

Identification of risk factors for hepatitis B and C in Peshawar, Pakistan

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Background: Hepatitis B and C need immediate worldwide attention as the infection rates are too high. More than 240 million people have chronic (long-term) liver infections. Every year, about 600,000 people die globally due to the acute or chronic consequences of hepatitis B and more than 350,000 people die from hepatitis C-related liver diseases.

Methods: Our study was designed as a case-control, descriptive study. It was conducted through formal interviews by using structured questionnaires. A total of 100 cases were included, with four controls for each case.

Results: This study confirms household contact, history of dental work, history of surgery, sexual contact, and history of transfusion (blood and its components) as the main risk factors which are responsible for the increased prevalence of hepatitis.

Conclusion: The important risk factors, responsible for the high prevalence of hepatitis B and C in our society are household contact, history of dental work, history of surgery, sexual contact, and history of transfusion (blood and its components). The odds ratio of probability for these risk factors are: 4.2 for household contact history, 4.1 for history of dental work, 3.9 for sexual contact, 2.7 for history of surgery, and 2.1 for history of transfusion. Associations of other predictor variables (diabetes status, education level, profession, contact sports, intravenous drug abuse, residence, immunosuppression, and skin tattoos) were not statistically significant.

Keywords: hepatitis B, hepatitis C, IV drug abuse, transfusion, dental work, surgery, sexual contact

Introduction

Hepatitis B and C viruses can lead to hepatocellular carcinoma^{1,2} and cirrhosis-related end-stage liver disease,^{2,3} which are potentially life-threatening liver diseases.⁴ Hepatitis B and C need immediate worldwide attention as the infection rates are too high.⁵ More than 240 million people globally have chronic (long-term) liver infections. Every year, about 600,000 people die because of the acute or chronic consequences of hepatitis B,⁶ and more than 350,000 people die from hepatitis C-related liver diseases worldwide.⁷

In the Middle East and the Indian subcontinent, an estimated 2%–5% of the general population is chronically infected with hepatitis B.⁶ Countries with the highest reported prevalence rates of hepatitis C are located in Africa and Asia; areas with lower prevalence rates of hepatitis C include industrialized nations in North America and Northern and Western Europe.⁸ Studies^{9–25} have been conducted in Pakistan to assess the prevalence as well as identify the various risk factors associated with hepatitis B and C. A meta-analysis²⁶ indicates that the prevalence of hepatitis B and C in the general population

in Pakistan is 2.4% (range, 1.4%–11.0%) and 3.0% (range, 0.3%–31.9%), respectively.

In most of these studies, however, very few risk factors were included in one study at a time. Many risk factors have been identified worldwide, eg, blood transfusion,²⁷ IV drug abuse,²⁸ profession (health care workers, barbers, etc),²⁹ household contact,³⁰ sexual contact,³¹ surgical procedures,³² dental procedures,³³ immune-compromised^{34,35} hemodialysis,³⁶ skin tattoos,³⁷ etc, but the ones responsible for the high prevalence of hepatitis B and C in our cities need to be identified. For this purpose, this study takes into account 13 variables (potential risk factors) all at once to find the association as well as the probability odds ratio.

Research design and methodology

Study design

Our study was designed as a case-control, descriptive study, and was conducted through formal interviews using structured questionnaires. A total of 100 cases (either hepatitis B or hepatitis C positive) were included, with four controls for each case.

Study population

Both outpatients and inpatients of Khyber Teaching Hospital, Peshawar, KPK, Pakistan, were included in the study.

Sampling method

For cases

Inclusion criteria were: aged 18 years and above; diagnosed for either hepatitis B or C through ICT/ELISA. Exclusion criteria were: anyone not in the Khyber Teaching Hospital, Peshawar.

For controls

Inclusion criteria were: aged: 18 years and above; Hepatitis B and C negative. Exclusion criteria were: anyone not in the Khyber Teaching Hospital, Peshawar.

