

Non-conventional Transmission of Hepatitis C: A true possibility ignored

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Abstract

Objective: The exact mode of hepatitis C virus (HCV) transfer remains elusive in a vast majority of cases. We examined the possibility of non-conventional transmission of HCV by person-to-person contact.

Method: A questionnaire based, prospective study was conducted at Pakistan Institute of Medical Sciences (PIMS) from July-October, 2006. Patients with compensated chronic hepatitis B (CHB) &/or C (CHC) were registered for 6 month interferon (IFN) therapy. All candidates furnished information about age, gender and mode of transmission. The unanswered queries were interpreted as "missing data". After omission of cases with hepatitis B virus (HBV) infection alone, the remaining persons included in the present study were placed in: Group-A: Multifactorial transfer involving conventional (blood borne) and non-conventional modes; Group-B: Unifactorial transfer by non-conventional routes only; Group-C: No identifiable risk factor. Unlike conventional routes, the non-conventional modes represented likelihood of CHB &/or CHC by exposure to household contacts, to persons with hepatic cirrhosis and during traveling.

Results: Initially, 879 patients (mean age: 35.52 ± 9.1 years) were registered. After exclusion of 25 subjects with HBV infection only, the remaining 854 were included. Of 854 cases, 830 (97.18%) were infected with HCV and 24 (2.81%) had co-infection with HBV & HCV. According to the mode(s) of transmission, Group-A: 515 (60.30%); Group-B: 136 (15.92%) and Group-C: 203 (23.77%) cases were identified. Dental treatment: 278 (32.55%) was the commonest conventional risk factor in Group-A. The non-conventional transfer of HCV in Group-A was mainly suggested by household contact: 222 (25.99%). Groups-A and -B combined, the sum of any non-conventional risk factor was comparable with and even higher than the leading haematogenous routes in Group-A. Groups-B and -C combined, HCV infection in 339 patients (39.69%) was apparently acquired by non-conventional modes, most probably by person-to-person interaction.

Conclusion: Non-conventional transmission of HCV is a genuine possibility which is currently underestimated (JPMA 59:430; 2009).

Introduction

HCV has infected 180 million people worldwide.¹ Seroprevalence of HCV is 4-7% in the local population.²⁻⁴ It accounts for 40-60% cases of chronic liver disease. The rate of chronicity is >76%.⁵ After 20 years, 6-8% patients with Chronic Hepatitis C (CHC) develop hepatocellular carcinoma.⁶ There are 10 million copies of HCV per ml and as little as 0.0001ml of blood can impart infection. The predicted half life of HCV is < 3 hours.⁷ Blood-to-blood contact, sexual route and vertical transmission are regarded as the principal modes of infection. The concept of non-conventional spread of HCV has not been adequately investigated. Similar to HBV in the past, the faecal-oral transmission of HCV is not accepted as the proven mode of infection. Based on this study, we provide evidence in support of our hypothesis that non-conventional spread of HCV also occurs by person-to-person contact.

Patients and Methods

A prospective study was conducted on out-patients, registered in the Department of Gastroenterology, Pakistan

Institute of Medical Sciences (PIMS) for 6-month IFN treatment of CHB and/or CHC. The expense on evaluation and treatment was sponsored by the Government of Pakistan between 19th July and 31st October, 2006. There was no financial support for our study. Interferon (IFN) therapy was offered to subjects with positive polymerase chain reaction (PCR) for HBV and/or HCV, normal or increased transaminases, platelet count >150,000/mm³ and without any contraindication to IFN and ribavirin. The persons with HBV infection alone and those with signs of hepatic decompensation were excluded from the study. On a questionnaire, the candidates were required to provide information about gender, age and the likely route(s) of transmission. The unanswered queries were entered as "missing data". Due to lack of education and conservative life style of local population, the questions were served in a simple and brief format. Highly personal and technical information was purposefully avoided to encourage participation of the registered candidates. Thus questions about breast feeding, sexual practices, social activities and habituation/ addiction were omitted which has added some bias to the study. The modes of transmission of HCV were divided as: (a)

conventional (blood borne) routes: dental treatment, major/minor surgery, childbirth and blood transfusion, (b) non-conventional routes (suggestive of inter-personal spread): household contact, exposure to patient with hepatic cirrhosis and domestic/foreign travel. According to the pattern of transfer of HCV, the patients were placed in three groups: Group-A: multifactorial transmission due to conventional and non-conventional risk factors; Group-B: unifactorial transfer by non-conventional risk factors only; Group-C: no identifiable risk factor. The "household contact" means regular, frequent or intimate "exposure" of our "on-treatment patients" to some well-compensated, domestic carrier(s) of HBV and/or HCV. The interaction with case(s) of "hepatic cirrhosis" means exposure of our "on-treatment patients" to persons with signs of hepatic decompensation. On the basis of frequency of exposure, the household contacts were divided into two subsets: (a) immediate contacts (frequent and regular exposure): father, mother, spouse, brother, sister, son, daughter and neighbour, (b) distant contacts (less frequent exposure): friend and relatives.

