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**Review Article** 

# Hepatitis C Virus Infection in Isfahan, Iran: A Review Article

Zary Nokhodian,<sup>1</sup> Farzin Khorvash,<sup>2</sup> Behrooz Ataei,<sup>1</sup> and Mohsen Janghorbani<sup>1,3,\*</sup>

<sup>1</sup>Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, IR Iran
<sup>2</sup>Nosocomial Infection Research Center, Isfahan University of Medical Sciences, Isfahan, IR Iran
<sup>3</sup>Department of Epidemiology, School of Public Health, Isfahan University of Medical Sciences, Isfahan, IR Iran

<sup>\*</sup> Corresponding author: Mohsen Janghorbani, Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, IR Iran, E-mail: janghorbani@hlth.mui.ac.ir

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# Abstract

**Context:** The hepatitis C virus (HCV) is a serious worldwide health problem. The HCV infection prevalence rate has been estimated to be approximately 0.16% in the general Iranian population. In this review, the authors summarize various epidemiological studies of HCV infection in Isfahan, Iran.

**Evidence Acquisition:** Published studies were accessed from PubMed, Ovid, EMbase, Google Scholar, Iranmedex, Magiran, and the Scientific Information Database (SID), as well as from a manual search using references cited in relevant papers.

**Results:** Twenty-eight studies, including 6, 17, 4, and 1, reported a prevalence of HCV in Isfahan province, and Isfahan, Kashan, and Foulad shahr cities. Sample sizes ranged from 73 to 542,705. The highest prevalence of HCV infection was reported in HIV-infected patients, and the lowest prevalence was found in laboratory workers.

**Conclusions:** The results of this study revealed the important role injection drug use plays as the main cause of HCV spread in Isfahan province. Effective harm reduction programs should be implemented to prevent new HCV infections. Considering the high prevalence of HCV infection among HIV patients, this group should receive special attention.

Keywords: Prevalence, Hepatitis C Virus, Isfahan, Iran

# 1. Context

The hepatitis C virus (HCV) is the most common bloodborne disease worldwide, with more than 170 - 200 million people affected (1). Most people with the HCV progress to a chronic infection, which can lead to hepatic fibrosis, cirrhosis, liver failure, hepatocellular carcinoma, and death (2). Despite declining incidence of new infections, prevalence of the HCV remains high and is expected to increase over the next decade, potentially causing substantial morbidity and mortality (1). The sources of the infection include transfusion of blood products and contamination during medical procedures, intravenous drug use, sexual exposure, and mother to child transmission (3).

Prevalence of the HCV varies from 0.2% - 40% depending on the country (1, 4), but it is lowest in developed nations and highest in developing nations (5). For example, in China (6, 7), Japan (8), and India (8), prevalence rates have been estimated to be approximately 1%, 0.49%, and 1.85%, respectively, among blood donors. In Malaysia (9), Singapore (10), and Thailand (11), prevalence has been reported to be as high as 1.6%, 0.54%, and 5.6%, respectively. In comparison, the prevalence rates in Saudi Arabia and Yemen are 1.8% and 2.1%, respectively (12, 13).

Studies on the prevalence of HCV infection in different

regions or among high-risk groups in Iran have been conducted and have estimated the prevalence rate to be approximately 0.16% in the general population (14). The first paper was published in 1994, using samples from Iranian blood donors (15). In 2007, the prevalence of HCV Ab was 1.62% among blood donors in a province in the north of Iran (16). In later reports, the rate of HCV infection was 0% in Tehran and Khuzestan (4, 17) but 1.3% in the Guilan province (18). The purpose of this brief review is to summarize various epidemiological studies of HCV infection in Isfahan, Iran.

# 2. Evidence Acquisition

#### 2.1. Search Strategy and Identification of Studies

To identify relevant studies, PubMed, Ovid, EMbase, Google Scholar, Iranmedex, Magiran, and the scientific information database (SID) were searched for all epidemiological studies on HCV prevalence dating up to June 2012, using the keywords: hepatitis C, HCV, HCV Ab prevalence, and epidemiology. The keywords were combined with Isfahan or Esfahan to limit the studies to those involving human subjects. Additionally, reference lists from the identified publications were reviewed for additional pertinent

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studies. The Iranian center for scientific documents and records (IranDoc) was also searched for students' theses. No language restrictions were imposed.

# 2.2. Eligibility Criteria

All epidemiological studies published in peerreviewed journals or students' dissertations that reported the prevalence of HCV infections based on HCV antibody screenings using ELISA or RIBA/PCR were selected. Because this study attempted to estimate the prevalence of HCV in Isfahan province, only studies with source populations resided in Isfahan were included. None of the study subjects had serious medical problems related to the liver and none took medication affecting liver enzymes.

