



ORIGINAL RESEARCH ARTICLE

Epidemiological Markers for HIV Infection among First-Time Antenatal Attendees in Sierra Leone: 2012-2015 Longitudinal Study

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Abstract

Globally it is estimated that 10% of Human Immunodeficiency Virus (HIV) infected patients are coinfecting with Hepatitis B Virus (HBV) which is the leading cause of chronic liver diseases including liver cirrhosis and hepatocellular carcinoma. In countries with high HBV endemicity the seroprevalence rate can be as high as 25% with approximately 10% of the HIV infected population coinfecting with HBV. HIV and HBV shares similar transmission route and co-infection is common. It has been reported that a high HBV seroprevalence positively correlates with HIV prevalence in many regions including Africa. This is a cross sectional study that analyzed anonymized laboratory records of 1,500 antenatal care (ANC) attendees that used formal and non-formal (traditional birth centers) healthcare facilities for antenatal services in Sierra Leone from April 2012 to August 2015. Coded STI risk assessment and demographic questionnaires were submitted to the ANC attendees in order to determine the risk for STI infection amongst ANC attendees whose blood samples were used for analysis in this study. We recorded seroprevalence rates for HBV and HIV of 5.3% and 11.2% respectively. Holding other covariates in the model constant, the adjusted odd ratio (AOR) for a HSV-2 infected ANC attendees being infected with HIV was 2.14 times (95% CI = 1.1-4.3, $p = 0.02$) greater than non HSV-2 infected ANC attendees; and HSV-2 infected ANC attendees were 1.54 more likely to become infected with HBV than non HSV-2 infected ANC attendees (95% CI = 1.0-2.3, $p = 0.03$). Our study shows an increased risk for HIV infection among first-time antenatal attendees across wide spectrum of women in Sierra Leone society. Our finding shows that HBV/HIV and HSV/HIV co-infection rates might grow if appropriate and current preventive and controlling mechanisms are not upscaled.

Introduction

Globally it is estimated that 10% of Human Immunodeficiency Virus (HIV) infected patients are coinfecting with Hepatitis B Virus (HBV) which is the leading cause of chronic liver diseases such as liver cirrhosis and hepatocellular carcinoma [1,2]. Currently, an estimated 400 million people are infected worldwide with HBV [2] many of them in Asia and Africa where the virus is endemic [3]. Approximately between 500,000-1,000,000 persons die annually of HBV-related liver disease [4]. Areas of high HBV endemicity are Asia (except Japan and India), Middle East, South America, Pacific Island Groups, Africa, and special populations such as Native Alaskans, Australian Aborigines, and Maoris in New Zealand [5]. In countries with high HBV endemicity the seroprevalence rate can be as high as 25% with approximately 10% of the HIV infected population coinfecting with HBV [1]. According to the World Health Organization there are 536 million people aged 15-49 infected with herpes simplex virus type 2 (HSV-2) worldwide [6]. HSV-2 is now considered a major co-factor for the heterosexual transmission of HIV. In spite of recent successes in HIV research, HIV anti-viral therapy appears to be suffering from progressive threat because of increasing HIV coinfection with HBV and HSV-2.

HIV and HBV Co-infection

HIV and HBV shares same transmission routes and

co-infection is also common. It has been reported that a high burden of HBV seroprevalence rate positively correlates with HIV prevalence rate in many regions including Africa [7,8]. The risk for chronic HBV infection inversely varies with age and is higher for infants infected in the perinatal period [9,10]. Treating HIV coinfection with HBV is fraught with challenges. Most antiviral treatments of HIV infection do not adequately suppress HBV which is worrisome for the 10% of HBV/HIV coinfecting subjects in Africa considering the fact that HIV coinfection with HBV is often associated with progressive liver diseases [11]. The up-scaling of antiretroviral therapy (ART) leading to the increased longevity of HIV infected persons has now being associated with the resurfacing of chronic HBV infection [1].

