

RAPID COMMUNICATION

Seroepidemiology of hepatitis C and its risk factors in Khuzestan Province, South-West of Iran: A case-control study

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extramarital sexual activities (2.4%), tattooing (3.6%) were found to be independent risk factors of being HCV-positive. No apparent risk factors could be demonstrated in 29 (11.2%) of the positive cases.

CONCLUSION: Our data indicate that a history of transfusion and iv drug abuse and haemodialysis are important risk factors for HCV infection in our area and that more careful pretransfusion screening of blood for anti-HCV must be introduced in our blood banks. Improvements in certain lifestyle patterns, and customs in this area may be essential to prevent transmission of the infection.

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Abstract

AIM: To evaluate possible risk factors for the spread of hepatitis C infection and to analyze the characteristics of the epidemiological and clinical patterns among the patients with hepatitis C infection.

METHODS: During a five-year period a cross-sectional study was conducted among HCV positive individuals referred to the Ahwaz Jundishapur University Hospitals (AJSUH) and Hepatitis Clinic from 1 Sept 1999 to 1 Sept 2003. The control group consisted of first time blood donors referred to the Regional Blood Transfusion organization. Enzyme-linked immunosorbent assay and recombinant immunoblot assay anti-hepatitis C virus (HCV) tests were performed for two groups. Positive serum specimens were retested using polymerase chain reaction (PCR) for HCV RNA. Risk factors were evaluated using a questionnaire. Reported risk factors among infected subjects ("HCV-positive") were compared to those of subjects never exposed ("HCV-negative") to HCV.

RESULTS: A total of 514 subjects were studied for HCV, of which 254 were HCV-positive and 260 HCV-negative donors comprised the control group. Mean age of the patients was 28.4 (Std 15.22) years. HCV-positive subjects were more likely to be of male gender (63% versus 37%). Transfusion 132 (52%), non-intravenous (n-iv) drug abuse and iv drug abuse 37 (14.5%), haemodialysis 25 (10%), receiving wounds at war and

INTRODUCTION

Hepatitis C virus (HCV) infection is responsible for considerable morbidity and mortality worldwide. HCV is a leading cause of liver failure and liver transplantation in adults. Identified risk factors for HCV infection include intravenous (IV) drug use, exposure to infected blood products, and intranasal drug use^[1]. High-risk sexual activity [multiple sexual partners, history of sexually transmitted disease (STD)], tattooing, and skin piercing have also been suggested to be associated with increased risk for HCV^[2]. In addition, mother-to-infant transmission has been demonstrated^[3,4], but the possibility of other transmission routes has not been thoroughly explored. With the use of RT-PCR or bDNA techniques, HCV RNA has been detected in many systemic fluids other than blood, including peritoneal fluids, seminal and vaginal secretion, urine, and feces. These observations, however, have not been confirmed by all investigators^[5]. The possibility of HCV replication in the mosquito alimentary tract has recently been demonstrated, but the epidemiological importance of this has not yet been

determined^[6]. The rate of HCV infection differs in particular countries. The prevalence in developed countries amounts to 0.2%-2.2%, while in developing countries it reaches 7%. In some regions or risk group the rate of occurrence may be as high as 30%-90%. In Iran, according to the latest data, it is estimated that between 0.12-0.89 percent of the general population present anti-hepatitis C virus antibodies, which corresponds to as many as 0.5 million chronic carriers^[7,8].

Risk factors associated with HCV infection may be specific to a country or region^[9]. Few data are available about the risk factors associated with HCV infection in our area. Hepatitis C is a common health problem in South-West of Iran, and needs proper attention to alleviate the suffering of the people. It is essential to assess the magnitude of the problem, which will help us in understanding the dynamics of its transmission and can be utilized to guide screening procedures as well as provide insight into the control and prevention of the disease.

Herein, we report results of our cross-sectional analyses of risk factors for HCV infection in our community in Khuzestan Province, South-West of Iran conducted during a five year period.

MATERIALS AND METHODS

During a five-year period a cross-sectional study was conducted among HCV positive individuals referred to the Ahwaz JundiShapour University Hospitals (AJSUH) and Hepatitis Clinic from 1 Sept 1999 to 1 Sept 2003. On the basis of a specially designed protocol, standard commercially available tests and physical examinations were performed. The analysis included data of medical history, physical examination and periodic evaluation clinically and serologically.

All subjects were evaluated using a face-to-face questionnaire about demographic (gender and age) and socioeconomic (education) aspects, parenteral exposure to blood or blood products, social and sexual behavior, occupational exposure, intravenous drug use, tattooing, acupuncture, surgery, previous hospitalization and parenteral administration of drugs, personal history of jaundice or hepatitis or history of these diseases in the cases' and controls' families. The control group consisted of first time blood donors referred to the Regional Blood Transfusion Organization. None of the control group subjects were HBsAg positive, HIV-positive or have any signs or symptoms of hepatitis.

