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High seroprevalence and associated risk factors for hepatitis B virus infection among pregnant women living with HIV in Mtwara region, Tanzania

Vulstan James Shedura^{1*} , Geoffrey Joseph Mchau² and Doreen Kamori¹

Abstract

Background Hepatitis B virus (HBV) infection continues to be a global public health problem. As of 2019, there were 296 million people chronically infected with HBV, resulting in nearly 1 million deaths from decompensated cirrhosis or hepatocellular carcinoma. The seroprevalence of HBV infection among pregnant women in Tanzania was reported to range between 3.8 and 8.03%. However, data on HBV infection in HIV-infected pregnant women is limited. We aimed to determine the seroprevalence and associated risk factors for HBV infection among HIV-infected pregnant women in selected health facilities in the Mtwara region. This was a health facility-based quantitative cross-sectional study conducted for three months (from February to April 2022). A structured questionnaire was used to collect information from the study participants. A total of 4 ml of blood was collected for HBV screening and confirmatory tests using rapid diagnostic tests and automated Enzyme-Linked Immunosorbent Assay (ELISA) tests, respectively. The logistic regression model was used to identify significant variables for HBV infection.

Results Two hundred and twenty ($n = 220$) pregnant women living with HIV were enrolled in this study, with a median age of 32.7 years (Interquartile range (IQR) 27.6–37.6). The seroprevalence of HBV, chronic, and acute HBV infections were 10.5%, 10.0%, and 0.5%, respectively. We found that the multiparous women [aOR 11.99: 95% CI 1.11–129.01, $p = 0.040$], being infected with syphilis [aOR 27.65: 95% CI 9.07–84.30, $p < 0.001$], and having HIV viral load of 1000 copies/ml and above [aOR 16.00: 95% CI 1.70–150.63, $p = 0.015$], are factors independently associated with HBV infection.

Conclusions The overall seroprevalence of HBV infection among pregnant women was 10.5%, which is high endemicity. Furthermore, the study revealed that having more than four children, a high HIV-1 viral load of ≥ 1000 cp/ml, and being infected with syphilis are significant risk factors associated with HBV infection among pregnant women living with HIV in the Mtwara region.

Keywords Seroprevalence, Hepatitis B virus infection, HIV infection, Pregnant women, Mtwara region, Tanzania

*Correspondence:

Vulstan James Shedura
vulstanshedura@gmail.com

¹ Department of Epidemiology and Biostatistics, School of Public Health and Social Sciences (SPHSS), Muhimbili University of Health and Allied Sciences, P.O. BOX 65001, 9 United Nations Road, Upanga West, 11103 Dar es Salaam, Tanzania

² Tanzania Food and Nutrition Centre (TFNC), Dar es Salaam, Tanzania

Background

Hepatitis B virus (HBV) infection is an infection of the liver that accounts for up to 80% of all cases of hepatocellular carcinoma worldwide, second after tobacco among the known human carcinogens (Kamal 2021; Petruzzillo 2018). As of 2019, there were 354 million people worldwide infected with hepatitis B or C, of which 296

million were chronically infected, and 1.5 million people were newly infected every year, which resulted in about 820,000 deaths (World Health Organization 2021a, b).

The WHO Global Health Sector Strategy for Viral hepatitis, launched in May 2016, aims to achieve a 90% reduction in new cases of chronic hepatitis B and C and to reduce mortality from hepatitis B and C by 2030. HBV infection is common in sub-Saharan Africa, and despite the introduction of the universal HBV vaccine and effective antiviral treatment, the overall seroprevalence of HBV infection remains high at 6.1% (95% Confidence Interval (CI) 4.6–8.5). Thus, integrated interventions are needed to achieve these goals (Spearman et al. 2017; World Health Organization 2016).

The studies conducted in different parts of Africa have shown that the seroprevalence of HBV infection ranges from 0.8 to 11.8%. For instance, the study conducted in Cameroon and Sudan showed a seroprevalence of 4.98% and 8.5%, respectively, among pregnant women (Mudardum and Mohammed 2019; Nlinwe and Lungle 2021). Other parts of Africa include; Ghana [10.6%], Northwest Ethiopia [8.3%], South Africa [0.8%], Hawassa [7.8%], Eritrea, Asmara [3.2%], Ethiopia, Gambela [7.9%], Halal City [6.3%], all of which show a moderate endemicity (Demeke et al. 2021; Diale et al. 2016; Fessehayee and Kenyatta 2018; Luuse et al. 2016; Metaferia et al. 2016; Ngalula et al. 2018; Tanga et al. 2019; Tiruye et al. 2018). In Tanzania, the seroprevalence of HBV infection in pregnant women was reported to vary between 3.8 and 8.03% (Geffert et al. 2020; Mirambo et al. 2016), whereas that of the general population varies between 5.5 and 20.0% (Froeschl et al. 2021; Tanzania Ministry of Health Community Development Gender Elderly and Children (MOHCDGEC) 2018).