Twenty-eight cross-sectional studies were considered for inclusion in this review (19-46). Six studies assessed the prevalence of the HCV in Isfahan province (30-34, 41), 17 studies assessed the prevalence in Isfahan city (21-25, 28, 29, 35-40, 42-44, 46), four studies assessed the prevalence in Kashan city (19, 20, 26, 45), and one study assessed prevalence of the virus in Foulad-Shahr city (27).

# 2.3. Data Extraction

Data were extracted pertaining to publication information (including the first author's last name, the year of publication, and the city or population studied), study design, and the number, age, and gender of the individuals involved. Information on study design, participant characteristics, prevalence of HCV infection, and laboratory measurements was extracted independently by two reviewers. Discrepancies were resolved by discussion.

#### 3. Results

After the studies were reviewed, 29 were found that discussed HCV prevalence in Isfahan province, including 25 articles (19-43), three student theses (44-46), and one research project (47). The research project (47) was excluded because it remains ongoing; therefore, 28 relevant studies of satisfactory quality were found. Seventeen investigations were chosen from studies conducted in Isfahan city (21-25, 28, 29, 35-40, 42-44, 46), four from Kashan city (19, 20, 26, 45), and one from Foulad-shahr city (27). Other studies were associated with other parts of Isfahan province. The sample sizes ranged from 73 - 542,705, and 25 studies were cross-sectional.

#### 3.1. The Prevalence of HCV Among Blood Donors

Seven studies (19-24, 44) were found during the literature review about HCV prevalence among blood donors in Isfahan province. Table 1 shows these search results. From

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these seven studies, five were performed in Isfahan city (21-24, 44) and two studies were performed in Khashan city (19, 20). Masaeli et al. (21) compared HCV Ab prevalence between regular, sporadic, and first-time blood donors in Isfahan city and found that the HCV Ab was less common among regular blood donors than sporadic and first-time donors. In a similar study in Isfahan, the frequency of HCV Ab in regular donors and first-time blood donors was 0.23% and 0.53%, respectively (23). Salehi et al. (22) evaluated blood samples from two groups of donors (routine and religious ceremony donors) for HCV Ab. The results of this study showed no statistical difference in HCV Ab prevalence between these two groups. In Ebrahimian's study, HCV Ab seropositivity was less common in volunteers referred to the Isfahan blood transfusion organization between 2004 and 2008 but more common from 2008 to 2009 (24). Similarly, the prevalence of HCV Ab infection among healthy volunteer blood donors referred to the Kashan blood bank significantly increased from 0.38% in 1996 to 1.71% in 2001 (19).

# 3.2. The Prevalence of HCV in High-Risk Populations

#### 3.2.1. Injection Drug Users

Injection drug use (IDU) is considered a primary cause of HCV infection (48). The prevalence of the HCV among injection drug users in Isfahan ranges from 23.3% - 75.5% (25-32). This wide range reported in studies is partially explained by variations in the duration of IDU among subjects. Younger age groups had a significantly lower prevalence of the HCV than older age groups, although age is likely associated with the duration of IDU. In fact, the study that found a 23.3% prevalence of HCV only included people younger than 30 years of age (29). Eight studies were found (25-32) on HCV prevalence among injection drug users in Isfahan province (Table 1). Khorvash et al. (28) and Meidani et al. (29) evaluated the frequency of HCV cases among drug users who were admitted to Al-Zahra Hospital in Isfahan from 2004 to 2005 and 2007 to 2008, respectively. A similar study was conducted in Kashan from 2001 to 2006 (26). Tayeri et al. (25) assessed the prevalence of HCV in HIV positive patients with a history of IDU and found it to be 75.5%. In Fadaei Nobari et al. (32), the prevalence of HCV was evaluated among intravenous drug users in Isfahan province.

#### 3.3. Incarcerated Populations

The true prevalence of the HCV in incarcerated populations is difficult to obtain because no mandated screening programs exist, and the number of studies that have investigated HCV prevalence in this population is limited. The only data from the Isfahan correctional system were from a cross-sectional study of 160 young prisoners from Isfahan

