



Original article

Association of blood groups with hepatitis C viremia

Mahnour^a, Mamoona Noreen^{a,*}, Muhammad Imran^b, Sher Zaman Safi^c,
Muhammad Amjad Bashir^d, Afrah Fahad Alkhuriji^e, Suliman Yousef Alomar^e, Hanan Mualla Alharbi^e

^a Department of Zoology, The Women University Multan, Multan, Pakistan

^b Department of Microbiology, University of Health Sciences, Lahore, Pakistan

^c Interdisciplinary Research Center in Biomedical Materials (IRCBM), COMSATS Institute of Information Technology, Lahore, Pakistan

^d Department of Plant Protection faculty of Agricultural Sciences Ghazi University Dera Ghazi Khan Punjab, Pakistan

^e Department of Zoology, College of Science, King Saud University, Riyadh, Saudi Arabia



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ABSTRACT

Hepatitis C virus remained a public health problem with approximately half of the patients untreated and undiagnosed. Chronic HCV is a leading cause of cirrhosis, fibrosis, hepatocellular carcinoma and other hepatic morbidities. Active HCV has a prevalence rate of about 1% (71 million). By July, 2019, 10 million population of Pakistan was declared to have active HCV infection. According to World Health Organization, 23,720 people died of hepatitis-related complexities in Pakistan in 2016. Individuals with certain types of ABO blood groups were more susceptible to diverse kinds of infections. For instance, blood types A and AB predisposed individuals to severe malaria, while type O conferred resistance to the many of the protozoan agent.

This study was designed to explore the association of hepatitis C viremia to blood groups, Rh factors, age and gender distribution among Pakistani population. Total 246 participants were screened for HCV in Taqwa diagnostics laboratory, Multan and 200 were found positive. They were divided into 4 groups on the basis of their age. First group included patients ranging from 17 to 25 (52), second, third and fourth group included patients from 26 to 34 (92), 35 to 43 (42) and 44 to above (14) respectively. Confirmed Hepatitis C patients were subjected to analysis of blood group, Rh factor and viral load. Results demonstrated that patients having 'O' blood group (60.37%) were reported for high viral load than any of the other blood groups in the patients of Southern Punjab, Pakistan. Furthermore, Rh-negative factor (26.42) was associated with high viral load than that of the Rh-positive factor (73.58). Disclosure practiced that age group (26–34) was reported for the high viral load than that of the any other group of this study. Females were more aggressively affected by HCV Viremia than male because the mean viral load among the females was higher than that of the males. Greater social awareness and gender-sensitive healthcare is necessary to improve the experiences of patients with HCV.

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1. Introduction

Hepatitis C virus (HCV), which belongs to *Flaviviridae* family is a hepatotropic, enveloped, positive-sense single-stranded RNA virus and it is the leading cause of liver diseases and chronic hepatitis globally (Dubuisson and Cosset 2014, Simmonds et al. 2017). For

the very first time HCV was identified in 1989 (Lindenbach and Rice 2013). In HCV, single open reading frame encodes a polyprotein of ~3000 amino acids. It is cleaved into 10 proteins namely the viroporin p7, core, envelope glycoproteins E1 and E2, and the nonstructural proteins such as NS2, NS3, NS4A, NS4B, NS5A and NS5B (Gottwein and Bukh 2008, Bartenschlager et al. 2013, Scheel and Rice 2013). Budding into the endoplasmic reticulum forms the particles of nascent HCV, these particles then fuse with the pre forms of very low-density lipoprotein (VLDL) particles. Thus, forming lipo-viro particles (LVPs) (Lindenbach and Rice 2013, Scheel and Rice 2013). These particles incorporate with (triglycerides (TGs) and cholesterol. Then, they bind to apolipoprotein and form lipoviroproteins (Fukuhara et al. 2015). Endoplasmic reticulum then buds these lipoviroproteins and transport it by

* Corresponding author.

E-mail address: mamoona.noreen@gmail.com (M. Noreen).

