

Sero-prevalence of Hepatitis B Surface Antigens (HBsAg) and Its Risk Factors among People Attending Voluntary Counselling and Testing (VCT) Centre and Anti-retroviral Therapy (ART) Clinics of Goba Hospital.

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Abstract

Hepatitis B Virus (HBV) infection is significant health problem, as it can lead to chronic hepatitis, liver cirrhosis, and hepatic carcinoma. Approximately 400 million person worlds wide have chronic HBV infection and up to 1 million die annually from HBV related liver disease (1). Factors associated with HBV propagation include blood and derivates transfusion, sexual contact, equipment contamination and contact among patients as well as between them and health-care workers. On the other hand acquired immune deficiency syndrome (AIDS) has been described as the most devastating disease human kind has ever faced (2). The aim of this study was to determine the prevalence of hepatitis B surface antigen (HBsAg) and its risk factors, among individuals visiting Goba Hospital. A cross-sectional analysis was performed on 168 VCT clients from June 01, 2009 to August 31, 2009. Sociodemographic and risk factors data were collected using structured questioner. Blood samples were collected and screened for HBsAg by commercially available rapid test kit and HIV screening was performed by rapid test kist as KHB for screening and positive samples were tested with STATPACK. Samples giving discordant results in the two tests were re-examined using tie-breaker, (Uni-Gold HIV). The prevalence of HBsAg in VCT clients was 7%, of the HBV infected persons 8(66.6%) were seropositive for HIV. In this study significantly high prevalence of HBsAg marker was observed on the occupation of individual's higher rate and the difference were found statistically significant, even though the result was statically non significant the prevalence of HBsAg was increased with the age. This study suggests that hepatitis B infection has high prevalence in VCT centres of Goba Hospital. Therefore, preventive measures program should be implemented at the Hospital, especially at the VCT centres and these patients should be identified early and managed appropriately so as to reduce the risk of long term complications like cirrhosis.

Keywords: HBsAg, HIV, Goba Hospital, Ethiopia

1. Introduction

Chronic viral hepatitis is the principal cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma in the world and now ranks as the chief reason for liver transplantation in adults. Of the five known hepatitis viruses; three can cause persistent infection and chronic hepatitis: the hepatitis B virus (HBV) the hepatitis C virus (HCV) and the hepatitis delta (hepatitis D) virus (HDV) (3). Hepatitis B virus (HBV) is one of the major diseases of mankind that has shown to cause serious public health problem (4). Approximately 400 million person worlds wide have chronic HBV infection and up to 1 million die annually from HBV related liver disease. In the United States, up to 1.25 million are infected with HBV and chronic hepatitis B accounts for 5 to 10 percent of chronic liver disease and cirrhosis (5,1). The global prevalence of HBV infection varies widely and its endemicity ranges from high (>8%) to intermediate (2-7%) and low (2%) (4). High endemic areas are those parts of the world where almost all infections occur during the preinatal period of early in childhood (example, South East Asia and sub-Saharan Africa). In most developed parts of the world such as Western Europe, USA, Australia, the endemicity of HBV infection is low and most infections occur among high risk adult populations that include injection drug users, person with multiple heterosexual patterns, and among homo sexual men (6). Hepatitis B is a serious and common infectious disease of the liver, affecting millions of people throughout the world. (7) The severe pathological consequences of persistent HBV infections include the development of chronic hepatic insufficiency, cirrhosis, and hepatocellular carcinoma (HCC). In addition, HBV carriers can transmit the disease for many years (7). More than 2 000 million people alive today have been infected with HBV at some time in their lives. Of these, about 350 million remain infected chronically and become carriers of the virus. Three quarters of the world's population live in areas where there are high levels of infection. Every year there are over 4 million acute clinical cases of HBV, and about 25% of carriers, 1 million people a year, die from chronic active hepatitis, cirrhosis or primary liver cancer (2). HBV may be the cause of up to 80% of all cases of hepatocellular carcinoma worldwide, second only to tobacco among known human carcinogens (8). HBV is transmitted through percutaneous or parenteral contact with infected blood, body fluids, and by sexual intercourse (7). Sexual intercourse with multiple partners or with persons who have multiple partners can be dangerous. One should not judge by appearance: most infected people look perfectly healthy and have no symptoms of disease, yet may be highly infectious. All persons who are hepatitis B surface antigen (HBsAg)

