

# A Case Control Study for the Identification of Novel Risk Factors Associated with Hepatitis C Viral Infection in Population of Lahore Pakistan

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## ABSTRACT

**Aim:** To investigate the most common as well as least common, unidentified risk factors contributing major part in HCV transmission.

**Method:** A case control study comprising 50 cases and 100 controls was conducted during May, 2011 to August, 2011. Informed consent was taken from all of the participants. Fifty cases and hundred controls were interviewed using pre-tested and specially designed questionnaire. Data was analyzed by using SPSS 16 version to measure the strength of association of various known and unidentified risk factors with HCV transmission. Cases were ELISA confirmed positive and controls were ELISA negative for anti-HCV antibodies. All participants were resident of same area (Lahore) and 16-70 year age. Not a single participant was missed.

**Results:** History of clinical symptoms (OR 7.39), history of sharing of straw (OR 4.321), History of blood transfusion (OR 3.6), history of alcohol consumption (OR 2.67), History of previous surgery (OR 2.42), history of body (including Ear/Nose) piercing/tattooing (OR 2.25), History of sharing of crack pipe (OR 2.23), history of sharing tooth brush (OR 2.11), history of sharing comb (OR 2.06) were significant risk factors associated for acquiring HCV infection.

**Conclusion:** In conclusion, history of presence of acute hepatitis like symptoms prior to illness, sharing of straw, blood transfusion, sharing of straw, crack pipes, tooth brush, comb, history of alcohol consumption, surgical procedures and blood transfusion remains most important vehicles for spread of the HCV in Pakistan. There is a dire need of awareness and effective surveillance and monitoring program at national level to reduce and ultimately control the HCV infection.

**Keywords:** Hepatitis C, risk factors, epidemiology, case control study

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## INTRODUCTION

Hepatitis C virus (HCV) was first identified in 1989<sup>1</sup>. HCV is a heterogeneous virus with at least 6 genotypes and number of subtypes identified globally<sup>2</sup>. According to the World Health Organization (WHO), a total of 170 million people are infected with chronic HCV infection. Hepatitis C is estimated to result in 366 000 deaths annually<sup>33</sup>.

Areas of higher prevalence include countries in the Far East, Mediterranean countries and certain areas in Africa and Eastern Europe<sup>35,36,37,38,39</sup>. Its prevalence is highest (17% to 26%) in Egypt, intermediate (1% to 5%) in Eastern Europe, the Middle East, the Indian subcontinent, low (0.2% to 0.5%) in Western Europe and North America. It has been estimated worldwide that 200 million people get

infected with the HCV<sup>3</sup>. The overall prevalence of anti-HCV antibodies was 2% in Spain<sup>4</sup>, 3.9% in Jakarta, Indonesia<sup>5</sup> and 1.25% in Zakynthos Greek<sup>12</sup>. Hospital based studies done in Mauritius<sup>7</sup>, Ethiopia<sup>8</sup> and South India<sup>9</sup> showed a seroprevalence of 5.9%, 6% and 4.8% respectively. WHO estimates indicate 10-24 million HCV-infected persons in India and seroprevalence of 2.4% in Pakistan. Given its large population (165 million) and intermediate to high rates of infection<sup>33,34</sup>. Pakistan is among the worst afflicted nations.

Administratively Pakistan is divided into five provinces, Punjab, Sindh, Khyber Pakhtoonkhwa, Balochistan, Gilgit Baltistan, as well as federally administered areas including the capital (Islamabad), Federally Administered Tribal Areas (FATA), and the Pakistan administered Jammu and Kashmir. Considering Pakistan's size and large growing population, there is a surprising dearth of information about hepatitis prevalence, although more is known about its risk factors.

