

SEROPREVALENCE OF HEPATITIS B VIRUS AND ITS CO-INFECTION WITH HEPATITIS D VIRUS AND HEPATITIS C VIRUS IN IRANIAN ADULT POPULATION

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ABSTRACT

CONTEXT: Hepatitis B virus (HBV) infection is one of the most prevalent public health problems worldwide (especially in developing countries). **AIMS:** This study was carried out to determine the seroprevalence of HBV and its co-infection with hepatitis D (HDV) and C (HCV) viruses in the northeastern part of Iran. **SETTING AND DESIGN:** A population-based cross-sectional study in Iran. **MATERIALS AND METHODS:** As many as 1,850 subjects were explored for HBsAg. Anti-HDV and anti-HCV antibodies were assessed in HBsAg-positive cases. **STATISTICAL ANALYSIS USED:** Proportions were compared by Chi-square and Fisher's exact tests. **RESULTS:** The mean age of subjects was 43.86 ± 11.2 years. The age- and sex-standardized prevalence for HBsAg positivity was 9.7%. It was higher in males than in females (OR: 1.28; 95% CI: 0.9-1.7). The risk of infection in singles was significantly higher than in married cases (OR: 2.13). Eight (5.8%) of HBsAg-positive cases were infected with HDV, and 17 (12.3%) were positive for anti-HCV antibody. **CONCLUSION:** This study demonstrates that the prevalence of HBsAg seropositivity in Golestan province of Iran is higher than the levels reported by WHO and previous studies from Iran. It is very important, especially for health providers and policy makers, to recognize the risk factors of HBV infection and its co-infection with HDV and HCV in this area and design effective preventive programs.

Key words: Co-infection, hepatitis B virus, hepatitis C virus, hepatitis D virus, Iran

BACKGROUND

Infection by hepatitis B virus (HBV) is a worldwide public health problem. It is a significant cause of morbidity and mortality,

especially in developing countries. It is estimated that 350 million people worldwide are chronic HBV carriers, representing approximately 7% of the total population.^[1] It causes 1 million deaths annually.^[2] About 1.3-

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8.69% of the Iranian population are chronic HBV carriers.^[3,4] As HBV and hepatitis C virus (HCV) have the same transmission routes, dual infection may occur. Patients co-infected with both HBV and HCV may have more severe liver disease and high mortality rate (10%).^[5,6] HCV infection is found in approximately 3% of the world population, accounting for 160 million people.^[7] The seroprevalence of HCV in Iranian blood donors was reported as 0.59%.^[8] Hepatitis D virus (HDV) is a defective RNA virus dependent on HBV infection for its replication and expression.^[9] It is known that coexistent infection with HDV tends to accelerate the progress of chronic HBV infection to chronic hepatitis, cirrhosis and hepatocellular carcinoma.^[10] More than 15 million patients are infected with HDV, and its prevalence in Italy, east of Europe and west of Asia is higher than the rest of the world.^[11] Its infection appears to be endemic in the Middle East.^[12]

This study was carried out to determine the seroprevalence of HBV and its co-infection with HDV and HCV in the northeastern part of Iran.

MATERIALS AND METHODS

A population-based cross-sectional study was conducted in Golestan province of Iran during 2004-2005. A total sample size of 2,500 subjects (15-65 years old) was enrolled using a single-stage cluster sampling method. For achieving this sample, 125 clusters were selected using a systemic random sampling according to the last census tract in Golestan province of Iran (2003). In each cluster, 20 persons were enrolled. 'Household' was the basic unit of a cluster. The first household

of the cluster was chosen randomly. Up to four persons in the target households were registered and invited to participate in the study. If a locked house was encountered, the next household in the same direction replaced it.

From these 2,500 cases, individuals aged higher than 25 years (1,850 subjects) were selected for getting enrolled in our study. Approximately 5 ml of blood sample was collected from each participant. Separation of serum was done under complete aseptic conditions. Serum samples were explored for HBV surface antigen using enzyme-linked immunosorbent assay (ELISA) kit, Diasorin, Italy (sensitivity: 100%; specificity: 98.8%). Anti-HCV and anti-HDV antibodies were assessed in HBsAg-positive cases by ELISA kits - DRG, Germany; and Radim, England, respectively (sensitivity: >98%; specificity: >98%). All data were analyzed by SPSS (Chicago, IL) software, version 13; and STATA, version 8. Proportions were compared by Chi-square and Fisher's exact tests. Values of 'P' less than 0.05 were considered significant.

