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ABSTRACT

***Background*: Hepatitis B Virus (HBV) and HIV spread in the same manner, but HBV is more infectious than HIV-1. Active HBV requires modification of HIV-1 therapy and is associated with increased risk for sexual transmission of HBV.**
***Objective*: To determine the prevalence and knowledge of HBV among HIV-1 discordant couples.**
***Design*: A cross-sectional study.**
***Setting*: Couple Counselling Centres in Nairobi and Thika clinics in Kenya.**
Subjects: HIV discordant couples attending Couples Counselling Centres in Nairobi and Thika clinics in Kenya.
***Results*: One hundred and sixty one couples with a mean age of 33 years (Standard Deviation 8.4) were enrolled into the study. HBV prevalence was higher among HIV positive women than among HIV negative women (10.2% vs. 5.9%, OR=0.5, 95% CI 0.2-1.0; p=0.05). However, among men, prevalence of HBV was higher among the HIV negative than the HIV positive participants (8.4 vs. 6.2%, OR=3.0, CI 1.3-6.5; p=0.04). There was no association between HBV and HIV (p=0.4) or gender (p=0.5). HIV positive participants were more likely to have adequate knowledge compared to HIV negative participants (13% vs. 3.7%, OR=2.7, 95% CI 1.95-7.9; p=0.05)**
***Conclusions*: Female index participants had the highest HBV prevalence. Knowledge on HBV was lacking, particularly among the HIV negative; a target group for health education regarding risk factors and prevention of HBV infection.**

INTRODUCTION

The World Health Organization (WHO) estimates that about two billion people worldwide are infected with the Hepatitis B Virus (HBV), and an estimated one million people die each year due to the acute or chronic consequences of Hepatitis B (1). Africa carries the major burden of HIV infection and, along with Asia, is the largest reservoir of chronic HBV. HBV is the most common cause of chronic liver disease worldwide with 400 million chronic carriers, of whom 50 million are estimated to reside in sub-Saharan Africa (2,3).

There are currently 35 million people infected with HIV-1, with over four million people newly infected and 1.5 million HIV-1 related deaths in 2013 (4). Worldwide HBV prevalence ranges from 0.1 to 20%. This wide range is largely due to differences in age at the time of infection (5). An estimated 10% of all HIV infected people have chronic HBV, implying that about 40 million people are HIV/HBV co-infected (6). Kenya has an active HBV prevalence of 10-15% (7)

Impact of HIV on HBV: HIV infected patients are less able to clear HBV infection compared to HIV uninfected people (8). An increase in the incidence of liver cancer and in patients with HIV-1 and HBV co-infection compared to HIV mono infection is well documented (9,10). Additionally, HIV increases the progression to liver cirrhosis and hepatocellular carcinoma (11). Liver disease due to chronic HBV infection is becoming a leading cause of death among persons co-infected with HIV-1 infection worldwide (12) with liver related mortality being higher among HBV/HIV co-infected patients (12,13).

Impact of HBV on HIV

Recent data does not show any impact of HBV

on HIV (14), though contrasting data exists on previous studies which concluded that HBV causes progression of HIV (15), while others did not show any impact on HIV progression (16). However, HBV co-infection requires modification of anti-retroviral regimens and may contribute to morbidity to HIV-1 infected individuals (17,18) , as well as increasing the risk for hepatotoxicity of HAART and likelihood of onset of an AIDS-defining illness, compared with infection with HIV-1 alone (7).

Studies on HBV among discordant couples in Kenya have not determined specific prevalence among stratified HIV infected or uninfected male and female participants. Knowledge of HBV was not determined from the studies.

Our study aimed to determine the prevalence of HBV and association between HBV infection and knowledge of HBV among HIV-1 discordant couples. For this study, previous HBV status was defined as a HBsAb positive test and active HBV status was defined as a HBsAg test positive.

MATERIALS AND METHODS

Study Area: The study took place in the Couple Counseling Centres in Nairobi and Thika clinics in Kenya where HIV-1 discordant couples were followed up.