Results

IFN therapy for CHB and/or CHC was initially recommended in 879 patients, 14-68 years of age (Mean 35.52 ± 9.1 years). There were 506 (57.56%) males and 369 (41.97%) females (missing data: 4: 0.45%). After omitting 25 cases with HBV infection alone, 854 were included in our study. Of 854 subjects, 830 (94.35%) were infected with HCV and 24 (2.81%) had co-infection with HBV and HCV

(Table-1). The division of cases according to mode of transfer was: Group A: 515 (60.30%); Group-B: 136 (15.92%); Group-C: 203 (23.77%) (Table-2). Dental treatment was the commonest blood borne route, observed in 278 (32.55%) persons in Group-A. It was followed by surgery: 231 (27.04%); childbirth: 191 (22.36%); blood transfusion: 124 (14.51%) (Table-3). The non-conventional risk factors in Group-A were: household contact: 222 (25.99%); exposure to patients with hepatic cirrhosis: 157 (18.38%); travel: 173 (20.25%). The non-conventional transmission in Group-B was due to: household contact: 76 (8.89%); exposure to patients with hepatic cirrhosis: 38 (4.44%); travel: 22 (2.57%). The sum of non-conventional risk factors in Groups-A and -B was: household contact: 298 (34.89%); exposure to patients with hepatic cirrhosis: 195 (22.83%); travel: 173 (20.25%) (Table-4). In Group-C, no risk factor was found in 203 (23.77%) cases (Table-1). Groups-B & -C combined, HCV infection was apparently not blood borne in 339 (39.69%) patients. There were 317 household contacts in this series (n=317): relatives: 161 (50.78%); spouses: 59 (18.61%); children: 39 (12.30%); friends: 25 (7.88%); parents: 12 (3.78%); neighbours: 11 (3.47%); siblings: 10 (3.15%). The disease status of household contacts was identified in 136 (42.90%) cases (n=317): HCV infection 114 (35.96%); co-infection with HBV and HCV: 12 (3.78%); HBV infection: 10 (3.15%). The number of domestic contacts was described as (n=854): 1/270 (31.61%); 2/16 (1.87%); 3/5 (0.58%) patients. In 67 (7.84%) cases, relationship between our patients and

Table-1: Preliminary data.

Registered cases	*Gender		Age (years)	**HBV patients	Study patients	Disease status	
	Male	Female				HCV	***Co- infection
879	506 (57.56%)	369 (41.97%)	14-68 (mean age= 35.52 ± 9.1 years)	25	854	830 (97.18%)	24 (2.81%)
		* Missing Data (4: 0.45%)	** Excluded from study		***HBV & HCV		

Table-2: Pattern of transmission of HCV: (n=854).

Group A	Group B	Group C
*Multifactorial transfer 515 (60.30%)	**Unifactorial transfer 136 (15.92%)	No identifiable risk factor 203 (23.77%)
	* Conventional & non-conventional risk factors	** Non-conventional risk factors

Table-3: Group A: Blood borne transfer of HCV: (n=854).

Risk factor	Patient response		*Missing data
	Yes	No	
Dental treatment	278 (32.55%)	535 (62.52%)	41 (4.09%)
Surgery	231 (27.04%)	588 (68.85%)	35 (4.80%)
Childbirth	191 (22.36%)	-	-
Blood transfusion	124 (14.51%)	667 (78.10%)	63 (7.37%)

* No response

Table-4: Non-conventional transfer: Groups A & B combined: (n=854)

Risk factor	Patient response		
	Yes	No	Missing data
Household contact	298 (34.89%)	544 (63.70%)	12 (1.40%)
Exposure to patient with hepatic cirrhosis	195 (22.83%)	599 (70.14%)	60 (7.02%)
Travel	173 (20.25%)	630 (73.77%)	51 (5.97%)

domestic contacts was adversely affected due to the disease process.

Discussion

We carefully selected four risk factors to encompass the haematogenous transmission of HCV. The omission of queries pertaining to shaving equipment, combs, razors, and circumcision appears to add bias to the present study albeit with ample justification to avoid such details in the questionnaire. Most of our patients belonged to suburbs with limited access to basic amenities of life, including facilities for education and medical care. In spite of this dismal background, the majority have responded unambiguously to the questions about their exposure to different risk factors. Several hundred negative answers support our observation in this behalf. They could confidently describe the disease status in household contacts. There was even an adverse impact of HBV and/or HCV disease on their relationship with domestic contacts. Such acceptable levels of awareness have resulted from publicity through media and nationwide immunization programme for HBV during the past decade. The association of HCV with socially and religiously unacceptable practices, like alcoholism, sexual promiscuity, homosexuality and drug abuse is increasingly recognized by the local people. Thus we had enough reason to keep the questionnaire in a brief format. In view of the non-availability of funds for our study, we put reliance on patients' response for identification of disease status amongst the household contacts. The actual problem seems to lie with logistics and affordability rather than general awareness. For example, seroprevalence of HCV in the western countries is reduced from >10% in 1993 to 1% after health reforms. On the other hand, the incidence of HCV in hospitalized patients in Pakistan remains >10% and <5% of blood transfusions are routinely screened for hepatotropic viruses.⁸ The traditional birth attendants ("dayas") conduct >80% of deliveries in smaller towns and villages.⁹ In spite of these alarming figures, our results show blood transfusion as the least common conventional risk factor, preceded by childbirth. It supports our concept of transmission of HCV by modes other than blood-to-blood contact. The issue of person-to-person transfer of HCV, however, appears controversial.¹⁰ There is no explanation for 20-40% of subjects with community-acquired HCV infection. Approximately 20-40% of cases have no identifiable risk factor(s).¹¹ This data is comparable with the number of patients in Group-C. We