HBV transmission most commonly occurs from mother to child at birth or from person to person during infancy in high-incidence areas. Although perinatal transmission accounts for more than one-third of chronic infections in low-endemic areas, sexual transmission and the use of contaminated needles are the main routes of infection in these settings, especially among injecting drug users (World Health Organization 2021b). Without precautions, vertical transmission of HBV is more likely to occur, especially among pregnant women who are positive for the hepatitis e antigen (HBeAg). In addition, maternal viremia is a determinant of vertical transmission of HBV (Veronese et al. 2021). The impact of pregnancy on the clinical course of HBV infection has been reported to be associated with an increased risk of intrahepatic cholestasis of pregnancy (ICP), gestational diabetes, and threatened preterm labor (Xiong et al. 2021). Furthermore, in previous studies, an increase in alanine aminotransferase (ALT) and HBV viral load were

observed during postpartum and in the late pregnancy period (Belopolskaya et al. 2021; Huang et al. 2021a, b).

Some risk factors have also been associated with the transmission of HBV infection in previous studies, for instance, history of surgical procedures, sexual behavior, tattoos, blood transfusion, tooth extraction, and jaundice (Alemu et al. 2020; Gedefaw et al. 2019). Hepatitis B virus and co-infection with other sexually transmitted infections (STIs) in pregnant women could occur since the modes of transmission are shared. A study done in Tanzania among pregnant women showed a significantly high HBV infection rate among HIV-infected women, which was also associated with a low CD4 count (Man-yahi et al. 2017).

Among the estimated 37 million people infected with HIV globally, 5–20% of them are also co-infected with HBV, with a significant impact on the natural history of chronic HBV infection compared to HBV mono-infection (Singh et al. 2017). Despite efforts to reduce HBV prevalence globally, the burden is still high. The risks of acquiring the infection include perinatal transmission from a pregnant woman. HIV-positive mothers co-infected with HBV are more likely to give birth to HBV-positive infants, who are more likely to fail to mount protective immunity following hepatitis B vaccination (Bhattacharya et al. 2021; National Institutes of Health (NIH) 2020). Among children who will become HBV carriers, 10% acquire their status perinatally, and only 52.5% would be protected by vaccination (Mahmud et al. 2021). In addition, individuals, including pregnant women who are co-infected with HIV, have higher levels of hepatitis B viremia; and progression to chronic hepatitis B infection is about five times that of mono-HBV infection. Furthermore, they have a higher risk of developing liver cirrhosis and hepatocellular carcinoma (Kim et al. 2021; Singh et al. 2017; Weldemhret 2021). Several studies have reported the HBV infection burden among blood donors and the general population (Kilonzo et al. 2021; Mremi et al. 2021). However, there is a scarcity of data in Tanzania on the burden of HBV infection among pregnant women, especially those living with HIV (Tanzania Ministry of Health Community Development Gender Elderly and Children (MOHCDGEC) 2018). Therefore, we aimed to determine the seroprevalence and associated risk factors for HBV infection among HIV-infected pregnant women attending Prevention of mother-to-child transmission (PMTCT) clinics in the Mtwara region. Study findings are essential baseline information to guide the need for scaling up screening and vaccination programs, including instituting HBV vaccine birth dose (rather than the current schedule of HBV vaccine in Tanzania that involves an initial dose at six weeks of life, followed by two consecutive doses at the interval of four months) in

neonates born from infected mothers, to prevent perinatal transmission.

Methods

Study design

This was a health facility-based quantitative cross-sectional study conducted between February 2022 and April 2022 among pregnant women living with HIV who were attending PMTCT clinics in selected health facilities in the Mtwara region, Tanzania.

Study site

Mtwara is one of the 31 regions of Tanzania located in the southern part of Tanzania, with a population of 1,270,854 according to the 2012 census and a size of 16,710 km² (National Bureau of Statistics Ministry of Finance 2013). Having the boundary with Mozambique to the south, to the west, Mtwara is bordered by the Ruvuma region, to the north by the Lindi region, and to the east is the Indian Ocean. The economy of the Mtwara region depends on commerce, fishing, small-scale cultivation, and tourism. Two hundred twenty-one health facilities provide PMTCT services in the Mtwara region. In this study, Likombe health center, Ndanda hospital, Mangaka hospital, and Mkomaindo hospital were selected purposefully because they provide PMTCT services to many clients compared to the other facilities in the Mtwara region. The facilities receive an average of 70 clients per month, which is a higher number compared with other regional PMTCT health facilities in the region.

Study population

The study population comprised pregnant women (≥ 18 years old) living with HIV attending PMTCT

clinics at Mkomaindo hospital, Ndanda hospital, Mangaka hospital, and Likombe health center in the Mtwara region from February 2022 to April 2022.

Inclusion criteria

All pregnant women (≥ 18 years old) of any gestation age (first, second or third trimester) living with HIV and on ART attending PMTCT clinics in selected study sites and who provided consent to participate in the study.

Exclusion criteria

Those with a prior history and records of hepatitis B vaccination were excluded from the study.

Sample size estimation and sampling method

Sample size estimation

We calculated the sample size using the Kish and Leslie formula based on the data from a prevalence study conducted in Mbeya, Tanzania, with an HBV prevalence of 5.0% (Froeschl et al. 2021). We used a two-sided 95% confidence interval, a marginal error of 3%, and by considering a 10% non-response rate. The resulting sample size was 220.