Data collection

Data were collected from respondents (patients) in Khyber Teaching Hospital using a questionnaire over a 5-month period (from October 2013 to February 2014). After verbal consent was obtained, a structured questionnaire was used to conduct face-to-face interviews. The questionnaire had closed-ended questions. It was translated into the mother tongue of the respondent and then retranslated into English, and due corrections were made.

Defining variables

Profession

Based on the established facts, professions were categorized as:

1. Health care professionals
2. Barbers
3. Sewage cleaners
4. Others

Education level

The respondents were grouped into the following categories based on educational level.

1. 0–4th grade: below primary
2. 5th–9th grade: primary
3. 10th grade: matric
4. 11th–14th grade: above matric
5. 15th grade or above: higher education

Diabetes

Respondents were considered to have diabetes if they had been told by a health care professional that they were diabetic. The criteria for this was to ask the individual respondents themselves and to cross-question them about the time of appearance of the symptoms and when the health care professional had diagnosed their diabetic condition. Accordingly, the respondents were categorized as:

1. Diabetics
2. Nondiabetics

Transfusion history

It included transfusion of whole blood or any of its components, eg, fresh frozen plasma.

Accordingly, they were categorized as:

1. Transfusion history – positive
2. Transfusion history – negative

Surgical history

In this category, only major surgeries that involve general anesthesia and respiratory assistance were considered.

They were categorized as:

1. Surgical history – positive
2. Surgical history – negative

Dental history

Anyone who had done professional cleansing, tooth filling, or tooth extraction, or had undergone dental surgery was considered as having positive dental history.

They were categorized as:

1. Dental history – positive
2. Dental history – negative

Contact sports

A contact sport is a sport such as football, hockey, or boxing that involves physical contact between players as part of normal play. Those who had a history of contact sports in the past 5 years were considered as having positive contact sports history.

Intravenous drug abuse

Anyone who disclosed a positive history of drug abuse was then assessed for injection drug abuse, and categorized as:

1. Injection drug abuse – yes
2. Injection drug abuse – no

Household contact

If someone had a family member (other than spouse) who was hepatitis B or C positive, then household contact was considered positive; otherwise negative.

Sexual contact

If someone's spouse was infected with hepatitis B or C, sexual contact was considered positive; otherwise negative.

Rural/urban

Rural areas are places away from cities/towns. On the other hand, towns/cities are called urban areas. Depending on where the respondents lived, they were categorized as:

1. Those living in places away from cities/towns – rural inhabitants
2. Those living in cities/towns – urban inhabitants

Sex

People were categorized as either male or female.

■ Hepatitis status positive ■ Hepatitis status negative

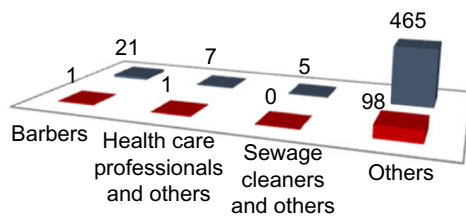
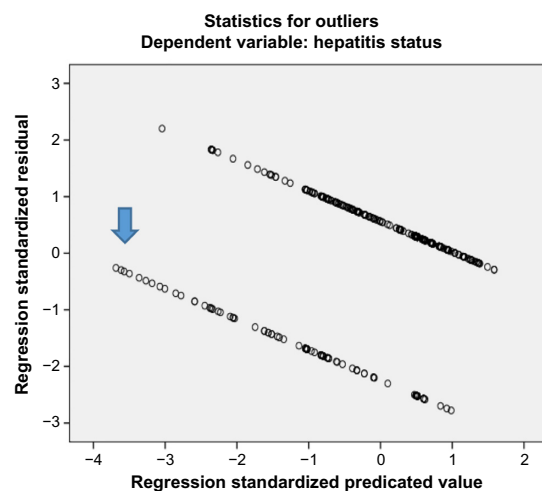


Figure 1 Profession versus hepatitis status.
Note: Data are presented as number of patients.

