

# Anti-HCV Antibody Positivity of Various Sections of Pakistani Patients

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## ABSTRACT

**Objective:** To determine the anti-HCV antibody status of various sections of the Pakistani population and patients as reported in various Pakistani studies.

**Study Design:** A meta-analysis.

**Place and Duration of Study:** Department of Medicine, Rawalpindi Medical College and Allied Hospitals, Rawalpindi, from July 2007 to July 2008.

**Methodology:** Data pertaining to anti-HCV antibody status of various sections of the Pakistani population and patients was collected from studies published till July 2008. To note anti-HCV antibody status, 15 groups of subjects like liver disease patients, general blood donors, adult screening, and community prevalence etc. were identified. The frequency of total and anti-HCV antibody positive subjects of each group was noted. Chi<sub>2</sub> was used as test of significance for comparison wherever appropriate.

**Results:** Data from 183 studies was collected; 1004391 subjects anti-HCV antibody status was retrieved. 4.27% (n=42982) of these were anti-HCV antibody positive. Major bulk of patients with liver disease (56.9%), 2.71% of general and 10.39% of professional blood donors groups were positive, (p < 0.05). Positivity in community and adult screening was 11.52 and 6.29% respectively.

**Conclusion:** According to the studies in consideration; 2.71% of Pakistani general blood donors and major bulk of liver disease patients are anti-HCV positive. Community based anti-HCV positivity is 11.52%.

**Key words:** Hepatitis C virus. Anti-HCV antibody. Review liver disease. Blood donor. Community.

## INTRODUCTION

Hepatitis C virus (HCV) was discovered in 1989 by investigators at Chiron. It is transmitted primarily by blood and blood products. Widespread use of injectable therapies and injection drug use are important risk factors for HCV infection.<sup>1</sup> Progression to chronic liver disease, cirrhosis, and hepatocellular carcinoma are frequent in HCV infected persons.<sup>2</sup> Despite important and continuous developments; currently available therapies for HCV infection remain costly, less effective, and associated with multiple side effects.<sup>3</sup>

Worldwide prevalence of HCV infection is 2.2-3%, though it varies in different countries.<sup>2,3</sup> In the USA, Central and South America, Europe, and Australia it is 1.6-1.8%, 6.4%, 1%, and 2.3% respectively.<sup>4</sup> The highest prevalence has been noted in Egypt.<sup>2</sup> Pakistan is currently the sixth most populous country in the world with an estimated population of 16,094,3000. According

to an estimate, about 10 million persons are infected with HCV in Pakistan.<sup>5</sup> The prevalence of HCV infection reported in various Pakistani studies varies from 2.2-14%.<sup>2,5</sup>

An evidence based appraisal of Pakistani data is required to plan strategies for managing HCV related diseases. The first Pakistani study focused on HCV was published in 1992. A review of published Pakistani literature focusing on HCV prevalence was published in 2002.<sup>6</sup> This included data of 17,933 subjects derived from 19 studies published before 2000. Since then extensive work on HCV and its related disease pattern has been done and the database required an update. This study was planned to determine the anti-HCV antibody status of patients and various sections of the Pakistani population, based on Pakistani studies published till July 2008.

## METHODOLOGY

This secondary research was conducted at the Department of Medicine, Rawalpindi Medical College and Allied Teaching Hospitals, Rawalpindi in collaboration with Pakistan Society of Hepatology from July 2007 to July 2008. Data from published studies regarding anti-HCV antibody status of various sections of the Pakistani population and patients was collected. Studies were found through library and internet based

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search employing Pubmed/Medline (www.ncbi.nlm.nih.gov/pubmed), and Pakmedinet (www.pakmedinet.com) search engines. Google search (www.google.com) was additionally performed in order to avoid missing data from studies published outside Pakistan in journals which are not Medline indexed. Hepatitis C, serology, anti-HCV antibodies, seroprevalence, chronic liver disease, hepatitis, cirrhosis, hepatocellular carcinoma, and epidemiology were key words used for the search.

Fifteen groups of subjects were identified from these studies i.e., general blood donors, liver disease patients, adult screening, and community prevalence etc. whose details are given in Table I. Frequency of total and anti-HCV antibody positive subjects of each group was noted. Data obtained in this way was converted into variables, which were analyzed using computer based statistical program, SPSS version 10.  $\chi^2$  was used to calculate p-value wherever appropriate. P-value < 0.05 was considered significant.

