ORIGINAL ARTICLE

Detection of Frequency of Hepatitis C Patients with Fatty Liver and Impact of Interferon on Fatty Liver Improvement

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ABSTRACT

Background: Hepatitis C virus (HCV) infection is one of the most common causes of chronic liver disease affecting approximately 130 million individuals worldwide, with 20% of these patients potentially progressing to cirrhosis. Currently, standard treatment includes a combination of pegylated interferon and ribavirin with a sustained viral eradication rate of 55%.

Aim: To determine the frequency of fatty liver in patients with chronic hepatitis C and also to determine the proportion of subjects with the clearance of fatty liver with standard interferon treatment.

Methods: A total of 120 patients were included in this study. Interferon and ribavirin combination therapy was started in the dose of 3 million units subcutaneously thrice a week and 400mg orally thrice a day respectively. Ultrasonography was carried out to differentiate the grades of fatty liver.

Results: Mean age of the patients was 36.9±5.0 years. Out of 120 patients, 49.2% were male and 50.8% were female. Fatty liver was noted in 68 patients (56.7%). Out of these 68 patients, 31 (45.6%) showed grade-II fatty liver and 37 (54.4%) had grade-III fatty liver. Post-treatment fatty liver grades were as follows: 4 patients (5.9%) of grade-I, 36 patient (53.0%) of grade-II, 9 patients (13.2%) of grade-III while clearance of fatty liver was observed in 19 patients (27.9%).

Conclusion: It was found that 56.7% of patients with chronic hepatitis C had fatty liver. Patients with hepatic stetosis were more frequently obese and had more severe hepatic fibrosis. Fatty liver clearance was found to be in 27.9% of patients after combination therapy.

Keywords: Hepatitis C, Fatty liver, Pegylated interferon, Stetosis

INTRODUCTION

The hepatitis C virus (HCV) is theforemost contributor of chronic liver disease and main public health concern issue.It is assessed about 180 million population is influenced worldwide[1]. HCVremained the prime source of deathsdue to liver disease and the important indicator for liver transplantation[2]. Some researchreports and data demonstrated the serious mortality rates due to HCV infection and it is documented as a significant factor for public health issue in Pakistani settings[3]. Hepatitis C is also considered as main cause of hepatitis including, acute hepatitis and chronic liver disease, cirrhosis and hepatic carcinoma. It is estimated that about 3-4 million people are newly infected each year[4].

Most recently, therapy of Pegylated interferon-γ (Peg-interferon-γ) combination with ribavirin is being used as a standard treatment for hepatitis C infection. It is observed that this combination is more alleviating to the patients with HCV genotype 2 and 3 infections with success rates of 75% and 90% respectively. However, the current combination therapy is not much effective for genotype 1 and 4 infections, showing frequency only 45% to 52% respectively [5]. This might be due to vast diversity in viral and host response. Antiviral response actually depends on HCV genotype and the pre-treatment viral load which is more for genotype 2 and 3 than for genotype 1. In Pakistan, the most common HCV genotype is 3a and the combination therapy is highly effective for genotype 3a[6].

Nonalcoholic fatty liver disease (NAFLD) is a type of fatty liver which is more evident in chronic hepatitis C patients showing 40% to 85%[5]. The connection of fatty liver and chronic hepatitis is due to the contribution of host and viral factors[7]. In fatty liver, in infection liable cells, the core protein of virus makes link with lipid droplets surface which results in virus-induced stetosis.Thisinvolves the triglycerides stacking in the liver and ameliorate the development of fibrosis in chronic hepatitis C patients. Various clinical investigationsshowed that virus-induced stetosis is considerably more severe in HCV genotype-3 patients rather than other[8].

In NAFLD, genotpye-3 is the only subtype revealed to be associated to a higher grade of stetosis without involvement of any other host-related

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factors. In these fatty liver patients, the severity of stetosis is mainly evident with viral load ofHCV-RNA. It has also been proposed that HCV genotype 3 may also lead to stetosis by haltingthe secretion of triglycerides.Certainly, antiviral treatment is responsive to viremia which ultimately subsides the stetosis[9].

