

Sero-prevalence of HBV and associated factors among HIV positive adults attending an ART clinic at Nekemte Specialized Hospital, Nekemte, Western Ethiopia

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Abstract

Background: Hepatitis B is a major global health problem and potentially life-threatening liver infection caused by hepatitis B virus. It is more common in HIV infected individuals. The aim of this study was to assess the sero-prevalence of hepatitis B infection and associated factors among HIV positive adults on Antiretroviral Therapy (ART).

Method: A hospital based cross-sectional study was conducted from March to June, 2021. Samples were taken from randomly selected HIV positive adults visiting an ART clinic using a single population proportion formula. Blood sample were tested for HBsAg and data entered into Epi-data software 3.1, transferred to SPSS version 20 and analyzed. A difference was considered statistically significant at p value < 0.05 .

Result: Among 384 HIV positive adults on ART selected for this study, 199 (51.8%) were males and 185 (48.2%) were females. Twenty-two (5.7%) individuals were sero-positive for HBsAg, of which 9 (2.3%) and 13 (3.4%) were females and males, respectively. Among the 384 adults, 22.7% of them had been married, and 9.1%, 40.9%, and 25% had been widowed, divorced and single, respectively and significantly associated with the presence of HBsAg at a 5% level of significance [AOR = 4.02; $P = 0.041$]. Similarly, regarding CD4 count, among the study subjects 0% of them had 200-250cells/ μ l and 251-300cells/ μ l, and 0.8%, 1.3%, and 3.6 % had < 200 cells/ μ l, 301-500cells/ μ l and > 500 cells/ μ l respectively and significantly associated with the presence of HBsAg at a 5% level of significance [AOR = 1.03; $P = 0.034$].

Conclusion: The prevalence of HBsAg was found to be moderate in HIV positive adults on ART. HBV infection had no significant effect on ART treatment progress or virological suppression. ART treatment had no association with HBV sero-negativity. CD4 counts had significant association with HBV infection. Provision of routine screening for HBV-HIV co-infected individuals and promoting awareness of this risk creation is necessary to advance treatment strategies.

INTRODUCTION

Hepatitis B is the most common serious liver infection in the world (1). It is caused by hepatitis B virus (HBV). The inflammation associated with a hepatitis B infection can lead to extensive liver scarring (cirrhosis), which may impair the liver's ability to function. However, HIV can still take a toll on the body, especially the liver. They often result in a build-up of fat in the liver, known as steatosis, which can lead to inflammation and scar tissue. In severe cases, this can progress to cirrhosis. Among the five different types of hepatitis viruses (A, B, C, D, and E), types B and C lead to chronic disease in hundreds of millions of people and, together, are the most common cause of liver cirrhosis and cancer. HBV is transmitted through exposure to infective blood, semen, and other body fluids. HBV can be transmitted from infected mothers to infants at the time of birth or from family members to infants in early childhood. Transmission may also occur through transfusions of HBV-contaminated blood and blood products, contaminated injections during medical procedures, and through injection drug use (2).

Because of shared routes of transmission, HBV coinfection among HIV-positive persons is common. In some settings, more than two-thirds of HIV-infected persons have markers of past exposure to HBV (3). Worldwide, an estimated 2 to 4 million people (~10% of HIV-infected individuals) are currently living with HBV-HIV coinfection (4, 5). HBV is reported to be 50–100 times more infectious than HIV; it can survive for several weeks even in dried blood (6, 7).

Most people are unaware of being infected with viral hepatitis and unknowingly transmit the infection to other people, so it is a silent epidemic due to its highly asymptomatic nature (8). Next to Asia, at least 65 million of all chronically infected individuals in Africa have the prevalence rate of between 8 and 20%. About 80% of countries globally and all countries in the African region have recognized viral hepatitis to be an urgent public health issue, responsible for 57% of liver cirrhosis and 75% of primary liver cancer cases, respectively (9).

