Hepatitis C in Pakistan: A Review of Available Data

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Hepatitis C virus (HCV) infection is increasingly recognized as a major health care problem, and is found frequently in Pakistani settings. In this article we reviewed published and unpublished data related to the seroepidemiology of HCV infection in Pakistan. For this article, data from 132 published studies and three unpublished data sets published/presented between the period 1992-2008 were utilized. Data of 1,183,329 individuals were gathered. Blood donors (982,481) and the general population (178,322) constituted the majority of these subjects. The frequency of HCV infection in blood donors and in the general population was 3.0 % (95% CI: 3.0-3.1) and 4.7 (95% CI: 4.6 -4.8), respectively. The frequency among 6,148 pregnant females was 7.3% (95% CI = 6.7 – 8.0). The frequency in healthy children ranged from 0.4 to 4.1% (95% CI = 1.4 – 2.3). Pakistani HCV serofrequency figures are significantly higher (P < 0.0001) compared to those of the corresponding populations in surrounding countries like India, Nepal, Myanmar, Iran and Afghanistan.

Keywords: Hepatitis C Virus, Anti-HCV, Pakistan, Serofrequency

Introduction

The World Health Organization (WHO) has compared hepatitis C to a "viral time bomb" and estimates that about 180 million people (some 3% of the world's population) are infected with hepatitis C virus (HCV), 130 million of whom are chronic carriers at risk of developing liver cirrhosis and/or liver cancer. Three to four million persons are newly infected each year, 70% of whom will develop chronic hepatitis. HCV is responsible for 50–76% of all liver cancer cases, and two thirds of all liver transplants in the developed world (1). World Health Statistics 2008 lists cirrhosis of the liver as the 18th commonest cause of mortality in the world, and it is estimated that by 2030, liver cancer will become the 13th commonest cause (2).

The prevalence of hepatitis varies from country to country, and at times it will also vary among different regions of the same country. The epidemiological estimates by WHO show that the prevalence of hepatitis C is low (<1%) in Australia, Canada and northern Europe, and about 1% in countries of medium endemicity, such as the USA and most of Europe. It is high (>2%) in many countries of Africa, Latin America, Central and South-East Asia. In these countries, prevalence figures between 5% and 10% are frequently reported (1).

Collecting and comparing health data from across a country is a way to describe health problems, identify trends and help decision-makers set priorities. The global epidemiology of hepatitis C is well established. However, its epidemiology in Pakistan is ill-defined.
Most of the data have come from hospital-based studies, because there is a dearth of community-based ones (3-5). Although the National Survey of Hepatitis has concluded, its results have not yet been officially published, except for a few presentations made by researchers at official meetings. This review summarizes the available data on the epidemiology of hepatitis C since the first report of its recognition in 1992.

HCV-Related Pakistani Data

All available Pakistani data published or unpublished till the writing of this article were collected by a literature search through electronic databases like Pubmed, Pakmedinet, Yahoo and Google etc. Unpublished data from any source, if accessible, were also reviewed. Data from 132 published studies and 3 unpublished data sets were gathered and grouped in six categories, based on the type of population studied i.e. 1) general population, 2) blood donors, 3) patients with liver diseases, 4) patients with diseases other than hepatic diseases, 5) pregnant women and 6) children. Most of the data (78.5%) pertained to the years 2001-2008. Year by year distribution of this data is given in Table 1.

Table 1. Distribution of studies and unpublished data sets by year of publication/data gathering/presentation.

| Year          | Number | Percent |
|---------------|--------|---------|
| 2005 – 2008   | 47     | 34.8    |
| 2001 – 2004   | 59     | 43.7    |
| 1996 - 2000   | 20     | 14.8    |
| 1995 and earlier. | 9   | 6.7     |
| Total         | 135    | 100.0   |

General Population

Twenty-five studies (6-30) pertained to the serofrequency of hepatitis C in the general population. Details are given in Table 2. The majority of these studies (92%) were conducted during the period 2000-2008. Two studies were conducted in the nineties (6, 7). The data of 178,322 persons were included in this group. Unfortunately, there was no study from any major city of Balochistan, or from the NWFP provinces. The frequency of HCV infection ranged from 0.4% in Karachi (6) to 33.7% in Jarwar (Sindh) (28). The mean frequency was 4.7% (95% confidence interval [CI]: 4.6 - 4.8).