Enzyme-linked immunosorbent assay (Organon/Teknica UB/HCV EIA) and recombinant immunoblot assay anti-hepatitis C virus tests were performed for two groups. Positive serum specimens were retested using polymerase chain reaction (PCR) for HCV RNA.

None of our patients showed any signs of HBV infection, or any other cause of acute or chronic liver disease, such as HAV, EBV, CMV infections, auto-immune diseases, alcohol and drug abuse, α 1-antitrypsin deficiency, Wilson's disease, or hemochromatosis. HBsAg, anti-HBc were determined by IMx analyzer (Abbott Lab., Abbott Park, IL, USA). HBsAg, anti-HBc were determined by IMx analyzer (Abbott Lab., Abbott Park, IL, USA).

Table 1 Demographic features and symptoms and signs of liver disease of the patients enrolled into the study

Variable	HCV positive (n = 254)	
	n	%
Sex		
Male	160	63
Female	94	37
Age group (yr)		
< 20	81	32
20-29	82	32.5
30-39	56	22
40-59	26	10
> 60	9	3.5
Total	254	100
Symptoms		
RUQ Pain	142	56
Malaise	93	36.6
Dyspepsia	58	22.8
Signs		
Splenomegaly	25	9.8
Jaundice	12	4.7
Hepatomegaly	8	3.1
Elevated serum ALT level	168	66
HIV positive	3	1.2

Reported risk factors among infected subjects ("HCV-positive") were compared to those of subjects never exposed ("HCV-negative") to HCV. Consent for an interview was taken from each participant, who was assured about the confidentiality of his information. Controls were briefed about the known modes of HCV transmission. The institutional Ethics Review Committee approved the study protocol.

Statistical analysis

Collected data were coded, analyzed and computed, using the Statistical Package for Social Sciences (SPSS) version 10 (SPSS Inc., Chicago, IL, USA). Simple statistics such as frequency, and standard deviation were used. We conducted a multivariate logistic regression analysis to identify factors associated with HCV infection. Chi-square and Student's *t*-tests were used for comparison.

RESULTS

A total of 514 subjects were studied for HCV, of which 254 were HCV-positive and 260 HCV-negative donors comprised the control group. Mean age of the patients was 28.4 (SD 15.22) years. Of the 254 patients, 225 (88.6%) had identifiable risks of exposure to HCV infection.

HCV-positive subjects were more likely to be of male gender (63% *vs* 37%). Transfusion 132 (52%), non-intravenous (n-iv) drug abuse and iv drug abuse 37 (14.5%), haemodialysis 25 (10%), receiving wounds at war and extramarital sexual activities 6 (2.4%), tattooing (3.6%) were found to be independent risk factors of being HCV-positive. The mean age was significantly younger in patients with transfusion (13.4 years) than the mean age of all the patients (28.4 years, *P* = 0.004), mainly those with thalassemia and received regular blood transfusion. No

Table 2 Risk factors possibly associated with HCV-positive in patients group

Variable	HCV-negative (n = 260)		HCV-positive (n = 254)	
	n	%	n	%
Risk factor				
Blood transfusions	6	2.3	132	52
Intravenous drug use	0	0	37	14.5
Extramarital sexual activities	1	0.4	3	1.2
Tattooing	2	0.8	9	3.5
Surgical procedures	5	1.9	5	2
Dental procedures	8	3.1	12	4
Hemodialysis	0	0	25	10
Receiving wounds at war	0	0	3	1.2
Endoscopy	14	5.4	1	0.4
Unknown	224	86.1	29	11.2
Total	260	100	254	100

apparent risk factors could be demonstrated in 29 (11.2%) of the positive cases.

The demographic features and the background characteristics of the patient population are displayed in Table 1. Differences in the distribution of risk factors were compared between the HCV positive and negative groups, with similarities observed for educational level, economic status, and residency.

Transfusion ($P < 0.002$), intravenous drug use ($P < 0.005$) and hemodialysis ($P < 0.008$) were the only three variables with a statistically significant correlation with the presence of HCV infection on univariate analysis. There were no other statistically significant differences between the HCV positive and HCV negative control group in terms of demographic characteristics or topic areas associated with HCV infection/transmission such as extramarital sexual activities, tattooing, endoscopy, surgical and dental procedures (Table 2).

DISCUSSION

Chronic HCV infection represents one of the major public health problems in Iran and according to the annual IBTO internal reports, it is estimated to be less than 0.2%^[8,10]. Approximately 20%-30% of patients with chronic HCV infection will progress to cirrhosis^[11], which can be further complicated by hepatic decompensation and development of hepatocellular carcinoma(HCC)^[12,13].