In Ethiopia, there is significant hepatitis B transmission and prevalence in both children and adults, with estimated seroprevalence of 6–12% hepatitis B surface antigen (HBsAg). Acute viral hepatitis, chronic viral hepatitis, cirrhosis of the

liver, and hepatocellular carcinoma (HCC) account for 12% of hospital admissions and 31% of mortality on medical wards (10, 11).

To date, there are two kinds of HBV vaccines, a first-generation plasma-derived vaccine, and a second generation recombinant vaccine. The recombinant vaccine was produced by expressing the *HBsAg* gene in the yeast *Saccharomyces cerevisiae* (12,13). Both vaccines are safe and effective.

The national survey and regional estimates conducted in Ethiopia have shown wide geographic and socioeconomic variations in hepatitis B prevalence, ranging between 5.7% and 10.8% (14). According to previous studies, the prevalence of HBV in Wolayita Sodo, in southern Ethiopia (15), and Mekele, in northern Ethiopia (16) were 6.9% and 5.9 %, respectively. HBsAg among PLWH. Also it was 8.4% at Hawassa, southern Ethiopia (17). The overall pooled prevalence of HBV was 6% including 5% of pregnant women, healthcare workers and HIV positive patients respectively (18).

To date there is no well-studied and documented assessment of the prevalence of HBV infection in Nekemte town. Nekemte Specialized Hospital, was chosen because of the presence of well-organized ART clinic and its provisions of a comprehensive package of health prevention, diagnostic and treatment services to the large communities, the four wollega zones.

Here, HIV/AIDS patients were treated with ART without prior screening for HBV infection. Furthermore, the impact of HBV on ART treatment progress and virological suppression, were not well studied in this study location. Therefore, the aim of this study was to assess the sero-prevalence of hepatitis B infection and associated factors among HIV positive adults on ART.

METHOD

Study Area

The study was conducted at Nekemte Specialized Hospital ART clinic, in the city of Nekemte, Western Ethiopia. Nekemte is located 328 km to the west of Addis Ababa, at 2088 meters above sea level, with a mean annual rainfall of 2022mm and mean annual temperature of 19.85°C. Nekemte Specialized Hospital is one of the renovated hospitals providing a comprehensive package of health prevention, diagnostic and treatment services to the community.

Study design and period

A hospital-based cross-sectional study was conducted from March through June, 2021, among HIV-positive patients attending the ART clinic at Nekemte Specialized Hospital.

Source and study population

All HIV-positive adults attending the ART clinic at Nekemte Specialized Hospital were considered the source population. The study population consisted of all HIV-positive adult ≥ 15 years attending the ART clinic during the study period.

Inclusion and Exclusion criteria

All HIV-positive adults ≥ 15 years who are found in the reproductive stage and could give informed consent were included. HIV-positive adults who were critically ill or unable to speak and hear were excluded.

Sample size determination and sampling technique

Calculation of sample size was done using a single proportion population equation ($n = Z^2 P (1-P) / d^2$). Here n = sample size, d = worst accepted value/marginal error, Z = is statistic value for level of 95% confidence, is 1.96; P = is expected prevalence or proportion which is 0.5. Since there were no published previous studies conducted in the area, 50% was assumed and 384 samples were generated using a 5% marginal error. A systematic random sampling technique was used to select the study participants among HIV patients attending the ART clinic, with a sampling interval of five.

Data collection

Prior to data collection, enrollment and sample collection training was given for health workers by laboratory professionals at the ART clinic. A pretested structured questionnaire containing socio-demographic characteristics was given to eligible HIV patients after verbal informed consent.

Specimen collection and processing

Three milliliters of venous blood was collected from each study subject by a trained laboratory technician and placed in a test tube. Following standard operating procedures, the blood specimens were allowed to clot at room temperature and subjected to centrifugation at 2500 rpm for 5 minutes to separate the serum.

