

# Seroprevalence and associated factors of hepatitis B virus infection among HIV-positive adults attending an antiretroviral treatment clinic at Wolaita Sodo University Referral Hospital

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**Background:** Hepatitis B virus infection (HBV) constitutes major public health problems in sub-Saharan Africa from different infections occurring in HIV positive patients. Ethiopia is a part of sub-Saharan Africa with 1.5% adult HIV prevalence, and also belongs to the intermediate to high HBV prevalence category. Hence, this study aimed to measure the seroprevalence and associated factors of HBV infection among HIV-positive adults attending an antiretroviral treatment (ART) clinic at Wolaita Sodo University Referral Hospital.

**Methods:** An institution-based cross-sectional study was conducted from October 15 to December 10, 2017 using a systematic random sampling technique. After getting informed written consent, data were collected by a structured and interviewer-administered questionnaire. Venous blood was collected and centrifuged to separate serum. Hepatitis B surface antigen (HBsAg) was detected from serum using an advanced quality one-step rapid test kit. Data were entered into EpiData version 3.01 and exported to SPSS version 20. Summary statistics, bivariate analysis, and multivariate analyses were performed. The variables having significant association of  $P < 0.05$  in the multivariate logistic regression were taken as independent factors. OR and 95% CI were used to measure the strength of the association.

**Results:** A total of 442 study participants, 187 males and 255 females, were included in this study. Overall prevalence of HBsAg was 37 (8.4%). Family history of HBV (adjusted OR=8.83, 95% CI=2.56–30.49), multiple sexual partners (adjusted OR=7.08, 95% CI=2.29–21.9), and CD4 count  $< 200$  cells/ $\mu$ L (adjusted OR=15.34, 95% CI=4.77–49.3) were found to be significantly associated with HBsAg positivity.

**Conclusion:** The prevalence of HBsAg in this study was high. Family history of HBV, multiple sexual partners, and CD4 count  $< 200$  cells/ $\mu$ L were independently associated with HBsAg positivity. Therefore, screening for HBV is recommended before initiation of ART in HIV patients and providing appropriate treatment for co-infection. Furthermore, accurate information on risk factors for HBV transmission should be provided.

**Keywords:** hepatitis B surface antigen, HIV, co-infection, HIV-positive adults, highly active antiretroviral treatment regimens, hepatitis B virus infection

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## Introduction

### Background

Viral hepatitis is an inflammation of the liver affecting millions of people every year. Of the five different types of hepatitis viruses (A, B, C, D, and E), hepatitis B virus (HBV) infects the liver more than other viruses. HBV is a DNA virus that replicates in the liver

cells and causes acute and chronic infections of the liver. It is a major cause of chronic hepatitis, cirrhosis, and hepatocellular carcinoma. Most people are unaware of their infection with viral hepatitis and unknowingly transmit the infection to other people, so it is a silent epidemic due to its highly asymptomatic nature.<sup>1-3</sup>

About 80% of countries, including all countries in the African region, have recognized viral hepatitis to be an urgent public health issue. Most persons who become chronic carriers of HBV live in Asia and Africa. Ethiopia, part of Africa, has significant hepatitis B transmission in both children and adults, displaying around 6–12% hepatitis B surface antigen (HBsAg) prevalence. It also displays 12% of hospital admissions and 31% of mortality on medical wards due to acute viral hepatitis, chronic viral hepatitis, cirrhosis of the liver, and hepatocellular carcinoma.<sup>4-6</sup>

HBV is reported to be 50–100 times more infectious than HIV; it can survive for several weeks even in dried blood.<sup>7,8</sup> Blood is the most important vehicle for its transmission. Semen, tears, and saliva are also possible vehicles for its transmission. Percutaneous contact with infected blood, unprotected sexual contact, infected mother-to-infant, unsafe blood transfusion, sharing razors, toothbrushes, needles, and syringes, tattooing, and body piercing are some modes of HBV transmission.<sup>1,2,9</sup>

The seromarkers and biomarkers associated with HBV infection are HBsAg, hepatitis B surface antibody, hepatitis E antigen, and hepatitis B core antigen. From these seromarkers, the presence of a confirmed HBsAg result is indicative of ongoing HBV infection. So, all HBsAg-positive persons should be considered infectious and it is the only serologic marker detected during the first 3–5 weeks after infection in newly infected persons.<sup>10</sup>

Because of common routes of transmission, frequent co-infection of viral hepatitis and HIV is common. An estimated 5–25% of people living with HIV are also infected with HBV (2–4 million). The mean HIV/HBV co-infection in 20 sub-Saharan African countries was reported as 15%.<sup>11</sup> Some hospital-based studies documented 3.9–14% HBsAg prevalence among HIV patients, which is intermediate to high prevalence, in Ethiopia.<sup>8,12</sup>

