Original Article

Previous history of surgery in females and roadside shaving in males are the commonest risk factors for hepatitis C infection: A cross-sectional retrospective study

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Abstract

Background and objectives: Hepatitis C virus (HCV) is a causative agent of hepatitis C disease of the liver. We have analysed the major risk factors including demographic, clinical and genotypic distribution among HCV seropositive patients and their distribution in Uttar Pradesh, India. **Methods:** This study was conducted by a questionnaire-based proforma, filled in Hepatobiliary Clinic, Department of Medicine, King Georg's Medical University, Lucknow, from 2014 to 2017. Demographic, clinical and laboratory data were recorded. Seropositivity was demonstrated through an anti-HCV IgG ELISA kit. Positive patients were further examined for HCV RNA by RT-PCR. **Results:** A total of 31,440 patients attended the hepatobiliary clinic. Among these, 310 (0.99%) patients were confirmed for HCV infection and there was no significant difference between males and females (50.3% vs. 49.7%). Previous surgery (49.0%), dental extraction (41.0%) and roadside shaving (38.1%) were the major risk factors for HCV infection. We also observed that previous surgery 143/154 (92.9%) in female and roadside shaving 118/156 (75.6%) in male was the commonest factor for HCV, however; dental extraction was comparable among male and female (65 [51.8%] vs 62 [48.2%], *P* value = 0.818). HCV RNA genotype 3 (81.6%) was the most frequent followed by 3a (11.3%), 3b (5.8%), 1 (0.7%) and 4 (0.7%). In the district-wise analysis, frequent cases were included from Lucknow with previous surgery and dental extraction as the commonest risk factor. **Interpretation and Conclusions:** Previous surgery among female and roadside shaving among males are the commonest risk factors for HCV. This study suggests a powerful and strict guideline, to avoid HCV infection.

Keywords: Dental extraction, HCV-genotype, hepatitis C virus, previous surgery, roadside shave, tattooing

Introduction

Hepatitis C is an infectious liver disease, triggered by the hepatitis C virus (HCV). HCV causes both acute and chronic infection of the liver. Acute HCV infection is usually asymptomatic and seldom associated with the life-threatening disease. Firstly, infection showed no symptoms, but once established, apparently, after many months to years, it becomes a chronic infection that can progress to blemishing of the liver followed by advanced scarring and cirrhosis. Approximately 15–45% of the infected persons spontaneously clear the virus within 6 months of infection without treatment. However, the remaining develop

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chronic HCV infection followed by the risk of cirrhosis of the liver in between 15–30% within 20 years. HCV infection is a globally prevalent pathogen and a leading cause of morbidity and mortality.[20] Worldwide approximately, per year 3–4 million people are infected with HCV.[4] World Health Organisation (WHO) observed that more than 6 million people of India infected with HCV and chronic infection accounts for 10–20% of liver cirrhosis cases and 12–32% of hepatocellular carcinoma (HCC).[5,6] It is also estimated that 15 million people are living with hepatitis C infection with 2.8 lakh new cases of HCV occurring every year in India with the highest incidence in the state of Punjab, India.[7] Uttar Pradesh (UP) [24] also shows a vulnerable population for the risk of HCV infection.

HCV is usually a blood-borne infection and its most common modes of infection include the transfusion of unscreened blood and blood products, high-risk sexual behaviour, unsafe intravenous drug abuse or reuse syringe practises including poor sterilisation of medical equipment. Injection drug use is the main mode of transmission of HCV in developed countries, transmitted through blood-to-blood contact, either via direct or indirect sharing of injecting equipment.[3] Earlier studies showed that unscreened blood transfusion, intravenous drug abuse, multiple sexual partners and homosexuality were highlighted as the major risk factors in the case of females.[1-3] However, high-risk sexual behaviour was a major risk factor for males. On the other hand, the most prevalent genotype is genotype 4, especially in northern, eastern and western parts, which is often followed by genotype 1 in the southern part of India.[8] These two genotypes are not only difficult to treat against anti-HCV therapy but also are aggressive in pathogenicity.

