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Infection of Pregnant Women with Human Immunodeficiency Virus, Hepatitis B Virus and Associated Risk Factors in Semi-rural Health District, Cameroon

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Abstract

Introduction: Human Immunodeficiency Virus (HIV), Hepatitis B (HBV) infection remains a public health problem worldwide and known to cause chronic hepatitis with high risk of mortality resulting from liver failure and hepatocellular carcinoma. Pregnant women, who are infected, can vertically transmit the disease to their babies. This study was conducted to determine the infection of pregnant women with HIV, HBV and associated risk factors in semi-rural health district.

Method: A cross-sectional, analytical study was conducted from May to July 2018 among pregnant women in Bafia Health District (BHD) after providing informed consent. Socio-demographic characteristics and associated risk factors were collected using a questionnaire. HIV was diagnosed and confirmed using determine and OraQuick HIV1/2 and HBV by Nova test© one step HBV-5 rapid diagnostic test Multi Panel. Statistical analysis was performed using Epi infoTM 7 and $p < 0.05$ was considered significant. The study of associations was performed by bivariate analyzes and associations between the variables were sought with the Odds Ratio (OR), expressed with 95% confidence interval (CI).

Results: Of the 145 pregnant women enrolled, 6.90% (3.36%-12.32%), 10.34% (5.91%-16.49%), and 2.76% (0.76%-6.97%) were positive for HIV, HBsAg, and HBeAg respectively. According to the associated risk factors, history of blood transfusion (OR: 11; 1.60-75.50, p=0.03), and previous surgery (OR: 11; 1.60-75.50, p=0.03) were statistically associated risk factors for HIV infection.

Conclusion: Infection of HIV and HBV in pregnant women remains high in semi-rural health district, reflecting a significant risk of vertical transmission. The primary measures would early diagnosis these two viruses during antenatal clinic (ANC).

Keywords: Infection; HIV; HBV; Associated Risk Factors; Pregnant Women; Cameroon

Abbreviations: Ab: antibody; AIDS: Acquired Immunodeficiency Syndrom; Ag: Antigen; ANC: Antenatal Clinic; BHD: Bafia Health District; DNA: Dexoyribonucleic Acid; EDTA: Ethylene Diamine Tetra Acetic; HBV: Hepatitis B Virus; HCC: Hepatocellular Carcinoma; HBeAg: Hepatitis B envelop antigen; HBsAg: Hepatitis B surface antigen; HBcAb: Hepatitis B core antibody; HBeAb: Hepatitis B envelop antibody; HBsAg: Hepatitis B surface antibody; HIV: Human Immunodeficiency Virus; IQR: Interquartile Range; MTCT: Mother-To-Child Transmission; OBI: Occult HBV Infection; PCR: Polymerase Chain Reaction; RNA: Ribonucleic Acid; SD: Standard Deviation; WHO: World Health Organization

Introduction

HIV and HBV infection remains major public health problems worldwide particularly in sub-Saharan Africa (SSA) [1,2]. While about 36.7 million HIV-infected individuals worldwide with 70% in SSA, the World Health Organization (WHO) estimates about 350 million people are chronically infected by HBV with high endemicity (8 to 15%) in Africa and Asia [1,3]. As HIV and HBV share common routes of transmission (blood transfusion, vertical transmission…), co-infection in pregnancy is associated with increased morbidity, mortality and untoward outcomes to a newborn. HIV co-infection increases HBV replication, leading to higher levels of detectable virus, and increases likelihood of perinatal transmission of HBV [4]. The prevalence of HIV-1 among infants from the prevention of mother to child transmission (PMTCT) is 11.5% (434/3789) in Cameroon [5], suggesting eventual impaired T-cell immunity and inferior response to vaccination in these potentially vulnerable populations [6]. Of note, babies born to mothers who are positive for both HBsAg and hepatitis B e antigen (HBeAg) are at a higher risk of acquiring infection (70–100% in Asia and 40% in Africa) than those born to HBsAg-positive mothers who have lost the HBeAg (5–30% in Asia and 5% in Africa) with HBV deoxyribonucleic acid (DNA) level (>200,000IU/ml, equivalent to 6 log copies/ml) [7,8].

