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Research Article

A case control study on non-alcoholic fatty liver disease in healthy individuals and in patients with metabolic syndrome

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ABSTRACT

Objective: To determine the prevalence of non-alcoholic fatty liver disease in healthy individuals and in patients with metabolic syndrome

Material and methods: This case control study was conducted at Department of Gastroenterology & Hepatology, Bahawal Victoria Hospital, Bahawalpur from November 2017 to May 2018 over the period of 6 months. Total 61 individual with metabolic syndrome (cases) and 61 individual without metabolic syndrome (control) having age >18 years either male or female were selected.

Results: Mean age of the subjects in metabolic syndrome group and non-metabolic syndrome group was 52.4±15.4 and 50.7±15.4years respectively. There were 27 females and 34 males in each of the groups. Mean Body mass index (BMI) for the subjects in metabolic syndrome group and non-metabolic syndrome group was 31.39±6.93 and 26.42±6.28kg/m2 respectively (P <0.05). Mean total cholesterol, triglyceride, and low density lipoprotein (LDL) cholesterol was higher in patients with metabolic syndrome when compared to patients without metabolic syndrome, and the difference was statistically significant (p<0.05).

Conclusion: Overall prevalence of NAFLD from current study was approximately 32%. The prevalence of NAFLD was significantly higher in persons with metabolic syndrome than in persons without metabolic syndrome. Present study strongly confirms well known association between metabolic syndrome and NAFLD, association between atherogenic dyslipidemia and metabolic syndrome and also emphasizes ever increasing prevalence of obesity, diabetes mellitus, dyslipidemia and liver disease in population in general and in those with metabolic syndrome in particular.

Key words: Metabolic syndrome, fatty liver, lipid profile, obesity

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.[1] NAFLD occurs as a histological spectrum of disease and includes the subtypes of simple steatosis and nonalcoholic

steatohepatitis (NASH). It was thought to be a benign condition but is now increasingly recognized as a major cause of liver-related morbidity and mortality. Studies introduced that NAFLD may progress to cirrhosis, liver failure, and hepatocellular carcinoma.[2]It has been shown that NAFLD is strongly associated to the features of metabolic syndrome. Insulin resistance is a key pathogenic factor in both NAFLD and metabolic syndrome. Available data from clinical, experimental and epidemiological studies indicate that NAFLD may be the hepatic manifestation of metabolic syndrome.[3]

Metabolic syndrome is a cluster of diseases oftenly seen in diabetes. The metabolic syndrome consist of metabolic derangements such as insulin resistance, hyperinsulinemia, abdominal obesity, impaired glucose tolerance, dyslipidemia, hypertension and a proinflammatory and prothrombotic state. Pathological change in lipord profile is a key component of metabolic syndrome. Dyslipidemia may occur in the form of hypertriglyceridemia, reduced HDL cholesterol and increased LDL cholesterol.[4]It may complicate in the form of atherosclerotic vascular disease and type 2 diabetes.[5]In obesity, the prevalence of metabolic syndrome is very high. [3] Its prevalence is increasing with worsening obesity.[6]Sedentary life style, excess of adipose tissue and genetically predisposition, all may lead to insulin resistance which is the key element of its pathogenesis.[5]

The current study aims to study the prevalence of non-alcoholic fatty liver disease in healthy individuals and in patients with metabolic syndrome and to establish a relationship between NAFLD and metabolic syndrome.

OPERATIONAL DEFINITION

Metabolic Syndrome:

The metabolic syndrome is a cluster, within the same individual, of cardiometabolic risk factors, including hypertension, abdominal obesity, dyslipidemia, insulin resistance and proinflammatory and prothrombotic states.

ATP III DIAGNOSTIC CRITERIA FOR METABOLIC SYNDROME

Metabolicsyndrome will be labeled when 3 of the following trait are present in a patient.