Variables: The study included active or previous HBV status as the outcome variable and HIV-1 status, knowledge of HBV infection, socio-demographic factors, gender, sexual behaviour and risk factors as potential predictors of HBV status.

Study population: The study population consisted of HIV-1 discordant couples where one partner was HIV-1 positive by two rapid tests and confirmed by double well Enzyme-linked immunosorbent assay (ELISA) test, and a negative HIV-1 partner whose two rapid tests are negative. The inclusion criteria into the study were guided by the parent clinical trial study.

Study procedures: We conducted an ancillary cross sectional study within the University of Washington Partners Pre-Exposure Prophylaxis (PrEP) study. The primary study was a phase III clinical trial, aimed at determining if administration of anti-retroviral (ARV) drugs to the negative partner will prevent HIV-1 acquisition. The clinical trial procedures have been described before (19). The PrEP study enrolled HIV sero-discordant couples aged between 18 and 65 years, and randomised the HIV negative participant to study drug or placebo. These couples were followed up for three to four years.

Laboratory procedures for HIV and HBV status were determined by the PrEP study as part of the initial screening and enrollment procedures. HIV-1 positive was determined by two rapid tests and confirmed by double well ELISA, while HIV-1 negative was determined by two negative rapid tests. HBsAb and HBsAg were determined by an ELISA (Murex HBsAg Version 3) for the detection of HBsAg in human plasma or serum. HBsAg and HBsAb have a specificity of about 97-99% and a sensitivity of 97-98% (20). Results of the tests were given to the patient prior to enrollment into the PrEP study.

Data collection and analysis: Quantitative data were acquired for the determination of prevalence rates of HBV, risk factors and knowledge of HBV infection in participants. Knowledge of Hepatitis B was determined by asking questions on HBV infection transmission, type of infection, prevention of HBV, organs primarily affected and complications of HBV. The first section of the questionnaires was administered to the couple together, and the section on risk factors was asked to each participant individually.

Purposive sampling was done as the patient came for their PrEP appointment visit. Information on risk factors predisposing the participants to possible infection was determined by asking questions on sharing of needles, history of blood transfusion, sexual behaviour by indication of sexual contacts per month, number of sexual partners since knowledge of discordance and use of condoms.

Socio-demographic, HBV and HIV status was gathered from the PrEP database, and linked to each participant by their unique identifying number. Data were entered onto the Windows XP Access data base computer programme and transported to STATA version 11.1 (StataCorp, College Station, TX, USA). Descriptive and inferential analysis was done using univariate logistic regression to determine the association between HIV infection, socio-demographic factors and risk factors with HBV prevalence with a two sided p-value and alpha value of 5%. Statistically significant associations at the p=0.05 level were added to a multivariate, logistic regression model to determine adjusted odds ratios.

Knowledge of Hepatitis B was determined by asking questions on 1) HBV infection transmission, 2) type of infection, 3) prevention of HBV, 4) organs primarily affected and 5) complications of HBV. Participants who answered three or more questions correctly were considered to have adequate knowledge

Ethical Considerations: Ethical clearance was sought from the Ethical Research Committee in Nairobi and University of Washington Review Board. Written consent in English or Kiswahili was mandatory from all the participants of the study. Consenting was done on reading and understanding the written informed consent form. Illiterate participants were required to insert a thumb print in the presence of an independent witness.

Participants who were included in this ancillary study had already signed and consented for HIV-1, HBsAg and HBsAb testing and blood draw procedures as per the protocol for the Pre-Exposure prophylaxis study.

RESULTS

One hundred and sixty one HIV discordant couples (322 participants) with a mean age of of 33 years (SD= 8.4) were included into the study; couples in which the HIV infected partner (index partner) was female accounted for 118 (37%) while couples in which the index partner was male was 43(13%).

Prevalence of HBV

Overall, 99 of 322 participants (31%) had a positive marker for Hepatitis B. Active HBV was observed in three of 322 participants (1%), and previous HBV was observed in 96 of 322 participants (30%) (Table 1).