Epidemiological data with risk assessment on HCV infection from India is very scarce and scanty; hence we conducted a proforma-based seroepidemiologic survey to estimate the prevalence and risk factors for hepatitis C in UP, a northern large and highly populated state of India. The specific objective of this study was to find out risk factors, genotypic distribution and seroprevalence of anti-HCV antibody among the patients with different demographic and clinical profiles. This study also helps us to predict the probable risk factors for hepatitis C infection in UP, India.

Material and Methods

Study population

This study was conducted in the Hepatobiliary clinic of the Department of Medicine, King Georg's Medical University, Lucknow, India between 2014 to 2017. The study was conducted following recommendations of the ethics research committee (**registration no. ECR/262/Inst/UP/2013**) and ethical clearance (**ref no. 537/Ethics/R/Cell-17**) was obtained from our institution. Consent was also obtained from all the participants for conducting the present study. A total of 31,440 patients attending the Hepatobiliary clinic in the above period, were tested for HCV infection. Out of these, 310 (0.99%) patients were positive against anti-HCV antibody detectable with the HCV RNA test and were finally enrolled for this study.

Clinical evaluation

Subjects, positive for the anti-HCV screening test were further guided for clinical evaluation. The detailed medical history was recorded, with special attention being given towards the symptoms of chronic hepatitis and various risk factors for the acquisition of the HCV. All the clinical and laboratory parameters like blood profile, especially haemoglobin (Hb), total leucocyte count (TLC), platelets (PLT), mean corpuscular volume (MCV), prothrombin time (PT) and international normalised ratio (INR) were measured. We have also collected biochemical profiles mainly alanine transaminase (ALT), aspartate amino transaminase (AST), alkaline phosphates (ALP), albumin, creatinine, serum sodium, potassium and total protein among all the patients.

Risk factor analysis

The questionnaire used to obtain data included information on basic demography, their original native place or district and also a habit of alcohol consumption. The information on risk factors was collected on proforma at the time of clinical evaluation. The previous history of any surgery, dental extraction, tattooing, blood transfusion, intravenous (IV) drug use or reuse syringe, roadside shaving and high risk of sexual behaviour were counted as a risk factor of HCV infection. Patients with a history of IV drug abuse were considered as a route of transmission of HCV. Transfusion was presumed to be the route of infection among subjects who had received blood or blood product transfusion at any prior time. Some patients had no memories of any source mentioned above. So, they were counted as the unknown reason for HCV infection. Some patients also recall more than one reason then we have mentioned duplicacy of the risk source; but, counted them separately.

Laboratory assessments for HCV infection and their genotyping

All patients were tested for immunoglobin G (IgG) anti-HCV by a third-generation enzyme-linked immunosorbent assay (ELISA) kit through the Department of Microbiology of our institute. Sera were also screened for hepatitis B virus infection using commercially available hepatitis B surface antigen (HBsAg) enzyme immunoassay kits. Anti-HCV positive subjects were further investigated for HCV RNA by real-time polymerase chain reaction (RT-PCR).

Statistical analysis

Discrete data were represented as frequencies and percentages. Continuous data were represented as mean ± standard deviation (SD), especially age, basel mass index (BMI) and biochemical parameters. Data were analysed using Microsoft Excel and Chi-square test by **IBM SPSS 20**. A 0.05 level of probability (*P*-value) was used as the criterion for statistical significance of studied data.