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secretory pathway (Lindenbach and Rice 2013, Scheel and Rice 2013). HCV is a blood born pathogen, 62–79 million persons in the world have become victim of this virus (Stanaway et al. 2016, Organization 2017). HCV is the leading cause of morbidities such as liver cancer, fibrosis and cirrhosis. This virus places a strain on our modern healthcare structure (Anwar, 2016; Bouvard et al., 2009; Lauer and Walker, 2001; Rosen and Martin, 2000; Organization, 2017). There are two types of this infection; Acute HCV infection and Chronic HCV infection. About 20–25% of patients face acute infection and about 15% of these infected patients develop symptomatic liver diseases (Maheshwari et al. 2008). About 75–85% of the patients facing persistent acute infection, lead to chronic HCV infection and approximately 10–20% of chronic HCV patients are progressed to hepatic cirrhosis, of which 1–5% develop hepatocellular carcinoma (Taherkhani and Farshadpour 2015).

71 million people are facing chronic infection across the globe. The world faces approximately 2 million new infections annually (McHutchison et al. 1998, Fried et al. 2002). In 2015, 1.75 million HCV infections were reported in the world (Global incidence: 23.7 per 100,000 persons) (Organization 2017, Polaris Observatory 2017). In Pakistan, 1 person in every 20 is its victim (Al Kanaani et al., 2018; Ayoub et al., 2018), Pakistan is second largest victim of HCV infection worldwide (Qureshi et al. 2010). Although the prevalence of HCV is being reduced in the 21st century as compared to the 20th century (Thrift et al. 2017). World Health Organization (WHO) has set the goals towards global elimination of HCV infection by 2030 (World Health 2016, Duffell et al. 2017). At national and regional levels, the WHO is considering analytical characterization of HCV epidemiology in Pakistan. Cost effective, targeted precautions and best treatment strategies are its major goals. Over a decade ago, only one population-based survey was conducted at national level (Qureshi et al. 2010). Association of blood groups with the pancreatic, gastric and the epithelial ovarian cancer was estimated (Vioque and Walker 1991, Edgren et al. 2010, Risch et al. 2013). Possible link between ABO blood group system and hepatocellular carcinoma was established. The distribution of ABO blood group system effects the frequency of that particular disease within the population and its resistance to that disease (Vogel and Strobel 1960, Bhattacharya et al. 1978). Distribution of ABO blood group system was largely studied in the infectious diseases. Studies demonstrated that bacterial, parasitological and viral infections are somewhat associated with blood groups (Lenka et al. 1981). In the case of chronic hepatitis C infection, severity of liver fibrosis is blood group associated (Poujol-Robert et al. 2006). Whether the statistical analysis support or not, there is increasing trend that ABO blood group system play biological role (Garratty 1994, Garratty 2000). Thus we aimed to explore the possible association of hepatitis C viremia to blood groups, Rh factors, age and gender distribution among Pakistani population.

2. Materials and methods

2.1. Collection of samples

This study was approved by ethical committee of The Women University, Multan. A consent form was filled by the patient to allow the research conducted on their blood samples. Total 246 participants were screened for HCV in Taqwa diagnostics laboratory, Multan and 200 patients were medically diagnosed to be positive for HCV. The natural history of these patients was recorded in terms of demographic variables.

2.2. Blood typing

Transparent slides were taken and three points were marked named A, B and Rh to that slide. Three drops of patients' blood were put separately at the marks. Anti A monoclonal blood grouping antisera (Cat No. ABO /005 Bridport, Dorset) was added to the first drop, anti B monoclonal blood grouping antisera (Cat No. ABO/020R Bridport, Dorset) to second drop and anti D monoclonal antibodies (Cat No.005 Bridport, Dorset) to the third drop of blood. Mixing allowed it to coagulate. It took 10 min to show reaction. By considering agglutination, all the blood samples were analyzed for their ABO blood group distribution. Third drop of blood was taken for Rh factor determination.