HIV-infected individuals are more likely to develop chronic hepatitis B than are HIV-negative individuals after infection with hepatitis B in both groups. HIV accelerates the progression of HBV-related liver disease. Cirrhosis is more common in co-infected cases than in HBV mono-infected cases. HIV/HBV co-infected men

are also more likely to die of liver-related causes compared to those mono-infected with HBV.<sup>13</sup>

HBV infection is a serious public health problem that occurs all over the world. According to the WHO estimation, more than 2 billion people are HBV infected and about 378 million people are chronic carriers of HBV in the world. There are approximately 620,000 HBV-related deaths each year. Approximately 4.5 million new HBV infections are occurring worldwide each year and a quarter progress to liver disease from these new infections. It was also estimated that more than 50% of liver cancers were caused by HBV.<sup>2</sup>

The introduction of HBV vaccines to prevent HBV infection in the 1980s is to be considered the major achievement.<sup>2</sup> The introduction of highly active antiretroviral treatment (ART) for treatment of HIV infection has decreased morbidity and mortality from HIV infection. However, the management of HIV/HBV co-infection has become increasingly important since the management of the co-infected patient is complex, as the presence of one infection can affect the management of the other in a number of ways.<sup>12,14,15</sup>

Since several antiviral agents have activity against HIV or HBV alone or HIV and HBV co-infection, the issues of HIV and HBV drug resistance must be considered when selecting therapeutic regimens. When stopping ART regimens in patients with HIV/HBV due to treatment failure, toxicity, or other reasons, agents with anti-HBV activity may be stopped together although the patient is positive for HBV. This causes a hepatitis flare reaction which is an elevation of aminotransferases to more than 10 times the upper limit of normal and more than twice the baseline value during the natural course of a chronic HBV infection. So, clinicians need to be mindful for this problem in HIV patients before stopping ART regimens containing agents effective against HBV.<sup>13,14</sup>

Approximately, 10% of the 40 million HIV-positive individuals in the world have chronic hepatitis B infection.<sup>15</sup> Their co-infection is reported as high as 10–20% in countries where HBV infection is either endemic or intermediate to high.<sup>15</sup> HBV constitutes a major public health challenge in sub-Saharan Africa from different infections in HIV patients.<sup>16</sup> Ethiopia is part of sub-Saharan Africa with 1.5% HIV prevalence in adult,<sup>17</sup> and also belongs in the intermediate to high HBV prevalence category<sup>8</sup> according to the global clustering of the prevalence of chronic HBV infection.

However, data on the prevalence of hepatitis B infection and associated risk factors among HIV/AIDS patients in Ethiopia are scarce. The majority of the previous studies on hepatitis B infection were conducted in

pregnant women and healthy blood donors in Ethiopia.<sup>18</sup> A few studies on HBV infection were conducted among HIV patients<sup>9,18,19</sup> but these studies have not well addressed the distribution and associated factors for HBV transmission in HIV-positive adults, particularly in the study setting. Thus, assessing the prevalence of HBV infection and associated factors among HIV-positive adults becomes most important, because they are productive age groups who can move from place to place and can be exposed to many risk factors for HBV infection including unsafe sexual intercourse. Once exposed, they can serve as a reservoir of HBV transmission due to the silent nature of the virus.

Moreover, since therapeutic management is dependent on the correct diagnosis and staging, the state of HBV infection in the HIV-infected individual should be accurately diagnosed and assessed.<sup>15</sup> However, treating of HIV/AIDS-infected individuals with ART without prior screening for HBV infection is common in many Ethiopian health facilities. This results in high ART drug resistance, and severe liver toxicity and cirrhosis.<sup>18</sup> So, early screening using serological markers and preventing transmission is very essential because HBV is preventable with a safe and effective vaccine available.

## Significance of the study

The quality of treatment and life in HIV patients co-infected with HBV can be improved by appropriate management and monitoring. Knowing the magnitude of HBV infection and associated risk factors for its transmission is fundamental data for health planners and health professionals working in the ART clinic for appropriate medical management and monitoring. Moreover, this can reduce the occurrence of multiple complications due to viral HBV co-infection in HIV patients and can also help to undertake effective prevention measures once the status of HBV infection is recognized.

Therefore, this study aimed to measure the seroprevalence and associated factors of HBV infection among HIV-positive adults attending an ART clinic at Wolaita Sodo University Referral Hospital (WSURH). Data from this study can also be the baseline for further large-scale study.

## Objectives of the study

This study aimed to determine the magnitude of HBV infection among HIV-positive adults attending an ART clinic at WSURH.

The study also aimed to identify associated factors of HBV infection among HIV-positive adults attending an ART clinic at WSURH.

## Methods and materials

### Study setting

The study was conducted at WSURH which is located in Sodo town, southern Ethiopia. The hospital has more than 200 beds for inpatient services which are in medical, emergency, and critical care units, pediatrics, surgical, gynecology, eye unit, and obstetric wards. Currently, there are 1445 HIV patients under the ART service, of which 112 are children and 1333 are adults.

### Study design and period

An institution-based cross-sectional study was conducted among HIV-positive adults attending an ART clinic at WSURH from October 15 to December 10, 2017.

