HEPATITIS C VIRUS IN IRAN: EPIDEMIOLOGY OF AN EMERGING INFECTION

Seyed-Moayed Alavian MD*, Peyman Adibi MD**, Mohammad-Reza Zali MD***

Hepatitis C infection has come to the top of virus-induced liver diseases in many parts of the world. In Iran, it seems that its prevalence in general population is less than 1%, which is much lower than in most of the regional countries. However, the infection is emerging mostly due to problem of intravenous drug abuse and needle-sharing in the country. On the other hand, an increase in number of centers providing hemodialysis and transfusion facilities for hemoglobinopathies generated new sources and susceptible populations in Iran. This article aims to summarize available data of Iran and to compare them with those of similar countries to find better preventive means.

Keywords: Epidemiology • drug abuse • hemodialysis • hepatitis C • prevention

Introduction

Hepatitis C infection is now the most common cause of end-stage liver disease in many countries. It is a blood-borne infection that was a well-known cause of posttransfusion hepatitis after introduction of hepatitis B screening in blood banking and before implementation of hepatitis C-sensitive screening laboratory methods. Since the discovery of hepatitis C virus (HCV) and the development of diagnostic tests, almost all of the non-A non-B (NANB) posttransfusion hepatitis cases were shown to be due to HCV infection. Recently, HCV infection has drawn great attention due to similar risk factors and coinfectivity with human immunodeficiency virus (HIV) infection. HCV infection is widespread throughout the world. World Health Organization (WHO) estimations suggest that up to 3% of the world’s population (170 million) have been infected with HCV. The prevalence of infection in healthy blood donors ranges from 0.01 – 0.02% in the northern Europe and 1 – 1.5% in southern Europe to 6.5% in parts of equatorial Africa.

Prevalence rates as high as 20% have been found in Egypt. This difference yields the need for different preventive methods, community interventions, and even selecting different therapeutic strategies based on economic and social variance.

Iran is located in the Middle-East in a position like a bridge between Indian subcontinent, Arab peninsula, Middle Asia, and Europe. This geographical situation, mass immigration from Afghanistan and Iraq, frequent travels in western borders to Turkey, and illegal drug traffic from eastern borders with Pakistan and Afghanistan have all affected epidemiology of HCV in our country.

Prevalence of HCV infection in the general population

Nearly all of studies regarding estimation of prevalence of HCV infection in general population in Iran have been conducted on healthy blood donors. In the first report that appeared in literature in 1994, Rezvan et al in Iranian Blood Transfusion Organization (IBTO) reported 0.3% of blood donors in Tehran to have positive anti-HCV
antibody (Ab).\(^5\) Recently, a study on 5,976 blood donors in Rasht, northern part of Iran, showed that 0.5% of the cases were positive.\(^6\) Others on North-West reported a prevalence of 0.97% positive HCV antibody.\(^7\) In another study in Shiraz in southern part of Iran on 7,897 cases, anti-HCV antibodies were found in 0.59%.\(^8\) The main problem with all of these studies is probability of selection bias and low positive predictive value of routine HCV Ab detection by enzyme-linked immunoassay (ELISA) tests in blood donors. All of Iranian blood donation clinics follow regulations of Iran’s Blood Transfusion Organization (IBTO) that exclude high-risk groups i.e. persons with history of jaundice, intravenous drug abuse, and high-risk sexual behavior, so the major bulk of positive cases are ruled out from the sampling; the exclusion rate reaches to 19.7% due to all causes in Tehran.\(^9\) It may be more prominent when looking at a recent report about relative frequency of positive anti-HCV antibody in excluded cases that were 9.2% positive.\(^10\) We found in our study that with more restrict regulations in blood donation, the prevalence may decrease to 0.12%.\(^11\) A study was done in Shahr-e-Kord (South-West of Iran) by Hosseini-Asl et al which showed 3.1% of gypsies were anti-HCV Ab positive. The very low level of socioeconomic status of this population together with profound health problems render them to acquire HCV infection.\(^12\)

Generally speaking, it seems that the whole population prevalence is less than 1% in Iran that is lower than that of the regional countries: 1.1% in Yemen,\(^13\) 0.9% in children to 1.8% in adult blood donors in Saudi Arabia,\(^14\)\(^15\) and, 4% of blood donors and 3% of college students in Pakistan.\(^16\)\(^17\) The reason may be accounted by lower rate of needle-sharing for injection in past, earlier implementation of safe blood transfusion, and using accurate testing in high-risk groups, although none of these are fully evidence-based.

