Original Article

Analysis of Liver Histology and Severity of Metabolic Syndrome in Patients Suffering from Nonalcoholic Fatty Liver Disease

Muhammad Awais Saleh[1], Amad Ul Haq Bhatti[2] and Ali Javaid Chughtai[3]

ABSTRACT

Objective: The basic aim of the study is to find the analysis of liver histology and severity of metabolic syndrome in patients suffering from nonalcoholic fatty liver disease.

Study Design: Comparative study

Place and Duration of Study: This study was conducted at the Allama Iqbal Memorial Teaching Hospital, Sialkot during October 2019 to May 2020.

Materials and Methods: This is a comparison analysis in which we explored specific relationships between hepatic histology and markers of the metabolic syndrome. There were total 50 patients that included in this study. The diagnosis was based on the histological presence of macrovesicularsteatosis, with or without lobular inflammation, hepatocellular degeneration, or fibrosis.

Results: In this study the data was collected from 50 patients with biopsy-proven NAFLD, a relationship between the severity of the metabolic syndrome and NAFLD was observed. While proportions of biopsy correlated with hepatic steatosis, hepatic inflammation and fibrosis were related with the presence and seriousness of the metabolic syndrome. This finding has clinical ramifications, since hepatic ultrasound and serum transaminases have restricted utility in foreseeing hepatic inflammation and fibrosis and there is current dependence on liver biopsies to affirm the analysis and show anticipation.

Conclusion: It is concluded that NAFLD is associated with a high prevalence of obesity. There was a trend towards an association between NASH and metabolic syndrome, in addition, patients with NAFLD with MetS were more likely to have severe steatosis and portal inflammation on liver biopsy.

Key Words: Liver, Metabolic, Syndrome, Obesity, Disease

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease since its prevalence is estimated to be 20-30% in general population of Western countries. NAFLD occurs as a histological spectrum of disease and includes the subtypes of simple steatosis and nonalcoholic steatohepatitis (NASH)[1].

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It was thought to be a benign condition but is now increasingly recognized as a major cause of liver-related morbidity and mortality[2]. The metabolic syndrome is a clustering of risk factors that greatly increases an individual's probability for developing atherosclerotic cardiovascular disease (ASCVD), type 2 diabetes mellitus and chronic kidney disease[3]. The predominant underlying risk factors appear to be abdominal obesity, atherogenicdyslipidaemia, hypertension, elevated plasma glucose, a prothrombotic state, and a proinflammatory state [4].

Non-alcoholic fatty liver disease (NAFLD) is now considered a hepatic component of metabolic syndrome (MS) because of the close association between the two conditions. Prevalence of metabolic risk factors including diabetes mellitus, obesity, etc. is rapidly increasing which is consequently increasing the prevalence of NAFLD in Asia [5]. Patients with NAFLD are at risk not only for the liver-related morbidity and mortality but also for the increased cardiovascular disease risk and increased incidence of diabetes mellitus on long-term follow-up[6].

NAFLD is strongly associated with obesity, metabolic syndrome (MetS), and cardiovascular risk factors and is

more common in obese patients. Nonetheless, a smaller, but significant, proportion of patients develop NAFLD despite having a relatively normal body mass index (BMI) [7]. This condition is often referred to as lean or non-obese NAFLD. Traditionally considered a condition unique in Asia, NAFLD has also been found in 10% of lean Americans in the National Health and Nutrition Examination Survey III[8]. Severity, factors associated with advanced disease, and prognosis of non-obese NAFLD are not well understood. A recent international study reported that non-obese NAFLD patients might have more-severe histological necro-inflammation and higher mortality than obese patients. Other smaller studies reported mixed results on the disease severity [9].

MATERIALS AND METHODS

This study was conducted at Allama Iqbal Memorial Teaching Hospital, Sialkot during October 2019 to May 2020. This is a comparison analysis in which we explored specific relationships between hepatic histology and markers of the metabolic syndrome i.e LDL, HDL, Cholesterol and TG. There were total 50 patients that included in this study. The diagnosis was based on the histological presence of macrovesicular-steatosis, lobular inflammation (with or without), hepatocellular degeneration and fibrosis.

Inclusion Criteria: All the patients who done the biopsy of liver and clinically proven were included in this study.

Exclusion Criteria: All patients having any major surgery, pregnant women and any other metabolic diseases were excluded from this study.

