



Prevalence of Hepatitis-B Virus Co-infection among People Living with HIV in Mthatha Region of South Africa

Ramprakash Kaswa^{1,2*} and Marietjie de Villiers³

¹Specialist, Department of Family Medicine and Rural Health, Walter Sisulu University, South Africa

²Department of Family Medicine and Primary Care, Stellenbosch University, South Africa

³Professor, Department of Family Medicine and Primary Care, Stellenbosch University, South Africa

***Corresponding Author:** Ramprakash Kaswa, Specialist, Department of Family Medicine and Rural Health, Walter Sisulu University, South Africa.

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Abstract

Background: Hepatitis-B virus (HBV) infection among people living with HIV (PLWH) is highly endemic in South Africa. Despite the availability of an effective vaccine for the last three decades, chronic HBV infection is a major cause of morbidity and mortality among PLWH. Although the majority of opportunistic infection has been reduced in an individual with HIV since the universal test and treat (UTT) programme implemented in South Africa. HBV co-infection among PLWH is still accounting for high morbidity and mortality in South Africa.

Methodology: This cross-sectional descriptive survey was conducted in King Sabata Dalindyebo (KSD) sub-district municipality in the Eastern Cape Province of South Africa to determine the prevalence of HBV Co-infection among people living with HIV.

Results: There were 602 PLWH participated in the study and two-third (65.5%) of them had screened for HBV coinfection. The mean age of the participant was 38.8 ± 10.5 years and the majority (75.1%) of them were female. The prevalence of HBV coinfection among PLWH was 12.2% and the males had three-time higher than female counterparts ($\chi^2 = 12.8$, $p = 0.001$). The HBV coinfection was more common among PLWH, who use alcohol, tobacco, and cannabis. The median CD4 count of participants was 508 (IQR = 307 to 715) and there was no significant association between HBV coinfection and CD4 count.

Conclusion: There is a high prevalence of HBV coinfection among PLWH in the Mthatha region of South Africa. The high prevalence of HBV coinfection recommends the need for routine screening of Hepatitis-B among HIV infected patients in South Africa.

Keywords: HBV; HIV; PLWH; UTT; Morbidity and Mortality

Introduction

Globally an estimated 257 million peoples are chronically infected with the hepatitis B virus (HBV). About 95% of these people are unaware of their HBV infection and do not have any health care interventions to reduce onward transmission. Around one-third of those chronically infected die as a result of serious liver disease [1,2]. According to the WHO global hepatitis report, HBV infection

responsible for 1.2 million deaths every year and which is similar to HIV/AIDs associated annual deaths (1.3 million) [2]. The Western Pacific and African regions together accounted for two-thirds (68%) global burden of HBV. A range of global prevalence (5.1% to 7.6%) was reported depending on gender, ethnicity and geographic areas. The highest prevalence of HBV infection was reported among black men and boys born in rural areas that placing further health care constrain on under-resourced rural settings [2,3].

HIV epidemic is accountable for higher HBV transmission rates and associated morbidity and mortality. HBV co-infection among PLWH has the potential risk of perinatal transmission [4]. It also promotes an aggressive disease course by increasing HBV replication and reactivation that leads to acute liver failure, progression to liver fibrosis and cirrhosis. Patient with chronic HBV infection is predisposed to hepatocellular carcinoma occurring at a younger age and higher risk of Antiretroviral therapy (ART) related hepatotoxicity [5].

Hepatitis B Virus (HBV) co-infection among PLWH remains a major health concern in sub-Saharan Africa including South Africa [6]. Both diseases have the same route of transmission and endemic in sub-Saharan Africa. An estimated 2.6 million PLWH has HBV coinfection in Sub-Saharan Africa [1,7]. A recent systemic review by Jean Joel Bigna A., *et al.* (2018) reported the prevalence of HBV coinfection among PLWH is ranging from 6% to 20% with variation within the different geographic regions in Africa [3].

There has been a recent clinical interest in HBV coinfection among PLWH due to its chronicity. Furthermore, there is evidence that HBV/HIV coinfection is associated with high morbidity and mortality than the individual infection alone [8]. Although the recent success of ART has dramatically decreased the opportunistic infection and increase survival among PLWH. This resurfaced the previously unrecognized chronic HBV infection in these groups. Importantly, the first-line ART can mask undiagnosed HBV co-infection, but there is a threat of Hepatitis flare up during change in ART regimen [9].

