

Viral Hepatitis in Khuzestan Province, South-West of Iran: A Review of Published Data

Mini Review

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Abstract

Introduction: Viral hepatitis is still remaining to be one of the major causes of chronic hepatitis worldwide and a potential cause of substantial morbidity and mortality in the future. This is a brief review of published DATA about viral hepatitis in Khuzestan province.

Methods: By searching scholar search engines from 1986 to 2012 for terms of Khuzestan Province, Hepatitis B, Hepatitis C and viral hepatitis.

Findings: Hepatitis B virus (HBV) prevalence has decreased dramatically in our population during the last decade, but Improvement of the people's knowledge about HBV risk factors, national vaccination program and vaccination of high risk groups should be continued. Hepatitis C infection is becoming the leading cause of liver diseases in many parts of the world. In Iran, it seems that its prevalence in general population is less than 1%. Khuzestan province in south west of Iran has special demographic and socioeconomic features. In this province different patterns of hepatitis viruses' distribution are found. Hepatitis A virus (HAV) infection is endemic but seropositivity for anti-HEV antibodies has been observed in volunteer blood donors. The Khuzestan region has a similar rate of HBV carriers in the country affecting mainly children and young adults, Hepatitis delta virus (HDV) is also highly endemic in our region with rates varying from 3.59% to 45.5% among HBs Ag carriers. Most of the HCV epidemiology relies mainly upon HCV seroprevalence studies in selected groups in our province so a population-based study representative of an entire community is needed.

Conclusion: The epidemiology of viral hepatitis in Khuzestan has not been well-characterized and high-quality studies of the seroprevalence and the major modes of transmission in this area should be made available. More emphasis should be given to the preventive measures of these diseases. We recommend to inform and educate the public and press regarding these diseases to create awareness among the general population by the use of media and/or training programs.

Keywords: Hepatitis; Epidemiology; Iran; Khuzestan

Abbreviations: HBV: Hepatitis B Virus; HAV: Hepatitis A Virus; HDV: Hepatitis Delta Virus; HEV: Hepatitis E virus; IDUs: Intravenous Drug Abuse; HCV: Hepatitis C Virus; HCC: Hepatocellular Carcinoma; TTI: Transfusion-Transmitted Infections; SLE : Systemic Lupus Erythematosus

Introduction

Despite considerable advances in medical technology and attempts to cure the diseases, viral hepatitis still affects billions worldwide and is associated with significant morbidity and mortality as well as high costs on medical expenditure and work loss [1]. Moreover, viral hepatitis frequently is asymptomatic until late in the disease course and is thus under diagnosed [2]. In spite to enormous advances in the understanding of viruses; development of sensitive assays, identification of new viral agents, safe and effective vaccines for hepatitis A virus (HAV) and hepatitis B virus (HBV), implementation of donor screening, effective inactivation of plasma derived products and

widespread use of universal precautions vastly contributed to the prevention and control of viral hepatitis, Khuzestan province has some specific significance in reference to seroepidemiology of viral hepatitis.

Khuzestan province is located in the southwest of Iran, a tropical area with an approximate population of 4.5 million (Census 2011). Khuzestan Province shares a land, river, and sea border with Iraq and Arabian countries along Persian Gulf. Khuzestan has suffered a lot of problems during a 8-year period of the Iran-Iraq War (1980-1988) [3]. During the war, many of the Iranian who were in battlefield had some trauma, and became wounded. As their treatment (surgery or transfusion) was done in emergency situation, some of the health standards were not observed for them [4].

Most acute and/or chronic hepatitis cases result from infection with one of the hepatitis viruses, named from A to E. In Khuzestan different patterns of hepatitis viruses' distribution are found throughout the province. Hepatitis A virus (HAV) infection

is endemic especially among low socioeconomic populations, although a decrease in its prevalence has been observed recently because sanitary conditions have been improving. Hepatitis E virus (HEV) is considered a major etiological agent of enterically-transmitted viral hepatitis in developing area. In Khuzestan, the seropositivity for anti-HEV antibodies has been observed in volunteer blood donors, but the occurrence of acute hepatitis E cases has not been notified [3]. In Iran, epidemiological studies have shown that the rate of hepatitis B infection ranges from 1.7% to 5% [5]. The Khuzestan region has a similar rate of HBV carriers in the country affecting mainly children and young adults, but there is no available data showing prevalence rate to address it. Hepatitis delta virus (HDV) is also highly endemic in the Khuzestan region with rates varying from 3.59% to 45.5% among HBs Ag carriers [6].

Most of the knowledge about hepatitis C virus (HCV) infection in Khuzestan has been acquired from seroprevalence studies carried out in thalassemic and hemodialysis patients and among intravenous drug users (IDUs) groups [3,7,8]. There is no study to show the HCV prevalence in general population in this region. In this article, we reviewed the available knowledge on present situation of the epidemiology of HBV and HCV viral hepatitis including certain occupations, behaviors and environmental risk factors and mode of transmission in the Khuzestan province. We searched Pubmed and Google Scholar search engines from 1986 to 2012 for terms of Khuzestan Province, Hepatitis B, Hepatitis C and viral hepatitis.