positive are potentially infectious. Many millions of people around the world who become HBV carriers are a constant source of new infections for those who have never contracted the virus (9). Blood is infective many weeks before the onset of the first symptoms and throughout the acute phase of the disease. The infectivity of chronically infected individuals varies from highly infectious (HBeAg positive) to often sparingly infectious (anti-HBe positive). Hepatitis B is the only sexually transmitted infection for which there is a protective vaccine (10). Following acute HBV infection, the risk of developing chronic infection varies inversely with age. Chronic HBV infection occurs among about 90% of infants infected at birth, 25-50% of children infected at 1-5 years of age and about 1-5% of persons infected as older children and adults. Chronic HBV infection is also common in persons with immunodeficiency (8). The world can be divided into three areas where the prevalence of chronic HBV infection is: high (>8%), intermediate (2-8%), and low (<2%) (10). High endemicity areas include south-east Asia and the Pacific Basin (excluding Japan, Australia, and New Zealand), sub-Saharan Africa, the Amazon Basin, parts of the Middle East, the central Asian Republics, and some countries in Eastern Europe. In these areas, about 70 to 90% of the population becomes HBV-infected before the age of 40, and 8 to 20% of people are HBV carrier (8). In countries such as China, Senegal, and Thailand, infection rates are very high in infants, and continue through early childhood. At that stage the prevalence of HBsAg in serum may exceed 25%. In Panama, New Guinea, Solomon Islands, Greenland, and in populations such as Alaskan Indians, infection rates in infants are relatively low and increase rapidly during early childhood (8). In Ethiopia, a previous population survey that examined for serological evidence of exposure to Hepatitis A, B and delta infection reported a prevalence rate of 6.2% and 39.8% for HBsAg and overall HBV markers respectively (11). Moreover, in Addis Ababa, a community based sero-epidemiological survey that addresses the transmission dynamics and control of hepatitis B virus infection estimated HBsAg prevalence rate of 7% for general population (12, 13). HBsAg prevalence rates of 5% in women attending clinics and 3.7% among pregnant were also reported in Addis Ababa and Jimma respectively (14). On the other hand Acquired Immuno deficiency Syndrome (AIDS) has been described as the most devastating disease human kind has ever faced (2). At the end of 2005, The joint United Nations Programme on HIV/AIDS and World Health Organization (UNAIDS, WHO) estimated 38.6 million persons have been living with human immune deficiency virus (HIV) globally, of whom more than 65% of cases live in sub-Saharan Africa (15). In Ethiopia, an estimated 1.59 million people were infected with prevalence rate of 4.6% in 2004 (16). According to, the prevalence of adult infections 2.1% (urban 7.7%, rural 0.9%) (17). In sub-Saharan Africa, including Ethiopia, heterosexual exposures are responsible for most HIV infections (18). HIV infected people are three to six times more likely to develop a Chronic or long term hepatitis B infection because of their weakened immune systems than individuals without HIV (19) and people co-infected with both hepatitis B and HIV are 14 to 17 times more likely to die than those with hepatitis B alone. In addition HIV co-infection with HBV has also been associated with increased hepatotoxicity to highly active anti retroviral therapy (HAART). Consequently, its recognition and treatment has increasingly received attention (1). HBV-related liver disease in HIV infected patients are more progressive, including the development of cirrhosis and its complications, compared to patients with HBV infection only; and thus contribute significantly to the morbidity and mortality of HIV infected patients (11). The increase in liver related mortality appears to be more pronounced when co-infected patients are treated with (HAART). This might be due to increased liver injury as consequence of immune restoration under HAART, and hepatotoxicity of certain anti-viral drugs. Moreover; the longer life expectancy of patients treated with HAART let them to develop complication of their liver disease (20).

More than 8 % of Ethiopia is infected by hepatitis B. You can have hepatitis B without feeling or looking sick. You can infect other people without knowing it. Therefore it is highly important for you to know if you have the virus in your system.

In Ethiopia, information on the magnitude of HBV infection at different risk group is scarce. Thus, studies to monitor the infection patterns and associated risk factors are important to undertake effective prevention and control measures. Since HIV and HBV have common means of transmission; they also have common means of prevention. Voluntary counselling and testing of HIV is advocated to play a great role in the effort to reduce and prevent the spread of HIV infection. Therefore, this study was conducted in clients of VCT centre Goba Hospital to determine the prevalence of hepatitis-B surface antigen (HBsAg) and its risk factors.

