

Prevalence of Hepatitis B Virus, HIV and HBV Coinfection and Associated Factors in Pregnant Women Attending Antenatal Care at the University Teaching Hospital, Lusaka, Zambia

V. Sichone,¹B. Vwalika²

¹University Teaching Hospitals, Women and Newborn Hospital, Lusaka.

²University of Zambia School of Medicine, Department of Obstetrics and Gynaecology, Lusaka

Abstract

Objectives: To explore the prevalence and associated socio-demographic factors of hepatitis B in HIV positive and HIV negative pregnant women attending antenatal care at the University Teaching Hospital, Lusaka, Zambia.

Methods: This was a comparative cross-sectional study with a total of 316 (158 HIV negative and 158 HIV positive) pregnant women, aged 16-46years. Participants were recruited from the antenatal ward using convenient sampling method from women with a known and documented HIV status. A structured questionnaire was administered for socio-demographic data and bloods for HBsAg screening were collected. Data collection was done between 15th Dec 2016 and 30th May, 2017. The relationship between study variables and presence of HBV and HBV/HIV coinfection was examined using logistic regression. The selection for entry into the logistic regression model was considered at level $p < 0.05$.

Results: Of the 316 study participants 11(3.5%) tested positive for HBsAg. There was no statistical difference in the prevalence of HBV in the HIV negative and HIV positive pregnant women (3.8% and 3.2% respectively, $P=0.76$). Similarly, there was

no association between the age, marital status, parity, residence, religion, education level or form of employment with HBV infection. Being on combined anti-retroviral therapy (cART) had a 91% reduced odds for HBV co-infection [OR = 0.09, CI = 0.01 – 0.63, $P=0.02$]

Conclusion: There was no significant difference in the prevalence of HBV between the HIV positive and HIV negative pregnant women. However, HIV antiretroviral treatment seems to have a protective effect on acquisition of HBV infection. Therefore, regardless of their HIV status or socio-demographic characteristics, all pregnant women should routinely be screened for HBV so that babies born to high risk mothers can receive the birth doses of HBV vaccine and immunoglobulins to prevent transmission to newborns.

INTRODUCTION

HIV and Hepatitis B virus (HBV) are a global public health problem, especially in the sub-Saharan Africa where they are known to be endemic.¹ According to WHO, it is estimated that about 2 billion people worldwide have been infected by HBV at some time in their lifetime with about 240 million remaining chronically infected.^{2,3} The major complications of chronic HBV infection are cirrhosis and hepatocellular carcinoma.³ HBV infected women

*Corresponding author:

Victor Sichone,

University Teaching Hospitals,

Women and Newborn Hospital,

P/ Bag RW 1X, Lusaka; vsichone@gmail.com

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like those who are HIV positive risk infecting their babies during pregnancy, delivery and puerperium with a consequence of developing fulminant hepatitis B infection especially if the woman is HBsAg positive and more so if the HBeAg is also positive.⁴ HBV is said to be about 50-100 times more infectious than HIV.⁵ Without vaccination, the risk of HBV infection is 10 to 20% if the mother is positive for HBsAg, and as high as 90% if she is also positive for the HBeAg.² If administered appropriately after birth, hepatitis B immunoglobulin (HBIG) plus hepatitis B vaccine (HB vaccine) can effectively prevent mother to infant transmission of HBV.⁶

The prevalence of chronic HBV infection ranges widely from 0.1–2% in low-prevalence areas like North America, Western Europe, Australia, and New Zealand to 10–20% in high prevalence areas like South East Asia, China, and sub-Saharan Africa. Intermediate-prevalence areas include; Japan, Central Asia, the Middle East, Central America, and South America.⁷ The mode of transmission differs among these geographic areas with; mother to child transmission predominating in high-prevalence areas, horizontal transmission in intermediate-prevalence areas and unprotected sexual intercourse and intravenous drug use in adults being responsible in low-prevalence areas.⁷ A review of some studies done in Africa showed that the prevalence of HBV infection in pregnant women falls in the intermediate or high endemicity. For example in Ethiopia, HBV infection prevalence was found to be 3.8% while HIV and HBV co-infection was 19%.⁸ In one study in South Africa, HBV prevalence was 5.3% and a 3.1% HBV and HIV coinfection was reported.⁹ A study in Malawi found 13% prevalence.¹⁰ In Yaoundé, Cameroon, HBV prevalence was 7.7% while HIV and HBV co-infection was 0.74%.¹¹ Another study in Nigeria found 6.9% prevalence of HBV and 0.8% co-infection with HIV and HBV.¹² With regards to association of HBV infection with socio-demographic characteristics, a study in Sudan found 5.6% of pregnant women were positive for HBsAg

