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FREQUENCY OF STEATOSIS IN CHRONIC HEPATITIS C PATIENTS IN KHYBER PAKHTOONKHWA. A CLINICAL AND HISTOLOGICAL STUDY

Naila Ismail[1], Farrukh Saeed[2], Hamid Hussain[3], Iqbal Mohammad[4], Farida Naseer[1], Fazal Ahmad[5]

[1]Department of Pathology, Khyber Medical College, Peshawar - Pakistan

[2]Department of Gastroenterology, Military Hospital, Rawalpindi - Pakistan

[3]Department of Community Medicine, Khyber Medical College, Peshawar - Pakistan

[4]Department of Pathology, Combined Military Hospital, Peshawar - Pakistan

[5]Department of Histopathology, Rehman Medical College, Peshawar - Pakistan

ABSTRACT

Objective: To assess steatosis histologically and correlate with body mass index in chronic hepatitis C patients.

Material and Methods: This was a prospective observational study conducted at Gastroenterology ward and Department of Pathology at Combined Military Hospital, Peshawar from May 2007 to September 2008. A total of 100 adult patients who were HCV-RNA positive fulfilling the pre-requisites for liver biopsy were admitted. Liver biopsy was performed and analyzed for necroinflammation, fibrosis and steatosis. Steatosis was correlated with BMI by using Chi Square test. P value of 0.05 was considered as significant.

Results: Fifty-four male and 46 female patients between ages of 13 to 70 years were studied. Forty-nine patients (49%) were overweight, 16 (16%) were obese. Twenty-nine (29%) patients showed grade I Steatosis, 8(8%) had grade II and 4 (4%) had grade III Steatosis. Strong correlation was found between Steatosis and BMI (P-value 0.0001). High BMI is strongly associated with females of >35 years of age, P-value 0.0001.

Conclusion: Steatosis is related to higher BMI and together with necroinflammation results in accelerated disease process in chronic hepatitis C patients. Steatosis should always be assessed histologically and included in clinical as well as research analysis.

Keywords: Steatosis, Body mass index, necroinflammation, chronic hepatitis C.

INTRODUCTION

Hepatitis C virus (HCV) is a major cause of chronic liver disease and its complications. One hundred and seventy million people are affected by HCV globally while 3-4 million people are infected every year[1]. Eighty percent of acutely infected individuals develop chronic disease of which 20%-25% progress to cirrhosis and hepatocellular carcinoma (HCC)[2]. In Pakistan, it is estimated that 10 million people i.e. 6% of the population are infected with HCV[3]. According to a number of studies conducted for prevalence of HCV, 14 million Pakistanis are HCV carriers[4]. Effects of HCV on liver are necroinflammation, fibrosis, steatosis and cirrhosis. Mild steatosis is seen as an aging process in obese and elderly. Extensive steatosis is seen in chronic hepatitis C (CHC) patients and is a risk factor for progression of disease[5]. Some data suggest that the pathogenesis of mild steatosis of most HCV infected patients may be metabolic as its severity correlates with body mass index (BMI) whereas only the moderate to severe steatosis typically found in patients with genotype 3 may be HCV related[6]. Thus steatosis observed in chronic hepatitis C is not always virally related as other factors may coexist. This is not surprising considering the frequency of liver steatosis in the general population (15%)[7]. Obesity and higher grades of steatosis are major factors responsible for development of fibrosis[8]. Steatosis in CHC patients is dependent on complex interaction of host and viral factors, like intravenous drug users (IVDU) infected with HCV showed moderate to severe steatosis[9]. In Pakistan, high prevalence of steatosis (65.7%) is seen in CHC patients and more alarming is that it may be a risk factor for HCC[10].

However, steatosis in chronic hepatitis C is almost invariably accompanied by some degree of necroinflammation. Thus steatosis may contribute to liver disease progression either directly or via a

Address for Correspondence:
Dr. Naila Ismail
Assistant Professor,
Pathology Deptartment,
Khyber Medical College, Peshawar - Pakistan
Cell: 0300-5987735
E-mail: drnismail@yahoo.com

synergistic effect with inflammation or other cofactors[11]. It has a negative impact on antiviral therapy along with increasing age[12]. Steatosis is a histological diagnosis and should be detected early and treated appropriately[10]. The objective of our study was to assess the frequency of steatosis in CHC patients and to evaluate the role of BMI in its pathogenesis.

MATERIAL AND METHODS

The study included 100 adult male and female patients who were HCV-RNA positive. The patients were admitted in the Gastroenterology ward fulfilling the criteria for liver biopsy, which included thorough history, physical examination, relevant biochemical and serological tests. Body Mass Index was calculated by recording height and weight. Subjects below 13 years and above 70 years of age with decompensated cirrhosis, diabetes mellitus, hemophilia, HBsAg positive, alcoholics and patients with other concomitant illnesses were excluded from the study.

Percutaneous Liver Biopsy was performed in the ward by trained gastroenterologist fulfilling the pre-requisites for the biopsy. A prebiopsy ulltrasonography for marking the biopsy site, prothrombin time and platelet count were done atleast 24 hours prior to biopsy. Analgesic i.e. aspirin and nonsteroidal anti-inflammatory drugs were stopped atleast 5 days before biopsy. The patient, according to the instructions laid down by the institution duly signed informed consent. Liver biopsy was performed using Modified Menghini needle (18 G). Adequate biopsy sample was obtained and send for histopathological evaluation. All the clinical and histological data were entered in proforma designed for the study. The liver biopsies (H & E, reticulin stained) were studied for necroinflammation, steatosis and fibrosis. Necroinflammation was graded according to Knodell's HAI[13]. Steatosis was graded according to Brunt's classification as grade 0 (<2% hepatocytes affected), grade 1 (3-29% hepatocytes affected), grade 2 (30-59%), grade 3 (>60% hepatocytes affected)[14]. Fibrosis was staged according to Metavir scoring system as: F0 (no fibrosis), F1 (marked portal fibrosis), F2 (occasional bridging fibrosis), F3 (marked bridging fibrosis, portal-portal or portal- central), F4 (incomplete cirrhosis/cirrhosis)[15].