**Table I:** Patient groups and selections.

| Patient group                     | Number of patient selections |
|-----------------------------------|------------------------------|
| Liver disease*                    | 61                           |
| General blood donors              | 38                           |
| Adult screening**                 | 34                           |
| Hospital based studies***         | 22                           |
| Children                          | 9                            |
| Contacts of HCV infected patients | 7                            |
| Renal failure                     | 6                            |
| Thalassemia                       | 6                            |
| Community prevalence              | 5                            |
| Ante-natal screening              | 5                            |
| Health care workers               | 4                            |
| Professional blood donors         | 4                            |
| Injection drug users              | 3                            |
| Hemophilia patients               | 3                            |
| Other****                         | 5                            |
| <b>Total</b>                      | <b>212</b>                   |

\* Chronic liver disease, hepatocellular carcinoma and acute hepatitis patients.

\*\* Controls, pre-employment screening, and screening of employees.

\*\*\* Various admitted/outpatient subjects i.e., surgical patients, gynecology, diabetic patients etc.

\*\*\*\* Lymphoproliferative disorder patients, prisoners, depressed patients, mothers and sex workers.

## RESULTS

Data from 183 studies published during the period January 1992 to July 2008 was collected. Two hundred and twelve selections of patients were made from these studies. The number of patient selections was more than number of included studies as studies pertained to a single type of case, multiple types of cases, and cases along with controls. Eighty two selections were made from Medline indexed journals. The maximum number of selections were from journals published in the year 2002 to 2004. In the majority of studies, second generation ELISA technique was used for detecting/confirming anti-HCV antibodies.

Data regarding anti-HCV antibody status of 1004391 subjects was analyzed. The maximum number of patient selections (28.77%) pertained to subjects with liver disease, whilst the majority of subjects (80.53%)

belonged to the blood donor group. Group wise distributions of total and anti-HCV antibody positive subjects are given in Table II. 2.71% (n=21938) of the 808,872 general blood donors and 10.39% (n=159) of 1529 professional blood donors were anti-HCV antibody positive, (p < 0.05).

**Table II:** Details of anti-HCV antibody status.

| Patient group                     | Number of subjects | Positive     | Percentage of positive |
|-----------------------------------|--------------------|--------------|------------------------|
| Liver disease                     | 13745              | 7821         | 56.9                   |
| General blood donors              | 808872             | 21938        | 2.71                   |
| Adult screening                   | 123144             | 7747         | 6.29                   |
| Hospital based studies            | 25746              | 1523         | 5.91                   |
| Children                          | 6389               | 118          | 1.84                   |
| Contacts of HCV infected patients | 1010               | 218          | 21.58                  |
| Renal failure                     | 613                | 194          | 31.64                  |
| Thalassemia patients              | 876                | 387          | 44.17                  |
| Community prevalence              | 16651              | 1919         | 11.52                  |
| Ante-natal screening              | 1400               | 98           | 7                      |
| Health care workers               | 676                | 38           | 5.62                   |
| Professional blood donors         | 1529               | 159          | 10.39                  |
| Injection drug users              | 562                | 489          | 87.01                  |
| Hemophilia patients               | 240                | 122          | 50.83                  |
| Other*                            | 2938               | 211          | 7.18                   |
| <b>Total</b>                      | <b>1004391</b>     | <b>42982</b> | <b>4.27</b>            |

\* Lymphoproliferative disorder patients, prisoners, depressed patients, mothers and sex workers.

## DISCUSSION

Epidemiological data collection and analysis in Pakistan is an uphill task due to the absence of established health management information system, and disease/death registries. Most Pakistani data, therefore, pertains to hospital-based studies and nationally representative population data is deficient. Data regarding anti-HCV antibody positivity of various sections of the Pakistani population and patients in context of sero-epidemiological status of HCV infection was collected.

Cumulatively, anti-HCV positivity of our patients with various liver diseases was 56.9%, although we noted up-to 97.1% positivity in studies focused on patients with liver disease and hepatocellular carcinoma.<sup>7</sup> According to data from India, HCV is the cause of chronic liver disease, liver cirrhosis and hepatocellular carcinoma in 43%, 3.3%-31.5% and 15.1-42% of cases respectively.<sup>8,9</sup> The prevalence of HCV infection in Iranian chronic liver disease and hepatocellular carcinoma patients is < 10-40.7% and 8.5% respectively,<sup>10,11</sup> while 16.2% positivity has been noted in Chinese liver disease patients.<sup>12</sup>

From the present results, it seems that HCV is the commonest cause of liver disease in Pakistan. In this regard, consideration should be given to the fact that studies from which this group was derived were mainly done at tertiary healthcare facilities and estimation based on these figures may be biased. Additionally, the diversity of patients in this group i.e. chronic liver disease, hepatocellular carcinoma, and acute hepatitis patients should also be kept in mind.

