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Original Article

Epidemiology of hepatitis C virus infection in a tertiary care hospital

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ABSTRACT

Background: There are epidemiological lacunae in literature of hepatitis C virus (HCV) infection. We report a prospective observational study of asymptomatic HCV infected patients from a tertiary care Government Hospital.

Methods: All consecutive asymptomatic antibodies to hepatitis C virus (anti-HCV) positive patients were studied from July 2011 to April 2016. Patients were reviewed for demographic factors including symptom profile, risk factors, family screening, and point prevalence in relation to various districts of Punjab and Haryana.

Results: One thousand twelve patients were studied with median age of 52 years (range:13–85) with a male to female ratio of 0.87. Eight hundred (79.25%) patients were from Punjab and 110 (10.67%) from Haryana. Forty percent patients were in 40–60 age group. Six hundred seventy patients (66.21%) did not have any apparent risk factor, 274 (27.08%) had one risk factor, and 68 patients (6.72%) had > 2 risk factors. Commonest risk factor was h/o surgery in 243 patients (24.01%), 32 patients had h/o IV drug abuse and 29 among them were < 30 years. Three hundred and sixty-seven families and children were screened, and 27 spouses and 16 children were found to be anti-HCV positive. The risk factor of IV drug abuse was more common in the younger adults with age ≤ 30 years as compared with age > 30 years ($p = 0.001$).

Conclusion: HCV infection was common in certain districts of Punjab and common in adults of 40–60 years. This finding needs to be confirmed in larger population-based study. The IV drug abuse is the risk factor of concern among young adults.

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Introduction

Approximately 17 crore people in the world are affected by hepatitis C infection, putting them at risk of developing liver cirrhosis and hepatocellular carcinoma (HCC) and hence making it a global health problem.^{1,2} It spreads mostly undetected, having a risk of cirrhosis after 20 years in 10%–15% of men and 1–5% in women,³ and 1–4% per year risk of developing HCC after development of cirrhosis. Globally, it causes approximately 3 lakh deaths per year and has also now become the leading indication for liver transplantation.³ The estimated prevalence of antibodies to hepatitis C virus (anti-HCV) varies from 0.3% to 5.6% across the world, though high endemic areas have prevalence of up to 12% and some even going up to 58%.⁴ The overall prevalence of HCV infection in India varies from 0.5% to 1.5%;⁵ though, in a study of voluntary blood donors, 2% of the samples were found to be anti-HCV positive.⁶ Among, high endemic areas of Arunachal Pradesh and Mizoram, 7.89% of the general population were found to be HCV infected,⁶ while, 71.2% of injection drug addicts showed HCV antibody positivity. There is paucity of epidemiological data and risk factors from Punjab and Haryana. Therefore, a need was felt to fill the lacunae in literature by a hospital-based epidemiological study of asymptomatic HCV patients.

Materials and methods

Aims

The aim is to study the epidemiological factors related to HCV infections.

Objectives of the study

1. To study the distribution of HCV infection in various districts of Punjab and Haryana.
- 2 To study the relationship of various risk factors with baseline variables.

This cross-sectional study was done at a tertiary care hospital in the Northern Part of the country from July 2011 to April 2016. All consecutive anti-HCV positive patients reporting from northern states of India including Punjab, Haryana, and Himachal Pradesh, who did not have primary liver disease-related symptoms during initial detection were included in the study. Patients who had age <10 years and >80 years, patients with decompensated HCV cirrhosis, HCV cirrhosis, HCC, pregnancy, HIV, or HBV co-infection and chronic kidney disease/on dialysis with HCV were excluded.

All such patients who were anti-HCV positive, HCV RNA detectable or both and fulfilling inclusion and exclusion criteria were subjected to detailed history, history for evaluation of risk factor and history for family screening, complete physical examination, hematological, biochemical investigations, and radiological investigations as per protocol. Upper gastrointestinal endoscopy and fibroscan was done in patients, whenever clinically indicated. HBsAg, anti-HCV, and HIV test was done by enzyme linked immunosorbent assay.