Table 1

Selected demographic characteristics of men and women in HIV-discordant couples

Participant Characteristic	n (%)
Age(mean(SD))	33.3(SD 8.4)
Sex	
Male	
HIV positive	43 (13)
HIV negative	118 (37)
Female	
HIV positive	118(37)
HIV negative	43 (13)
Level of Education	
Primary and below	175 (54)
Secondary and above	147 (46)
Employment	
No employment	64 (19)
Self employed	227 (71)
Formal employment	30 (9)
Marital status	
Married with 1 partner	136 (42)
Married, more than 1 partner	7 (2)
co-habiting	179 (56)
Couple characteristics	
Concordant HBV positive	19 (12)
Discordant HBV positive	61(38)
Concordant HBV negative	81 (50)

The presence of a positive serological marker for HBV among the HIV positive participants and negative participants was 53 of 161 (33%) and 46 of 161 (29%) respectively.

Among the HIV negative participants, there was a significantly higher prevalence of HBV among the men -20 of 118 (16.8%) than the women 5 of 43 (11.8%) (Odds Ratio (OR)=2.6, 95%, Confidence Interval (95% CI)=1.2-5.9, p<0.01), while among the HIV positive participants there was a significantly higher prevalence of HBV among the women - 24 of 118 (20.5%) than the men 5 of 43 (12.4%) (OR=0.4, 95% CI=1.2-9.8, p=0.03).We noted a significant difference in the prevalence of HBV between HIV positive women and HIV negative women (10.2% vs. 5.9%, OR = 0.5, 95% CI 0.2-1.0, p=0.05). However, among the men, there was a higher prevalence of HBV among the HIV negative than the HIV positive participants (8.4 vs. 6.2% OR=3.0, CI 1.3-6.5, p=0.04) (Table 2). We found increasing prevalence of HBV

with increasing age (OR=1.6, CI 1.2-2.1, p=0.001,) There was no association between HBV and any of the socio-demographic characteristics. HBV and HIV infection were not associated (p value=0.4). We found that 61(38%) couples were discordant for HBV, 81 (50%) couples were concordant negative for HBV and 19 (12%) couples were concordant positive for HBV

Knowledge of HBV: Of all respondents, 62.1% had heard of HBV but only 8% of them had adequate knowledge of HBV. There was a significant difference in HBV knowledge by HIV status, as 13% of HIV positive participants had adequate knowledge compared to 3.7% of HIV negative participants (OR=2.7,CI 1.95-7.9, p=0.05). Those who had at least one positive serological marker for HBV were not statistically significantly more likely to have adequate knowledge of HBV than those without a marker. Similarly, no difference was found when comparing men and women. (Table 2)

Table 2
Prevalence of a positive serological marker of HBV among HIV discordant couples

Participant Characteristic	Total (n)	HBV prevalence (%)	OR	95% CI	P-value
HIV Negative Participants					
Women	43	5(11.8)	1		
Men	118	20(16.8)	2.6	1.2-5.9	<0.01
HIV positive participants					
Men	43	5(12.4)	1		
Women	118	24(20.5)	0.4	1.2-9.8	0.03
Men					
HIV positive	43	3(6.2)	1		
HIV negative	118	10(8.4)	3.0	1.3-6.5	0.04
Women					
HIV negative	43	3(5.9)	1		
HIV positive	118	12(10.2)	0.5	0.2-1.0	0.05
Knowledge of HBV	n (%)				
Adequate knowledge	16(8)				
Inadequate knowledge	184(92)				
Participant characteristic	Total n	Adequate Knowledge of HBV (n) (%)	OR	95%CI	p-value
HIV status					
HIV uninfected	27	1(3.7)	1		
HIV infected	31	4(13)	2.7	1.9-7.9	0.03
HBV status					
negative	11	1(9.3)	1		
positive	20	1(5)	0.4	0.2-3.8	0.36
Gender					
Male	13	1(7.5)	1		
Female	12	1 (8.5)	0.81	0.6-5.4	0.44

DISCUSSION

Overall prevalence of HBV: In this study, we found an overall HBV prevalence of 31% among HIV discordant couples. One percent of all HIV discordant couples had active HBV. These results are slightly lower than a similar study done at Aga Khan University Hospital, Nairobi, Kenya, which found a co-infection prevalence of active HBV infection with HIV-1 of 6% (21). Additionally, the prevalence of the serological marker HBsAb was 30% in our study compared to 40% in HIV discordant couples in Kisumu, Kenya (22).

