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Epidemiology of Hepatitis C in Iran and the World.

Alavian SM *, Fallahian F*.

* Research Center for Gastroenterology and Liver Disease, University of Medical Sciences, Baqiyatallah Baqiyatallah Research Center for Gastroenterology and Liver Disease, Baqiyatallah University of Medical Sciences.

Correspondence: Dr. S. M. Alavian, Professor of Internal Medicine, Gastroenterology and Hepatology. Baqiyatallah Research Center for Gastroenterology and Liver Disease, Tehran, Iran, Telephone: +98(21) 8894-5186, Fax: +98(21) 8894-5188, E-mail: alavian@thc.ir

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Abstract:

Hepatitis C virus (HCV) infection creates a significant burden to health care system. The epidemiological characteristics and risk factors for transmission vary across countries. A literature review of published scientific reports on HCV epidemiology in Iran and summarize of findings of some countries was performed. Prevalence of hepatitis C in Iran ranges from 0.5% to 0.97% in blood donors, 19.3% in patients with thalassemia, 19.6% in patients on maintenance hemodialysis, 31.5% of drug abuser inmates in a prison of Hamadan, 45.4% of inmates and 88.9% of intravenous drug abusers of a prison in Guilan were HCV antibody positive. The risk of infection related to injection drug use and health care serving are the most important for still growing number of infected persons. Expansion of harm-reducing interventions for drug users, and educating preventive programs in targeted high-risk behaviors populations will improve infection spread in our country. Design appropriate public health strategies by involvement of regional health agencies for education, supervising addiction control and establish policies for the appropriate use of injections, sterile principles in health-care-related procedures, and improvement in blood transfusion safety in countries with high drug trafficking and insufficient health and social resources is needed. Control of HCV transmission requires continuous monitoring, surveillance and prevention.

Keywords: Epidemiology, hepatitis C virus, transmission, risk behaviors, Iran, world

Introduction:

Hepatitis C is a global health problem affecting over 170 million people worldwide.[1] Most hepatitis C virus is spread parenterally, either through intravenous drug use or, in lesser-developed countries, through blood contamination during medical procedures. Despite a declining incidence of new infections, the burden of disease, both in terms of mortality and in terms of cost, is expected to increase over the next decade.[1] HCV is a potential cause of substantial morbidity and mortality in the future. The complexity and uncertainty related to the geographic distribution of HCV infection and chronic hepatitis C, determination of its associated risk factors, and evaluation of cofactors that accelerate its progression, underscore the difficulties in global prevention and control of HCV. Most persons who acquire acute HCV infection either have no symptoms or have a mild clinical illness. However, chronic HCV infection develops in 75%-85% of those acutely infected.[2] HCV-infected people serve as a reservoir for transmission to others. It has been estimated that HCV accounts for 27% of cirrhosis and 25% of HCC worldwide. HCV infection has likely been endemic in many populations for centuries.[3] The focus of primary prevention efforts should be safer blood supply in the developing world, safe injection practices in health care and other settings, and decreasing the number of people who initiate injection drug use.[4]

In this manuscript studies about epidemiology, transmission and risk behaviors of hepatitis in Iran and other countries would be reviewed.

Methods:

A review of literature was performed in 2008 to summarize scientific reports on epidemiology of the HCV infection in Iran and other countries. Articles indexed in the PubMed database and Google and Iran Medex for medical journals. Papers published during recent years (1994-2008) were searched by using the following key words: hepatitis C, epidemiology, prevalence, transmission, Iran. Country-specific information was searched by adding a country name to the search. The search was restricted to few countries in each continent. To obtain information on risk groups, the terms injecting drug users, sex workers, prisoners, tattooing, immigrants, hemodialysis, blood transfusion, blood donors, and health care workers were added to the search. The search was restricted to publications written in English and Persian.