HIV-infection increases the transition to the chronicity of acute hepatitis B by increasing viral replication. It also increases the frequency of HBV reactivation in inactive HBV carriers, and accelerates the rate of progression of fibrosis, the development of cirrhosis and HCC [9]. Cameroon is located in an area of high endemicity for HBV and HBsAg prevalence rate among pregnant women attending the ANC ranges from 7 to 12% [10-12]. These studies were limited to looking only for HBsAg. However, HBsAg alone does not make it possible to assess the epidemiology of HBV in a pregnant woman. The prevalence of HIV-infection during pregnancy in Africa (7.8% in Cameroon) suggests significant rates of vertical HIV-infection, in the context of ongoing risks of MTCT [13].

Materials and Methods

Study Design and Population

A cross-sectional, analytical study was conducted from May to July 2018 among 145 pregnant women attending the BHD. Bafia is a city of Cameroon located in the Center region, Mbam and Inoubou department, 120 km north of Yaoundé. The BHD include: a health center within it, the district hospital of Bafia, main health structure of the city which is endowed with the main specialties (general medicine, pediatrics, gynecology, odonto-stomatology, surgery, etc.) and several integrated health centers in certain neighborhoods and villages.

Sample Size Determination and Strategy of Enrollment

The minimum sample size was calculated using the following formula:

$n = \frac{z^2 \times P(1-P)}{d^2}$. With ‘’z”= the standard deviation of 1.96 (95% confidence interval), ‘’P”= the prevalence of HIV among pregnant women in center region, Yaoundé-Cameroon (11.9%) found by [13] and ‘’d”= tolerable error or precision (6%). Applying the formula, the minimum sample size obtained was ‘’n”= 111.82. However, one hundred and forty five pregnant women attending the BHD were consecutively recruited during the study period. The enrollment of study participants was the interview face to face with a questionnaire containing socio-demographic characteristics and associated risk factors data (age, marital status, education level, gestational age, parity, occupation, history of blood transfusion, scarification, tattoo and/or piercing, previous surgery, knowledge of the disease). Were included all pregnant women attending the BHD who gave their written informed consent. Moreover, informed consent from parental or legal representative was obtained for pregnant women under 21 years old. All pregnant women who decided during the process, withdrew their consent were excluded in this study.

Samples Collection and Storage

The minimum sample size was calculated using the following formula:

A total of four milliliters (4ml) of whole blood was collected aseptically by veno-puncture into vacutainer dry tube and a tube under anticoagulant including ethylene diamine tetra acetic (EDTA) previously labelled. After centrifugation of the whole blood in the dry tubes, the sera was immediately separed in eppendorf tubes, previously labelled with the identification code and stored in a -20c freezer until analysis.

Laboratory Diagnosis Tests

HIV Screening

HIV was tested using standard operational procedures (SOP) of rapid test kits and national HIV test algorithm [14]. The serial algorithm involving tree tests was used to confirm HIV sero-positivity and the determine Abbott HIV-1/2 was the first screening test used. Determine Abbott HIV-1/2 is a lateral flow chromatographic immunoassay sandwich used for the qualitative detection of anti-HIV-1/2 antibodies in the serum/plasma after 15 minute turnaround time [15]. A second rapid HIV test was performed on antenatal patients who had a positive determine test. For any indeterminate results, “OraQuick ADVANCE® HIV-1/2” test (manufactured by OraSure Technologies, PA 18015 USA, Item 3001-1203 rev.03/16) was used as third test [14].

