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ORIGINAL ARTICLE

Seroepidemiology of Hepatitis B Virus Infection in Khuzestan Province, Southwest of Iran

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Background and Aims: **Hepatitis B is a disease of public health importance in Iran. We conducted this study to determine the epidemiology, clinical presentations of hepatitis B infection in Khuzestan province, Southwest of Iran.**

Methods: **A cross-sectional study was conducted on hepatitis B virus (HBV) positive individuals referred to the Ahwaz Jondishapour University Hospitals (AJSUH) and Hepatitis Clinic from February 2002 to May 2007. Based on a specially-designed protocol, standard commercially-available tests and physical examinations were performed. All subjects were evaluated using a face-to-face questionnaire about demographic aspects. The analysis included data on past medical history, physical examination and periodic evaluation clinically and serologically.**

Results: **1264 patients infected with hepatitis B virus participated in the study. The patients consisted of 874 male and 390 female patients with the age range of 8-72 years. The most frequent age group was 20-40 years (56.4%). Anti-delta antibodies were observed in 4.7% of the carriers (59/1264), anti hepatitis C virus (anti-HCV) antibodies in 0.9% (12/1095) and anti human immunodeficiency virus (anti-HIV) antibodies in 0.1% (1/1095) of active carriers, respectively. Of 1264 patients infected with hepatitis B virus, 71 (5.6%) were also hepatitis B e antigen (HBeAg) positive, no difference in female to male ratio was observed between HBeAg-positive and HBeAg-negative patients with chronic hepatitis B.**

Conclusions: **The family history of hepatitis, dental procedures and a history of transfusion are important risk factors for HBV infection in our area. More careful screening and preventive measures, strict attention to asepsis, evaluation of risk factors, and improvements in certain lifestyle patterns and customs in this area may be essential to prevent transmission of the infection.**

Keywords: **Hepatitis B Virus, Risk Factors, Seroprevalence, Iran, Khuzestan**

Introduction

More than 350 million persons are chronically infected with hepatitis B virus (HBV) worldwide [1]. Nearly15%-40% will develop serious sequelae, from cirrhosis-related complications to hepatocellular carcinoma [2].

Chronic HBV infection is a major problem on health delivery system in our country. Hepatitis B is the leading cause of chronic hepatitis, cirrhosis and mortality in Iran [3].

In Iran, epidemiological studies have shown that the rate of hepatitis B infection ranges from 1.7% in Fars to 5% in Sistan-o-Baluchestan [4, 5].

In the Islamic Republic of Iran, 46% of patients with hepatocellular carcinoma and 51% of those with cirrhosis are reported to be hepatitis B surface

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antigen (HBsAg) positive. HBV is also recognized as the most frequent cause (70%-80%) of chronic hepatitis in the country [5, 6].

Factors determining clinical outcome are largely unknown and epidemiological characteristics of HBV are scarce in our area-Khuzestan province, Southwest of Iran.

The objective of this study was to describe current epidemiological and clinical features of patients with chronic HBV infection observed in our hepatitis clinics.

Materials and Methods

Study population

A cross-sectional study was conducted on HBV-positive patients referred to the Ahwaz Jundishapour University Hospitals (AJSUH) and Hepatitis Clinic from February 2002 to May 2007.

Based on specially-designed protocol, standard commercially-available tests and physical examinations were performed. The analysis included data on past medical history, physical examination and periodic evaluation-clinically and serologically.

All subjects were evaluated using a face-to-face questionnaire about demography (gender and age), geographic origin, and socioeconomic (educational) aspects, parenteral exposure to blood or blood products, social and sexual behavior, occupational exposure, intravenous drug use, tattooing, acupuncture, surgery, previous hospitalization and parenteral administration of drugs, alcohol consumption, past history of jaundice or hepatitis or history of these diseases and date and mode of discovery of HBsAg positivity, duration of HBV infection when available, and duration of HBsAg positivity.

The requirement for inclusion in the study was having a hepatitis B serology test for at least six months before.

In either circumstances, the patients were cared for by Hepatitis Clinic physicians. All subjects were also evaluated for any signs and symptoms related to liver diseases.

Laboratory studies

Serum sample of each patient was checked by commercially-available enzyme-linked immunosorbent assay (ELISA) kit for HBsAg, hepatitis B e antigen (HBeAg) or anti-HBe antibodies, hepatitis B core antibody (HBcAb), and polymerase chain reaction (PCR) assay (commercially available kit was used: Roche Diagnostics, GmbH; UK) for detection of HBV-DNA in the serum. Patients were also tested for hepatitis C virus antibodies (anti- HCV) by ELISA. Anti-HCV reactive samples were retested for confirmation by Abbott MATRIX immunoblot assays and also for HCV-RNA by PCR. Presence or absence of delta antibodies and co-infection with human immunodeficiency virus (HIV) was also recorded.

