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Original Research Article

Study of non-alcoholic fatty liver disease in metabolic syndrome

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ABSTRACT

Background: Metabolic syndrome is a clustering of risk factors that increase an individual's probability of developing atherosclerotic cardiovascular disease, type 2 diabetes mellitus and all cause mortality. Since primary NAFLD has strong association with metabolic syndrome as a whole and various components of metabolic syndrome, it is being debated whether NAFLD is a hepatic component of metabolic syndrome. Hence this study was done 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.
Methods: A total of 122 patients - 61 with metabolic syndrome and 61 without metabolic syndrome fulfilling inclusion and exclusion criteria who presented to the Medicine outpatient Department of Ramaiah Medical College, Bangalore, between October 2014 and September 2016 were included in the study. Baseline variables, laboratory parameters, ultrasound abdomen findings were compared between the groups.
Results: Mean age of the subjects in metabolic syndrome group and non-metabolic syndrome group were 52.4±15.4 and 50.7±15.4years respectively. Mean triceps skin fold thickness (in cms) for the subjects in metabolic syndrome group and non-metabolic syndrome group were 19.16±6.1 and 7.59±2.57 respectively (P <0.05). Prevalence of fatty liver on ultrasonography in metabolic syndrome and non-metabolic syndrome were 42.62 % and 21.31% respectively. Overall prevalence of NAFLD was 31.97 %.
Conclusions: Overall prevalence of NAFLD from current study was 31.97%. The prevalence of NAFLD was significantly higher in persons with metabolic syndrome than persons without metabolic syndrome.

Keywords: Fatty liver, Metabolic syndrome, NAFLD

INTRODUCTION

Metabolic syndrome (MS) is considered as a major public health concern since the prevalence has reached epidemic proportions in the past decade and ever increasing. The pathogenesis of metabolic syndrome is multi factorial. However, insulin resistance is considered as a cornerstone in the pathogenesis.[1] Non-alcoholic fatty liver disease, the commonest cause currently for cryptogenic cirrhosis, is also strongly associated with insulin resistance. Since insulin resistance forms the cornerstone in the pathogenesis of both metabolic syndrome and Non-Alcoholic Fatty Liver Disease (NAFLD), the prevalence of NAFLD seem to be higher in those with metabolic syndrome than common population.

NAFLD is a clinical entity characterized by the occurrence of alcohol like liver disease characterized by accumulation of fat in hepatocytes, among those who are not heavy drinkers (consuming less than 20grams of ethanol per day). NAFLD is now considered the most common liver disease world over.[2] Once thought to be a benign entity, NAFLD is now increasingly recognized as a major cause of hepatic morbidity and mortality.

Various studies have reported the prevalence of NAFLD among Indian population between 10-32%.[3,4] However there are few Indian studies on the prevalence of NAFLD in patients with metabolic syndrome. 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.

METHODS

Study was a hospital based prospective case control study conducted at Ramaiah Hospital over a period of 2 years from October 2014 to September 2016. A total of 122 cases were enrolled into current study. The study cohort was divided into two groups - study group - individuals with metabolic syndrome, and control group - individuals without metabolic syndrome.

Inclusion criteria

Patients aged above 18 years and diagnosed to have metabolic syndrome according to new International Diabetes Federation (IDF) criteria.[5] MS was defined as presence of central obesity; defined as waist circumference ≥90cm for men and ≥80cm for women PLUS any two of the following four factors -

- Raised triglyceride level (TG) ≥150mg/dl (1.7mmol/L) or specific treatment for this lipid abnormality.
- Reduced HDL cholesterol: <40mg/dl (1.03mmol/L) in males, <50mg/dl (1.29mmol/L) in females, or specific treatment for this lipid abnormality
- Raised blood pressure - systolic ≥130 mmHg or diastolic >85mmHg or treatment for previously diagnosed hypertension.
- Raised fasting blood sugar (FBS) ≥100mg/dl (5.6mmol/L) or previously diagnosed type 2 diabetes mellitus.

Exclusion criteria

- Patients who had abusive alcohol consumption (>20grams/day),
- patients who have acute and chronic liver disease,
- patients who were treated with hepatotoxic drugs and
- Pregnant patients were excluded from the study.

Total of 122 patients fulfilling inclusion and exclusion criteria were included. Purpose of the study was explained to the patients and informed consent was obtained.

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.

Statistical analysis

In the statistical analysis of our study, continuous variables are presented as mean for parametric data and median if the data is non-parametric or skewed. Student t test was applied for calculation of statistical significance whenever the data followed normative distribution. Mann whitney test was applied whenever data followed non-normative distribution.

Categorical variables are expressed as frequencies and percentages. Nominal categorical data between the groups was compared using chi-square test or fisher's exact test as appropriate. P <0.05 was taken to indicate a statistically significant difference. Minitab version 17 was used for computation of statistics.

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/m^2 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 statistically

significant (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: 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*

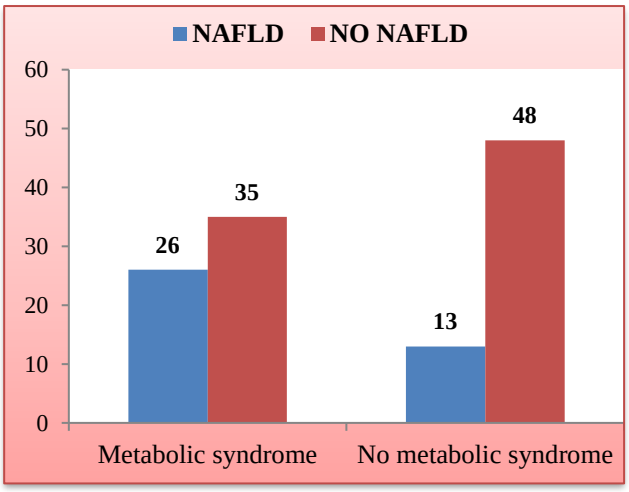

Figure 1: Fatty liver on Ultrasonography.

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.

DISCUSSION

The mean BMI was significantly higher in metabolic syndrome group (31.39±6.93kg/m^2), in comparison to control group (26.42±6.28kg/m^2). 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. The typical Indian body phenotype is thought to have higher body fat percentage at lower BMI and high waist hip ratio at low waist circumference. A study conducted by Dudeja A et al, among Asian Indians in India showed that for mean BMI of 23.3 kg/m^2, 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.[3]

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%.[2,6]

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 Indian and Asian studies.[7-11]

The prevalence of NAFLD is estimated between 20-35% among general population in India by various studies.[3,4] 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.[12] In a study done by Mishra S et al, on 119 individuals with metabolic syndrome, 27% of them had NAFLD.[13] 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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