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Association of Sexual Behavior with HBV Infection Among Adults: Results from the NHANES study

Wei Zhao[1], Zhi-Qin Xie[2], Hong Gao[1], Lin Wu[1], Liang Zhao[1], Bin Feng[2], and Yu-Qing Zhou[1]

[1]Chongqing Emergency Medical Center
[2]Zhuzhou Central Hospital

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Abstract

Background and Aims: Although it is known that hepatitis B virus (HBV) can be transmitted through sexual behavior, limited research has been conducted on the specific types of sexual behavior that facilitate transmission. The purpose of the research was to analyze the association of sexual behavior with HBV infection in US adults. **Method:** Four cycles (2009-2016) of National Health and Nutrition Examination Surveys (NHANES) were collected, and 16569 participants were finally included. HBV infection was determined by a positive HBV core antibody and participants were categorized into two groups: "yes" and "no" group. Data pertaining to sexual behaviors were gathered. The sexual identity group comprised individuals with no sex, heterosexual, homosexual, bisexual, or unclear. The sexual type group consisted of individuals with no sex, heterosexual vaginal sex, heterosexual oral sex, heterosexual anal sex, heterosexual multiple types, bisexual sex, male homosexual sex, female homosexual sex, or unclear. Multivariable logistic regression was used to analyze the association of sexual identity/type with HBV infection by adjusting different covariates. **Results:** The present study comprised a sample of 16,569 individuals between the ages of 18 and 69. Participants with HBV infection were more likely to be 40-69 years predominant, men, non-Hispanic Black. Additionally, these individuals were more likely to have co-infections with HIV or HCV, engage in drug use or current smoking, identify as homosexual or bisexual. After full adjustment, it was found that homosexual men were associated with a higher risk of HBV infection (odds ratio [OR]: 4.00, 95% confidence interval [CI]: 2.09-7.64) compared to men without sexual behavior. Bisexual men (OR: 5.65, 95% CI: 2.13-15) and men with heterosexual anal sex (OR: 4.52, 95% CI: 1.12-18.2) were associated with a higher risk of HBV infection. Notably, women engaging in any type of sexual behavior with men or women did not have a significantly higher risk of HBV infection compared to women without sexual behavior. **Conclusion:** The study showed that homosexual men, bisexual men, and men with heterosexual anal sex were found to be correlated with a higher risk of HBV infection. These results may offer valuable insights for the pursuit of HBV elimination.

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Wei Zhao[1+], Zhi-Qin Xie[2+], Hong Gao[1], Lin Wu[1], Liang Zhao[1], Bin Feng[2*], Yu-Qing Zhou[1*]

[1]Department of Hepatobiliary Surgery, Chongqing Emergency Medical Center, Chongqing, China

[2]Department of Hepatobiliary and Pancreatic Surgery, Zhuzhou Hospital Affiliated to Xiangya School of Medicine, Central South University, Zhuzhou City, Hunan Province, China

+These authors have contributed equally to this work and share first authorship.

*Correspondence: Bin Feng, fengbin19720303@163.com; Yu-Qing Zhou, zhouyuqing1977@hotmail.com

Abstract

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Conclusion: The study showed that homosexual men, bisexual men, and men with heterosexual anal sex were found to be correlated with a higher risk of HBV infection. These results may offer valuable insights for the pursuit of HBV elimination.

Key words: sexual behavior, sexual identity, sexual type, hepatitis B virus

INTRODUCTION

Chronic viral hepatitis B is a global affliction that imposes a significant economic and medical burden on society. The persistence of HBV infection in some individuals may result in chronic hepatitis B, which can progress to cirrhosis and even liver cancer[1]. HBV and hepatitis C virus (HCV) are the primary etiologic agents of liver cancer and overall mortality. Despite the efforts of the US government to combat HBV, a considerable number of individuals remain infected with the virus[2, 3]. Between 2001 and 2016, an estimated 7.6 million US adults aged 20-59 years were afflicted with HBV infection[4]. The challenge of eradicating HBV is formidable.

HBV, an infectious disease, can be transmitted through multiple routes. The primary mode of transmission is from mother to neonate. Contaminated blood products also pose a risk for HBV transmission. Furthermore, drug use and sexual behavior are significant routes of transmission[5].