Despite the availability of safe and effective vaccines from the last three decades, Chronic HBV infection is a major cause of morbidity and mortality. HBV co-infection among PLWH had a higher risk of HBV infectivity and reactivation due to the alteration of immunity by HIV infection [4]. The HBV coinfection among HIV positive pregnant women is more important as it determines the vertical transmission of infection in utero and during parturition [5]. In May 2016, the WHO created a global health sector strategy on viral hepatitis with aims to achieve a 90% reduction in new infection and a 65% reduction in mortality due to HBV by 2030. WHO recommended routine HBV screening in countries where prevalence is higher than 2% to identify who are infected [2].

The vaccine is freely available in South Africa, as part of the childhood Expanded Programme on Immunizations (EPI) since April 1995 [10]. The burden of chronic hepatitis B infection among

PLWH in South Africa (SA) is mostly underestimated. This is further complicated by the lack of routine screening and surveillance, especially in primary health care settings.

Aim of the Study

This study aimed to determine the prevalence of HBV co-infection among PLWH who attending primary health care settings in the Mthatha region of South Africa.

Methods

Study design

A cross-sectional descriptive survey.

Settings

The study was conducted at the HIV Outpatient Clinic at Ngangelizwe and Mbekweni Community Health Centre (CHC) at King Sabata Dalindyebo (KSD) sub-district municipality in the Eastern Cape Province of South Africa. Mthatha is the main town in the KSD sub-district municipality. IsiXhosa is the dominant language of communication and most people depend on social welfare grants. Most people depend on state facilities for health care services.

Sample size

The sample size was calculated with a proportion of 50% of patients, 95% confidence intervals and a 5% margin of error then a sample of 385 was required. The sample size was further increased by 50% to overcome the poor response rate.

Selection of patients

A simple random sampling method was used. Every tenth patient, who visited the HIV clinic (between 15 June to 15 August 2018) was invited to participate in this study. Eligible subjects included HIV-infected adults (≥ 18 years) and on ART for more than six months. A patient who is severely ill or refused to give the consent was not included in the study. The study was approved by the Health Research Ethics Committee (HREC) of Stellenbosch University (HREC reference number: S18/01/001).

Clinical and laboratory measurement of participants

A structured questionnaire was administered by trained research assistants. The questionnaire included questions regarding age, sex, history of present or past self-described smoking, alcohol and other substance use. Laboratory-based hepatitis B surface antigen (HBsAg), CD4 count and viral load results from the last 12

months were retrieved from clinical records.

Data analysis

Descriptive statistical analysis was performed using SPSS version 18. Categorical data were reported as frequency and percentages and scale data were reported as mean and standard deviation or median and interquartile ranges if not normally distributed. Differences in demographic and clinical characteristics between patients with and without HBV infection were assessed using the chi-squared or Fisher's exact test for categorical variables and p-value <0.05 considered at significance level.

Results

Six hundred and two HIV infected patients participated. Amidst 208 (32.4%) patients were excluded because of no clinical records of HBV screening, the remaining 394 (65.6%) were analyzed for prevalence of HBV coinfection. The mean age of the participant was 37.8 years (SD \pm 10.5). The majority of participants were female (75.1%), unemployed (70.8%), and education level secondary school (85.2%). The prevalence of HBV coinfection among PLWH was 12.2% and the male had a three-time higher infection than female counterparts with a statistically significant difference ($\chi^2 = 12.8$, $p = 0.001$). The majority of HBV coinfection among PLWH were in age between 26 and 45 years. Although people younger than 26 years had the lowest prevalence of HBV coinfection and it increased with age but there the difference is not statistically significant. The HBV coinfection was more common among PLWH who smoke tobacco and cannabis. Although, there was a slightly higher prevalence of HBV coinfection among PLWH who used alcohol the difference was not statistically significant. The median CD4 count of participants was 508 with Inter Quadrantile Range (IQR) 307 to 715. The prevalence of HBV coinfection was marginally high among PLWH who had a viral load of ≥ 1000 copies/ml. Table 1 represents the demographic and clinical characteristics of a lifetime and current substance use among PLWH.