HIV and HSV-2 Co-infection

HSV-2 seroprevalence rate data worldwide varies. The disease is one of the most common sexually transmitted diseases and most common cause of genital ulcer disease globally [12,13]. HSV-2 prevalence rate varies from < 15% in most European countries [12] to > 40% and higher in some resource-poor countries [14,15]. HSV-2 infection is an important driver in the dynamics of HIV infection. HSV-2 has been implicated for increasing both susceptibility to and transmission of HIV infection [16]. Given these epidemiological synergies between HIV and HBV, and HIV and HSV-2, raising public health awareness about these infections alongside the treatment of HBV and HSV for the purpose of reducing HIV transmission and decrease its progression may be of significant public health benefits [17].

Sierra Leone, HIV and HBV

Unlike most African countries Sierra Leone has a low national HIV prevalence. The national HIV seroprevalence rate for person of the age group 15-59 years is 1.5% [17]. One independent investigation has documented alarming seroprevalence rates for HBV infection for different population groups in Sierra Leone [18]. The use of ARVs for HBV treatment is on the increase in recent time. One survey in Sierra Leone observed that HBsAg patients with primary education recorded highest (27.05%) treatment failure (died) during HBsAg lamivudine monotherapy compared to HBsAg patients who were non-educated or had other educational levels [19]. Knowing one's HIV status is important in reducing the spread of STIs. In Sierra Leone however, in spite of scaling up HIV Testing and Counselling (HTC) capacity, majority of Sierra Leoneans don't know their HIV status. Seventy-eight percent of HIV infected adults in Sierra Leone are unaware of their HIV status [20]. There is paucity of integrated data on HBV/HIV and HIV/HBV coinfection epidemiology in Sierra Leone. Few studies have shown that Sierra Leone is showing signs of a nascent HBV epidemic [21]. There is a high seroprevalence rate of hepatitis B among HIV/AIDS patients nowadays especially in developing countries with negative conse-

quences for treatment outcome [22]. However, unlike many countries HIV infected patients on ARVs in Sierra Leone are rarely screened for HBV.

Methods

This is a cross sectional study that analyzed anonymized laboratory records of 1,500 first time antenatal care (ANC) attendees that used formal and non-formal healthcare facilities (traditional birth centers) services in Sierra Leone from April 2012 to August 2015. Both formal and non-formal ANC healthcare facilities provided data for this study. Data for this study were obtained from laboratory results done on blood specimen collected routinely from ANC attendees attending these antenatal healthcare facilities. The collected blood specimen were anonymously tagged and hence could not be traced to their source. The collected blood samples were used for haematological, serological and serum tests. Haematology tests conducted on blood samples includes blood cells count and blood typing. Serological tests were done for syphilis diagnosis. Serum samples were used for HIV, HBV and HSV-2 diagnosis. Coded STI risk assessment and demographic questionnaires were submitted to the ANC attendees in order to determine the risk for STI infection amongst ANC attendees whose blood samples were used for analysis in this study. Data from the STI risk assessment and demographic questionnaires were subsequently used for both explorative and descriptive statistical analysis.

Ethic and privacy

The Njala University Institutional Review Board in Sierra Leone approved this study; provided ethical clearance and waived the requirement for informed consent on the grounds that the study involves minimal health risk on the participants and is a retrospective study.

HIV assay and diagnosis

HIV assay test was done on all blood samples using the HIV and other STI screening tests guideline and recommendations of the WHO/UNAIDS. Given that this was a preliminary screen stage testing and that the expected prevalence of HIV was less than 10%, Strategy II of the WHO recommendation was utilised [23]. Each blood sample was initially tested with an ELISA assay [24] and all reactive blood samples were considered positive. Discordant blood samples were retested with a rapid assay kit [25]. All HIV positive tests for both ELISA and the rapid kit were tested with a second ELISA assay (Equipar EIA, Sarrano, Spain) as confirmatory test. The analytical sensitivity and specificity for the ELISA assay and rapid kit are 95% and 99%; 95% and 99% respectively.