Laboratory detection of hepatitis B virus

The serum was then used for an enzyme-linked immunosorbent assay (ELISA) and a rapid serological HBsAg test (Wantai AiD™ HBsAg ELISA of Beijing Wantai Biological Pharmacy Enterprise co., Ltd (ACON®HBsAg Rapid test cas-

sette of ACON Laboratories, Inc. USA). The test results were interpreted and reported as positive or negative based on the manufacturer's instruction. For HBsAg serum samples that tested positive on the initial test, the tests were duplicated before reporting the samples as positive using the 4th generation ELISA assay.

Quality control

Data quality was maintained by training the data collectors before the actual data collection was begun. The SOP of pre-analytical to post-analytical quality control techniques of the laboratory were strictly followed. Negative internal (manufacturer's) control and known positive and negative control serum samples and internal controls for HBsAg were confirmed by ELISA at Nekemte Blood Bank and run together with the patients' serum. Every newly opened kit was checked before use by these control samples. So ELISA and rapid tests results were assured using positive and negative controls according to the manufacturer's manual.

Data analysis

The data entered into Epi-data software 3.1 were transferred to Statistical Package for Social Science (SPSS) software version 20. Bivariate analysis was conducted to check the association of each independent variable with the dependent variable. Independent variables that had associations with the dependent variable at a P-value of 0.05 were entered into multivariate logistic regression to control for possible effects of confounding. The OR and 95% CI were used to measure the strength of the association.

RESULTS

Socio-demographic characteristics

All of the 384 study participants responded to the interview, of which 199 (51.8%) were male, and 185 (48.2%) female. The majority, 154 (40.1%), were between 35 - 44 years old, of which 167 (43.5%) were married, 91(23.7%) were divorced, 65 (16.9%) were widowed, and 61(15.8%) were single. Concerning family size, 88 (22.9%) had one member, 76 (19.8%) had two members, 56 (14.6%) had three members, 96 (25%) had four members and 68 (17.7%) had five and greater members. The majority (89.06%) were urban residents (Table 1).

HBV Sero-Prevalence

The prevalence of HBsAg was found to be 22 (5.7%); of which 13 positive individuals (59.1%) were males and 9

(40.9%) were females. With respect to age, the prevalence of HBsAg was 2 (9.1%) in age category of 15-24 years, 7 (31.8%) in age category of 25 – 34 years and 35-44 years, and 6 (27.3%) for ≥ 45 years old. These data suggest the infection is more prevalent between the ages of 25-44 years old. Concerning marital status, the prevalence of HBsAg was 6 (25%) among singles, 5 (22.7%) among married individuals, 9 (40.9%) among those who were divorced, and 2(9.1%) among those who were widowed. Marital status related seroprevalence showed higher HBV prevalence among HIV patients who were divorced (40.9%) compared to those who were married (22.7%) and single (25%) and the difference between HBV infection and marital status was statistically significant ($p < 0.05$). On the other hand, HBV rates were not significantly correlated with educational attainment levels. The majority of the participants positive results with HBsAg 19(86.4%) live in urban areas (Table 1).

Associated risk factors & clinical characteristics

Among the participants, 242(63%) had good knowledge about HBV, but the nearly one-thirds of them 116 (30.2%) think that infection with HBV is more serious than HIV and highly severe in PLWH. One hundred-fifty seven (40.9%) did not know whether HIV positivity contributes to HBV infection or not. Regarding routes of transmissions of HBV, more than half 232 (60%) of participants were not well informed. From 16(72.7%) HBV positive cases, only 10(2.8%) of these participants understood the diseases can be transmitted through sexual intercourse, and only 79(20.6%) of the participants understood different routes of transmission were possible (contact with blood, saliva, sweat and body fluid). In case of CD4 counts, 45.6% of the participants had CD4 > 500 cell/ μ l, of which 14(3.6%) tested positive for HBV; 13.5% had 301-500cell/ μ l from which 5(1.3%) tested positive for HBV, and 25.5% had CD4 < 200 cell/ μ l, of which 3(0.8%) tested positive for the virus

About 18(4.7%) were positive for HBsAg and had started ART before two years and 22(5.7%) were had good Adherence to ART drug (Table 2).