## Population

### Source population

All HIV-positive adults attending an ART clinic at WSURH were considered the source population.

### Study population

The study population consisted of all HIV-positive adults aged 15 years and older attending an ART clinic at WSURH during the study period.

## Eligibility criteria

### Inclusion criteria

HIV-positive adults aged 15 years and older who signed informed consent and were able to answer the questionnaire were included.

### Exclusion criteria

HIV-positive adults who were critically sick or were unable to speak and hear were excluded.

## Study variables

### Dependent variable

Infection by HBV was the dependent variable.

### Independent variables

Sociodemographic variables (age, sex, residence, marital status, occupation, education, income), route-associated factors (history of sharing sharp instruments, history of blood transfusion, multiple sexual partners, family history of HBV,

history of hospital admission, surgical history, tattooing, tooth extraction, ear piercing, circumcision, unsafe therapeutic injection), and clinical characteristics (history of opportunistic infection, years lived with HIV virus, history of sexually transmitted infection [STI], CD4 count, and highly active ART regimens) were independent variables.

## Sample size determination

The sample size was calculated for both objectives

### Sample size for first specific objective

The sample size was calculated using a single population proportion formula by assuming the prevalence of HBV to be 6.9%,<sup>19</sup> with 95% CI and 2.5% marginal error, and considering 10% contingency for possible nonresponse. Since the source population of the study population was 1333, which was less than 10,000, a finite population correction formula was used to adjust the necessary sample size. After considering a contingency of 10% for the nonresponse rate, the final sample size became  $303 + 303 \times 10\% = 333$ .

### Sample size for second specific objective

The sample size was calculated using OpenEpi version 3.03, and using factors statistically associated with HBsAg positivity among HIV patients taken from Mekelle Hospital<sup>18</sup> and Hawassa University Referral Hospital.<sup>19</sup> The study in Mekelle Hospital found a history of multiple sexual partners and the study in Hawassa University Referral Hospital found a history of surgical procedure and opportunistic infection were statistically associated with HBsAg prevalence.

The 442 participants calculated as the maximum sample size would have better representativeness taken as the final sample size.

## Sampling technique

A systematic random sampling technique was used to select the study participants among HIV patients attending an ART clinic, with a sampling interval of three. Of the first three subjects, one study participant was selected by lottery method, and then every third study participant was selected to participate in the study. Duplication was controlled by marking on the patient's card.

## Data collection method

### Enrollment and data collection procedure

Prior to data collection, 1 day of training was given to two nurses holding a BSc degree in nursing for data collection,

one MPH student for supervision, and one laboratory technologist for laboratory analysis, respectively. Then, a pretested structured questionnaire containing sociodemographic and other explanatory variables was delivered to eligible HIV patients after informed consent was taken to collect data through face-to-face interview by two trained BSc nurses working at the ART clinic. Then, the patients were ready to give blood samples.

### Specimen collection and processing

Five milliliters of venous blood was collected following standard operational procedures by a trained laboratory technologist from each study subject. 3 mL was added into a red top vacutainer tube for HBsAg test and 2 mL was added into a K<sub>3</sub>EDTA test tube for CD4<sup>+</sup> count. The blood specimen for the HBsAg test was allowed to clot at room temperature and serum was separated by centrifugation at 5000 rpm for 15 min. The collected serum specimen was tested for HBsAg using an advanced quality one-step rapid test kit according to the manufacturer's guidelines.<sup>20</sup>

For the CD4<sup>+</sup> count, the whole blood was incubated in a CD4<sup>+</sup>/CD8<sup>+</sup> reagent vial and a fixative was added to measure the CD4<sup>+</sup> count using a FACS count analyzer (BD FACS count; BD Biosciences, San Jose, CA, USA) according to the manufacturer's instruction.

### Laboratory testing method

Sample testing for HBsAg was done using an advanced one-step HBsAg test which is 98.89% sensitive and 98.87% specific.<sup>20</sup> This is a colloidal gold enhanced immunoassay for the determination of HBsAg in human whole blood, serum, or plasma. Goat anti-HBsAg antibody is immobilized in the test region on a nitrocellulose membrane. During the assay, the specimen was allowed to react with the colored conjugate (antibody–colloidal gold conjugate); the mixture then migrated chromatographically on the membrane by capillary action. An HBsAg-positive specimen produced a distinct color band in the test region, formed by the specific antibody–HBsAg-colored conjugate complex. Absence of this colored band in the test region suggested a negative result. A colored band in the control region served as procedural control regardless of the test result.

## Data quality control

The questionnaire was translated into Amharic language to make it appropriate and understandable; a pretest was made on 5% of the sample size at Sodo Health Center 1 week before actual data collection. Necessary modifications were

made to the questionnaire after conducting the pretest. Close supervision was undertaken during data collection to avoid bias. Standardized procedures were strictly followed during blood sample collection, storage, and the analytical process.

