

## Hepatitis C virus in Pakistan: A systematic review of prevalence, genotypes and risk factors

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### Abstract

In Pakistan more than 10 million people are living with Hepatitis C virus (HCV), with high morbidity and mortality. This article reviews the prevalence, genotypes and factors associated with HCV infection in the Pakistani population. A literature search was performed by using the keywords; HCV prevalence, genotypes and risk factors in a Pakistani population, in Pubmed, PakMediNet and Google scholar. Ninety-one different studies dating from 1994 to May 2009 were included in this study, and weighted mean and standard error of each population group was calculated. Percentage prevalence of HCV was  $4.95\% \pm 0.53\%$  in the general adult population,  $1.72\% \pm 0.24\%$  in the pediatric population and  $3.64\% \pm 0.31\%$  in a young population applying for recruitment, whereas a very high  $57\% \pm 17.7\%$  prevalence was observed in injecting drug users and  $48.67\% \pm 1.75\%$  in a multi-transfused population. Most prevalent genotype of HCV was 3a. HCV prevalence was moderate in the general population but very high in injecting drug users and multi-transfused populations. This data suggests that the major contributing factors towards increased HCV prevalence include unchecked blood transfusions and reuse of injection syringes. Awareness programs are required to decrease the future burden of HCV in the Pakistani population.

**Key words:** Hepatitis C virus; Prevalence; Genotypes; Blood transfusions; Injections

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### INTRODUCTION

Hepatitis C virus (HCV) was discovered in 1989 as the major causative agent of non-A, non-B hepatitis<sup>[1]</sup>. It belongs to the *Flaviviridae* family and is a plus-stranded RNA virus<sup>[2]</sup>. About 200 million people are infected with HCV worldwide, which covers about 3.3% of the world's population<sup>[3,4]</sup>. HCV infection leads to chronic hepatitis in 50% to 80% of individuals<sup>[5]</sup>. It was estimated by the WHO in 2004 that the annual deaths due to liver cancer caused by HCV and cirrhosis were 308 000 and 785 000 respectively<sup>[6]</sup>.

Pakistan is a developing country of 170 million people with low health and educational standards. According to the human development index of the United Nations, it was ranked 134th out of 174 countries<sup>[7]</sup>. In Pakistan 10 million people are presumed to be infected with HCV<sup>[8]</sup>. Public health authorities are creating awareness about hepatitis through print and electronic media<sup>[9]</sup>, but still tremendous efforts are required to increase the awareness regarding various risk factors involved in HCV transmission. In developing countries, due to non-implementation of international standards regarding blood transfusion, reuse of needles for ear and nose piercing, reuse of syringes, injecting drug users, tattooing, shaving from barbers, unsterilized dental and surgical instruments are the main source of transmission of HCV. This article briefly presents the prevalence, genotypes and risk factors associated with HCV transmission in the Pakistani population.

### LITERATURE SEARCH

Articles were searched for in Pubmed, Google scholar and PakMediNet (for non-indexed Pakistani journals),

by using the key words; HCV in Pakistan, prevalence of HCV in Pakistan, epidemiological patterns of HCV in Pakistan, HCV in multi-transfused Pakistani population, HCV in general Pakistani population, HCV in Pakistani injecting drug users (IDUs) population, HCV in Pakistani health care workers, sexual transmission of HCV, injection use in Pakistan, blood banks/transfusion in Pakistan, awareness about HCV in Pakistani population and HCV genotypes in Pakistan. Inclusion criteria entailed the studies demonstrating the prevalence, genotypes and risk factors of HCV in the Pakistani population while studies with incomplete references were excluded. Two hundred and eighty-one different articles/abstracts/reports were obtained from the literature search, out of which 91, published from 1994 to May 2009, were included in this study.

## ANALYSIS

Table 1 includes various reports showing the percentage prevalence of HCV in different groups. Weighted mean of each population was calculated by using the formula:

$$\bar{x} = \frac{\sum_{i=1}^n \omega_i x_i}{\sum_{i=1}^n \omega_i}$$

Standard error of mean was calculated by using the formula:

$$SE_{\bar{x}} = \frac{s}{\sqrt{n}}$$

Results of each population group are presented in the form of mean  $\pm$  SE with 95% confidence interval.