RESULTS

Of the 1,850 subjects enrolled in the study, 877 (47.4%) were men and 973 (52.6%) were women, with mean \pm SD age of 43.86 ± 11.2 years. Characteristics of the participants are detailed in Table 1.

One hundred sixty-four of 1,850 cases were positive for HBsAg. The age- and sex-standardized prevalence for HBsAg positivity was 9.7% (95% CI: 0.07-0.11). The age-standardized prevalence of HBV seropositivity was 10.8% (95% CI: 8-13) in males and 8.6%

Table 1: Socio-demographic characteristics of participants in the study

Variables		Number	Percent
Sex	Male	877	47.4
	Female	973	52.6
Age groups	25-34	475	25.7
	35-44	471	25.5
	45-54	464	25.1
	55-65	440	23.8
Marital status	Married	1707	92.3
	Single	143	7.7
Place of resident	Rural	967	52.3
	Urban	883	47.7

(95% CI: 6-10) in females. This difference was not statistically significant (OR: 1.28; 95% CI: 0.9-1.7). The age- and sex-standardized prevalence for HBsAg positivity was 8.1% (95% CI: 5-10) in rural and 11.4% (95% CI: 8-14) in urban area, although no significant relationship was seen between them ($P > 0.05$). The risk of HBV infection in singles was significantly higher than in married cases (OR: 2.13; 95% CI: 1.29-3.5). The highest prevalence of HBsAg positivity was seen in the age group 25-34 years, but there was no significant relationship between age and HBV seropositivity [Figure 1]. All HBsAg-positive subjects were in a chronic asymptomatic carrier state.

Because of inadequacy or loss of some serum

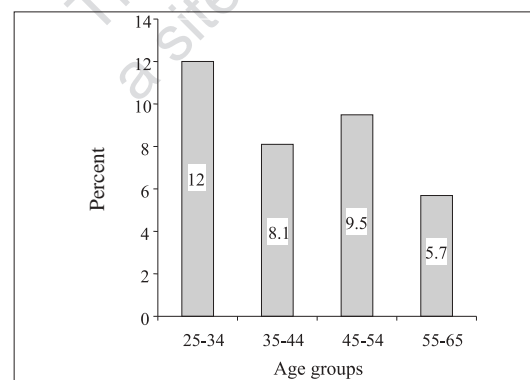


Figure 1: Age distribution of HBsAg-positive cases in Golestan province

samples, only 139 and 138 HBsAg-positive cases (instead of the total 164 ones) were assessed for anti-HDV and anti-HCV antibodies respectively. Eight (5.8%) cases were infected with HDV (95% CI: 2.5-11.0%). Anti-HDV antibody was positive in 7 (9.9%, 95% CI: 4.1-19.3%) of the females and 1 (1.5%, 95% CI: 0.04-7.9%) of males, but the difference was not statistically significant ($P = 0.06$). The prevalence of HDV seropositivity in rural population tended to be higher than in urban population, although no significant relationship was seen ($P = 0.48$). Seroprevalence of HDV did not significantly differ between age groups. Ten percent of singles and 5% of married subjects were positive for anti-HDV antibody, but the difference was not significant ($P = 0.38$) [Table 2].

Anti-HCV antibody was positive in 17 (12.3%) of HBV-infected subjects. There was no significant relationship between sex and HCV seropositivity ($P = 0.51$). The prevalence of HCV seropositivity in rural population tended to be higher than in urban population but it was not statistically significant. No significant relationship was seen between seroprevalence of HCV and age, marital status [Table 2]. Only 1 HBsAg-positive subject (0.6%) was positive for both HDV and HCV.