BMI (weight in kg/height in meter^2 was calculated and patients were categorized according to WHO guidelines into normal (BMI 18.5-24.9), overweight (25-29.9), obese (30-39.9), morbidly obese (>40)[16]. The data was analyzed using SPSS version 13.0. The study data was categorized and correlated by applying Pearson's Chi-square. P values of < 0.05 were considered significant.

RESULTS

The study included 100 adult patients with mean age of 34.59 years ± 9.4 SD. Fifty-four were male and 46 were female patients. Fifty-four patients were upto 35 years of age and 46 patients were >35 years of age. 41 patients had steatosis of various grades whereas 59 patients had no steatosis. 29 out of 41 patients were in grade 1 steatosis, 8 were in grade 2 and 4 patients were in grade 3 steatosis. Out of 100 patients 35 had normal BMI, 49 patients were overweight and 16 were obese. Higher grade of steatosis is significantly associated with high BMI, P-value is 0.0001, coefficient of correlation (p) 0.555. Table 1 shows distribution of steatosis in males and females of various age groups, suggesting females of >35 years with high BMI have higher grades of steatosis. The correlation of BMI with gender is highly significant (Fig. 1), P-value is 0.0001, p- 0.685. Impact of steatosis on necroinflammation was also observed, suggesting that higher grade of steatosis is seen with progression of necroinflammation and this correlation is significant P-value 0.003. Patients with higher grades of steatosis did not show advanced fibrosis. This correlation of steatosis with fibrosis was non-significant, P-value 0.116.

Table 1: Distribution of steatosis

Steatosis	Total No. of patients with %ages
No Steatosis	59(59%)
Grade 1	29(29%)
Grade 2	8(8%)
Grade 3	4(4%)

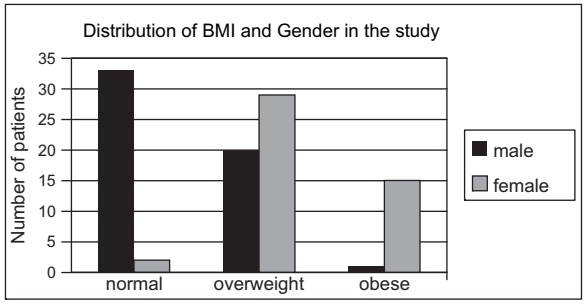

Fig. 1: Body Mass Index

DISCUSSION

Steatosis was observed histologically in 41 of 100 patients (41%) in this study. The results of this study matched the recent studies by Alia Zubair suggesting steatosis in 46% of patients[17]. These results also matched Samiullah Sheikh's study, which suggested steatosis in 45% of patients of CHC[11]. Most of the patients (80%) with normal BMI had no steatosis. Similarly 57.17% of patients in overweight category did not have steatosis. Higher grades of steatosis were seen in obese category (87.5%). A strong correlation

was found between BMI categories and various grades of steatosis (P-value 0.0001). The present study results matched with study by Osland et al. suggesting that elevated BMI is associated with increased incidence of steatosis in patients with CHC[18]. He also suggested that modest weight reduction showed improvement in steatosis and serum ALT levels. This provides a change in clinical protocol taking into account anthropometry (height, weight and waist circumference), weight management and monitoring the disease progression, forming an important aspect of the care of such patients attending liver clinics. Females present in the study were mostly in overweight and obese category and presented in higher grades of steatosis. This matched with the study results by Codes et al. suggesting that steatosis was more frequent in females with elevated BMI who were menopausal[19]. Similar results were shown by Rodriguez suggesting that individuals with >75 kg body weight achieved lower SVR rates because of higher relapse rates, hence increase in weight is a predictor for non-response to antiviral therapy[20].

The correlation of steatosis with fibrosis was also evaluated in the study. This correlation was found non-significant (P-value 0.116) which was similar to study results by Westin et al[21]. They however, found significant correlation between steatosis and necroinflammation in all HCV patients. The possible explanation for this insignificant result may be due to small number of patients in steatosis group presented with fibrosis. A study by Hourigan et al. also revealed that patients with chronic hepatic C presenting with steatosis showed necroinflammatory activity but hepatic fibrosis was non-significant[22].

Sorsi et al suggested that increasing age was associated with higher BMI and was a negative predictor of therapeutic response[12]. A study conducted by Rinella also showed that steatosis was missed on imaging techniques like 30% of patients missed in MRI group and 24% in the CT group failed to show steatosis, which was diagnosed on liver biopsy[23]. These results match the results of our study in which almost 93.7% steatosis cases were missed on sonographic examination. 7.3% of the sonographic results showed enlarged liver with no definite diagnosis of steatosis. Such studies suggest that liver biopsy cannot be avoided in individuals with elevated BMI in presence of risk factors, as biochemical and imaging techniques are currently inadequate to determine the severity of steatosis.

CONCLUSION

Steatosis is a frequent histological finding in HCV RNA positive patients and shows significant correlation with BMI. Steatosis should always be included in histological assessment of liver biopsy for clinical and research purposes. Anthropometry must become an essential part of liver clinics. Future studies are required to assess steatosis quantitatively and study its relationship with other morphological features especially fibrosis in CHC patients.

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