Results:

Epidemiology, prevalence, and transmission of hepatitis C in Iran

The prevalence rate for anti-HCV positive in blood donors as a mean figure for samples from the whole country of Iran in 1994 was 0.3% reported by Rezvan et al.[5] The prevalence of anti-HCV among 7897 healthy voluntary blood donors in Shiraz, Iran, using a second-generation enzyme-linked immunosorbent assay was 0.59% in 1998.[6] In a study in blood donors: transfusion, undergoing endoscopy, extramarital sexual activities, non-intravenous (IV) drug abuse, IV drug abuse, and receiving wounds at war were found to be independent risk factors of being HCV-positive (Odds ratio: 17, 4,

42.2, 34.4, 52.8 and 5.2, respectively). No apparent risk factors could be demonstrated in 24.5% of the positive cases. [7] 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.[8] The prevalence of HCV infection in Iranian hemophilic patients is from 15.6% in Fars [9], southern district of Iran, 44.3% in Kerman [10], 29.6% in Zahedan [11], 59.1% (12) in Hamadan, 71.3% (13) in Guilan to 76.7% in North-West of Iran in different studies and roughly 50% in the country.[14-17] Thalassemic patients are at high risk for hepatitis C infection and 19.3% in seven hundred and thirty-two patients with beta-thalassemia from five provinces of Iran are infected.[18] The collected data of all hemodialysis patients in Iran showed the prevalence of positive HCVAb decreased from 14.4% in 1999 to 4.5% in 2006.[19] Positive HCV antibody in 548 patients on maintenance dialysis in Tehran was present in 19.6%. Prevalence of HCV antibody seropositivity was not different in patients with or without history of blood transfusion. It seems that nosocomial transmission is the main route of infection in patients on dialysis in Iran.[20] In study 300-household contacts of 60 index cases of HCV infection and 360 pair-matched controls in Ahwaz, Iran, only 4 of 300 (1.33%) cases of household contacts were positive for HCVAb. The anti-HCV prevalence in parents, spouses, children of the index cases was 0.87% (1/115), 3.39% (2/59) and 0.79% (1/126), respectively. The prevalence of positive HCVAb among household contacts (1.33%) was not significantly higher than that in the controls (1%). Interfamilial transmission of HCV is not the significant transmission route and sexual transmission does not seem to play a role in the interfamilial spread of HCV infection.[21] In a study of 254 HCV positive subjects in Ahwaz, Iran; independent risk factors of being HCV-positive were more male gender, received transfusion, non-intravenous drug abuse and i.v. drug abuse, on maintenance haemodialysis, receiving wounds at war and extramarital sexual activities, tattooing. In 29 (11.2%) of the positive cases no apparent risk factors was found.[22]

In 3.1% of 226 gypsies HCV Ab was positive. Because of permanent immigration, poor socioeconomic status and the special life style, gypsies should be considered a high risk group for HCV infection.[23] Many studies in Iran are reported; the intravenous drug users (IDUs) had HCV infection between 38% and 47%.[24] In a study, 34.9% of inmates in Hamedan Prison were injection drug abusers and 65.1% were non-injection drug abusers. Of all injection drug abusers, 31.5% and of non-injection drug abusers, 29.1% had serological evidence of HCV infection.[25] Of 460 inmates in a prison in Guilan, 45.4% were HCV antibody positive and 88.9% of intravenous drug abusers were infected. HCV-positive status in drug abusers admitted to prison in Guilan was significantly associated with intravenous drug use, having skin tattoos and number of times in prison.[25] In a study of 292 Iranian drug users seeking treatment through a general practice clinic in Marvdasht, Iran (34% IDU, 31% DU and

35% non-drug users), the mean age of the sample was 30 years. Of the IDU sample, 67% reported sharing a needle or syringe, 19% of these had done so in prison. Mean age of first drug use was 20 years. The first drugs most commonly used were opium (72%), heroin (13%) and hashish/ other cannabinoids (13%). IDU were more likely than DU to report having ever been imprisoned (41% vs 7%) and 41% to have used drugs in prison. The expansion of services for drug users in Iran such as needle and syringe programs and pharmacotherapies are likely to be effective in reducing the harms associated with opium use and heroin injection.[24]