**HCV in chronic liver disease**

In a study that was done in 1999 among 162 chronic hepatitis and cirrhotic patients, HBsAg, anti-HBe Ab, and anti-HCV Ab were positive in 56.2%, 70%, and 40.7% of cases, respectively.\(^18\) When comparing with reports from other countries in the neighborhood of Iranian borders, the differences will appear. The prevalence of antibody to hepatitis C virus (HCV) in patients with chronic liver disease (CLD) and hepatocellular carcinoma in Saudi Arabia was 30.4%\(^9\); another study found that 63.6% of similar patients were positive for anti-HCV, a significantly higher prevalence than the rate of 3.9% observed in 488 asymptomatic volunteer blood donors.\(^20\) In a study on Pakistani patients with chronic liver disease and hepatocellular carcinoma, 24% of the patients had detectable HCV RNA.\(^21\)

**Modes of transmission**

Hepatitis C virus is a blood-borne pathogen and the main risk factors predominantly are through exposure to infected blood or blood products, such as: transfusion with unscreened blood and blood products,\(^22\) needle-sharing among drug abusers as a major risk factor for infection,\(^23\) and needle-stick injuries in health care workers.\(^24\) Persons at increased risk of acquiring hepatitis C include hemodialysis patients,\(^25\) hemophilia patients,\(^26\) infants of mother with HCV infection,\(^27\) and promiscus persons.\(^28\) Percutaneous procedures (e.g. ear and body piercing, circumcision, and tattooing) may be important.\(^11\) It seems that HCV may also spread iatrogenically through the use of nondisposable needles and syringes, and practice of traditional healing techniques involving puncture of skin. For example, in Egypt HCV may have been spread via contaminated needles used to administer antimony as schistosomiasis treatment.\(^29\)

Today, intravenous drug abuse is the major risk factor for HCV infection. Intravenous drug abusers not only have the highest prevalence of HCV infection but also constitute a potential reservoir of HCV in the community. The incidence varies between 31% and as high as 89% in different parts of the world. The prevalence of HCV infection increases proportionally with the duration of intravenous drug abuse.\(^30\) About 50 – 100% of IDUs are anti-HCV positive all over the world. In England injecting drug abuse is the most common risk factor found in HCV-infected patients, which counts for 80% of cases. Among frequent injection users 50 – 80% are infected in the first 12 months of beginning injection.\(^31\)

In early reports from Tehran in 2001 by Zali and colleagues, positive HCV Ab by ELISA test was found in 45% of imprisoned IDUs, with 12% having a history of jaundice. It is interesting that 54% of IDUs with positive HCV Ab had a positive history of blood donation.\(^32\) In another study in Hamadan in western part of Iran, about 38% of IDUs prisoners were HCV Ab positive whereas the rate in non-IV-drug abusers in prison was 0.71%.\(^33\)
Recently, a study was published from Zanjan, a North-West city of Iran, in which the HCV infection was found in 47% of drug abuser prisoners, of whom 1.2% had HCV-HIV coinfection. Although the rate is high, it is lower than that of western countries and even available reports from the region. For instance, in Saudi Arabia HCV Ab was positive in 74.6% of similar cases. The anti-HCV prevalence in drug-dependent patients who did not use the intravenous route was 10.5%. The anti-HCV prevalence in healthy Saudi males and in healthy non-Saudis was 1.7% and 3.2%, respectively. The condition may be accounted mainly by low prevalence of infection in the community, low cost of syringe, and probably community sampling in early stages of an epidemic. Since needle-sharing is frequent in prisons, it may be considered that the infection will increase significantly in future years, and the country will encounter local or nationwide epidemic due to transmission within IDUs and from them to persons in close contact with them.

The probability of HCV transmission through sexual intercourse is very low but not absent within monogamous long-term sexual contact, and the physicians should inform the patients that there is some risk. Sexual transmission is more frequent among those with high-risk sexual behaviors such as multiple sexual partners, history of other sexually transmitted diseases, working as a prostitute, unprotected sexual contact, and sexual activities with trauma. Regarding these data, the sexual transmission of HCV in prostitutes and homosexuals is not as high as IDUs. Such data suggest a limited role for sexual transmission in general population. However, having multiple sexual partners, attending sexually transmitted disease clinic, and prostitution are associated with an increased risk of HCV infection. This seems to be very important in Iranian IDUs since they report such high-risk behaviors and play as a source of infection for the whole community. Zero point twelve percent of Iranian blood donors had a positive anti-HCV antibody and one of the important risk factors by this case-control study was sexual promiscuity (defined as one or more extramarital sexual relationships and/or sex with prostitutes, according to Iranian culture). The overall rate of anti-HCV positivity appears low in sexual partners of HCV-infected hemophiliacs, unless there is coexistent HIV infection.