Table 2. Sero-Prevalence of HCV in General Population

| Author                  | Year | Place      | Number | Anti HCV (%) | Reference |
|-------------------------|------|------------|--------|--------------|----------|
| Agboatwala et al.       | 1994 | Karachi    | 258    | 0.4          | (6)      |
| Luby                    | 1997 | Hafizabad  | 313    | 6.5          | (7)      |
| Adam                   | 2001 | Lahore     | 488    | 16.0         | (8)      |
| Adam                   | 2001 | Gujranwala | 1,922  | 23.8         | (8)      |
| Ali et al.              | 2002 | Rawalpindi | 5,370  | 3.3          | (9)      |
| Khan                   | 2004 | Mandan     | 700    | 9.0          | (10)     |
| Khokhtar               | 2004 | Islamabad | 47,538 | 5.3          | (11)     |
| Muhammad               | 2005 | Buner      | 16,400 | 4.6          | (12)     |
| Fareeq et al.           | 2005 | Khudar     | 665    | 3.3          | (13)     |
| Hashim et al.           | 2005 | Attock     | 4,552  | 4.0          | (14)     |
| Ahmad                  | 2006 | Swat       | 41,613 | 2.2          | (15)     |
| Feyza et al.            | 2006 | Bahawalpur | 2,086  | 6.3          | (16)     |
| Tariq & Janjua          | 2006 | Rawalpindi | 15,550 | 3.7          | (17)     |
| Jaffri et al.           | 2006 | Karachi    | 3,533  | 1.6          | (18)     |
| Shereef & Tariq        | 2006 | Rawalpindi | 2,558  | 2.8          | (19)     |
| Zaman                  | 2006 | Bahawalpur | 6,815  | 4.4          | (20)     |
| Ahmad et al.            | 2007 | Faisalabad | 300    | 16.0         | (21)     |
| Atif et al.             | 2007 | Hyderabad | 2,835  | 5.2          | (22)     |
| Minra et al.            | 2007 | Bahawalpur | 1821   | 2.5          | (23)     |
| Malik et al.            | 2008 | Pano Aqil | 5,237  | 4.8          | (24)     |
| Hakim et al.            | 2007 | Karachi    | 4,000  | 5.2          | (25)     |
| Butt & Amin             | 2008 | DI Khan   | 5,707  | 1.7          | (26)     |
| Khan et al.             | 2008 | Azad Kashmir | 425   | 3.3          | (27)     |
| Anees et al.            | 2008 | Lahore    | 6,817  | 14.6         | (28)     |
| Ahluwia  et al.          | 2008 | Jarwar (Sindh) | 873 | 33.7        | (29)     |
| Alam et al.             | 2008 | Miranwali | 697    | 1.9          | (30)     |
| Total                   | 178,322 |          | 4.7 (95% CI: 4.6-4.8) | (31)     |

Blood Donors

Blood donor data constituted the largest data set. There were 27 studies and 3 unpublished data sets in this group. The total population covered in this group was 982,481 over the period 1996-2008 (Table 3). The studies covered all provinces of Pakistan. The serofrequency of HCV ranged from 0.3% in Multan (31) to 12.5% in Islamabad (32). The mean frequency was 3.0% (95% CI: 3.0- 3.1). Only five studies (29, 32-35) showed a frequency of > 5%.

Patients with Liver Diseases

Forty-one studies (36-68) dealing with the frequency of hepatitis C among patients with liver diseases were found, covering 7,765 patients over a period of 27 years from 1992 to 2008 (Table 4, and 5). Liver diseases included cirrhosis, chronic liver disease, chronic active hepatitis and hepatocellular carcinoma.

Fourteen studies (37-50) pertained to cirrhosis patients. The number of individuals included in these studies was 1,902. HCV serofrequency in these individuals ranged from 10.5-79.6%, with
an overall prevalence of 44.9% (95% CI = 42.6 –
47.2). Eleven studies (39, 51-59, 69) covering 3,144
patients with chronic liver disease showed a range
of 13.3% to 86.0% HCV serofrequency. The mean
frequency was 52.9% (95% CI : 51.1–54.7).