In a study, 105 of 202 (52.0%) of injecting drug users were positive for HCV-antibody in Tehran in 2004. HCV infection was associated with length of drug injection (more than 10 years) [odds ratio (OR), 3.25; 95% confidence interval (CI), 1.43-7.38], length of lifetime incarcerations (more than a year) (OR, 3.44; 95% CI, 1.68-7.06), and a history of being tattooed inside prison (OR, 1.96; 95% CI, 1.06-3.62).[26]

Epidemiology, transmission and risk behaviors of hepatitis C in other countries

Approximately 3% (170 million) of the world's population has been infected with HCV (table 1).[27] Prevalence is higher (up to 15%) in some countries in Africa and Asia, and highest (over 15%) in Egypt.(28-29) The overall prevalence of anti-HCV in a survey during 1988 to 1994 in the USA was 1.8 percent. Among subjects 17 to 59 years of age the strongest factors associated with HCV infection were illegal drug use and high-risk sexual behavior. Neither sex nor racial-ethnic group was independently associated with HCV infection.[30] In another survey in from 1999 to 2002 in the USA, the prevalence of anti-HCV was 1.6% (95% CI, 1.3% to 1.9%). A total of 48.4% of anti-HCV-positive persons between 20 and 59 years of age reported a history of injection drug use. Other significant risk factors included 20 or more lifetime sex partners and blood transfusion before 1992.[31] The most frequent mode of transmission in the United States is through sharing of drug-injecting equipment among injecting drug users.[31] For international travelers, the principal activities that can result in blood exposure include receiving blood transfusions that have not been screened for HCV; having medical or dental procedures or engaging in activities (e.g., acupuncture, tattooing, or injecting drug use) in which equipment has not been adequately sterilized or disinfected or in which contaminated equipment is reused; and working in health-care fields (e.g., medical, dental, or laboratory) that entail direct exposure to human blood.[4] Among Central and South America, a recent community based study in San Juan, Peurto Rico, showed that estimated prevalence of HCV in 2001-2002 was 6.3%.[32] Multivariate logistic regression revealed that tattooing practices, lifetime cocaine use, blood transfusions prior to 1992, lifetime heroin use, and history of imprisonment remained significantly associated with HCV seropositivity.[34] In Mexico, the reported prevalence was about 1.2%.[33] Anti-HCV was detected in 0.49% of the first-time blood donors in Japan during 1995-2000.[34] In a cohort

study after 5 years of following 375 subjects living in a hyperendemic area of HCV in Japan, the prevalence of anti-HCV was (23.4-24.0%), and seroconversion rate was 0.28% per year. Seroconversion rates of HCV in a hyperendemic area of HCV were extremely high, and medical treatment was considered to be a causative route of HCV transmission.[35] A study mentioned the vertical transmission of HCV from infected mothers to their babies, and that the risk of transmission is correlated with the titer of HCV RNA in the mother.[36]

In China, the prevalence rates was low, around 1% among donors in Beijing and Wuhan, but was higher in certain areas such as the Hubei province (30.13%) and Inner Mongolia Autonomous Region (31.86%).[37,38,39] In a longitudinal cohort of 597 young injection drug users (IDU) from southern China, HCV prevalence was 72%. HCV prevalence within one year of starting heroin use was 57% for any route of administration, and 80% if restricted to injectors. After two 6-month follow-up visits, 56 out of 159 baseline HCV seronegative individuals (148.9 total person years [py]), underwent seroconversion at an incidence rate of 37.6 per 100 py. Individuals who reported injection drug use were more likely to undergo HCV seroconversion (rate ratio [RR] = 6.59).[40] A cohort of 333 HIV-seronegative IDU was followed for 36 months from 2002 in a drug trafficking city in southwest China. Predictors of HCV seroconversion included being female, greater frequent drug use in the past 3 months seven or more times per week, and frequent sharing of needles or syringes in the past 3 months one or more times per week.[41]