Sexual behavior is a prevalent biological phenomenon in human beings, serving various purposes such as the perpetuation of offspring, expression of emotions, and others. Within society, the majority of individuals identify as sexually heterosexual, while a sexual minority exists, including those who identify as homosexual or bisexual[6]. Furthermore, individuals have explored alternative forms of sexual activity, such as oral and anal sex, as a means of avoiding vaginal sex, satisfying male pleasure, and preventing unwanted pregnancy[7, 8]. However, sexual behavior may also result in the transmission of various diseases, including HIV, HCV, HPV, and other sexually transmitted infections[9-11], as well as certain cancers, such as anal cancer and cervical cancer[7, 8, 12, 13].

The transmission of HBV through sexual activity has been firmly established, particularly in the context of anal sex among homosexual individuals[14-16]. The European Union has recognized men who have sex with men as a high-risk population for HBV infection[17]. However, limited research has been conducted on the

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relationship between sexual identity/type and HBV infection among homosexual, bisexual, and heterosexual individuals. It was the first study to research the association between sexual behavior and HBV infection among US adults, stratified by sexual identity/type.

METHODS

Study Population

The present study utilized data from the National Health and Nutrition Examination Surveys (NHANES) spanning from 2009 to 2016. NHANES is a nationally recognized center that examines demographic characteristics, population health, and certain diseases, and provides publicly available data. The investigation included a total of 40,439 participants; however, due to age restrictions on certain questionnaires, individuals under the age of 18 or over the age of 69 (N=19,791) were excluded. Additionally, participants without complete responses to the sexual behavior questionnaire regarding "ever had vaginal, anal, oral sex" (N=3,241) and those with missing data on anti-HBc examination (N=838) were also excluded. Finally, 16,569 participants were included (Figure 1).

Primary Exposure

In the "sexual behavior" questionnaire, men were asked by" ever had vaginal sex with a woman", "ever had oral sex with a woman", "ever had anal sex with a woman", "ever had any sex w/man: anal, oral", and women were asked by "ever had vaginal sex with a man", "ever had oral sex on a man", "ever had anal sex with a man", "ever had any kind of sex w/woman". Based on the sexual behavior of the population, we categorized individuals into two groups: sexual identity and sexual type. The sexual identity group comprised individuals with no sex, heterosexual, homosexual, bisexual, or unclear. The sexual type group consisted of individuals with no sex, heterosexual vaginal sex, heterosexual oral sex, heterosexual anal sex, heterosexual multiple types, bisexual sex, male homosexual sex, female homosexual sex, or unclear.

Outcomes

As per the AASLD 2018 guidelines on hepatitis B, the presence of positive HBV core antibody (anti-HBc) serves as an indicator of HBV infection, including previous or present infection[18]. A detailed description for anti-HBc detection has been reported in previous study[4]. Positive anti-HBc was classified under the "yes" group for HBV infection, while negative anti-HBc was categorized under the "no" group.

Covariates

In the study, according to previous literature, several covariates were included to adjust the models that described the association of sexual behavior with HBV Infection. First, demographic characteristics including age, gender, race/ethnicity, education, marital status, poverty income ratio (PIR) were selected. The age group was classified into three categories, namely 18-39, 40-59, 60-69 years. Race/ethnicity was divided into five categories, including Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other Races, comprising non-Hispanic multiracial. Education was classified into three categories, namely less than high school, high school graduate, and more than high school. The categorization of marital status comprised the subsequent classifications: married, widowed/divorced/separated, never married, and living with a partner[19]. poverty income ratio (PIR) was classified into <1.3, 1.3-1.8, and >1.8[20]. Body mass index (BMI) was categorized as <25, 25-30, and [?]30. Smoking status was classified as never smoking, former smoking, and current smoking. Second, human immunodeficiency virus (HIV) infection, HCV infection, and drug use were collected[6]. All these variables were categorized as "yes" and "no" group. Third, indicators of liver function, including albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), total bilirubin (TBIL), were included.

Statistical Analysis

Categorical variables were described as weighted percentages accompanied by a 95% confidence interval, and their comparison was computed utilizing the chi-square test. Continuous variables were characterized by their weighted mean ± standard deviation (SD), and their comparison was calculated using a weighted

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linear regression model. The association between sexual behavior and HBV infection was analyzed using multivariable logistic regression models. The final model was adjusted for age, race/ethnicity, education, marital status, PIR, HIV infection, HCV infection, drug use, BMI, and smoking status. All statistical analyses were conducted by Empowerstats 2.2 and STATA 17.0. The complex survey design was represented using appropriate examination weights, and statistical significance was determined at a level of $p < 0.05$.

