ORIGINAL ARTICLE

FREQUENCY AND SEVERITY OF STEATOSIS IN PATIENTS WITH CHRONIC HEPATITIS-C

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Background: Hepatitis-C viral infection is a global health problem. It has been estimated that approximately 170 million individuals are infected with hepatitis-C virus. Hepatic steatosis is a frequent histological feature in patients with chronic hepatitis-C infection. Histological examinations show that up to 50% of these patients have variable degrees of hepatic steatosis, even in the absence of other possible steatogenic factors like alcohol, drugs or metabolic syndromes. The objective of this study was to determine the frequency and severity of steatosis in patients with Chronic Hepatitis-C. **Methods:** This cross sectional study was carried out from 1st January 2010 to 1st July 2010 at the department of Gastroenterology PIMS, Islamabad. A total of 127 patients of chronic hepatitis-C were enrolled in the study after taking informed written consent. Frequency and severity (mild, moderate and severe) of steatosis was assessed on the basis of liver biopsy. **Results:** A total of 127 patients were included in the study. Mean age of the patients was 36.24 years. Out of 127 patients, 48(38%) were male and 79(62%) were female. Steatosis was present in 50(39%) patients with chronic hepatitis-C infection. whereas steatosis was absent in 77(61%) patients. **Conclusion:** The presence of steatosis on liver biopsy in patients with chronic hepatitis-C is common (39% patients) and female patients had slightly more severe degree of steatosis as compared to male patients.

Keywords: Chronic hepatitis-C, Steatosis, Frequency, Severity

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INTRODUCTION

Hepatitis-C viral (HCV) infection is a global health problem. It has been estimated that 170 million people are chronically infected with HCV and up to 350,000 deaths occur every year due to all HCV-related causes.[1] Unfortunately, HCV infection is not a notifiable disease in Pakistan and there is no national data collection system for evaluation of routine risk factors. It is estimated that approximately ten million people in Pakistan (6% of the population) have been living with HCV infection.[2]

Chronic hepatitis-C (CHC) virus infection is a predominant cause of chronic liver disease in many parts of the world including Pakistan.[3,4] It often presents with the complications of portal hypertension and hepatic failure. The sources of spread include unsafe injections and transfusions, body tattooing and acupuncture.[5] Histological features of chronic hepatitis-C include lymphoid follicles, bile duct injury and fibrosis which may differ in various regions.[6,7] Steatosis (accumulation of macro or micro vesicular intracytoplasmic fat droplets in hepatocytes) as a part of histological feature of chronic hepatitis-C has been described and it correlates with both patient factors (e.g., obesity), as well as viral factors (HCV genotype).[8,9] The degree of steatosis has been linked to the extent of hepatic fibrosis and patients with steatosis and genotype 3 were found to be at risk of accelerated fibrosis. In addition, it has also been noted that steatosis may reduce response to HCV therapy.[10]

The pathophysiology of hepatitis-C related steatosis is still elusive. It is proposed that HCV core protein may be interacting with Apolipoprotein resulting in steatosis. Anther proposed mechanisms is the interaction between the core protein and retinoid X receptor α (RxRα) which is a transcriptional regulator of lipid metabolism. Other theories propose that the core protein induces oxidative stress within the mitochondria contributing to lipid accumulation.[11]

The objective of this study was to determine the frequency and severity of steatosis in patients with chronic hepatitis-C in our setup.

MATERIAL AND METHODS

This cross sectional study was conducted on indoor and outdoor patients of department of Gastroenterology, Pakistan Institute of Medical Sciences (PIMS), Islamabad, from 1st January to 1st July 2010 with patients selected through non-probability consecutive sampling technique. Patients included in the study were of both genders, between 18 and 65 years of age, those having positive serum HCV antibodies, those having HCV-RNA detectable in the serum by qualitative polymerase chain reaction (PCR) and those willing to undergo antiviral therapy.Patients who were excluded were having: clinical or biochemical evidence of decompensated liver disease, diabetes mellitus, hyperlipidaemia, Body Mass Index (BMI) of more than 30, deranged coagulation profile, ingested more than 20 g/day of alcohol within the previous 6 months, autoimmune disorders, uncontrolled depression or psychosis, cardiac disease or any other debilitating

medical condition. Those using any medication known to cause steatosis (corticosteroids, oestrogen, amiodarone, nifedipine, diltiazim), and those who received any kind of treatment for hepatitis-C were also excluded.

All patients diagnosed with chronic hepatitis-C underwent a detailed history taking and physical examination, including age, gender, diabetes mellitus, hypertension, alcohol intake, endocrine disorders, psychosis and use of drugs. BMI was calculated and in addition, liver function tests, coagulation profile, fasting lipid profile and blood sugar levels were also checked.