The sample size distribution per PMTCT facility

Figure 1 shows a scheme showing pregnant women living with HIV and on ART during the study period. In brief, a total of 450 pregnant women living with HIV were enrolled in four PMTCT clinics in the Mtwara region, of whom 400 were aged more than 18 years. Of the 400 women, all were enrolled in ART. Of whom 174 had previous records of hepatitis B vaccination, one refused to participate in the study, and five participants, their samples were inadequate for laboratory testing.

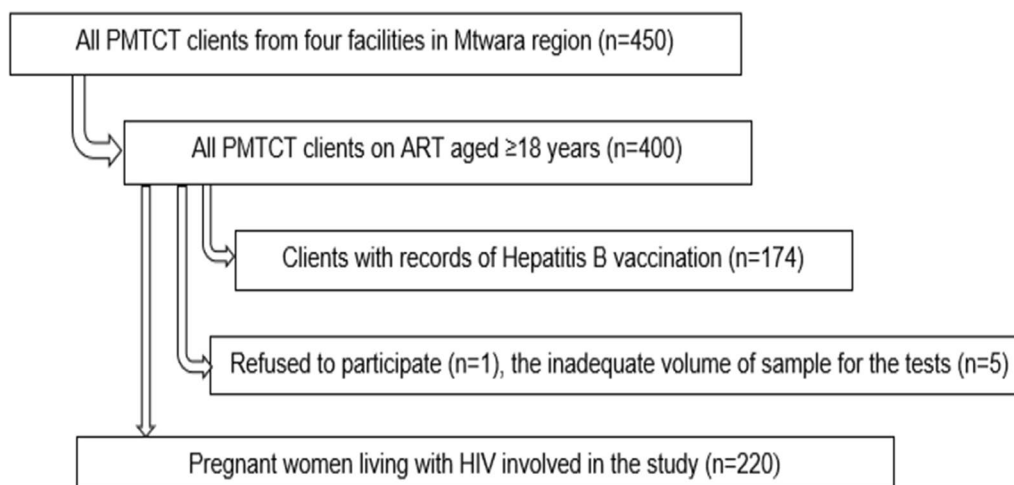


Fig. 1 A scheme showing the data of HIV-infected pregnant women attending PMTCT clinics in the Mtwara region

All the remaining (220) pregnant women were included in the present study (Fig. 1). Probability Proportional to size (PPS) was used to calculate the sample size for each health facility by the following formula;

$$N_i = \frac{N_h \times 220}{N_t}$$

N_i =number of study participants (sampled in each health facility), N_h =number of pregnant women LWHIV at a selected health facility, N_t =total number of pregnant women LWHIV from the selected health facilities in the Mtwara region.

Their distribution per facility was as follows: Likombe health center ($n = 39$, 17.7%), Mangaka hospital ($n = 36$, 16.4%), Mkomaindo hospital ($n = 75$, 34.1%), and Ndanda hospital ($n = 70$, 31.8%).

Sampling method

We used a systematic random method to attain study participants based on their attendance at the PMTCT clinic for their scheduled antenatal clinic follow-up. Once the number of women LWHIV sampled in each facility was obtained, the list of pregnant women (aged ≥ 18 years) attending the PMTCT clinic was asked, and a unique identification number based on the registration was assigned. The sampling fraction was determined by dividing the total number of pregnant women attending the PMTCT clinic within the study period from each selected health facility by the sample size in each health facility, allocating randomly from 1 to the obtained factor (k th interval = $N_h/N_i = 2$) to determine the starting unit and arrange the study participants based on their order of coming to the clinic for each health facility. Each study participant was selected at every defined interval (obtained factor = 2) using systematic random sampling. If an attendant declined to participate, the next attendant in a defined interval after her was selected.

Data collection tools and procedures

A structured questionnaire was used to solicit socio-demographic characteristics, clinical information (sexual history, gestation age, obstetrics history (gravity, parity, abortion), history of sexually transmitted infections (STIs), surgical history, and socio-cultural information (history of tattooing)) from the study participants. Clinical parameters such as recent HIV viral load, WHO clinical staging of HIV, ART regimen, and recent CD4 count results were obtained from the study participants' care and treatment cards (CTC2) and the CTC2 database.

Variables

Dependent variable

The dependent variable was HBV seropositivity. A binary outcome was categorized as HBV seropositive status or HBV seronegative status.

Independent variables

The independent variables were as follows: socio-demographic characteristics such as age (categories; 18–39, ≥ 40), marital status (categories; married, single, divorced or cohabiting), occupation status (categories; self-employed or unemployed), place of residence (categories; rural or urban), education status (categories; non-formal, primary, secondary, college or university), facility name (categories; Likombe health center, Mangaka hospital, Mkomaindo hospital or Ndanda hospital) and income per day in Tanzanian shillings (categories; < 2400 , 2400–12,000, or $> 12,000$). Clinical information and parameters included the variables such as the history of blood transfusion (categories; yes or no), WHO clinical staging of HIV disease (categorized into; stage-1, stage-2, stage-3 or stage-4), recent CD4 count in cells/mm³ (categories; < 200 , 200–499 or ≥ 500), recent HIV viral load (HVL) status in copies/ml (categories; < 50 , 50–999 or ≥ 1000) and syphilis status (categories; positive or negative). Other variables from the clinical information of the study participants included; the number of sexual partners (categories; one, two, or more than two), history of sexually transmitted infections (categories; yes or no), number of live children (categories; one, two to three, four or more), history of dental procedure (categories; yes or no), history of body tattooed (categories; yes or no), history of abortion (categories; yes or no), gestation period (categories; first trimester, second trimester or third trimester), ART regimen (categories; first line or second line), duration on ART in months (categories; < 6 , 6–12 or > 12) and surgical history (categorized in to yes or no).