Table 1 Collinearity diagnostics for ruling out related predictor variables

Parameters	Tolerance	Variance inflation factor
Sexual contact	0.959	1.042
Surgical history	0.771	1.297
Transfusion history	0.768	1.303
Dental history	0.876	1.141
Diabetes mellitus status	0.632	1.583
Education level	0.881	1.136
History of contact sports	0.944	1.060
Household contact	0.950	1.053
Immunosuppression	0.634	1.576
IV drugs abuse history	0.940	1.064
Profession	0.954	1.048
Residence	0.978	1.023
Skin tattoos	0.945	1.058



Notes: As indicated by the arrow, there are very few outliers (Criteria: 3.3 standard deviations), which can be ignored in a large sample. Hence, both assumptions for binary logistic regression are met.

Immunosuppression

Respondents were considered immunosuppressed, if they had obvious signs and symptoms of immunosuppression (eg, opportunistic infections) and the following blood counts.

1. Neutrophils <1,000 cells/μL of blood³⁸ or
2. CD4 T-lymphocytes <350 cells/μL of blood³⁹

Skin tattoos

Tattoos are designs on the skin made with needles and colored ink. The criterion was to ask and then see the skin tattoo objectively.

Statistical analysis

The data were sampled and entered into the SPSS worksheet for analysis. The alpha criterion was set at 0.05 (95% confi-

Table 2 Variables in the equation for the binary logistic regression

Parameters	B	SE	Wald	df	Significance	Exp(B)	95% CI for Exp(B)	
							Lower	Upper
Dental history	1.402	0.320	19.234	1	0.000	4.063	2.172	7.603
Household contact	1.437	0.352	16.617	1	0.000	4.208	2.109	8.396
Sexual contact	1.376	0.541	6.474	1	0.011	3.959	1.372	11.424
Surgical history	0.999	0.320	9.725	1	0.002	2.717	1.450	5.091
Transfusion history	0.749	0.340	4.835	1	0.028	2.114	1.085	4.119
Diabetes mellitus status	0.261	0.370	0.498	1	0.480	1.299	0.629	2.683
Education level			5.065	4	0.281			
Below primary	-0.351	0.684	0.264	1	0.607	0.704	0.184	2.689
Primary	-0.456	0.727	0.394	1	0.530	0.634	0.153	2.634
Matric	-0.062	0.770	0.006	1	0.936	0.940	0.208	4.255
Above matric	2.042	1.306	2.445	1	0.118	7.705	0.596	99.614
History of contact sports	-1.338	1.073	1.554	1	0.213	0.262	0.032	2.150
Immunosuppression	-0.221	0.417	0.282	1	0.595	0.801	0.354	1.814
Profession			1.823	3	0.610			
Health care professionals	1.441	1.079	1.785	1	0.182	4.226	0.510	35.014
Barbers	-0.220	1.180	0.035	1	0.852	0.803	0.079	8.110
Sewage cleaners	18.463	17,466.171	0.000	1	0.999	104,341,396.887	0.000	-
Residence	0.099	0.272	0.132	1	0.716	1.104	0.648	1.881
Skin tattoos	-0.965	0.751	1.649	1	0.199	0.381	0.087	1.662
Constant	-1.238	1.590	0.606	1	0.436	0.290		

Abbreviations: SE, standard error; CI, confidence interval; df, degree of freedom.

dence interval [CI]). After constructing a 2×2 contingency table, chi-square without Yates correction was used to find the association between the potential risk factors and hepatitis status.

Whenever the assumption (of expected count being not less than five in each cell) did not meet the chi-square without Yates correction, Fischer's exact test was used to find the association. Binary logistic regression was used (after meeting the assumptions) to find the influence of each statistically significant predictor variable in terms of the "odds ratio of probability".