Positive and negative control samples within the test kit were run to assess the performance of the test kit as an internal quality control. Known positive and negative serum samples for HBsAg confirmed by ELISA were obtained from the Ethiopian Red Cross Society Blood Bank, Arba Minch branch. These known serum samples were analyzed before the actual investigation as an external quality control of the test kit.

## Data management

The completeness and consistency of questionnaires were checked by the principal investigator and supervisor on each day of data collection. After checking the completeness, accuracy, and clarity, the data were entered into EpiData version 3.01.

## Data analysis procedure

The data entered into EpiData version 3.01 were exported to Statistical Package for Social Science (SPSS) software version 20 for analysis. Summary statistics such as frequencies and percentages were computed. Bivariate analysis was conducted to check the association of each variable with the dependent variable. Variables that had association with the dependent variable at a  $P$ -value of 0.25 were entered into multivariate logistic regression to control for possible effects of confounding. The final model was then tested for its goodness of fit by the Hosmer and Lemeshow test, and  $P > 0.05$  was taken as best fit. The variables which had significant association with  $P < 0.05$  in the multivariate logistic regression were considered independent factors. The OR and 95% CI were used to measure the strength of the association.

## Ethical consideration

This study was conducted in accordance with the Declaration of Helsinki that provides guidance for researchers to protect research subjects. The study was approved by the institutional research review committee of Wolaita Sodo University. Then, the participants were informed that participation is on a voluntary basis, and about the benefits and harms of participation. Sample collection was done based on their agreement. Samples were handled properly and participants and physicians

were informed of results based on permission of the participants for their benefit. Each respondent was informed about the objective of the study and informed written consent was obtained. Confidentiality and voluntariness were kept at each step of data collection and processing. The participant was interviewed alone to keep privacy and all participants did not pay for the test. Finally, positive HBsAg test results of the study participants were communicated to the clinicians who are working at the ART clinic of the hospital for further diagnosis and better management of the patients.

## Results

### Sociodemographic and economic characteristics

A total of 442 HIV-positive adults comprising 187 (42.3%) males and 255 (57.7%) females were included in this study. The mean ( $\pm$ SD) age of study participants was 36.79 ( $\pm$ 9.97) years with the highest category of age being 35–44 years. 361 (81.7%) were living in an urban setting, 236 (53.4%) were married, and 116 (26.2%) were housewives. 117 (26.5%) study participants had no formal education. Of 442 study participants, 182 (41.2%) had  $\leq$ 500 ETB average monthly income, as shown in [Table 1](#).

### Route-associated risk factors

From a total of 442 study participants, 210 (47.5%), 20 (4.5%), 50 (11.3%), and 86 (19.5%) had a history of hospital admission, blood transfusion, surgical procedure, and sharing sharp materials, respectively. 35 (7.9%) had family members with HBV infection. Those who had a history of tattooing, ear piercing, and tooth extraction were 123 (27.7%), 233 (52.7%), and 221 (50%), respectively. 235 (53.2%) had more than one sexual partner, as shown in [Table 2](#).

### Clinical characteristics

318 (71.9%) had a history of opportunistic infections (OIs) since their HIV status had been known. 137 (31%) had a history of STIs other than HIV and HBV infections. The mean ( $\pm$ SD) years that study participants lived with HIV was 8.4 ( $\pm$ 3.7) with a range of 1–20 years. Of the total study participants, 87 (19.7%) had CD4 count  $< 200$  cells/ $\mu$ L. For the treatment protocol, 35.3% were taking TDF, 3TC, and EFV, 30.8% were taking AZT, 3TC, and NVP, 11.5% were taking AZT, 3TC, and EFV, and 12.7% were taking second-line ART drugs, as shown in [Table 3](#).



**Table 1** Sociodemographic and economic characteristics of HIV-positive adults attending an ART clinic at WSRH from October 15, 2017 to December 10, 2017

Variable (n=442)	Categories	Frequency	Percentage
Age (years)	15–24	22	5
	25–34	149	33.7
	35–44	176	39.8
	≥45	95	21.5
Sex	Male	187	42.3
	Female	255	57.7
Residence	Urban	361	81.7
	Rural	81	18.3
Marital status	Single	58	13.1
	Married	236	53.4
	Divorced	69	15.6
	Widowed	79	17.9
Occupational status	Government/NGO employee	80	18.1
	Merchant	79	17.9
	Farmer	24	5.4
	Daily laborer	50	11.3
	House wife	116	26.2
	No job	46	10.4
	Others, specify*	47	10.6
Educational status	No education	117	26.5
	Primary	165	37.3
	Secondary and above	160	36.2
Monthly income (ETB)	≤500	182	41.2
	501–999	49	11.1
	1000–1999	80	18.1
	>2000	131	29.6

**Note:** \*Students, prisoners, commercial sex workers, etc.

**Abbreviations:** ART, antiretroviral therapy; NGO, nongovernmental organization; WSRH, Wolaïta Sodo University Referral Hospital.