Laboratory methods

A total of 4mls of a blood sample from each participant was collected into a plain vacutainer tube (red-top tubes), labeled with a unique participant identification number, and then sent to the laboratory at the selected study site (hospital). In the laboratory, the sample was processed into serum by centrifugation at 3000 revolutions/minute for 10 min using a centrifuge machine (Thermo Scientific™ 75,004,503 Megafuge 40 Centrifuge, Cole-Parmer Pvt. Ltd. India). The processed serum was transferred into two cryogenic tubes and stored temporarily at -80 °C until an adequate number of samples was obtained for testing. Screening for Hepatitis B surface antigen (HBsAg) was done at the laboratory of each

selected health facility using HBsAg rapid test (HBsAg Meril Diagnostics Pvt. Ltd. India). The screening provided qualitative results that indicated whether the participant was negative or positive for hepatitis B virus infection. HBV infection was confirmed by Enzyme-linked immunosorbent assay (ELISA). In addition, for the participants who did not have syphilis test results, a non-treponemal test (Bioline syphilis 3.0 test; Standard diagnostics Inc. (SD). Korea) was done at the laboratory of each health facility selected. The rapid HBsAg and syphilis tests are lateral flow chromatographic immunoassays that qualitatively detect antigens or antibodies in human serum or plasma. The tests were done according to the manufacturer's instructions; briefly, about 0.5 ml of serum was taken with a plastic pipette, one drop was dropped on the test cassette, and the result was read after 15 min. If the test cassette shows both control (C) and test (T) bands, it is considered positive; if only the C band develops, it is negative; if no C band appears, it is considered invalid. All screening tests were done using a rapid diagnostic test (with relative sensitivity and specificity ranging 98.5–99.0% and a lower detection limit of 2 ng/ml = 1.66 IU/ml) according to the laboratory standard operating procedure (SOP) of each laboratory and manufacturer's instructions. All the HBV-positive samples were confirmed using an automated ELISA (Abbot ARCHITECT PLUS[®] i2000SR immunoassay analyzer, USA) at National blood transfusion services (NBTS)-Southern zone laboratory (SADCAS accredited) and Ligula regional referral hospital laboratory (KENAS accredited) in Mtwara region. HBV serological parameters included; HBsAg, Hepatitis B core antibody of immunoglobulin M type (HBcAb-IgM), total anti-HBc (HBcAb-IgG&IgM), and Hepatitis B envelope antigen (HBeAg). Abbot ARCHITECT PLUS[®] i2000SR immunoassay analyzer has a sensitivity of $\geq 99.5\%$, a specificity of 100%, and a lower detection limit of 0.05 IU/ml by using laboratory standard operating procedures (SOP). Samples that were positive for syphilis were also confirmed by using an automated ELISA test (Abbot ARCHITECT PLUS[®] i2000SR immunoassay analyzer, USA). For the participants who were confirmed to have HBV infection, ALT testing was performed at Ligula regional referral hospital laboratory (LRRHL) using an Abbot ARCHITECT[®] ci4100[™] chemistry analyzer.

Data quality assurance

The data collection tools were validated by conducting a pilot (pre-testing) before actual data was collected from the study participants to ensure that they could give desired results. All testing procedures, including calibration and quality control, were performed, whereby the Abbot ARCHITECT PLUS[®] i2000SR immunoassay

analyzer, USA. Positive Control 1, 2, and Negative Control were run to verify the calibration. Furthermore, a single sample of each control was tested once every 24 h on each day of use as per the manufacturer's recommendations. The assay Control values were reviewed and ensured that are within the concentration ranges specified in the Control package insert before testing samples from the study participants. All results were recorded carefully before data entry, and the data were double-checked by different personnel before analysis.

Data processing and analysis

Data cleaning and analysis were performed using the Microsoft (MS) excel[®] version 2019 and STATA version 15 package (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: Stata-Corp L.L.C.). Frequency and proportion for categorical variables were calculated, whereas continuous variables were summarized using the median (interquartile range) as a measure of central tendency. Bivariate and multivariate logistic regression models were used to predict the relationships between dependent and independent variables. Bivariate analysis was conducted primarily to check the association of each independent variable with the dependent variable. Variables with p values less than 0.20 in the bivariate analysis were included in the multivariable analysis, whereas variables with a p value ≤ 0.05 were measured as statistically significant risk factors for HBV infection, with a 95% CI. We excluded the missing records of CD4 counts and HVL in the analysis.

Results

Socio-demographic characteristics of the study participants

Between February 2022 and April 2022, a total of 220 pregnant women living with HIV in the Mtwara region were enrolled. The study participants' median age was 32.7 years (IQR 27.6–37.6). The majority, 34.1% (75/220) and 71.4% (157/220) of the participants were from Mko-maindo hospital and attained only a primary school level of education, respectively. 47.7% (105/220) were unemployed, 51.8% (114/220) were living in urban areas, and 45.5% (100/220) were married.