In this study, 254 anti-HCV-positive patients between 1999 and 2003 were investigated. The ages of these patients, at the time of data analysis, ranged from 7 to 68 years with a mean age of 28.4 years. Our study included 160 males and 94 females, with a male:female ratio of 1:7. This male preponderance in HCV-infected patients was also reported by others^[14,15].

Our study indicated blood transfusion was the leading risk factor for HCV acquisition in our patients as 52% of them were diagnosed with chronic haemolytic anemias, mainly thalassemia and received regular blood transfusion. It should be emphasized that these cases most probably,

had contracted the infection before testing for HCV antibodies was performed routinely. Screening for HCV has been a routine for all blood donors since 1995 in Iran^[8]. Although it is not clear whether all the HCV-positive subjects in our study population with a positive history of transfusion had had their transfusion before 1995, the date of transfusion was not determined in our study. Therefore, more careful pretransfusion screening of blood for anti-HCV must be introduced in our blood banks.

Injection drug users (IDUs) constitute the largest group of persons at high risk for acquiring HCV infection in developed countries^[14,15]. Intravenous drug use was the second most frequent risk factor for HCV acquisition in our patient group (14.5%) and all of them were male, which is consistent with other reports. The male patients tended to have a history of IDU, whereas, female patients tended to have a history of transfusion^[16,17]. The data on route of drug administration were based on selfreporting. One must always consider the possibility that injection drug use is underreported and that some of the HCV infection among the non-injection drug users (NIDUs) may have actually occurred through injection of drugs^[18,19]. Although it is certainly possible that some of the NIDUs in this study may have injected drugs and become infected with HCV *via* injection of drugs, it does not appear that underreporting of injection drug use is a viable explanation for the results of this study.

As reported in several studies, HCV infection is a significant health problem in dialysis units in our country with a high prevalence rate (13.2%) among this population^[20]. It was reported that blood transfusion and duration of dialysis treatment are important risk factors for HCV infection in patients on haemodialysis^[21,22]. The more units transfused, the higher the risk for HCV infection.

Besides, we cannot exclude the possibility of nosocomial transmission of the virus over time in this group. This is supported by the fact that 8.8% of infected patients in this population had no history of blood transfusion. Patient-to-patient transmission was prospectively shown in some incidence studies in hemodialysis patients^[17]. Some strategies to reduce the risk of HCV infection in patients on hemodialysis such as early screening of patients for anti-HCV, reduction of transfusion by the use of erythropoietin or screening with more sensitive methods to detect HCV; and reducing the duration of the hemodialysis period by early transplantation should be considered in this group.

No apparent risk factors could be demonstrated in 29 (11.2%) of the positive cases (called sporadic infections), which is similar to those reported previously^[17]. In sporadic infections with no apparent risk factors, other routes of transmission and other factors, such as use of the same razor or tooth brush, or careless dressing of cuts and wounds or the family environment, where the infection risk increases along with exposure time should be noted^[24]. Another possible explanation for this percentage of sporadic infections is failure of the questioning process in our study. We found no significant relationship between sex, previous endoscopy, receiving wounds at war, marital status with the risk of HCV infection as independent risk

factors in our cases in comparison with controls.

Although the serological, epidemiological and possible risk factors of HCV infection here obtained were related to a small population, this study was justified by the lack of information about HCV infection in Khuzestan Province, South-West of Iran. Other limitations of the study are linked to the difficulties inherent in self-reporting of behaviors such as sexual activity and drug use. It is also possible that the patients receiving blood transfusion in the study may not be representative of the population of Khuzestan Province. Genotyping was not performed in our studied cases due to limitations in our area but the genotypes of HCV were investigated in Iranian patients with histologically proven chronic hepatitis, genotype (1a) has been identified in the majority of the patients^[25].

In conclusion, we provide epidemiologic features of hepatitis C and its risk factors in Khuzestan Province in South-West of Iran. These data are useful for understanding the risks of transfusion, hemodialysis, and other lifestyle patterns that predispose people to a number of HCV risk factors. These findings could be utilized to primary prevention program focused on identified risk factors, may help curtail the spread of HCV infection in this and other similar settings in developing countries. These results suggest that further study on the mode of transmission of hepatitis C should focus on patients who deny intravenous drug use or apparent risk factors. This information contributes to our understanding of the worldwide prevalence of hepatitis C. It demonstrates the importance to continue this study in order to establish routine procedures that can be applied to the screening and confirmation of the diagnosis, as well as to provide an applied methodology for the epidemiological investigation of the virologic profile of HCV-infected patients.

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