## HCV PREVALENCE IN VARIOUS GROUPS

### General population

Ten different studies showed that the percent prevalence of HCV in the general adult population was  $4.95\% \pm 0.53\%$ <sup>[10-19]</sup>, while six studies showed a percent prevalence of  $1.72\% \pm 0.24\%$  in the pediatric population<sup>[20-25]</sup>. In Pakistan, military recruits are screened for HCV before induction; six different studies showed a percent prevalence of  $3.64\% \pm 0.31\%$  in candidates for military recruitment<sup>[26-31]</sup>. About 5% of infants obtained HCV infection transmitted from a mother carrying both HCV antibody and HCV RNA<sup>[32]</sup>; four studies in pregnant women showed the percent prevalence to be  $4.54\% \pm 3.5\%$ <sup>[33-36]</sup>. Volunteer blood donors are the healthiest population in a community and HCV prevalence in these individuals is a true reflector of a general population's health<sup>[9]</sup>; twelve different studies showed the percent prevalence to be  $3.78\% \pm 0.41\%$  in blood donors<sup>[17,37-47]</sup>.

### IDUs

It was estimated that there were about 5 million drug users in Pakistan, out of which 15% were regular IDUs<sup>[48]</sup>. There has been an increased shift among addicts from inhalatory to injectable drugs due to decrease in quality and availability of heroin (common inhalatory drug used in Afghanistan and Pakistan)<sup>[49]</sup>. The effect of injecting drugs is more intense and satisfying, and young drug users who switch over to injectables usually adopt it as the

main route of their drug administration<sup>[50]</sup>. Approximately 50% of IDUs reported by Altaf *et al*<sup>[51]</sup> in 2007 were in a treatment program; the majority of them wanted to get rid of their addiction but could not do so due to non availability or high charges by rehabilitation centers. The main reason for relapse was the economic crisis which most addicts suffer because the rehabilitation centers are not involved in the development of vocational skills among addicts. Four different reports showed a high  $57\% \pm 17.7\%$  prevalence of HCV among the IDUs<sup>[52-55]</sup>.

### Multi-transfused population

Thalassemic and hemophilic patients require life-long blood transfusions, so it is necessary to obtain screened blood from a reputable source, because the multi-transfused population is more prone to blood-borne pathogens. Arif *et al*<sup>[56]</sup> reported that only 15.8% of parents of thalassemic children knew the importance of blood screening. Six different reports showed an HCV percent prevalence of  $48.67\% \pm 1.75\%$  among the thalassemic and hemophilic population<sup>[56-62]</sup>.

### Health care workers

Health care workers are at high risk of HCV infection because they are dealing with blood, blood-related products and instruments which may carry transmissible pathogens. Hamid *et al*<sup>[63]</sup> reported that recapping of syringes is the key factor for receiving needle stick injuries in health care workers and that transmission of HCV by needle stick injury ranges from 2% to 10%. Two different reports showed an HCV percent prevalence of  $5.2\% \pm 0.63\%$  in health care workers<sup>[64,65]</sup>.

### Sexual transmission

It has been reported from the US that up to 20% of new HCV infections are due to sexual activity<sup>[66]</sup>. Two different reports from the USA and Congo indicate low HCV prevalence among commercial sex workers<sup>[67,68]</sup>. The main problems in Pakistan are illiteracy, lack of awareness about sexually transmitted diseases and low use of condoms among the sex workers. Saleem *et al*<sup>[69]</sup> reported in 2005 that 17% of female sex workers, 3% of male sex workers and 4% of hijras (transgender men) consistently used condoms during the previous month; 67% of female sex workers were illiterate, 34% of female sex workers were suffering from sexually transmitted infections. Homosexual activities were very high among street children who are sexually victimized or indulge in such activities; later on they adopt commercial sex in order to raise their income. Condom usage among the male homosexual population was very low. Four different studies showed an interspousal percent prevalence of  $17.24\% \pm 7.98\%$ <sup>[70-73]</sup>.

