ORIGINAL ARTICLE

Assessment of hepatitis C risk factors in center of Iran: A case–control study

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Background: Hepatitis C virus (HCV) infections remain as one of the major public health problems worldwide. The current study aimed at investigating the potential risk factors of HCV+ in a sample of Iranian patients. **Materials and Methods:** In a case–control study, 436 HCV-infected patients and 531 age-matched HCV antibody negative controls were recruited in a central region of Iran. Sociodemographic characteristics, blood and therapeutic factors, underlying diseases, and behavioral risk factors were evaluated through a standard checklist and compared between two study groups. **Results:** Although among studied potential risk factors, many of them were significantly associated with infected with HCV; however, in multivariable logistic regression model in the presence of other variables being male gender (odds ratio [OR]: 4.1; 95% confidence interval [CI]: 2.2–7.8), illiterate or less educated (OR: 62.64; 95% CI: 5.94–660.35), having history of intravenous (IV) drug addiction (OR: 33.0; 95% CI: 5.43–250.0), and tattooing (OR: 14.29; 95% CI: 1.82–90.91) increased risk of infection with HCV. **Conclusion:** In total, the current case–control study documented that socioecomical factors including economical state, marital status, education, and ethnicity and also other expected factors such as hospitalization, imprisonment, dialysis, tattooing, needle sharing, IV drug abuse, and extramarital sexual relationship represent an important source of HCV infection among adults in a central region of Iran. Thus, we suggest further considerations for prevention of HCV infection as most of related factors are preventable by close considerations.

Key words: Case–control studies, hepatitis C, Iran, risk factors

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INTRODUCTION

Hepatitis type C is one of the most considerable clinical diseases, with an incidence of above 170 million worldwide.[1] Cirrhosis is a common complication of hepatitis C virus (HCV)-positive patients which can lead to liver failure and hepatocellular carcinoma.[2] HCV infection has highly variable long-standing complications which consequently lead to chronic hepatitis. In some cases, patients have HCV viremia with no complication.[3] However, 70% of all chronic HCV infections lead to chronic liver diseases and cirrhosis in 20%–30% of infected patients.[4]

Apart from physical health issues, HCV also has a notable economic burden on world health system.[5]

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Many factors are thought to be in association with the acquisition of HCV. These risk factors are pivotal to distinguish, due to their role in population health and causing serious complications. In various studies, different factors have been presented to be correlated with disease course. Some studies found that sociodemographic characteristics such as age, sex, and migration have a great impact on HCV progression.[6-8] Other evaluations suggest that blood risk factors such as blood transfusion, accidents, and dialysis are also correlated with HCV incidence.[8] Iatrogenic risk factors including history of therapy, organ transplantation, and intravenous (IV) drug abuse also correlate to HCV prevalence.[7,8] Other HCV risk factors are underlying diseases, for example, other types of hepatitis, diabetes

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as well as sexually transmitted disorders. Hazardous social behaviors such as imprisonment and unsanitary tattooing are also involved as considerable risk factors in HCV development. New findings also suggest family history as one of the most noticeable factors due to susceptibility.[9,10]

In asymptomatic patients, HCV detection should be considered in early stages as this group as HCV carriers may transmit this disease and thus burden of it to other persons and community. Therefore, due to its complications and effects on the health system, studying potential risk factors would be one of the best approaches to decrease affliction rate and toward prevention. In this manner, we have aimed to investigate potential risk factors of HCV infection in a large study population case-control study in center of Iran.

MATERIALS AND METHODS

In a case–control study, $n = 436$ were selected from hepatitis C positive patients (diagnosed since 2007) who referred to Hepatitis-C Infectious Diseases Research Center, Isfahan University of Medical Sciences. Controls (n = 531) with negative results for both anti-HCV and HBsAg were selected randomly among people who attended to outpatients with problems other than liver disease (i.e., irritable bowel disease, peptic ulcer, food allergies, dyspepsia, and gallstones) or laboratories and blood banks and matched by age; however, we could not able to match them with case group based on gender due to low prevalence of HCV+ among women in Isfahan city.