The predominant role of blood transfusion and injection drug use in the transmission of HCV has consistently been reported worldwide<sup>10</sup>. Risk factors

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as reported by various researchers are parenteral drug abuse<sup>11</sup>, blood or blood product transfusion<sup>4,5,12</sup>, tattooing<sup>13</sup> surgical procedures<sup>14</sup> reused/contaminated syringes<sup>15</sup> and dental procedure<sup>13,17</sup>. According to reports in over 40% of cases the risk factor(s) cannot be identified<sup>37,39</sup>.

**MATERIAL AND METHODS**

After considering the standard protocol required as per Declaration of Helsinki (2002), blood samples from 150 patients of a tertiary care hospital were collected by non-random, convenience sampling from May 2011 to June 2011. After applying selection criteria 50 known anti-HCV positive Patients from medical outdoor were selected and confirmed as case by using 3rd generation ELISA for the qualitative detection of anti-HCV antibodies in serum while 100 known anti-HCV negative patients from surgical outdoor were taken as control. A pretested questionnaire was filled after taking informed consent from all cases and controls. The data analysis and summary statistics was carried out by using SPSS Version 16.0 for windows. Chi Square and Fisher's Exact tests were used for categorical variables that measured association among categorical variables. The results for all variables were given in the form of rates (%) and all data is presented as Odds ratio with 95% Confidence interval. P-values less than 0.05 were considered significant. No case of control was missed.

**RESULTS**

Case control ratio was 1:2 comprising 50 cases and 100 controls. There were overall 124(82.7%) males and 26 (17.3%) females. Among male participants,

34 were cases and 90 were controls while 16 female participants were taken as case and 10 as controls. The mean age was 30 years (range 16-70). Out of these 150 patients, 46% were married and 54% were unmarried, 75% had Punjabi as mother tongue while 18% had Urdu, 7% had Pashto (Table 1). Our results show that hepatitis C viral infection is more in male, unmarried and between 21-30 years age group.

Statistical analysis of all the risk factors reveals significant but unusual results. History of acute hepatitis like symptoms had (OR 7.39), sharing of straw (OR 4.321), receiving blood transfusion (OR 3.619), consumption of alcohols (OR 2.667), history of surgery (OR 2.42), history of body piercing/tattooing (OR 2.250), sharing of crack pipes (OR 2.232), sharing of tooth brush (OR 2.111), sharing of comb (OR 2.068), history of jaundice in family (OR 1.80), sharing of Spoon (OR 1.560), history of cuts during shave (OR 1.45), sharing of towel (OR 1.397), sharing of razor (OR 1.317), history of traveling outside of Pakistan (OR 1.28), history of receiving intramuscular/intravenous injections (OR 1.19), Use of eye/contact lens (OR 1.17), history of road accident (OR 1.15), sharing of drinking glass (OR 1.096), history of street drugs usage (OR 0.980), use of unprescribed drugs (OR 0.711), use of new needle for injection (OR 0.62), history of pricks by needle/sharps (OR 0.50), history of attending beauty saloon (OR 0.419), history of blood donation (OR 0.360) and use of new blade by barber (OR 0.22) were measured (Table-2). Analysis showed strongest association of HCV with acute hepatitis like symptoms, sharing of straw, crack pipes, comb, tooth brush, history of blood transfusion, alcohol consumption, history of surgery and sharing of crack pipes. In general donating blood and attending beauty saloon were not strongly associated with risk of infection.

Table 1: Distribution of demographic variables

	<b>Variables</b>	<b>Overall</b>	<b>Cases</b>	<b>Controls</b>
Gender	Male	82.7%	34 (68%)	90 (90%)
	Female	17.3%	16 (32%)	10 (10%)
Marriage	Married	46%	33 (66%)	36 (36%)
	Not married	54%	17 (34%)	64 (64%)
Ethnicity	Punjabi	75%	42 (84%)	70 (70%)
	Urdu	18%	6(12%)	21 (21%)
	Pashto	07%	2 (4%)	9 (9%)

Table 2: Risk factors for HCV infection.

