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A Review of Hepatitis C Virus: Prevalence, Genotype, Risk Factors in Pakistan Last Quarter of Century

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Abstract

Hepatitis C virus has infected over 200 million people worldwide and is the most common blood-borne disease. Pakistan has the HCV prevalence rate of over 8%. A literature search has been performed using different keywords in different databases i.e. PubMed, Google Scholar, and NCBI. 6.2% prevalence rate was found in the general population, 4.13% in healthcare workers and a higher prevalence rate was observed in injection drug users and multi transfusion population. Use of injection was very frequent among the Pakistani population, reuse and sharing of syringes have an association with HCV infections. In Pakistan most prevalent genotype of HIV was 3a. Knowledge about HCV and its risk factors also varies with the educational background. Blood donors should be screened for HCV, awareness campaigns about different risk factors should be initiated at the government level, and strict regulation on healthcare waste should be implemented, these might help in preventing its spread to healthy individuals.

Keywords: *Hepatitis C, Pakistan, Prevalence, Genotypes, Risk factors, Injection, Transfusion.*
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I. INTRODUCTION

Hepatitis C virus (HCV) was first identified in the early 1990s and it was associated with blood transfusion (Alter *et al.*, 1992). HCV is among the most common blood-borne disease, approximately 200 million people are affected by HCV worldwide. Most affected areas are Eastern Mediterranean including Lebanon, Syria, Palestine, Israel, and Egypt, and prevalence rate in the European region is 1.5%. (Hajarizadeh *et al.*, 2013). In Pakistan, the prevalence rate of HCV is over 8% (Arshad and Ashfaq, 2017). A recent report on HCV indicates that deaths from HCV now exceeded than Human immunodeficiency virus in USA (Ly *et al.*, 2012). According to a survey that was conducted from 1999-2002 by National Health and Nutrition Examination there were 3.2 million people affected by chronic HCV (Armstrong *et al.*, 2006). The recent survey reported that the number of individuals affected by HCV increased to 71.1 million which is an alarming situation (Zeuzem *et al.*, 2017).

Genotype 1 is the most prevalent genotype globally. Previous studies reported that only 15% patients can clear the virus in initial stage; rest 85% are unable to clear the virus and ultimately virus start growing inside the body and leading towards the cirrhosis and then hepatocellular carcinoma (NIH, 2002). HCV belongs to genus Hepacivirus and family Flaviviridae. Hepatitis C virus is an enveloped virus, contains RNA genome (+ssRNA) of 9.6kb, which encodes for a long chain protein of 3010 amino acids. The genome of HCV encodes 10 proteins, 3 of them are structural while 7 are nonstructural (Murphy *et al.*, 2015).

HCV has 7 genotypes, the last one was reported recently in Canada (Moosavy *et al.*, 2017). A study was conducted in Central Africa and reported the subtype of the 7th genotype of HCV, they classified the prototype sequence QC69 as 7a genotype (Saitou and Nei, 1987). The prevalence of HCV genotypes varies among different geographical regions (Simmonds *et al.*, 2005). Asia and South Africa has the higher prevalence of genotype 5 and 6 while Genotype 4 has higher prevalence rate in the Middle East and Africa (Hajarizadeh *et al.*, 2013; Li *et a*l, 2009; McOmish *et al.*, 1993). In Australia, HCV prevalence is < 2% while Egypt has the highest HCV prevalence > 14% (Guerra *et al.*, 2012; Mohamoud *et al.*, 2013) in the world. Asia has

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HCV prevalence rate a bit greater than 2%, there is an exception in case of Mongolia with a prevalence rate of HCV is above than 10% (Lavanchy, 2011). Recent studies reported that the prevalence rate of HCV worldwide increased to 6% of the total world's population. China has 29.8 million, India has 18.2 million and Indonesia has 9.4 million affected individuals reported in their countries and they are among the highest HCV prevalent countries (Lavanchy, 2011). Japan has a low prevalence of HCV and most of the affected individuals are above 55 years of age (Tanaka *et al.*, 2004). According to systematic data available on different databases, approximately 8.8 million population of Europe is affected by HCV (Mühlberger *et al.*, 2009). The study is conducted to give an up to date insight of HCV prevalence, genotypes, and risk factors associated with the HCV transmission in Pakistan.

