

Hepatitis B and C Viral Infections in Tihamet Aseer, South-Western Saudi Arabia: Are There Gender Differences?

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ABSTRACT

Background: Hepatitis B virus (HBV) infection is endemic in Saudi Arabia. Many studies have shown varying results in gender differences in HBV and hepatitis C virus (HCV) infection. The objective of this study was to determine if gender differences exist in HBV and HCV infection and to elucidate any related risk factors in Tihamet Aseer, south-western Saudi Arabia.

Materials and Methods: The study was a cross-sectional study of a representative sample of males and females in Tihamet Aseer, south-western Saudi Arabia. A comprehensive questionnaire was completed by all participants. Blood samples were taken and sera were tested for hepatitis B surface antigen and HCV antibodies by fourth-generation enzyme immunoassays.

Results: The study included 1532 participants from the Tihamet Aseer area. An overall seroprevalence of 7.9% and 1.7% was found for HBV and HCV infections, respectively. In logistic regression analysis, no gender differences were found for HBV seroprevalence. Identified risk factors for HBV infection included a history of blood transfusion and lack of hepatitis B vaccination. On the other hand, females were more prone to become seropositive for HCV (adjusted odds ratio = 5.034, 95% confidence interval: 1.042–9.321). Other identified risk factors for HCV infection were illiteracy and a history of blood transfusion.

Conclusion: The prevalence and HBV and HCV infection is high compared to the national figures. Gender differences were only observed in HCV infection. It is recommended to have an active educational and media campaign. A “catch-up” vaccination program against HBV should be introduced for adults as a strategy to achieve the herd immunity effect in the affected area.

Key words: Gender, hepatitis B virus, hepatitis C virus, Tihamet Aseer

ملخص البحث:

تهدف هذه الدراسة المقطعية إلى معرفة إن كان هناك اختلافات بين الجنسين في الإصابة بالتهاب الكبد الوبائي ب و ج والتعرف على عوامل الخطورة ذات العلاقة في تهامة عسير بالمملكة العربية السعودية. تم اخذ عينات دم من المشاركين واختبارها للأجسام المضادة لالتهاب الكبد ب و ج الوبائي. خلصت الدراسة إلى وجود معدل عال للإصابة بالتهاب الكبد الوبائي ب و ج مقارنة بالمعدلات الوطنية، كما بينت فروقات بين الجنسين في التهاب الكبد الوبائي ج. يوصي الباحثون بالاستمرار في حملات التوعية الخاصة بهذه الأمراض. وكذلك بتصميم وتفعيل برنامج لتطعيم البالغين ضد التهاب فيروس الكبد ب.

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INTRODUCTION

Hepatitis B virus (HBV) is endemic in Saudi Arabia, and studies have shown that the highest rate of infection is in the southern region.^[1] In the last two decades, studies have addressed various aspects of HBV infection in Saudi Arabia, such as its prevalence in the general population, age groups infected, blood donors, health-care workers, pregnant women, virus genotypes and its relation to hepatocellular carcinoma (HCC).^[1-11]

One year before the addition of the HBV vaccine to the expanded program of immunization in 1990, the prevalence of HBV infection among children was approximately 7%.^[11] A steady decline of infection among children was subsequently observed.^[12] A recent survey conducted in regions of different HBV endemicity in Saudi Arabia documented a zero prevalence of hepatitis B surface antigen (HBsAg) among students (16–18 years of age).^[13] In 2013, the Saudi Ministry of Health reported an incidence rate of 16.29 and 5.45/100,000 for HBV and hepatitis C virus (HCV) infections, respectively, in the Aseer region.^[14] Despite limitations in studies from various regions of the Kingdom, in 2009, Madani reported a mean rate of 124 HCV cases per 100,000 population and observed a slight steady increase during the period 1995–2005, followed by a plateau.^[15]

The objective of this study was to determine whether gender influences the rate of HBV and HCV infection and to elucidate any related risk factors in Tihamet Aseer, south-western Saudi Arabia.

MATERIALS AND METHODS

This was a cross-sectional study carried out on a representative sample of males and females in Tihamet Aseer, south-western Saudi Arabia. The Aseer region is located in the southwest of Saudi Arabia covering an area of more than 80,000 km². The region is located to the northeast of Jizan. Tihamah refers to the Red Sea coastal plain of Saudi Arabia from the Gulf of Aqaba to the Bab el Mandeb Strait. The region is sometimes subdivided into two parts: Tihamet Al-Hejaz (northern part) and Tihamet Aseer (southern part). The temperatures in Tihamah are probably some of the hottest on Earth. The present study included Tihamah areas in Al Farsha of Sarat Ebeida and Al-Majarda areas of the Aseer region, where the climate is hot and humid most of the year, and the majority of the

inhabitants are farmers who raise domestic animals for a livelihood.