Patients with incomplete checklist, those who did not agree to participate in the study, and who were found positive for both anti-HCV and HBsAg were excluded from the study, and also the controls whose tests were positive during the initial assessment were excluded from the study.

This study has been conducted based on proposal code 941436 approved by Ethical Committee of Isfahan University of Medical Sciences. The current study protocol conforms ethical guidelines of the 1975 Declaration of Helsinki and all participants in this study were assured that collected information and their answers to the questions were confidential and written informed consent was obtained from all study participants; also Bioethics Committee of Isfahan University of Medical science was approved the study protocol.

Epidemiologic data collection

Demographic, clinical, and possible different risk factor data were collected from both patients and controls through a questionnaire based on interviewer-administered approach by a trained staff. (1) Sociodemographic data included age, gender, education, nationality, ethnicity, living in urban or rural areas, immigrant or nativity, economic status (according to their income), marital status, and wide varieties of risk factors of HCV in different domains were collected including blood type and a history of travel abroad. (2) Blood risk factors such as blood transfusion history, piercing, cupping, skin cut in the laboratory (Needlestick), acupuncture, assault or accidental wounding, and a history of dialysis. (3) Therapy-related risk factors (iatrogenic): a history of hospitalization, surgery, cesarean section, stillbirth and abortion, organ transplantation, immunodeficiency, drug injection, dental treatment, and circumcision for the male. (4) A history of liver diseases (hepatitis, cirrhosis, jaundice, etc.), history of any infectious diseases, sexually transmitted diseases, and other ailments. (5) Checking all kinds of hazardous behaviors such as IV drug addiction, sharing needles, extramarital sexual relationship, history of imprisonment, and history of tattooing. (6) History of hepatitis in the person's family members, history of jaundice, and imprisonment in partners. The time required to fill the checklist was about 10–15 min. After obtaining and reviewing the checklists, if any incomplete answering was found, the participants were requested to complete the checklists. The researchers who admitted checklists were blind to the participants' HCV results.

Statistical analysis

Quantitative and categorical data were presented as mean ± standard deviation and frequency (percentage). Quantitative normally distributed variables were compared between two groups using independent samples t-test, while categorical ones using Chi-square or Fisher's exact tests. In association analyses, those variables with sufficient frequency and significant at $P < 0.01$ in univariable analyses were entered in multivariable analysis. Multiple logistic regression was used for identifying determinates of HCV+. Odds ratio (OR) and 95% confidence interval [CI] for ORs were reported as the quantity of the estimated association. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS version 16; SPSS Inc., Chicago, IL, USA).

RESULTS

Table 1 presents the results of comparison of basic sociodemographic variables of the study participants in case and control groups. Two groups were similar age distributed but significantly different in terms of other studied variables except nationality and place of residence ($P < 0.001$). Majority of recruited patients were male (95%), had low income (86.3%), and less educated or illtreated (70.3%). Results of multiple logistic regression presented in Table 1 shows that lower levels of education are in association with higher risk of HCV infection.

Table 1: The comparison of sociodemographic characteristics between healthy and hepatic groups and their association with hepatitis C virus +