The risk of vertical transmission seems to be low (< 6% of children becoming HCV positive) unless the mother is HIV positive or has a particularly high level of viremia.

HCV is transmitted primarily by exposure to infected blood. Since 1990, when anti-HCV screening of blood donors became mandatory, the incidence of posttransfusion HCV declined to < 1% but not completely eliminated. As a result of improvements in HCV antibody assays in 1992 and again in 1996, the risk fell to 1 in 103,000 units.

The blood donation, screening, transfer, and transfusion are totally under supervision of IBTO. The organization bases all over the country follow similar regulations for blood donation and testing that include exclusion of high-risk cases according to history taking and physical examination, and screening blood units for HBsAg, HIV Ab, and HCV Ab using ELISA. Fortunately, blood donation in Iran is not paid and the donors are volunteer, which makes it safer. On the other hand, in one of our studies, transfusion was found to be an independent risk factor for hepatitis C in Iran, but it seems that these transfusions have been performed before implementation of blood screening in 1996.

**HCV infection in special diseases**

Hepatitis C virus (HCV) is a major cause of chronic liver disease among chronic renal failure (CRF) patients undergoing maintenance hemodialysis. The prevalence of HCV infection among dialysis patients varies markedly from country to country, ranging from 3% in north-western Europe to more than 76% in Asia (Indonesia).

There are few studies involving large multicenteric sampling that provide epidemiological aspects of HCV infection among hemodialysis patients in Iran. The prevalence is from 5.5% to 55.9% in different cities. History of blood transfusion, the number of transfused units, longer dialysis duration, and history of previous renal transplantation were risk factors for HCV positivity in hemodialysis patients. HCV infection does not seem to influence patient and graft survival within a medium-time follow-up in living allograft recipients, and anti-HCV-antibody positive status (alone) is not a contraindication for renal transplantation.

Patients with hemophilia constitute a high-risk group for acquisition of HCV infection. Transmission of HCV via blood products has been
a significant source of hepatitis C infection for patients with hemophilia. During last decade, several cross-sectional studies have been published in the world concerning the prevalence of hepatitis C among hemophilic patients, indicating a wide range from 25% to 100%. The older hemophiliacs are exposed to HCV infection for a longer time compared with the younger ones, and it seems that the prevalence of HCV should be higher in this group. Most of the infected hemophilic patients are asymptomatic. Natural history of hepatitis C in hemophiliacs has been investigated in several studies. Eyster reported that risk factor of developing liver failure is more common in patients who were infected with HCV and HIV. Screening of these patients has a critical importance as infected patients should be identified, followed, and treated.

The prevalence of HCV infection in Iranian hemophilic patients is from 15.65% in Fars, a southern district of Iran to 76.7% in North-West of Iran in different studies (Table 1). Before the introduction of compulsory testing for HCV, adolescent and adult patients with thalassemia received multiple blood transfusions with a high risk of HCV transmission and 60 to 80% of thalassemic patients were anti-HCV Ab positive according to various reports. Chronic posttransfusion hepatitis C is a progressive disease and dramatically increases morbidity and mortality rate among thalassemics due to liver failure or hepatocellular carcinoma. The countries with a higher HCV prevalence in thalassemia had a higher prevalence rate among general population, too. For instance, a study in Egypt reported 75% of HCV prevalence among thalassemic cases, considering the fact that the prevalence in their blood donor population was 14.5%. Whereas, in India with a low HCV prevalence among blood donors (1.78%), the prevalence in thalassemics was reported relatively low (25.5%).

In Iran, a recent report from northern part showed 63.8% positive HCV Ab in thalassemics in comparison with the prevalence of blood donors (0.5%). A confirmatory immunoblotting test was employed using HCV-positive cases, which showed that 92.6% of samples were positive. Karimi and Ghavanini from Shiraz reported 73 of 466 thalassemic children with a history of multiple transfusions (15.7%; 95 CI = 12.6 – 19.2) positive for HCV Ab. Five years before this study, in the same location, Saber-Firooz et al reported 27.1% of cases were positive for anti-HCV antibody. Mean age, duration, and mean amount of blood transfused were significantly higher in patients with HCV infection. The relative risk of HCV infection for each unit of blood transfusion was 0.2%. In our experience on Iranian thalassemic patients in Tehran, 24.2% of them were anti-HCV positive. Anti-HCV Ab-positive patients had a significantly longer duration (mean difference 38 months) of transfusion compared with anti-HCV Ab-negative cases. It should be mentioned that after initiation of donors screening for HCV in 1995 and exclusion of high-risk groups from donation pool, the prevalence of HCV infection in thalassemic patients had decreased significantly and no case has been infected after that time.