No.	Component	Diagnostic criteria
1.	Abdominal/central obesity	Waist circumference: >102 cm (40 inches)in men, >88 cm (35 inches) in women
2.	Hypertriglyceridemia	>150 mg / dL * or drug treatment for increased triglycerides
3.	Low HDL cholesterol	<40 mg /dL for men, <50 mg /dL for women
4.	High blood pressure	> 130/85 mm Hg** or documented use of antihypertensive therapy
5.	High fasting glucose	> 100 mg / dL. Or drug treatment for increase blood sugar level.

Key:* mg/dL= milligram per deci-Liter, **mm Hg= millimeter of mercury

Nonalcoholic Fatty Liver Disease (NAFLD)

on ultrasonography, hyperechogenicity of the liver relative to the kidneys, ultrasound beam attenuation, and poor visualization of intrahepatic vessel borders and left ventricular diastolic dysfunction was diagnosed by using pulse wave Doppler on the basis of : E/A ratio of less than 1, mitral deceleration time (DT) >240 mitral and Isovolumic relaxation time (IVRT) > 90 msec.

MATERIAL AND METHODS

This case control study was conducted at Department of Gastroenterology & Hepatology, Bahawal Victoria Hospital, Bahawalpur from November 2017 to May 2018 over the period of 6 months. Study is approved by ethical committee of the hospital. Written informed consent was taken from every patient. Total 61 individual with metabolic syndrome (cases) and 61 individual without metabolic syndrome (control) having age >18 years either male or female were selected. Patients with alcohol use, patients with acute and chronic liver disease, patients who were treatedhepatotoxic drugs and pregnant women were excluded from the study.There after

patients were assessed, vital parameters measured, and anthropometric measurements done and blood samples for complete blood count, lipid profile, fasting blood glucose, and liver function test was sent. Clinical parameters, laboratory investigations, and ultrasonographic findings were compared among the two groups.

All the collected data was entered in SPSS version 20 and analyzed. Mean and SD was calculated for numerical data and frequencies and percentage were calculated for categorical data.

RESULTS

Mean age of the subjects in metabolic syndrome group and non-metabolic syndrome group was 52.4±15.4 and 50.7±15.4years respectively. There were 27 females and 34 males in each of the groups. From the current study, no statistically significant difference was noted between two groups in terms of age and gender distribution. Though the mean age in control group was slightly lower than metabolic syndrome group, this didn't have a statistical significance (p=0.546). Thus, in the current study design, age and gender were not significant confounding factors.

Mean Body mass index (BMI) for the subjects in metabolic syndrome group and non-metabolic syndrome group was 31.39±6.93 and 26.42±6.28kg/m2 respectively (P <0.05). 46 subjects (75.41%) in metabolic syndrome group and 28 subjects (45.9%) in non-metabolic syndrome group had abnormal waist circumference (P <0.05). 52 subjects (85.25%) in metabolic syndrome group and 34 subjects (55.74%) in non-metabolic syndrome group had abnormal waist hip ratio (P <0.05).

Triceps skin fold thickness was another anthropometric variable studied in this study which showed statistically significant elevations in metabolic syndrome group. Mean triceps skin fold thickness for the subjects in metabolic syndrome group and non-metabolic syndrome group was 19.16±6.1 and 7.59±2.57cms respectively (p<0.05). 36 subjects (59.01%) in metabolic syndrome group and 12 subjects (19.67%) in non-metabolic syndrome group had diabetes. 40 subjects (65.57%) in metabolic syndrome group and 13 subjects (21.31%) in non-metabolic syndrome group had hypertension.

Mean total cholesterol, triglyceride, and low density lipoprotein (LDL) cholesterol was higher in patients with metabolic syndrome when compared to patients without metabolic syndrome, and the difference was statisticallysignificant (p<0.05). Mean high density lipoprotein (HDL) cholesterol was lower in subjects with metabolic syndrome, when compared to subjects with no metabolic syndrome (36.9±4.02 and 39.21±4.12mg/dl respectively) and the difference was statistically significant (Table 1).

Among the various Liver function parameters studied, AST (aspartate aminotransferase) and total bilirubin were significantly elevated in Metabolic syndrome group when compared to subjects with no metabolic syndrome. (Table 1).