The seroprevalence of hepatitis B virus infection among the study participants

The seroprevalence of hepatitis B virus infection (HBsAg-positive) among pregnant women living with HIV attending PMTCT clinics in the Mtwara region was 10.5% (23/220). Twenty-two out of 220 (10%) participants tested positive for HBsAg, total anti-HBc (HBcAb-IgG & IgM), and negative for HBcAb-IgM, suggesting HBV chronic infection. Furthermore, 0.5% of the participants tested

positive for HBeAg, HBcAb-IgM, and HBsAg-HBeAg serological markers, suggesting acute HBV infection.

Clinical and behavioural characteristics of the study participants

The majority (40.5%) of the study participants were in the second trimester of their pregnancy, 77.7% were multigravida, 58.6% had live children ranging from two to three, and 85% had no history of abortion. Most participants (80.0%) had no prior history of body tattoos, and 81.8% had no history of surgical procedures. In addition, most participants had no history of blood transfusion (80.9%) and jaundice (95.0%). Furthermore, 61.8% of the study participants had only one sexual partner; and only 6.8% reported a history of sexually transmitted infections.

Clinical and immunological parameters of the study participants

Most participants were in WHO clinical stage one of HIV (86.4%). Ninety percent (90%) of the participants had HIV-1 viral load of less than 50 copies/ml (with a median of 40 copies/ml (IQR (20–70)) and CD4 counts median of 384 cells/mm³ (IQR (220–593)). All study participants were on ART, and the majority, 88.2% (194/220), were on the first-line ART regimen for more than 12 months. In this study, most of the participants with HBV infection (positive HBsAg) had normal ALT levels (91.3% (21/23)). Forty-five (0.20%) participants were missing their CD4 counts and HIV-1 viral load records; among these, 0.07% (3/45) were positive for HBV infection. In addition, five participants (5/220) had their HIV-1 viral load records missing, and one (1/5) was positive for HBV.

Risk factors associated with hepatitis B virus infection

Among the variables assessed in this study were the socio-demographic characteristics of the study participants, whereby bivariate and multivariate logistic regression was conducted. The results of the multivariate logistic regression showed that none of the socio-demographic factors was significantly associated with HBV infection (Table 1). Having four children and above was significantly associated with HBV infection, whereby pregnant women LWHIV and who had four children and above were 11 times more likely to acquire HBV infection than those who had only one child [aOR 11.99: 95% CI 1.11–129.01, $p=0.040$]. However, other variables such as; having a history of surgical procedure, dental procedure, blood transfusion, body tattooing, number of sexual partners, and history of STIs were not significantly associated with HBV infection among the pregnant women population LWHIV in Mtwara region (Table 1).

This study revealed that having a high HIV viral load (1000 copies/ml and above) is significantly associated

with HBV infection among pregnant women LWHIV. Hereby, pregnant women LWHIV who had an HIV viral load of 1000 copies/ml and above were 16 times more likely to have HBV infection than those with an HIV viral load of less than 50 copies/ml [aOR 16.00: 95% CI 1.70–150.63, $p=0.015$]. Furthermore, the findings show that being infected with syphilis is significantly associated with HBV infection among the pregnant women LWHIV in the Mtwara region, whereby those infected with syphilis were 27 times more likely to acquire HBV infection than those who had no syphilis [aOR 27.65: 95% CI 9.07–84.30, $p<0.001$]. In this study, other factors, including CD4 level, WHO clinical staging of HIV, ART regimen, and ART duration, were not significantly associated with HBV infection among pregnant women LWHIV in the Mtwara region (Table 1).

Discussion

The present study demonstrated that the seroprevalence of HBV infection among pregnant women LWHIV was 10.5%; per WHO's criteria for HBV severity, the seroprevalence of 10.5% indicates high endemicity (World Health Organization 2021b). These findings are consistent with the studies done in Ethiopia, Cameroon, China, and Ghana, which reported the seroprevalence of 9.2%, 9.3%, 11.3%, and 14.9%, respectively, among the HIV-infected pregnant women population (Frempong et al. 2019; Kfutwah et al. 2012). However, the seroprevalence of HBV infection among HIV-infected pregnant women is much higher than in previous studies in sub-Saharan Africa. The intermediate endemicity of HBV infection has been shown by previous studies conducted in South Africa, Uganda, the Democratic Republic of Congo (DRC), and Ethiopia, whereby a seroprevalence of HBV infection among pregnant women population was reported to range from 0.8 to 7.8%, respectively (Diale et al. 2016; Metaferia et al. 2016; Ngalula et al. 2018; Kayondo et al. 2020; Nlinwe and Lungle 2021).

