Wrath of Hepatitis C in Jammu: A Hospital Based Population Study

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Abstract
Background and Objective: Currently, India harbors an anticipated 10-15 million chronic carriers of HCV whereas reported prevalence rates vary broadly from 0.09% to 2.02% (Mukhopadhyaya, 2008). Although various studies for seroprevalence are there but still a paucity of data from large multi-centric studies in India remains. The main aim of this study was to estimate the seroprevalance of HCV in the district of Jammu (J&K); as very scarce data regarding the prevalence of HCV in the state of J&K is present.

Methodology: The present study was conducted from January 2014 to December 2016 amongst the patients attending various departments of GMC, Jammu and were referred by them to Viral Research and Diagnostic Lab., Deptt. of Microbiology for anti-Hepatitis C Virus ELISA. The serum was separated for the qualitative detection of HCV antibody by ELISA.

Results: During this study a seroprevalence of 1.158% was determined. Among 235 positive samples 170 (72.34%) were males and 65 (27.65%) were females with an overall seropositivity of 0.83% and 0.32% indicating a male preporederance. The maximum number of HCV positive patients were in the age group of 41-60 (53.24) followed by 18-40 years (31.01%) and 61-80 years (15.74%) and above 80 years none was reported. Among the samples screened 755 (3.72%) were from HIV care and 6 among which was found to be positive (0.79%).

Conclusion: Control of HCV infection requires a comprehensive approach that incorporates primary prevention of transmission through enhanced infection control and injection safety in healthcare settings and in the community, universal screening of blood and blood products, harm reduction programs, and increased public awareness about risk factors for HCV infection.

Introduction
Hepatitis C virus (HCV) infection is a major global health concern and the second most widespread chronic viral disease in the world after Hepatitis B. World Health Organisation (WHO) estimates that HCV accounts for approximately
15% - 20% cases of acute Hepatitis, ((http://www.who.int) of which 50% - 80% of patients develop chronic infection and in 3% – 11% there is progression to liver cirrhosis within 20 years along with the risk of liver failure and Hepatocellular Carcinoma (HCC) (Dore et al., 2002). WHO estimates that, 3,50,000 to 5,00,000 people die each year from HCV related liver diseases, most affected being Central and East Asia and North Africa, although the virus is prevalent worldwide (http://www.who.int/mediacentre/factsheets/fs164 _apr2014/en/). The natural history of HCV is prejudiced by a wide variety of factors viz., host factors which include age at infection, gender, race, obesity, steatosis, insulin resistance/diabetes, genetics, alanine aminotransferase levels and exercise; viral factors include HCV RNA level, quasispecies/genotype, coinfection with HBV and coinfection with HIV and environmental factors like use of alcohol, cigarette, cannabis, caffeine and herbal product (Lingala and Ghany 2015). Among the HCV-infected patients, approximately 15%-45% are able to clear the virus impulsively within 6 months of infection without any treatment, and the remaining 55% - 85% of persons may progress to continual chronic infection. It is estimated that the risk of developing cirrhosis of the liver within 20 years is 15%-30% in those with chronic HCV infection (http://www.who.int/mediacentre/factsheets/fs164 _apr2014/en/), and the risk of developing hepatocellular carcinoma is 1% - 4% per year (Lingala and Ghany, 2015). The viral evolutionary dynamics and host genetic polymorphisms, e.g., the interleukin 28B (IL28B) gene, are important in determining the outcomes of HCV infection (Saito and Uneo, 2013).