Risk factor	Odds ratio	Confidence interval		P-Value
		Lower	Upper	
History of symptoms like acute hepatitis	7.39	3.46	15.79	0.000
History of Straw (Share)	4.321	2.098	8.899	0.000
History of Received blood transfusion	3.619	1.118	11.718	0.010
History of Alcohols consumption	2.667	0.683	10.407	0.145
History of surgery	2.42	1.17	5.03	0.015
History of Body piercing/Tattooing	2.250	1.004	5.044	0.046
History of Crack Pipes (Share)	2.232	1.073	4.644	0.030
History of Tooth brush (Share)	2.111	0.582	7.664	0.247
History of Comb (Share)	2.068	0.780	5.486	0.138
History of jaundice in family	1.80	0.88	3.69	0.106
History of Spoon (Share)	1.560	0.721	3.373	0.257
History of Cuts during shave	1.45	0.73	2.89	0.288
History of Towel (Share)	1.397	0.694	2.812	0.348
History of Razor (Share)	1.317	0.477	3.635	0.594
History of traveling outside of Pakistan	1.28	0.40	4.13	0.681
History of Receiving Intramuscular/Intravenous injections	1.19	0.43	3.32	0.74
History of Use of eye/contact lens	1.17	0.46	3.01	0.744
History of road accident	1.15	0.55	2.40	0.705
History of Glass (Share)	1.096	0.390	3.079	0.862
History of Street drugs (Use)	0.980	0.942	1.020	0.614
History of Unprescribed drugs (Use)	0.711	0.351	1.443	0.344
History of Use of new needle during injection	0.62	0.28	1.41	0.254
History of Prick by needle/sharps	0.50	0.25	1.00	0.049
History of attending beauty saloon	0.419	0.168	1.040	0.056
History of Blood donation	0.360	0.162	0.800	0.024
History of Use of new blade by barber	0.22	0.10	0.51	0.000

Note. OR= Odds Ratio; CI= Confidence interval

## DISCUSSION

The outlook is not all bright, according to the latest WHO statistics; The Hepatitis C virus infection appears to be endemic in most parts of the world with an estimated overall prevalence of 3% and is responsible for a 3 to 4 million new cases of chronic liver disease worldwide<sup>38</sup>.

Different studies suggest that HCV spread may be associated with different transmission routes. The prevalence rate, risk factors and sharing of utensils are known to vary considerably from country to country, probably because of cultural and socioeconomic differences that influence HCV transmission<sup>19</sup>. There was a trend of increasing prevalence of HCV with age<sup>5,6</sup> significantly higher prevalence reported from Zakynthos, a Greek island<sup>6</sup>. According to reports, in over 40% of cases the risk factor(s) cannot be identified (lemon, Purcell). In comparison with others, our study raises two important issues regarding prevention of HCV infection. The first issue relates findings about the presence of acute hepatitis like symptoms (lack of appetite, fever, abdominal pain) before onset of illness in general population and second is sharing of straw among general population. Although risk factors are almost common in the countries of same

region but they differ slightly due to difference in their socioeconomic and health status. The poverty itself invites all diseases. Incomplete treatment, lack of awareness, lack of hygienic measures and diagnostic facilities, care free attitude and limited access to healthcare facilities are imparting their role in increase of HCV spread so it was seen that although acute hepatitis like symptoms had appeared in the patients but due to certain factors mentioned above, the patients were not diagnosed in time and in turn they progressed to the disease complications. So it is concluded that insufficient awareness and limited diagnostic healthcare facilities are major contributing factors towards HCV transmission at large.

It has been discussed by various researcher but not all case-series or case-reports have reported the possibility that HCV can be spread by sharing of straw. The sharing is common between the low or middle class population so further research is required on this aspect. Difference of study design, age, and definition of severity of disease, small sample population and difference in baseline histological characters of liver imparts their pivotal role for the difference of findings in addition to socioeconomic differences.