Previously, large number of reports highlighted the reduction of stetosis from 13% to 48% in enrolled patients for treatment. Apparently, there is no large scale study carry out to define the clearance of fatty liver/stetosis by interferon and ribavirin combination therapy[10].

The present study was to assess the rate of incidence of fatty liver in individuals with chronic hepatitis C (genotype 3) in Pakistani population. According to the published data, there are no reports about the frequency of fatty liver in chronic hepatitis patients and the efficacy of Pegylated interferon to resolve and clear the fatty liver pattern. If the frequency is found high, treatment with interferon could be initiated to prevent long term complication of fatty liver like non-alcoholic stetotic hepatitis which could have added effects on disease progression.

SUBJECTS AND METHODS

Prior to start of the study, ethical approval was obtained from Services Institute of Medical Sciences, Lahore, Pakistan.

Study population: A total of 120 patients of chronic hepatitis C were investigated for this study. Patients with age group of 30-60 years with PCR diagnosed HCV positive and have to receive HCV therapy without any complications were selected for analysis. Patients with history of other liver injuries, hepatitis or hypertension and receiving interferon therapy were not taken. The population included was statistically calculated bykeeping confidence level 95%, error chance 6% and interferon induced stetosis clearance by taking expected percentage in genotype 3 and13% dropout rate.

Data collection: All the patients were enrolled according to the inclusion criteria aftertaking written informed consent and are registered atHepatitis clinic of Services Hospital, Lahore, Pakistan. The frequency of fatty liver was documented by Ultrasonography which was done by a single radiologist in every registered chronic hepatitis patient. After that, combination of Peg-interferon and ribavirin therapy was initiated with the dose of 3 million units subcutaneously thrice a week of Peg-interferon and ribavirin 400mg taking orally thrice a day. Ultrasonography was done after week 6 and 12 of the start of therapy and then finally at the completion of treatment after 24 weeks. Presence or absence of stetosis was documented on ultasonographic features of liver.

Statistical analysis was carried out by using SPSS version 16. Quantitative variable like age was given Mean±S.D, while qualitative variables were given as percentage variation and variable frequencies. Data was grouped for age (group-1, 30-45 years) and (group-2, 46-60 years) and by grading fatty liver (I, II, III) to address effect modifiers.

RESULTS

In present study, total 120 patients with chronic hepatitis C were selected for analysis. For age distribution, they were divided in to two groups. Out of total 120 patients, 112 patients (93.3%) were 30-45 years while 8 patients (6.7%) were 46-60 years of age. Mean age of the patients was 36.9±5.0 years. On the basis of gender distribution female cases (50.8%) were more than male patients 49.2%. From total patients, 68 patients were demonstrated for fatty liver and grad-III fatty liver was present in higher percentage (Table 1).

Table 1 Frequency of different parameters in cases with chronic hepatitis C

Parameters	n	%age
Age in years		
30-45	112	93.3
46-60	08	6.7
Gender		
Male	59	49.2
Female	61	50.8
Fatty liver		
Yes	68	56.7
No	52	43.3
Fatty liver grades		
Grade-II	31	45.6
Grade-III	37	54.4

Table 2: Distribution of Fatty liver grades with different time duration in chronic hepatitis C cases

Parameters	n	%age
Fatty Liver Grades at 6 weeks of treatment		
Grade-I	09	13.2
Grade-II	47	69.2
Grade-III	12	17.6
Fatty Liver Grades at 12 weeks of treatment		
Grade-I	24	35.3
Grade-II	32	47.1
Grade-III	12	17.6

After starting of interferon and ribavirin treatment, grades of Fatty liver were noted at 6 weeks and at 12 weeks. There were 9 cases of grade-I after 6 weeks of treatment while 24 cases of grade-I after 12 weeks of treatment. This shows that there is continuous improvement in fatty liver after the

interferon and ribavirin treatment (Table-2).Post-treatment fatty liver grades were as follows: 4 patients (5.9%) of grade-I, 36 patient (53%) of grade-II, and 9 patients (13.2%) of grade-III while clearance of fatty liver was observed in 19 patients (27.9%) (Table 3).