HBV assay and diagnosis

HBV was tested for by the presence of the viral surface antigen (HBsAg) in blood/serum using parallel testing with latex slide agglutination and immunochro-

matic strips [26]. A seropositive latex slide agglutination and immunochromatographic strips HBV test result is indicated by the appearance of an agglutination reaction and coloured line respectively. Discordant samples are re-tested first to eliminate technician error and re-tested with a third assay - HBsAg Haemagglutination assay [27], which use sensitized chicken erythrocytes. The analytical sensitivity and specificity for the HBsAg Haemagglutination assay is 95% and 99% respectively.

HSV2 assay and diagnosis

HSV2 was assayed using an ELISA kit (Worldwide Diagnostics, USA). This utilised antigen coated wells to capture antibodies present in the sample. A positive sample would bind with the antigen to form a complex that reacted with a substrate in a colour change enzymatic reaction. The colour was read spectrophotometrically and the value of the optical density calculated. Values below the cut off were reported negative and those above were said to be positive. The analytical sensitivity and specificity for the HBsAg Haemagglutination assay is 96% and 99% respectively.

Results

Descriptive characteristics of subjects

We analyzed 1,500 anonymized laboratory results of first time ANC attendees that used formal and non-formal healthcare facilities (traditional birth centers) for antenatal services in Sierra Leone between April 2012 to August 2015. Majority (73.4%) of the ANC attendees were HSV-2 seropositive. The seroprevalence rates for HIV and HBV were 5.3% and 11.2% respectively.

Majority of the HBsAg positive ANC attendees belong to the age bracket 20-24 years (27.9%), had secondary school education (39.0%), were in cohabiting relationship (44.3%), in a monogamous relationship (71.5%) had 2-5 pregnancies (58.9%) (Table 1).

Multivariate analysis of STI risk of infection

AIC-backward stepwise logistic multivariate regression analysis was done to determine the risk of being infected with one STI as a result of being infected with another. Adjusting for other covariates in the model there was a strong association between being infected with HSV-2 or HSV and becoming infected with HIV; as well as being infected with HSV-2 and becoming infected with HBV (Table 2). Holding other covariates in the model constant, the adjusted odd ratio (AOR) for a HSV-2 infected ANC attendees being infected with HIV was 2.14 times (95% CI = 1.1-4.3, $p = 0.02$) greater than non HSV-2 infected ANC attendees. Also, adjusting for other covariates in the model, HBV infected ANC attendees were 2.81 more likely to become infected with HIV than non HBV infected ANC attendees (95% CI = 1.6-4.9, $p = 0.001$). Additionally, HSV-2 infected ANC attendees were 1.54 times more likely to become infected with HBV than non HSV-2 infected ANC attendees (95% CI = 1.0-2.3, $p = 0.03$) holding other covariates in the model constant.

Table 1: Demographic characteristics of ANC attendees and their HB seroprevalence.

Characteristics	HBV Seroprevalence n (%)
Age group	
13-19	38 (24.1)
20-24	44 (27.9)
25-29	40 (25.3)
30-34	23 (14.6)
35-48	13 (8.2)
Educational status	
None	65 (41.1)
Primary	26 (16.5)
Secondary	62 (39.2)
Post-secondary	5 (3.2)
Marital status	
Married	65 (41.1)
Relationship/cohabiting	70 (44.3)
Single	22 (14.6)
Type of union relationship	
Monogamous	113 (71.5)
Polygynous	33 (20.9)
Unknown pattern	14 (7.6)
Parity	
Primigravid	59 (37.3)
2-5 Pregnancies	93 (58.9)
6-12 Pregnancies	9 (3.8)

Table 2: Multivariate analysis of STIs associated with diagnosed HIV, HSV-2 and HBV among antenatal care users.