These variations between several studies may be due to differences in the study population, as most previous studies were conducted among the pregnant women population regardless of their HIV serostatus. In addition, sampling methods and variations in laboratory testing technology may have contributed to the disparities in study findings among previous studies conducted in sub-Saharan Africa. Nonetheless, a systematic review and meta-analysis of the seroprevalence of HBV infection among pregnant women population showed that the pooled seroprevalence of HBV infection across the studies was 6.49% (95% CI 4.75–8.46%; $I^2=96.7%$, $p=0.001$; $n=20$) (Olakunde et al. 2021). These results suggest that in most African countries, the seroprevalence of HBV infection varies from intermediate to high endemicity

Table 1 Bivariable and Multivariable analysis of risk factors for HBV infection among HIV-infected pregnant women attending PMTCT clinics in the Mtwara region from February to April 2022 (N = 220)

Variable	HBV infection		Bivariate		Multivariate	
	Negative n (%)	Positive n (%)	cOR (95% CI)	p value	aOR (95% CI)	p value
<i>Age category (in years)</i>						
18–39	59 (88.1)	8 (11.9)	1.25 (0.50–3.10)	0.634		
≥ 40	138 (90.2)	15 (9.8)	1			
<i>Residence status</i>						
Rural	96 (90.6)	10 (9.4)	0.81 (0.34–1.93)	0.634		
Urban	101 (88.6)	13 (11.4)	1			
<i>Facility name</i>						
Likombe health center	34 (87.2)	5 (12.8)	1			
Mangaka hospital	31 (86.1)	5 (13.9)	1.10 (0.29–4.15)	0.892		
Mkomaindo hospital	67 (89.3)	8 (10.7)	0.81 (0.25–2.67)	0.732		
Ndanda hospital	65 (92.9)	5 (7.1)	0.52 (0.14–1.93)	0.331		
<i>Occupation status</i>						
Self-employed	93 (90.3)	10 (9.7)	0.76 (0.32–1.82)	0.540		
Unemployed	92 (87.6)	13 (12.4)	1			
<i>Education level</i>						
Non-formal	13 (100.0)	0 (0.0)	1		1	
Primary	138 (87.9)	19 (12.1)	2.82 (0.63–12.63)	0.175	3.23 (0.64–16.38)	0.158
Secondary	41 (95.4)	2 (4.6)	0.12 (0.01–1.07)	0.060	0.14 (0.02–1.37)	0.092
College or University	5 (71.4)	2 (28.6)	8.20(0.94–71.73)	0.057	6.87 (0.69–68.07)	0.100
<i>Marital status</i>						
Married	91 (91.0)	9 (9.0)	1		1	
Single	47 (88.7)	6 (11.3)	1.29 (0.43–3.84)	0.647	1.32 (0.42–4.20)	0.637
Divorced	15 (75.0)	5 (25.0)	3.37 (0.99–11.44)	0.051	3.45 (0.96–12.36)	0.057
Cohabiting	42 (93.3)	3 (6.7)	0.72 (0.19–2.81)	0.638	0.83 (0.20–3.35)	0.790
<i>Income status per day (in Tsh)</i>						
< 2400	111 (89.5)	13 (10.5)	0.27 (0.06–1.19)	0.084	0.25 (0.04–1.50)	0.131
2400–12,000	79 (91.9)	7 (8.1)	0.21 (0.04–0.98)	0.047	0.19 (0.03–1.15)	0.071
> 12,000	7 (70.0)	3 (30.0)	1		1	
<i>History of surgical procedure</i>						
No	164 (91.1)	16 (8.9)	1		1	
Yes	33 (82.5)	7 (17.5)	2.17 (0.83–5.70)	0.114	2.78 (0.95–8.15)	0.063
<i>History of blood transfusion</i>						
No	157 (88.2)	21 (11.8)	1		1	
Yes	40 (95.2)	2 (4.8)	0.37 (0.08–1.66)	0.196	0.36 (0.07–1.83)	0.218
<i>Dental procedure</i>						
No	90 (86.5)	14 (13.5)	1		1	
Yes	107 (92.2)	9 (7.8)	0.54 (0.22–1.31)	0.172	0.49 (0.19–1.26)	0.139
<i>History of body tattooed</i>						
No	159 (90.3)	17 (9.7)	1			
Yes	38 (86.4)	6 (13.6)	1.48 (0.55–4.00)	0.443		
<i>Number of sexual partners</i>						
One	120 (88.2)	16 (11.8)	1			
Two	35 (94.6)	2 (5.4)	0.43 (0.09–1.95)	0.274		
More than two	42 (89.4)	5 (10.6)	0.89 (0.31–2.59)	0.835		
<i>History of STIs</i>						
No	183 (89.3)	22 (10.7)	1			
Yes	14 (93.3)	1 (6.7)	0.59 (0.07–4.74)	0.623		

Table 1 (continued)