Results

Demographic characteristics

In this study, we enrolled 310 (0.99%) participants, positive for the anti-HCV antibody. We found similar cases among male vs. female (156 [50.3%] vs. 154 [49.7%], *P* = ns). HBV coinfected patients were excluded from our study. The mean age of the studied population was 40.8 years ± 12.2 years. However, the male was younger than the female (37.2 ± 12.6 vs. 44.4 ± 10.6, *P* < 0.001). BMI was also comparable among men and women (22.09 ± 2.8 vs. 21.74 ± 4.07, *P* = ns) [Table 1]. The behaviour of alcohol consumption was not accepted by any confirmed patients.

Clinical and biochemical profile

Clinical and biochemical parameters across gender represented as mean and standard deviation showed nonsignificant differences among blood profile [Table 2]. The rest of the other biochemical liver function tests like AST, ALT, ALP, serum protein and albumin also showed comparable values among men and women [Table 2].

Risk factor profile

Figure 1 showed the different risk factor and their percentage among patients. In which, the previous history of surgery was a more common risk factor 152 (49.0%) followed by dental extraction 127 (41.0%) and roadside shaving 118 (38.1%) for HCV infection. However, high-risk sexual behaviour 8 (2.6%) and blood transfusion 15 (4.8%) was the least common risk factor of HCV. Although 16 (5.2%) patients said that they have not memorised any idea about the consecutive source of HCV infection, counted as the unknown reason. When we analysed our data based on gender-wise distribution, we found that previous history of surgery 143 (92.9%) in female and roadside shaving 118 (75.6%) in males was the commonest factor for HCV infection. The other major high-risk factor for male were dental extraction 65 (41.7%) and IV drug/reuse syringe 31 (19.9%); however, previous surgery 9 (5.8%), tattooing 6 (3.9%) and high-risk sexual behaviour 8 (5.1%) were a least common risk factor for HCV infection. On the other hand, dental extraction 62 (40.3%) followed by tattooing 30 (19.5%) were the second and third most common risk factors for females. Dental extraction was comparable among male and female (65 [41.7%] vs 62 [40.3%], *P* value = 0.818). Males have not accepted that they have any history of blood transfusion and history of high-risk sexual behaviour and the unknown reason was absent in the female.

Viral load and Genotype

When focusing on the issue of viral load, only 294 patients showed an active viral load of HCV-RNA [Table 3]. The median viral load was 375002 IU/mL. We found that males and females had a similar viral load of all types of genotypes (349501 IU/mL

Table 1: Demographic representation

Risk factor	Total patients	Distributions among gender		*P**
		Male	Female	Male vs Female
*Gender distribution	310	156 (50.3%)	154 (49.7%)	0.473
Age in years (Mean±S.D**)	40.78±12.17	37.2±12.62	44.4±10.56	<0.001
BMI*** (Mean±S.D)	21.92±3.5	22.09±2.8	21.74±4.07	0.379

**P*=Chi-square test; ***S.D*=Standard deviation; ****BMI*=Basel mass index

Table 2: Biochemical and laboratory parameters

	Unit	Normal value	Mean ± S.D			*P* (Male Vs. Female)
			Total No. of cases (*n*=310)	Male (*n*=154)	Female (*n*=156)	
Haemoglobin	g/dL	13-17	11.7±2.3	11.9±2.2	11.5±2.3	0.876
TLC	Cells/mm^3	4000-11000	7838±2980	7741±2982	7935±2984	0.567
PLT	Lac Cells/mm^3	1.5-4.5	167922±65620	170460±62828	165351±68442	0.494
MCV	ft	80-100	90±8.7	89.8±8.2	90.2±9.2	0.712
Creatinine	mg/dL	0.5-1.5	0.9±0.4	1.0±0.4	0.9±0.4	0.161
Sodium	n mol/L	135-145	141±6	142±6	141±5	0.518
Potassium	n mol/L	3.5-5.3	4.2±0.5	4.3±0.5	4.2±0.5	0.249
Bilirubin	mg/dL	0.3-1.4	1.2±1.4	1.1±1.4	1.2±1.5	0.402
AST	IU/L	0-40	97.6±83.3	98.9±91.9	96.3±73.9	0.778
ALT	IU/L	0-45	93.2±83.1	92.0±83.3	94.4±84.0	0.800
ALP	IU/L	0-270	210.6±128.6	216.1±123.3	205.1±134.0	0.455
Protein	gm/dL	6.0-7.8	7.5±1.1	7.5±1.0	7.4±1.1	0.322
Albumin	gm/dL	3.5-5.0	4.0±0.8	4.0±0.7	4.1±0.9	0.289
PT	sec	11-15	14.9±2.1	15.0±2.4	14.8±1.8	0.325
INR	-	-	1.1±0.3	1.1±0.3	1.1±0.2	0.826