Risk factors	Correlates	AOR	95% CI	P value
HSV-2 ⁺	HIV	2.14	1.1-4.3	0.02
HBV ⁺	HIV	2.81	1.6-4.9	0.001
HIV ⁺	HBV	2.91	1.7-5.3	0.06
HSV-2 ⁺	HBV	1.54	1.0-2.3	0.03

There was no statistically significant difference in becoming infected with HBV as a result of being infected with HIV. ANC attendees who are infected with HIV were 2.91 times more likely to be infected with HBV than ANC attendees without HIV (95% CI = 1.7-5.3, $p = 0.06$).

Multivariate analysis of reproductive characteristics and HBV

There were differences in risk for acquiring HBV as a result of the number of pregnancies an ANC attendee had (Table 3). Holding other covariates in the model constant, an ANC attendee who had 2-5 pregnancy was 0.7 times more likely to be infected with HBV than ANC attendees without 2-5 pregnancy (95% CI = 0.5-1.1, $p = 0.01$); ANC attendee who had > 6 pregnancy was 0.33 times more likely to be infected with HBV than ANC attendees who don't have > 6 pregnancy (95% CI = 0.2-0.7, $p = 0.01$).

Socio-demographic factors and HBV infection risk

There was no statistically significant difference in HBV infection due to whether attendee had previously experience the death of a child within the past five

Table 3: Multivariate analysis of reproductive characteristics of antenatal care users and HBV seropositive antenatal care users.

Risk factors	Correlates	AOR	95% CI	P value
Primigravid	HBV	1.00	-----	-----
2-5 pregnancy	HBV	0.70	0.5-1.1	0.01
≥ 6 pregnancy	HBV	0.33	0.2-0.7	0.01
Single partner	HBV	1.00	-----	-----
Multiple partner	HBV	0.37	0.2-0.7	0.01
Not applicable	HBV	0.75	0.3-2.1	0.01

Table 4: Association between socio-demographic factors and diagnosed HBV antenatal care users.

Risk factors	HBV seroprevalence n (%)	AOR	95% CI	P value
Occupation				
Business	94 (11.5)	1.0	-----	-----
Salary worker	8 (9.9)	0.8	0.4-1.8	0.9
None	58 (10.9)	0.9	0.7-1.3	0.8
Partner occupation				
Salary	26 (7.8)	1.0	-----	-----
Business	77 (10.9)	1.1	0.7-1.8	0.2
Forces	14 (8.8)	0.9	0.5-1.8	0.1
Distant driver	21 (17.5)	1.9	1.1-3.6	0.2
Infant mortality in ≤ 5yrs				
No	126 (11.4)	-----	-----	-----
Yes	34 (10.3)	0.9	0.6-1.3	0.6
Spouse death				
No	150 (11.1)	-----	-----	-----
Yes	9 (16.1)	1.5	0.7-3.2	0.3
Dependents				
No	80 (11.6)	-----	-----	-----
Yes	64 (9.8)	0.8	0.6-1.2	0.5
Not applicable	7 (13.5)	1.2	0.5-2.7	0.5

years, or death of a spouse, or had dependents living with her (Table 4). Adjusting for other covariates in the model, the risk for being infected with HBV is 0.9 times higher for ANC attendees who received monthly salary than ANC attendees who didn't (95% CI = 0.4-1.8, $p = 0.9$). Also, adjusting for other covariates in the model, ANC attendees whose partners are distance drivers are at higher risk (AOR = 1.9) of being infected with HBV compared to ANC attendees whose partners are not distance drivers (95% CI = 1.1-3.6, $p = 0.2$); while the risk for HBV infection among ANC attendees who had previously experience the death of a child is 0.9 times higher than ANC attendees who had not experienced the death of a child within the past five years (95% CI = 0.6-1.3, $p = 0.6$); ANC attendee whose spouse have died are 1.5 times more likely to have HBV compared to ANC attendees whose spouse are still alive (95% CI = 0.7-1.2, $p = 0.5$). Adjusting for other covariates in the model, ANC attendees with dependents are 0.8 times more likely to have HBV compared to ANC attendees without dependents (95% CI = 0.6-1.2, $p = 0.5$).