A community-based study in Hafizabad, Punjab of Pakistan found a 6.5% seroprevalence of HCV infection.[42] General seroprevalence of anti-HCV in healthy adult male population from the northern Pakistan was 5 percent for anti-HCV.[43] This reflects that the population at large is exposed to the same risk factors. Community trends like reuse of disposable or glass syringes, repeated use of potentially contaminated razors by barbers, improper dental practices are risk factors.[44]In a study of 464 adult injection drug users (IDUs) in Kabul, Afghanistan from 2005 to 2006, prevalence of HIV and HCV were 3.0% (95% confidence interval [CI] 1.7%-5.1%), 36.6% (95% CI 32.2%-41.0%); respectively. Needle sharing, injecting for > or = 3 years, and receiving injections from nonmedical providers were independently associated with increased risk for HCV infection.[45] Of 1214 patients with viral hepatitis identified in Saudi Arabia during 2000 to 2005, HBV was the most predominant type of hepatitis (49.3%), followed by HCV (40.7%).[46]

The prevalence for anti-HCV antibodies in 8862 subjects at Hail region of Saudi was 5.09%. Egyptians had a high prevalence of 26% as compared to other expatriates. The prevalence of anti-HCV in blood donors was 4.3%, in medical staff 2.2%, and dialysis patients 6.9%.[47] There has been very high prevalence rates of HCV reported in Egypt in the past (28%).[48]

There have been fewer studies out of Africa, 1.6% among blood donors in

Ethiopia and 0.9% in Kenya.[49-50]The estimated prevalence in Australia recently reported as 2.3%.[51] Almost 250,000 HCV cases were notified by 24 European Union (EU) and European Economic Area/European Free Trade Association (EEA/EFTA) countries in 1995-2005. During this period a steady increase in the incidence of reported HCV cases was observed.[52] The data from Europe indicate a wide variation in HCV prevalence between the countries, ranging from 0.1 to 6.0%. The lowest HCV prevalence (≤ 0.5%) estimates are from Scandinavian countries, Austria and the Netherlands, and the highest (≥ 3%) from Bulgaria, Greece, Italy and Romania.[53] Prevalence of HCV antibody is 0.87% (1993-1994) in Belgium [54], 3.2% in Northern Italy [55], and 1.3% in France.[56] Prisoners often have prevalence rates of antibodies to HCV comparable to those of IDUs due to a high proportion of IDUs among this group.[58,59] In Germany, Spain and in the UK the anti-HCV prevalence in sex workers ranged from 0.7 to 9.0 %; with the lowest estimate in Germany.[60] HCV infections in sex workers have been shown to be associated with injecting drug use.[61] In a study conducted on 433 subjects in the Italian and foreign inmates of the prison of Bologna, Italy; 31.1% of inmates were HCV positive. Anti-HCV positive was is more common among Italian vs. foreign inmates, and among IDU vs. not IDU.[62] Of 1366 inmates in the prison population of the Republic of Ireland, prevalence of antibodies to hepatitis C virus was 442/1193 (37%; 34.3% to 39.9%). The most important predictor of being positive for hepatitis C was a history of injecting drug use.[63] Acquiring a tattoo in prison was common and the reports of sharing the tattooing needle and ink was high, placing prisoners at risk of acquiring HCV through tattooing in prison.[64]

Table 1- Hepatitis C estimated prevalence and number infected by WHO Region. Source: Weekly Epidemiological Record. N 49, 10 December 1999, WHO