Sera from all patients were tested for the following liver function tests at the patients' first visit to our outpatient clinic: Serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), g-glutamyl transpeptidase (G-GTP), total bilirubin (TBil), total protein (TP), albumin (Alb), and γ-globulin (γ-glob). Ultrasonographic examination was performed in all patients to investigate hepatic shape and space occupying hepatic lesions. The results of liver biopsy performed before any antiviral treatments were also recorded. Informed consent was obtained from all patients after the purpose and methods of the study were explained. The institutional Ethics Review Committee approved the study protocol.

Statistical analysis

Collected data were coded, analyzed and computed using SPSS ver 10.0 (SPSS Inc., Chicago, IL, USA). The χ^2 and unpaired *Student's* t test were used for statistical analyses. Differences were considered statistically significant when $P<0.05$.

Results

1264 patients infected with HBV participated in the study. The mean follow-up of the total population was 5.3 years.

The patients consisted of 874 males and 390 females. The age distribution of patients is shown in Figure 1. The most frequent age group was 20-40 years (56.4%). The mean±SD age of participants was 37±13.8 (range: 8-72) years.

The clinical presentation of patients at the time of study was noted for all of patients in the study and is given in Table 1.

Of 1264 studied patients, 1059 (83.8%) were classified as probable HBsAg inactive carriers, whereas 205 patients (16.2%) presented with chronic liver disease. Anti-delta antibodies were observed in 4.7% of the carriers (59/1264), anti-HCV antibodies in 0.9% (12/1095) and anti-HIV antibodies in 0.1% (1/1095) of active carriers, respectively. The discovery of HBsAg during pregnancy accounted for 7% of patients in our cases.

Of the 1264 patients infected with HBV, 71 (5.6%) were also HBeAg-positive, indicating wild

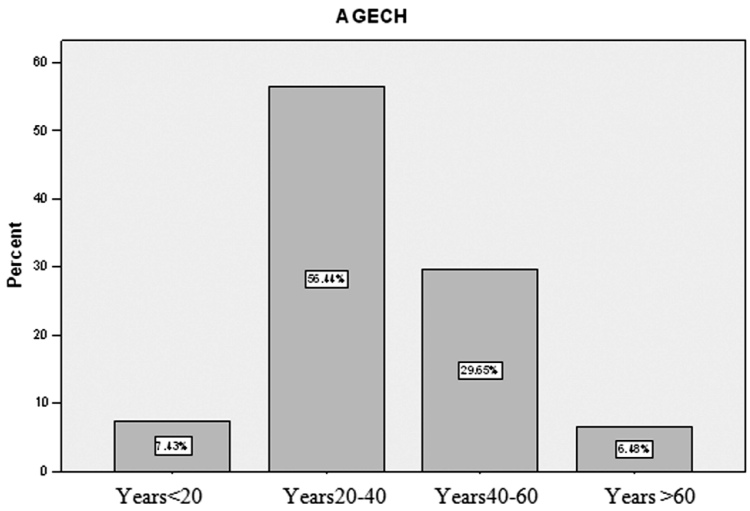

Figure 1. Age distribution of patients.

Table 1. Clinical presentation of patients at the time of study.

HBV-related liver disease sub-group (n)	HDV non-reactive individuals n (%)	HDV reactive individuals n (%)
Chronic inactive carriers	1059 (83.8)	38 (64.4)
Chronic active hepatitis	80 (6.3)	8 (13.6)
Cirrhosis	109 (8.6)	12 (20.3)
Hepatocellular carcinoma	16 (1.3)	1 (1.7)
Total	1264 (100)	59 (100)

type condition in these subjects. No difference in the female to male ratio was observed between HBeAg-positive and HBeAg-negative patients with chronic hepatitis B.

Table 2. Risk factors of hepatitis B infection in our studied group.

Variable	n=1264 group	Total %
Unknown	952	75.3
Family history of hepatitis	225	17.8
Dental procedures	35	2.8
Blood transfusion	18	1.4
Surgical procedures	13	1
Intravenous drug abuse	5	0.4
Tattooing	4	0.3
Wounded at war	9	0.7
Needle stick	2	0.2
Hospitalization	1	0.1

Statistical analysis showed that family history of hepatitis, dental procedures, blood transfusion and surgical procedures are greatest risk factors for hepatitis B infection (Table 2).

Hepatitis D virus (HDV) antibody was found positive in 59 patients positive for HBsAg (4.7%).

A higher proportion of individuals positive for antibodies to HDV was observed among males (n=41, 69.5%) and females (n=18, 30.5%) compared with males (n=833, 69.1%) and females (n=372, 30.9%) negative for the antibodies (P=0.953).

The mean age of those positive for antibodies to HDV (41.6 yrs) was significantly (P<0.01) higher than non-reactive individuals (37.0 yrs).

Discussion

Despite considerable advances in medical technology and attempts to find "the magic bullet" to cure the disease, viral hepatitis still remains a major public health problem with its worldwide high morbidity and mortality.

Around one million people die each year of HBV infection, making it the 9th leading cause of death worldwide [7].

It has been estimated that over 35% of Iranians have been exposed to the HBV and about 3% were chronic carriers [8].