Discussion

To the best of our knowledge, this is the first study to investigate trends of HIV, HBV, and HSV seroprevalence rates and coinfections among first-time antenatal attendees in Sierra Leone. We discovered a 10.5% HBV seroprevalence rate among first-time antenatal attendees who used both traditional and non traditional clin-

ics between April 2012 to August 2015 in Sierra Leone. None of the HBV seropositive study participants had detectable HBsAg antibodies thus indicating a chronic HBV status. Our findings shows marked decrease in HBV seroprevalence rate among women of child-bearing age compared to result of a similar study done in 2014. A 47.5% HBsAg seroprevalence rate in Sierra Leone has been reported previously [20]. This decrease in the HBV seroprevalence rate among first-time antenatal attendees over time in our study is explainable by the upsurge in routine STI screening for women in the child bearing age bracket as well as increase in public health campaigns against HIV and other STIs that shared similar mode of transmission. Additionally, the drop in HBV seroprevalence rate in our study could be attributed to the fact that following the emergence of HIV infection in Sierra Leone in the late nineties the government implemented a policy for thorough blood screening prior to transfusion throughout the country thus leading to the reduction of STIs among high risk population. Also, the upscale use of ARVs especially the therapeutic cocktails that includes lamivudine to treat HBV and other viral infections in Sierra Leone could also have contributed to the reduction of HBV seroprevalence rate in our study. One study on lamivudine monotherapy to treat HBV in Sierra Leone showed encouraging result if started within the first year of reported HBV infection [18]. Lamivudine has also been documented to be effective in treating chronic HIV and HBV infections as well as for

the prevention of perinatal transmission of these infections [28,29].

We recorded a wide range of risk which can serve as epidemiological markers for HIV infection due to infection with HBV or HSV. We found high risk for HIV infection amongst HBV (AOR = 2.81, (95% CI = 1.6-4.9, $p = 0.001$) and HSV (AOR = 1.54, 95% CI = 1.0-2.3, $p = 0.03$) infecteds. Our finding is similar to those of previous studies on different risk groups and geographic areas with high STI endemicity [8,12,30,31]. In regions with high-HBV endemicity including Asia and Africa, the risk for HIV as a result of HBV or HSV infections reflects the background seroprevalence of HBV or HSV in the general population [30,31]. The risk for HIV infection amongst HBV and HSV infecteds is high because they share the same route of infection; and HBV and HSV increases the transmissibility of HIV [16]. Findings from our study show that it is prudent to prevent HBV and HSV acquisition in the general population in order to reduce HBV/HIV liver-related mortality in Sierra Leone. Expanding on ongoing national expanded immunization programs to cover both adults and infants could help reduce this risk and bring down the seroprevalence rate of HBV/HIV and HSV/HIV coinfections in Sierra Leone. Sierra Leone like many other developing countries experience limited access to HBV vaccination although this is improving gradually. HBV vaccination is now available in 171 countries and approximately 60-65% of the world population have access to it compared to 3% in 1992 [31]. The risk for HBV infection as a result of being infected with HIV compared to non HIV infected ANC attendees was not statistically significant although it was high (AOR = 2.91, 95% CI = 1.7-5.3, $p = 0.06$). One limitation to this study is that we are unable to comment on the trend of HSV or HIV infections among antenatal attendees since no literature on such trend exist.

Conclusion

This study shows that there is still an increased risk for HIV infection among first-time antenatal attendees across wide spectrum of women in Sierra Leone society in spite of the decreased in HBV seroprevalence rate. The finding from this study shows that HBV/HIV and HSV/HIV co-infection rates might grow if appropriate and current preventive and controlling mechanisms are not up-scaled. Additionally, further epidemiological investigations are needed to ascertain those behaviors that put antenatal attendees at elevated risk for STIs.

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