## Prevalence of HBsAg

From 442 HIV-positive study participants included in this study, the overall prevalence of HBsAg was 37 (8.4%). The prevalence of HBV infection was 16 (8.6%) among males and 21 (8.2%) among females, respectively. The highest prevalence was detected among participants with CD4 count <200 cells/μL (25.3%) followed by family with HBV history (22.9%) followed by second-line drug users (19.6%), respectively. It was also high among those who had a history of sharing sharp materials (16.3%) and those who had a history of multiple sexual partners (13.2%), respectively, as shown in Figure 1.

**Table 2** Route-associated risk factors of HBV infection among HIV-positive adults attending an ART clinic at WSRH from October 15, 2017 to December 10, 2017

Variable (n=442)	Categories	Frequency	Percentage
History of hospital admission	Yes	210	47.5
	no	232	52.5
History of blood transfusion	Yes	20	4.5
	no	422	95.5
History of surgical procedure	Yes	50	11.3
	no	392	88.7
History of sharing sharp materials	Yes	86	19.5
	no	356	80.5
Family history of HBV	Yes	35	7.9
	no	407	92.1
History of tattooing	Yes	123	27.8
	no	319	72.2
History of ear piercing	Yes	233	52.7
	no	209	47.3
History of tooth extraction	Yes	221	50
	no	221	50
History of circumcision	Not	37	8.4
	Traditional	357	80
	modern	48	10.9
History of multiple sexual partners	Yes	235	53.2
	no	207	46.8
History of unsafe therapeutic injection	Yes	70	15.8
	no	372	84.2

**Abbreviations:** ART, antiretroviral therapy; HBV, hepatitis B virus; WSRH, Wolaïta Sodo University Referral Hospital.

## Multivariate analysis of variables associated with HBV infection

In the bivariate analysis, occupational status, hospital admission, sharing sharp materials, family history of HBV, tooth extraction, multiple sexual partners, OIs, STIs, CD4 count <200 cells/μL, and second-line ART drugs have shown statistically significant association ( $p < 0.25$ ) with HBsAg seropositivity. When these significantly associated variables were entered into the multivariate model, family history of HBV (adjusted OR [AOR]=8.83, 95% CI=2.56–30.49,  $p=0.001$ ), multiple sexual partners (AOR=7.08, 95% CI=2.29–21.9,  $P=0.001$ ), and CD4 count <200 cells/μL (AOR=15.34, 95% CI=4.77–49.3,  $P=0.000$ ) were found significantly associated with HBsAg positivity.

Although there was no statistically significant association, those taking AZT, 3TC, and EFV (AOR=2.41, 95%

**Table 3** Clinical characteristics of HIV-positive adults attending an ART clinic at WSURH from October 15, 2017 to December 10, 2017

Variable (n=442)	Categories	Frequency	Percentage
OIs	Yes	318	71.9
	No	124	28.1
STIs	Yes	137	31
	No	305	69
Years lived with HIV	<5	108	24.4
	5–10	182	41.2
	>10	152	34.4
CD4 count	<200	87	19.7
	200–350	79	17.9
	351–499	84	19
	≥500	192	43.4
ART drugs	AZT, 3TC, and NVP	136	30.8
	AZT, 3TC, and EFV	51	11.5
	TDF, 3TC, and NVP	43	9.7
	Second-line drugs*	56	12.7
	TDF, 3TC, and EFV	156	35.3

**Note:** \*TDF/3TC/tazanvir/kalteza, AZT/3TC/tazanvir/kalteza and ABC/3TC/ATV, etc.

**Abbreviations:** ART, antiretroviral therapy; STI, sexually transmitted infection; WSURH, Wolaita Sodo University Referral Hospital; OIs, opportunistic infections.

CI=0.56–10.43) and those taking second-line ART drugs (AOR=2.47, 95% CI=0.72–8.42) showed an increased HBsAg positivity compared with those who were taking