HCV RNA analysis was done by real-time polymerase chain reaction in patients. The study was done through a semi-structured questionnaire designed/reviewed by experts and validated for criterion, construct, and content validity through a pilot test. Pilot test was also used to determine the reliability of the questionnaire.

Patients were reviewed for HCV acquisition, viz. blood transfusion, surgery, needle stick injury, self-reported dental procedure, tattooing, acupuncture, unprotected intercourse with multiple sexual partners, and intravenous drug abuse. Patients with significant alcohol intake were defined as those who were consuming regularly >20 g of alcohol per day for at least 10 years, prior to presentation. Statistical analysis: descriptive statistics was used for various parameters. Chi-square test was used to derive association between variables. The p values < 0.05 and p values = 0.05 were considered significant. For statistical analysis, STATA software (ver 13) was used.

Results

A total of 1012 patient were studied. The demographics are depicted in Table 1 and age distribution in Table 2. The mean age of the study population was 49.88 years with a median of 52 years (range 13–85 years). The male to female ratio was 0.87:1. Eight hundred (79.25%) were from Punjab, 110 (10.67%) were from Haryana, and 102 (10.2%) were from other parts of the country. Table 3 depicts distribution of cases as per districts of Punjab and Haryana, respectively. A schematic diagram showing relative distribution of cases in various districts of Punjab and Haryana, respectively, are shown in Figs. 1 and 2. The relative prevalence of cases in Punjab was more common in the Majha belt of Punjab, adjoining the international boundary. The risk factor profile is depicted in Table 4. 66.2% did not have an apparent risk factor for HCV infection, whereas 27.08% had at least one risk factor and 68 (6.72%) patients had more than two risk factors. A total of 243 (24.01%) patients had history of operation in the past, 91 (0.89%) had history of jaundice 10–40 years before presentation, 40 patients (0.39%) had history of tattooing, 32 (0.29%) patients had history of IV drug abuse, and 19 (0.18%) had past history of blood transfusion.

History of alcohol consumption was available in 995 patients of which 31 had history of alcohol abuse, 17 had social consumption of alcohol, and 957 did not consume alcohol. Thirty-two patients had history of IV drug abuse among these HCV positive patients, of which 29 were less than 30 years, and three were females. Two patients were from Haryana, two from other states, while 27 were from Punjab, and eight had other associated risk factors such as tattooing (five) and jaundice (three) in the past, and one had history of operation in the past. It was interesting to see that none of the above patients were consuming alcohol.

Data on symptoms were available for 995 patients, of which only 36 patients had non-specific symptoms such as fatigue, pain abdomen, or non-specific loss of weight. 44.93% families of patients had been screened. A total of 261 spouses were screened, and only 27 (1.03%) were found to be anti-HCV positive, while of 367 families where 433 children were

Table 1 – Patient demographics.

Serial No	Variable	Distribution	Number (N-1012)	Percentage (%)
1	Age	13–85	1012 (Median 52 y)	—
2	Sex	Male	471	46
		Female	541	54
3	States	Punjab	802	79.27
		Haryana	108	10.67
		Others	102	10.08
4	Symptoms (n = 995)	Non-Specific ^a	38	3.82
		Nil	957	96.18

^a Non-specific symptoms: fatigue, pain abdomen, and non-specific weight loss.

Table 2 – Age distribution of the study group.

Age group	Number (n)	Percentage (%)
<20 years	2	0.20
20–29 years	99	9.78
30–39 years	154	15.22
40–49 years	176	17.39
50–59 years	313	30.93
60–69 years	187	18.48
70–79 years	77	7.61
>80 years	4	0.40

screened, only 16 (0.37%) children were found to be anti-HCV positive, which is shown in [Table 5](#).

