the processing and statistical analysis were carried out using the STATA software with 2013 model. The data analyses were carried out with the t-student test for the comparison of quantitative variables and the exact Fisher test for the comparison of ratios. The level of significance was set at 5 percent.

3. Results

The total number of Hbs Ag positive pregnant women included in the study was 91 patients. The age bracket between 20 - 39 years was the most represented (92.31%), the age average of 30, 10 years and extremes of 18 years and 44 years. More than 2/3 of Hbs Ag positive pregnant women included in the study came from the public teaching hospitals and 51.65% among them had an average monthly income. More than 1/3 of the spouses of the Hbs Ag positive pregnant women were working in the informal sector (36.26%). Only one patient was not educated or was illiterate, the majority had a university level (59.34%). The large majority of pregnant women carrying the Hbs Ag was living with a spouse (73.63%). Almost 2/3 (64.84%) of pregnant women with Hbs Ag had already got at least a previous pregnancy. Sixty-one pregnant women with HbsAg positive (62.64%) had already given birth to a baby at least once. All the pregnant women in this study had been exposed at a given moment to a viral B amount mostly by using a sharp material in 83.52% of cases. Excluding two pregnant women who were screened for before pregnancy, all the others, that is to say, 97.80% of cases were screened for during the prenatal check-up. Most of the pregnant women included (85) did not know their viral B status before screening for. Among those who knew about their viral B status (6), 4 knew they were carrying VHB. In the majority of cases (82.42%), screening for the VHB among our patients was carried out in the second term of pregnancy. All these socio-demographic characteristics are shown in Table 1.

In almost cases Hbe Ag has become negative, only (3.30%) pregnant women with Hbs Ag positive had the HBe antigen positive. The viral load was high

Table 1. Socio-demographic features of Hbs Ag positive pregnant women.

Variables	n	Frequency (%)	variables	n	Frequency (%)
Age			**Marital status**		
<20 years	3	3.30	As a couple	67	73.63
20 - 29 years	35	38.46	Cohabitation	24	26.37
30 - 39 years	49	53.85			
≥40 years	4	4.40			
Origin			**Gestity**		
Abidjan CHU	64	70.33	G1	32	35.16
Private Clinics	27	29.67	>G1	59	64.84
Women's profession			**Parity**		
Whithout	3	3.30	P0	30	37.36
Informal	41	45.05	P1	38	41.76
Average-salaried woman	47	51.65	>P1	19	20.88
Profession of husband			**Past history**		
Whithout	1	1.10	Tatooing	5	5.4
Informall	33	36.26	Scarification	14	15.38
Salaried	47	51.65	Excision	14	15.38
			Sharp material	76	83.52
Senior executive	10	10.99	Tooth extraction	20	21.98
			Transfusion	2	2.20
Educational level			**Screening during**		
Not educated	1	1.10	**BPN**		
Primary	4	4.40	No	2	2.2
Secondary	32	35.16	Yes	89	97.8
University	54	59.34			
Sreening period			**HVB status known**		
1st term	14	15.38	No	85	93.41
2nd term	75	82.42	Yes	6	6.59
3rd term	2	2.20			

among 21 (23.03%) patients, that is to say, at least superior to 2000 UI/ML. The co-infection VHB-HIV was found with 3 (3.30%) pregnant women with Hbs Ag positive. The co-infection VHB-VHC was but found in one pregnant woman with Hbs Ag positive. Only 19 (20.88%) pregnant women with Hbs Ag positive were able to bring back the results of the additional virology check-up in a deadline of less than one month. One found a cytise with ALAT superior to 1.5N in 4 pregnant women carrying Hbs Ag. All the pregnant women with HBsAg + had a normal amount of prothrombin and number of platlets. We noticed a hypoproteinemia in about 1/3 pregnant women with Hbs Ag positive. All of these biological data are summarized in Table 2.

Table 2. Virologic and biochemical features.

Variables	n	Frequency (%)	Variables	n	Frequency (%)
Ag HBe status			**ALAT (UI/ml)**		
Négative	88	96.70	>1.5 N	4	4.40
Positive	3	3.30	Normales	87	95.60
Viral load (UI/ml)			**Protidemia (g/l)**		
>2000	21	23.08	Normal	30	32.97
≤2000	70	76.97	Low rate	61	67.03
Coinfection HVB-HIV			**Taux de prothrombine (%)**		
VIH positive	3	3.30	Low	00	0
VIH négative	88	96.70	Normal	91	100
Coinfection HVB-HVC			**Platelet (nb/mm^3)**		
VHC positive	1	1.09	<150,000	00	0
VHC négative	90	98.01	≥150,000	91	100
Deadline while awaiting the additional check-up					
≤2 semaines	19	20.88			
]2-4] semaines	60	65.93			
]4-8[semaines	12	13.19			

4. Discussion

The global prevalence of hepatitis B is high in Cote d'Ivoire [4] [5]. The mother-to-infant of hepatitis B is the cause of more than 1/3 of chronic infections via the hepatitis B virus in the world [7]. The perinatal infection is considered as a major transmission way in the areas of high prevalence like most Sub-saharan countries in Africa [8]. Positivity with HBeAg is associated with a high risk perinatal transmission of VHB in infants born from mothers positive to HBsAg and HBeAg showing a probability of 70% and 90% perinatal acquisition of infection through VHB [9] [16]. The global prevalence of hepatitis B is high in Cote d'Ivoire [4] [5]. The vertical transmission of VHB can be reduced by an early screening for mothers carrying chronic hepatitis B and through preventative measures [17] [18]. The objective of our study was to estimate the transmission risks from mother-to-infant of VHB in pregnant women positive to HbsAg in order to show a more efficient preventative attitude.