Blood donors constituted a majority of the subjects with, 2.71% being positive. In relatively large Pakistani studies (of more than 100000 subjects) 3.99%, 1.8% and 4.1% anti-HCV positivity was noted. These figures are high compared to neighbouring countries like India (around 1%), Iran (0.5 to 0.97%), and China (generally 1%, upto 31% at some places).<sup>5,10,13</sup> Data regarding anti-HCV antibody status of many countries is extrapolated from blood donor screening. Epidemiologically, this data is not representative of the general population as children, old persons, and those suffering from different illnesses generally do not donate blood. Professional blood donors whether in Pakistan or regional countries have higher anti-HCV positivity.<sup>13</sup>

A proportion (12.9%) of data pertains to screening of healthy adults. Male subjects applying for overseas jobs or employed in the armed forces constituted the bulk of this group. This kind of data is retrieved from hospital or laboratory records.<sup>14</sup> The noted positivity in this group was 6.29%. These figures are double that of general blood donors. The difference between the two groups pertains to the facts that on one hand every adult regardless of health status tries to get a job due to the current Pakistani economic scenario, while on the other hand only healthy persons go for voluntary blood donation as discussed earlier. This selection is thus more representative of the adult male population.

The group of hospital based studies was very diverse as it included various admitted/outpatient subjects like surgical patients, gynaecology, and diabetic patients etc. It was thus not possible to compare with similar data from other countries. HCV-antibody positivity in this group was 5.91%.

Anti-HCV positivity in children is generally less because of fewer chances of exposure to risk factors like injections, and blood transfusion etc. Hence 0.3-5.4% positivity rates have been documented in studies done on children.<sup>15</sup> Positivity in children was 1.84%.

The family contacts of patients with HCV related chronic liver disease have an increased risk of acquiring infection. This risk is particularly increased if; duration of residence with index case is prolonged after diagnosis of liver disease, index case has cirrhosis, and contact consumes alcohol. Sixteen percent of contacts in an Indian study tested positive for anti-HCV antibodies.<sup>16</sup> In an Iranian study, prevalence of HCV infection among household contacts without percutaneous risk factors was 1.33%.<sup>10</sup> The positive percentage in household contacts of HCV infected patients was 21.58%.

Advent of various renal replacement therapies has remarkably improved life expectancy of patients with end stage renal disease on one hand, while on the other, chances of acquiring viral hepatitis and its sequel have also increased. In studies from India, and Iran 4.3-

46%, and 24.8% positivity has been noted in renal failure patients respectively.<sup>11,13</sup> Higher proportion i.e. 31.64% of renal failure patients were positive for anti-HCV antibodies in the local studies.

Regular blood transfusions significantly improve survival in thalassemia. Transfusion related complications like acquisition of HCV infection are important causes of mortality and morbidity in thalassemia patients. In Iranian and Indian studies 10.6-63.8, and 16.7-21% thalassaemics have been noted as being anti-HCV positive,<sup>13,17,18</sup> while 44.17% of Pakistani thalassaemia patients were positive.

Community studies are the best indicators of the sero-epidemiological status of a country. Few population/community based studies regarding sero-epidemiology of HCV have been done in south East Asia. In a systematic study by Chowdhury *et al.*, 0.87% overall prevalence of HCV infection was noted in the general population of eastern India.<sup>13,19</sup> In related studies from China, 3.1-12.6% positivity has been noted.<sup>12,20</sup> Based on various studies and estimates, community prevalence of anti-HCV positivity in Iran is < 1%.<sup>10</sup>

Data gathered from 5 of such studies mainly represented Punjab province with 4.7-22.19% positivity. The anti-HCV positivity in this group is much higher i.e., 11.52%. Epidemiological design as well as sensitivity and specificity of diagnostic tests applied have probably skewed the results. There is definite need for further nationally representative studies in this context which should take care of age, gender, district, urban, and rural stratification as positivity in this cohort was greater than general blood donor and adult screening groups.

Prevalence of HCV infection is higher in individuals of reproductive age. Chances of transmission of HCV from mother to offspring are 7-8%. Life time risk of severe liver disease is likely to be high in babies who are infected at birth. In a large-scale, single hospital based Indian study, seroprevalence of hepatitis C virus-specific antibodies in an urban population of pregnant women was 1.03%.<sup>21</sup> The local studies showed 7% positivity.