HBV Testing

The one step HBV-5 (Nova test©) rapid diagnostic test Multi Panel (sensivity: 98.4%, specificity: 98.3%, ISO13485: 2016 certified medical diagnostic in USA, Atlas link technology co., Ltd, Lot: 20170503; Expiration: 05/2019) is lateral flow chromatographic immunoassay with 100µl of serum/plasma (10-20 minute turnaround time) for the qualitative detection of HBsAg, HBsAb, HBeAg, HBeAb, and HBcAb assembled in one cassette. Each strip of the panel member is composed of a sample pad, colloid gold conjugate pad, nitrocellulose membrane (NC membrane) strip pre-coated with control band (C band) and test band (T band), and absorbent pad. The HBeAg, HBsAb, HBsAg are based sandwich immunoassay and the HBeAb, HBcAb are based competitive immunoassay [16].

Detection of HBsAg

HBsAg marker was used to qualitatively detect any pregnant woman infected with HBV, using lateral flow chromatographic immunoassay HBsAg Gold Rapid Screen (collodial gold), with 100µl of serum. Validated results were reported as HBsAg reactive (HBV-positive) or non-reactive (HBV-negative).

Detection of HBeAg

HBeAg marker was used to qualitatively detect any pregnant woman with HBV replication, using lateral flow chromatographic immunoassay sandwich with 100µl of serum. The test utilizes a pair of anti-HBeAg antibodies to detect HBeAg in the test specimen. A burgundy colored T band indicates an HBeAg positive test result and absence of the T band suggests a negative result.

Statistical Analysis

The data compiled on the data sheets were entered in a Microsoft Excel version 2007 and transported to the analysis software Epi infoTM version 7.2.1.0. The statistical test used to compare frequencies was Fisher's exact test corrected by Yates test calculation online for any value less than five in the contingency table. The probability was significant for all values of $p<0.05$. The study of associations was done by bivariate analyzes and associations between the variables were sought with the Odds Ratio (OR), expressed with 95% confidence interval (CI).

Results

Socio-Demographic Characteristics of the Study Population

A total of 284 pregnant women seen at the BHD, 51.05% (145/284) were finally enrolled in this study. The age of the study participants range from 15 to 41 years old with a mean age of 25±5.96 years and the predominant age group was 15-23 years old (46.21%; 95%CI: 37.90% -54.67%). One hundred of pregnant woman were married (68.96%; 95%CI: 53.58% - 85.64%) and 112 (77.24%; 95%CI: 69.55% - 83.79%) were secondary education level. Moreover, seventy two (49.66%; 95%CI: 41.25 - 58.07%) were first trimester of gestational age, seventy nine (54.49%; 95%CI: 39.04% -79.04%) of them were housewives and sixty seven (46.21%; 95%CI: 37.90% - 54.67%) were multiparous (Table 1).

Variables	Total N=145 (%)	HIV		p-value
		Positive (%) 10 (6.90)	Negative (%) 135 (93.10)	
Age groups (in years)				
15-23	67 (46.21)	02 (2.99)	65 (97.01)	p=0.45 X^2=1.57
24-32	61 (42.07)	06 (9.84)	55 (90.16)	
33-41	17 (11.72)	02 (11.76)	15 (88.24)	
Marital status				
Married	100 (68.96)	08 (8.00)	92 (92.00)	p=0.66 X^2=0.18
Single	45 (31.04)	02 (4.45)	43 (95.55)	
Education level				
Primary	28 (19.31)	0 (0.00)	28 (100.0)	p=0.52 X^2=1.29
Secondary	112 (77.24)	09 (8.04)	103 (91.96)	
University	05 (3.45)	01 (20.00)	04 (80.00)	
Gestational age				
1st trimester	72 (49.66)	04 (5.56)	68 (94.44)	p=0.55 X^2=1.18
2nd trimester	43 (29.66)	02 (4.65)	41 (95.35)	
3rd trimester	30 (20.68)	04 (13.33)	26 (86.67)	