Table 3 Variables having no association with the Hepatitis B/C as per this study

Variable	Frequency	Chi-square value	P-value for chi-square	P-value for Fischer's exact ^a
Diabetes mellitus status	500	1.42	0.23	-
Education level	500	<3.84	>0.05	-
Profession	500	-	-	>0.05
History of contact sports	500	-	-	0.61
IV drugs abuse history	500	-	-	1.00
Residence	500	0.36	0.55	-
Immunosuppression	500	0.09	0.76	-
Skin tattoos	500	-	-	1.00

Notes: ^aFischer's exact test was used whenever the assumption for chi-square "expected count not less than 5 in each cell" did not meet. Alpha criterion =0.05.

Results

The two-tailed *P*-value for Fischer's exact test of profession: "Barber and others" and "hepatitis status" equals 0.061. Thus, the association between professions: "Barber and others" and "hepatitis status" is not considered to be statistically significant (Figure 1, Tables 1 and 2). The two-tailed *P*-value for Fischer's exact test of profession: "health care professionals and others" and "hepatitis status" equals 1. Thus, the association between professions: "health care professionals and others" and "hepatitis status" is not considered to be statistically significant (Figure 1, Tables 2 and 3). The two-tailed *P*-value for Fischer's exact test of profession: "savage cleaners and others" and "hepatitis status" equals 0.59. Thus, the association between professions: "savage cleaners and others" and "hepatitis status" is not considered to be statistically significant (Figure 1 and Tables 1–3).

Table 4 Education level versus hepatitis level

Education level	Hepatitis status		Total
	Positive	Negative	
Illiterate, count (% of total)	71 (14.2%)	223 (44.6%)	294 (58.8%)
Primary, count (% of total)	16 (3.2%)	65 (13.0%)	81 (16.2%)
Matric, count (% of total)	9 (1.8%)	47 (9.4%)	56 (11.2%)
Above matric, count (% of total)	1 (0.2%)	40 (8.0%)	41 (8.2%)
Higher education, count (% of total)	3 (0.6%)	25 (5.0%)	28 (5.6%)
Total, count (% of total)	100 (20.0%)	400 (80.0%)	500 (100.0%)

Applying Pearson’s chi-square without Yates correction test on education level: “illiterate and primary” and “hepatitis status” shows chi-square equals 0.69 with 1 degree of freedom. The two-tailed *P*-value equals 0.41. Thus, the association between education level: “illiterate and primary” and “hepatitis status” is not considered to be statistically significant. Applying Pearson’s chi-square without Yates correction test on education level: “illiterate and matric” and “hepatitis status” shows chi-square equals 1.74 with 1 degree of freedom. The two-tailed *P*-value equals 0.19. Thus, the association between education level: “illiterate and matric” and “hepatitis status” is not considered to be statistically significant (Tables 1, 2, and 4). Applying Pearson’s chi-square without Yates correction test on education level: “illiterate and above matric” and “hepatitis status” showed chi-square equals 10.05 with 1 degree of freedom. The two-tailed *P*-value equals 0.002. Thus, the association between education level: “illiterate and above matric” and “hepatitis status” is considered to be statistically significant (Tables 1, 2, and 4). Applying Pearson’s chi-square without Yates correction test on education level: “illiterate and higher education” and “hepatitis status” showed chi-square equals 2.61 with 1 degree of freedom. The two-tailed *P*-value equals 0.11. Thus, the association between education level: “illiterate and higher education” and “hepatitis status” is not considered to be statistically significant (Tables 1, 2, and 4).

Applying Pearson’s chi-square without Yates correction test on diabetes and hepatitis showed chi-square equals 1.42 with 1 degree of freedom and the two-tailed *P*-value equals 0.23. Thus, the association between diabetes and hepatitis status is not statistically significant (Tables 1–3, and 5).

Applying Pearson’s chi-square without Yates correction test on transfusion history and hepatitis status shows chi-square equals 29.72 with 1 degree of freedom. The two-tailed *P*-value equals less than 0.001. Thus, the association between transfusion history and hepatitis status is considered to be statistically significant with an odds ratio of 3.98 (95% CI: 2.36–6.71) (Figure 2, Tables 1, 2, and 6).