Variable	HBV infection		Bivariate		Multivariate	
	Negative n (%)	Positive n (%)	cOR (95% CI)	p value	aOR (95% CI)	p value
<i>Number of live children</i>						
One	66 (93.0)	5 (7.0)	1		1	
Two–three	113 (87.6)	16 (12.4)	1.87 (0.65–5.34)	0.243	2.02 (0.48–8.46)	0.337
Four or more	18 (90.0)	2 (10.0)	1.47 (0.26–8.20)	0.166	11.99 (1.11–129.01)	0.040*
<i>History of abortion</i>						
No	169 (90.4)	18 (9.6)	1			
Yes	28 (84.9)	5 (15.2)	1.68 (0.58–4.88)	0.343		
<i>Gestation period</i>						
First trimester	70 (100.0)	0 (0.0)	1		1	
Second trimester	72 (80.9)	17 (19.1)	2.16 (0.80–5.85)	0.128	1.82(0.64–5.21)	0.264
Third trimester	55 (90.2)	6 (9.8)	0.46 (0.17–1.25)	0.130	0.45 (0.16–1.23)	0.120
<i>CD4 levels within the last 6 months (in cells/mm³)</i>						
< 200	27 (87.1)	4 (12.9)	1.93 (0.45–8.31)	0.380		
200–499	76 (86.4)	12 (13.6)	2.05 (0.63–6.72)	0.234		
≥ 500	52 (92.9)	4 (7.1)	1			
<i>HVL status within last 6 months (in number of copies/ml)</i>						
< 50	181 (91.4)	17 (8.6)	1		1	
50–999	10 (83.3)	2 (16.7)	2.13 (0.43–10.52)	0.354	3.52 (0.54–22.86)	0.187
≥ 1000	2 (40.0)	3 (60.0)	15.97 (2.49–102.28)	0.003	16.00 (1.70–150.63)	0.015*
<i>WHO clinical staging of HIV</i>						
Stage-1	173 (91.1)	17 (8.9)	1		1	
Stage-2	22 (81.5)	5 (18.5)	2.31 (0.78–6.89)	0.132	1.83 (0.44–7.62)	0.404
Stage-3	2 (66.7)	1 (33.3)	5.09 (0.44–59.06)	0.193	4.82 (0.20–115.99)	0.332
<i>ART regimen</i>						
First-line	194 (89.8)	22 (10.2)	1			
Second line	3 (75.0)	1 (25.0)	2.94 (0.29–29.49)	0.359		
<i>Duration on ART (in months)</i>						
6–12	17 (89.5)	2 (10.5)	0.97 (0.21–4.49)	0.968		
> 12	173 (89.2)	21 (10.8)	1			
<i>Syphilis status</i>						
Negative	186 (94.9)	10 (5.1)	1		1	
Positive	11 (45.8)	13 (54.2)	21.98 (7.89–61.23)	< 0.001	27.65 (9.07–84.30)	< 0.001*

The significance of bold is to indicate variables that were statistically significant during multivariate analysis

cOR crude odds ratios, aOR adjusted odds ratios, HVL HIV viral load

*p value < 0.05 statistically significant

and thus requires prompt interventions in pregnant women LWHIV.

However, the seroprevalence of chronic infection in the present study is relatively higher compared to a previous study conducted in Mwanza, Tanzania (3%) among pregnant women (Geffert et al. 2020; Kinfe et al. 2021; Xiong et al. 2021). The higher number of pregnant women with HBV chronic infection warrants regular screening of pregnant women to ensure early detection and management to prevent perinatal transmission since most of the pregnant women are asymptomatic. Furthermore, the

present study revealed that most HIV-infected pregnant women who tested positive for HBV also had Syphilis infection. These findings suggest an increased risk of HBV infection, especially among pregnant women who are infected or living with HIV, as shown by the findings of the previous study done in Rwanda (Mutagoma et al. 2017).

One participant (0.5%) had positive HBeAg; this usually indicates high viral replication and may also indicate delayed HBeAg seroconversion that suggests chronic HBV infection, which was associated with

gestational diabetes mellitus (GDM) and intrahepatic cholestasis of pregnancy (ICP) among pregnant women in previous (Huang et al. 2021a, b). However, the higher number of HBeAg- (95.7%) among HBsAg+ participants with normal ALT levels may suggest HBeAg seroconversion, which indicates a good prognosis (World Health Organization 2017).

The high endemicity of HBV among pregnant women LWHIV suggests that infections could occur in infants through perinatal transmission. Therefore, we recommend instituting an HBV screening program at PMTCT clinics, HBV prophylaxis and treatment, and introducing hepatitis B immune globulin (HBIG) and HBV vaccine birth dose in newborns born to HBV-infected mothers, which could minimize the magnitude of the HBV infection not only among pregnant women but also in the general population.

In the present study, there was no significant association between the socio-demographic characteristics of the study participants and HBV infection. This result is similar to the two studies in Ghana that showed no significant association between socio-demographic characteristics and HBV infection among the HIV-infected pregnant women population (Anabire et al. 2019; Dortey et al. 2020). In contrast, similar studies in Ethiopia, Congo, and Uganda found significant associations between socio-demographic factors such as marital status, age, and occupation with HBV infection among the HIV-infected pregnant women population (Gedefaw et al. 2019; Kayondo et al. 2020; Manyahi et al. 2017; Ngalula et al. 2018). This variation of findings may have occurred due to differences in sampling methods and laboratory techniques used among the previous studies. The present study revealed that mothers having more than four children were 11 times more likely to acquire HBV infection than those with only one child. This could be because multiparous women may have been exposed to unsafe sex, multiple sexual partners, surgical procedures, and blood transfusions which may pose risks for HBV transmission as described by previous literature (Demeke et al. 2021; Gedefaw et al. 2019; Tiruye et al. 2018). These findings are similar to the study conducted in Nyamagana District Hospital in Mwanza, Tanzania, which showed a significant difference in seroprevalence of HBV infection between uniparous and multiparous women (0.8% vs. 8.6%, $p=0.017$), respectively (Mirambo et al. 2016). Furthermore, a previous study conducted in Rwanda showed that women with more than two pregnancies were potentially associated with HBV/HIV co-infection compared to those with less than two pregnancies (Mutagoma et al. 2017). However, a similar study conducted in Ethiopia among the pregnant women population showed no significant

association between multiparous women and HBV infection (Gedefaw et al. 2019).