It is estimated that over 2,000million people have been infected with HBV, that there are over 300 million carriers of the virus and more than 2 million deaths occur every year as a direct result of HBV infection (21). The Global HBV endemicity ranges from high (>8%) to intermediate (2-7%) and low (< 2%) (22). In North America and Western Europe, the prevalence of the hepatitis B surface antigen (HBsAg) carrier state is 0.1% to 0.5% while in Sub Saharan Africa, Asia, the Middle East and the Mediterranean regions, it is 5% to 20%, with a tendency to be higher in the evidence of past exposure to HBV infection (23). In Ethiopia, different population based studies revealed medium to high endemicity of HBV infection, depending on age and sex, the HBsAg carrier state is between 8% and 12% and the overall HBV marker prevalence is between 42% and 79% in the general population (Tsega et al., 1991). In the study conducted at St. Paul's General Specialized Hospital, the prevalence of HBsAg and anti HBe in VCT clients was 5.7% and 44.8%, respectively and among HIV infected

persons, 3.9% were sero positive for HBsAg (24). The HBsAg carrier state is 2:1 in favor of males (25). The prevalence of HAV and HBV markers increases with age. Infection rates between 72% and 87% were reported for normal adults from population surveys and from among blood donors and hospital staff and from 13% to 31% for normal children below 15 years of age (25). Also, of 5270 military recruits from all regions of Ethiopia and within a restricted age range (18-30 years) the prevalence of HBsAg and overall HBV markers were 10.8% and 73.3%, respectively (26). In Addis Ababa also there was a study carried out a community-based sero epidemiological survey of Addis Ababa, Ethiopia was conducted in 1994 to inform on the transmission dynamics and control of hepatitis B virus (HBV) infection. Venous blood from 4736 individuals under 50 years of age from 1262 households, selected using stratified cluster-sampling, was screened for HBV markers using commercial ELISAs. HBsAg prevalence was 7% (95% CI 6-8), higher in males (9%; 7-10) than females (5%; 4-6). HBeAg prevalence in HBsAg positive was 23% (18-29), and less than 1% of women of childbearing age were HBeAg positive. Overall HBV sero-prevalence (any marker), rose steadily with age to over 70% in 40-49 years old, indicating significant childhood and adult transmission. Estimated instantaneous incidence was 3-4/100 susceptible/year, higher in males than in females in 0-4 years old, and peaking in early childhood and young adults. The age at which 50% had evidence of infection was around 20 years. And the herd immunity threshold is approximated at 63-77%. Addis Ababa is of intermediate-high HBV endemicity, with negligible prenatal transmission. Our main findings are the identification of a significant difference between males and females in the age-acquisition of HBV infection, and marked difference between age groups in HBV incidence rates. These results should target future research studies of underlying risk factors. Furthermore, we generate a crude estimate of the level of coverage of HBV vaccine that would be required to eliminate the virus from study population (27)

Statement of the problem

The prevalence of HBV infection varies markedly throughout regions of the world. Hepatitis B is highly endemic in developing countries with large population such as South East Asia, China, sub-Saharan Africa including Ethiopia and the Amazon Basin, where at least 8% of the population are HBV chronic carrier. In these areas, 70–95% of the population shows past or present serological evidence of HBV infection. Most infections occur during infancy or childhood. Since most infections in children are asymptomatic, there is little evidence of acute disease related to HBV, but the rates of chronic liver disease and liver cancer in adults are high (28).

Sub-Saharan Africa is with the highest rates of HCC incidence >50/100,000 population (29). A prospective study in Taiwan (30). Showed that relative risk of HCC among men who were positive for both HBsAg and HBeAg (RR=60.2) were much higher than that among men who were positive for HBsAg alone (RR=9.6). In co infected patients, HBV infection is more likely to take a chronic course (31) and has a higher replication rate (32). In addition, a liver disease due to HBV in HIV infected patients are more progressive and ultimately leads to higher morbidity and mortality, particularly in those receiving anti retroviral therapy (ART) (33).