Sharing of tooth brush (OR 2.1) and comb (2.0) were significantly associated with HCV transmission

which in turn suggests to avoid sharing of these items with hepatitis C patients. The trend of this type of sharing was seen most commonly among HCV positive husbands or wives who previously had shared their comb in routine and tooth brushes on occasional basis.

Hepatitis is spread through direct exposure of infected blood to salubrious. Through receiving blood transfusion, infected medical equipments, blood products, organ transplantation from infected donors, vulnerability to blood especially through contaminated needles, having sex with an infected partner, blood splatters in health care settings, horizontal and vertical transmissions are also responsible for hepatitis, lack of appropriate testing compels the patients to use unscreened blood in emergency situation. Penury is one of the major causes of using undiagnosed blood in developing countries.

Although limited alcohol production is permitted in this country and permission is granted only to some minorities but odds ratio 2.667 was surprisingly high for drinking of alcohol products. Not in near past but now alcohol usage is now very much common in our country. Alcohol consumption is major contributor towards hepatitis. Crapulence causes ascetic liver complications like cirrhosis, hepatocellular carcinomas, and liver fibrosis leading to death.

History of surgery also reflects significantly high risk in spreading hepatitis. Use of un-sterilized and contaminated equipments in healthcare settings should be stopped to minimize the risk of transmission of infectious diseases. Awareness programs are required at large for the medical professionals as well as for general population too.

Odd ratios of body piercing and tattooing are 2.250 in our country. Due to lack of hygienic conditions and un-sterilized equipments, population becomes exposed to the infected blood. Tattooing dyes, inks and piercing of nose, ears plays a critical role in transmission of disease.

Although not common nor still investigated saliva can act as a source for transmission of disease in developing countries. Sharing of personal article like tooth brush can transmit a disease to the household healthier person even if little blood is present as reflected in our study and supported by the OR 2.11.

Sharing of personal care items such as razors (OR1.13), comb (OR 2.0), towels (OR 1.397), and cuts while shaving (OR 1.45) although not found strongly associated with HCV transmission but in turn suggests avoiding sharing of these items with hepatitis C patients because they may come in contact with the infected blood

The sharing was seen common between the population visiting low or middle class restaurants.

History of sharing of spoon (1.56), sharing of glass used for drinking water (1.09) shows that our society costumes, allows family members and household contacts to easily share their kitchen utensils. Although still not proven but results show that it could be common tool for HCV transmission and need further research. Kitchen utensils must be washed properly with the detergents.

History of blood Transfusion, surgical operation, dental procedure with inadequately sterilized instruments, repeated injection (reused), shaving barber and unhygienic sexual relation have been well known risk factors for HCV transmission<sup>4,5,12,20,21,26,27,28,29,30,31</sup>. People who visit regularly for any kind of dental procedure had more prevalence rate of HCV<sup>16,17,21,22</sup> as compared to those who do not visit for any kind of dental procedure and we found this the case in our study. History of surgical operation was recorded as risk factor as seen in other studies<sup>4,22,23</sup>. Similarly our finding of symptoms like lack of appetite, fever, abdominal pain as a common symptom of HCV is consistent with earlier reports<sup>24,25,26</sup>.

## CONCLUSION

The significant risk factors were sharing of straw, crack pipe, tooth brush, alcohol consumption, reused syringes, blood recipients, dental procedures and surgical operations. The common and more important was history of symptoms appearance. As there is no vaccine available for HCV, the prevention of HCV infection can be achieved by blood screening for HCV before donation, avoiding sharing tooth brush, straw, needles or any injecting equipment and following safe sexual practices.

These results indicate that there is a dire need of education programs for awareness amongst general public as well as to healthcare professionals. There should be vaccination of Hepatitis A and B to the Hepatitis C patients. Better management of Hepatitis Patients by medical professionals, Vaccine production against HCV and prevention policies implementation through Government is utmost necessity of the era for healthy society.

Although this study has a number of limitations as the convenience sample of participants may not be representative of all the population. Questions about previous months may result in recall bias, either over or underestimation of events and subjective responses.

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