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REVIEW: EPIDEMIC STATUS OF HCV IN PAKISTAN

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ABSTRACT

Society faces an immense burden of hepatitis C virus (HCV) infection-related morbidity and mortality. Transmission of HCV is ongoing, and the incidence of HCV infection has been increasing in recent years. In Pakistan, hepatitis C virus (HCV) distribution appears to present a wide range of prevalence. The scale and nature of HCV disease burden is poorly known in Balochistan and Azad Kashmir. The aim of this review is to provide a systematic overview of HCV prevalence in different regions of Pakistan. Linkage to care and treatment for those identified with infection through testing would have a profound impact in reducing HCV disease burden The results highlight the need for more robust surveillance studies to quantify the HCV disease burden more accurately.

INTRODUCTION

HCV is an RNA virus member of the Hepacivirus genus and Flaviviridae that is divided into seven phylogenetically distinct GTs (GT1-GT7) and a vast series of subtypes (67 subtypes). Hepatitis C virus (HCV) causes both acute and chronic infection. Acute HCV infection is usually asymptomatic, and is only very rarely associated with life-threatening disease. A significant number of those who are chronically infected will develop liver cirrhosis or liver cancer. Molecular epidemiology and phylodynamic analysis have revealed that HCV genomic types and subtypes have distinctive patterns of geographical distribution (Lavanchy, 2011; Smith *et al.,* 2014) and the genotype of HCV is a major predictive factor for natural and in HCV infection treatment evolution (Pybus *et al.,* 2001; Cochrane *et al.,* 2002). Several epidemiological studies in different contexts have identified at-risk populations with a higher prevalence of HCV infection than the general population (Baldo et al., 2008). HCV is primarily transmitted via parenteral routes. Blood transfusions without previous HCV screening, and reuse and sharing of gloves, syringes and other material that can become contaminated are the most commonly documented routes of HCV infection (Allison *et al., 2012;* Prati, 2006). Injecting drug users are known to be the population most at risk of HCV infection, with prevalence estimated between 60% and 80% (Nelson et al., 2011; Ghany et al., 2009). The smoking, snorting (Scheinmann *et al.,* 2007; Caiaffa *et al.,* 2011) and, in particular, the intravenous use (Boodram *et al.,* 2010; Maher et al., 2006) of cocaine is also a well-established HCV infection risk factor (Morissette *et al.,* 2007). Other routes of HCV infection have been reported, such as sexual and mother-to-child, but less frequently (Murakami *et al., 2012;* Terrault *et al., 2013)*. After HCV screening tests were added to the routine protocols of blood centers, and blood donors were screened clinically and epidemiologically based on knowledge of HCV transmission, the rate of post-transfusion hepatitis was significantly reduced (Prati, 2006). The prevalence of HCV infection is higher in drug-using than in non-incarcerated drug users (Fazel & Baillargeon, 2010). Other practices such as tattooing and piercing in prisons, homes and other potentially non-sterile settings are also suspected of being HCV transmission risk factors (Tohme & Holmberg, 2012).

METHODOLOGY

Inclusion Criteria:

People infected with HCV in Pakistan were included in the study.

Search Strategy:

PubMed was searched with 'HCV' and 'HIV in Pakistan' phrases starting from 2000 to 2015. Clinical trials, reviews, meta-analyses, letters, editorials, and practice guidelines were all considered. In reading the articles, the reference lists were checked to identify any other articles that may have been relevant to the topic.

RESULTS

Worldwide status:

130–150 million people globally have chronic hepatitis C infection. Approximately 500 000 people die each year from hepatitis C-related liver diseases. Antiviral medicines can cure approximately 90% of persons with hepatitis C infection, thereby reducing the risk of death from liver cancer and cirrhosis, but access to diagnosis and treatment is low (WHO, 2015). About 15–45% of infected persons spontaneously clear the virus within 6 months of infection without any treatment. The remaining 55–85% of persons will develop chronic HCV infection. Of