The relative importance of the two most common exposures associated with the transmission of HCV has changed over time. Blood transfusion, which accounted for a substantial proportion of HCV acquired more than 10 years ago, accounts for only a small proportion of recently-acquired infection. In contrast, illegal drug use has accounted for a substantial proportion of HCV during both the remote and recent past.

### Table 1. Prevalence of anti-HCV in different groups in Iran.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year(s)</th>
<th>Type of subject</th>
<th>Number tested</th>
<th>Percentage positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rais-jalali et al</td>
<td>1999</td>
<td>Hemodialysis patients</td>
<td>182</td>
<td>5.5</td>
</tr>
<tr>
<td>Ansar et al</td>
<td>1997 – 1998</td>
<td>Hemodialysis patients</td>
<td>93</td>
<td>55.9</td>
</tr>
<tr>
<td>Alavian et al</td>
<td>2003</td>
<td>Hemodialysis patients</td>
<td>838</td>
<td>13.2</td>
</tr>
<tr>
<td>Mansour-Ghanaei et al</td>
<td>1999</td>
<td>Hemophilic patients</td>
<td>101</td>
<td>71.3</td>
</tr>
<tr>
<td>Ebrahim-poore et al</td>
<td>1997</td>
<td>Hemophilic patients</td>
<td>80</td>
<td>76.7</td>
</tr>
<tr>
<td>Karimi et al</td>
<td>1999 – 2000</td>
<td>Hemophilic patients</td>
<td>47</td>
<td>15.65</td>
</tr>
<tr>
<td>Alavian et al</td>
<td>2000 – 2001</td>
<td>Hemophilic patients</td>
<td>176</td>
<td>60.2</td>
</tr>
<tr>
<td>Karimi et al</td>
<td>1999 – 2000</td>
<td>Thalassemic patients</td>
<td>466</td>
<td>15.7</td>
</tr>
<tr>
<td>Saber-firooz et al</td>
<td>1997</td>
<td>Thalassemic patients</td>
<td>90</td>
<td>27.1</td>
</tr>
<tr>
<td>Alavian et al</td>
<td>2001</td>
<td>Thalassemic patients</td>
<td>95</td>
<td>24.2</td>
</tr>
<tr>
<td>Ansar et al</td>
<td>1997 – 1998</td>
<td>Thalassemic patients</td>
<td>105</td>
<td>63.8</td>
</tr>
</tbody>
</table>

Molecular genotyping of HCV in Iran

The nucleotide sequence of HCV may vary considerably from one isolate to another, forming the basis for at least six known genotypes. In the
first report in Iranian patients, the prevalence of specific genotypes in 15 samples was studied by Zali and his group in Tehran and the results were as follows: Type I/1a in seven cases, Type II/1b in three cases, and Type V/3a in four patients. One sample disclosed Type 4. A recently published article by Samimi-Rad et al. in Iranian patients with anti-HCV Ab positive from Tehran and five cities from different locations of Iran, showed that genotype 1a was predominant (47%), and 3a, 1b, and 4 were 36%, 8%, and 7%, respectively. The patterns of our genotypes are similar to those of England, but different from other Middle-East countries such as Republic of Yemen, Kuwait, Iraq, and Saudi Arabia, where genotype 4 is the most prevalent. HCV genotype 4 was detected in 50% and genotype 1b was found in nearly 40% of Saudi patients.

Conclusion

Better understanding of the mode of spread of HCV disease will assist in minimizing HCV spread globally. The overall burden on the society both financially and socially to support and manage individuals with HCV is another recommendation. It is suggested to have a strategy to inform and educate the public and press regarding this disease to have HCV awareness program. Educating personnel of dialysis centers for more health caution to prevent nosocomial transmission and minimizing transfusion requirements by judicious use of erythropoietin are very important. Availability of inexpensive sensitive and specific tests for detection of HCV infection will help in diagnosis and prevention of transmission. Finally, the main comment is to consider the IUD patients as a source for transmission in general population and we should try to prevent needle-sharing by addicted persons and to change pattern of addiction to a less harmful one (harm reduction program).

References


Bell J, Batey RG, Farrell GC. Hepatitis C virus in intravenous drug users. 