TLC=Total leukocyte count, PLT=platelets, MCV=mean corpuscular volume, AST=alanine aminotransferase, ALT=alanine transaminase, ALP=alkaline phosphates, PT=Prothrombin Time, INR=international normalized ratio

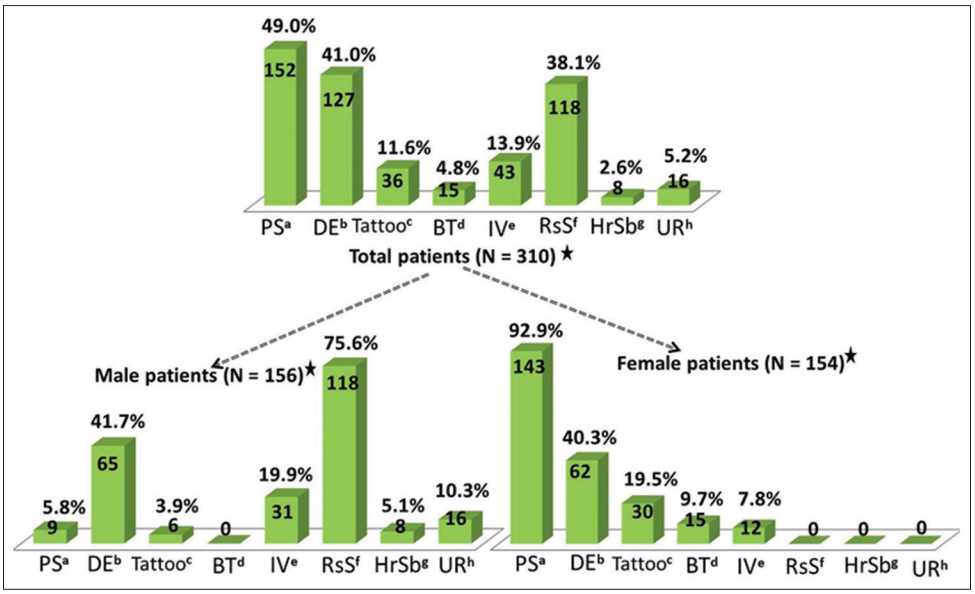

Figure 1: Frequency of risk factors responsible for HCV transmission Many patients gave the response against more than one questionnaire, so we have added every response separately in our frequency representation. **Abbreviations used**: aPS: Previous Surgery, bDE: Dental extraction, cTattoo: Tattooing in body, dBT: Transfusion of blood or blood products, eIV: Intravenous drug or reuse syringe, fRsS: Roadside Shaving, gHrSb: High risk sexual behaviour, hUR: Unknown region

vs. 397501 IU/mL, $P = 0.634$). Genotype was not detected in 16 patients due to low viral load or viral load below the detection limit. Table 3 also shows the genotypic distribution in the north Indian population. The majority of patients enrolled in our study, found to have HCV RNA genotype 3 (81.6%) was the most frequent followed by 3a (11.3%), 3b (5.8%), 1 (0.7) and 4 (0.7%), respectively. However, genotype distributions were comparable among men and women [Table 3].