However, the recent studies showed that the rate of hepatitis B carriers varied between zero and 3.9% with an average of 1.7% [9]. This decrease might be due to implementing of screening programs with focus on high risk groups [10].

In this survey, 1264 patients infected with HBV were studied. The mean follow-up of the studied sample was 5.3 years.

The age of our patients ranges from 8 to 72 years. The mean ± SD age of the population was 37 ± 13.8 years.

The highest rate (56.4%).was observed in 20-40-year-old age group, higher in males followed by older age groups which is similar to other reports [11].

A large number (n=952, 75.3%) of our patients have been infected with hepatitis B with unknown risk factors, showing the complex nature of HBV transmission and warranting the need for checking of the risk factors for HBV spread, as well as implementing strong screening programs with more

focus on high-risk groups to control the disease in our area. In our study, the frequency of infected patients with unknown risk factors was 75.3% which is clearly higher than that reported by other studies [12].

In cases with no apparent risk factors, other routes of transmission and other factors, such as use of common razor or tooth brush, careless dressing of cuts and wounds or the family environment, where the risk of infection increases with the exposure time should be noted. Another possible reason for the observed high rate might be for failure in correct questioning process in our study.

The second most important risk factor for HBV infection was contact with an infected family person in our study (n=225, 17.8%) which is similar to other studies carried out in Iran and other countries [12-14]. This might suggest that horizontal transmission of the infection may be an important route of transmission in children and young adults in our province.

Interfamilial exposure, especially history of jaundice in husbands was an important risk factor among pregnant women in recent studies [12]. The discovery of HBsAg during pregnancy accounted for 7% of our patients.

Such results confirm the significance of the screening in pregnant women. It has been shown in several studies, that dental care is a risk factor for HBV acquisition [15, 16]. Our study also revealed that dental visit, especially visit by an "experimental dentist" is an important risk factor for the transmission of HBV infection, either as a result of patient-patient exposure by inadequately sterilized instruments or of dentist-patient exposures by intimate contacts with HBsAg carriers. So we should increase the public knowledge by health education about improvement in personal hygiene and strict attention to asepsis and sterilization in our province in this regard. However, other studies conducted in Karaj Hepatitis Center showed that routine dental care was not a risk factor for the spread of HBV infection [12, 17].

The results of the present study showed the significant prevalence (4.7%) of co-infection with HBV and HDV, proved by the presence of HDV antibody.

This seroprevalence of HDV antibody indicates the endemicity of HDV infection in Khuzestan province. The rate was approximately the same as other reports from Golestan province (Northeast of Iran) and Tabriz (Northwest of Iran), but was higher than that reported in other Iranian studies which they detected HDV antibodies in less than 2.5% of HsAg carriers [18-21].

This increasing in the prevalence of HBV/HDV co-infection in recent years in Iran might be noted.

HDV, a defective RNA virus that requires the HBV for packaging and transmission [22], plays an important role in the development of fulminant hepatitis and the progression of chronic liver damage in patients with chronic hepatitis B [23].

A higher proportion of patients with HDV were male (69.5%) similar to that of non-reactive individuals. However, the mean age of individuals positive for antibody to HDV (41.6 yrs) was significantly ($P<0.01$) higher than non-reactive individuals (37.0 yrs).

Treatment options for patients who have dual infection of HDV and HBV are limited due to the presence of HDV and because of such a high rate of HDV infection in our province, all patients with HBV should be screened for HDV before treatment decision for the former is taken.

Our results showed that 5.6% were also HBeAg-positive, indicating the wild type condition in these subjects. This rate was obviously lower than other reports [5].

In several studies in healthy Iranian blood donors, HBeAg has been detected in 9.4%-13.8% of chronic hepatitis B carriers [21, 24].

HBeAg is a marker of active HBV replication and infectivity, especially in mother to child transmission. It has been shown that the probability of development of hepatocellular carcinoma is many folds higher in persons who are HBeAg-positive than those who are only HBsAg-positive and HBeAg-negative [25].

Of the 1264 patients infected with HBV, 1193 (94.4%) were HBeAg-negative. No difference in the female to male ratio was observed between HBeAg-positive and HBeAg-negative patients with chronic hepatitis B.

An important feature of HBV epidemiology is the emergence and increasing significance of HBeAg-negative mutants. The prevalence of this HBeAg-negative chronic hepatitis B and its molecular basis varies geographically. In Iran, nearly 58% of the HBeAg-negative infections are associated with the pre-core mutants [26]. This rate is 50% in the Far East and 25% in the USA [27, 28]. Several factors may account for the higher frequency of HBeAg-negative chronic hepatitis B and altered epidemiology of HBV infection in our country that should be investigated.

Khuzestan province is classified as "intermediate" in terms of HBsAg prevalence. Therefore, general preventive measures including health education, improvement of personal hygiene and strict attention to asepsis and evaluation of risk factors in

HBV-infected people are recommended to better control this potentially serious disease.

Despite the limitations of this study, we recommend a larger study of risk factors in which further information about the transmission routes of hepatitis B infection and efforts for understanding HBV genotypes will be investigated.

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