Variables	Total N=145 (%)	HIV		p-value
		Positive (%) 10 (6.90)	Negative (%) 135 (93.10)	
Parity				
Primiparous	28 (19.31)	01 (3.57)	27 (96.43)	p=0.86 X^2=0.28
Pauciparous	50 (34.48)	03 (6.00)	47 (94.00)	
Multiparous	67 (46.21)	06 (8.96)	61 (91.04)	
Occupation				
Pupils	27 (18.62)	0 (0.00)	27 (100.0)	p=0.53 X^2=5.04
Student	03 (2.07)	0 (0.00)	03 (100.0)	
Housewives	79 (54.49)	05 (6.33)	74 (93.67)	
Dressing	04 (2.76)	0 (0.00)	04 (100.0)	
Dressmaking	23 (15.85)	02 (8.69)	21 (91.31)	
Nurses	02 (1.38)	01 (50.00)	01 (50.00)	
Teachers	07 (4.83)	02 (28.57)	05 (71.43)	

Table 1: Socio-demographic characteristics and sero-prevalence of HIV

Socio-Demographic Characteristics and Sero-Prevalence of HIV

Out of 145 samples tested, the overall HIV-positive was 6.90% (95%CI: 3.36%-12.32%; 10/145) with no statistically significant between socio-demographic characteristics (p>0.05). Meanwhile, sero-prevalence of HIV was observed in the age group of 24-32 years old (9.84%, 6/61) compared to other age groups (p=0.45). Among one hundred married pregnant women, 8.00% (08/100) was HIV-positive. We also note that, higher sero-prevalence of HIV was recorded in secondary education level and no HIV-positive was observed in primary education level (Table 1).

Socio-Demographic Characteristics and Sero-Prevalence of HBV

The HBsAg positive was simultaneously increasing significantly with age groups of study population, with women aged between 33-41 years (35.29%; 6/17) having the highest HBV sero-prevalence compared to other age groups (p=0.001). We have also registered higher sero-prevalence of HBV in married women and secondary education level (Table 2).

Variables	Total N=145 (%)	HBsAg	p-value	HBeAg	p-value
		Positive (%) 15 (10.34)		Positive (%) 04 (2.76)	
Age groups (in years)					
15-23	67 (46.21)	05 (7.46)	p=0.001** X^2= 12.95	04(5.97)	p=0.3 X^2=2.37
24-32	61 (42.07)	04 (6.56)		0(0.00)	
33-41	17 (11.72)	06 (35.29)		0(0.00)	
Marital status					
Married	100 (68.96)	10 (10.00)	p=0.92 X^2=0.008	03(3.00)	p=0.77 X^2=0.08
Single	45 (31.04)	05 (11.11)		01(2.22)	
Education level					
Primary	28 (19.31)	03 (10.71)	p=0.96 X^2=0.06	0(0.00)	p=0.56 X^2= 1.13
Secondary	112 (77.24)	12 (10.71)		04(3.57)	
University	05 (3.45)	0 (0.00)		0(0.00)	
Gestational age					
1st trimester	72 (49.66)	06 (8.33)	p=0.65 X^2=0.34	02 (2.78)	p=0.84 X^2=0.83
2nd trimester	43 (29.66)	04 (9.30)		01 (2.33)	
3rd trimester	30 (20.68)	05 (16.67)		01 (3.33)	
Parity					
Primiparous	28 (19.31)	04 (14.29)	p=0.73 X^2=0.61	02 (7.14)	p= 0.4 X^2= 1.72
Pauciparous	50 (34.48)	05 (10.00)		02 (4.00)	
Multiparous	67 (46.21)	06 (8.96)		0 (0.00)	