believe that hepatitis C is exclusively rather injudiciously linked with blood transfusion and invasive procedures.^{12,13} The possibility of non-conventional transmission has, therefore, not gained acceptance despite well documented intrafamilial clustering of HCV.¹⁴ These figures compare favourably with a large number of household contacts in our study. It is pertinent to recall that hepatitis B was initially labeled as "syringe hepatitis". The faecal-oral transmission of HBV was acknowledged only after several decades.¹⁵ All males in a Muslim society (like ours) undergo circumcision. Episiotomy is performed in majority of the primigravida during childbirth. The parturition involves some serious steps, like instrumentation, cord excision, evacuation of placenta and the need for blood transfusion. Theoretically, circumcision and childbirth should constitute a 100% risk of HCV infection amongst our men and women. However, practically it does not hold true. The presence of dental treatment as a more significant route than childbirth in Group-A favors our argument in spite of the fact that oral hygiene is generally neglected by the local population. Moreover, the frequency of childbirth and blood transfusion is comparable with the non-conventional modes in Group-B. These findings imply that HCV possibly spreads by direct exposure to the infected individuals. The intrafamilial spread of HCV is attributed to domestic environment, household exposure, infected children, sex partners and intercourse with intravenous drug users. It is also linked with horizontal transmission, old age and ethnicity.¹⁶⁻¹⁸ Illiteracy and crowded living are thought to be responsible for the persistence of HCV amongst low socio-economic groups.¹⁹ In South Asia, the incidence of HCV has, therefore, increased in the past decade.²⁰ There are similar reports from other regions²¹ where blood transfusions are routinely screened and the people are aware of transfer of blood borne viruses. Our hypothesis is further supported by some well-established viral characteristics. HCV survives outside the body from 7 days to 3 months. HCV RNA is stable at room temperature for 5 hours²² and the virus can sustain pH 2.4 for 6 hours. These features suggest that HCV can sustain external environment and gastric pH for a sufficient length of time. A splash of blood or body fluid into the eyes, nose or mouth is regarded as an "exposure". Thus HCV is likely to contaminate food, water and scores of items shared in the domestic environment. It can be similarly acquired during long distance travelling. Our figures for infected spouses vs domestic contacts may not be compatible with other studies²³

yet they represent a greater likelihood of HCV transfer by interpersonal exposure vis-à-vis sexual activity. The duration of co-habitation is proportional to the risk of infection under such circumstances. In our opinion, the mother-child pairs and sex partners constitute classic examples of intimate bodily contact. The alcoholics and drug addicts also have frequent and regular physical exposure similar to the residents of a family. The incidence of hepatitis C is reported higher in frequently hospitalized children without undergoing invasive procedures.²⁴ The patients with hepatic cirrhosis constitute a long term domestic reservoir of infection even in our urban areas. The risk of transmission of HCV from such cases is related to the viral load.²⁵ Other examples may be the correctional facilities, geriatric houses, mental hospitals and mass congregations. Thus it is inconceivable to us that HCV is not transmitted by day-to-day contact, closeness, kissing and other non-conventional routes. Our view point is supported by the large number of patients in Groups B and/or C with no evidence of blood borne transfer of HCV. By adding cases due to non-conventional risk factors from Group-A to the sum of Groups-B and -C, we appreciate that the non-conventional routes were operative in more than 50% of patients in the present study. However, we admit that a limited number of cases of hepatitis-C may have resulted from the haematogenous routes, omitted from our questionnaire. CHC due to childhood infection often results in hepatic decompensation at 35-45 years. This possibility is less likely in our patients because of the mean age above 35 years and a well compensated liver disease in all treatment candidates. Further studies are required to establish the association of a particular risk factor with the onset of hepatitis C. How many risk factors interact and under what optimal conditions does the transmission occur are some other questions, which need to be answered for a more reliable prophylaxis against HCV.

Conclusion

It is concluded that regular and intimate interpersonal exposure is an important route of transmission of HCV. The concept of non-conventional transfer of HCV is supported by our results, special viral characteristics and endemicity of HCV irrespective of the socio-economic conditions.

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