In Ethiopia, a previous population survey that examined for serological evidence of exposure to Hepatitis A, B and delta infection reported a prevalence rate of 6.2% and 39.8% for HBsAg and overall HBV markers respectively (11). In this country, information on the magnitude of HBV infection at different risk group is scarce or under reported. Hence, studies are important to monitor the infection patterns and associated risk factors to undertake effective prevention and control measures. So, that this study was designed and conducted in this country.

Methods and Materials

Description of the Study area

The study was conducted at Goba Hospital, which is found in Bale Zone, Oromia Regional State, Robe is the capital town of the Zone and found at distance of 430 km South-East of Addis Ababa, Ethiopia. Goba is found at 445 km South-East of Ethiopia. The hospital delivers service nearly for about 800,000 populations in the catchments area. When we look at man power of the hospital: Different health professionals are 90 (ninety) including 3 (three) specialists. Supportive staff is about 86 (eighty six). Generally, the overall population distribution in the zone is 88.9% Oromo, 7.6 % Amhara, and 3.5% other Ethiopian Nations and Nationalities (34). The health service coverage of the Zone reaches at 80%. In the hospital the VCT centres routinely deliver HIV counselling and testing. People whose results become positive for HIV infection were transferred to the ART clinics for clinical and laboratory investigations to monitor their disease status; those who are eligible received ART. Hepatitis B testing was not routine activity of the hospital so far.

Duration of the study

The study period was from June 01, 2009 to August 30, 2009

Study design

A hospital based cross-sectional study was conducted.

Study population

The study population was all individuals attending VCT centre of Goba Hospital.

Sample size and sampling technique

Sample size was calculated by single proportion formula 50% prevalence assumption, 95% CI and $p \leq 0.05$ (35)

$$N = \frac{Z^2 \cdot p \cdot \text{expe.} (1 - p \cdot \text{expe.})}{d^2}$$

Where N= sample size,

Z= statistic for a level of confidence,

P= expected prevalence and

d= precision

Based on the above formula, sample size was determined with 95% confidence interval and a precision of 5% is calculated using the seroprevalence of HBsAg is estimated to be 50%. Since there was no HBsAg study conducted in the area, so estimated prevalence of HBV in VCT clients was set at 50% to yield maximum sample size (n=385).

Data Collection

Socio-demographic characteristics and risk factors were assessed. Counsellor nurses interviewed the study subjects using pre tested structured questionnaire on socio-demographic characteristics and other risk factors including family history of hepatitis infection, blood transfusion and others.

Specimen collection and processing

About 5ml of blood sample was collected by vein-puncture from each of the participants. Whole blood was used for HIV screening tests while sample used for HBsAg screening was centrifuged and serum was separated.

Serological test

At the VCT site, HIV status of all participants was obtained from the counsellor nurse using client's identification number. The hospital routinely uses commercial HIV test kits as (KHB, shangha Kehua Bio engineering Co., Ltd. China) for screening and positive samples were re-tested with STAT-PACK.

Samples giving discordant results in the two tests were re-examined using tiebreaker, (Uni-Gold HIV, Trinity Biotech PLC, Co. Wicklow, Ireland). All sera were screened for HBsAg using commercially available HBsAg screening rapid test kit.

Quality Control

To ensure quality, routine checkups for completeness, consistency, accuracy and clarity of the data was checked. Pre-tested questioner was conducted before actual data collection to ensure the quality of the questionnaire. Trained and experienced laboratory technologists have performed laboratory tests.

Data analysis

Data were coded entered, cleaned and analyzed using SPSS version 20 (IBM, USA). Descriptive statistics like; numerical summary measures and frequencies were used for describing the study population. The result was summarized using descriptive statistics.

Ethical clearance

The Ethical committee of Mada Walabu University assured or certified, also Separate permission was obtained from MWU, Health Science College. The purpose of the study was explained to the participants and written consent was obtained before sampling. The participants were assured that all the information was kept confidentially and the samples were utilized only for research purpose.