RESULTS

Characteristics of Participants

A total of 16,569 participants were included in the study, with 50.09% (95%CI: 49.08%-51.1%) being men and 49.91% (95%CI: 48.9%-50.92%) being women, and an average age of 42.76 ± 14.57 years. **Table 1**summarizes all characteristics of the study stratified by HBV infection (yes or no). The prevalence of HBV infection (including previous or present infection) among US adults was approximately 4.04% (95%CI: 3.72%-4.38%). The majority of outcomes exhibited statistically significant differences when stratified by HBV infection. Participants with HBV infection were more likely to be 40-69 years predominant, men, non-Hispanic Black, with education less than high school, with a poverty income ratio (PIR) <1.3. Additionally, these individuals were more likely to have co-infections with HIV or HCV, engage in drug use or current smoking, identify as homosexual or bisexual, and exhibit elevated levels of ALT, AST, and GGT. The study found that while no statistically significant difference was observed in sexual behavior (yes or no) among individuals with HBV infection, statistically significant differences were observed in sexual identity and sexual type.

Furthermore, the characteristics of participants were compared and stratified by sexual identity, as presented in **Table 5** . The results indicated that the rates of HIV and HCV infection were significantly higher among homosexual and bisexual individuals compared to those without sexual behavior.

Associations Between Sexual Identity and HBV Infection

Sexual identity was classified into five groups, including no sex (3.94%), heterosexual (88.43%), homosexual (0.83%), bisexual (6.71%), and unclear (0.09%). In comparison to participants without sexual behavior, the present study found that individuals who identified as homosexual or bisexual had a significantly higher risk of HBV infection across three models. Model 1 revealed that homosexual individuals had an OR of 4.22 (95%CI: 1.99-8.94) and bisexual individuals had an OR of 1.73 (95%CI: 1.15-2.59). Model 2 showed that homosexual individuals had an OR of 5.75 (95%CI: 2.63-12.55) and bisexual individuals had an OR of 2.23 (95%CI: 1.46-3.42). Model 3 demonstrated that homosexual individuals had an OR of 4.83 (95%CI: 1.86-12.57) and bisexual individuals had an OR of 1.78 (95%CI: 1.09-2.92). Notably, heterosexual individuals did not exhibit a significant difference in HBV infection risk when compared to participants without sexual behavior across all three models.

Upon stratification by gender, it was observed that among the men population, individuals who identified as homosexual (OR=5.61, 95%CI: 2.53-12.48) or bisexual (OR=4.32, 95%CI: 2.51-7.44) exhibited a increased risk of HBV infection in model 1, as compared to men without sexual behavior. This trend persisted in models 2 and 3, where homosexual (models 2: OR=7.96, 95%CI: 3.51-18.05; models 3: OR=5.89, 95%CI: 2.21-15.66) and bisexual (models 2: OR=4.45, 95%CI: 2.48-7.99; models 3: OR=4.2, 95%CI: 2.2-8.03) individuals continued to demonstrate a significantly elevated risk of HBV infection. Conversely, heterosexual individuals did not exhibit a significant difference in HBV infection risk as compared to men without sexual behavior across all three models.

However, in the women population, compared with women without sexual behavior, whether heterosexual, or bisexual, no statistically differences were observed across three models.

Associations Between Sexual Type and HBV Infection

According to the questionnaire, sexual type was classified into nine groups, individuals with no sex (3.94%), heterosexual vaginal sex (10.23%), heterosexual oral sex (0.59%), heterosexual anal sex (0.04%), heterosexual

multiple types (77.36%), bisexual sex (6.71%), male homosexual sex (0.74%), female homosexual sex (0.09%), and unclear (0.3%).

In comparison to participants without sexual behavior, we found that bisexual sex and male homosexual sex were found to be linked with an increased likelihood of contracting HBV infection. Specifically, in model 1, bisexual sex (OR=1.73, 95%CI: 1.15-2.59) and male homosexual sex (OR=4.82, 95%CI: 2.25-10.31) were identified as having a higher risk of HBV infection. In model 2, bisexual sex (OR=2.2, 95%CI: 1.44-3.36) and male homosexual sex (OR=6.58, 95%CI: 2.99-14.46) were correlated with an increased risk of HBV infection. Similarly, in model 3, bisexual sex (OR=1.69, 95%CI: 1.04-2.76) and male homosexual sex (OR=5.23, 95%CI: 1.95-13.99) were correlated with a higher risk of HBV infection. Conversely, there were no significant differences observed in heterosexual vaginal sex, heterosexual oral sex, heterosexual anal sex, or heterosexual multiple types across the three models.