II. Literature Review Collection

Relevant data about HCV searched from different databases including PubMed, Google Scholar, NCBI by using different keywords i.e. HCV, HCV genotypes, HCV prevalence in Pakistan, risk factors of HCV, transmission of HCV, HCV genome and life cycle, prevalent HCV Genotypes in Pakistan, blood transfusion-related disease, HCV prevalence in general public, HCV prevalence in healthcare workers, HCV in drug users, HCV prevalence globally. Articles demonstrating the prevalence, genotypes and risk factors of HCV in Pakistan were included, articles with irrelevant/incomplete data were excluded. Selected articles were published between the time frame of 1994-2018.

III. Prevalent Hcv Genotypes

A study conducted in Hazara division showed significant results. It was reported that HCV genotype 3a was most prevalent in the region with 54.4% of the total cases. The age group which was most affected was 31-40 years in this study. Viral load with respect to other genotypes was less. These less prevalent genotypes included genotype 1a, 1b, 1c, and genotypes 2a. 2b (Ali *et al.*, 2011). Similar results were obtained in another study, in which it was shown that genotype 3a was the most prevalent HCV genotype in the Pakistani population. In Punjab, it constituted 68.9% of the HCV cases, 76.8% in Sindh, 58% in Khyber Pakhtunkhwa and 60.7% in Baluchistan. It was also observed that genotype 1 had a high prevalence as well with 12.1% of the cases, affected with It and there was an increase in its incidence (Attaullah *et al.*, 2011).

Similar results with respect to genotype 3a were obtained in another study in which it was seen that genotype 3a was more prevalent as compared to other subtypes. Prevalence of genotype was 65.1% followed by genotype 1 that was 21.4% and genotype 2 that was 11.6% (Safi *et al.*, 2012).

A study was conducted in district Mardan, to find the prevalent genotypes in that region. It was found out that genotype 3a was the most prevalent one. It constituted 90.3 % of the cases. Genotype 1a constituted about 5.6% of the cases (Afridi *et al.*, 2013). An expansion in the classification system was performed to classify HCV genotypes. HCV has 7 genotypes and based on the genetic differences present in the HCV genome it is classified into 67 subtypes (Smith *et al.*, 2014). Another study was conducted to find out the prevalent genotypes in different regions of Pakistan. It was found out that 3a was the most prevalent genotype, comprising of 39.4%. Genotype 2a constituted 24.9%. it was also reported that genotype 3a was prevalent in Punjab and Sindh (Khan *et al.*, 2014).

Another study claimed HCV genotype 3a as the most prevalent subtype. It constitutes 61.3% of the cases according to this study. There is also evidence of an increase in the frequency of other subtypes like 2a. In Khyber Pakhtunkhwa, the prevalence of 2a was 17.3% while in Sindh it was 11.3% (Umer and Iqbal, 2016). It was reported in a study that the most predominant genotype in Malakand was 3a, the prevalence was 63.3%. Other genotypes that were detected were 1a, 1b, and 3a but these were not predominant as 3b (Nazir *et al.*, 2017).

IV. Hcv Prevalence Among Various Groups

A. Arevalence among the general public

It was reported that the prevalence of HCV among the general public in Pakistan was 6% (Haqqi *et al.*, 2019). The prevalence of the high-risk clinical population was 34.5%. Those at intermediate risk had a prevalence of 12.8%. Special clinical populations had a prevalence of 16.9% (Al Kanaani *et al.*, 2018). It was also found that active HCV infection was 6% among the population while seroprevalence among adult population was 6.8% (Umer and Iqbal, 2016).

B. Health care workers

Prevalence among the health care workers (HCW) reach to 4.13% as positive for HCV antibodies while 2.79% prevalence of HCV RNA was observed in the workers The most prevalent genotypes found were 3a and 2a (Khan *et al.*, 2011).