## RISK FACTORS

### Unsafe and unnecessary needles

The reuse of syringes and needles was a major factor contributing towards increased HCV prevalence<sup>[74,75]</sup>. It was reported that there are several small groups involved in recycling and repacking of used unsterilized

**Table 1 Percentage prevalence of HCV among different communities in Pakistan**

Population type	Author	Region	Methods	Population size	HCV (%)
General population	Luby <i>et al</i> <sup>[10]</sup> , 1997	Hafizabad	RIBA	309	6.50
	Parker <i>et al</i> <sup>[11]</sup> , 2001	Lahore	EIA	417	6.70
	Khokhar <i>et al</i> <sup>[12]</sup> , 2004	Islamabad	ELISA	47538	5.31
	Muhammad <i>et al</i> <sup>[13]</sup> , 2005	Buner	ELISA	16400	4.57
	Hashim <i>et al</i> <sup>[14]</sup> , 2005	Attock	ELISA	4552	4.00
	Zaman <i>et al</i> <sup>[15]</sup> , 2006	Bahawalpur	ICT	6815	4.41
	Alam <i>et al</i> <sup>[16]</sup> , 2006	Central Punjab	ELISA, ICT	2038	4.41
	Chaudhary <i>et al</i> <sup>[17]</sup> , 2007	Rawalpindi	MEIA	1428	2.52
	Hakim <i>et al</i> <sup>[18]</sup> , 2008	Karachi	ELISA,ICT,PCR	3820	5.20
	Tunveer <i>et al</i> <sup>[19]</sup> , 2008	Lahore	ICT	203	1.48
Pediatric population	Agboatwalla <i>et al</i> <sup>[20]</sup> , 1994	Karachi	ELISA	236	0.44
	Khan <i>et al</i> <sup>[21]</sup> , 1996	Lahore	EIA,RIBA	538	4.09
	Parker <i>et al</i> <sup>[22]</sup> , 1999	Lahore	ELISA	538	1.30
	Hyder <i>et al</i> <sup>[23]</sup> , 2001	Lahore	ELISA	171	0.58
	Jafri <i>et al</i> <sup>[24]</sup> , 2006	Karachi	ELISA	3533	1.60
	Aziz <i>et al</i> <sup>[25]</sup> , 2007	Karachi	EIA	380	1.40
Recruitment	Ali <i>et al</i> <sup>[26]</sup> , 2002	Rawalpindi	ICT	5371	3.29
	Zakaria <i>et al</i> <sup>[27]</sup> , 2003	Karachi	ICT-ELISA	966	2.20
	Masood <i>et al</i> <sup>[28]</sup> , 2005	Lahore	ELISA	4552	4
	Mirza <i>et al</i> <sup>[29]</sup> , 2006	Mardan	ELISA	15550	3.69
	Sharif <i>et al</i> <sup>[30]</sup> , 2006	Risalpur	ELISA	2558	3.40
	Alam <i>et al</i> <sup>[31]</sup> , 2006	Sargodha	unknown	2038	4.41
Pregnant women	Zafar <i>et al</i> <sup>[33]</sup> , 2001	Lahore	PCR	300	4
	Khokhar <i>et al</i> <sup>[34]</sup> , 2004	Islamabad	ELISA	503	4.80