Upon stratification by gender, in the men population, comparing with men without sexual behavior, heterosexual anal sex (OR=14.42, 95%CI: 3.66-56.81), bisexual sex (OR=4.32, 95%CI: 2.51-7.44) and male homosexual sex (OR=5.61, 95%CI: 2.53-12.48) exhibited an increased risk of HBV infection in model 1. Heterosexual anal sex (OR=4.75, 95%CI: 1.22-18.47), bisexual sex (OR=4.34, 95%CI: 2.43-7.77) and male homosexual sex (OR=7.75, 95%CI: 3.43-17.52) were found to be linked with an increased risk of HBV infection in model 2. Heterosexual anal sex (OR=4.52, 95%CI: 1.12-18.2), bisexual sex (OR=4.00, 95%CI: 2.09-7.64) and male homosexual sex (OR=5.65, 95%CI: 2.13-15) were found to be linked with an increased risk of HBV infection in model 3. No significant differences were observed in heterosexual vaginal sex, heterosexual oral sex, or heterosexual multiple types across all three models.

However, among the women population, compared with women without sexual behavior, whether heterosexual vaginal sex, heterosexual oral sex, heterosexual multiple types, bisexual sex, no statistically differences were observed across three models.

Associations Between Gender and HBV Infection

Table 1 indicated a higher proportion of HBV infection in men compared to women, while in model 1, 2, and 3 of table 4, women were found to have a lower risk of HBV infection (OR=0.78, 95%CI: 0.66-0.92; OR=0.71, 95%CI: 0.6-0.85; OR=0.79, 95%CI: 0.64-0.97).

DISCUSSION

In the sexual identity group, it was observed that individuals identifying as bisexual or homosexual had a significantly higher prevalence of HBV infection compared to those without any sexual behavior. To account for the potential impact of gender, the data was stratified by gender, revealing that bisexual and homosexual men had a significantly higher prevalence of HBV infection compared to men without any sexual behavior. However, no significant difference was observed among women of all sexual identities. Further analysis was conducted by grouping heterosexual individuals into heterosexual vaginal sex, heterosexual oral sex, heterosexual anal sex, and heterosexual multiple types. The incidence of HBV infection was found to be significantly higher in men with heterosexual anal sex as compared to those without sexual behavior, but no significant difference was observed in three other groups. Bisexual men, homosexual men and men with heterosexual anal sex may be focus populations for the elimination of HBV targets.

It is noteworthy that HBV infection has affected approximately 250 million individuals globally. HBV infection is one of the main causes of liver cirrhosis and liver cancer, increasing the economic burden of the people and the medical burden of the society. Despite the widespread dissemination of HBV medical information and the existence of professional organizations dedicated to the treatment of HBV infection[1], there remains a significant portion of the population who are unaware of their HBV infection status. This lack of awareness poses challenges to follow-up treatment, increases costs, and may even result in secondary transmission[21]. Therefore, it is imperative to expand the dissemination of information regarding HBV screening, transmission routes, vaccination, and the consequences of infection, in order to raise awareness and promote prevention efforts.

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Certain studies have suggested that sexual behavior is a significant risk factor for the transmission of HBV[17, 22], and recent data from the United States indicates that approximately one-third of acute HBV infections were associated with sexual behavior during 2013-2018[23]. Despite this, limited research has been conducted on the relationship between sexual type/identity and HBV infection.

Our findings indicate that men with heterosexual anal sex were 4.52 times more likely to contract HBV than men without sexual behavior. However, no significant differences were observed in the risk of contracting HBV through heterosexual vaginal sex, heterosexual oral sex, or heterosexual multiple types of heterosexual sexual behavior. These results suggested that heterosexual anal sex may be a particularly high-risk factor for HBV infection. A literature also reported that heterosexual anal sex contributed to the transmission of HIV[24]. Furthermore, the prevalence of HBV infection was found to be 5.23 times higher in male homosexual sex and 1.69 times higher in bisexual sex compared to men without sexual behavior. Homosexual and bisexual men were identified as being at a greater risk of HCV and HIV infection, which is consistent with the findings of a survey[25]. A research also revealed that the rate of HBV infection in individuals with HIV was 6.5 times higher than in those without HIV[26]. The potential correlation between decreased counts and dysfunction of CD8+ and CD4+ T cells resulting from HIV infection and an increased susceptibility to HBV infection has been suggested as a contributing factor to the higher incidence of HBV co-infection among homosexual and bisexual men[27, 28]. In light of this, preventative measures such as condom use and health screenings for high-risk groups should be prioritized to mitigate transmission.