Result

This study was conducted at Goba Hospital VCT center. 168 individuals were approached and screened for their HBsAg and HIV sero status. The Majority of participants were from Goba town and surroundings. Of the total, 56% and 44% female and male respectively. Among the study subjects 39.2% married, 25% single, 20% divorced and 16% widowed. The majority (37%) of the participants belong to 30-39 years of age. The details of sociodemographic characteristics of the participants were presented in table 1. Out of 168 participants 81(48%) of clients found to be seropositive to HIV, but 87(52%) were found to be negative. The prevalence of HBsAg among attendants was found to be 12 (7%). From which 8(66.6%) and 4 (33.4%) were female and male respectively. The distribution of hepatitis B surface antigen in different risk factors was shown in table 2. Among HBsAg 8(66.6%) was found to be positive to HIV as well and 4(33.4%) were negative to HIV, indicated in table 3.

Table 1: Socio-demographic characteristics and proportion of Hepatitis B surface antigen (HBsAg) among different categories of the study subjects at Goba Hospital, 2009

Characteristics	Total%	Total (%) positive for HBsAg	P- value
Age			P>0.05
<20	18(10.7%)	%	
20-29	43(25.5%)	3(7%)	
30-39	62(37%)	5(8%)	
40-49	24(14.2%)	3(12.5%)	
>50	21(12.5%)	1(4.7%)	
Marital Status			P > 0.05
Single	42(25%)	%	
Married	66(39.2%)	7(25%)	
Divorced	33(20%)	3(9%)	
Widowed	27(16%)	2(7.4%)	
Religion			P > 0.05
Muslim	38(23%)	%	
Orthodox	111(66)	7(25%)	
Protestant	19(11.3%)	3(9%)	
Other	38(23%)	2(7.4%)	
Occupation			P< 0.05
Merchant	35(21%)	5(14.2%)	
Farmer	24(14%)	3(12.5%)	
Gov.employee	21(12.5%)	%	
Driver	2	%	
Daily labourer	44	2(4.5%)	
Other	42	2(4.7)	

Table 2: Distribution of Hepatitis B virus (HBsAg) in subjects with different risk factors at Goba Hospital

S.No	Characteristics	Total (%)	No (%) of positive for HBsAg	P-value
1	Family history regarding hepatitis B infection			P > 0.05
	Yes	6 (4%)	1 (17%)	
	No	162 (96.4%)	11 (7%)	
2	Contact with infected blood (blood transfusion)			P > 0.05
	Yes	20 (12%)	1 (5%)	
	No	148 (88%)	11 (7.4%)	
	Unsafe injection			P > 0.05
	Yes	29 (17.2%)	2 (7%)	
	No	139 (83%)	10 (7.1)	
3	Have you ever had sex with hepatitis B virus infected individuals			P > 0.05
	Yes	1 (0.5%)	1 (100%)	
	No	167 (99.4)	11 (7%)	

Table 3: Hepatitis B virus surface antigen markers in HIV positive and HIV negative individuals at Goba Hospital

HBsAg in HIV Positive subjects	HBsAg in HIV negative subjects	HBsAg in both subjects (total positive individuals)
8 (66.6%)	4 (33.4%)	12 (71%)

Discussion

In this study, the rate of hepatitis B virus infection among VCT clients of Goba Hospital was determined. The result showed an overall prevalence of 7% for hepatitis B virus infection. The current finding agree or par with the Previous survey at Addis Ababa that community based sero-epidemiological survey which address the transmission dynamics and control of hepatitis B virus, (12,13), reported HBsAg prevalence rate of 7% for