District-wise risk analysis in the state of UP, India

UP is the most populated state of India with 199.58 million population (According to 12th Indian Census) and the sex ratio was 908 females per 1000 males (2011 census) which are lower than the national average of 933 (www.censusindia.gov.in). So, we have also analysed our data based on the patient's home district or reported in the registration of OPD. According to our study, most of the patients attended the clinic from Lucknow and least from Gorakhpur and Kanpur [Table 4]. Among the patients attending from Lucknow, surgery (17.67%) and dental extraction (15.48%) were the most common risk factors, followed by tattooing (2.9%) and 1.94% blood transfusion [Table 4].

Discussion

The present cross-sectional retrospective analysis of prospectively collected data revealed that (a) Previous history of surgery is the primary or leading risk factor followed by dental extraction, and roadside shaving is the second most common risk factor for HCV transmission, (b) High-risk sexual behaviour and blood transfusion was the least common risk factor of HCV infection, (c) Based on gender-wise distribution, previous history of surgery in female and roadside shaving in male was the commonest factor for HCV infection, (d) Dental extraction was equally frequent among male and female, (e) HCV Genotype 3 (81.6%) was most frequent followed by Genotype 3a (11.3%), 3b (5.8%), 1 (0.7%) and 4 (0.7%) in our north Indian state – UP population and (f) Lucknow is the most HCV affected district in UP firstly by previous surgery and dental extraction equally and secondly by tattooing and blood transfusion.

As previously reported studies in India that HCV infection spreads due to the flaws in the blood banking system, exposure to blood or body fluids i.e., mainly by surgery, an unscreened blood transfusion and blood product, unsafe therapeutic injections, injection drug uses, reuse of injection accessories and by unprotected sex and healthcare-related procedures.[9-12] Mandatory testing for HCV was started in 2002 in blood banks of India.[12] Therefore, HCV screening of blood products is compulsory; however, blood transfusion and injection drug use are gradually becoming the major route of HCV infection.[13] In our study, previous surgery, dental extraction and roadside shaving are the leading risk factors of HCV infection. Other study data Basu *et al.* (2015) reported the four most common risk factors for HCV positivity, were sharing syringes, reuse of injections accessories, blood transfusions and drug abuse. However, blood transfusion, IV drug or reuse syringes and high-risk sexual behaviour showed lower risk factor of HCV transmission in our study.

The previous history of surgery followed by dental extraction was the major cause of infection among female. It was observed that HCV infection in females is associated with previous surgery including lower uterine segment caesarean section (LSCS), hysterectomy, surgery of ovarian cyst cancer, fibroid and prolapse uterus. Another study data revealed that roadside shaving among

Table 3: HCV-RNA viral load among patients with HCV infection

HCV-RNA Load Median (IU/mL)		Total no. of patients	Distributions among gender		*P*
		294*	Male (146)	Female (148)	
		375002	349501	397501	0.634
Genotype distribution	Types of genotype				
	1	2 (0.7%)	0	2 (100%)	-
	3	253 (81.6%)	134 (53.0%)	119 (47.0%)	0.220
	3a	35 (11.3%)	13 (37.7%)	22 (62.9%)	0.117
	3b	18 (5.8%)	7 (38.9%)	11 (61.1%)	0.338
	4	2 (0.7%)	2 (100%)	0	-

*Out of 310, genotype was not detected in 16 patients due to low viral load or viral load below detection limit, so only 294 patients had shown the HCV-RNA viral load