Applying Pearson’s chi-square without Yates correction test on surgical history and hepatitis status shows chi-square

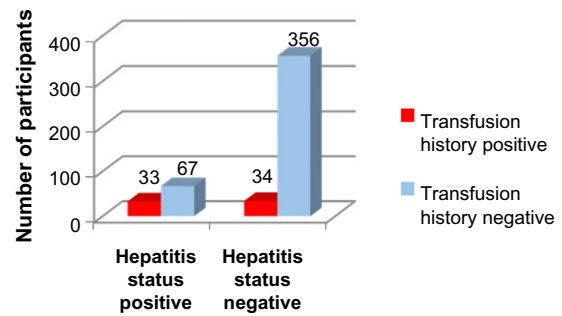


Figure 2 Transfusion history versus hepatitis status.

Table 6 Significant variables

Variable	Frequency	Chi-square value*	P-value	OR	95% CI of OR
Transfusion history	500	29.72	<0.001	3.98	2.36–6.71
Surgical history	500	36.32	<0.001	4.28	2.60–7.03
Dental history	500	51.86	<0.001	6.01	3.55–10.18
Household contact	500	26.38	<0.001	4.18	2.35–7.45
Sexual contact	500	17.14	<0.001	5.32	2.23–12.70

Notes: *Chi-square value with 1 degree of freedom. Alpha criterion =0.05, so any variable with *P*<0.05 is statistically significant.

Abbreviations: OR, odds ratio; CI, confidence interval.

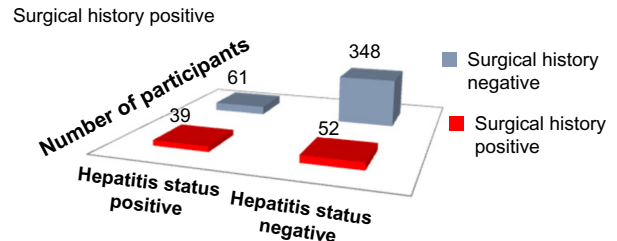


Figure 3 Surgical history versus hepatitis status.

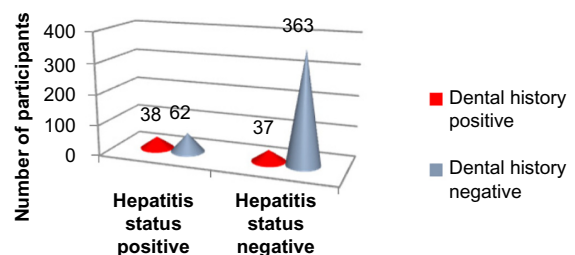


Figure 4 Dental history versus hepatitis status.

Table 5 Diabetes mellitus status versus hepatitis status

Diabetes mellitus status	Hepatitis status		Total
	Positive	Negative	
Diabetic, count (% of total)	26 (5.2%)	82 (16.4%)	108 (21.6%)
Nondiabetic, count (% of total)	74 (14.8%)	318 (63.6%)	392 (78.4%)
Total, count (% of total)	100 (20.0%)	400 (80.0%)	500 (100.0%)

Table 7 Dental history versus hepatitis status

Dental history	Hepatitis status		Total
	Positive	Negative	
Positive, count (% of total)	38 (7.6%)	37 (7.4%)	75 (15%)
Negative, count (% of total)	62 (12.4%)	363 (72.6%)	425 (85%)
Total, count (% of total)	100 (20%)	400 (80%)	500 (100%)

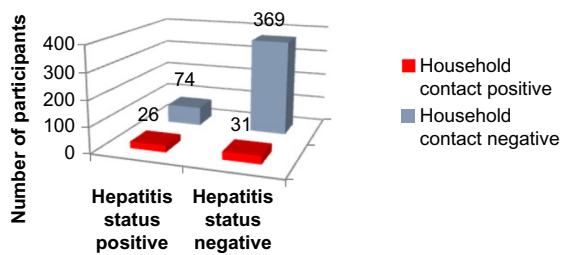


Figure 5 Household contact history versus hepatitis status.

