Hepatitis C virus transmission and its risk factors within families of patients infected with hepatitis C virus in southern Iran: Khuzestan

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Abstract

AIM: To determine whether hepatitis C virus (HCV) infection of index cases increases intrafamilial transmission (sexual and nonsexual contacts) of HCV.

METHODS: In a case-control descriptive study we enrolled 300-household contacts of 60 index cases (40 males and 20 females) of HCV infection and 360 pair-matched controls in Ahwaz Jundishapur University Hospitals from August 1, 1998 to September 1, 2003. The control group consisted of first time blood donors referred to the Regional Blood Transfusion Organization. Serum samples and demographic data and a medical history including the existence of risk factors for HCV (after a questionnaire on the risk factors for parenteral exposure) were obtained from each subject. Antibodies to HCV were detected employing a commercially available second-generation enzyme immunoassay (EIA, Abbott II). Positive serum specimens were retested using a second-generation recombinant immunoblot assay (RIBA-2) and a polymerase chain reaction for HCV RNA. Data analysis was carried out for intra-household clustering.

RESULTS: Only 4 of 300 (1.33%) cases of household contacts without percutaneous risk factors were positive for HCV Ab while the remaining 296 family contacts were negative for anti-HCV. The mean age of the index cases was 28.4 (Std 15.22) years. The anti-HCV prevalences in parents, spouses, children of the index cases were 0.87% (1/115), 3.39% (2/59)) and 0.79% (1/126), respectively. Among couple partners negative for anti-HCV antibodies, the mean duration of the sexual relationship was 6 years.

The two-couple partners positive for anti-HCV antibodies married the index cases for longer than 15 years. The prevalence of positive HCV Ab among household contacts (1.33%) was not significantly higher than that in the controls (1%) (P > 0.06).

CONCLUSION: Intrafamilial transmission of HCV is not the significant transmission route and sexual transmission does not seem to play a role in the intrafamilial spread of HCV infection. Intrafamilial transmission of HCV is possible but occurs at a low rate.

Key words: Intrafamilial transmission; Hepatitis C virus; Khuzestan; South-west of Iran

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INTRODUCTION

One of the most substantial problems in public health is hepatitis C virus (HCV) infection, which affects approximately 1%-5% of the world's population and occurs in all countries. Epidemiological information on HCV is essential for strategic prevention of chronic hepatitis, liver cirrhosis and cancer. 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 in risk groups the rate of occurrence may be as high as 30%-90%.[1,4]

HCV infection is acquired mainly parenterally by transfusion of infected blood, rupture of the continuity of skin or mucous membrane, infected medical equipment despite strict hygienic control, intravenous drug abuse, hemodialysis or organ transplantation. HCV infection is an important cause of post-transfusion hepatitis. Transmission through sexual contacts has been implicated, although this may be a rather inefficient mode of transmission.[5,6] HCV has also been detected in persons in whom no clear risk factor has been defined, and these cases constitute about 40%-45% of HCV infections.[4]. According to
the published data, the prevalence of HCV infection in Iran is 0.59%-0.8%[9]. Mother-to-infant transmission has also been demonstrated[9] 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 in blood, including peritoneal effusion, seminal and vaginal secretion, urine, feces and typhoid secretion. At least 20% of hepatitis C patients develop cirrhosis with the associated risk of developing hepatocellular carcinoma (HCC)[10]. Despite primary hepatotropism, HCV can affect tissues and organs such as kidneys, thyroid, salivary glands, eyes, or the hematopoietic and lymphatic systems other than the liver[10]. HCV infection seems to be connected with several autoimmune diseases[9].

To our knowledge little information is available about HCV infection due to contacts of patients infected with HCV in southern Iran: Khuzestan. Because HCV may be transmitted by the non-parenteral routes such as sexual and non-sexual household contacts, this study was undertaken to investigate whether intrafamilial transmission occurs via the usual contacts between patients and their household members who are unaware of the potential infectious state of the patients, to determine the prevalence of antibody to HCV in the contacts of HCV positive cases (index patients) and to evaluate the potential risk factors associated with intrafamilial transmission of HCV.

### MATERIALS AND METHODS

#### Subjects

During a 5-year period in a case-control descriptive study we enrolled 300 household contacts of 60 index cases (40 males and 20 females) of HCV infection and 360 pair-matched controls in Ahwaz JundiShapur University Hospitals from August 1, 1998 to September 1, 2003. The control group consisted of first time blood donors referred to the Regional Blood Transfusion Organization.

#### Methods

Serum samples and demographic data and a medical history including the existence of risk factors for HCV (after a questionnaire on the risk factors for parenteral exposure) were obtained from each subject. The questionnaire consisted of questions regarding demographic variables, household behaviors and extra-familial factors including various potential parenteral exposures to blood or blood products (such as past hospital admission, operation, injuries needing hospital interventions, blood or blood product transfusion), history of parenteral injections and intravenous drips, travel history outside Iran, as well as dental treatment, tattooing and ear piercing. All these factors are known to be associated with HCV infection. All index cases and household contacts and controls answered the questionnaire and had their blood tested for anti-HCV. Antibodies to HCV were detected employing a commercially available second-generation enzyme immunoassay (EIA, Abbott II). PCR for HCV RNA and a second-generation recombinant immunoblot assay (RIBA-2) were performed in all index cases and positive serum specimens were obtained from each subject. The Amplicor HCV RNA assay was used to detect HCV RNA in index case serum (Roche Diagnostic Systems). None of our cases (household contacts and index cases) revealed any signs of HBV infection (MEIA, Abbott IMX) or any other causes of acute or chronic liver diseases such as HAV, EBV and CMV infections, autoimmune diseases, alcohol and drug abuse, α1-antitrypsine deficiency, Wilson’s disease, or hemochromatosis. All these index cases were still receiving follow-up at the time of our study.