those with chronic HCV infection, the risk of cirrhosis of the liver is 15–30% within 20 years (Liakina et al., 2015). In 2011, reported estimation of HCV infected population of 130–170 million people worldwide causing approximately 350 000 deaths each year (The state of hepatitis B and C in Europe: report from the hepatitis B and C summit conference, 2011). The estimated prevalence of HCV infection worldwide is 2.8% (Mohd Hanafiah *et al.*, 2013). Region-specific estimation ranges from less than 1.0% in northern Europe to more than 3.0% in North Africa (Lavanchy, 2011*;* Mohd Hanafiah *et al.*, 2013). The largest population-level prevalence of HCV infection in the world is found in Egypt with 14.7% of the adult population being exposed to the infection (El-Zanaty, 2009; Mohamoud *et al.*, 2013). China has the largest number of HCV-infected people (29.8 million) (Hajarizadeh *et al.*, 2013). Each genotype has its distinct geographical distribution, that is, HCV-1 and HCV-2 are the most common genotype in USA, Europe, and Japan. HCV-3 is predominant in Asia while HCV-5 and HCV-6 are mostly confined to Southeast Asia and South Africa. HCV-4 is the predominant genotype in the Middle East and North Africa with exception to Algeria (HCV-1b) (Rouabhia *et al.*, 2013). In the United States, it is estimated that 2.7 to 3.9 million persons are living with HCV infection, of whom 45% to 85% are unaware they are infected resulting in more than 15 000 deaths per year (Smith *et al.*, 2012; Mohd Hanafiah *et al.*, 2013). The prevalence of hepatitis C virus (HCV) infection is disproportionately higher in African Americans, with 3% being affected compared to 1.5% of the non-Hispanic White population in United States (Armstrong *et al., 2006*). In Europe, an estimated 8 million people (1.3%) are infected by HCV (The state of hepatitis B and C in Europe: report from the hepatitis B and C summit conference, 2009). Intermediate-to-high prevalence rates were reported in Eastern and Southern Europe, Western and Northern Europe reported low prevalence rates (≤1.0%) (Hajarizadeh & Grebely, 2013). Prevalence of HCV infection in India has been variously estimated as 0.9 and 1.9% (Chigurupati et al., 2014).

HCV prevalence in Pakistan:

Viraemic prevalence has been reported to be 4.2% in Pakistan. The total reported cases in Pakistan are 7 001 000 cases (Liakina *et al.*, 2015). In 2011, this prevalence was about 5%, with most individuals being infected with HCV genotype 3a (Inamullah *et al.*, 2011). Reported genotype 3a (34.1%) as the most prevalent genotype in district Swat followed by genotypes 2a (8.1%), 3b (7%), 1a (5.4%) and mixed genotype (7.6%) (Inamullah *et al.*, 2011). In district Swat, prevalence of genotype is found to be 49.5% (Ahmad et al. 2010). In Khyber Pakhtunkhwa, 57.83% prevalence of genotype 3a, followed by 6.2% of genotype 3b has been reported (Ali *et al.*, 2010). Genotype 3a is 62%, 3b is 9%, 1a is 3%, 2a is 2.144% and mixed genotype is 4.718%, prevalent among HCV positive samples in Pakistan (Afridi *et al., 2009*). The incidence of genotype 2a is increasing in our country with decrease in the incidence of genotype 3a (Khan et al., 2014). A higher incidence of HCV various genotypes are among male patients and those younger than 45 years. Almost 58.1% of HCV patients suffer from the infection due to multiple uses of needles especially syringes. Almost 16.7% of the patients suffer the infection due to surgeries (both major and minor). About 3.3% gets HCV due to blood and blood products infectivity. While in 23.1% patients the mode of spread was not known and therefore were sporadic (Ali *et al.*, 2010).The foremost mode of contamination in patients with HCV genotype 3a and 3b was multiple use and re-use of needles/syringes that was 70% and 60% respectively. All the genotype 1a and about 75% 1b infected patients got their infection during surgeries. Sixty percent of the patients having dual infections were sporadic where the route of infectivity was unknown to them. Majority (58.1%) of untypable patients were infected due to contaminated needles and syringes followed by surgeries and dental procedures (Ahmed *et al.*, 2010). About 25.7% of HCV infected individuals were present in Gilgit Baltistan province in 2008 and 2009 (Akbar et al., 2009; Batool et al., 2008). In Quetta region, 1.5% HCV infected individuals are present (Qureshi et al., 2013; Kazmi et al., 1997). High prevalence of HCV genotype 3a in the different divisions of Punjab has been reported with a prevalence rate of 88.1% (Aziz *et al.*, 2013). Prevalence of genotype 3 is almost 87% (Shah *et al.*, 1997). The second most prevalent HCV genotype in Pakistan is genotype 1 (Aziz *et al.*, 2013; Idrees & Riazuddin, 2008). In Islamabad, age groups of 21–30 and 40–50 years showed highest frequency of HCV (Jafar *et al.*, 2014). Other studies also documented high prevalence in age group of 22–30 and age group above 40 (Gull *et al.*, 2009; Pennap *et al.*, 2010; Al-Ajlan, 2011). Married patients are more prone to infection (Jafar *et al.*, 2014; Raja *et al.*, 2007). HCV seropositivity prevalence of females in Islamabad is 62 (24.6%) (Hashmi *et al.*, 2010). In Islamabad, Pakistan showed the prevalence of HCV in pregnant women to be 6%. In North West Frontier Province, the distribution of HCV genotypes in Mardan, Charsadda, Peshawar, Sawabi and Nowshehra districts is different. Genotype 3a and 3b, 1a, 1b and 2a are the common genotypes in NWFP (Sher Zaman *et al.*, 2012). In NWFP, 3a is less frequent while 3b is more frequent than other provinces of Pakistan. The seroprevalence of HCV among pregnant population was found to be 4.7% in Hyderabad Sindh. HCV positive women were more likely to have a history of blood transfusion, history of therapeutic injection use, history of surgery and history of sharing household products (Bibi et al., 2013). In 2011, prevalence of 24% was in rural Sindh (Nangrejo *et al.*, 2011). The total prevalence of Hepatitis C in 2012 is found to be 12.99% (Naeem *et al.*, 2012). In Karachi, overall seroprevalence of HCV in