Findings from the present study showed no significant association between abortion and HBV infection. However, several studies have shown a significant association between abortion and HBV infection. For example, a previous study conducted in Northern Ethiopia showed that having a history of abortion was significantly associated with HBV infection (Kinfu et al. 2021). This could occur since abortion involves invasive procedures, which may escalate the transmission of HBV, especially when a non-medical specialist does it. In the present study, factors such as the history of surgical procedures, blood transfusion, dental procedure, history of body tattoos, and the number of sexual partners were not associated with HBV infection among pregnant women LWHIV. These findings are similar to those found in studies done in Sudan and southern Ethiopia that showed that these factors were not significantly associated with HBV infection (Metaferia et al. 2016; Mudardum and Mohammed 2019). However, other studies in different parts of Africa showed a significant association between these factors and HBV infection. For example, factors such as having multiple sexual partners, history of body tattoos, history of blood transfusion, and history of jaundice were associated with HBV infection in different studies done in Kenya, South Sudan, and Ethiopia (Demeke et al. 2021; Gatheru et al. 2018; Machar 2021).

The findings in the present study showed that having a higher HIV viral load ($HVL \geq 1000$ cp/ml) is significantly associated with HBV infection among pregnant women LWHIV in the Mtwara region. These findings are similar to those of a previous study conducted in the Eastern-Amhara region in Ethiopia that showed a significant association of HIV viral load with HBV infection, whereby the HIV-infected pregnant women with high HIV viral load were seven times more likely to be infected with HBV as compared to those who had low HIV viral load (HVL) (Anteneh et al. 2021). Furthermore, the present study revealed that; being infected with syphilis is significantly associated with HBV infection. This suggests that pregnant women LWHIV co-infected with opportunistic infections such as syphilis may easily be infected with HBV. The previous study conducted in Rwanda showed that women who tested positive for syphilis were also associated with HBV-HIV co-infection (Mutagoma et al. 2017).

These findings could be because high HIV viral load and syphilis may have affected the body's immunity of the pregnant woman to fight against pathogens, including HBV, and it could also be because they share the same mode of transmission as shown in previous studies (Anteneh et al. 2021; Mutagoma et al. 2017). Therefore,

these findings suggest scaling up screening of opportunistic infections (OIs), including syphilis and HBV, during antenatal clinics, as well as regular testing for HVL and CD4 counts among pregnant women LWHIV. All these could minimize the risk of perinatal transmission. The present study has some limitations; it did not involve advanced tests (like DNA PCR tests), which would have helped to reveal cases of occult hepatitis B infection. Additionally, the study identified those who did not receive hepatitis B vaccination based on their medical records and verbally, and did not include hepatitis B antibody testing thus, the interpretation of the results should be taken care of this consideration.

Conclusions

The present study revealed that the seroprevalence of HBV infection is 10.5%, which is high endemicity. Having children of more than four, a higher HIV viral load (≥ 1000 cp/ml), and being infected with syphilis are risk factors independently associated with HBV infection among pregnant women living with HIV. Taken together, the results of the present study contribute to the basic knowledge about the seroprevalence of HBV among pregnant women with HIV in Tanzania and provide empirical evidence that may stimulate further research into this disease.

Abbreviations

ALT	Alanine transaminase
ART	Antiretroviral therapy
aOR	Adjusted odds ratio
CI	Confidence interval
cOR	Crude odds ratio
HBV	Hepatitis B virus
HIV	Human immunodeficiency virus
HVL	HIV viral load
ICP	Intrahepatic cholestasis of pregnancy
KENAS	Kenya accreditation service
LWHIV	Living with HIV
PMTCT	Prevention of mother-to-child transmission
SADCAS	The southern African development community accreditation services

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Author contributions

VJS, GJM, and DDK developed the study concept and design. VJS and GJM interviewed the study participants during data collection; VJS and DDK performed data entry, cleaning, and analysis; VJS, GJM, and DDK prepared the draft of the manuscript and reviewing to the final manuscript. All authors have contributed to the review and approval of the final manuscript and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final manuscript.

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Availability of data and materials

Data generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Ethical approval for the study was sought from the Institutional Review Board (IRB) of the Muhimbili University of Health and Allied Sciences (MUHAS-Research and Ethics Committee) with Approval Number MUHAS-REC-02-2022-978. Permission to conduct the study was sought and obtained from the Regional administrative secretary's office (RAS-Mtwara region), District Medical Officers of all selected districts, and medical officers in charge of Mkomaindo hospital Ndanda hospital, Mangaka hospital, and Likombe health center. Data were anonymized before being accessed, and all respondents provided informed, written consent and were assured of confidentiality. Seropositive results were reported to the clinician or nurse at the respective hospital within 48–72 h.

Consent for publication

Not applicable.

Competing interests

All authors declare that they have no commercial or other associations that may pose a conflict of interest.

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