In 10 studies (36, 39, 40, 42, 60-65) The HCV
serofrequency in 739 cases of hepatocellular carcinoma
was investigated (T able 5), and it ranged from 24%
 to 67.9%. The mean frequency in this subgroup
was 50.6% (95% CI: 46.9–54.3). One thousand
nine hundred and eighty patients with acute/chronic
hepatitis from 6 studies had 58.2% (95% CI : 55.7–
60.4) HCV serofrequency (46, 51, 57, 66-68).

Patients with Diseases Other than Hepatic Diseases

Sixteen studies focused on HCV serofrequency in
patients with various diseases other than liver diseases
(Table 6) (10, 70-85). These studies spanned a period
of 8 years, from 1999 to 2006, and covered major cities.
The mean frequency of HCV infection in patients
with various medical diseases was 20.4% (95% CI : 18.4–22.5), 38% in haematological diseases (95% CI :
33.6–42.5), 7.9% among surgical diseases (95% CI : 6.9 – 9.0), and 1.3% in dental diseases.

Pregnant Women

Eleven studies (86-96) dealing with the
serofrequency of HCV among pregnant women
were found (Table 7). These studies spanned a period
of 13 years from 1996 to 2008 and covered 6,148
women. The frequency in this group ranged from
3.3% to 29.1%. Overall serofrequency in this group
was 7.3% (95% CI = 6.7 – 8.0).

Children

Data from four studies (18, 86, 97, 98) covering
4,472 healthy children were analyzed (Table 8). HCV
serofrequency among children ranged from 0.4% to
### Table 4. Sero-Prevalence of HCV in Liver Disease.

| Author          | Year | Place          | Number | Anti HCV (%) | Reference |
|-----------------|------|----------------|--------|--------------|-----------|
| **Cirrhosis**   |      |                |        |              |           |
| Malik           | 1992 | Northern Areas | 24     | 13.3         | (38)      |
| Malik           | 1995 | Rawalpindi     | 220    | 48.0         | (39)      |
| Makki           | 1995 | Karachi        | 67     | 10.5         | (40)      |
| Hussain         | 1998 | Lahore         | 50     | 52.0         | (14)      |
| Farooqi & Farooqi| 1998 | Peshawar      | 410    | 43.9         | (42)      |
| Umar et al.     | 1999 | Rawalpindi     | 120    | 58.0         | (43)      |
| Mahmood et al.  | 1999 | Karachi        | 202    | 37.7         | (44)      |
| Liaqat          | 2000 | Karachi        | 250    | 43.0         | (45)      |
| Shah et al.     | 2002 | Islamabad     | 108    | 79.6         | (46)      |
| Iqbal           | 2002 | Peshawar      | 100    | 41.0         | (47)      |
| Khan            | 2002 | Lahore        | 94     | 68.0         | (56)      |
| Farooqi & Kahan | 2002 | Swat          | 55     | 59.0         | (49)      |
| Khurram         | 2003 | Rawalpindi     | 142    | 34.1         | (50)      |
| Mashud et al.   | 2004 | DI Khan       | 60     | 13.3         | (125)     |
| **Total**       |      |                | 1902   | 44.9         | (95% CI = 42.6 – 47.2) |

| **Chronic Liver Disease** |      |                |        |              |           |
| Malik           | 1995 | Rawalpindi     | 45     | 13.3         | (39)      |
| Tong et al.     | 1996 | Rawalpindi     | 105    | 22.0         | (52)      |
| Sultana et al.  | 2000 | Islamabad     | 108    | 29.6         | (53)      |
| Younas et al.   | 2001 | Lahore        | 100    | 65.0         | (94)      |
| Tahir et al.    | 2001 | Lahore        | 104    | 43.3         | (55)      |
| Khan et al.     | 2001 | Islamabad     | 323    | 28.7         | (56)      |
| Khokhar         | 2002 | Islamabad     | 354    | 86.0         | (51)      |
| Khan            | 2003 | Hazara        | 614    | 40.8         | (57)      |
| Shalik          | 2003 | Larkana       | 1,074  | 51.0         | (69)      |
| Bakhtiar et al. | 2003 | Rawalpindi     | 97     | 68.1         | (58)      |
| Wazir et al.    | 2003 | Hyderabad     | 510    | 59.0         | (59)      |
| **Total**       |      |                | 3144   | 52.9         | (95% CI = 51.1 – 54.7) |