Our study was carried out during a period of 7 months (February 2016-August 2016) at the end of which 91 pregnant women carrying HBsAg were included.

In relation to our results, the research done at Tokombéré (a rural area in the Great North of Cameroon) like in Ibadan in the South-West in Nigeria reported high rates of HBeAg respectively 22.7% and 26.7, this suggests a high risk of perinatal transmission of VHB [19] [20]. Another study carried out in urban sur-

rounding in Cameroon also found a high rate of infectivity by VHB, 28% $HBsAg^+$ pregnant women being $HBeAg^+$ [21]. These results corroborate the literature exploring the perinatal transmission risk of VHB based on estimates of HBeAg prevalence in all the areas worldwide. It showed that in 2005, 22.7% to 29.9% HBsAg positive women at childbearing age in Sub-Saharan Africa were HBeAg positive [22]. Our study found a lower rate of infectivity of VHB, with a global HBeAg prevalence in our sample which was 3.7%. This suggests that the probability of TME VHB was high but in a low count in our population of study. This result corroborates Hannachi's [23] who had found 4.3% HBeAg positive in our study with a population of 92 pregnant women carrying HBsAg. Other studies in Tunisia [24] and in Greece [25] [26] had reported similar rates of HBeAg among pregnant women. This HBeAg rate is all the same below 14.7% in Cote d'Ivoire in its group of 61 $HBsAg^+$ pregnant women [10], 11.1% in Burkina Faso [27] and 12.1% in the north of Cameroon [28]. The natural story of the viral B infection could explain these different results, mostly in our countries with a high VHB endemicity where infection is passed on most often at birth or during infancy. Thus at manhood at the moment of screening VHB, in the absence of viral reactivation, the patient is in a phase of inactive carrying with HBeAg negative, seroconversion having certainly occurred in infancy [1] [10] [29].

In our study, none of the HBsAg positive pregnant women carrying HIV was not HBeAg positive, this suggests that perinatal transmission plays a minor role in the burden of VHB in Cote d'Ivoire. We must note that the present recommendation of the vast programme of vaccination in Cote d'Ivoire to vaccinate all the new-borns aged 6, 10 and 14 weeks is probably based on the proof that the horizontal transmission during early infancy could be the most current mechanism of the infection by VHB in Sub-Saharan countries in Africa [30] [31] [32]. The contradictory data about infectivity of VHB among pregnant women and the mother-to-infant transmission in Sub-Saharan countries in Africa demand deeper surveys.

In the litterature the threshold of the viral load of VHB from which the transmission risk becomes significant is not clearly expressed. Some authors consider that the vertical transmission risk is high when the DNA VHB > 2.105 UI/ml [33]. This transmission risk reaches 28% to 50% for a viral load > 2.108 UI/ml [1] [6]. Other authors in an Asian study, evaluated the significant transmission risk from a DNA of VHB about 7 - 8 Log UI/ml [34]. The WHO (World Health Organisation) in its recommendation in 2015 defined as eligible for a BHV anti-viral treatment any $HBsAg^+$ patient having a viral load > 20,000 UI/ml with or without HBeAg associated with a persistent cytolysis [35]. Finally MAUSS while synthetizing different recommendations, defined as eligible for a VHB anti-viral treatment, any $HBsAg^+$ patient having a viral load > 2.000 UI/ml with or without HBeAg associated with a persistent cytolysis or a hepatic fibrosis. Twenty-one pregnant women, that is to say 23.08% had a high viral load (>2.000 UI/ml) in our study. This ratio of $HBsAg^+$ pregnant women with DNA VHB > 2000 UI/ml, therefore likely to pass the VHB on to their infant during

delivery is not insignificant.

Considering that intrauterine transmission is the main way of transmitting the BHV from mothers to their foetus or new-born, particularly in countries where VHB is endemic like in Cote d'Ivoire, all the pregnant women must be screened for the hepatitis B [36]. The immunization of the new-born with the vaccine against the hepatitis B should be the absolute priority in the highly endemic areas where the engagement of the perinatal transmission with a global load of morbidity is the highest. However, even in the countries where the hepatitis B chronic prevalence is relatively low, implementing a vaccine dose at birth against the hepatitis B brings about an extra reduction of 10 to 20% in mortality by the VHB [37] [38]. Considering the viral hepatitis impact due to the main way of the mother-to-infant transmission, the design and implementation of intervention strategies to reduce the vertical transmission of the VHB assume a fundamental importance. This deals with administering the VHB infected mothers the prophylaxis at birth of the new-born with a specific immunoglobulin and vaccine, together with the administration of antivirals (tenofovir or Lamuvidine) to the mother in the third term of pregnancy (in case of a high viral load in mother) [39]. Treatment in the third term can be considered as a help to prevent the perinatal transmission, this seems to be the most recommended to mothers having a high viral load [40]. The strategies aiming at disrupting the mother-infant transmission could considerably reduce the number of new infections and put an end to the suffering imposed by the disease to individuals, families and society.

5. Conclusions

According to our work, the virologic profile of $HBsAg^+$ pregnant women in Cote d'Ivoire is characterized by an important viral duplication objectified by a high viral load among about 23% pregnant women, a neutralization of the HBe antigen among 96.6% of them. It is recommended to vulgarise vaccination before pregnancy and systematically screen for the HBsAg in all pregnant women. For $HBsAg^+$ and $HBeAg^-$, it is important to study the viral load in order to assess the perinatal transmission risk and prevent with a seroprophylaxis from birth, even an antiviral treatment during pregnancy.

However, we think that these risk factors will have to be reevaluated inside a more important serie before finding a true consensus as for the antiviral treatment to the pregnant women carrying VHB.

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