Using the WHO manual for Sample Size Determination in Health Studies with a conservative anticipated population proportion of 4% and with an absolute precision of 1% at 95% confidence interval (CI), the minimal sample size required for the study was calculated to be 1476 cases.^[16,17] To meet the inclusion target, it was planned to include a total of 1500 participants in the study. In 2014, 1500 patients and their relatives attending the outpatients' clinics of hospitals and relevant primary health-care centers in the selected study areas for any reason (attending clinics, laboratory investigation, blood donation and premarital screening) were included in the study group.

A comprehensive questionnaire was given to all participants. The questionnaire included socio-demographic data and a history of relevant exposures, blood transfusions, surgical operations, tooth extraction, wet cupping and hepatitis B vaccination.

The study was reviewed and approved by the ethical committee of King Khalid University, which is located in the Asir Province in south-western Saudi Arabia. Written informed consent was obtained from each participant or, in the case of children, their guardian.

Approximately 5–10 ml venous blood sample was extracted in plain tubes and allowed to clot at room temperature (range 18°C–20°C). Sera were aliquoted and stored at –20°C until transportation in ice boxes to the Virus Lab of Abha College of Medicine, King Khalid University. HBsAg was tested by a fourth-generation enzyme immunoassay (ELISA) obtained from DIA.PRO Diagnostic Bioprobes (Sr1 Via G. Carducci, Milano, Italy). The manufacturer's protocols were strictly followed in testing and interpreting the results.

The laboratory diagnosis of HCV infection was performed utilizing fourth-generation ELISA. Kits were obtained from DIA.PRO Diagnostic Bioprobes. The assay detects IgG class antibodies against the viral structural protein c-22-3 derived from the genomic core region and three nonstructural proteins c-33c, c100-3 and 5-1-1 derived from the NS3 and NS4 regions of the viral genome. The manufacturer's protocols were strictly followed in testing and interpreting the results. All positive and equivocal HCV serology results were further confirmed by reverse transcription-polymerase chain reaction.

Data were coded, validated and analyzed using the Statistical Package for the Social Sciences (SPSS) version 13.0 (SPSS Inc., Chicago, IL, USA). The frequency, percentage, arithmetic mean and mode are used to present the data. Chi-square test and Fisher's exact tests were used as tests of significance at a 5% level of significance. Binary logistic multivariate analysis, adjusted odds ratio (aOR) and antecedent 95% CIs were used to identify potential risk factors for HBsAg and HCV seropositivity.

RESULTS

The present study included 1,532 participants from the Tihamet Aseer area, south-western Saudi Arabia. Their age ranged from 5 to 81 years with an average of 34.6 ± 11.4 years and a median of 31 years. There were 876 males (57.2%) and 656 females (42.8%) and the majority of the participants were married (1,240, 81%).

Table 1 shows that 14.1% (122) of males were aged <20 years compared to 17.3% of females (112). The illiteracy rate among females was higher (37.8%, 248) compared to males (22.7%, 198), which was statistically significant ($\chi^2 = 42.006$, $P = 0.001$). History of wet cupping among males (5.3%, 46) was higher than that of females (2.6%, 17), which was also statistically significant ($\chi^2 = 6.729$, $P = 0.009$) compared with females (6.4%, 42). On the other hand, females had a significantly higher rate of hepatitis B vaccination and a history of yellow eyes in adulthood (30.8% and 12.5%, respectively) compared with males (24.5% and 8.3%, respectively).

Figure 1 shows that 69 males were positive for HBsAg, giving a seroprevalence of 7.9%. Among females, 40 were positive for HBsAg, giving a seroprevalence of 6.1%. The gender difference was not statistically significant ($\chi^2 = 1.797$, $P = 0.181$). Figure 1 shows that two males were found to be positive for hepatitis C giving a prevalence of 0.2%. Among females, 11 cases were positive, giving a seroprevalence rate of 1.7%. The gender difference was statistically significant (Fisher's exact 2 tailed $P = 0.003$).