Discussion

In the present study, the mean age was 49.88 years with a median of 52 years (range 13–85 years). This is very similar to a study of symptomatic patients (56% Cirrhotic, 37%

chronic hepatitis and 7% HCC),⁷ where median age was 49 (range:15–95) years and similar to three other studies of CKD with HCV with median age of 48 years.⁸ In asymptomatic patients, the mean age was 41.89 ± 18.38 years and 38 years in a hospital-based and a population-based study,^{9,10} respectively, such that the mean age was at least 10 years younger than in the present study. The maximal prevalence was in the older age group 40–59 years group (48.32%), followed by 25% in the 20–39 years age group and 18.48% in the 60–69 years age group, with only 0.4% patients more than 80 years and 0.20% in less than 20 years age group. The prevalence was commonest in the age group 41–60 years in the above quoted population-based study¹⁰ and is similar to another population-based study⁵ with 41.3% patients being 41–60 years age group and 2.2% less than 20 years and 1.1% more than 80 years. The figures in a hospital-based study⁹ of 516 asymptomatic incidental patients was also similar, where 44.8% of them were between 41 and 60 years, signifying the long asymptomatic phase and high frequency of implied risk factors during this age.

Table 3 – District-wise distribution in Punjab (n-800) and Haryana (110).

Serial No	District of Punjab	Numbers (n)	Percentage (%)	Districts of Haryana	Numbers (n)	Percentage (%)
1	Amritsar	140	17.5%	Ambala	8	7.27%
2	Ferozepur	22	2.75%	Bhiwani	1	0.90%
3	Fazilka	9	1.125%	Faridabad	0	0
4	Fatehgarh	13	1.625%	Fatehabad	2	1.80%
5	Gurdaspur	50	6.25%	Gurugram	0	0
6	Hoshiarpur	20	2.5%	Hisar	2	1.80%
7	Jalandhar	14	1.75%	Jhunjhunu	0	0
8	Ludhiana	52	6.5%	Jhajjar	1	0.90%
9	Pathankot	1	0.125%	Jind	28	25.45%
10	Sangrur	89	11.125%	Kurukshetra	28	25.45%
11	SBS Nagar	4	0.5%	Kaithal	17	15.45%
12	Taran Taran	144	18%	Karnal	5	4.54%
13	Moga	46	5.75%	Mahendargarh	0	0
14	Mansa	24	3%	Mewat	0	0
15	Muktsar	21	2.625%	Palwal	0	0
16	Patiala	56	7%	Panchkula	5	4.54%
17	Kapurthala	24	3%	Panipat	3	2.70%
18	Faridkot	18	2.25%	Rewari	0	0
19	Ropar	19	2.375%	Rohtak	2	1.80%
20	Mohali	10	1.25%	Sirsa	1	0.90%
21	Chandigarh	6	0.75%	Sonapat	1	0.90%
22	Bhatinda	16	2%	Yamunanagar	5	4.54%
23	Barnala	2	0.25%	Charkhi Dadri	1	0.90%
24	—	—	—	Hansi	0	0

Fig. 1 – Schematic distribution of frequency of HCV infection in districts of Punjab in a hospital-based study. HCV, hepatitis C virus.

The male to female ratio in this study was 0.86:1, which is contrary to what most studies have reported. A study of treatment naïve HCV patients from Northern India¹¹ showed a male to female ratio of 79:18, while other studies on demography in India, among blood donors,^{12,13} showed male predominance of 66% and 68.3%, respectively. This could be explained by a referral bias of male preponderance in medical care, as so in the donor population. The only other studies which showed a similar male to female prevalence as the present study were population-based studies on HCV prevalence in Punjab¹⁴ and from West Bengal.⁵ What is important to understand is that most population-based studies have shown similar male and female prevalence, and the difference in hospital-based/donor studies can be attributed to a male bias in both these situations.