Variables	Total N=145 (%)	HBsAg	p-value	HBeAg	p-value
		Positive (%) 15 (10.34)		Positive (%) 04 (2.76)	
Occupation					
Pupils	27 (18.62)	02 (7.41)	p=0.99 X^2=0.74	01 (3,70)	p= 0.24 X^2= 7.92
Student	03 (2.07)	0 (0.00)		0 (0.00)	
Housewives	79 (54.49)	09 (11.39)		02 (2.53)	
Dressing	04 (2.76)	0 (0.00)		0 (0.00)	
Dressmaking	23 (15.85)	03 (13.04)		01 (4.35)	
Nurses	02 (1.38)	0 (0.00)		0 (0.00)	
Teachers	07 (4.83)	01 (14.29)		0 (0.00)	

Table 2: Socio-demographic characteristics and sero-prevalence of HBV

Associated Risk Factors with HIV and HBV Infection

To assess independent associated risk factors for HIV and HBV infection, bivariate logistic regression was performed. History of blood transfusion (OR: 11; 95%CI: 1.60-75.50; p= 0.03), previous surgery (OR: 11; 95%CI: 1.60-75.50; p= 0.03) were statistically significant risk factors for HIV infection (Table 3). Alarming fact, sero-prevalence of HIV was more observed in study participants with knowledge of the disease (8.82%) compared to 2.33% (1/43) for those do not have knowledge of the disease (OR: 4.06; 95%CI: 0.49-33.12; p=0.29) (Table 3). No statistical significant association was found between associated risk factors and HBV-infection in this study (p>0.05).

Variables	Total N=145 (%)	VIH		OR (95%CI)	p-value
		Positive (%) 10 (6.90)	Negative (%) 135 (93.10)		
History of blood transfusion					
Yes	05 (3.45)	02 (40.00)	03 (60.00)	11 (1.60-75.50)	0.03**
No	140 (96.55)	08 (5.71)	132(94.29)		
Scarification					
Yes	16 (11.03)	02 (12.50)	14 (87.50)	2.16 (0.41-11.19)	0.67
No	129 (88.97)	08 (6.20)	121(93.80)		
tattoo and/or piercing					
Yes	06 (4.14)	02 (33.33)	04 (66.67)	8.18 (1.29-51.62)	0.07
No	139 (95.86)	08 (5.76)	131(94.24)		
Previous surgery					
Yes	05 (3.45)	02 (40.00)	03 (60.00)	11 (1.60-75.50)	0.03**
No	140 (96.55)	08 (5.71)	132(94.29)		
Knowledge of the disease					
Yes	102 (70.34)	09 (8.82)	93 (91.18)	4.06 (0.49-33.12)	0.29
No	43 (29.66)	01 (2.33)	42 (97.67)		

Legend: %: percentage; OR: Odds Ratio; CI: Confidence Interval; p: p-value; **significant (<0.05)
Table 3: Associated risk factors for HIV among pregnant women

Discussion

The present study was designed to determine the infection of pregnant women with HIV, HBV and to identify the associated risk factors among pregnant women in semi-rural health district. In the current study, the HIV sero-prevalence of 6.90% (95%CI: 3.36%-12.32%) was recorded. In comparison in other studies conducted in Cameroon, this result was higher than that reported by Abongwa, *et al.* [17] and Jodie, *et al.* [18] who found HIV sero-prevalence of 6.60% and 6.00% (95%CI: 3.0–10.2%) respectively among pregnant women in the North and South West regions of Cameroon. Meanwhile, our results are very lower than the sentinel study conducted in the ten regions of Cameroon by [13] who found HIV prevalence of 7.8%. Despite the estimated HIV prevalence of 7.8% reported by [13] among pregnant women in Cameroon, there is regional variability in HIV prevalence. The center region ranks first with an estimated prevalence of 11.9% [13]. Our result could be explained by the implementation of the new WHO recommendations requiring the treatment of any HIV-infected person in order to reach the global target "90-90-90" in 2020 [19].