Epidemiological studies also imply that HCV is related with a number of Inflammatory and related extrahepatic manifestations including insulin resistance, type 2 diabetes mellitus (T2DM), glomerulopathies, oral manifestations (Carrozzo and Scally., 2014; Ozkok and Yildiz, 2014) fatigue, cognitive impairment, depression, impaired quality of life, polyarthritis/ fibromyalgia, and cardiovascular disorders (i.e., stroke and ischemic heart disease) (Cacoub and Comarmond 2016). Immune-related extrahepatic manifestations include mixed cryoglobulinemia, cryoglobulinemic vasculitis, B-cell NHL, Sicca syndrome, arthralgia/myalgia, autoantibody production (i.e., cryoglobulins, rheumatoid factor, and antinuclear, anticycldiolipin, antithyroid and anti-smooth muscle antibodies), polyarthritis nodosa, monoclonal gammapathies, and immune thrombocytopenia. Recent studies suggest that HCV infection leads to increased risk of developing cardiovascular diseases and has been linked to increased risk of mortality caused by these diseases (Petta et al., 2016)

HCV is an enveloped positive stranded icosahedral virus of 55-65 nm size, a ~ 9.6 kb single-stranded RNA genome, a member of the Flaviviridae family and genus Hepacivirus. (Lindenbach et al., 2007). The HCV nucleocapsid is surrounded by a lipid bilayer; wherein two enveloped glycoproteins, E1 and E2, anchored as a heterodimer play a major role in HCV entry (Lavie et al., 2007). HCV is transmitted mostly through the parenteral route due to iatrogenic exposures in 20% - 80% (transfusion/ needle stick accidents/ transplantation/dialysis of infected blood/ blood products or organs/tissues, use and sharing of contaminated injections/equipment). Sexual and Maternal-infant transmission of HCV are less frequent (Gowe et al., 2014).

On the basis of sequence homology, six major HCV genotypes (1-6) and numerous distinct subtypes exist whose distribution is highly variable. Genotypes 1-3 are distributed globally and contribute to the majority of HCV infection, whereas genotypes 4 and 5 are restricted to Middle East and Africa, while as genotype 6 occurs predominantly in South China and Southeast Asian countries (Zein 2000; Akkarathamrongsin et al., 2010). Subtypes 1a and 1b are most common in Europe, USA and Japan, whereas subtypes 2a and 2b are predominant in Japan, North America and Europe, while subtype
3a is most prevalent in the Indian subcontinent and Thailand (Khan et al., 2009). The mode of HCV transmission is associated with genotype distribution; for example, evolutionary analysis has suggested that HCV subtype 1a may spread via blood transfusion and unsafe medical practices (Romano et al., 2010) while subtypes 1a and 3a are prevalent in young individuals particularly in injecting drug users (IDUs) (Shustov et al., 2005). Currently, India harbors an estimated 10 - 15 million chronic carriers of HCV. In India, reported prevalence rates vary broadly from 0.09% to 2.02% (Mukhopadhyaya, 2008). Although various studies for seroprevalence are there but there is still a paucity of data from large multi-centric studies in India. The main aim of this study was to estimate the seroprevalence of HCV in the district of Jammu (J&K); as very scarce data regarding the prevalence of HCV in the state of J&K is present. The district of Kashmir has a reported prevalence of 1.9% (Shah et al., 2017). The prevalence among healthy blood donors in Jammu was reported to be 0.51% (Malik et al., 2011). Thus, making surveillance method useful to recognize cases or clusters of cases that need interventions, assess the public health impact of health events, demonstrate the need for public health intervention, monitor effectiveness of prevention and intervention strategies, identify high-risk population groups and develop hypotheses leading to analytic studies about risk factors for disease causation or progression.

Materials and Methods

Study population
The present study was conducted from January 2014 to December 2016 amongst the patients attending various departments of GMC, Jammu and were referred by them to Viral Research and Diagnostic Lab., Deptt. of Microbiology for anti-Hepatitis C Virus ELISA. A detailed questionnaire was designed which highlighted age, sex, marital status, residence, occupation, lifestyle and past history of travel and disease (if any). Results of anti-HCV sero testing were shared with the patient and the concerned doctor.

Serological testing
The serum was separated for the qualitative detection of HCV antibody by ELISA. The sera and controls were incubated in the wells and antibodies if present bind to the antigens on the microwell. After washing, conjugate is further added which binds to the specific IgG already bound to the antigen on the well. After washing again 3,3’,5,5’- tetramethylbenzidine (TMB) and hydrogen peroxide is added which in wells with bound conjugate gives a blue to bluish green colour. This colour further turns yellow to orange after the stop solution (H2SO4) is added. After incubation, the colour is read spectrophotometrically. The intensity of colour produced is directly proportional to the concentration of antibody to HCV in the sample. Wells containing negative sample remain colourless.