the paediatric population from 12 to 18 years is 0.4%. The prevalence of HCV antibody positivity in our antenatal population is estimated at around 4–6% (Jaffery *et al.*, 2005).

DISCUSSION

It has to be recognized, however, that surveillance systems for HCV are prone to underestimation due to the generally asymptomatic nature of acute infections, the marginalization of at risk populations or simply a lack of informative campaigns and testing for HCV. So, not only is data on the incidence of HCV infection limited, but data on its prevalence and subtype distribution is also incomplete (Seeff *et al.*, 2002). The presence of estrogen receptor α enables females to attain spontaneous clearance or persistent HCV infection (Tang *et al.*, 2014). Chronic HCV infection develop more rapidly in men than in women and disease complications like cirrhosis are more pronounced in men and post-menopausal women (Shimizu, 2003).

The presence of poor quality of care provided and a massive need to educate general population including patients as well as health professionals and allied health workers for controlling, combating and preventing the wild epidemic of HCV has been observed (Hashmi *et al.*, 2010). Use of unsterile equipment for medication, barbers and previous history of hospitalization were the main risk factors for HCV transmission in North West Frontier Province. The level of awareness about various modes of transmission of HCV among the population is found to be very low (Sher Zaman *et al.*, 2012). People in NWFP have the least of the above mentioned facilities, awareness and educational standards to combat the infection of HCV by self-care and appropriate interferon therapies. Several shortcomings have been noted with the existing HCV screening and prevalence literature, emphasizing a need for more representative population samples, appropriate use of diagnostic tests, and better stratification by gender and race/ethnicity (Lavanchy, 2011). Timely transfusion of blood saves millions of lives, but unsafe transfusion practices place millions of people at risk of transfusion-transmissible infections such as HCV and HIV. Donor selection begins with education of the public about transfusion-transmissible diseases (Bihl *et al.*, 2007). Shaving or trimming nails can generate trauma or microtrauma on the skin surface, resulting in exposure to HCV on blades or nail scissors contaminated by asymptomatic infected family members or other people who are unknowingly infected and who frequent barbershops and beauty salons. In Brazil, Italy, Pakistan and Nigeria, HCV transmission by sharing razor blades and other cutting instruments, as well as other forms of viral dissemination due to a lack of public awareness, have been reported as risk factors for infection (Bari *et al.*, 2001).

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