Hepatitis B surface (HBsAg) is one of the most HBV-biomarkers frequently performed tests laboratory for HBV infection. In this study, we recorded HBAg sero-prevalence of 10.34% (95%CI: 5.91%-16.49%). This is relatively high in view of the fact that a vast majority of study participants were asymptomatic [11]. In accordance to WHO interpretation, the finding grades the study setting an area with high HBV (HBsAg) disease endemicity [20]. In comparison to other studies carried out in Cameroon, the

results (10.34%) obtained in this study was higher than that found by Noubiap, *et al.* [12], Frambo, *et al.* [11] and, Fomulu, *et al.* [10] who found HBsAg prevalence of 10.20% (33/325), 9.7% (95%CI: 5.7-15.0) and 7.7% (74/959) respectively. On the other hand, in comparison with other countries situated in SSA, similar finding was reported in Mauritania (10.7%) and, in Ghana (10.6%) [21,22]. These results show the variability of HBV prevalence in different region and in different group from the same population. This may be due to the variability of ethnic origin, socio-economic conditions and the high rate of emigration due to urbanization [23]. Our study found HBeAg sero-prevalence of 2.7% (95%CI: 0.76%-6.91%). This sero-prevalence of HBeAg is almost twice than that observed by Noubiap, *et al.* (1.2%) [12]. This suggests that the probability of HBV transmission remains in our study.

According to socio-demographic characteristics, the majority of study participants were young with a mean age of 25± 5.96 years old (range from 15 to 41 years old). Sero-prevalence of HIV was higher among pregnant women between 24-32 years with 9.84% (6/61). This prevalence is contrary to the work conducted by [13] who found high prevalence of 11.3% among pregnant women aged 35-39 years. However, the similar result was observed by the National Statistics Survey [24] among pregnant women aged 30-39 (9.1%). This result could be explained by the fact that women in these age groups are more sexually active and they may have higher chance of multiple sexual partners [25]. In the current study, higher HIV sero-prevalence, 9.84% (6/61) was observed in the age group of 24-32 years (p=0.45). However, HBsAg infection (35.29%; 6/17) was recorded in the age group 33-41 years (p=0.001). This age group correlates with the highest age of sexual activity, suggesting the role of sexual intercourse in HBV transmission [17]. This result could be explained by the fact that women in these age groups are more sexually active and they may have higher chance of multiple sexual partners [25].

Bivariate analysis of associated risk factors among pregnant women show that history of blood transfusion and previous surgery were statistically associated risk factors with HIV infection. Pregnant women with history of blood transfusion or previous surgery had a high chance of 11 times (OR: 11; 1.60-75.50; p=0.03) to contact HIV. This result could be explained by the fact that, blood is transfused to pregnant women to replace blood lost during labor and prevent maternal mortality. The study conducted in Ethiopia by [26] showed an increase of HIV infection among pregnant women who had a history of blood transfusion (AOR = 19.52, 95%CI: 1.80-150.6). In the current study, some limitations were reported: the investigation of HBV-DNA PCR assay did not allow us to determine the contribution of occult HBV infection (OBI) on the epidemiological burden of HBV during pregnancy in this semi-rural setting. Moreover, the small sample size did not allow us to have some statistically significant results.

Conclusion

Among pregnant women receiving ANC in semi-rural health district, sero-prevalence of HIV, HBsAg, and HBeAg were respectively 6.90% (10/145), 10.34% (15/145), and 2.76% (4/145) reflecting a significant risk of vertical transmission. Bivariate analysis shows that, associated risk factors like history of blood transfusion and previous surgery were statistically associated with HIV infection. The primary measures would early diagnosis these viruses during antenatal care and prevention vertical transmission.

Ethics Approval and Consent to Participate

Ethical approval was obtained (Reference: N°2018/07/1059/CNERSH/SP) from the National Ethics Committee of Research on Human Health of Cameroon. A written information note, informed consent from adult, parental consent or guardian for children (age under 21years old) were obtained. Confidentiality was secured by the use of unique identification codes attributed to each study participants.

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