### Table 5. Sero-Prevalence of HCV in Hepato-cellular Carcinoma and Acute/Chronic Hepatitis.

| Author           | Year | Place         | Number | Anti HCV (%) | Reference |
|------------------|------|---------------|--------|--------------|-----------|
| **Hepato cellular Carcinoma** |      |               |        |              |           |
| Malik            | 1991 | Karachi       | 25     | 24.0         | (40)      |
| Malik            | 1995 | Rawalpindi    | 64     | 25.0         | (39)      |
| Mujeeb et al.    | 1997 | Karachi       | 54     | 33.0         | (60)      |
| Farooqi & Farooqi| 2000 | Peshawar     | 56     | 67.9         | (42)      |
| Mumtaz et al.    | 2001 | Rawalpindi    | 44     | 54.0         | (61)      |
| Khokhar et al.   | 2003 | Islamabad    | 67     | 67.0         | (72)      |
| Siddiqui         | 2005 | Karachi       | 100    | 43.0         | (36)      |
| Bilal            | 2006 | Faisalabad    | 100    | 66.4         | (74)      |
| Almani et al.    | 2008 | Hyderabad    | 100    | 52.0         | (64)      |
| Abbas et al.     | 2008 | Karachi       | 129    | 51.2         | (65)      |
| **Total**        |      |               | 739    | 50.6         | (95% CI = 46.9 – 54.3) |

| **Acute/Chronic Hepatitis** |      |               |        |              |           |
| Haidet et al.      | 1994 | Lahore        | 94     | 6.4          | (79)      |
| Umer              | 1999 | Rawalpindi    | 710    | 70.0         | (67)      |
| Almani et al.     | 2002 | Jamshoro      | 100    | 9.0          | (112)     |
| Khokhar           | 2002 | Islamabad    | 354    | 86.0         | (51)      |
| Shah et al.       | 2002 | Islamabad    | 108    | 79.6         | (115)     |
| Khan et al.       | 2003 | Abbotabad     | 614    | 40.8         | (57)      |
| **Total**         |      |               | 1980   | 58.2         | (95% CI = 55.9 – 60.4) |
36.25%. The mean frequency was 1.8% (95% CI = 4.6 – 7.5). One study from Lahore in 1996 reported a 4.1% perinatal transmission of HCV in children of HCV-positive mothers. The serofrequency of HCV in thalassemics, and hemophiliacs was 35-42% (75-78) and 25% (79), respectively.

Discussion

Many researchers have tried to derive a national or regional figure for HCV serofrequency based on the available data (99-101). In 2005, Umar M and Khaar HTB (99), from Rawalpindi, collected data from various studies and reported a 9.8% frequency in 79,192 individuals. In 2006, Hafeez (99), from Islamabad, collected data from 98 studies and produced an estimate of 5.3%. Raja and Janjua (101), from Essex (UK), analyzed studies available on Medline from 1970 to 2005, and observed that the prevalence of HCV infection ranges from 0.4% in children, to 1.2% in healthy blood donors. Ali et al.

Table 6. Seroprevalence among patients of diseases other than Liver Disease.

| Author          | Year | Place     | Disease          | Number | Anti HCV (%) | Reference |
|-----------------|------|-----------|------------------|--------|--------------|----------|
| Khan            | 2004 | Mardan    | General          | 700    | 9.0          | (10)     |
| Mumtaz & Aftab  | 2005 | Rawalpindi| General          | 264    | 28.6         | (70)     |
| Gul & Iqbal     | 2003 | Lahore    | Renal Failure    | 50     | 68.0         | (71)     |
| Khokar et al.   | 2005 | Islamabad| Renal Failure    | 97     | 23.7         | (72)     |
| Qazi et al.     | 2004 | Bahawalpur| Diabetes 2       | 250    | 27.6         | (73)     |
| Bilwani et al.  | 2004 | Karachi   | Lymphoprolifreative | 143    | 29.2         | (89)     |
| **Total**       |      |           |                  | 1504   | 20.4         | (95% CI = 18.4-22.5) |