Anti-HCV positivity of health care workers (HCW) corresponds to that of the general population. In Iran, 0.37% positivity has been noted in HCW.<sup>10,11</sup> 4-5.4% of Indian HCW are anti-HCV positive.<sup>13</sup> Local HCWs had 5.62% positivity.

Injection drug users (IDU) are at risk of acquiring infections like hepatitis B, C and HIV. Injection drug use is the predominant mode of HCV transmission in developed countries like the United States, Australia, and Europe compared to unsafe injectable therapies in developing countries like ours.<sup>1</sup> An estimated 5.8% of Indian, 36.6% Afghani, and 30% Irani IDU have been noted positive in various studies.<sup>9,10,22</sup> while 87.01% of local IDU were positive.

Use of plasma derived products in hemophilia patients leads to an increased risk of acquiring HCV infection. reported frequency of anti HCV positivity from Iran and India varies from 22.8-100%,<sup>11,13,23</sup> while 50.83% of local hemophilia patients were positive.

Comparing present data with related Pakistani data reviewed by Shah and Shabbir generated interesting results.<sup>6</sup> That review included studies published between 1992-2000 which constituted a minor part of this data as the total number of subjects included in this study are 56 times more (1004391:17933).<sup>6</sup> The cumulative anti-HCV positivity in this study is less (4.27%:12%), while positivity in liver disease patients is very high (56.9%:8.67%). Positivity in general blood donors (2.7%:2.2%), professional blood donors (10.39%:9.35%), and HCW (5.62%:4%) groups is greater. Positivity in renal failure (31.64%:37.05%) and thalassemia patient (44.17%:60%) groups is less. The general population group data is not comparable as it includes studies focusing on healthy adult screening, liver disease patients, and surgical patients.

This study clearly shows high anti-HCV positivity not only in patients with various liver diseases but also in the apparently healthy population. Most figures are high when compared with neighbouring countries. An alarming situation becomes evident if figures of anti-HCV positivity are compared with various Pakistani demographics (Table III).<sup>4,7,24,25</sup> Possible reasons for this are multiple therapeutic injections, use of contaminated/reused/unsterilized needles/surgical/dental equipment, behavioural/environmental (body piercing [mainly pierced ears], shared shaving/hair cutting instruments) and socioeconomic factors.<sup>1-3,7</sup>

**Table III:** Group wise data and Pakistani demographics.

| Type of data                       | Disease burden/population characteristics           |
|------------------------------------|---|
| Liver disease                      | Major cause of morbidity and mortality*             |
| Blood donors                       | 1.5 million transfusions/year**                     |
| Adult screening                    | 90270 thousand population over 18 years age         |
| Hospital based studies             | ---   |
| Children                           | <15 years old constitute 42.3% of population        |
| Contacts of HCV infected patients  | 36 > 40% of Pakistani population***                 |
| Renal failure                      | 15-20% of population ≥ 40 years age has reduced GFR |
| Thalassemia                        | 5% population carries beta thalassemia              |
| Community prevalence               | 160 million total population                        |
| Ante-natal screening               | 4358 thousand births/year                           |
| Registered health care workers**** | About 220561 in number                              |
| Injection drug users               | 3 million   |
| Hemophilia patients                | 10500   |

\* Chronic liver disease is one of the top four adult medical causes of health life years (HeaLYs) loss.  
 \*\* 20% from professional blood donors.  
 \*\*\* Estimate based on approximate prevalence of anti-HCV in community/general population (6%), and average Pakistani household size (6.83).  
 \*\*\*\* Registered doctors, nurses, midwives, and lady health visitors.

As evident from this study, since the year 2000, HCV is increasingly recognized as the cause of liver disease in this scenario. This is causing immense pressure on the resource deficient health system. Health policy makers, medical organizations, medical practitioners, and the community can utilize the data to plan programs for

limiting HCV related morbidity and mortality. Preventive measures like the screening of blood and blood products, infection control practices, testing of persons at risk, and health education need to be implemented and maintained. If strict and effective steps are not taken now, the management of HCV related liver diseases will not be possible in the near future with our resources.

Despite limitations of publication bias, it is the largest collection of such data.

## CONCLUSION

Hepatitis C virus infection is an important health care issue in Pakistan requiring urgent attention and concrete steps. Based on an analysis of cumulative data, the major bulk of liver disease patients (56.9%), and 2.71% of general blood donors are anti-HCV antibody positive. Positivity in community based studies and adult screening is 11.52 and 6.29% respectively.

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