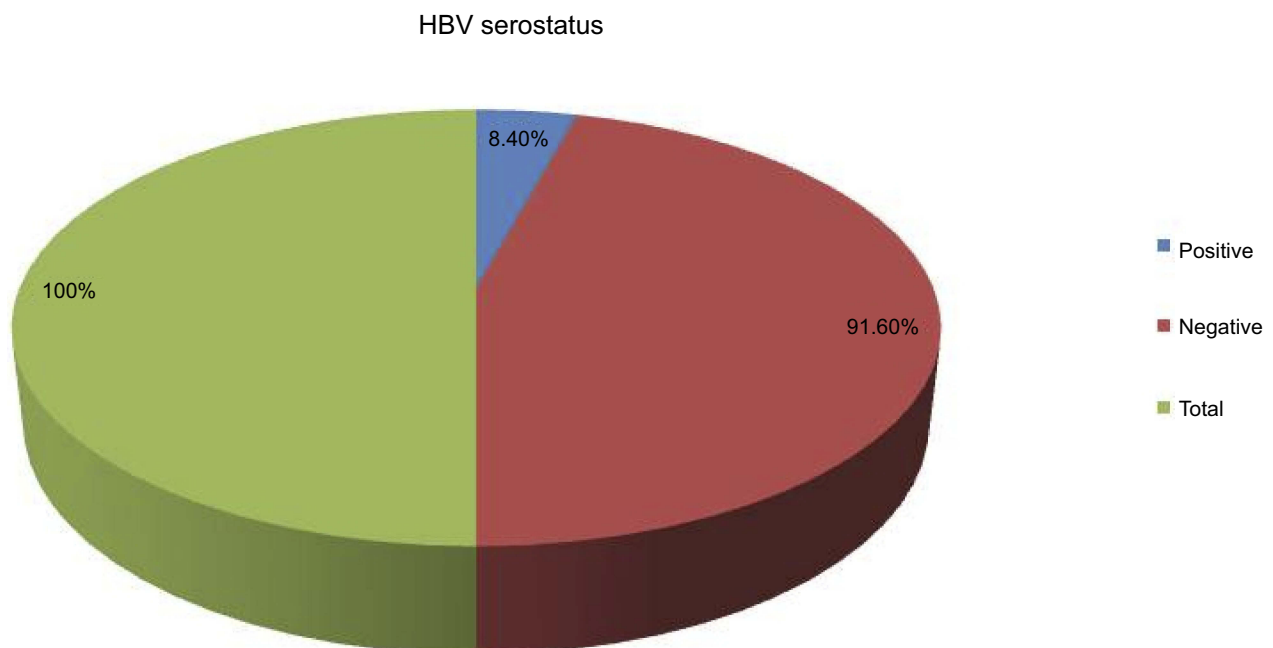
TDF, 3TC, and EFV based combined ART therapy, as displayed in Table 4.

## Discussion

The overall prevalence of HBsAg among 442 HIV-positive adult study participants in this study was 37 (8.4%). It was 8.6% among males and 8.2% among females. The finding of the present study is similar to previous studies conducted in Uganda (8.3%),<sup>22</sup> in Vietnam (8.4%),<sup>23</sup> in Myanmar (8.7%),<sup>24</sup> and in Taiwan (7.8%)<sup>25</sup> among HIV-infected patients.

On the other hand, this finding was relatively higher as compared with studies conducted in Tigray (5.9%),<sup>18</sup> in Hawassa (6.9%),<sup>19</sup> in Gondar (6.1%),<sup>9</sup> and in Addis Ababa (3%)<sup>11</sup> among HIV-infected patients in Ethiopia. It was also relatively higher than studies done in Brazil (2.5%),<sup>26</sup> in Canada (5.5%),<sup>27</sup> and in Botswana (5.3%)<sup>28</sup> among HIV patients. This might be due to the low awareness about transmission and prevention of HBV in our study population. The other possible reason might be lack of hepatitis B vaccine which is a cornerstone for HBV prevention in our study setting.

The finding of this study was also higher compared to some studies done among different population groups in Ethiopia like 3.7% in Jimma,<sup>29</sup> 4.3% in Arba Minch,<sup>30</sup> and 6% in Jigjiga among pregnant women attending an

**Figure 1** Prevalence of HBsAg among HIV-positive adults attending an ART clinic at WSURH from October 15, 2017 to December 10, 2017.

**Abbreviations:** ART, antiretroviral therapy; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; WSURH, Wolaita Sodo University Referral Hospital.

**Table 4** Multivariate analysis of variables associated with HBV infection among HIV-positive adults attending an ART clinic at WSURH from October 15, 2017 to December 10, 2017