Multivariate binary logistic regression analysis was used to identify potential risk factors associated with HBsAg seropositivity [Table 2]. After adjusting for other potential risk factors, the study showed that participants with a history of blood transfusion had more than two times the risk of becoming seropositive for HBsAg (aOR = 2.75, 95% CI: 1.379–5.482). Similarly,

Table 1: Distribution of the study sample of males and females in Tihamet Aseer, south-western Saudi Arabia by demographic data and relevant exposures

Variable	n (%)		P
	Males (n = 876)	Females (n = 656)	
Age (<20 years old)	122 (14.1)	112 (17.3)	0.093
Level of education (illiterates)*	198 (22.6)	248 (37.8)	0.001
History of blood transfusion	51 (5.8)	42 (6.4)	0.638
History of surgical operations	88 (10.0)	69 (10.5)	0.413
History of teeth extraction	155 (17.7)	101 (15.4)	0.130
History of wet cupping*	46 (5.3)	17 (2.6)	0.009
History of yellow eye in adulthood*	73 (8.3)	82 (12.5)	0.005
History of hepatitis B vaccination*	215 (24.5)	202 (30.8)	0.004

*Significant ($P < 0.05$)

Table 2: Multivariate analysis, adjusted odds ratio and antecedent 95% confidence intervals of potential risk factors determining seropositive HBsAg in Tihamet Aseer, south-western Saudi Arabia

Variable	aOR	95% CI	
		Lower	Upper
Gender: Males versus females	1.285	0.813	1.984
Age: >20 years versus <20 years	1.854	0.829	4.147
Education: Illiterates versus educated	1.209	0.769	1.871
History of blood transfusion*: Yes versus no	2.75	1.379	5.482
History of any surgical operation: Yes versus no	0.626	0.314	1.249
History of tooth extraction: Yes versus no	1.423	0.857	2.363
History of wet cupping: Yes versus no	1.413	0.630	3.712
History of yellow eye in adulthood: Yes versus no	1.439	0.689	3.005
History of hepatitis B vaccination*: No versus yes	3.922	1.889	8.196

*Significant ($P < 0.05$). aOR – Adjusted odds ratio; CI – Confidence interval; HBsAg – Hepatitis B surface antigen

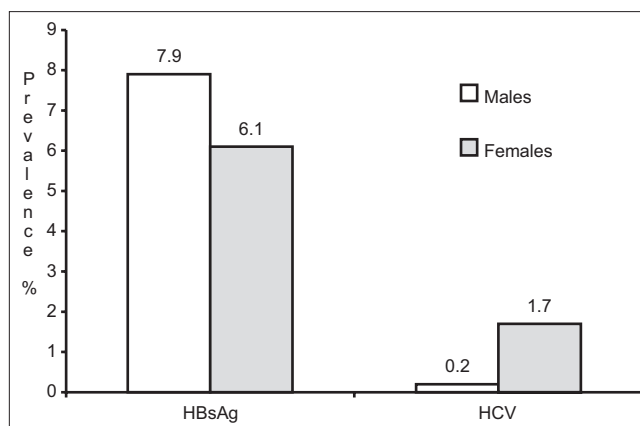


Figure 1: Seroprevalence of Hepatitis B (hepatitis B surface antigen) and C Viral Infections among the study sample of males and females in Tihamet Aseer, south-western Saudi Arabia.

persons lacking a history of hepatitis B vaccination had more than three times the risk of becoming seropositive for HBsAg (aOR = 3.922, 95% CI: 1.889-8.196). On the other hand, gender, age, education and history of other exposures were found to be of no significance in developing seropositive HBsAg.

Table 3 shows that after adjusting for other potential risk factors, females had more than five times the risk of becoming seropositive for HCV (aOR = 5.034, 95% CI: 1.042–9.321). Similarly, illiterate persons had more than four times the risk of becoming seropositive for HCV (aOR = 4.973, 95% CI: 1.256–10.411). The study showed that participants with a history of blood transfusion had more than 11 times the risk of becoming seropositive for HCV. On the other hand, age and history of other exposures were found to be of no significance in developing seropositive HCV.