irrespective of their age, parity and socio-demographic characteristics.¹³ However, a study in the United States of America, noted that the prevalence of HBsAg among pregnant women in urban areas varied by race and ethnicity. The highest rate was 5.79% for Asian Americans while 0.97% was noted among African Americans, 0.6% for whites and 0.14% for Hispanics.¹⁴ In Zambia, there was paucity of data as regards to the prevalence of HBV more especially in the pregnant women population. Most pregnant women are unaware of their HBV infection and thus risk infecting their offspring and presenting late for care with advanced disease. The paucity of data seems to be partly due to limited access to routine screening and treatment availability. Most of the studies done on HBV in Zambia were in the non-pregnant and HIV infected adult population. One recent study at the Paediatric Centre of Excellence (PCOE) at the University Teaching Hospital (UTH) in Lusaka found the HBV infection in HIV infected children to be 5.9%.¹⁵ Another study at the University Teaching Hospital (UTH) found that 9.9% of the HIV infected adults had active HBV infection.¹⁶ A study on prevalence of HBV in HIV seropositive and seronegative pregnant women in Zambia conducted in five rural district hospitals and 3 urban health centres found the prevalence of Hepatitis B surface antigen positivity in pregnant women at 6.5% and it was noted that HBsAg positivity ranged from 3.3% to 13.6% among the sites, with higher prevalence in the rural district hospitals than urban health centres in Lusaka.¹⁷ Another study looking at the prevalence of HBV and HCV co-infections among HIV positive pregnant women admitted to labour ward in Kitwe in the Copperbelt province of Zambia found the prevalence of HBV to be 9.3%.¹⁸

This study aimed at determining the prevalence of HBV, HBV and HIV coinfection and associated sociodemographic factors in pregnant women attending antenatal care at the University Teaching Hospital.

METHODS

This was a comparative cross-sectional study with a total of 316 (158 HIV negative and 158 HIV positive) pregnant women. A convenient sampling method was employed and recruitment was done in the antenatal clinic between 15th December, 2016 and 30th May, 2017. A structured questionnaire was administered for socio-demographic factors and blood for HBV screening was collected. No matching was done for age, parity, marital status, education level, form of employment or HBV vaccination status. Statistical Package for Social Sciences (SPSS) version 23.0 was used for statistical analyses. The Pearson's chi-squared test was used to study associations between categorical variables. The Fisher's exact test was used when one or more of the cells had an expected frequency of five or less. The relationship between study variables and presence of HBV and HBV and HIV co-infection was examined using logistic regression. The selection for entry into the logistic regression model was considered at level $p < 0.05$.

RESULTS

A total of 316 pregnant women participated in the study. The socio-demographic characteristics of the study population are shown in Table 1. Bivariate analysis for the association with HBV infection was conducted and results shown in Table 2. There was no study variable associated with HBV infection at 5% significance level including HIV status ($P = 0.99$). Among the 158 HIV positive participants, 5 (3.2%) were co-infected with HBV while 6 (3.8%) were positive for HBV among the HIV negative participants, $P = 0.76$. Table 3 shows the bivariate analysis for association with HBV co-infection. At 5% significance level, only cART status was significantly associated with co-infection ($P = 0.04$) while residential area was marginally associated with co-infection ($P = 0.05$). Backward logistic regression conducted with residential area and cART status showed that only cART status was independently associated with co-infection. Compared to women not on cART, women on cART

had on average 91% reduced odds for HBV co-infection (odds ratio = 0.09, 95% confidence interval = 0.01 – 0.63, P -value = 0.02).