Of all the patients from the state of Punjab, the six districts which had maximum frequency were 144 in Taran Taran

(18%), 140 in Amritsar (17.5%), 89 in Sangrur (11.125%), 56 in Patiala (7%), 52 in Ludhiana (6.5%), and 50 in Gurdaspur (6.25%). The prevalence of HCV seropositive person was higher in Mansa (13.6%), Muktsar (12.4%), Moga (8.8%), and Sangrur (5.7%) in a population-based study of Punjab reported in 2012¹⁴, which is different from the present study. The prevalence of HCV infection rose from 1.1% to 1.4%–1.9% in 2014 in District Amritsar and from 1.8% to 2.3%–2.9% from 2014 to 2016 in District Taran Taran, respectively, as reported by State AIDS(PSACS),¹⁵ which could explain the difference in the above two studies. The frequency of HCV infection (N = 516) in yet another hospital-based study from Ludhiana¹⁶ was highest in Ludhiana (30.4%), Moga (17.83%), Sangrur (11.63%), and Firozpur (6.98%), and these differences in the hot spots could also be attributed to a referral bias. However, in the present study, three of the six districts were most distantly placed from the study location and in some way may

Fig. 2 – Schematic distribution of frequency of HCV infection in districts of Haryana in a hospital-based study. HCV, hepatitis C virus.

represent the true prevalence. Of the 109 patients in Haryana, Kurukshetra (25.45%), Jind (25.45%), and Kaithal (15.45%) were maximally represented, suggesting high prevalence in these districts. The only other study from Haryana of patients

referred for cataract surgery in Hissar¹⁷ reported high prevalence in the above three districts, besides Fatehabad, Hisar, and Jind districts (these being adjacent districts to place of study).

Table 4 – Risk factors associated with hepatitis C virus infection.

Serial No	Risk factors		Numbers	Percentage
1	Presence of risk factors ^a	No risk factors	670	66.21
		Single risk factor	274	27.08
		Two or more risk factors	68	6.72
2	Alcohol consumption (n = 995)	Alcohol abuse	31	3.12
		Social	17	1.71
		No alcohol	947	95.18
3	IV drug abuse		32	0.32

^a Risk factors—H/o Operation, jaundice, blood transfusion, IV drug abuse, tattooing, alcohol.

Table 5 – Seropositivity/concordance in family.

Serial No	Seropositivity/concordance in family	Numbers	Percentage
1	Spouse positivity (n = 261)	27	1.03
2	Seroconcordance in children (n = 433)	16	0.37

In the present study, 66.21% of patients had no risk factor, 27.08% had one risk factor, and 6.72% had more than two risk factors. Surgery (24.01%), history of jaundice in the past (0.89%), history of tattooing (0.39%), history of IV drug abuse (0.29%), and history of blood transfusion (0.18%) were the most significant risk factors. Analysis in another study¹³ revealed increasing age; alcoholism, blood transfusion, and dialysis as significant risk factors. A study of pregnant women¹⁸ showed 61.9% had no identifiable risk factors, similar to our study. In a study of blood donors,¹⁹ sharing of shaving kits or visit to a roadside barber was present in 32%, history of surgical procedures in 25.8%, and drug abuse in 6.4%, and none had prior history of blood transfusion. The risk factors in a study of preoperative evaluation for cataract surgery²⁰ were shaving from barber (79%), dental procedures (54%), injection from unqualified health-care worker (36%), surgery (19%), and blood transfusion (2%). In another population-based study from Uttarakhand,²¹ 27.3% had h/o blood transfusion, 36.4% had past surgery, and 13.6% had either tattooing/piercing or frequent visit to barbers. A study from Kerala²² did not show history of jaundice or hospitalization as a risk factor. History of injection from the local practitioner (70.3%) and dental treatment (66.7%) were two most common risk factors for HCV infection in another study.²³ The variation in various studies on possible risk factors is also related to social and cultural practices of that region and the variability in collection of data, hence the incongruity. Shaving from barbers, injection from local practitioners, and dental procedures were not studied in our patient population, hence the gap in this data in the present study.

