Original Article

Analysis of Liver Histology and Severity of Metabolic Syndrome in Patients Suffering from Non-alcoholic Fatty Liver Disease

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ABSTRACT

Objective: To analyze 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 Idris Teaching Hospital of Sialkot Medical College, Sialkot and Lahore General Hospital, Lahore from January 2018 to December 2018
Materials and Methods: This is a comparative analysis in which we explored specific relationships between hepatic histology and markers of the metabolic syndrome. There were total 50 patients 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 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.
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

Nonalcoholic 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]. It was thought to be a benign condition but is now increasingly recognized as a major cause of liver-related morbidity and mortality[2].

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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, atherogenic-dyslipidaemia, hypertension, elevated plasma glucose, a prothrombotic state, and a proinflammatory state[4].

Nonalcoholic 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]. The 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 Idris Teaching Hospital, Sialkot Medical College, Sialkot and Lahore General Hospital, Lahore from January 2018 to December 2018. The data was collected from Idris Teaching Hospital, Sialkot Medical College, Sialkot and pathological work was done at Pathology Department of Lahore General Hospital, Lahore. This is a comparison analysis in which we explored specific relationships between hepatic histology and markers of the metabolic syndrome. There were 50 patients that were included in this study. The diagnosis was based on the histological presence of macrovesicularsteatosis, with or without lobular inflammation, hepatocellular degeneration, or fibrosis.

All subjects were negative for viral hepatitis, anti-nuclear antibody, anti–smooth muscle antibody, and anti-mitochondrial antibody and had normal iron and copper studies. Nine male subjects and eight female subjects had preexisting type 2 diabetes. Out of these five managed their diabetes with diet alone, and 12 were taking metformin. Each subject and their respective control was given a score of 1 for each feature of the metabolic syndrome, for a maximum score of 5, with a score of ≥3 being diagnostic of the metabolic syndrome. Informed consent of each patient was considered before the start of study. The permission of Ethical Committee was also considered.

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-proven NAFLD, a relationship between the severity of the metabolic syndrome and NAFLD was observed. The mean age of selected patients were 42.44±9.24years and men accounted for 63.0%. The mean BMI of patients was 26.90± 3.45. All the demographic values of selected patients are explained in table 01. 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. 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. We collected all the laboratory values of selected patients.

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

Laboratory values	Mean±SD	p Value*
Age (years)	42.44 ± 9.24	≤ 0.078
Male (%)	67.7	0.004
BMI	26.90 ± 3.45	≤ 0.001
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

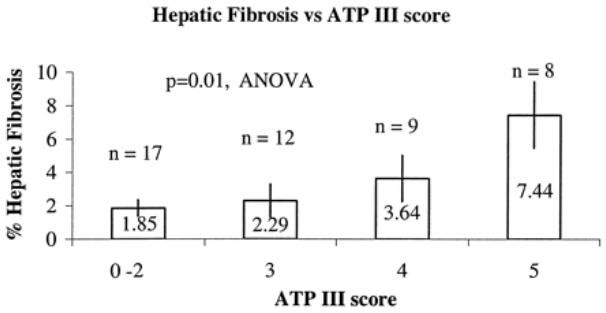

Figure No.1: Features of the metabolic syndrome compared with the degree of hepatic fibrosis.

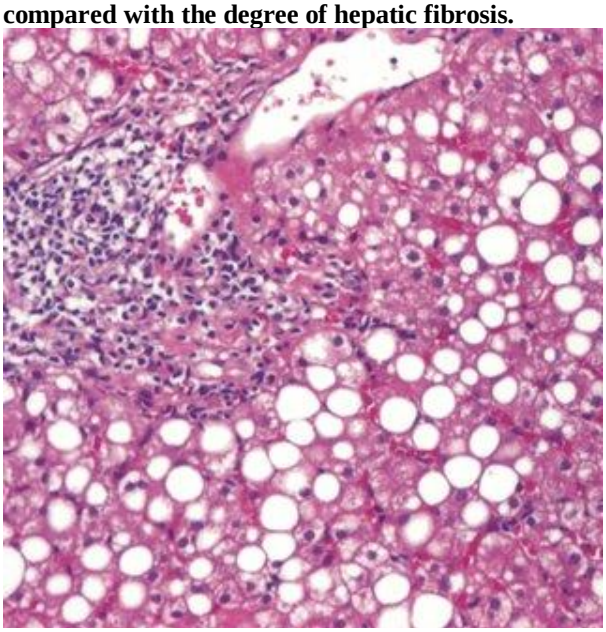

Figure No.2: Histological analysis of liver suffering from NAFLD.

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[10]. 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[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]. Ninety 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 NAFLD is associated with a high prevalence of obesity and MetS. 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.

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Author's Contribution:

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Revisiting Critically:	Kashif Aziz Ahmad, Akmal Khurshid Bhatti
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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