2.3. Serological assay for the detection of HCV

3 ml of patient's blood sample in a serum separating gel tube (5 ml) was taken and allowed to coagulate for 10 min. After coagulation the blood sample was centrifuged by using centrifuge machine (Thermo Lindberg Blue M Demos, China) for 10–15 min. Bob transfer pipette was used to suck supernatant to the transparent cups (500 µl). This supernatant was serum extracted from the venous blood of the patient. Patients ID was mentioned to each cup containing extracted serum. A commercially available Mindray kit (DEIA015, Shenzhen and Nanjing, China) of antibody to HCV (CLIA) was used in the fully automatic Mindray analyzer (CL900i, Shenzhen and Nanjing, China) to detect the presence of HCV in the patient's serum. Following the instructions of the manufacturers, reagents were loaded. Program was selected. And the samples, ID and positions were checked before the name of the patient. After selecting particular program samples were placed to the particular slot given in that analyzer. Serum cups (500 µl) were placed one by one. 50 serum samples were loaded at a time. The system attached to that immunoassay analyzer started to record the patient's value for the viral load. Results were noted.

2.4. Statistical analysis

Statistical analysis was done to analyze all the variables in the study groups. All the presented data was tabulated and analyzed by Microsoft excel 2010 and IBM SPSS version 1.1. Pie chart and histograms were constructed on SPSS and excel 2010 to profile the relationship of variables.

3. Results

200 Hepatitis C patients attending the outpatient diagnostics were examined for the prevalence of blood groups in the hepatitis C viremic patients and to find any possible association between the occurrence of viral load and the blood groups. Correlation between HCV patients to the age and gender was also assessed. Prevalence of ABO blood group and Rh factor was determined in patients. Among all the patients, blood group A (10%) was found to be least and blood group O (60%) was found to be most frequent (Fig. 1).

Results displayed that range of signal strength was maximum among Rh negative factor than Rh positive factor containing patients (Fig. 2).

200 HCV viremic patients were divided into 4 groups on the basis of their age. Group 1 included patients ranging from 17 to 25. Group 2 included patients ranging from 26 to 34. Group 3 included patients of age ranging from 35 to 43. While the group 4 included patients of age ranging from 44 and above. Results illustrated that group 2 exhibited high range for signal strength than any of the other group. It displayed that high signal strength was witnessed among patients of age group 26 to 34. We also inquire

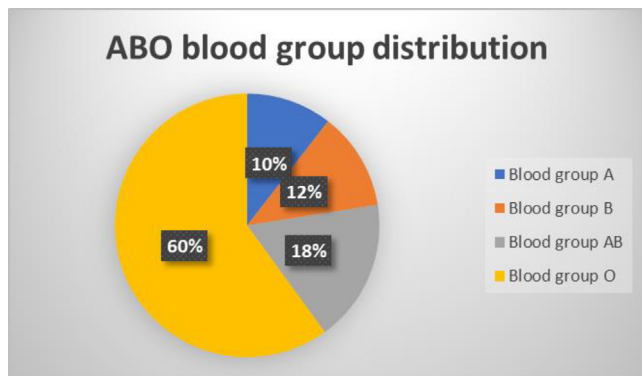


Fig. 1. Blood group distribution among 200 study subjects.

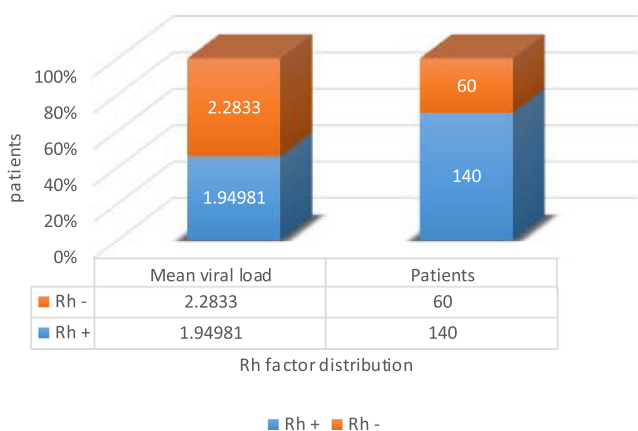


Fig. 2. Distribution of viral load among Hepatitis C patients with different Rh factors.