A total of 261 spouses were screened, and only 27 (1.03%) were found to be anti-HCV positive, while of 367 families where 433 children were screened, only 16 (0.37%) children were found to be anti-HCV positive. Twenty (16%) of the willing 125 first degree relative contact of a total of 272 patients in a study²⁴ who agreed to participate tested positive for anti-HCV. Alcohol consumption by contact, longer duration of residence with the index case after the diagnosis of liver disease, and presence of cirrhosis in the index case were associated with increased risk of HCV infection among contacts in another study.²⁵ Similarly, 52 family contacts (17%) of a total of 307 family members of 102 index patients were positive for anti-HCV in a study²⁶ in Taiwan. 54% of parents, 28% of spouses, 6.9% of children, and 6.4% of other contacts were affected in that study. 14% of spouses and none of the children showed HCV positivity in a study²⁷ from Egypt. Various studies bring out differences in relation to intrafamilial prevalence in contacts in relation to sexual exposure, infection because of blood transfusion, percutaneous exposure in index cases, and possibly stage of disease in index cases suggesting duration of infection and hence exposure, which explains the difference in the results of the present study.

Thirty-one of 995 patients whose records were available had history of alcohol abuse, 17 had social consumption of alcohol, and 957 did not consume alcohol. Thirty-two of 1012 (0.31%) patients had history of IV drug abuse, 29 (90.6%) of

these were aged less than 25 years, and three (9.4%) were females. 84.6% of these were from Amritsar, Taran Taran, Sangrur, and Fatehgarh Sahib districts of Punjab. None of them were consuming alcohol, though 25% had other associated risk factors like tattooing and jaundice and history of operation. 98% and 13.7% of IV drug abusers in a study from Manipur²⁸ and from Assam,²⁹ respectively, were found to be anti-HCV positive, while, IV drug abuse was not shown to be a risk factor for HCV prevalence in a population-based survey in Uttarakhand.²¹ 29% and 49% of 1155 IV drug abusers were HIV and HCV antibody positive, respectively, and 12% of young intravenous drug user (IDU) (<19 years) were HIV antibodies positive with 27% of them being HCV antibodies positive in a study from Punjab.³⁰ It is interesting to note that this is the first study to show that a very high proportion of young patients who were found to be anti-HCV positive were IV drug abusers, and most of them were not consuming alcohol.

Most patients were asymptomatic, and this may represent the true epidemiological profile of such patients, along with its risk factors. However, certain risk factors have not been analyzed in this study which may be a shortcoming of the study. Though, the frequency of reporting from some distant parts may be because of population referred elsewhere, the fact of high reporting from certain districts cannot be overlooked. The sheer numbers in this study may have reduced the biases likely in a hospital-based study, though this continues to be a limitation of the study.

Conclusion

It is concluded from this present study that the 40–60 years of age group are the most prevalent in asymptomatic HCV infected patients and have similar male female prevalence. There are certain high frequency pockets in Punjab and Haryana, where interfamilial prevalence of HCV infection has been shown to be low and where risk factors for acquiring infection as brought out appear to be linked to history of jaundice/surgery in the past, blood transfusion, tattooing, and of course IV drug abuse in the young population. The authors believe that there is a need to have a larger population-based study involving the whole state and in turn the country for understanding in depth the true contribution and relevance of these risk factors for HCV infection. Finally, once the two are known, this may be used to reduce the prevalence of HCV infection in the country, reduce the morbidity and mortality, and in turn the overall health of these high prevalence areas of HCV infection.

Future directions

The future lies in reducing the overall HCV-related morbidity and mortality in the country, and since HCV vaccination is

as of now not in sight, the only way forward is to understand the epidemiology of HCV infection and role of each of the risk factors in the propagation of this infection. These then can be used to reduce the HCV disease burden in the country.

Conflicts of interest

The authors have none to declare.

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