Haematological Diseases

| Author et al.   | Year | Place     | Disease          | Number | Anti HCV (%) | Reference |
|-----------------|------|-----------|------------------|--------|--------------|----------|
| Moarter et al.  | 1999 | Karachi   | β-Thalassemia    | 100    | 35.0         | (106)    |
| Muhammad J      | 2003 | Peshawar (Thalassemia) | 80    | 36.2         | (126)    |
| Younus et al.   | 2004 | Islamabad| β-Thalassemia    | 75     | 42.0         | (94)     |
| Burki et al.    | 2005 | Islamabad| β-Thalassemia    | 180    | 41.7         | (74)     |
| Hussain         | 2001 | Peshawar  | Haemophilia      | 40     | 25.0         | (14)     |
| **Total**       |      |           |                  | 475    | 38           | (95% CI = 33.6-42.5) |

Psychological Diseases

| Author et al.   | Year | Place     | Disease          | Number | Anti HCV (%) | Reference |
|-----------------|------|-----------|------------------|--------|--------------|----------|
| Shah & Dar      | 2004 | Islamabad| Depression       | 135    | 22.9         | (80)     |

Surgical Diseases

| Author et al.   | Year | Place     | Disease          | Number | Anti HCV (%) | Reference |
|-----------------|------|-----------|------------------|--------|--------------|----------|
| Hussain & Fatima| 2005 | Karachi   | Surgical Diseases| 750    | 16.2         | (81)     |
| Talpur et al.   | 2006 | Nawabshah | Surgical Diseases| 180    | 11.9         | (82)     |
| Khan et al.     | 2007 | Abbottabad| Orthopaedic Diseases| 1630  | 3.1          | (83)     |
| Daudpota & Soomro| 2008| Jacobabad | Surgical Diseases| 150    | 14.0         | (84)     |
| **Total**       |      |           |                  | 2710   | 7.9          | (95% CI = 6.9-9.0) |

Dental Diseases

| Author et al.   | Year | Place     | Disease          | Number | Anti HCV (%) | Reference |
|-----------------|------|-----------|------------------|--------|--------------|----------|
| Khizar et al.   | 2005 | Peshawar  | Dental Diseases Diseases| 1498  | 1.3          | (85)     |

Table 7. Seroprevalence among Pregnant women.

| Author          | Year | Place     | Number | Anti HCV (%) | Reference |
|-----------------|------|-----------|--------|--------------|----------|
| Khan            | 1996 | Lahore    | 417    | 9.3          | (56)     |
| Parker          | 1999 | Lahore    | 417    | 4.0          | (90)     |
| Zafar et al.    | 2001 | Lahore    | 300    | 6.0          | (88)     |
| Bilal           | 2002 | Peshawar  | 352    | 5.1          | (74)     |
| Rizvi           | 2002 | Karachi   | 120    | 6.6          | (80)     |
| Fayyaz          | 2004 | Lahore    | 100    | 7.0          | (91)     |
| Khokar et al.   | 2004 | Islamabad| 503    | 4.8          | (92)     |
| Jaffery         | 2005 | Islamabad| 947    | 3.3          | (93)     |
| You PROFAN et al.| 2006| Hyderabad | 103    | 29.1         | (94)     |
| Hakeem et al.   | 2006 | RY Khan   | 450    | 18.2         | (41)     |
| Batool et al.   | 2008 | Lahore    | 2,439  | 7.3          | (99)     |
| **Total**       |      |           | 6,148  | 7.3          | (95% CI = 6.7 – 8.0) |
reviewed data from 139 studies from 1994 to 2007 and concluded that the weighted average for hepatitis C antibody positivity was 3.0% (range 0.3-31.9%). Rates in the high-risk subgroups were far higher (100).

The data analyzed in this article shows HCV positivity (95% CI: 4.6 – 4.8) among 178,322 healthy individuals and 3.03% positivity (95% CI: 3.00 – 3.06) among 982,481 healthy blood donors. This figure is significantly lower (P < 0.0001) than the figure of 9.8% quoted by Umar M and Khaar HTB (99). However, our estimates are significantly higher (P < 0.00001) than the 3% figure quoted by Ali et al. (100) for healthy individuals. Our estimates are closer to the figure of 5.3% given by Hafeez (99). According to several studies, HVC genotype 3 is the most frequent genotype found in Pakistan (Table 9).