Variable	Control group (*n*=531), *n* (%)	Hepatitis C positive (*n*=436), *n* (%)	*P**	OR (95%CI for OR)**
Age	34.58±11.04	34.24±8.70	0.60	-
Gender				
Female	304 (57.3)	22 (5)	<0.001	1
Male	227 (42.7)	414 (95)		4.1 (2.2-7.8)
Economic status				
Low income (<1 million Tomans [about 270 $] per month)	252 (51.3)	404 (86.3)	<0.001	6.55 (0.44-97.03)
Middle income (1-3 million Tomans [about 270-800$] per month)	209 (42.6)	20 (4.3)		1
High income (more than 3 million Tomans [about 800$] per month)	29 (5.9)	1 (0.2)		-
Marital status				
Married	424 (77.4)	267 (54.9)	<0.001	1
Single	119 (21.7)	218 (44.9)		4.69 (0.26-84.70)
Widowed/divorced	5 (0.9)	1 (0.2)		10.28 (0.6-176.00)
Education				
Academic degree	308 (55.8)	29 (6)	<0.001	1
Diploma (12-year formal education)	149 (27)	115 (23.7)		13.3 (2.66-66.55)
Less educated or illiterate	95 (17.2)	341 (70.3)		62.64 (5.94-660.35)
Nationality				
Iranian	531 (100)	433 (99.4)	0.19	-
Others	0	3 (0.6)		
Ethnicity				
Fars	474 (89.2)	426 (97.6)	<0.001	-
Others	57 (10.8)	10 (2.2)		
Place of residence				
Rural	509 (95.8)	426 (97.7)	0.12	-
Urban	21 (4.2)	10 (2.3)		

*Resulted from independent *t*-test for continuous and Chi-square test or Fisher's exact test for categorical variables, **Resulted from multivariable logistic regression. OR=Odds ratio; CI=Confidence interval

Table 2 shows the results of the comparison of prevalence of wide varieties of hepatitis C risk factors between case and control groups and the results of association analysis using multivariable logistic regression analysis. As can be seen, the frequency of majority of risk factors was significantly higher among HCV-infected patients, in particular, history of hospitalization, undergoing surgery, accidental injuries, blood transfusion, IV drug addiction, needle sharing, extramarital sexual relationships, injection, history of prison, dental treatment, tattooing, and cupping ($P < 0.05$); although some potential risk factors such as travel to foreign countries and dialysis were significantly more prevalent among healthy group. However, the significant associations in the multivariable setting were seen only for RH+ (OR: 7.17; 95% CI: 5.59–10.39), drug addiction (OR: 33.0; 95% CI: 5.43–250.0), and tattooing (OR: 14.29; 95% CI: 1.82–90.91). Table 3 is presenting odds ratio of risk factors of hepatitis C infection among those with positive HCV.

DISCUSSION

Hepatitis C has become one of the world's considerable health problems bearing negative consequences on the society. With day-to-day increase of the infection among all countries, clinician scientists are still trying to find definitive treatments and approaches. However, before the disease can be treated, we have to pay close attention to risk factors having a possible role in HCV development. We evaluated common demographic factors among infected group and compared them to healthy control group. Our evaluations showed that the presence of HCV was significantly higher in males. Likewise, Rezaee-Zavareh and Alavian[11] have reported a similar higher prevalence of males. However, according to a study conducted on the general population of Northern Spain, no significant difference was reported regarding gender.[12] Another study done in Southern Taiwan stated that the incidence of HCV was higher in females.[13]

Furthermore, our results demonstrated that economic status had a significant effect on HCV infection incidence. In other words, wealthy people were less likely to be

Table 2: Comparison of potential risk factors between two groups (healthy and hepatic) and their association with hepatitis C virus +