C. Injecting drug users

It has been reported that prevalence rate of HCV was 53.6% among the drug users in Pakistan (Al Kanaani *et al.*, 2018). Prevalence among the population of Lahore which have largest population was reach to 36.09% in drug users (Akhtar *et al.*, 2016).

D. Sexual transmission

HCV transmission through sexual activity has been reported many times. A study was conducted in Rawalpindi, it was seen that 34% of homosexuals were affected by sexually transmitted diseases. These types of activities were linked to low wages in the country. The use of protectives was only 4% among homosexual. Illiteracy and lack of awareness were also seen as an important reason for such unsafe practices (Saleem *et al.*, 2008).

E. Blood donors

In a study, it was found out that seroprevalence among the blood donors was 2.4% among the population (Umer and Iqbal, 2016). In another research, carried out on the population of Quetta, it was found out that blood donors have HCV prevalence of 20.8%. the highest prevalence was observed in the age group of 25, with a value of 26.3% (Khan et al, 2013). It has also been reported that HCV is also prevalent of among blood donors in Khyber Pakhtunkhwa and FATA region. It was recorded that HCV antibodies were found in 3.1% of the study population, and 1.89% found by ELISA and active HCV infection had a prevalence of 1.65% (Khan *et al.*, 2011).

F. Liver diseases

A study showed that the prevalence of HCV among people with liver-related diseases was 55.9% (Al Kanaani *et al.*, 2018). A study was conducted to find the relation between hepatocellular carcinoma and HCV genotypes. It was found out that genotype 3a had a relation with carcinoma. Prevalence of HCV-3a was found to be 81.4% among the study population (Khan *et al.*, 2009).

G. Multi transfused population

People going through blood transfusions are a high risk of HCV transmission. It was seen that patients with thalassemia had a mean prevalence of 42.4% of HCV. People going through hemodialysis had a prevalence of 28% (Al Kanaani *et al.*, 2018).

H. Injections

Unnecessary use of injections is considered as a major risk factor in the Pakistani population. It has been reported that Pakistan is among those countries who have the highest prevalence of injection used having an average of 9 injections per person annually (Khan *et al.*, 2000), approximately 94.2% of the injections administrated were unnecessary (Altaf *et al.*, 2006). There were certain groups who were involved in the recycling and selling of waste syringes to healthcare waste dealers. It has been found that major clinical laboratories were dumping their waste in municipal waste sites which can cause an increased risk of disease load (Mujeeb *et al.*, 2003). It was observed that household members who received four injections annually had 11.4% higher chances of developing HCV (Pasha *et al.*, 1999) while approximately 44% of the Pakistani population preferred injections over oral medicines although both have equal effectiveness (Khan *et al.*, 2000). Jilani et al reported that 77% of the pregnant women acquire HCV because of injections (Jilani *et al.*, 2017). Reuse of syringes by the general practitioners clinics caused infection in 26% of the HCV patients (Idrees *et al.*, 2008).

Use of unsafe medical and major or minor surgical practices was another common risk factor in HCV infections. The chances of infection for both patients and medical staff increased due to unsafe practices. HCV seroprevalence was 5-6% in health care workers (Aziz *et al.*, 2002). The possible practices that cause HCV infections in health care works were use of unsterilized instruments, poor handling of infected blood samples and medical waste, unsafe injections practices, nonprofessional behaviour (Mujeeb *et al.*, 1998). Injection sharing is very common among injecting drug users and these people have higher chances of getting HCV infections. HCV Prevalence among IDUs has been different in different cities of Pakistan. It was reported that in twins cities around 72% of the people who inject drugs have HCV present in their serum (Waheed *et al.*, 2017). The prevalence of HCV among IDUs in Lahore was 36% (Akhtar *et al.*, 2016). Khyber Pakhtunkhwa province of Pakistan has 24% HCV prevalence among IDUs (Ur Rehman *et al.*, 2011) while Quetta has 60% prevalence rate among IDUs (Achakzai *et al.*, 2007).