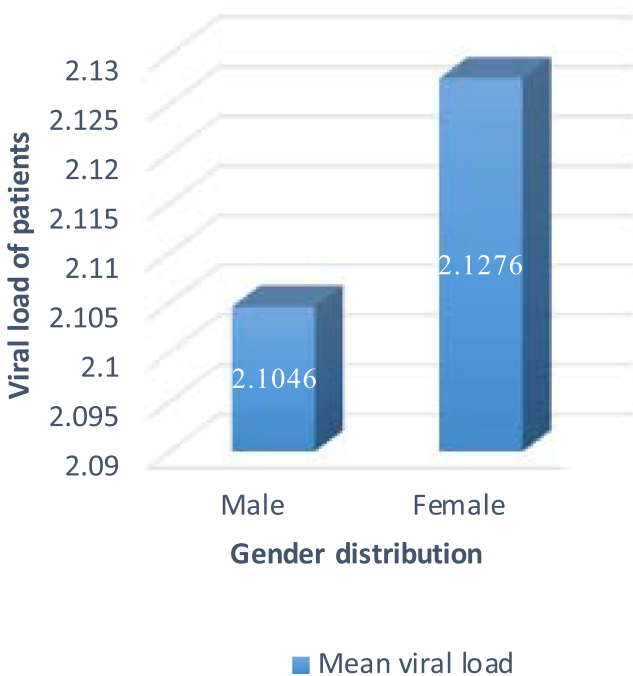


Fig. 3. Viral load among males and female patients of hepatitis C.

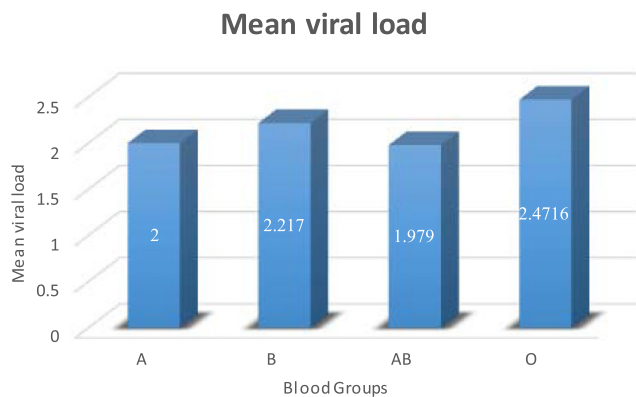


Fig. 4. Viral load among different blood groups of hepatitis C patients.

age and sex as potential factors that may effect on HCV viral load in two subjected groups. 26–34 age group was the most prevalent age range in HCV infected patients with frequency greater than 50%.

A correlation between the viral loads and the patients' gender was also analyzed. Results demonstrated that mean signal strength was slightly higher among females than males. The female gender was found to be a risk factor for sustaining higher levels of the virus than male. The mean viral load among male subjects was 2.10 log₁₀ IU/ml compared to 2.13 log₁₀ IU/ml among female patients (Fig. 3).

Current study revealed that viral load was highest among patients of 'O' blood group than any of the other blood group. Patients having blood group "O" showed higher mean viral loads, which was 2.47 log₁₀ IU/ml. Patients having blood group 'A', 'B' and 'AB' showed 2, 2.22 and 1.989 respectively. These results indicated that male patients having blood groups 'A', 'B' and 'AB' were more likely to have lower viral loads of HCV (Fig. 4).