All participants were screened for opportunistic infection (OI). Of these, 93(24.2%) participants had a history of opportunistic infection, including 54(14.1%) with tuberculosis, 7 (1.8%) with candidiasis, 24(6.3%) with diarrhea $>$ one month and 14(3.6%) with other opportunistic infections such as herpes zoster. All those who had history of other opportunistic

infections were treated. But HBV infection has no significant association with history of opportunistic infections 4(1.04) compared to those without opportunistic infections 18(4.7), $P > 0.05$ (Table 3). On the other hand, the majority of participants had healthy nutritional status with 20(5.2%) positive result. No linear association was found between viral suppression and HBsAg positivity since all HBsAg positive participants were adherent to ART treatment and virologically suppressed ($P > 0.05$) (Table 3).

Table 1: Socio-demographic characteristics of study participants relative to HBsAg test results (n=384)

Variables	HBV test result		Total	P-value	AOR	95%CI Lower	95%CI Upper	
	Positive n(%)	Negative n(%)						
Sex	Male	13 (59.1)	186 (51.4)	199 (51.8)	0.642	0.35	0.075	1.626
	Female	9 (40.9)	176 (48.6)	185 (48.2)				
Age	15-24	2 (9.1)	15 (4.1)	17 (4.4)	0.477	0.049	0.002	1.326
	25-34	7 (31.8)	98 (27.1)	105 (27.3)				
	35-44	7 (31.8)	147 (40.6)	154 (40.1)				
	≥45	6 (27.3)	102 (28.2)	108 (28.1)				
Family size	1	6 (25.0)	82 (22.8)	88 (22.9)	0.633	9.363	0.92	95.3
	2	3 (12.5)	73 (20.3)	76 (19.8)				
	3	2 (8.3)	54 (15.0)	56 (14.6)				
	4	6 (27.3)	90 (24.9)	96 (25.0)				
	≥5	5 (22.7)	63 (17.4)	68 (17.7)				
Marital Status	Married	5 (22.7)	162 (44.8)	167 (43.5)	0.041	17.83	1.83	175.51
	Widowed	2 (9.1)	63 (17.3)	65 (16.9)				
	Divorced	9 (40.9)	82 (22.7)	91 (23.7)				
	Single	6 (25.0)	55 (15.3)	61 (15.9)				
Educational Level	Illiterate	2 (9.1)	49 (13.5)	51 (13.3)	0.286	2.001	0.044	90.31
	Primary school	14 (63.6)	147 (40.6)	161 (41.9)				
	Junior School	3(13.6)	55(15.3)	58(15.1)				
	Secondary School	1(4.2)	50(13.9)	51(13.3)				
	College above	2.(9.1)	61(16.9)	63(16.4)				
Residence	Urban	19(4.9)	322(89)	341(88.8)	0.709	0.422	0.23	2.02
	Rural	3(13.6)	40(11)	43(11.2)				

Table 2: CD4 count, ART and clinical conditions of study participants with HBsAg sero-status (n=384)