DISCUSSION

This study demonstrates that the prevalence of HBsAg seropositivity in Golestan province of Iran is higher than the levels reported by WHO. It is also higher than results of previous studies from Iran^[13] and India.^[14] Increase in sexual high-risk behaviors and communication with neighbor countries may be probable causes

Table 2: Relationships of hepatitis C virus and hepatitis D virus seropositivity with socio-demographic characteristics in HBsAg-positive cases in Golestan

Variables		Hepatitis C virus seropositivity				Hepatitis D virus seropositivity			
		Number (percent)	Odds ratio	95% CI	P-value	Number (percent)	Odds Ratio	95% CI	P-value
Sex	Male	7 (10.4)	1	-	-	1 (1.5)	1	-	-
	Female	10 (14.1)	1.4	0.5-3.93	0.35	7 (9.9)	7.32	0.87-61.23	0.06
Age	<30	5 (15.6)	1.98	0.55-7.03	0.23	3 (9.4)	4.24	0.42-42.84	0.21
	30-50	6 (8.6)	1	-	-	4 (6.2)	2.69	0.29-24.92	0.35
	>50	6 (16.7)	2.13	0.63-7.17	0.18	1 (2.4)	1	-	-
Marital status	Married	15 (12.7)	1.31	0.28-6.22	0.54	6 (5)	1	-	-
	Single	2 (10)	1	-	-	2 (10)	2.03	0.39-11.18	0.39
Place	Rural	8 (15.4)	1	-	-	4 (7.5)	1	-	-
	Urban	9 (10.5)	1.55	0.56-4.32	0.28	4 (4.7)	1.67	0.40-6.99	0.48

of this increase in prevalence. Complementary studies are recommended to understand the causes of these differences and find out the common mode of transmission.

In this study, the prevalence of HBsAg positivity was higher in males than in females. In developing countries, particularly in the Islamic region, multi-partnership is unusual in women. In Iran also, risk factors such as intravenous drug usage, being shaved by common barbers, traveling, etc., are more prevalent in men than in women, which may explain this difference.^[13] This result is similar to that reported from Turkey.^[15] In this study, the seroprevalence of HBV was higher in singles than in married. It may be due to high-risk sexual behavior in singles.

The seroprevalence of anti-HDV antibody in our study was considerably high when compared with some previous similar Iranian studies.^[16-18] Recently, Alavian *et al.* have reported 5.7% of HDV seropositivity among HBV-infected subjects in Iran.^[19] In other parts of the world, the seroprevalence of HDV among HBsAg-positive cases was 1.5, 1.6 and 2.2% in Yugoslavia,^[20]

Spain^[21] and Taiwan^[22] respectively.

Analysis of sex-related seroprevalence of HDV antibody in our study showed that the females (9.9%) were more infected than males (1.5%). This finding was not in conformity with earlier reports from Babol, Iran,^[16] and Pakistan.^[23] In the present study, subjects living in rural areas showed a higher prevalence of HDV seropositivity than the urban population. This is consistent with findings of Mumtaz *et al.*^[23] from Pakistan. Our results showed that the prevalence of anti-HDV antibody tended to be higher in young and single population. It was found that this was due to high-risk behaviors (sexual activity, IV drug abuse) among them. Mumtaz^[23] from Pakistan had reported similar findings. But, Gaeta *et al.*^[11] reported an inversely higher HDV seroprevalence in older subjects than in younger subjects.

Anti-HCV antibody was positive in 12.3% of HBV-infected subjects that participated in the present study. This is in line with worldwide prevalence (>10%) reported by the World Health Organization.^[24] HCV seropositivity among HBsAg-positive cases was reported as

2.7% by Barros *et al.*^[25] Seroprevalence of HCV in the same population from Taiwan was 8%.^[26] In contrast with these studies, de Miguel *et al.*^[19] from Spain had detected anti-HCV antibody in 16% of HBV-infected subjects (higher prevalence rate than ours). In the present study, the seropositivity of HCV in HBsAg-positive females was higher than in males; but Barros *et al.*^[25] had reported inversely higher prevalence rate in males.

The prevalence of triple infection with HBV/HCV/HDV in our study was 0.6%. Gaeta *et al.*^[27] similarly reported both HDV and HCV seropositivity in 6 of 837 (0.7%) HBsAg carrier subjects.

It was not possible for us to determine the causes of relatively high prevalence of HBV infection and its co-infection with HCV and HDV. So other complementary studies are required to clarify the risk factors of these viral infections.

CONCLUSION

It is very important, especially for health care providers and policy makers, to recognize the risk factors of HBV infection in this area and design effective preventive programs. Also, the risks of dual infection with HCV and HDV in HBV-infected patients should be acknowledged by practitioners and all health care managers in our area.

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