The box and whiskers plot in figure 1 demonstrated that young male was more likely to be co-infected with HBV than their older counterparts. More outliers were noticed in both genders in Hepatitis B negative groups. Figure 2 demonstrated that male participants had lower median CD4 than female counterparts but there is no difference in CD4 count and HBV infection in both genders.

	Hepatitis-B		χ^2	P-value
	Positive	Negative		
Age (Years)				
18 - 25	4(9.5%)	38 (90.5%)	1.81	0.6
26 - 35	16 (11.8%)	120 (88.2%)		
36 - 45	20 (15.0%)	113 (85.0%)		
46 and above	8 (9.6%)	75 (90.4%)		
Gender				
Male	22 (22.4%)	76 (77.6%)		
Female	26 (8.8%)	270 (91.2%)	12.85	0.001*
CD4 count				
< 200	6 (14.3%)	36 (85.7%)	0.41	0.52
≥ 200	34 (10.9%)	277 (89.1%)		
Viral Load				
< 1000	32 (10.7%)	268 (89.3%)	1.6	0.19
≥ 1000	6 (18.2%)	27 (81.8%)		
RPR				
Positive	3 (14.3%)	18 (85.7%)	0.28	0.5
Negative	18 (10.5%)	154 (89.5%)		
Alcohol use				
Yes	28 (14.2%)	169 (85.8%)	1.4	0.2
No	20 (10.2%)	176 (89.8%)		
Tobacco use				
Yes	20 (17.4%)	95 (82.6%)	4.1	0.04*
No	28 (10%)	251 (90%)		
Cannabis use				
Yes	6 (27.3%)	16 (72.7%)	4.9	0.02*
No	42 (11.3%)	329 (88.7%)		
*P < 0.05				

Table 1: Demographic characteristics of Hepatitis-B co-infection among people living with HIV (n = 394).

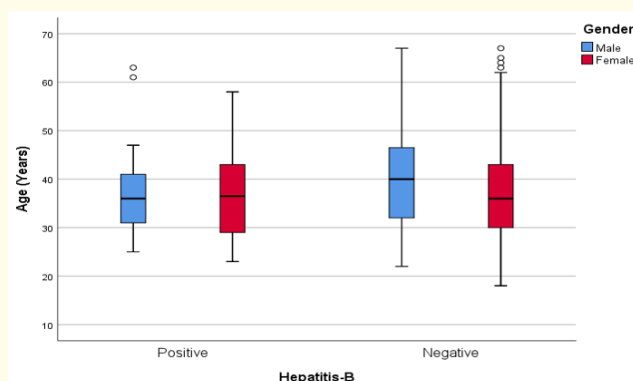


Figure 1: Age and gender distribution of Hepatitis-B coinfection among PLWH.

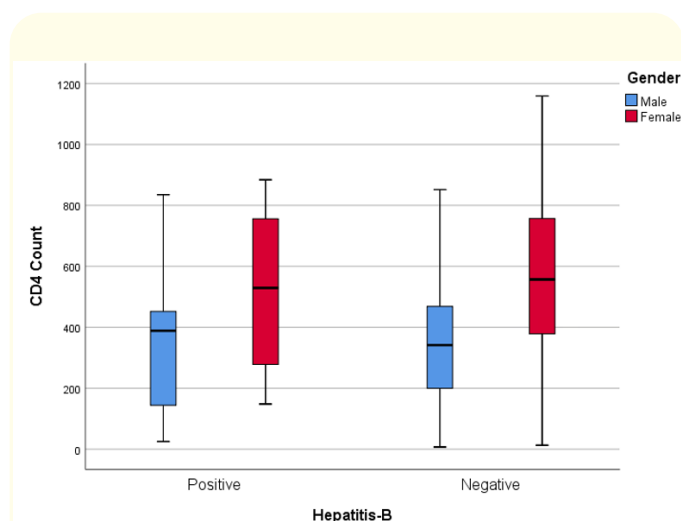


Figure 2: CD4 count and gender distribution of Hepatitis-B coinfection among PLWH.