Source	Year of Publication	City	Study Population	Number of Participants	No. (%) of HCV Cases	Age, y
Mojtabavi et al. (43)	2007	Isfahan Province	Hemophilic patients	553	553 (22.6)	$23.4 \pm 12.9$
Afzali et al. (19)	2001	Kashan city	Regular blood donors	43,731	43.731 (1.1)	
Yazdani et al. (41)	2012	Isfahan Province	Hemophilic patients	350	350 (66)	24
Ataei et al. (40)	2012	Isfahan city	Patients with beta thalassemia	466	463(8)	$17.46 \pm 8.3$
Ataei et al. (33)	2010	Isfahan Province	HIV-infected patients	130	130 (77)	$50.23 \pm 8.81$
Lenjani et al. (44)	1999	Isfahan city	Regular blood donors	579	579 (1.73)	
Rahimi et al. (46)	2000	Isfahan city	Hemophilic patients	150	150 (72)	
Hashemi et al. (45)	2002	Kashan city	Hemodialysis patients	73	(8.22)	
Tayri et al. (25)	2008	Isfahan city	Injection drug users	106	106 (75.5)	$50.8 \pm 8.1$
Moniri et al. (20)	2004	Kashan city	Regular blood donors	600	600 (0.5)	
Sharif et al. (26)	2009	Kashan city	Injection drug users	200	200 (-)	$36.5 \pm 10.2$
Masaeli et al. (21)	2006	Isfahan city				
		-	Regular blood donors	16,620	16.620 (0.19)	
			Sporadic blood donors	5,742	5,742 (0.31)	
			First-time blood donors	7,096	7.096 (0.31)	
Salehi et al. (22)	2011	Isfahan city		1,-5-	,1151(1151)	
	2011	isanan city	Regular blood donors	2,635	- (0.15)	
			R.C.B.D	2,173	-(0.41)	
	2005	Info have also	KC.D.D	2,175	-(0.41)	
Pourazar et al. (23)	2006	Isfahan city	Denvie bland daman	12.156	(2,455 (0,22))	20 + 10
			Regular blood donors	43,456	43.455 (0.23)	38±19
			First-time blood donors	7,997	7.997 (0.53)	31.8 ± 13
Hariri et al. (34)	2006	Isfahan Province				
			Thalassemic patients	616	616 (10.9)	15.5±8
			Hemophilic patients	120	120 (64)	$22\pm14$
Khorvash et al. (28)	2009	Isfahan city	Injection drug users	92	92 (57.6)	$31.7\pm2$
Ebrahimian et al. (24)	2009	Isfahan city				
			Regular blood donors	54,2705	- (0.18)	•
			Regular blood donors	54,2705	-(0.15)	
			Regular blood donors	54,2705	-(0.13)	
			Regular blood donors	54,2705	-(0.11)	
			Regular blood donors	54,2705	-(0.09)	
			Regular blood donors	54,2705	- (0.11)	
Ataei et al. (36)	2010	Isfahan city	Street children	386	386 (1)	$12.62\pm3.23$
Ataei et al. (35)	2008	Isfahan city	Transit heavy vehicle drivers	235	235 (1.3)	$41.8\pm9$
Meidani et al. (29)	2009	Isfahan city	Injection drug users	150	150 (23.3)	$30.7\pm7.09$
Zamani et al. (27)	2010	Foulad-Shahr city	Injection drug users	118	118 (59.4)	-
Nokhodian et al. (30)	2012	Isfahan Province	Injection drug users	531	531 (47.1)	$31.77 \pm 8.51$
Nokhodain et al. (39)	2012	Isfahan city	Young prisoners	160	160 (4.4)	$16.59 \pm 1.24$
Kalantari et al. (38)	2011	Isfahan city				
			Thalassemic patients	545	545 (9.17)	$18.7\pm6$
			Hemophilic patients	615	615 (80.5)	$27.1 \pm 12.8$
Kassaian et al. (31)	2012	Isfahan city	Injection drug users	943	943(41.6)	32.6
Fadaei Nobari et al. (32)	2012	Isfahan Province	Injection drug users	1,747	595 (34)	$35\pm9.4$
Kassaian et al. (37)	2011	Isfahan city	Women exhibiting illegal social behavior	100	100 (9.9)	30.84 ± 9.34
Shoaei et al. (42)	2012	Isfahan city	Laboratory healthcare workers	203	203 (0.00)	35.8 ± 9.54

Table 1. Cross-Sectional Studies of the Prevalence of HCV Infection in Isfahan Province That Satisfied the Eligibility Criteria for Inclusion in This Systematic Review

correctional facilities, conducted in 2012, which showed a prevalence of HCV of 4.4% (39). Because prisoners do not undergo routine screening for the HCV, these results are difficult to interpret and are inherently biased.

# 3.4. Homeless Children

A homeless child is a child who does not have a nighttime residence or resides in a homeless shelter or temporary housing. One study involved 386 homeless children and found the prevalence of HCV among these children to be 1% (36) (Table 1). There were no data for HCV prevalence among homeless adults in Isfahan. The low rate of HCV in homeless children may be due to the fact that children are less likely to engage in high-risk activities that would predispose them to the HCV.

# 3.5. The Prevalence of HCV Among Others Groups

Thirteen studies (33-45) related to the prevalence of HCV in Isfahan province were found to include other populations (Table 1). The smallest and the largest sample sizes were 73 and 616 for hemodialysis and thalassemic patients, respectively. Reported HCV prevalence ranged from 0% for laboratory healthcare workers to 80.5% for hemophilic patients. One study reported no cases of the HCV among 203 laboratory healthcare workers (42).