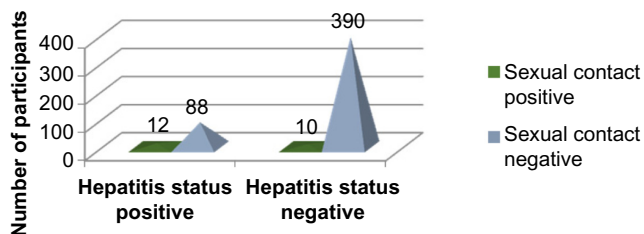


Figure 6 Sexual contact history versus hepatitis status.

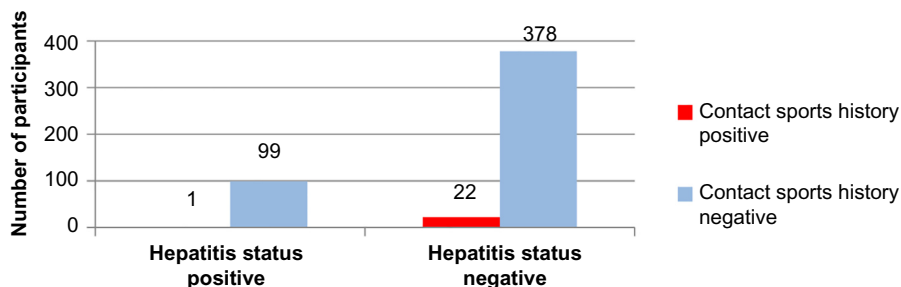


Figure 7 Contact sports history versus hepatitis status.

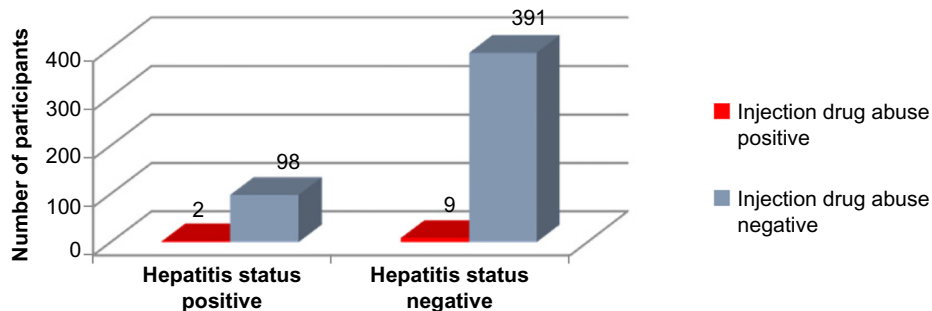


Figure 8 Injection drug abuse history versus hepatitis status.

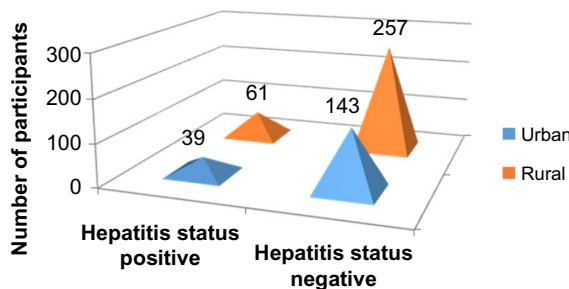


Figure 9 Residence versus hepatitis status.

equals 36.32 with 1 degree of freedom. The two-tailed *P*-value equals less than 0.001. Thus, the association between surgical history and hepatitis status is considered to be statistically significant with an odds ratio of 4.28 (95% CI: 2.60–7.03) (Figure 3, Tables 1, 2, and 6).