Table-3: Post-treatment effects on fatty liver

Parameters	n	%age
Post-treatment fatty liver grades		
Grade-I	04	5.9
Grade-II	36	53.0
Grade-III	09	13.2
Clearance of fatty liver after treatment		
Yes	19	27.9
No	49	72.1

DISCUSSION

In chronic hepatitis C, stetosis is a histological feature in patients and harmfullyinfluences the virologic response rates to anti-HCV therapy [11].Fatty liver is a condition in which fat builds up in the liver cells. It is not known exactly what causes the liver to accumulate fat, but predisposing factors include diabetes, high triglycerides and alcohol abuse. A fatty liver is common, and often causes no symptoms. Some symptoms may include fatigue, abdominal pain or weight loss. Some people can live with a fatty liver without complications, but in some cases it can cause inflammation and scarring[12].

It is obvious that gold standard diagnosis of fatty liver remains histological evaluation of liver. Ultrasonography can detect moderate-to-severe fatty changes in the liver and its sensitivity increases with optimal (at least 33%)stetosis[13]. Indeed, low sensitivity of ultrasonography indicated less prevalence of fatty liver.Usually, patients affected with HCV genotype 3 have a higher rates of liver stetosis than other genotypes.

Castera et al., (2003)noted that fatty liver was noted in 54% CHC patients and the prevalence of fatty liver in present report was only 56.7% which is comparable with the study by Castera[14]. In another report, it was noted significantly increased prevalence of fatty liver patients with HCV genotype 3 in comparison to other genotypes, which consequently indorse the association of HCV genotype 3 with fatty liver in chronic hepatitis individuals[15].. Previously, fatty liver progression has been documented in viral load (HCV genotype and core protein) and in host factors like metabolic syndrome. In present study, we excluded the predisposing factors of metabolic syndrome including insulin resistance, obesity, type 2 diabetes mellitus, hyperlipidemia, and hypertension.

In 1998, a 'two-hit' hypothesis was anticipated to explicate the pathogenesis of fatty liver, established on prevailing human and animal studies [16]. The first hit was reflected to insulin resistance (IR) which is due to predisposition of genetic variations that lead to developmentof obesity and resistance. In complex biological cascades, hyper-insulinemia and resistance augmented peripheral lipolysis with transport of free fatty acids to the liver and raised endogenous hepatic synthesis of fatty acids ultimately appears to decrease mitochondrial β-oxidation of fatty acids and VLDL synthesis and secretion[17]. Finally, IR (first 'hit') increase the liability to the liver for oxidative stress (second 'hit'), which develops liver fibrosis. Hyperinsulinemia may block the interferon-mediated inhibition of HCV replication by interrelating with the interferon-inducible regulatory factors, averting its activation by interferon[18].

In a study, it was observedthat the patients with severe stetosis were more predisposed to have steto-hepatitis. It was suggested that the severity of stetosis can be employed as a substitutetarget in drug development[19]. In future prospective, it might be adopted to assess quantitative stetosis during clinical trials. In present study, baseline grades of stetosis was un-importantly higher in chronic hepatitis patients with substantial fibrosis progression.

For NAFLD studies, it persists the utmost challenge because it is difficult to assess the alcohol consumption in each patient. A study by Hayashi et al (2004) reported that some NAFLD patients actually showed ALD pattern when it was evaluated forentire lifealcohol intake assessment [20]. At present NAFLD is diagnosed on the fat infiltration of liver by excluding the relevant causes. Diagnosis of NAFLD is set with a specific threshold of alcohol consumption. Due to increasing prevalence of NAFLD, it is strongly recommended the modifications of lifestyle to all patients which reduces the risk to type 2 diabetes and also intense dietary intervention might also improve the liver histology[21].

CONCLUSION

It is concluded that frequency of fatty liver was 56.7% in chronic hepatitis C patients. Patients with hepatic stetosis were more frequently obese and had more severe hepatic fibrosis.Pegylatedinterferon and ribavirin combination therapy showed fatty liver clearance in 27.9% of patients.

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