Table 4: District-wise distribution of different risk factor

Districts of Uttar Pradesh	No of cases	Number of agreements* and percentage of risk assessment (on recall basis)							
		Previous Surgery	Dental extraction	Tattoo-ing	Blood Transfusion	IV Drug	Sexuality	Road-side shaving	Unknown reason
Ambedkar Nagar	14	6 (1.9)	7 (2.26)	4 (1.29)	1 (0.32)	4 (1.29)	-	5 (1.61)	-
Lucknow	127	61 (19.67)	48 (15.48)	9 (2.9)	6 (1.94)	19 (6.13)	4 (1.29)	52 (16.77)	6 (1.94)
Sitapur	33	19 (6.13)	15 (4.83)	4 (1.29)	2 (0.64)	3 (0.97)	1 (0.32)	13 (4.19)	1 (0.32)
Basti	4	4 (1.29)	2 (0.64)	3 (0.97)	1 (0.32)	-	-	4 (1.29)	-
Bareilly	5	3 (0.97)	4 (1.29)	-	-	2 (0.65)	1 (0.3)	3 (0.97)	-
Faizabad	6	3 (0.97)	3 (0.97)	1 (0.32)	-	-	-	1 (0.32)	1 (0.32)
Pilibhit	7	4 (1.29)	3 (0.97)	2 (0.65)	-	-	-	3 (0.97)	-
Unnao	21	11 (3.55)	7 (2.26)	3 (0.97)	2 (0.64)	3 (0.97)	-	6 (1.94)	2
Raibareli	5	2 (0.65)	3 (0.97)	-`	-	1 (0.32)	-	1 (0.32)	1 (0.32)
Amethi	6	2 (0.65)	2 (0.65)	-	-	1 (0.32)	-	2 (0.65)	-
Bahraich	6	2 (0.65)	3 (0.97)	1 (0.32)	-	-	-	4 (1.29)	-
Balrampur	2	2 (0.65)	-	1 (0.32)	-	-	-	1 (0.32)	-
Barabanki	22	11 (3.55)	8 (2.58)	1 (0.32)	2 (0.64)	3 (0.97)	0	7 (2.26)	2 (0.65)
Gorakhpur	2	1 (0.32)	1 (0.32)	-	-	-	-	-	1 (0.32)
Kushinagar	2	1 (0.32)	1 (0.32)	-	-	-	-	-	-
Lakhimpur khiri	2	1 (0.32)	2 (0.65)	1 (0.32)	-	-	-	-	-
Hardoi	4	1 (0.32)	3 (0.97)	-	-	1 (0.32)	-	2 (0.65)	-
Mahoba	4	2 (0.65)	3 (0.97)	-	-	-	-	3 (0.97)	-
Siddharth nagar	4	2 (0.65)	3 (0.97)	1 (0.32)	-	-	-	1 (0.32)	-
SantKabir Nagar	4	2 (0.65)	-	1 (0.32)	-	-	-	-	2 (0.65)
Muradabad	4	2 (0.65)	3 (0.97)	-	-	1 (0.32)	-	2 (0.65)	-
Shahjahanpur	3	2 (0.65)	1 (0.32)	-	-	-	-	1 (0.32)	-
Udhamsinghnagar**	4	2 (0.65)	2 (0.65)	-	-	1 (0.32)	1 (0.32)	2 (0.65)	-
Kanpur	10	2 (0.65)	1 (0.32)	1 (0.32)	1 (0.32)	1 (0.32)	0	1 (0.32)	-
Azamgarh	3	1 (0.32)	0	1 (0.32)	0	2 (0.64)	1 (0.32)	1 (0.32)	0
Sultanpur	6	3 (0.97)	2 (0.65)	2 (0.65)	0	1 (0.32)		3 (0.97)	
Total		152	127	36	15	43	8	118	16

*Number of agreements means some patients have agreed that they have faced more than one previous history of risk of HCV transmission, so we have added every response separately in our frequency representation; **Udhamsinghnagar currently comes in Uttarakhand state, India

male patients was the commonest factor for HCV infection in the studied population. One of the reason of above observation that mostly roadside saloon shops uses single blades for more than one customers, so regular practise of contaminated blades with blood of one infected person to another healthy person like HIV and other hepatitis, maybe an explanation of this high-risk factor. Dental extraction was an equally higher risk factor of HCV infection among males and females. A dental extraction is a common cause of dental trouble in our population, and people mostly go to local unhygienic or nonqualified practitioners who use the same equipment for multiple people, thus it becomes the main source of infection for diseases like HCV. Its infection could also occur at different stages of tattooing due to the reuse of non-disposable and unsterilised needles, or reuse of needle which is contaminated with blood from an infected person.[14-17] In this study, the risk factor for tattooing in males is 3.9% and in the female is 19.5% cases and this may be a source of infection.