	Jaffery <i>et al</i> <sup>[35]</sup> , 2005	Islamabad	ELISA,PCR	947	3.27
	Yousfani <i>et al</i> <sup>[36]</sup> , 2006	Hyderabad	ICT, ELISA	103	16.50
Blood donors	Mujeeb <i>et al</i> <sup>[37]</sup> , 1996	Karachi	EIA	839	2.40
	Bhatti <i>et al</i> <sup>[38]</sup> , 1996	Rawalpindi	EIA	760	4.80
	Mujeeb <i>et al</i> <sup>[39]</sup> , 2000	Karachi	ELISA	7047	2.40
	Ali <i>et al</i> <sup>[40]</sup> , 2003	Quetta	ELISA	1500	1.87
	Asif <i>et al</i> <sup>[41]</sup> , 2004	Islamabad	MEIA	3430	5.14
	Ahmad <i>et al</i> <sup>[42]</sup> , 2004	Peshawar	MEIA	4000	2.20
	Zaidi <i>et al</i> <sup>[43]</sup> , 2004	Peshawar	ELISA	49037	2.60
	Chaudry <i>et al</i> <sup>[44]</sup> , 2005	Lahore	ELISA	890	6.06
	Abdul Mujeeb <i>et al</i> <sup>[45]</sup> , 2006	Karachi	ELISA	7325	3.60
	Chaudhary <i>et al</i> <sup>[17]</sup> , 2007	Rawalpindi	MEIA	1428	2.52
	Sultan <i>et al</i> <sup>[46]</sup> , 2007	Different Areas	EIA	41498	4.99
	Khattak <i>et al</i> <sup>[47]</sup> , 2008	Different Areas	ELISA	103858	4
	IDU	Kuo <i>et al</i> <sup>[52]</sup> , 2006	Lahore	ELISA	351
Achakzai <i>et al</i> <sup>[53]</sup> , 2007		Quetta	ELISA	50	60
Altaf <i>et al</i> <sup>[54]</sup> , 2009		Karachi	ELISA	161	94
Platt <i>et al</i> <sup>[55]</sup> , 2009		Abbottabad	ELISA	102	8
Platt <i>et al</i> <sup>[55]</sup> , 2009		Rawalpindi	ELISA	302	17.30
Thalassemic	Bhatti <i>et al</i> <sup>[58]</sup> , 1995	Rawalpindi	ELISA	35	60
	Muhammad <i>et al</i> <sup>[59]</sup> , 2003	Peshawar	ELISA	80	36
	Shah <i>et al</i> <sup>[60]</sup> , 2005	NWFP	ELISA	250	57
Hemophilia	Hussain <i>et al</i> <sup>[61]</sup> , 2008	Islamabad/Peshawar	ELISA	180	41.70
	Hussain <i>et al</i> <sup>[62]</sup> , 2003	Peshawar	ELISA	40	25
Health care workers	Malik <i>et al</i> <sup>[57]</sup> , 2006	Lahore	ELISA	100	56
	Mujeeb <i>et al</i> <sup>[64]</sup> , 1998	Karachi	EIA	114	4.40
Sexual/spousal	Aziz <i>et al</i> <sup>[65]</sup> , 2002	Karachi	ELISA	250	5.60
	Irfan <i>et al</i> <sup>[70]</sup> , 2004	Islamabad	PCR	23	4.30
	Kumar <i>et al</i> <sup>[71]</sup> , 2004	Karachi	MEIA	50	18
	Khokher <i>et al</i> <sup>[72]</sup> , 2005	Islamabad	ELISA	227	4.40
Qureshi <i>et al</i> <sup>[73]</sup> , 2007	Karachi	EIA/PCR	153	38	

