PREVALENCE OF VARIOUS HCV GENOTYPES IN HEPATITIS C PATIENTS ATTENDING HAYATABAD MEDICAL COMPLEX PESHAWAR FOR ANTIVIRAL TREATMENT.

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ABSTRACT

Objective: To know the frequency of various HCV genotypes in our local set up.

Subjects and Methods: This study comprising of 92 patients was carried out in OPD of gastroenterology unit HMC Peshawar from November 2013 to March 2015. Patient age more than 17 years, both genders, treatment experienced patients with normal hematologic and radiological parameters were included in the study. Patients age more than 70 years, with uncontrolled depressive and other medical illness, pregnant ladies, treatment naïve patients and decompensated cirrhotics were excluded from the study. Patients were evaluated for treatment with pegylated and ribavirin by history, clinical examination, routine laboratory investigations, ultrasound abdomen, HCV genotyping and upper GI endoscopy where considered necessary. Patients who fulfilled the inclusion criteria were included in the study.

Results: Total of 92 patients, 46(50.0%) male and 46(50.0%) female were included in this study. The mean age was 40.57±9.60 with minimum age of 18 years and maximum age of 60 years. Genotype 3a was the most frequent genotype, present in 54 (58.69%) patients followed by untypeable genotype which was present in 24(28.7%) patients and genotype 2a was present in 4(4.34%)

Conclusion: Genotype 3a is the most frequently occurring genotype in our local set up patients followed by untypeable genotype.

Keywords: HCV, Genotype, Interferon, structural protein, non-structural proteins.

INTRODUCTION

HCV infection is among life threatening public health problems worldwide, with over 170–200 million infected people[1]including about 17 million from Pakistan[2]. HCV is considered the leading cause of liver cirrhosis and hepatocellular carcinoma. It has been estimated to cause approximately 27% of cirrhosis and 25% of hepatocellular carcinoma cases worldwide[3]. Each year about 350,000 people die due to HCV[4].

HCV is a small enveloped, positive sense single stranded RNA virus and has been classified as a separate genushepacivirus in the Flaviviridae family[5]. The HCV genome is approximately 9.6 kb, encoding a polyprotein of about 3010 amino acids and is flanked by short untranslated regions at the 5′ and 3′ terminus [6]. This polyprotein is posttranslationally processed by viral and cellular proteins to generate the structural proteins (C, E1, E2, and p7) and nonstructural proteins (NS2, NS3, NS4A, NS4B, NS5A, and NS5B)[7].

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HCV shows high degree of genetic heterogeneity; consequently six major genotypes and multiple subtypes of HCV have been identified so far in world[8]. Distribution of HCV genotypes and subtypes in different regions of the world is variable. The common subtypes found in North and South America, Europe, Russia, China, Japan, Australia, and New Zealand are 1a, 1b, 2a, 2c, and 3a[3]. Genotype 4 is predominant in Egypt, North Africa, Central Africa, and Middle East[9]. Genotype 5 in South Africa[10] and genotype 6 in Southeast Asia[11] have been identified. Genotype 3 is the most prevalent genotype in India, Bangladesh, Pakistan, and Nepal[12-15]. Subtypes of genotypes 1, 2, 3, and 6 have been found prevalent in Thailand[16], Vietnam, Indonesia, and Burma[1] respectively. Genotype 1b is the most prevalent genotype in China; however genotype 2 has also been reported from some regions of China[1].

In Pakistan, the prevalence of HCV infection has been estimated to be 8% and is increasing gradually due to deficiency in basic health care resourses and lack of the general public awareness about safety measures[8].

Until 2011, the combination of pegylated interferon-alpha and ribavirin was the approved and effective therapeutic regimen for infection with hepatitis C virus, which yields sustained virologic response (SVR) in up to 56% of patients in genotype 1[17,18], and 70 to 80% in genotype 2 and 3, but the treatment is now changing with development of oral protease and polymerase inhibitors

to only oral antiviral which are more effective, having less hematological and no neuropsychiatric adverse effects and can even be given in decompensated cirrhosis as well and some of which are now also available in Pakistan for the treatment of hepatitis C. The primary goal of HCV therapy is to cure the infection, which is generally associated with resolution of liver disease in patients without cirrhosis. Patients with cirrhosis remain at risk of life threatening complications, albeit at a lower rate, even after viral infection has been eradicated.

The main purpose of this study was to find out baseline information on the prevalence of HCV genotypes in our local set-up because accurate HCV genotyping can be used in better understanding of HCV infection, for creating awareness in the general public and subsequently for implementation of preventive and therapeutic strategies for Chronic hepatitis C infection.