Variable	Labels	HBV test Result		Total n (%)	P-Value	AOR	95%CI
		Positive n (%)	Negative n (%)				
CD4 Count	<200cells/μl	3(0.8)	94(24.5)	97(25.3)	0.046	1.508	1.008-2.256
	200-250cells/ μl	0	35(9.1)	35(9.1)			
	251-300cells/ μl	0	25(6.5)	25(6.5)			
	301-500cells/ μl	5(1.3)	47(12.2)	52(13.5)			
	>500cells/ μl	14(3.6)	161(42)	175(45.6)			
Months with HIV	<6months	0	2(5)	2(5)	0.984	0.986	0.266-3.659
	6-12months	0	2(5)	2(5)			
	12-18months	1(0.3)	3(0.8)	4(1)			
	18-24months	0	7(1.8)	7(1.8)			
	>24months	21(5.5)	348(90.6)	369(96.1)			
Months on ART	initial/new	3(0.8)	82(21.4)	85(22.1)	0.66	1.179	0.56-2.46
	<6months	0	5(1.3)	5(1.3)			
	6-18months	1(0.3)	5(1.3)	6(1.6)			
	18-24months	0	9(2.3)	9(2.3)			
	>24months	18(4.7)	261(68)	279(72.7)			
Adherence to ART drug	Poor	0	2(0.5)	2(0.5)	0.727		
	Good	22(5.7)	360(93.8)	382(99.5%)			

Table 3: Clinical feature and health status of the of study participants in accordance with HBsAg (n=384)

Variables	Labels	HBsAg test Result		Total n (%)	p-value	AOR	95%CI
		Positive n (%)	Negative n (%)				
History of OI	Yes	4(1.04)	89(95.7)	93(24.2)	0.484	0.407	0.33-5.049
	No	18(4.7)	273(71.1)	291(75.8)			
Type of OI	Tuberculosis	2(0.52)	52(13.5)	54(14.1)	0.218		
	Candidacies	0	7(1.8)	7(1.8)			
	Diarrhea >1month	0	24(6.3)	24(6.3)			
	Others	1(0.2)	13(3.4)	14(3.6)			
	Not applicable	19(4.9)	266(69.3)	285(74.2)			
Prophylaxis to OI	Anti TB (CPT)	2(0.5)	52(13.5)	54(13.5)	0.726	0.889	0.46-1.72
	Amoxicillin	0	2(0.5)	2(0.5)			
	Ceftriaxone	2(0.5)	9(2.3)	11(2.8)			
	Cotri..	0	24(6.3)	24(6.3)			
	Anti-Fungi	0	7(1.8)	7(1.8)			
Initial viral load result	Suppressed	18(4.7)	261(68)	279(72.7)	0.856		
	mild suppressed	0	11(2.9)	11(2.9)			
	High(not suppressed)	1(0.3)	5(1.3)	6(1.6)			
	Unknown	3(0.8)	85(22.1)	88(22.9)			
Current health status	Sick	1(0.3)	2(0.5)	3(0.8)	0.69		
	Intermediate	0	1(0.3)	1(0.3)			
	Good	11(2.9)	182(47.4)	193(50.3)			
	Healthy	10(2.6)	177(46.1)	187(48.7)			
Nutritional status	severe malnutrition	0	5(1.3)	5(1.3)	0.93		
	Moderate	2	15(3.9)	17(4.4)			
	Mild	0	6(1.6)	6(1.6)			
	Normal	20(5.2)	333(86.7)	353(91.9)			
	Over weight	0	3(0.8)	3(0.8)			
Current Viral load result	Suppressed	22 (5.7)	357(93)	379(98.7)	0.99	2.69	0.00

Discussion

The study showed that the sero-prevalence of HBV-HIV co-infection was 5.7 %. This is similar to previous studies in Tigray 5.9% (16), and Southern Nation and Nationalities and Peoples Region (SNNPR) 6.9%(15), and less than that done in SNNPR region Hawasa 8.4%, (17) in Ethiopia. However, this value is higher than the prevalence in Eastern Mediterranean (3.3%), south East Asia (2%), East Asia (0.4%), Latin America (0.9%), and Europe (1.6%) (7).The relative higher prevalence in Ethiopia could be associated with factors like differences in awareness of study participants about the virus as reported in (14) or/and the slow rate

of screening and follow up for the virus which is estimated to 12.5% (19). Other factors could be the low knowledge level, estimated at about 60.4% of study participants, about HBV transmission. On the other hand, Egypt has significantly higher rate (17.5%) of prevalence of the co-infection (20).