Result
The present study is hospital based conducted from January 2014 to December 2016. A total of 20291 anti HCV ELISA tests were conducted during this period (5281, 7268 and 7742 in the years 2014, 2015 and 2016 respectively) among which a total of 235(1.158%) (Fig 1) samples were found be positive. Seroprevalence was 1.060%; n=56, 1.210%; n=88 and 1.175; n=91 in 2014, 2015 and 2016 respectively (Fig.2). Among 235 positive samples 170 (72.34%) were males and 65 (27.65%) were females (Fig.3) with an overall seropositivity of 0.83% and 0.32% indicating a male preponderance. The maximum number of HCV positive patients were in the age group of 41-60 (53.24%) followed by 18-40 years (31.01%) and 61-80 years (15.74%) and no case was reported above 80 years (Fig.4). Among the samples screened 755 (3.72%) were from HIV testing laboratory and 6 among which were found to be positive (0.79%) (Fig. 5).
Fig. 1: Graph depicting total number of samples screened and total positives obtained during 2014-2016

Fig. 2: Graph depicting total suspected samples and total positive samples for Anti HCV from 2014-2016

Fig. 3: Gender wise distribution of Anti HCV positive samples (2014-2016)
**Fig 4:** Distribution of positive samples obtained among different age groups.

**Fig. 5(a)** Distribution of HIV patients among the total tested samples (2014-2016).

**Fig. 5(b)** Total number of HCV positives HIV patients (2014-2016).
Discussion

Even after twenty four years of its discovery, HCV continues to be a major cause of concern and a huge burden on public health systems worldwide. WHO estimates that a minimum of 3% of the world’s population is chronically infected with HCV (WHO 1999; Alter 2007). HCV is known to cause infection in two phases, first acute attack that last for few weeks and if untreated may persist for long time and is termed as chronic Hepatitis C further leading to chronic liver disease (CLD) and eventually towards hepatic failure (Kamal 2008). It is estimated that only 30–50% of individuals infected with HCV are sentient of their disease (Rajesh, 2012). There is a dearth of population-based studies on Hepatitis C from assorted regions of India and as such the exact number of pretentious masses and the estimates are under-reported.

In the current study, a total sero prevalence of 1.158% was reported which is similar to (1.57%) another hospital based study by Mishra et al (2002). Sachdeva and Mehta, 2012 screened 150,000 residents of Fatehabad district in Haryana for anti-HCV positivity and found a population prevalence of 1%. On the contrary in another study by Gowri et al., 2012 a sero prevalence of 0.22% was reported while Patil et al., 2017 reported a seroprevalence of 0.46% from a tertiary care centre at Western Maharashtra. This seroprevalence is much similar to that reported in an earlier study from Jaipur (Rajasthan)(0.28%) (Sood and Malvankar 2010). Another study from Mangalore, Karnataka, reported seroprevalence of 0.2%. (Roche et al., 2012) Few studies done in the tribal population of India have depicted anti-HCV positivity (7.89% in Lisu community in Changland district of Arunachal Pradesh and 2.02% in Lambada tribe in Andhra Pradesh) (Phukan et al., 2001; Chandra et al., 2003). On the contrary in a hospital-based study from South India; seroprevalence of was 4.8% (Bhattacharya et al., 2003) was reported.

The seroprevalence of HCV among general population is 5.5% in Africa, 4.6% in the Eastern Mediterranean region, 4% in the Western Pacific region, 2% in South East Asia, 1.7% in the United States of America (USA), 1% in Europe, 28% in Egypt (Sy et al., 2006), 3% to 7% in different parts of Pakistan (Iqbal 2003) 5.9% Mauritius (Schwarz et al., 1994) and 6% in Ethiopia (Frommel et al., 1993) The seroprevalence of HCV has a considerable geographical variation, which may be explained by different distributions and different contributions of risk factors in different study regions.