Most of the available Pakistani data on HCV pertains to blood donors, probably because for reasons of convenience and access to a large sample size, and may not truly represent the general population (100). If high-risk blood donors are screened out (those with jaundice, injection drug users etc), the frequency in the general population may be underestimated. If professional blood donors (who are often injection-drug users who sell their blood to make money) are included, the figures may be overestimated.

The number of subjects studied, other than healthy blood donors, appears very small, and also there is a lack of representation from across the country (101). The frequency of HCV positivity in Pakistan is significantly higher (P < 0.0001) when compared to the corresponding populations in the surrounding countries (Table 10).

We noted a highly variable sero频率 in different studies of similar populations, even within the same province. One of the reasons for such variability in the results has been explained by Ali et al. (100). The authors observed that unlike highly contagious diseases like measles that have a more predictable sero-prevalence, blood-borne illnesses like hepatitis and HIV are transmitted sporadically or in microepidemics. According to them these microepidemics may account for wide variations in prevalence within a nation, a province, or even a community, and methodological differences in sampling strategies may also contribute to differences in sero-prevalence within similar regions or populations (100).

| Author     | Year | Place | Number | Genotype (%) | Reference |
|------------|------|-------|--------|--------------|-----------|
|            |      |       |        | 1  | 2  | 3  | 4  | 5  | 6  | Mixed |          |
| Azzam      | 2003 | Bahawalpur | 105    | 6.0 | 4.8 | 69.6 | 2.4 | -  | 0.8 | -       | (122)    |
| Ansari     | 2002 | Karachi   | 255    | 12.0 | 2.3 | 77.6 | 2.3 | 0.4 | 2.7 | 2.3     | (127)    |
| Khokhar    | 2002 | Islamabad | 148    | -  | -  | 64.1 | -  | -  | -   | -       | (125)    |
| Zuberi     | 2002 | Karachi   | 215    | 8.4 | -  | 79.5 | -  | -  | -   | 8.8     | (88)     |
| Nasir      | 2001 | Rawalpindi | 39     | 5.1 | 2.6 | 59.9 | 5.2 | 12.8 | 15.4 | -       | (128)    |
| Mammmaz    | 2005 | Karachi   | 725    | 7.9 | 1.2 | 87.8 | 5.0 | -  | 0.8 | -       | (129)    |
| Total      |      |         | 1,487  | 7.7 | 1.6 | 80.5 | 3.1 | 0.9 | 1.3 | 1.7     |          |

*Due to missing data in some studies, percentages do not add to 100.

| Country     | Year | Population       | Number | Prevalence (%) | Reference |
|-------------|------|------------------|--------|----------------|-----------|
| Myanmar     | 2006 | Healthy Adults   | 362    | 2.5            | (130)     |
| India       | 2003 | Blood Donors     | 28,956 | 0.66           | (126)     |
| Nepal       | 2004 | Healthy Adults   | 103    | 1.0            | (131)     |
| Iran        | 2006 | Healthy Adults   | 1721   | 0.87           | (132)     |
| Afghanistan | 2006 | Healthy Women    | 4452   | 0.31           | (133)     |
| Pakistan    | 2009 | Healthy Adults   | 178,322| 4.7            | This review|

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According to the “Burden of Disease Study” carried out by Hyder and Morrow in 2001, chronic liver diseases are the 5th commonest cause of premature mortality in Pakistan and the 11th commonest cause of disabilities (102). Although between 75-85% of infections move on to chronic hepatitis C, the progress may be slow. Hence most people who are infected do not experience symptoms and are unaware of their infection. They are not able to benefit from available treatment that may clear them of the virus. They may also unknowingly spread the virus to others. Currently, there is no vaccine to prevent HCV infection. Effective but costly treatment is available. The high frequency and its contribution to premature mortality and disability call for massive awareness campaigns to combat the menace of this infectious disease.

Conclusions

The frequency of hepatitis C infection in Pakistan is high (4.7%), varying from 0.4% - 33.7%, indicating pockets of infections. The frequency is significantly higher than in surrounding countries. The contribution of this high frequency to premature mortality and disability calls for massive awareness campaigns.

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