SUBJECTS AND METHODS

This cross sectional descriptive study comprising of 92 patients was carried out in the Out-patients Department of Gastroenterology Unit Hayatabad Medical Complex Peshawar from November 2013 to March 2015 on those chronic HCV patients who visited our OPD for free pegylated interferon. Patients of age more than 17 years, both male and female gender, previously treatment experienced patients either non-responders or relapsers and with normal hematologic and radiological parameters were included in the study. Patients age more than 70 years, patients with uncontrolled depressive and other medical illnesses, pregnant ladies, treatment naïve patients and decompensated cirrhotics were excluded from the study. Informed consent was taken from all patients and were evaluated for treatment with pegylated interferons and ribavirin by taking detailed history, clinical examination, routine laboratory investigations including FBC, liver enzymes, liver synthetic function tests, renal function tests ,blood glucose level, ultrasound abdomen, and upper GI endoscopy where considered necessary and besides this, blood samples were also sent for HCV genotyping. All those patients who fulfil the inclusion criteria and gave consent were included in the study. Patients were started on pegylated interferon-alpha 2a 180ug subcutaneously once a week with oral ribavirin 800mg in two daily divided doses for genotype 2, 3 and untypeable and 1200mg in three daily divided for genotype 1. Though our main aim in this study was to know the frequency of various genotypes in HCV patients, so besides knowing the genotypes the patients were followed in the treatment duration for any side effect of treatment and treated accordingly if occurred. After completion of the study, data was analyzed by using statistical software (SPSS version 10). Mean±SD was calculated for continuous variables like age and Frequencies were calculated for categorical variables genotype.

RESULTS

Total of 92 patients were included in this study. Out of 92 patients 46 (50.0%) were male and 46 (50.0%) were female with a male to female ratio of 1:1 (Table 1). The mean age was 39.05±8.54.The minimum age in this study was 18 years and the maximum age was 60 years. Majority of the patients, 52 (56.52%) were in the age range 31-45 followed by age range 46-60 having 22 (23.91%) patients (Table 1I).

Genotype 3a was the most frequently occurring genotype in our study which was present in 54 (58.69%) patients followed by untypeable genotype which was present in 24(28.7%) patients and genotype 2a was present in 4(4.34%) while genotype2b, 1a and mixed type genotype was the least frequent genotypes each of which was present in 2(2.17%)) patients in our study (Table (Table III).

Table No 1: Distribution of patients according to gender

Gender	No.	%
Male	46	50
Female	46	50

Table No 2: Distribution of patients according to age

Age	No.	%
18 – 30	18	19.56
31 - 45	52	56.52
46 - 60	22	23.91
Mean±SD	40.57±9.60	

Table No 3: Distribution of patients according to genotype

Genotype	No.	%
Genotype 1a	2	2.17
Genotype 2a	4	4.34
Genotype 2b	2	2.17
Genotype 3a	54	58.69
Genotype 3b	10	10.86
Genotype unbeatable	24	28.7
Mixed	2	2.17

DISCUSSION

The molecular epidemiological studies have reported that significant regional differences appear to be present in the frequency distribution of HCV genotypes. Moreover, determination of HCV genotypes in geographically diverse regions facilitates therapeutic decisions and preventive strategies[19]. It has been

reported that there are variations in disease outcome and response to antiviral therapy of HCV genotypes[20]. However, in Pakistan treatment of HCV infected patients is based on qualitative or quantitative viral detection and genotypes are usually not determined prior to treatment. Therefore variable response rates of HCV infected patients to antiviral therapy cannot be detected. The present study was conducted to determine baseline data on the prevalence of HCV genotypes in chronic HCV patients attending the out-patients department of Hayatabad Medical complex peshawar Khyber Pakhtunkhwa and this baseline information will be utilized in the better understanding of HCV infection, awareness in the general public and subsequent control and treatment strategies.

The distribution of HCV genotypes was found variable among studied patients. The genotype 3a was found to be the most prevalent genotype followed by 3b and 2a while genotype 1a and mixed type was found to be less prevalent (table.III). Results of the present study are in conformity with results of previous studies reported from different cities of Pakistan like study done by afridi et al in Mardan[21], Shamin Saleha et al in Bannu[22] and by Idress M[23] in Lahore, which means that HCV genotype 3a is the most prevalent genotype in the chronic HCV patients attending our out-patients department for HCV treatment, but our study was showing different genotype distribution to the study done by Sajid ali et al[24] in peshawar in which Genotype 2a was the most prevalent HCV genotype and this need a large province based study to know about the exact genotype distribution. Our study was also showing similiar results to the studies conducted previously in India, Bangladesh, and Nepal where genotype 3 was also the most prevalent genotype[12-14]. Howeve in our study the assay used could not determine HCV genotypes among a considerable number of HCV patients 24 (28.7%) and similarly untypeable genotypes have previously been also reported in another study conducted in Pakistan[24]. So, there is a need to use more reliable and sensitive assay for genotyping of HCV and more studies are needed to further clarify the distribution of untypeable genotype in our local set up.

In conclusion Genotype 3a is the most frequently occurring genotype in the chronic HCV patients attending the outpatients department of HMC for management, while a significant no of patients is also having untypeable genotype ,so a large province based study is needed to know about the exact distribution of various HCV genotypes.

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