In this study, 350(91.1%) participants were on tenofovir-based ART regimen (TDF-3TC-DRG), a highly active ART therapy. Of these study participants, only 21(5.5%) tested positive for HBsAg. This low percentage may be due to the global scale-up of ART for PLWH using a tenofovir-based ART regimen which provides an opportunity to simultaneously treat those HBV-HIV co-infection (16). Another result from the African Temprano Trial, showed that starting HIV/AIDS treatment (TDF was one of the drugs they used) at a

CD4 cell count above 500 reduced the risk of serious illness and death by 44 % when compared to starting treatment according to WHO guidelines, CD4 cell counts <350 cells/ μ L (21). The investigated demographic factors such as age, educational level, monthly income, knowledge and attitude had no significant association with prevalence of HBsAg. Positive association was found with those who were divorced (40.9%) compared to those who were married (22.7%) and single (25%) with HBsAg similar to the report of Omatola in Nigeria (22). Besides intermediate endemicity, previous opportunistic infections were significantly associated with the presence of HBsAg(17), but not in this study which was about 4(1.04). Regarding the CD4 Count, >500cells/ μ l 14(3.6) was significantly associated with increased risk for positive HBsAg, unlike the study report from Mekele Hospital (16) and other studies (18). However, the roles of CD4 cell count and HIV viremia in HBV–HIV co-infected individuals are limited and contradictory with several study findings (23,24).

Concerning the clinical outcome of ART follow up and treatment, respondents' adherence to the ART drug was 99.5%. Of these participants, 22(5.7%) were positive for HBsAg which indicates the absence of relationship between adherence and HBsAg sero-positivity ($P>0.05$). This is similar to studies which demonstrated that HBV co-infection has no impact on the natural history of HIV disease progression (25). In contrast to this, another study found that chronic HBV and resolved status of HBV–HIV co-infected subjects were associated with increased risk of AIDS and death particularly in those immune-compromised individuals (26). No significant relationship ($p>0.05$) also seen between HBV infection and effect of virological suppression of HIV.

Socio-demographic characteristics like age, residence, education and occupation were not significantly associated to HBsAg positivity. Likewise, of knowledge about routes of HBV transmission, its severity, vaccination history to the virus, nutrition, and history of opportunistic infection did not show statistically significant association with HBV infection. This was consistent with studies done in Goba, Ethiopia (27).

Conclusion

In this study the prevalence of HBV infection was moderate among HIV positive adults on ART.

Marital status related seroprevalence showed higher HBV prevalence among HIV patients who were divorced compared to those who were married and single. Also, CD4 cell count above 500 reduced the risk of serious illness when compared to starting treatment and remained statistically significant. No association was seen between HBV infection and viral load suppression. The majority of participants had poor knowledge about the disease and its transmission. They also lacked awareness about the value of vaccination for the disease. The present study may be one part of strengthening efforts toward eradication of HBV in the absence of detectable HBsAg in HBV–HIV co-infected individuals. Since hepatitis HBV is typically asymptomatic, screening of the disease should be required for HIV positive patients before initiation of ART.

Abbreviations:

AIDS- Acquired immunodeficiency syndrome

ART-Anti retroviral Therapy

ELISA- Enzyme-linked immune-sorbent assay

HBsAg- Hepatitis B surface antigen

HBV-Hepatitis B virus

HCC- *Hepatocellular carcinoma*

HIV-Human Immune Virus

SOP-Standard operating procedures

WHO-World Health Organization

Ethics approval and consent to participate

Ethical approval was obtained from Wollega University Research Ethics Review Committee with a Ref/No. of: WU, RD, 225, 2013 EC. In addition, positive cases for HBV infection were treated and confidentiality of data and information from this study was maintained. Written informed consent was obtained from each study participants.

Competing interests

The authors have no competing interests

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