Variable	Control group (*n*=531)	Hepatitis C group (*n*=436)	*P*	OR (95% CI for OR)
Blood type/blood group				
A	147 (31.6)	24 (30.4)	0.08	-
B	89 (19.1)	12 (15.2)		
AB	51 (11)	3 (3.8)		
O	178 (38.3)	40 (50.6)		
RH factor				
Positive	324 (87.8)	42 (66.7)	<0.001	7.17 (5.59-10.39)
Negative	45 (12.2)	21 (33.3)		1
Travel to foreign countries				
No	305 (56.7)	333 (87.2)	<0.001	0.92 (0.78-1.07)
Yes	233 (43.3)	49 (12.8)		1
Hospitalization				
No	309 (59.1)	240 (48.4)	0.001	1
Yes	214 (40.9)	256 (51.6)		2.50 (0.66-10.01)
Undergoing surgery				
No	291 (54.9)	274 (54.8)	0.973	-
Yes	239 (45.1)	226 (45.2)		
Accident injuries				
No	475 (90.3)	361 (73.2)	<0.000	1
Yes	51 (9.7)	132 (26.8)		2.16 (0.44-10.67)
Blood transfusion				
No	474 (91)	425 (86.2)	0.017	1
Yes	47 (9)	68 (13.8)		2.37 (0.51-14.28)
IV drug addiction				
No	466 (87.1)	46 (9.1)	<0.001	1
Yes	69 (12.9)	459 (90.9)		33.0 (5.43-250.0)
Needle sharing				
No	526 (100)	180 (36.5)	<0.001	-
Yes	0	313 (63.5)		
Extramarital sexual relationship				
No	482 (91.1)	304 (60.6)	<0.001	-
Yes	47 (8.9)	198 (39.4)		1.49 (0.17-12.35)
Drugs injection				
No	424 (88)	421 (98.6)	<0.001	-
Yes	58 (12)	6 (1.4)		
Vaccination against hepatitis B				
No	284 (68.8)	265 (64.3)	0.176	-
Yes	129 (31.2)	147 (35.7)		
Prison records				
No	514 (97.7)	192 (40.6)	<0.001	-
Yes	12 (2.3)	281 (59.4)		
Spouse's prison records				
No	485 (99.4)	272 (97.8)	0.057	-
Yes	3 (0.6)	6 (2.2)		
Dialysis				
No	509 (97.7	452 (99.3)	0.037	-
Yes	12 (2.3	3 (0.7)		
Dental treatment				
No	82 (15.1)	18 (3.6)	<0.001	1
Yes	461 (84.9)	476 (96.4)		4.76 (0.44-50.0)
Tattooing				
No	494 (93.4)	240 (48.9)	<0.001	1
Yes	35 (6.6)	251 (51.1)		14.29 (1.82-90.91)

Contd...

Table 2: Contd..

Variable	Control group (*n*=531)	Hepatitis C group (*n*=436)	*P*	OR (95% CI for OR)
Cupping				
No	424 (79.5)	254 (52)	<0.001	1
Yes	109 (20.5)	234 (48)		1.39 (0.25-3.44)
History of hepatitis				
No	510 (96.0)	418 (95.9)	0.91	-
Yes	21 (4.0)	18 (4.1)		
History of sexullay transmitted infection				
No	515 (96.0)	430 (99.2)	0.22	-
Yes	16 (3.1)	1 (0.8)		

*Resulted from Chi-square test, **Resulted from multivariable logistic regression. OR=Odds ratio; CI=Confidence interval

Table 3: Odds ratios and 95% confidence intervals for risk factors of hepatitis

	Significant	OR	95% CI	
			Lower	Upper
Sex male/female	0.000	4.1	2.2	7.8
IV drug addiction/no	0.000	14.4	8.6	24.1
Prison yes/no	0.000	8.9	4.3	18.4
Dentistry yes/no	0.005	3.4	1.4	8.1
Tattooing yes/no	0.000	3.3	1.7	6.3

OR=Odds ratio; CI=Confidence interval

affected than normal income stratum or the poor. Marital and educational status was also significantly different between patients and controls. In agreement with our findings, Gheorghe *et al*. declared that both mentioned sociodemographic characteristics were significantly different between the participants within the two groups.[14]