I. Barbers

HCV prevalence has an association with the barbers. People who shave from barbers have higher risk of HCV infections (Mele *et al.*, 1995). In Pakistan mostly, male visited barber shop for shaving and hair cutting, barbers were mostly illiterate or did not know the health risk of using the same razor for many customers. This could be a reason why there are more male than female who were infected by HCV (Idrees *et al.*, 2008). It has been reported that only 13% of the barbers knew that contaminated razors could be a cause of HCV Infection. (Janjua and Nizamy, 2004), while 42% had some knowhow about hepatitis, 90% did not wash their hands, and 66% of the barbers were using the same towel for all the customers (Wazir *et al.*, 2008).

J. Blood transfusion

Blood transfusion in critical situations has been very important for the survival of the person but if the blood is not properly stored or not screened for bloodborne pathogens then it could cause some other life-threatening diseases in the recipient. As reported by national blood bank data collection report, approximately 1.4 million blood transfusions have been carried out in Pakistan annually (Sufi et al, 2016). Almost half of the blood transfusion was not screened for bloodborne pathogens. Patients who need frequent blood transfusion i.e. hemophilia and thalassemia were at a higher risk of developing HCV infections (Alaei *et al.*, 2017). It has also been reported that 50% of the donors in blood banks of Karachi, Pakistan, were paid while 25% were collecting blood from volunteers. 23% of the blood banks have the facilities to screen for HCV, only 8% of the blood banks asked for injection drug use from their donor while none of the blood bank have asked donors about high risk sexual behaviors. 29% of the blood banks were not storing the blood at a temperature recommended by WHO (Luby *et al.*, 2000). Blood donors in Pakistan have HCV prevalence rate of 3% (Umar *et al.*, 2010).

K. Needle Stick Injuries (NSI)

It is reported that 64% of the HCW have had needle stick injury once in their carrier while 73% of health care workers had NSI two or more times (Afridi *et al.*, 2013). 45% of the HCWs have needle stick injury and the frequency was higher among the doctors. The main causes of these injuries were careless handling, stress, and workload (Zafar *et al.*, 2008).

42% of NSI were caused when injecting or drawing blood while 37% were during recapping of needles. Poor safety practices i.e. inadequate vaccination and lack of infection control guidelines were reported (Afridi *et al.*, 2013).

L. Vertical transmission of HCV infections

It has been reported that in the year 2007 5.1 million live births occurred and among them, 19708 children were HCV positive which is 3.73% of the total births. While in 2012 the percentage of HCV positive children were 3.87%. The prevalence of HCV in pregnant women was found out to be 1.42%. In these cases the infection was present in the mother during child birth (Ahmad *et al.*, 2016). 65% of the vertical transmission has been reported in rural areas but this can also be attributed to non-sterilized equipment in the labour room as the infection rate in the mothers is reported as 1.42% as mentioned before. Among all the reported cases approximately 72.5 % were in Punjab while the lowest percentage of vertical transmission has been reported in Baluchistan (<2%) (Benova *et al.*, 2017).

M. Other risk factors

There are certain other risk factors which have association with HCV infection like ear and nose piercings (Umar *et al.*, 2010). Awareness can be considered as a risk factor and it has been reported that the knowledge about HCV infection was associated with educational background (Zuberi *et al.*, 2008). Awareness activities about risk factors of HCV and their prevention must be organized to lower the disease burden.

V. CONCLUSION

This study reviewed the genotype, prevalence and risk factor associated with HCV transmission in Pakistan. It was concluded that 3a is the most prevalent genotype found in Pakistan and the overall HCV prevalence in Pakistan is around 8%. Among different groups highest HCV prevalence was observed in IDUs, the probable reason is the reuse and sharing of syringes. In Pakistan, the use of injection is very common because the majority of the population think that injection could cure their disease better and due to that use of injection per person annually was very high. Lack of awareness, poor infrastructure and limited health facility in rural areas are also playing their part in HCV transmission. HCV can be transmitted through various routes. Blood donors should be screened for HCV, awareness campaigns about different risk factors should be initiated at the government level, and strict regulation on healthcare waste should be implemented, these might help in preventing its spread to healthy individuals.

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