Table 1: Frequency distribution of socio-demographics characteristics

Variable	Frequency	Percentage(%)
Age group		
Less than 24 years	87	27.5
25 - 34 years	174	55.1
35 and above years	55	17.4
Marital status		
Single	42	13.3
Married	274	86.7
Parity		
0	82	25.9
1	81	25.6
2	69	21.8
3	46	14.6
4+	38	12
Education level		
None	16	5.1
Primary	78	24.7
Secondary	143	45.3
Tertiary	79	25
Employment		
Formal	59	18.7
Informal	45	14.2
Not employed	212	67.1
Residence		
High density	181	57.3
Medium density	77	24.4
Low density	33	10.4
Rural density	25	7.9
HBV status		
Negative	305	96.5
Positive	11	3.5
Vaccination against HBV		
Yes	2	0.6
No	242	76.6
I dont know	72	22.8
Age (n,mean,SD)	316, 28.7, 5.92	

Table 2: Bivariate Analysis for association with HBV infection

Variable	HBV negative		HBV positive		P-value
	n	%	n	%	
Age group					
Less than 24 years	86	28.2%	1	9.1%	0.34 ^f
25 - 34 years	167	54.8%	7	63.6%	
35 and above years	52	17.0%	3	27.3%	
Marital status					
Single	41	13.4%	1	9.1%	0.99 ^f
Married	264	86.6%	10	90.9%	
Parity					
0	80	26.2%	2	18.2%	0.68 ^f
1	79	25.9%	2	18.2%	
2	67	22.0%	2	18.2%	
3	43	14.1%	3	27.3%	
4+	36	11.8%	2	18.2%	
Education level					
None/Primary	91	29.8%	3	27.3%	0.68 ^f
Secondary	139	45.6%	4	36.4%	
Tertiary	75	24.6%	4	36.4%	
Employment					
Formal	55	18.0%	4	36.4%	0.33 ^f
Informal	44	14.4%	1	9.1%	
Not employed	206	67.5%	6	54.5%	
Residence					
High density	178	58.4%	3	27.3%	0.09 ^f
Medium density	73	23.9%	4	36.4%	
Low density	31	10.2%	2	18.2%	
Rural density	23	7.5%	2	18.2%	
HIV status					
Negative	152	49.8%	6	54.5%	0.99 ^f
Positive	153	50.2%	5	45.5%	
Age					
mean, SD	28.6, 5.93		31.5, 5.15		0.10 ^t

Table 3: Fisher's exact test for co-infection association with HBV/HIV

Variable	No Co-infection		Co-infection		P-value
	n	%	n	%	
Age Group					
Less than 24 years	43	28.1%	0	0.0%	0.35
25 - 34 years	77	50.3%	3	60.0%	
35 and above years	33	21.6%	2	40.0%	
Marital status					
Single	24	15.7%	0	0.0%	0.99
Married	129	84.3%	5	100.0%	
Parity					
0	32	20.9%	1	20.0%	0.27
1	42	27.5%	1	20.0%	
2	40	26.1%	0	0.0%	
3	19	12.4%	2	40.0%	
4+	20	13.1%	1	20.0%	
Education level					
None	7	4.6%	0	0.0%	0.45
Primary	46	30.1%	3	60.0%	
Secondary	76	49.7%	1	20.0%	
Tertiary	24	15.7%	1	20.0%	
Employment					
Formal	23	15.0%	1	20.0%	0.65
Informal	25	16.3%	1	20.0%	
Not employed	105	68.6%	3	60.0%	
Residence					
High Density	96	62.7%	1	20.0%	0.05
Medium Density	29	19.0%	3	60.0%	
Low Density	17	11.1%	0	0.0%	
Rural Density	11	7.2%	1	20.0%	
On cART					
Yes	144	94.1%	3	60.0%	0.04
No	9	5.9%	2	40.0%	
Duration on cART					
Less than 6 months	42	29.2%	1	33.3%	0.99
Between 6 and 12 months	21	14.6%	0	0.0%	
More than 12 months	81	56.3%	2	66.7%	
cART started before pregnancy					
Yes	104	72.2%	2	66.7%	0.99
No	40	27.8%	1	33.3%	

DISCUSSION

This study found that the overall prevalence of Hepatitis B virus among the pregnant women attending antenatal care at the University Teaching Hospital was 3.5%. There was no statistical difference in the prevalence of HBV in the HIV positive (3.2%) and HIV negative (3.8%) ($P=0.76$). In addition, there was also no significant association between HBV infection and socio-demographic factors. However, being on cART appeared to have a protective effect on acquisition of new HBV infection. Compared to women not on cART, women on cART had on average 91% reduced odds for HBV co-infection (OR = 0.09, 95% CI = 0.01 – 0.63, $P=0.02$).