HCV: Hepatitis C virus; RIBA: Recombinant strip immunosorbent assay; ICT: Immunochromatographic test; ELISA: Enzyme linked immunosorbent assay; MEIA: Micro-enzyme immunoassay; EIA: Enzyme immunoassay; PCR: Polymerase chain reaction.

syringes, which were available in various drug stores. It was difficult for the public to differentiate between new sterilized syringes and recycled unsterilized syringes<sup>[76]</sup>. Janjua *et al*<sup>[77]</sup> reported that 68% of individuals received injections during the previous three months in Digri and Mirpur khas, two districts of Pakistan, out of which only 54% were from freshly opened syringes. The incidence

of sharing of injection equipment for the last injection was 8.5% in Hyderabad and 33.6% in Sukkur<sup>[54]</sup>.

In Pakistan, the number of estimated injections per person per year ranged from 8.2 to 13.6, which was the highest among developing countries, out of which 94.2% were unnecessary<sup>[51]</sup>. Household members who received four injections per year were 11.4% more prone

to HCV infection than who did not receive injection<sup>[78]</sup>. Khan *et al*<sup>[74]</sup> reported that if both oral and injectable medicine were equally effective, 44% of the Pakistani population preferred injectable medicine.

In 2000, the WHO recommended that countries should implement strategies to change the behavior of health care workers and patients in order to decrease the over-use of injections, to ensure the practice of sterile syringes and needles, and to properly destroy sharp waste after use<sup>[79]</sup>. It was reported that 59% of syringes were dumped into the general waste and not properly disposed of in the healthcare waste. Scavengers seeking valuable things from the waste are at high risk of receiving needle stick injuries from contaminated needles<sup>[76]</sup>.

### Blood transfusion

People in developing countries are mostly anemic, and are more prone to traumatic injuries and obstetric complications. Blood transfusion in these situations is life-saving. If blood is not properly stored or is carrying blood-borne pathogens, then the situation becomes more complicated. According to the WHO office in Pakistan about 1.2 to 1.5 million transfusions are carried out annually in Pakistan<sup>[80]</sup>. In 2000, Luby *et al*<sup>[81]</sup> reported that 50% of blood banks in Karachi recruited paid donors, 25% of donations were from volunteer donors and only 23% of the blood banks screened for HCV while 29% of them were storing blood outside the WHO recommended temperature.

In developing countries, blood transfusion is still a problem due to lack of organized infrastructure, continuous supply of electricity, and properly trained and educated staff. In Pakistan the main source of blood donations are replacement donors and the majority of these are friends and relatives of the patient. These donors donate blood due to fear of death of a relative, chance of further complication of disease or under family pressure. These donors mostly hide their health conditions from their relatives. Selection of donor and their proper screening are key factors to ensure safe transfusion. Safe blood donors are those whose donations are repeatedly negative on screening<sup>[17]</sup>. Sixty-six percent of Pakistanis are residents of rural areas where there is less access to blood transfusion services. To provide proper transfusion facilities to underdeveloped areas requires economic growth. Efforts are required to eliminate the transfusions from paid donors, to improve the safety of the blood supply<sup>[81]</sup>. These conditions can be overcome by development of a fair and organized system of blood screening and transfusion.

### Barbers

In third world countries like Pakistan, most of the barbers are illiterate and unaware of transmission of infectious agents through the repeated use of razors and scissors for different customers without sterilizing them first<sup>[82]</sup>. Janjua and Nizamy reported that only 13% of the barber community knew that hepatitis is a liver disease and that it could be transmitted by contaminated razors; 11.4% of them were cleaning razors with antiseptic solution while 46% of them were re-using razors<sup>[83]</sup>. Recent reports suggested that only 42% knew about hepatitis, 90% did

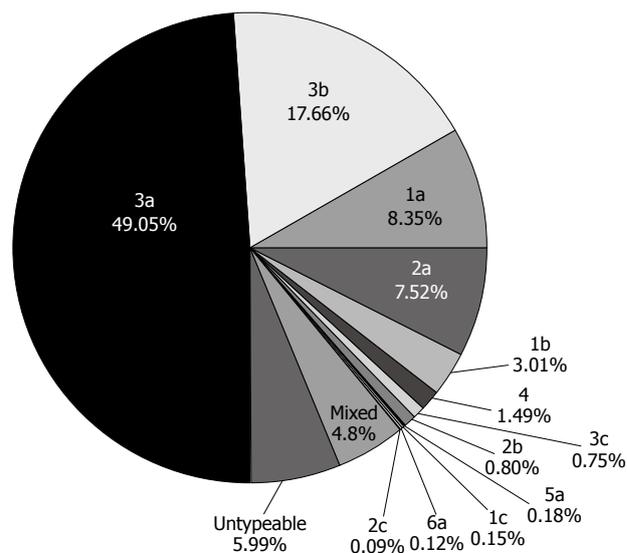


Figure 1 Hepatitis C virus (HCV) genotypes in Pakistan (2008)<sup>[95]</sup>.