Data Collection: All subjects were negative for viral hepatitis and they also had normal values for copper and iron. All subjects expended <14 standard drinks of alcohol every week. Nine male subjects and eight female subjects had prior sort 2 diabetes, five dealt with their diabetes with diet alone, and 12 were taking metformin. Each subject and their particular control was given a score of 1 for each element of the metabolic syndrome, for a most extreme score of 5, with a score of ≥3 being indicative of the metabolic syndrome

Biochemical Analysis: A pathologist blinded to subject details scored liver biopsies, allotting a score from 0 to 4 for inflammation, steatosis, and fibrosis as previously described. For additional fibrosis assessment, all biopsies were stained with Masson's Trichrome, percent fibrosis was calculated in triplicate by microscopy and image analysis and data were expressed as mean percentages.

Statistical Analysis: The data of the different baseline variable was analyzed on SPSS 11 packages. Data of 50 patients was expressed as mean and SD. Significance was set at 0.05.

RESULTS

In this study the data was collected from 50 patients with biopsy-demonstrated NAFLD, a connection between the seriousness of the metabolic syndrome and NAFLD was watched. While proportions of adiposity correlated with hepatic steatosis, hepatic inflammation and fibrosis were related with the presence and seriousness of the metabolic syndrome. This finding has clinical ramifications, since hepatic ultrasound and serum transaminases have restricted utility in foreseeing hepatic inflammation and fibrosis and there is current dependence on liver biopsies to affirm the analysis and show anticipation. We propose that highlights of the metabolic syndrome would potentially be a superior guide in figuring out which patients ought to be considered for biopsy as well as likely explicit treatment. We collect all the lab values of selected patients.

Table No.1: Laboratory value differences between NAFLD participants with and without metabolic syndrome

Laboratory values	Mean±SD	p Value*
Triglycerides (mg/dL)	185.1±103.6	<0.001
Cholesterol, total (mg/dL)	196.8±42.3	0.86
Cholesterol, HDL (mg/dL)	41.2±10.2	<0.001
Cholesterol, LDL (mg/dL)	121.2±35.3	0.66
Cholesterol, HDL/LDL	37.0±15.6	<0.001
Fasting glucose (mg/dL)	96.6±14.6	<0.001
Fasting insulin (μU/mL)	27.2±31.4	<0.001
Fasting C peptide (mg/dL)	4.6±1.6	<0.001
HOMA-IR (mg/dL×μU/mL/405)	6.5±7.4	<0.001
HbA1c (%)	5.6±0.5	0.04
Alanine aminotransferase (U/L)	77.6±47.9	0.47
Aspartate aminotransferase (U/L)	53.6±34.4	0.69
Alkaline phosphatase (U/L)	85.1±32.8	0.43
γ-Glutamyltransferase (U/L)	60.3±39.6	0.15
Albumin (g/dL)	4.17±0.39	0.04
Serum iron (μg/dL)	90.5±31.1	0.006
Serum ferritin (ng/mL)	236.3±265.4	0.27
Transferrin saturation (%)	25.6±10.4	0.008
Albumin (g/dL)	4.17±0.39	0.04

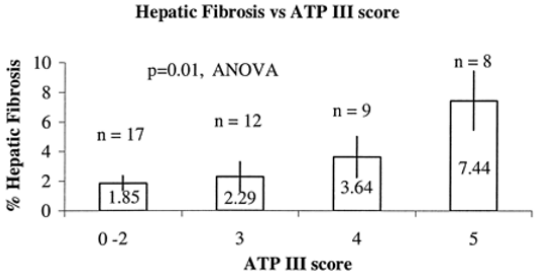

Figure No.1: Features of the metabolic syndrome compared with the degree of hepatic fibrosis