WHO Region	Total population (millions)	Hepatitis C prevalence Rate %	Infected Population (Millions)	Number of countries by WHO Region where data are not available
Africa	602	5.3	31.9	12
Americas	785	1.7	13.1	7
Eastern Mediterranean	466	4.6	21.3	7
Europe	858	1.03	8.9	19
South-East Asia	1 500	2.15	32.3	3
Western Pacific	1 600	3.9	62.2	11
Total	5 811	3.1	169.7	57

Discussion and conclusion:

Very high rates of HCV antibody reactivity (>70%) have been reported in injecting drug users and in hemophiliacs. Intermediate prevalence of 20 to 30% has been observed in patients receiving hemodialysis. The incidence is declining since transmission by blood products has been reduced to almost zero and universal precautions in medical settings are followed.[65] Transfusion-associated cases occurred prior to donor screening. Now they are very rare where blood is

screened with 2nd and 3rd generation EIAs, about 0.004% to 0.0004% per unit transfused. Most new infections are the consequence of high risk drug behavior (60%) or unsafe injection practices.[66]

In a review of IDUs in 57 countries and in 152 sub-national areas, HCV prevalence of at least 50% detected among IDUs in 49 countries or territories. Regional estimates varied widely, from 10 to 96% in Eastern Europe and Central Asia, from 10 to 100% in South and South-East Asia, from 34 to 93% in East-Asia and the Pacific, from 5 to 60% in North Africa and the Middle-East, from 2 to 100% in Latin America, from 8 to 90% in North America, from 25 to 88% in Australia and New Zealand, and from 2 to 93% in Western Europe. Only in Colombia and Lebanon were all HCV prevalence estimates below 20%. In China, Poland, Puerto Rico, Russia, Spain, Switzerland, Thailand and Viet Nam, estimates of the prevalence of HIV/HCV co-infection among IDUs reached 90%.[67] Implementing substitution treatment with concomitant effects and treatment elements such as drug history-taking, dosage setting, co-use of other psychoactive substances (alcohol, benzodiazepines, cocaine), management of 'difficult patient populations', and integration into the social environment, and involvement of self-help groups in the process of successful substitution treatment is recommended.[68] The prisoners' health must urgently be dealt with and particularly as regards infectious diseases, vaccination check-up, campaign against drug addiction health and nutrition education and dental care. As the number of intervening medical and social personnel, is increasing in prisons, coordination inside the walls as well as on the regional and national levels would prove useful.[69]

According to present data review, injecting drug use is a major risk of HCV exposure in both developed and developing countries. In developing and underdeveloped countries unsafe medical procedures and transfusion are still important routes of HCV transmission. Thus in countries that HCV infection is more prevalent in their old age group, it may be due to their inappropriate previous therapeutic injections, dental treatment, hospitalization, and medical procedures; the situations that still exist in some developing countries. Half of the more than 16 billion injections administered in the developing world have been estimated to be unsafe.[28]

The estimation of global real incidence and burden of HCV is difficult because of limited screening activities, accurate testing methods, legal aspects of reporting, and presence of asymptomatic cases that can serve as a reservoir for infection. In developing countries with limited access to disposable hospital devices, unsafe injections and contaminated equipments used in medical procedures, and insufficient laboratory services, transmission of HCV by high risk groups would get widespread and they not even endanger their friends and families to HCV exposure but also the general population.

In Iran, family practitioners at primary health care units along with midwives engaged in educating. Screening of high risk groups as hemophiliac, thalassemic patients, patients on hemodialysis, pris-

oners and addicts is performed through a network is started in our country. Implementing harm-reducing interventions, standardized substitution treatment programs for drug users, psychosocial counseling, and medical follow-up of specific co-morbidity is necessary. Educating preventive programs in targeted high-risk behaviors populations will further improve spread of infection in our country. It seems the majority of world-wide new cases of HCV are related to injection drug use, and health care serving. The large prevalence of HCV infection observed in our neighboring countries suggests that HCV infection is an emerging public health concern now and in future. Control of HCV transmission requires to structure monitoring, surveillance and preventive public health strategies.

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