DISCUSSION

HBV is the causative agent of one of the world's major infectious diseases, with approximately 350 million people being chronic carriers of the virus. It is the tenth leading cause of death worldwide. The prevalence of HBV and its modes of transmission vary geographically, and it can be classified into three endemic patterns: high, moderate and low. Certain types of practices increase the risk of contracting HBV, including the use of contaminated needles, lifestyle choices and blood transfusion.^[18]

Hepatitis C is one of the major causes of chronic liver diseases. Cirrhosis and HCC in HCV-infected individuals are of particular concern. The burden of HCV for the

patient, society and health-care systems is substantial. Approximately, 150 million people worldwide suffer from chronic HCV infection.^[18]

Regarding gender differences, studies in HBV infection have shown varying results. Kussak *et al.* did not report any gender differences in HBV infection in Lebanon, whereas Yang *et al.* did report a significant gender difference in China.^[19,20] In contradistinction to HBV infection, gender differences in HCV infection have been observed in prevalence rates and in virus clearance.^[21,22] In a large population-based cross-sectional study in Egypt, Butterfield *et al.* found that HCV clearance was significantly higher among women than men.^[23]

The present study investigated gender differences in HBV and HCV infections conducted in Tihamet Aseer, a deprived area in south-western Saudi Arabia. The Aseer region is considered to have one of the highest rates of HBV and HCV infections in Saudi Arabia.^[1] Furthermore, the study also cast light on some risk factors that were associated with these infections.

The study documented gender background differences regarding the level of education, history of wet cupping and lack of HBV vaccination. Males performed more wet cupping and had a lower rate of vaccination than females, and thus were more susceptible to acquiring HBV infection. Antenatal care, at least in part, might have been the reason for this disparity because HBV vaccination is offered in the Kingdom to those who were found to be seronegative. Women are informed that if they become infected, their babies might acquire the infection during delivery.

Multivariate analysis in the present study failed to identify a gender difference associated with HBsAg seropositivity. However, other studies have reported a gender difference in some aspects of HBV infection, such as virus clearance, the development of cirrhosis and HCC, where males significantly prevailed. The explanation given was related to the influence of estrogen in the protection and defense of hepatic cells against the development of chronic liver disease.^[24] Other molecular mechanisms have also been suggested.^[25] Gender disparity related to HBV infection with male prevalence has also been observed in the Arab world, China and Iran.^[22,26,27]

On the other hand, multivariate analysis in the present study has shown that patients who had no history of hepatitis B vaccination and those with a history of

Table 3: Multivariate analysis, adjusted odds ratio and antecedent 95% confidence intervals of potential risk factors determining hepatitis C virus infection in Tihamet Aseer, south-western Saudi Arabia

Variable	aOR	95% CI	
		Lower	Upper
Gender*: Females versus males	5.034	1.042	9.321
Age: >20 years versus <20 years	1.801	0.217	14.960
Education*: Illiterates versus educated	4.937	1.256	10.411
History of blood transfusion*: Yes versus no	11.761	2.936	27.109
History of any surgical operation: Yes versus no	0.150	0.194	1.812
History of tooth extraction: Yes versus no	0.463	0.081	1.668
History of wet cupping: Yes versus no	4.853	0.735	12.063
History of yellow eye in adulthood: Yes versus no	0.651	0.096	4.398

*Significant ($P < 0.05$). aOR – Adjusted odds ratio; CI – Confidence interval

blood transfusion were significantly more susceptible to acquiring HBV infection.

Hepatitis B vaccination is the most effective measure to prevent HBV infection and its consequences. HBV vaccines have long-term and stable efficacy. Widespread immunization programs against HBV have been implemented in more than 100 nations and have dramatically reduced the occurrence of chronic HBV infection.^[23]

Blood and blood products used to be a major cause of the spread of HCV infection in Arab countries. The major route for HCV infection was through blood transfusions due to the absence of adequate screening procedures. In addition, due to the regions' customs, when a patient's relatives and friends donate blood for the patient, the donor may be reticent about disclosing high-risk behaviors, such as lifestyle and drug use.^[22]

Concerning gender differences in HCV infection, the present study has shown that females had more than five times the risk to become seropositive for HCV infection. The multivariate analysis has also documented that being a female, illiterate and having had a history of blood transfusion were significant risk factors for acquiring HCV infection. The observed gender difference can be attributed to higher exposures of females to blood transfusion.

CONCLUSION

The study documented an intermediate endemicity of HBV infection and revealed the prevalent figure of HCV in the area. Gender differences were only found in HCV infection.

Based on the findings of this study, it is recommended to have an active educational and media campaign about the risks of HBV and HCV infections, routes of transmission and methods of protection. It is also recommended that a "catch-up" vaccination program against HBV should be implemented for adults as a strategy to achieve the herd immunity effect which will enhance the control of infection and transmission. Furthermore, increasing vaccination of high-risk groups, screening for HBV infection during pregnancy and intensifying surveillance of hepatitis B infected individuals will further decrease the prevalence of the disease in the affected area.

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Conflicts of interest

There are no conflicts of interest.

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