Applying Pearson’s chi-square without Yates correction test on dental history and hepatitis status shows chi-square equals 51.86 with 1 degree of freedom. The two-tailed *P*-value equals less than 0.001. Thus, the association between dental history and hepatitis status is considered to be statistically significant with an odds ratio of 6.01 (95% CI: 3.55–10.18). (Figure 4, Tables 1, 2, and 7).

Applying Pearson’s chi-square without Yates correction test on household contact and hepatitis status shows chi-square equals 26.38 with 1 degree of freedom. The two-tailed *P*-value equals less than 0.001. Thus, the association between household contact and hepatitis status is considered to be

statistically significant with an odds ratio of 4.18 (95% CI: 2.35–7.45) (Figure 5, Tables 1, 2, and 6).

Applying Pearson's chi-square without Yates correction test on sexual contact and hepatitis status shows chi-square equals 17.14 with 1 degree of freedom. The two-tailed *P*-value equals less than 0.001. Thus, the association between sexual contact and hepatitis status is considered to be statistically significant with an odds ratio of 5.32 (95% CI: 2.23–12.70) (Figure 6, Tables 1, 2, and 6).

The two-tailed *P*-value for Fischer's exact test of contact sports and hepatitis status equals 0.61. Thus, the association between contact sports and hepatitis status is not considered to be statistically significant (Figure 7 and Tables 1–3).

The two-tailed *P*-value for Fischer's exact test of injection drug abuse and hepatitis status equals 1. Thus, the association between injection drug abuse and hepatitis status is not considered to be statistically significant (Figure 8 and Tables 1–3).

Applying Pearson's chi-square without Yates correction test on residence and hepatitis status shows chi-square equals 0.36 with 1 degree of freedom. The two-tailed *P*-value equals 0.55. Thus, the association between residence and hepatitis status is not considered to be statistically significant (Figure 9 and Tables 1–3).

Applying Pearson's chi-square without Yates correction test on immunosuppression and hepatitis status shows chi-square equals 0.09 with 1 degree of freedom. The two-tailed *P*-value equals 0.76. Thus, the association between immunosuppression and hepatitis status is not considered to be statistically significant (Figure 10 and Tables 1–3).

The two-tailed *P*-value equals 1.0 for Fischer's exact test of skin tattoos and hepatitis. Thus, the association between skin tattoos and hepatitis status is not considered to be statistically significant (Figure 11 and Tables 1–3).

Binary logistic regression

As not a single value in “tolerance” is less than 0.10 and not a single value in “variance inflation factor” is greater than 10, it signifies that there is no collinearity between the independent variables. Hence, the assumption of multicollinearity has been met for the binary logistic regression (Table 4). The assumption for outliers has also been met.

Based on the results obtained from binary logistic regression, the odds ratios of probability (Table 5) for the statistically significant predictor variables are as follows:

- Dental history: 4.063 (95% CI =2.172–7.603)
- Household contact: 4.208 (95% CI =2.109–8.396)
- Sexual contact: 3.959 (95% CI =1.372–11.424)
- Surgical history: 2.717 (95% CI =1.450–5.091)
- Transfusion history: 2.114 (95% CI =1.085–4.119)

Discussion

We found that in our society, the important risk factors for hepatitis B and C are household contact, history of dental work, history of surgery, sexual contact, and history of transfusion (blood and its components).

The individual risk factor was stratified to know the degree of its influence using binary logistic regression. It was found that the odds ratio of probability for household contact is 4.2 (this means that if a person has a history of household contact, then he is 4.2 times more likely to have the disease as compared with a person without a history of household contact). For history of dental work, sexual contact, history of surgery, and history of transfusion, the odds ratios of probability are 4.1, 3.9, 2.7, and 2.1, respectively. In the past, studies^{14–18,21,23,26} were conducted in Pakistan to find the prevalence of disease or to find the