#### Statistical analysis

The data were analyzed statistically using SPSS, version 9. Comparison was made using the Student’s t-test and chi-square test. P < 0.05 was considered statistically significant.

### RESULTS

All the 60 index patients gave positive reactions in the second generation anti-HCV EIA. We assumed that most of them were chronically infected with HCV. A total of 300 household contacts of the index patients were subjected to the second generation anti-HCV EIA. Only 4 of 300 (1.33%) cases of household contacts without percutaneous risk factors were positive for HCV Ab while the remaining 296 family contacts were negative for anti-HCV. The mean age of the index cases was 28.4 (Std 15.22) years. The anti-HCV prevalences in parents, spouses, children of the index cases were 0.87% (1/115), 3.39% (2/59), and 0.79% (1/126), respectively. Among the couple partners negative for anti-HCV antibodies, the mean duration of the sexual relationship was 6 years. The two-couple partners positive for anti-HCV antibodies married the index cases for longer than 15 years. PCR for HCV RNA and second-generation recombinant immunoblot assay (RIBA-2) were performed in household members of two cases, one wife and one daughter (Table 1). The prevalence of positive HCV Ab among household contacts (1.33%) was not significantly higher than that in the controls (1%) (P > 0.06).

### DISCUSSION

HCV infection, a world-wide spread liver disease, is most
often asymptomatic in adults. It leads to serious clinical consequences that often occur later. About 50%–70% of mild infections progress to chronic phase and long term observations of natural history of the disease have confirmed that HCV is the risk factor for cirrhosis and primary hepatic carcinoma. However, there is a paucity of data on risk behaviors associated with HCV transmission through household contacts. HCV may be transmitted by the parenteral and other routes similar to that of HIV and HBV. Studies on family members of patients with chronic B hepatitis indicate that this virus can be transmitted both by vertical from mothers positive for hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) and by horizontal (sexual and non-sexual) routes. Spouses and siblings of HBsAg-positive subjects are frequently found to have a high prevalence of serological markers of current or past HBV infection[10,11]. But the epidemiological relevance of intrafamilial transmission of HCV has not been clearly established.

This study estimated (1.33%) HCV seroprevalence among the household contacts of HCV-seropositive index cases, which is lower than the finding of other studies reporting that HCV seroprevalence is 16% and 20% among contacts of HCV-seropositive index patients[12,13]. Our results differ from those in these studies reporting a higher rate of HCV infection in the family members of adult patients with chronic hepatitis C. This difference could be attributed to one or more of the following limitations in studies, i.e. a small-sized study, inadequate duration, intensity of potential contact with adult patients, low infectivity of HCV in blood, genotypes, and unknown sensitivity of the hepatitis C radioimmunoassay used for detecting HCV infection[14]. Although intrafamilial HCV transmission through nonsexual contacts has been recognized as a major route in the Saudi population and elsewhere, the mechanisms underlying such transmissions have not been elucidated. Another study has reported an elevated prevalence of 5.7% among household contacts, compared with HCV seroprevalence of 0.5% in the general population[15-17]. There are conflicting data in the literature concerning the role of sexual contacts in the spread of HCV infection. The prevalence of positive anti-HCV in spouses is different and may be a consequence of many factors such as sexual behavior and duration of marriage[18,19].

In this study, we found that spouses of anti-HCV positive patients were more likely to be infected with HCV than other family members and the infection rate increased with duration of marriage. In agreement with other authors[20], we found that positive anti-HCV increased in spouses with their length of marriage. In particular, a significant difference was found in the prevalence of positive anti-HCV between spouses married for more than 15 years and those married for a shorter time. Homology analysis on HCV nucleotide sequence is important in the study of sexual transmission of HCV[21], but we did not perform homology analysis in our studied cases. It is not easy to explain the increased rate of HCV infection in couples married for a longer time. Other authors reported that there is no prevalence in two groups of sexual partners married respectively for 13 and 15 years[1,2].

Marriage usually includes a sexual relationship, but also other kinds of body contact and exposure to the same risk factors (i.e. sharing the same personal tools such as toothbrushes, razors, dental appliances, etc.) as suggested by recent findings in Taiwan[22,23]. We did not perform genotyping in our studied cases but in Iran, genotype (1a) has been identified in the majority of chronic HCV patients[24]. HCV genotyping between the index cases and infected family contacts can clarify whether the infection is acquired in or out of the family setting. The HCV seroprevalence among the contacts of HCV-seropositive index patients is lower in our study than in populations elsewhere.

Our data suggest that sexual and nonsexual contacts with HCV-infected hemophilia patients within households are not associated with an increased risk for HCV infection. Further study is needed to assess the extent and the causes of nonparenteral transmission of HCV. Implementation of an education program based on the identified risk factors may reduce the spread of HCV in our area.

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