Epidemiological aspects of hepatitis B in Khuzestan

Since its discovery, hepatitis B has been recognized as a major cause of chronic liver disease worldwide. The most recent WHO estimate of the prevalence of HBV has shown that more than 2 billion people are infected with this virus among them 350 million are chronic carriers (hepatitis B surface antigen (HBsAg) positive) [9]. Although HBV is endemic worldwide, there is a large degree of geographic variability in its distribution. Iran is an area of low endemicity for hepatitis B infection (<2% HBsAg positive) [10]. We have no data available to validate assumptions about the burden of disease in the Khuzestan province. It is estimated that more than ninety thousand people are suffering from this infection.

Most descriptions of HBV epidemiology rely heavily upon HBV seroprevalence studies. These studies are typically cross-sectional in design and are done in selected populations-e.g. Intravenous Drug Users [8] or hemodialysis patients [11], patients with chronic liver disease [12] -which are not representative of the community or region in which they reside. A population-based study representative of an entire community is needed in our area. Although HBV infection has both acute and chronic forms, most of the complications associated with infection are realized through the development of chronic liver disease in a subset of infected people years after initial acquisition of the infection. Thus, a major determinant of the future burden of disease is the past and present incidence of infection.

However, establishing the incidence of HBV infection is difficult because most infections are initially asymptomatic and we would not be able to distinguish acute from chronic

or resolved infection. Acute disease reporting systems can underestimate the incidence of HBV infection, even in countries with well-established registry systems [13]. HBeAg is a marker of active HBV replication and infectivity, especially in mother to child transmission. In several studies in healthy Iranian blood donors, HBeAg has been detected in 9.4%-13.8% of chronic hepatitis B carriers [14]. HBeAg negative mutants were reported highly prevalent in Khuzestan comparable to other part of the country. Hajiani, et al. [12] reported the median prevalence of HBeAg positive chronic hepatitis to be 5.6% in the Khuzestan province. HBV infection is implicated in the prevalence of Hepatocellular carcinoma (HCC) in many countries, including Iran, where the proportion attributable to HBV ranges from 50% to 70 % [15]. In a study of the clinical characteristics of the patients with HCC in Khuzestan, 52.1% of the patients were anti-HBV (HBc Ab or HBsAg) positive [16].

General public vaccination effectively has decreased the carrier rate of this infection among our population, but it continues to be a significant health problem whose new cases are still being reported throughout the province. It seems that the average age of the infected individuals has increased. The epidemiology of infection is also changing from a vertical to horizontal route [17]. So it is of our health priorities to find the routes of its transmission and possible risk factors responsible for its spread to prevent this disease in our province.

Risk factors of hepatitis B infection transmission in Khuzestan

The risk factors most frequently cited as accounting for the bulk of hepatitis B transmission worldwide are blood transfusions from unselected donors, sexual and prenatal, injection drug use, unsafe therapeutic injections, and other health related invasive procedures. In most part of our country the evidence has shown the predominant source of new HBV infections within their population over the past few decades was history of contact with hepatitis B infected subject [18]. Other possible risk factors including older age groups, male sex, marital status (being married), extramarital sexual activity, intravenous (i.v.) drug use, major surgery, hemodialysis, experimental dentist visit and some jobs (police, barber, and driver had a substantial role in HBV transmission) [19,20].

In a study, 1264 cases infected with HBV were studied in Khuzestan province [13]. A large numbers (75.3%) of the studied group 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 this area. 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 [21]. Another possible reason for the observed high rate might be failure in correct questioning process in that study.

Other Factors predicting HBV infection was contact with an infected family person (17.8%). This might suggest that

horizontal transmission of the infection may be an important route of transmission in children and young adults in our province. This study also revealed that dental visit; especially visit by an “experimental dentist” was 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 aseptic and sterilization methods in our province in this regard (Table 1).

Table 1: Risk factors of hepatitis B infection in the studied group.

Risk Factor	Number (Total 1264)	Percent
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 in War	9	0.7
Needle Stick	2	0.2
Hospitalization	1	0.1

Epidemiological features and risk factors of hepatitis C transmission in Khuzestan

The most recent WHO estimate of the prevalence of HCV infection is 2-3%, representing 170 million people and HCV is the leading cause of liver transplantation in developed countries [22]. HCV infection is a slowly progressive disease and the second common cause of end-stage liver disease after hepatitis B infection in Iran and many countries [23]. HCV infection leads to chronic hepatitis in 50% to 80% of individuals [24]. It is estimated that the annual deaths due to liver cancer caused by HCV and cirrhosis are 308 000 and 785 000 respectively [25].

There is no study showing exact prevalence of HCV in the general adult population of the province. Most of the HCV epidemiology relies mainly upon HCV seroprevalence studies which are typically descriptive in design and are done in selected groups-e.g. multi-transfused patients or intravenous drug abuse (IDUs), patients with chronic liver disease-which are not representative of the community or region in which they reside so population-based studies representative of an entire community should be done. Regarding to estimation of prevalence of HCV infection in general population, one study in Shiraz in southern part of Iran (our neighbor province) has been performed on healthy blood donors. In this study on 7,897 cases, anti-HCV antibodies were found in 0.59 % [26].