Patients fulfilling the inclusion criteria were enrolled after taking informed written consent. Under aseptic condition, using 18G lumbar puncture needle liver biopsy was performed. After biopsy patients were retained in the ward in right lateral position for four hours and pulse and blood pressure monitoring was done half hourly. Biopsy specimens were sent in formalin for histopathology. Report on biopsy was given by a consultant histo-pathologist. Steatosis was graded on histopathology as mild (steatosis in <33% of hepatocytes), moderate (steatosis in 33-66% of hepatocytes) and severe (steatosis in >66% of hepatocytes). Data was analysed using SPSS-12.0

RESULTS

A total of 127 patients were included in the study. Mean age was 36.24 ±8.61 years ranging from 18–65 years. There were 48 (38%) were males and 79 (62%) females.

Steatosis was present in 50(39%) patients. Of these, 31 (24%) patients had mild steatosis, 18(14%) had moderate degree of steatosis and only 01(0.8%) had severe degree of steatosis. In the case of males, 18(38%) patients had steatosis whereas in females, 32(40%) patients had steatosis.

Analysis of the severity of steatosis by gender is shown t in table-1. With respect to steatosis in age group 21–30 years, 12, in 31–40 years, 15, in 41–50 years of age group, 18 patients, in 51–60 years, 4, and in 61–70 years of age group, one patient had steatosis.

Table-1: Severity of steatosis by gender

Severity of Steatosis	Gender of the patients		Total
	Male	Female	
No Steatosis	30 (39.0%)	47 (61.0%)	77 (100.0%)
Mild	10 (32.3%)	21 (67.7%)	31 (100.0%)
Moderate	8 (44.4%)	10 (55.6%)	18 (100.0%)
Severe	0 (.0%)	1 (100.0%)	1 (100.0%)
Total	48 (37.8%)	79 (62.2%)	127 (100.0%)

DISCUSSION

Chronic hepatitis-C (CHC) virus infection is a predominant cause of chronic liver disease in Pakistan as in rest of the world.[12,13] Hepatic steatosis, defined as excessive lipid accumulation in the cytoplasm of hepatocytes, is a frequent histological feature in patients with CHC infection.[14,16] Histological examinations show that up to 50% of CHC patients have variable degrees of hepatic steatosis even in the absence of other possible steatogenic factors, like alcohol, drugs or metabolic syndromes.[17]

According to our analysis steatosis was present in 39%. A study by Matos et al reported the prevalence of steatosis as 67%. This difference in the frequency of steatosis in both studies might be due to the severity of the disease, prevalence of predominant age group and genotyping.[18] High frequency was also found in other studies conducted internationally.[19] Hourigan *et al*. observed steatosis in 41% of patients with hepatitis-C.[20] The result of this study is consistent with our study. Same is the case with Carpenter who compared the histological lesions found in hepatitis-B, C and autoimmune hepatitis and observed the predominance of steatosis in hepatitis-C.[21]

Female gender (62%) was more prevalent in our study. This was in contrast to analysis conducted locally showing 57% male and 43% female (Khokhar *et al*).[22] Our study showed slightly increased prevalence of steatosis in female patients as compared to male patients (40% vs. 38%). An association between female gender and the presence of steatosis has also been demonstrated by other investigators.[23,24]

Our analysis showed variable degree of steatosis on liver biopsy. A study conducted locally showed slight different results with 39% patients did not have any steatosis, 32% had mild steatosis, 0.9 % had moderate steatosis, and 28% had severe steatosis. The main cause of difference of steatosis between study populations might be the age difference, most prevalent age group and disease duration. In our study, mean age was 36 years where as mean age in the aforementioned study was 44 years and the disease was in advanced stage so that is why many patients had severe steatosis.

It has been shown that HCV genotype 3 is independently associated with hepatocellular steatosis in patients with chronic hepatitis-C and the severity of steatosis in these patients is directly related to the burden of the HCV RNA load.[25,26] This relationship between the HCV viral load and the magnitude of steatosis was not observed in other HCV genotypes.[27]

The severity of steatosis is also variable among two genders and our analysis showed that females had somewhat more severe steatosis. This might be due to the high BMI and status of the hepatitis-C infection.

Steatosis has been independently associated with advanced fibrosis in chronic HCV

infection.[28] In our study, we did not analyze the relationship between hepatic steatosis and hepatic fibrosis. In another study 80% of the patients who had hepatic fibrosis had steatosis in the past. Another study showed the high prevalence of hepatic steatosis in patients with HCV-HIV co infected patients as compared with only HCV patients (72% vs. 52 %).[29]

CONCLUSION

Steatosis is a frequently encountered histological feature in chronic HCV-infection. Hepatic Steatosis in CHC is slightly more prevalent in female patients as compared to the male patients. Most of our patients belonged to very younger age group as compared to other analyses. Patients with mild degree of steatosis were more prevalent followed by moderate degree of steatosis. Female patients had slightly more severe degree of steatosis as compared to male patients.

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