In our study male predominance was observed with a reported seroprevalence of 0.83% and 0.32% in males and females respectively. Similar results were observed by Patil et al., (2017) where in a sero prevalence of 0.67% in males and 0.33% in females was reported. Numerous studies have reported male preponderance in Hepatitis C infection (Sood and Malvankar 2010; Roche et al., 2012; Sharma et al., 2007; Singh et al.,2014; Mindolli and Salmani 2015). In a similar study, by Sandhu et al., 2016 among a total of 4303 patients screened 155(3.60%) were positive for anti- HCV antibodies, among which 96 (2.23%) were males and 59 (1.37%) females thus indicating male dominance. On the contrary, Alsamarai et al., 2016 reported a slight dominance of females (0.72%) over males (0.41%) in a study from Iraqi population. According to studies, men have consistently lower clearance rates than women reasons remnents to be resolute. It is anticipated that high levels of estrogen may contribute to HCV clearance (Kong et al., 2014). In support of this possibility is data that the most potent physiological estrogen, 17 beta-estradiol, inhibits HCV replication in an Era-dependent manner in vitro (Fan et al., 2003). Clearly, indicating towards a warranted research in this important area.

In the present study maximum number of HCV positive patients were in the age group of 41-60 (53.24%) followed by 18-40 years (31.01%) and 61-80 years (15.74%) and none was reported above 80 years of age. In a similar study by Patil et al., 2017 the highest seroprevalence of 1.12%
was found to be among the age group 41–50 years. Sharma et al., 2007 in their study reported 70.38% of seropositive individuals above 35 years of age (Sharma et al., 2007). Patil et al., 2014 reported the maximum seroprevalence of HCV (1.5%) in the age group of 41-50 years. In a study conducted at West Bengal study maximal prevalence was in the older age group > 60 years (1.5%) (Chowdhary et al., 2003). The prevalence seems to enhance with age either because of the continuing risks of exposure or due to a cohort effect, with a decline in risk in recent times. The high prevalence in the older age group, may be due to late diagnosis and lack of knowledge in the earlier decades.

Both HIV and HCV infection share the same routes of transmission and thus its co-infection is common. In the current study a low prevalence of only 0.79% was reported of HIV- HCV co-infection. The occurrence of HCV in HIV patients has been very erratic. Two studies from Lucknow (1.61%) and Chennai (2.2%) showed fairly low rates of co-infection respectively. (Saravanan et al 2007; Tripathi et al 2007). Both these studies were done in patients with low incidence of IV drug use. However, a report from Imphal studied co-infection of HIV and HCV in injecting IV drug users and found a very high rate of 52.4% (Devi et al 2005). Another study was based in a STD clinic and showed that the seroprevalence of HCV in HIV positive individuals was 21.4% (Bhattacharya et al 2003). The HIV epidemic in India is fast reaching gigantic magnitude. It is estimated that India has 2.5 million of people living with HIV infection (Cohen 2007). Hepatitis C infection is expected to ride piggy-back on the HIV epidemic and is bound to be a major cause of morbidity in India.

Conclusion
HCV continues to cause substantial morbidity and mortality worldwide, and transmission continues unabated in many countries. Control of HCV infection requires a comprehensive approach that incorporates primary prevention of transmission through enhanced infection control and injection safety in healthcare settings and in the community, universal screening of blood and blood products, harm reduction programs, and increased public awareness about risk factors for HCV infection. For the 130–170 million persons already infected, newer, more effective therapies are available. However, lack of access to screening, care, and treatment limit the use of these therapies for most persons living with HCV infection globally, and deaths from preventable cirrhosis and liver cancer continue to increase. Governments need to address viral hepatitis comprehensively by improving surveillance, prevention, care, and treatment. Healthcare providers must be mindful of the global lumber and epidemiology of HCV infection and pursue current screening care and treatment recommendations.

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