4. Discussion

Chronic hepatitis C (CHC) is a leading cause of fibrosis, cirrhosis, hepatocellular carcinoma and other hepatic morbidities (Akram, 2017). Plenty of medical research is being done to find the correlation of ABO blood group system to the any of the medical disorder regarding the health of the general population. In China, an association between ABO blood type and HCC risk was found in CHC patients. The results of their hospital-based case-control study revealed a significantly increased risk for development of HCC in Chinese CHC patients with blood type A compared to that in Chinese CHC patients with blood type O, as these were reported for pancreatic, gastric and epithelial ovarian cancers (Vioque and Walker 1991, Edgren et al. 2010, Risch et al. 2013). In India, 20,000 random blood donors were screened for HCV status and were correlated with individual demographics such as sex, age and blood group. The study showed 0.34% anti-HCV seropositivity in healthy blood donors which was in accordance with previous reports from North India (ranging from 0.3% to 5.1%). (Choudhury et al. 1995, Makroo et al. 1999, Jain et al. 2003).

There have been immense researches done to correlate ABO blood group system to the blood born viral and other infectious diseases. Around a single country, there are marked differences in the distribution of ABO blood group system. Demographic variables (age and gender) and blood group types were determined to find correlation with the viral load of the hepatitis C patients. Our results showed that blood group 'O' was strongly associated with the HCV viremia (Fig. 1). Association of viral load with the Rh factor suggests that high viral load was associated with the Rh factor of the patients. Negative Rh factor was strongly associated with the

maximum range of signal strength than the positive Rh factor, which showed maximum frequency of HCV patients. More Rh-positive patients were seen with persistent HCV, but their signal strength was lower than the Rh negative factor. Rh negative patients were less prone to HCV infection but they displayed maximum range for signal strength. There were 140 (70%) HCV patients with Rh positive blood group and 60 (30%) HCV patients were Rh negative. There were 28 (14%) male HCV patients of Rh-negative blood group and 78 (39%) were Rh positive. In the case of female population, there were 32 (16%) patients having Rh negative blood group and 62 (31%) patients with Rh positive blood group (Fig. 2).

Age factor was also another determining factor in this study. Results suggested that middle aged population was largely infected with this infectious virus than that of the young population. High incidence rate for HCV infection was seen among the patients of age 26–34 years. Very low incidence rate was seen among patients of age above 50. But the average incidence rate was seen among the patients ranging from 17 to 25 years of age. There was age specific incidence rate among the study population. Two factors could demonstrate this fact. As patients with high HCV viral load would meet their death before reaching to this age or there is greater susceptibility for the middle-aged population to become its victim.

Greater incidence rate among males could be clearly seen from the data as 106 (53%) of the infected patients were male. While 94 (47%) patients were female, which portrayed that male members were more susceptible towards HCV viremia than the female patients. Gender specification is another contributing factor towards HCV susceptibility. Sharing of same syringe among drug addicted community also became its contributing factor for the enhanced transmission of this virus among male population than the female population. Results demonstrated that female exhibited maximum signal strength than the male population (Fig. 3).

ABO blood group system showed the positive correlation with the viral load of the patient. There were total 121 (60.5%) HCV patients with blood group 'O' in this data set. 34 (17%) HCV patients were seen with 'AB' blood group. While 21 (10.5%) and 24 (12%) HCV patients had blood group 'A' and 'B' respectively. Statistical analysis also illustrated the significant value among the blood groups and the viral load of the patients. Graphical demonstration also threw light on the strong association of blood group 'O' to the viral load of the patient. While patients of 'A' and 'B' blood group demonstrated mean signal strength of 2 and 2.17 respectively. 'AB' blood group demonstrated mean signal strength of 1.97 (Fig.4). In this study, the relationship of HCV viremia with gender (male and female), Rh factor (Rh positive or Rh negative), age and the ABO blood group system is investigated. Higher signal strength had a positive correlation with the ABO blood group system.

Thus ABO blood group system suggested contributing role of blood group system in the case of HCV viremia. Present study strongly correlates the role of blood group to the viral load of the patients.

We found that the risk of hepatitis C viremia in Pakistan is associated with the patient's ABO blood type and Rh factor. Furthermore, we found that HCV patients with blood type O are more susceptible to high viral load than patients with other blood types.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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