Nonetheless, the study found no statistically significant disparities among women, regardless of their sexual identity or sexual type. In the study, participants with HBV infection were more likely to be men predominant. The authors, Robin Brown et al., attributed this gender dimorphism to variations in sex hormone levels and immune factors, which may account for the observed differences in HBV infection rates between men and women[29, 30]. Specifically, estrogen and its interaction with estrogen receptors may have a suppressive impact on HBV.

Furthermore, the prevalence of drug use was observed to be higher in the HBV infection group compared to the non-HBV infection group, as reported by Jaimie Z. Shing et al[4]. The study revealed that approximately 20% of adults with a history of drug use were infected with HBV, which was significantly higher than the proportion observed in the general population. Drug use was identified as one of the common modes of HBV transmission[5]. Additionally, previous research has demonstrated that the proportion of smokers is higher in individuals with hepatitis B infection, which aligns with our findings. Furthermore, smoking was correlated with an increased risk of hepatitis B-related liver cancer[31, 32].

To achieve the objective of the World Health Organization to eliminate HBV by 2030, it was imperative to implement measures aimed at reducing the transmission of HBV through sexual behavior pathways[5]. Furthermore, vaccination and regular screening were deemed crucial.

However, our study was subject to certain limitations. The employment of cross-sectional design in NHANES data enabled us to establish a potential association between sexual behavior and HBV infection, but not a causal relationship. Sexual behavior was from questionnaire, maybe some bias existed. Furthermore, the absence of data on protective measures, such as condom use, leading to the absence of this important variable as covariates for the analysis.

CONCLUISION

In conclusion, the study findings indicated that homosexual men, bisexual men, and men with heterosexual anal sex were found to be linked with an increased risk of HBV infection. They should be the focus populations for World Health Organization's goal of eliminating HBV by 2030.

AUTHOR CONTRIBUTIONS

WZ and Z-QX contributed to the conception and design, the acquisition, analysis, interpretation of the data, the drafting of the article, or critical revision for important intellectual content. HG, LW, LZ, and H-ZZ collected data. BF and Y-QZ contributed to the conception and design, the reviewing of the article,

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or critical revision for important intellectual content. All authors approved the final version and agreed to be accountable for all aspects of the work.

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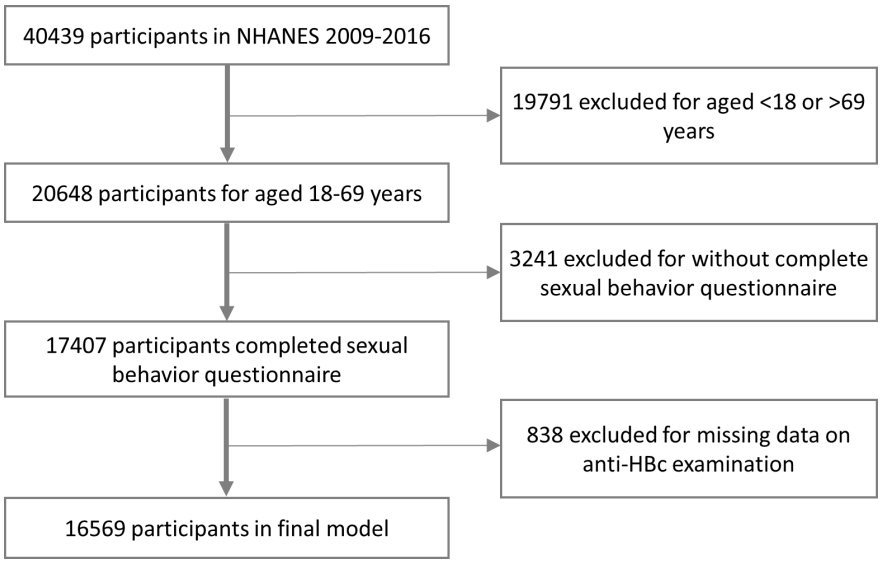
Figure 1 A flowchart showing the selection of study participants. NHANES, National Health and Nutrition Examination Survey.



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