general population. Again this study more or less agree with study done in Gondar city showed that of the 302 street dwellers examined 33 (10.9%) were found to be positive for HBsAg. The 28.9% prevalence in females was significantly higher than the 8.3% prevalence in males (OR=4.5, 95%CI 1.8-11.0 P=0.001). The seroprevalence of HBsAg consistently increased with an increase in age (Table 1). However, there was no significant association between HBV infection and the number of sexual partners. Similar to HIV infection and syphilis, educational status was not a factor for HBV infection in this specific population (36). On the other hand the current finding is disagree with the study conducted in Addis Ababa and Jimma on the prevalence of HBsAg among pregnant women rate of 5% and 3.7% were reported in respectively (14). This might be due to the methodological difference and study subjects or purposive sampling method. Again our finding is at par with study conducted at Shashemane on the prevalence of HBsAg in VCT clients at Shashemane General hospital the prevalence was reported 5.8% (37). Although quantitative comparison was difficult due to methodological difference, however, the result of the prevalence of this study showed similarity with the other studies done at different sites of the country. This might indicate that, the study subjects have similar risk factors with those in Addis Ababa, Shashemane and Jimma. The prevalence of HBV in the general US population (0.4%) and prevalence of HBV in HIV infected pregnant women was (1.5%) (1), however, the prevalence of HBV found in this study is higher compared to studies done in US. This could be due to the fact that in most developed parts of the world (example, Western Europe, USA, Australia), the endemicity of HBV infection is low and most infections occur among high risk adult populations that include injection drug users, person with multiple heterosexual patterns, and among homo sexual men (6). In this study, higher HBsAg (66.6%) positivity rate was observed among HIV positive individuals. This is comparable with study done by (6) which documented an increased occurrence of HBV among HIV positive individuals. This could be due to the fact that both HBV and HIV shares common means of transmission and risk factors. However, in contrast to this study (11) in Addis Ababa, and other study from South Africa (38) showed lower prevalence rate of HBV among HIV positive individuals. This might be partly due to effect that some HIV drugs such as; lamivudine had effect on HBV and in turn, on elimination of HBsAg (39). This current agreed with other study conducted in Ethiopia showed that of total of 500 individuals from five different regions of Ethiopia were studied. Demographic and clinical data were recorded and serologic tests were carried out to detect antigen and antibody markers of hepatitis B virus, hepatitis A virus, and the delta agent. Data on the economic status, number of rooms per household, number of persons per household, type of water supply, and mode of excreta disposal revealed that the majority of the population surveyed lived with economic hardship, overcrowding and poor hygiene. Only 36 persons gave a past history of jaundice. The mean carrier rate of hepatitis B surface antigen (HBsAg) was 6.2%, the mean overall hepatitis B virus marker prevalence was 42%, and in those over 14 years of age it was 76%. Among those who were positive for HBsAg, there was a tendency for hepatitis B e antigen (HBeAg) to decrease and the corresponding antibody (anti-HBe) to increase with advancing age. No woman more than 15 years of age had demonstrable hepatitis B antigen in serum. Antibody to hepatitis A virus was detected in 84%. Three HBSAg-positive individuals were found to have antibody to the delta agent (27).

The current study also revealed a slightly higher rate of HBsAg in females when compared with male participants. This higher rate of HBsAg in females may be attributed to the greater chance to become infected and might be due to slightly larger sample size of female, than male in this study. On top of this, majority of the females sampled were commercial sex workers in the Goba town. Analysis of age related seropositivity for HBsAg marker showed a tendency to increase, as the individuals get older though the difference was non-significant. The prevalence of HBsAg is higher in the age group of 30-39 (8 %) and this is comparable with the study done in Kosovo among blood donors (40). This might be explained by the fact that risk of exposure to HBV infection increase with time. In this study we found that occupation has played great roll in the prevalence of HBsAg and the difference was found statistically significant ($P < 0.05$). Individuals who had multiple sex partners, blood transfusion, and unsafe injection and having sexual contact with HBV infected person were infected with HBV at higher rate, although the difference was no significant. But the transmission was found to be 100% in the case of having sexual contact with HBV infected person. This may also support the hypothesis that horizontal transmission is the major source of HBV infection in the community (41).

Conclusion and Recommendation

This study was conducted in Goba Hospital for two months (June to August, 2009). With the overall objective of to determine the prevalence of HBsAg and its risk factors among people attending VCT centre and ART. The prevalence of hepatitis B infection was found to be high at VCT centre of Goba Hospital. Also its prevalence was found higher in HIV infected individuals. This study identified family history, having multiple sexual partners, occupations, having sex with infected individuals and unsafe injection were as risk factors for HBV infection.

It can also be concluded from this study that there is high prevalence of HBV in the area and preventive measures should be advocated targeting the high-risk groups also routine HBV screening program should be

implemented at the hospital, especially at the VCT centre and these patients should be identified early and managed appropriately so as to reduce the risk of long term complications like cirrhosis. High risk groups like health care workers should get vaccine for HBV. Awareness creation through health education about its transmission and prevention methods is also believed to reduce the prevalence of the HBV infection among the general population. Additionally, these data contribute to the mapping of viral hepatitis prevalence in this geographic area and therefore helpful in planning public health interventional strategies. Lastly, further studies should be conducted to determine the magnitude of HBV and its risk factors among VCT clients in the zone.

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