Variable (n=442)	Category	HBV serostatus		COR (95%CI)	AOR (95%CI)	P-value
		Positive (%)	Negative (%)			
Occupation	Employed	7 (8.8)	73 (91.2)	2.16 (.43–10.8)	3.17 (.40–24.92)	0.273
	Merchant	11 (13.9)	68 (86.1)	3.64 (.77–17.2)	6.87 (.86–54.65)	0.069
	Farmer	3 (12.5)	21 (87.5)	3.21 (.50–20.7)	4.86 (.47–49.7)	0.183
	Daily laborer	4 (8)	46 (92)	1.96 (.34–11.2)	2.17 (.24–19.6)	0.490
	Housewife	7 (6)	109 (94)	1.44 (.29–7.2)	2.36 (.30–18.78)	0.416
	No job	3 (6.5)	43 (93.5)	1.57 (.25–9.86)	1.54 (.16–14.99)	0.711
	Others	2 (4.3)	45 (95.7)	1	1	
Hospital admission	Yes	24 (11.4)	186 (88.6)	2.17 (1.1–4.4)	1.95 (.81–4.67)	0.136
	No	13 (5.6)	219 (94.4)	1	1	
Sharing sharp materials	Yes	14 (16.3)	72 (83.7)	2.8 (1.38–5.7)	2.43 (.97–6.05)	0.057
	No	23 (6.5)	333 (93.5)	1	1	
Family history of HBV	Yes	8 (22.9)	27 (77.1)	3.86 (1.6–9.3)	8.83 (2.56–30.5)	0.001*
	No	29 (7.1)	378 (92.9)	1	1	
Tooth extraction	Yes	22 (10)	199 (90)	1.5 (.766–3.0)	1.54 (.63–3.76)	0.341
	No	15 (6.8)	206 (93.2)	1	1	
Multiple sexual partners	Yes	31 (13.2)	204 (86.8)	5.1 (2.1–12.5)	7.08 (2.29–21.9)	0.001*
	No	6 (2.9)	201 (97.1)	1	1	
OIs	Yes	30 (9.4)	288 (90.6)	1.74 (.74–4.1)	1.79 (.61–5.26)	0.289
	No	7 (5.6)	117 (94.4)	1	1	
STIs	Yes	21 (15.3)	116 (84.7)	3.3 (1.65–6.5)	2.02 (.876–4.66)	0.099
	No	16 (5.2)	289 (94.8)	1	1	
CD4 count	<200	22 (25.3)	65 (74.7)	12.7 (4.6–35)	15.3 (4.77–49.3)	0.000**
	200–350	7 (8.9)	72 (91.1)	3.64 (1.12–12)	3.51 (.94–13.12)	0.062
	351–499	3 (3.6)	81 (96.4)	1.4 (.32–5.9)	1.64 (.32–8.29)	0.550
	≥500	5 (2.6)	187 (97.4)	1	1	
ART drugs	AZT, 3TC, and NVP	10 (7.4)	126 (92.6)	1.3 (.5–3.3)	1.03 (.336–3.18)	0.953
	AZT, 3TC, and EFV	4 (7.8)	47 (92.2)	1.4 (.4–4.7)	2.41 (.56–10.43)	0.238
	TDF, 3TC, and NVP	3 (7)	40 (93)	1.2 (.32–4.74)	0.88 (.16–4.89)	0.886
	Second-line drugs	11 (19.6)	45 (80.4)	4 (1.56–10.2)	2.47 (.72–8.42)	0.149
	TDF, 3TC, and EFV	9 (5.8)	147 (94.2)	1	1	

**Note:** \*Significant at  $p < 0.05$ ; \*\*significant at  $p < 0.05$ .

**Abbreviations:** AOR, adjusted odds ratio; ART, antiretroviral therapy; COR, crude odds ratio; HBV, hepatitis B virus; STI, sexually transmitted infection; WSURH, Wolaita Sodo University Referral Hospital; OIs, opportunistic infections.

antenatal clinic, 4.2% in Bahir Dar<sup>31</sup> among military personnel, and 2.4% in Addis Ababa<sup>32</sup> among health professionals. This is an indication that the prevalence of HBsAg seropositivity among HIV-infected individuals is higher than among the general population.

However, the prevalence of HBsAg was found lower compared to 14% in Shashemene<sup>8</sup> and 19% in Bahir Dar<sup>31</sup> in Ethiopia among HIV-infected patients. It was also similarly lower compared to studies conducted in different areas in Nigeria among HIV patients; 26.5% in Gombe,<sup>33</sup>

20% in Nsukka,<sup>34</sup> 12.1% in Uyo,<sup>7</sup> and 12.3% in north-western Nigeria.<sup>16</sup> It was also lower than studies done in Sudan (11.7%),<sup>35</sup> in Iran (35.5%),<sup>36</sup> and in India (19.5%).<sup>37</sup> The high prevalence of HBV in these studies compared to our study might be due to the more advanced diagnostic tools they used like the HBV DNA real-time PCR and HBsAg ELISA technique, but in our study we used only a one-step rapid HBsAg serological kit. The lower rate of HBsAg prevalence in this study might also be due to the effect of Tenofovir, which is active against



both HBV and HIV. In our study, 199 (45%) were using Tenofovir, a nucleotide reverse-transcriptase inhibitor, with potent in vitro activity against lamivudine-resistant HBV. The other possible reasons could be due to the lower proportion of high-risk groups such as intravenous drug users and homosexual men in the study setting.

The present study found a statistically significant association between HBsAg and family history of HBV (AOR=8.83, 95% CI=2.56–30.49,  $P=0.001$ ). This finding is supported by a study conducted in central Brazil.<sup>26</sup> This might be due to close contact of family members with the HBV-positive patient in the family (family environment).