not wash hands, 80% were not changing aprons and 66% were not changing towels after each customer. Circumcision is a very important religious procedure performed during early infancy both in rural and urban areas, and the barber community performing this procedure are mostly unaware of transmission of hepatitis by contaminated instruments<sup>[84]</sup>. Bari *et al*<sup>[85]</sup> identified the risk factors involved in transmission of HCV and reported that 70% and 48% of HCV patients had histories of facial and armpit shaving from barbers respectively.

### Awareness

In the Pakistani population there was moderate knowledge about HCV infection whereas awareness about various HCV risk factors was very low<sup>[31,86,87]</sup>. In a survey conducted at a family medicine clinic in Karachi, most of the participants had some educational background and were living in Karachi city. It was reported that 61% of participants believed that HCV was a viral disease, 49% believed that it could be transferred by needles and injections, 5.3% believed that it could be transmitted by ear and nose piercing, and 20.6% knew that it can cause cancer<sup>[86]</sup>. Kuo *et al*<sup>[82]</sup> reported in 2006 that HCV awareness was only 19% in the IDU population of Lahore and Quetta. Zuberi *et al*<sup>[88]</sup> reported that knowledge about HCV infection was related to the educational background of the participants. Public awareness programs are required to decrease the future burden of HCV infection in the Pakistani population.

## GENOTYPES

HCV is classified into eleven different genotypes, of which six are the major genotypes and these genotypes are further classified into many subtypes<sup>[89,90]</sup>. In 1997 it was reported in a small study that 87% of the individuals in Pakistan had genotype 3<sup>[91]</sup>. In 2004, a panel of 30 top gastroenterologists of the country met at a conference and reported that 75%-90% of HCV patients in Pakistan had genotype 3a<sup>[8]</sup>. Qazi *et al*<sup>[92]</sup> reported in 2006 that 71%

of patients had genotype 3 while only 10% had genotype 1. In 2007 it was reported that 81% of individuals had genotype 3 while only 9.5% had genotype 1<sup>[93]</sup>. Hakim *et al*<sup>[18]</sup> reported in 2008 that 51% of HCV patients had genotype 3a; 24% had 3a/3b co-infection and 16% had genotype 3b, while similar results were also reported by Afridi *et al*<sup>[94]</sup> who stated that 50% of HCV patients had genotype 3a followed by 3b and 1a. The most detailed study was conducted by Idrees and Riazuddin in 2008, who performed genotyping of 3351 patients and reported that genotype 3a was the most prevalent genotype in Pakistan; their results are summarized in Figure 1<sup>[95]</sup>.

## CONCLUSION

This study reviewed the seroprevalence of HCV among various population groups, along with risk factors and genotypes in Pakistan. HCV prevalence was observed in nearly 5% of the general population which is in parallel with the WHO estimates of HCV in Pakistan. High prevalence was observed in IDUs and the multi-transfused population, suggesting that the reuse of syringes was common among the injecting drug users, and that blood transfusions were not properly screened. Most prevalent genotype of HCV was 3a. The majority of HCV-positive patients had a history of facial and armpit shaving by barbers suggesting that the barbers shop was the key place for viral transmission. Condom usage was very low among the commercial sex workers and there was low awareness about sexually transmitted diseases amongst this group. In Pakistan, the number of estimated injections per person per year was very high because most Pakistanis think that injectable drugs are more efficacious than oral drugs. There was low awareness in people about the various risk factors associated with HCV transmission. Treatment of hepatitis is very expensive and is creating a huge burden on the country's economy. More emphasis should be given to the preventive measures of the disease in order to decrease the future health and economic burden; these include screened blood transfusions, proper sterilization techniques in clinics and hospitals, use of disposable syringes and razor blades. The government should take aggressive steps to create awareness among the general public by the use of media or by modifying the school syllabus.

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