There was an association of HBV prevalence and increasing age, meaning that older participants were more likely to have a positive marker for HBV. This is not surprising given that this study used previous and active HBV markers and would include cumulative figures. These findings are similar to another study that determined the HBV prevalence in Kenya increased with increasing age (23) (24). Another study in the USA showed that HBV infection was positively associated with older age (25). No association was found between HBV prevalence and other socio-demographic factors in the USA study.

Prevalence by HIV status: Among the HIV positive participants in this study, 29% had a positive marker for HBV infection. There was no association found between HBV and HIV. This is consistent with a study done in Tanzania to determine if there is an association between HIV status and HBV among different population groups (26). Similar outcomes were found in two recent cohort studies (14) (16). Though HBV and HIV have common risk factors, these studies show that having HBV doesn't increase chances of having HIV and vice versa.

Interaction of Gender, HIV and HBV: The difference in the prevalence of HBV among females (32.3%) and males (29.2%) was not statistically significant. This compares with a similar study done in Thika, Kenya that determined the prevalence of HBV among HIV-1 discordant couples where the difference in HBV prevalence was not significant between males and females (27). However, in this study, couples containing a HIV negative male have are three times more likely to have HBV than couples with a HIV positive male.

HIV positive females had a higher HBV prevalence compared to HIV positive males. This concurred with a study conducted in Tanzania to determine the association of HBV and HIV in different populations which observed that HBV prevalence was 66.7% among HIV positive women (28).

Among the HIV positive participants, there was a difference in HBV prevalence where the female was more likely to have a higher prevalence of HBV than males, while among HIV negative participants, males were two to three times more likely have a higher prevalence rate than the HIV negative females. It is possible that HIV positive females had higher prevalence of HBV due to social and physiological reasons such as poverty and dependence on the male bread winner, hence making them more vulnerable to Sexually Transmitted Infections (29). HIV negative males are more likely to be HBV positive than HIV negative females, a situation that may be explained by other factors such as male sexual behaviour of multiple sexual partners compared to women (30), thus exposing the male to greater chances of contracting HBV infection.

Knowledge of HBV: Knowledge on HBV was inadequate, as only 8% of the study population had adequate knowledge. A study to determine knowledge of HBV among healthcare and public health professionals in China corroborated the findings in this study, where it found that 89% of 200 participants did not know the cause of HBV (31).

HIV positive participants had higher HBV knowledge adequacy compared to HIV negative participants. However there were no significant differences in knowledge adequacy by HBV status and sex. HIV positive participants were more likely to be interested in HIV discussion and more likely to remember it than HIV negative participants. They are also more likely to have contact with a health worker or teacher (32).

Concordance and discordance in couple HIV status: The study showed that 38% of the couples were discordant for HBV, meaning one participant in the couple had a positive marker for HBV. Concordant negative and positive were 50% and 12% respectively. These findings contrasted with the distribution in a study done to determine the correlation of HBV among HIV discordant couples in New Jersey where concordant negative and positive was 33% and 14% respectively (33). A similar study in Thika, Kenya found HBV discordance of 15%, HBV concordant negative of 83% and concordance positve of 1% (34) . The reason for this variance could be difference in sampling and distribution of participants between the two studies, along with socio-cultural factors across multiple countries.

CONCLUSIONS AND RECOMMENDATIONS

Female index participants had the highest HBV prevalence. HBV knowledge was inadequate especially among the HIV negative participants, a target group for preventive interventions and health education regarding risk factors of HBV infection.

LIMITATIONS

The design of the parent PrEP study required that no HIV negative participant with active HBV infection

was enrolled because they were required to take study drug. This therefore limited the analysis of active HBV among HIV negative participants.

The parent PrEP study did not differentiate if HBsAb was acquired due to a previous infection or vaccination. We believe this difference was negligible and therefore may not have affected the overall outcome. We therefore did not distinguish between the two.

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