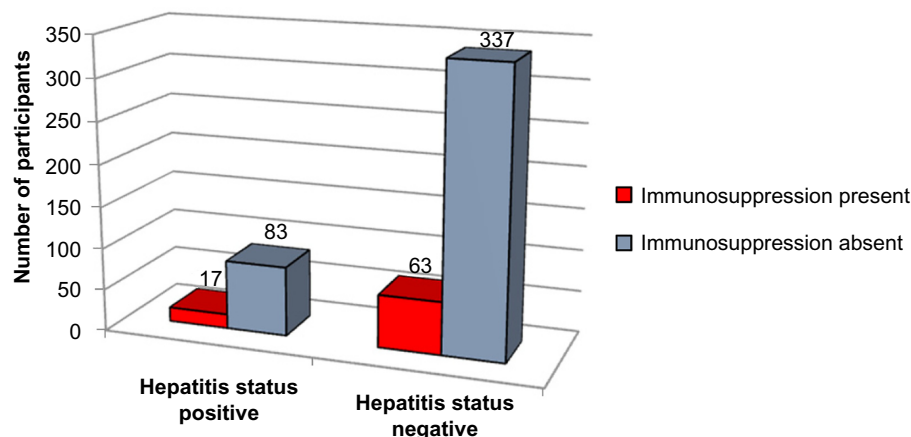


Figure 10 Immunosuppression versus hepatitis status.

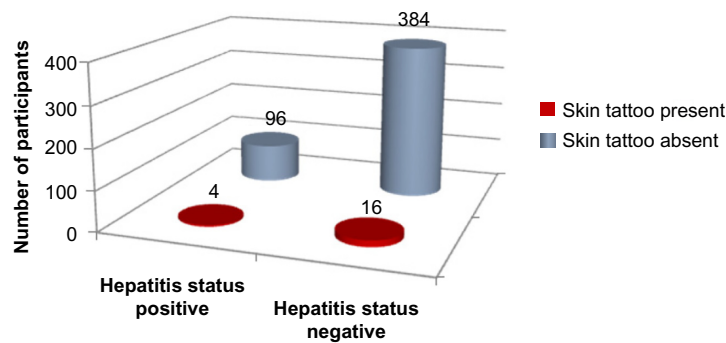


Figure 11 Skin tattoos versus hepatitis status.

association of a single risk factor.^{9–13,20–22,24,25} However, very few studies²⁶ have been conducted in Pakistan to include many possible risk factors in one study, even then the individual risk factor was not stratified (to find the degree of its influence).

We took many predictor variables all at once and identified the risk factors for our region. Based on the results, a targeted approach can be adopted in health prevention implementation. The predictive ability of our logistic model is 83%, which makes it a very good model.

Our study had funding limitations, and data collection was done by interns and final-year students along with their busy schedules. Because of deficiencies in the medical records, hepatitis B-positive patients and hepatitis C-positive patients were not separated during the analysis, and both were labeled as hepatitis positive. Because of the strict social norms in the city, data on sexual behavior (use or not of condoms, number of sexual partners) were not collected.

This study confirms household contact, history of dental work, history of surgery, sexual contact, and history of transfusion (blood and its components) as the main risk factors responsible for the increased prevalence of hepatitis. Therefore, all necessary precautions (eg, screening before dental and surgical procedures) should be taken not only at the individual level but also at the level of the whole population, and awareness should be increased in the general population to ensure the safety of precious lives.

Conclusion

The important risk factors responsible for the high prevalence of hepatitis B and C in our society are household contact, history of dental work, history of surgery, sexual contact, and history of transfusion (blood and its components). The odds ratio of probability for these risk factors are: 4.2 for household contact history, 4.1 for his-

tory of dental work, 3.9 for sexual contact, 2.7 for history of surgery, and 2.1 for history of transfusion. Associations of other predictor variables (diabetes status, education level, profession, contact sports, IV drug abuse, residence, immunosuppression, and skin tattoos) were not statistically significant.

Acknowledgment

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Disclosure

The authors report no conflicts of interest in this work.

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