Discussion

The study reported that HBV coinfection is common among PLWH. Although the prevalence of HBV coinfection was lower than many recent studies reported in South Africa. A study conducted by Chonco and Rangiah reported a much higher (25%) prevalence of HBV coinfection among PLWH in Durban [8]. Another study from Limpopo reported about 20% PLWH to have HBV coinfection [11]. The prevalence of HBV infection among PLWH reported from a range of 6% to 20% in the different geographic regions of Africa. A systemic review and meta-analysis by Bigna JJ, *et al.* (2018) reported that an overall 12.9% PLWH in Africa has HBV coinfection and these findings are similar (12.2%) to this study [3].

Despite the WHO recommendation of baseline screening of HBV in a country where prevalence is more than 2%, about one-third (32.4%) participant had not screened for HBV coinfection. Recently American and European guidelines also recommended routine screening of HBV infection among newly diagnosed HIV patient [1,2]. It is recommended routine screening of HBV among PLWH, even in resource-limited settings where hepatitis is endemic. There is a large reservoir of chronic HBV infection in sub-Saharan Africa [1]. The identification is very difficult because chronic HBV infection is asymptomatic and only presenting when

complications arise. To prevent the life-threatening complications of HBV coinfection among PLWH such as cirrhosis, liver failure, and hepatocellular carcinoma, it is essential to early identification of the individuals who are infected [5,12]. An integrated screening programme is needed to determine the real impact of HBV on the HIV epidemic in South Africa.

A significant gender difference ($p = 0.001$) in the prevalence of HBV co-infection among PLWH was demonstrated in the current study. The HBV coinfection was three-time higher among males compared to their female counterparts. The most study conducted in South Africa demonstrated a similar trend of male predominant HBV/HIV coinfection [11,12]. Polygamy and multiple sexual partners is a common practice in many African cultures and the sexual root of transmission could be a possible explanation of the high prevalence of HBV coinfection among male participants.

Importantly, we found that the median age of HBV coinfecting people in both genders was between the age group of 26 and 45 years. The people born before 1995 (older than 25 years) had had a high prevalence of HBV coinfection and this age distribution may reflect the protective effect of childhood HBV vaccination. Since 1995 the Hepatitis-B vaccine is part of the expanded programme on immunization (EPI) in South Africa [10].

The study showed that the majority of the participant had CD4 count more than 200 cells/mm³ in both genders. These results support the universal test and treat (UTT) programme rollout in South Africa. Since the UTT implementation the average CD4 count of HIV patients has been raised [13]. Since most of the study in South Africa was conducted before the rollout of the UTT programme when ART usually initiated with CD4 less than 200 cells/mm³ and findings from these studies support an association between low CD4 count and HBV coinfection. In this study, we found that median CD4 count among male participants was lower than female counterparts but there was no difference between HBV coinfection and median CD4 count in both genders.

It is well documented that the natural history of HBV infection can be influenced by the presence of HIV and the severity of immunosuppression [2,12]. Although our study reported that there is a slight high prevalence of HBV coinfection among PLWH who presented with high viral load (≥ 1000 copies/ml) but it was not statistically significant.

Furthermore, the study stated that HBV coinfection was more common among PLWH who use the substance (Alcohol, tobacco, and cannabis). Most studies supported the association between alcohol and cannabis use and risky sexual behavior that leads to a high prevalence of HBV coinfection in this group of population [6,14].

Conclusion

There was a high prevalence of HBV coinfection among PLWH, who attending primary health care settings in the Mthatha region of South Africa. Despite the high burden of HBV coinfection, there was a lack of routine screening of HBV among PLWH in primary health care settings. Therefore, a comprehensive and integrated HBV screening programme is recommended for adequate management and follow-up of hepatitis B infection among PLWH. Hence, primary prevention through vaccination is showing the yield by decreasing HBV coinfection among people who born after 1995. It is recommended to the policymaker to scale up the vaccination coverage to interrupt the transmission of HBV infection among PLWH.

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Conflict of Interest

The authors declare no conflict of interest.

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Authors' Contribution

Dr. R Kaswa was responsible for the project design, data collection, and initial draft design. Prof. Marietjie de Villiers made a major contribution and corrections of the manuscript writing.

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