Patients undergoing chronic hemodialysis are at increased risk for contracting the HCV based on the length of time patients receive dialysis and the number of blood transfusions they receive (49). In one study, the prevalence of HCV among 73 hemodialysis patients was found to be 8.2% (46). Similarly, patients with hemophilia are blood transfusion dependent and are at an increased risk for HCV infection. Four studies were found that measured the prevalence of the HCV in hemophilic patients, which ranged from 22.6% to 72.0% (34, 41, 43, 46).

#### 4. Discussion

HCV infection is a major public health concern in many countries, particularly in developing nations. There is no vaccine and no post-exposure prophylaxis for the HCV; therefore, in many countries, preventive strategies are based on healthcare policy. More attention is often paid to diagnose, screen, and treat high-risk groups rather than the general population, which is the basis of preventive strategies in Iran (50). The purpose of this study was to provide an accurate estimate of the HCV disease burden in Isfahan, including among those in high-risk groups. The results indicated that the infection may be more prevalent than previously thought and underscores the importance of more comprehensive studies among people at a high risk for contracting chronic HCV infections.

One of the transmission routes of the HCV is through blood transfusions. In Iran, a blood donor screening program was implemented in all Iranian blood transfusion centers in 1996 (14). Some studies on the prevalence of HCV infection have shown that the rate was significantly lower after this program was enacted, compared to previous blood screening methods (51). One of the main causes of improvement in Iran is the screening process and the elimination of high-risk donors. The present research showed an increase in the prevalence of the HCV from 1996 to 2001, during which time blood donors were referred to the Kashan blood bank (19). In contrast, from 2004 to 2008, Ebrahimian et al. (24) reported a decline in the prevalence of the HCV among blood donors referred to the Isfahan blood transfusion organization. The prevalence of anti-HCV antibodies among blood donors was 0.12% and 0.5% in Tehran and Babol, respectively (52). This is much lower than the prevalence rate of the HCV among blood donors in some developing countries, which ranges between 1% and 7% (53-56). Reasons for lower prevalence rates in Iran may be due to better trained healthcare staff, increased nonremunerated repeat donors, better supply of instruments and laboratory equipment for suitable blood transfusion, routine screening for the HCV using sensitive screening kits, and the establishment of donor deferral criteria.

Intravenous drug users not only have the highest prevalence of HCV infection but also constitute a potential reservoir for the HCV in the community. In the developed world, IDU is the primary mode of transmission for HCV infection (5). A systematic review showed a prevalence of HCV infection in drug user populations ranging from 1.9% - 100% (57). A number of recent studies have assessed HCV prevalence in drug users in Iran, which ranges from 11.2% - 88.9% (58-60). Based on this high prevalence, IDU plays an important role in the transmission of HCV infection. Therefore, harm reduction programs should be considered to control and decrease the spread of the HCV among drug users. Additionally, an understanding of HCV prevalence in each local high-risk population will be important to decision-making about appropriate strategies.

Prevalence of the HCV among hemophilic patients is high throughout Isfahan province. In the different cities and provinces of Iran, the prevalence of HCV ranges from 15.6% - 83.3%, with the highest rate being found in Tehran and the lowest in Fars (61-63). The prevalence of the HCV in thalassemic patients in Isfahan province decreased from 2004 (34) to 2011 (41), but the current prevalence rate among Iranian thalassemic patients is between 15.7% - 63.8% (64, 65). Although HCV infection is a significant issue among patients with congenital bleeding disorders who need to receive blood products, research has shown that the rate of infection is higher in patients with hemophilia because of the frequent use of blood products (41). Some Iranian healthcare policies have focused on screening transfused blood that is used for hemophilic and thalassemic patients to help maintain or decrease the prevalence of HCV infection (50).

A number of limitations to this study must be considered. First, estimates are based on cross-sectional studies that may not be representative of each respective group. Second, conclusions regarding the prevalence of chronic HCV infections were unable to be obtained because many studies did not include information on HCV RNA levels. Similarly, some studies did not confirm anti-HCV positivity with a confirmatory RIBA test while others did. The RIBA data were used, when available; thus, a number of false positives could be present in this study's dataset. Additionally, viable studies that investigated the prevalence of the HCV in hospitalized patients were not available.

Despite these limitations, this study demonstrates the significant role that IDU plays as the main contributor to HCV infection in Iran. To combat this, effective harm reduction programs should be implemented to prevent new HCV infections. Considering the high prevalence of HCV infection among HIV patients, healthcare policy makers should pay more attention to this group, in particular.

# Footnote

**Authors' Contribution:** Study concept and design: Zary Nokhodian; analysis and interpretation of data: Mohsen Janghorban; study supervision: Behrooz Ataei, Farzin Khorvash.

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