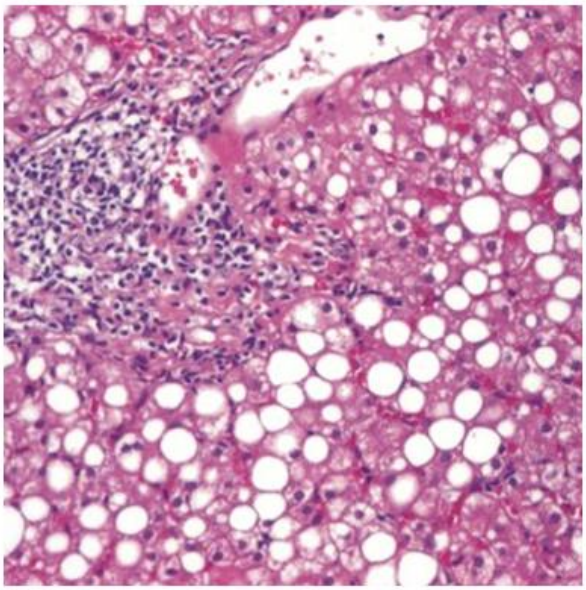

Figure No.2: Histological analysis of liver suffering from NAFLD

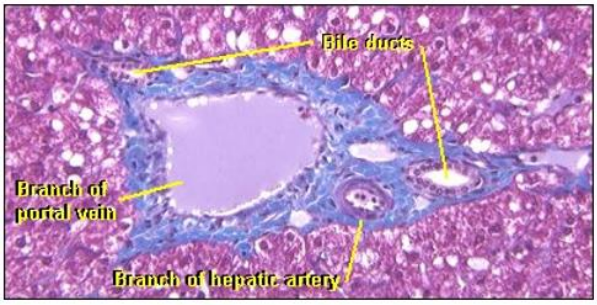

Figure No.3: In the section of equine liver below (Masson's trichrome stain), the capsule and septae are stained blue, while hepatocytes are magenta. Notice how the capsule extends as a septum into the liver about one-third of the way from left, immediately below a large capsular blood vessel

DISCUSSION

In this cross-sectional study of 50 patients with biopsy-proven NAFLD, a relationship between the severity of the metabolic syndrome and NAFLD was observed. While measures of adiposity correlated with hepatic steatosis, hepatic inflammation and fibrosis were associated with the presence and severity of the metabolic syndrome. This finding has clinical implications, since hepatic ultrasound and serum transaminases have limited utility in predicting hepatic inflammation and fibrosis, and there is current reliance on liver biopsies to confirm the diagnosis and indicate prognosis[10-11]. We suggest that features of the metabolic syndrome would potentially be a better guide in determining which patients should be considered for biopsy and/or potential specific therapy[12].

Recent studies have pointed that NAFLD, in its whole spectrum ranging from pure fatty liver to non-alcoholic steatohepatitis (NASH), might represent another feature of MS[13]. Pathophysiologic considerations, clinical associations, and laboratory investigations support that insulin resistance and hyperinsulinaemia have a central role in pathogenesis of both MS and non-alcoholic fatty liver. Studies concluded that NAFLD, in the presence of normoglycaemia and normal or moderately increased body weight, is characterized by clinical and laboratory data similar to those found in diabetes and obesity such as impaired insulin sensitivity and abnormalities in lipid metabolism[14]. Ninty percent of individuals with NAFLD have at least one risk factor of MS, and 33% have all the features of MS. Study concluded that liver fat content is significantly increased in subjects with the MS as compared with those without the syndrome, independently of age, gender, and body mass index[15]. In 304 NAFLD patients without diabetes mellitus the prevalence of metabolic syndrome increased from 18% in normal weight individuals to 67% in obese individuals[16]. The presence of multiple metabolic disorders such as diabetes mellitus, obesity, dyslipidaemia[17] and hypertension is associated with a potentially progressive, severe liver disease[18]. Obesity is found in 30-100% of subjects with NAFLD[19]. In obese persons steatosis is 4.6 fold higher than in normal weight persons[20].

CONCLUSION

It is concluded that there was a trend towards an association between NASH and MetS; in addition, patients with NAFLD with MetS were more likely to have severe steatosis and portal inflammation on liver biopsy. Systematic histological evaluation, full consideration of clinical and laboratory parameters, and good communications with hepatologists are crucial for making an accurate diagnosis of NAFLD and all other medical liver diseases.

Author's Contribution:

Concept & Design of Study:	Muhammad Awais Saleh
Drafting:	Amad Ul Haq Bhatti
Data Analysis:	Ali Javaid Chughtai
Revisiting Critically:	Muhammad Awais Saleh, Amad Ul Haq Bhatti
Final Approval of version:	Muhammad Awais Saleh

Conflict of Interest: The study has no conflict of interest to declare by any author.

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