In this study, 53.2% of HIV patients had a history of multiple sexual partners. Among patients with this exposure, the prevalence of HBsAg was 13.2% which is significantly higher than those without such exposure (13.2% versus 2.9%, AOR=7.08, 95% CI=2.29–21.9,  $P=0.001$ ). This finding is in line with similar studies conducted in South Gondar, Ethiopia,<sup>9</sup> in Brazil,<sup>38</sup> and in Mexico.<sup>39</sup> This finding supports the fact that people who have multiple sexual partners will be prone to HBV infection and other sexually transmitted disease.<sup>40</sup> It also supports the fact that adolescents having sex with multiple partners are at higher risk of acquiring STDs including HIV and unplanned pregnancy.<sup>41</sup>

A higher prevalence of HBsAg was seen in HIV patients with CD4 count <200 cells/ $\mu$ L than in those with CD4 count  $\geq$ 500 cells/ $\mu$ L; this study showed statistically significant association between HBV infection and low CD4 count (AOR=15.34, 95% CI=4.77–49.3,  $P=0.000$ ). This finding is similar to studies done in Tigray, northern Ethiopia,<sup>18</sup> in Nepal,<sup>42</sup> and in Thailand.<sup>43</sup> This significant association might be due to the fact that at a lowered CD4 count, re-emergence of HBV replication occurs due to spontaneous reverse seroconversion marked by the disappearance of anti-hepatitis B surface antibodies and reappearance of HBsAg.

Furthermore, the seroconversion rate of HBsAg between study participants who were taking AZT, 3TC, and EFV and second-line drugs was compared with those who were taking TDF, 3TC, and EFV combined ART therapy. Although there was no statistically significant association observed between those taking AZT, 3TC, and EFV (AOR=2.41, 95% CI=0.56–10.43) and those taking second-line ART drugs (AOR=2.47, 95% CI=0.72–8.42), there was an increased HBsAg positivity compared with those who were taking TDF, 3TC, and EFV-based combined ART therapy. This was similar to studies done in Tigray<sup>18</sup> and in Kenya.<sup>44</sup>

The reason for this can be justified by the efficacy difference between these three treatment regimens. The

HIV antiretroviral drugs tenofovir (TDF), lamivudine (3TC), and emtricitabine (EFV) are the backbone of nucleoside/nucleotide analogues effective against both HIV and HBV. Tenofovir plus emtricitabine or tenofovir plus lamivudine and efavirenz is the preferred first-line therapy for HIV/HBV co-infected patients.<sup>14,45</sup> Starting from 2010, the WHO also recommended that tenofovir should be contained in the first-line regimen for HIV patients.<sup>46</sup>

## Conclusion

The prevalence of HBsAg among HIV-positive adults was high compared with the intermediate endemicity among the general population in previous studies in Ethiopia. Family history of HBV, history of multiple sexual partners, and CD4 count <200 cells/ $\mu$ L were significantly associated with HBsAg positivity among HIV-positive adults.

HBsAg seropositivity was also higher among the AZT, 3TC, and EFV users and second-line ART drug users than the TDF, 3TC, and EFV combination ART drug users due to the high efficiency of TDF. So, early screening of HBV and providing appropriate treatment for HIV/HBV co-infection are essential. Moreover, health education about the transmission and prevention of HBV is needed.

## Recommendations

- The ART clinic should screen HIV-positive patients for HBV before ART initiation.
- The ART clinic should provide two active HBV agents, TDF plus 3TC or TDF plus EFV, for co-infected individuals when ART is initiated.
- Health institutions giving HIV-related services should provide accurate awareness on risk factors such as family with HBV, having multiple sexual partners, and low CD4 count.
- Federal Ministry of Health should incorporate routine HBV screening into the ART treatment guideline.
- WSU should provide a hepatitis B vaccination service for HIV patients not infected with HBV.
- Further study should be conducted using advanced modern machines.

## Abbreviations list

ABC, Abacavir; AIDS, Acquired immune deficiency syndrome; ALT, Alanine aminotransferase; AOR, Adjusted odds ratio; ART, Antiretroviral therapy; ARV, Antiretroviral; ATV, Atazanavir; AZT, Zidovudine; CI, Confidence Interval; DNA, Deoxyribonucleic acid; EDTA, Ethylene diamine tetra acetic acid; EFV, Efavirenz; ELISA,

Enzyme linked immunosorbant assay; HAART, Highly active antiretroviral therapy; HBcAg, Hepatitis B core antigen; HBeAg, Hepatitis B e antigen; HBs, Hepatitis B surface antibody; HBsAg, Hepatitis B surface antigen; HBV, Hepatitis B virus; HCC, Hepatocellular carcinoma; HCV, Hepatitis C virus; HIV, Human immunodeficiency virus; OR, Odds ratio; PCR, Polymerase Chain Reaction; RPM, Revolution per minute; SPSS, Statistical Package for Social Science; STI, Sexually transmitted infection; WHO, World Health Organization; WSURH, Wolaita Sodo University Referral Hospital.

## Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki that provides guidance for researchers to protect research subjects. The study was approved by the institutional research review committee of Wolaita Sodo University. Then, the participants were informed, as participation is on a voluntary basis, about the benefits and harms of participation. Sample collection was done based on their agreement. Samples were handled properly and participants and physicians were informed of results based on permission of the participants for their benefit. Informed written consent is obtained from participants aged  $\geq 18$  years, and for those younger than 18 years old, informed written consent was obtained from parents or guardians.

## Disclosure

The authors report no conflicts of interest in this work.

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