Whereas ALT (alanine aminotransferase) and ALP (alkaline phosphatase) levels were identical in both the groups. (Table 2) Of the total 122 subjects included in the current study, 39 had sonological evidence of NAFLD. Thus, the overall prevalence of NAFLD was approximately 32%. 26 subjects (42.62%) in metabolic syndrome group and 13 subjects (21.31 %) in non-metabolic syndrome group had fatty liver (Figure 1). Chi square test was applied and p value of less than 0.011 was obtained. Hence, the difference was statistically significant. (Fig. 1)

Table 1: Lipid profile.

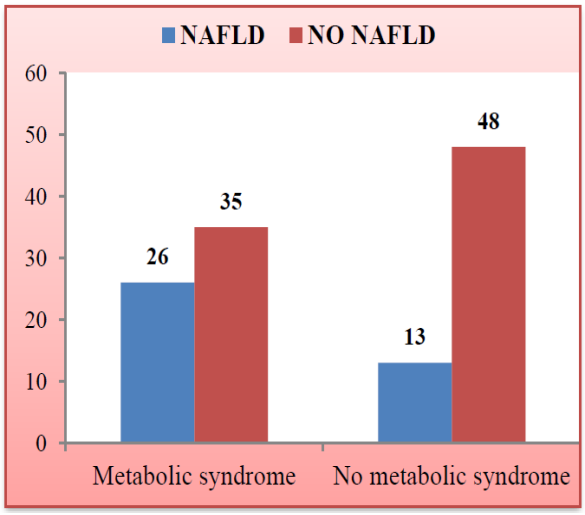
Lipid profile	Patients with metabolic syndrome (n=61)	Patients without metabolic syndrome (n=61)	P value
Total cholesterol (mg/dl)	233.28±28.10	143.98±20.40	<0.005*
Triglyceride (mg/dl)	193.80±40.80	101.70±27.50	<0.005*

HDL (mg/dl)	36.90±4.02	39.21±4.12	<0.005*
LDL (mg/dl)	157.60±24.40	84.30±18.30	<0.005*

Table 2: Liver function test.

Lab Parameters	Patients with metabolic syndrome (n=61)	Patients without metabolic syndrome (n=61)	P value
Total Bilirubin	0.362±0.0773	0.327±0.0767	0.012*
Aspartate transaminase	17.64±4.63	16.28±2.83	0.053*
Alanine transaminase	16.25±2.66	16.26±2.62	0.973
Alkaline phosphatase	56.60±10.10	56.90±16.00	0.904
Gamma glutayl transferase	24.05±5.60	26.36±5.86	0.028*

Figure 1: Fatty liver on Ultrasonography.



DISCUSSION

The mean BMI was significantly higher in metabolic syndrome group (31.39±6.93kg/m2), in comparison to control group (26.42±6.28kg/m2). This is an expected result from the study as obesity forms a diagnostic component of metabolic syndrome. It can be noted from the study that the mean BMI of the control group too falls in overweight category emphasizing the epidemic proportions achieved by obesity. A study conducted by Dudeja A et al, among Asian showed that for mean BMI of 23.3 kg/m2, the mean body fat was estimated at 35%. These observations in the past have resulted in revising the various anthropometric criteria employed in diagnosis of Metabolic syndrome particularly waist circumference for Asian population.[7]

Triceps skin fold thickness is another anthropometric variable studied in this study which shows statistically significant elevations in metabolic syndrome group. The mean triceps skin fold thickness (TSF) in metabolic syndrome group was 19.16cms±6.10 while in control group 7.59cms±2.57 (p=0.00). Thus, TSF seems to have a positive correlation with occurrence of metabolic syndrome. TSF has been used as a convenient anthropometric tool for many decades in nutritional assessment of both under nutrition and obesity.

The prevalence of diabetes was 59% in metabolic syndrome group and 19.6% in control group. The higher prevalence of DM in metabolic syndrome group was an anticipated result. Surprising finding from current study is that the prevalence of diabetes is high even in control group (19.6%),

in comparison to global prevalence and significantly higher than national prevalence of 9%. This increase in overall prevalence of DM can be attributed to the fact that majority of the patients in the current study belonged to 4th to 6th decade of age, an age group considered to be at risk for diabetes.