HCV genotype was an important factor in determining treatment duration in the interferon era but is still relevant as we have to see the long-term outcome of currently available antiviral drugs. In our study, the most frequent genotype in the north Indian population is genotype 3 followed by 3a, 1 and 4. However, genotype 2 was not found in our study. A study on samples from

many parts of India also found a high prevalence of genotype 3. We did not evaluate for genotype 5 and 6. If we are talking about subgenotype of 3, 3a are more prominent than 3b and, in the case of subgenotype 1b is less than 1. It has previously been established that genotype 3 is most widely prevalent in India, followed by genotype 1 and then genotypes 2, 4, 5 and 6, respectively.[18] Our study findings are similar to other studies and suggest that genotypes 3 and 1, constitute approximately 80%, however; genotype 4 is very less shown only in two cases i.e., about 1% and needs further study.

The district Lucknow showed the highest number of HCV infections occurring via previous surgery and dental extraction (19.67%) [Table 4]. There was no case of IV drug abuse, sexual and roadside shaving as a risk factor, it may be due to awareness about the mode of transmission of HCV among people of Lucknow. Hepatitis C is an emerging disease in UP with plenty of HCV infected asymptomatic persons, who can act as a pool for its continuous transmission. However, the limitation of this finding is that the studied tertiary care hospital is situated in Lucknow. So, frequent cases are included in the same city. Other frequent cases were also referred from neighbouring districts like Ambedkar Nagar, Sitapur and Unnao and Barabanki.

Patients with confirmed HCV infection were 0.99% in our study which is similar to 1% infected population of the world as well as previous studies of India. Previous surgery, dental extraction and roadside shaving were the major risk factor for HCV infection. We also observed that previous surgery among female and roadside shaving among males was the commonest factor for HCV, however; dental extraction was comparable among those. HCV RNA genotype 3 was the most frequent followed by 3a, 3b, 1 and 4. In the district-wise analysis, frequent cases were included from Lucknow with previous surgery and dental extraction as the commonest risk factors of HCV infection. So, there is a need to increase the awareness about the mode of HCV infection among the public, physicians, surgeons and paramedical health workers. However, there still exists a gap, that needs to be addressed. Further, it is advised, improvement in basic hygiene and strict adherence to universal precautions is essential to prevent iatrogenic transmission of the infection. There is no vaccine available for HCV till date.[19] So, primary care physicians can prevent the HCV infection by alertness about hygienic and uninfected operative theatre before surgery, avoiding sharing of blades and dental equipment and screening of blood before surgery. We must plan a powerful and strict guideline in India, to avoid HCV infection.

Conclusions

Previous surgery among females and roadside shaving among males are the commonest risk factors for HCV. This study suggests a powerful and strict guideline to avoid HCV infection. Hence, there is a need to increase the awareness about the mode of HCV infection among the public, physicians, surgeons and paramedical health workers. However, there still exists a gap, that needs to be addressed.

Key Points

1. Patients with confirmed HCV infection were 0.99% in our study which is similar to 1% infected population of the world as well as previous studies of India
2. There is a need to increase the awareness regarding the mode of HCV infection among the public, physicians, surgeons and paramedical health workers. However, there still exists a gap, that needs to be addressed.
3. Primary care physicians can prevent the HCV infection by alertness about hygienic and uninfected operative theatre before surgery, avoiding sharing of blades and dental equipment and screening of blood before surgery.

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Conflicts of interest

There are no conflicts of interest.

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