The 3.5% prevalence of HBV among the pregnant women attending antenatal care at the UTH found in the study, puts it among the intermediate endemic regions where low is 0.1-2%, intermediate is 2-10% and high being 10-20% and the result is in agreement with other earlier studies done on HBV in Zambia which found 6.5% and 9.3%.^{7,17,18} Another study done in Lusaka, Zambia in the non-pregnant population also found an intermediate endemic prevalence of HBV infection in HIV infected children.¹⁵ In Zambia, most of the health facilities do not offer routine screening of HBV during antenatal care and hence the real burden is not known. Although this was a hospital based study, the intermediate endemic result which is similar to the earlier studies calls for the deliberate introduction in all health facilities of routine antenatal HBV screening regardless of HIV status. All antenatal care clinics should ensure that counselling of all pregnant women on hepatitis B is done concurrently as the HIV counselling is taking place to increase awareness. The Ministry of Health through Medical Stores Limited should also make sure that Hepatitis B vaccine and Immunoglobulin is made available to hospitals so that neonates from mothers who test positive for HBsAg and especially those that are also positive for HBeAg receive the birth dose vaccine within twelve hours of birth as is recommended by WHO. The result is also

consistent with findings of studies in Africa with similar settings.^{8,9,11,12}

Comparing the prevalence between the HIV positive and HIV negative, the study found HBV seropositivity was 3.2% and 3.80% respectively showing no statistical significance ($P=0.76$). The finding is in agreement with similar studies in the sub-Saharan region.^{17,19,20} The expectation would have been to see a higher prevalence among HIV positives since HIV and HBV share common modes of transmission and HBV is more transmissible than HIV.⁵ The finding may seem to contradict a systematic review and meta-analysis of sixty studies of Hepatitis B/C and HIV in sub-Saharan Africa which found that among HIV-infected individuals, the mean HBsAg prevalence rate were 15% and concluded that many HIV-positive individuals in sub-Saharan Africa are HBV co-infected and that HIV is associated with a higher prevalence of HBV in this region. However, other similar recent studies in Africa have shown a lower coinfection of HBV and HIV.^{9,12} The WHO, suggests that in counties where HBV prevalence is high (>5%), infection is usually acquired perinatally or during early childhood, and precedes HIV infection in most cases and the prevalence of chronic HBV infection in HIV positive persons is close to that observed in the general population.³ This therefore, calls for stronger concerted efforts to prevent perinatal transmission of hepatitis B by routinely screening all pregnant women and administration of birth dose vaccines to babies born to mothers who are seropositive to HBsAg.

This study also found no significant association between HBV infection and socio demographic factors (i.e. parity, marital status, education level, employment status, religion) similar to a study in Sudan which found that 5.6% of pregnant women were positive for HBsAg irrespective of their age, parity and socio-demographic characteristics.¹³ However, A study in Zambia found that HBsAg positivity ranged from 3.3% to 13.6% among the sites, with higher prevalence in the rural district hospitals than urban health centres in Lusaka. This

calls for rolling out of routine HBV screening countrywide regardless of the socio-demographic characteristics of the populations.

Being on cART was independently associated with HBV/HIV co-infection in this study. Women on cART had on average 91% reduced odds for HBV co-infection, (OR = 0.09, 95% CI = 0.01 – 0.63, P = 0.02) compared to women not on cART. This finding therefore suggests that being on cART may have a role in preventing new HBV infections in the HIV positive pregnant women since the ARVs that are used as first line cART in Zambia (Tenofovir, Lamivudine) have anti-HBV activity. However, this type of conclusion would require a cohort or randomized controlled trial study. The duration of being on cART did not seem to have any association. In the study, 67% of those coinfecting with HBV/HIV were on cART for more than 12 months and 33% for less than six months. It would have been interesting to follow up these patients with HBeAg measurements. The presence of a positive HBeAg test would indicate active HBV replication and high infectivity. ARVs are effective inhibitors of HBV replication and seldom result in cure, and therefore clearance of HBsAg is rare.³ Long term therapy is required to delay the progression of cirrhosis, reduce incidence of hepatocellular carcinoma and improve long term survival.³ Thus being on cART and not duration on cART appeared to be the important protective factor in terms of acquisition of new HBV infection.

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