On the other hand, many risk factors were analyzed between healthy subjects and patient group and noticeable findings were demonstrated in Table 2. The frequencies of all mentioned risk factors were evaluated between healthy individuals and patients with HCV. The key factors such as hospitalization history, injury, extramarital sexual relationship, immunodeficiency, blood donation, drug injection, imprisonment, and dialysis were considerably of difference in terms of frequency. In many countries, studies have shown that all mentioned risk factors above are common among potential risk factors of HCV infection incidence.[15] A study in Mexico showed that hospitalization and history of received blood transfusion were in association with HCV infection.[16] Another study stated that a history of surgery, dialysis, blood transfusion, and male gender were statistically in association with occurrence of infection.[17] A study in rural North Vietnam on HCV risk factors revealed that job, hospitalization, and tattooing were the main potential risk factors of HCV incidence.[18] In Thailand, a multicentric case–control study reported that blood transfusion, IV drug abuse, unsafe injections, sharing of razors, and unsafe sex were found to be risk factors for HCV infection.[19]

The key point to our study was to evaluate the main risk factors of hepatitis, which is shown in Tables 1 and 2. Male gender is over four times more susceptible to be affected by HCV. This fact may have happened due to extremely higher rate of IV drug abuse by males. Furthermore, it should be mentioned that, due to transitional zone happening in Iran, this rate may change in the near future. This hypothesis is due to increasing rate of Iranian IV drug abuser females and also increasing rate of unsafe sexual activity. Nevertheless, Kim *et al*. in the study among Koreans also found that being female is a risk factor.[20] In Libya, a study on more than 65,000 people showed that the presence of HCV in females and males was 51% and 49%, respectively.[21] Contrary findings of mentioned studies can probably be attributed to cultural factors.

History of IV drug addiction was found to be another effective risk factor for HCV with OR of 33. Furthermore, it is clear for everyone that the only way of HCV transmission is through blood secretions, but the use of unsafe repetitious needles, which is very usual event among IV drug abusers in Iran, may play an important role in this high number of OR compared with other assessed risks. On the other hand, hazardous behaviors such as having multisexual partners or even a history of imprisonment should not be underestimated.[16] These results are in accordance with the study conducted in Italy that HCV infection was directly in accordance with IV-drug abuse. In the study of Italy, they also presented close association of IV drug abuse duration and incidence of HCV infection.[22] In contrast, multivariate analysis of HCV risk factors in blood donors of the Republic of Georgia declined any association between history of the imprisonment and HCV infection incidence.[23] Our assessment demonstrated that history of imprisonment was in association with HCV infection incidence that again may be attributed to the use of repetitious needles as new needles may not be provided to prisoners and also homosexuality.

A history of dentistry was one of the potential HCV infection risk factors. Strict controls on the use of sterile and individualized utensils can play a significant role in HCV prevention due to dentistry. It seems that these results

are belonging to previous decades as nowadays, hygiene is better considered by both dentists and supervisions. Determination of risk factors for HCV in Pakistani males revealed that dental procedures had a significant association with hepatitis C occurrence.[24]

The last assessed risk factor of HCV infection with similar probability with dentistry was tattooing. Mechanism of both risk factors is similar, and hygiene is the most important factor in this area. The fact that tattooing is illegal in Iran and hygiene consideration occurs less. Thus, these close OR of dentistry and tattooing would separate in the near future. In a case–control study on HCV risk factors among Koreans, it has been shown that tattooing was one of the potential risk factors;[25] however, in Morocco evaluation of potential risk factors did not show any significant association between tattooing and HCV infection.[26]

According to our results, it seems to be important to diagnose HCV at early stages because various reports have declared the lack of knowledge in HCV transmission ways among people, as it has previously declared that screening hepatitis C in high-risk persons may result in early identification of patients and prevents from further liver injury and its consequences.[27]

CONCLUSION

Eventually, the current case–control study documented that socioecomical factors including economical state, marital status, education, and ethnicity and also other expected factors such as hospitalization, imprisonment, dialysis, tattooing, needle sharing, IV drug abuse, and extramarital sexual relationship represent an important source of HCV infection among adults in a central region of Iran. Thus, we suggest further considerations for the prevention of HCV infection as most of the related factors are preventable by close considerations.

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Conflicts of interest

There are no conflicts of interest.

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