Intravenous drug abuse (Idus)

Injection drug use is the primary mode of transmission for HCV infection in the world. HCV infection is thought to occur rapidly after initiating injecting behavior, based on a

seroprevalence of 38% and 47% observed in several studies in Iran among injection drug users [27].

In a recent report from Ahwaz by Alavi et al, positive HCV Ab by ELISA test was found in 34.5% of IDUs [28]. In this study on 333 IDUs, 115 have been infected with HCV, they were mostly male, with a mean age of 24.8y. More than 65% had a history of imprisonment. Hepatitis B prevalence in this study was 3.6%. This study showed that viral hepatitis in the IDU population is associated with sharing injection equipment, a long duration of drug usage, a long duration of prison stay, HIV co-infection, history of surgery, and blood or blood products transfusion. The authors believed that these variables may be the main risk factors for viral hepatitis acquisition in the IDU population in the study region. In another study of 254 HCV positive subjects in Ahwaz, I.V. drug abuse was independent risk factors of being HCV positive in 14.5% of the cases [29].

Multi-Transfused population

Most cases of hepatitis C virus is spread parenterally specially through blood contamination during medical procedures. In an analysis of Transfusion-transmitted infections (TTI) over a 9-year period in Iran, HCV was the most prevalent TTI and remains a major health problem for these patients [30]. This mode of transmission is a highly effective means of transmitting HCV infection. Blood is now so safe in most of the countries, because numerous measures over the past four decades have resulted in progressive reductions in the risk of transfusion transmitted HCV infection [31].

Thalassemic patients are at highest risk for hepatitis C infection. In a study conducted by Ghafourian on 206 patients with beta thalassemia in Khuzestan the overall prevalence rate of anti-HCV was 28.1% [32]. Our data of hemodialysis patients in the province shows that the prevalence of positive HCV Ab is about 7.9% [11]. In this descriptive (2005-2006) study which was conducted in 214 hemodialysis patients referred to the dialysis centers of the province, the infection rate was lower than other Iranian centers. The duration of hemodialysis was significantly associated with HCV seropositivity. In this study 41.1% of HCV patients had genotype 1a followed by 3a (35.2 %) and 1b (23.5%).

In a study during 2006 to 2008, we performed genotyping of 223 patients and found the genotype distribution as follows: HCV genotype 1a: 41.7%; 1b: 2.7%; genotype 2: 4.1%, 3a: 31.4%, genotype 4: 1.8% and 42 samples (18.84%) were not classified into any of the known HCV subtypes [33]. The patterns of our genotypes are similar to those of other parts of Iran.

Sexual transmission and household contacts

Transmission through sexual contacts has been implicated, although this may be a rather inefficient mode of transmission [34]. In our study on 300-household contacts of 60 index cases of HCV infection and 360 pair matched controls in Ahwaz, only 4 of 300 cases of household contacts were positive for HCV Ab. The prevalence of positive HCV Ab among household contacts (1.33%) was not significantly higher than that in the controls (1%). Intrafamilial transmission of HCV was not the significant transmission route and sexual transmission does not seem to

play a role in the intrafamilial spread of HCV infection [35].

HCV infection in special diseases

Hepatitis C virus (HCV) is a major cause of chronic liver disease among chronic renal failure patients undergoing kidney transplantation. The impact of pretransplant hepatitis C virus (HCV) infection on the outcome of kidney transplantation is controversial. We studied a group of patients to determine the impact of pretransplant HCV infection on the patient and graft survival at a single center in Ahvaz [36]. Our findings showed that pretransplant minimal HCV infection had no detrimental effect on the short-term patient and graft survival. Autoimmune manifestations are common in patients chronically infected by hepatitis C virus (HCV). These manifestations can be dominant, while the hepatic disease can be quiescent or mild. More recently, there has been growing interest in the relationship between HCV and systemic lupus erythematosus (SLE) [37].

In a prospective study (2003–2005), we evaluated the prevalence and the clinical significance of chronic HCV infection in patients with SLE. We studied 124 SLE patients and compared them with the control group. Six of 124 (4.8%) patients were seropositive for anti-HCV which did not differ significantly from the prevalence of HCV in the general population (less than 1%) [38]. The potential contribution of HCV in pathogenesis of HCC is particularly evident in many countries. In this area we found that HCV infection accounts for as much as 8.5% of all cases of HCC [16].

Conclusion

This paper reviewed the epidemiological features of viral hepatitis among various population groups, along with risk factors in Khuzestan province. The underpinning of any effort to prevent and control viral hepatitis is accurate epidemiological data. The epidemiology of viral hepatitis in Khuzestan has not been well-characterized, and resources for high-quality studies of the seroprevalence and the major modes of HCV transmission in this area should be made available. More emphasis should be given to the preventive measures of these diseases in order to decrease the future health and economic burden. It is suggested to have a strategy to inform and educate the public and press regarding these diseases to create awareness among the general population by the use of media or training programs.

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