In consistence with other studies, the prevalence of hypertension was higher in metabolic syndrome group (metabolic syndrome group with hypertension, n=40, control group with hypertension n=13, p=0.0000014). The prevalence of hypertension in metabolic syndrome from the current study is 65.5%. Various studies have estimated the prevalence of hypertension among individuals with metabolic syndrome from 56-85%.[8-9]

The present study shows that metabolic syndrome is strongly associated with atherogenic dyslipidemia. The atherogenic dyslipidemia is defined by elevated LDL cholesterol, tryglyceride, apolipoprotein B and lower HDL-C levels. This constellation of risk factors termed atherogenic dyslipidemia is an independent risk factor for future occurrence of Arteriosclerotic cardiovascular disease (ASCVD).

The principal research question of the current study was to study the association between NAFLD and metabolic syndrome. Of the total 122 subjects included in the current study, 39 had sonological evidence of NAFLD. Thus, the overall prevalence of NAFLD from current study was approximately 32%. This prevalence correlates with various Asian studies.[10-14]

The prevalence of NAFLD is estimated between 20-35% among general population in India by various studies.[7,15] The overall prevalence of 21.31 % in control group from present study shares similarity with the already existing data.

In present study, the prevalence of NAFLD was significantly higher in metabolic syndrome group, 46.6% versus 21.3% in control group. (p=0.011). Similar finding was noted in a study done by Uchil D et al, in which the prevalence of NAFLD was 47% in those with metabolic syndrome and 23% in controls.[16] In a study done by Mishra S et al, on 119 individuals with metabolic syndrome, 27% of them had NAFLD.[17] This association between metabolic syndrome and NAFLD can be explained from the fact that insulin resistance forms the key pathogenetic factor for both these disease entities.

In fact, various authors have debated whether NAFLD should be considered as a separate entity or should be included as a diagnostic criterion for Metabolic syndrome. Few studies have also suggested that sonological evidence of NAFLD often predates the occurrence of overt metabolic syndrome and DM. This observation suggests the possibility of utilizing sonological evidence of NAFLD as predictor for development of overt DM and metabolic syndrome in future.

Recent studies have concluded that NAFLD might represent another feature of metabolic syndrome. Pathophysiologic considerations and clinical associations support that insulin resistance and hyper-insulinaemia have a central role in pathogenesis of both metabolic syndrome and NAFLD.

Since it was a case control study with small sample size, to what extent the observations from current can be generalized to population at large remains unclear. However current study strongly confirms well known association between metabolic syndrome and NAFLD, association between atherogenic dyslipidemia and metabolic syndrome and also emphasizes ever increasing prevalence of obesity, diabetes mellitus, dyslipidemia and liver disease in population in general and in those with metabolic syndrome in particular

NAFLD and metabolic syndrome affect a sizeable portion of the general population and are considered as public health concerns by now.

Patients with NAFLD not only frequently suffer from insulin resistance but also have increased overall mortality. Although NAFLD seems a benign entity in short term follow up, on the long

run, it can progress to active hepatitis, NASH and ultimately to cirrhosis in some patients and Hepatocellular carcinoma (HCC). Because of the long-term consequences of the disease, strong association with ASCVD risk, we emphasize the importance of early detection of NAFLD in high-risk groups, including obese patients, as well as those with evidence of insulin resistance or other components of metabolic syndrome.

CONCLUSION

Overall prevalence of NAFLD from current study was approximately 32%. The prevalence of NAFLD was significantly higher in persons with metabolic syndrome than in persons without metabolic syndrome. Present study strongly confirms well known association between metabolic syndrome and NAFLD, association between atherogenic dyslipidemia and metabolic syndrome and also emphasizes ever increasing prevalence of obesity, diabetes mellitus, dyslipidemia and liver disease in population in general and in those with metabolic syndrome in particular.

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