Original Research Article

Metabolic syndrome and Non alcoholic fatty liver disease among asymptomatic adults in North Kerala

Sarosh Kumar K K[1], Sarin S M [1*], Kadeeja Beevi B[1], Balakrishnan Valliyot[2]

[1]Associate Professor, Dept of Medicine, GMC Kannur,Kerala, India
[2] Professor, Dept of Medicine, GMC Kannur,Kerala, India

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Abstract

Background: Non-alcoholic fatty liver disease [NAFLD] is considered as the hepatic component of Metabolic syndrome (MS) and is a common cause of Chronic Liver Disease. Early identification of NAFLD in patients having metabolic syndrome is important in reducing the long-term morbidity.**Methods:** A cross sectional observational study of apparently healthy subjects attending routine health check in the hospital clinic between the age group of 18 years and 65 years for a period of six months was done. Data including medical history, anthropometric measurements, biochemical investigations and ultrasound scan abdomen were collected. Patients were categorised as metabolic syndrome based on IDF consensus criteria (2009) using population and country specific definition for waist circumference.**Results:** 168 consecutive subjects attending the clinic were studied out of which 75.60% (127) had NAFLD. Out of the study subjects, 80 (47.62%) had metabolic syndrome according to IDF 2009 criteria. There is a significant difference between the prevalence of NAFLD among subjects with and without metabolic syndrome (p=0.002). Logistic regression analysis showed that BMI and waist circumference were significantly contributing to the prediction model for the occurrence of NAFLD. **Conclusion:** Prevalence of NAFLD in those with metabolic syndrome is considerably higher than those who do not satisfy the criteria for metabolic syndrome. The study points to the importance of screening and aggressive life style intervention in patients with abdominal obesity to prevent the development of NAFLD and Metabolic Syndrome.

Keywords:NAFLD, Metabolic syndrome, BMI, Waist circumference

Introduction

Non-alcoholic fatty liver disease [NAFLD] is a major cause of chronic liver disease and it is considered as the hepatic component of Metabolic syndrome (MS). Non-alcoholic fatty liver disease has been defined as the accumulation of fat in the absence of recent or ongoing intake of a significant amount of alcohol [1]. Significant alcohol consumption is considered as ongoing or recent consumption of >14 standard drinks per week in women and >21 standard drinks per week in men (14 gm of alcohol is considered as one standard drink) [2]. Metabolic syndrome is a clustering of risk factors that greatly increases an individual's probability for developing atherosclerotic cardiovascular disease and type 2 diabetes mellitus [3]. Even at lower BMI, South Asians have been found to have a high percentage of body fat compared to other populations, so we have used IDF consensus criteria (2009) for defining metabolic syndrome based on population and country specific definition for waist circumference [4].

IDF Consensus Worldwide Definition of the Metabolic Syndrome-2009:
Subjects were diagnosed having MS when they meet at least 3 of 5 criteria:

Table 1:Measure and categorical cut points

Measure	Categorical cut points
1)Elevated waist circumference	Population/country specific definitions *
2)Elevated triglycerides	150 mg/dL (1.7 mmol/L)
3)Reduced HDL-C	40 mg/dL (1.0 mmol/L) in males; 50 mg/dL (1.3 mmol/L) in females
4)Elevated blood pressure	Systolic 130 and/or diastolic 85 mm Hg
5)Elevated fasting glucose	>100 mg/dL

* For South Asian population the recommended waist circumference is >90cm in males and >80 cm in females.

**Correspondence*
Dr. Sarin S M
Associate Professor, Dept of Medicine, GMC Kannur, Pariyaram, Kannur, Kerala,India
E-mail:sarinsm@gmail.com

Metabolic syndrome and Non-alcoholic fatty liver disease appear to have a common pathophysiology arising mainly from insulin resistance. Rapid urbanization along with change in diet and physical activity has led to an increase in obesity and metabolic abnormalities in Indian population leading to an increase in the prevalence of both NAFLD and MS. Nearly 90.0% of the NAFLD patients have at least one feature of metabolic syndrome and 33.0% of them usually have

all features of the MS according to previous reports. With the presence of MS in an individual the risk of developing NAFLD increases to almost 4–11 times [5]. Kerala the southern state of India; being a rapidly urbanizing society with high prevalence of Type 2 diabetes and other metabolic disorders even in rural community, the coexistence of both NAFLD and Metabolic syndrome will be expected to be high [6]. The state has a high number of Non-resident Indians working in many foreign countries especially Middle East countries who are generally observed to have high abdominal obesity rate than resident Indians. All these factors make this population vulnerable for the development of both NAFLD and MS. Since both NAFLD and MS remain asymptomatic for a long period in majority, early recognition of these conditions and early intervention in these subjects will be needed to prevent development of atherosclerotic cardiovascular complications. Hence in this study we intend to find out the hospital-based prevalence of both metabolic syndrome and NAFLD and association between NAFLD and MS in asymptomatic apparently healthy subjects attending routine health check-up.

Materials and methods

This is a cross sectional observational study conducted in a tertiary care academic institution in North Kerala for a study period of 6 months. All asymptomatic apparently healthy subjects attending routine health check in the hospital clinic between the age group of 18 years and 65 years were included in this study. Subjects with past history of chronic significant alcohol intake, known chronic liver disease, previous history of hepatitis or drug induced hepatic injury were excluded. Clinical examinations including anthropometric measurements were done. Body mass index (BMI) was calculated using the Quetelet index formula using weight in Kilogram and height in centimeters with light clothes and standing bare feet. Waist circumference (WC) in centimeters was measured at the midpoint between the lower border of the rib cage and the iliac crest. After an overnight fasting, blood samples were collected for Hemogram, Lipid profile, Fasting plasma glucose and Liver function tests. Ultrasound abdomen was conducted for all patients and based on the report presence of NAFLD was ascertained. Data were collected in a well validated proforma and analyzed by PSPP open-source statistical software. Descriptive statistics like frequencies and percentages were used for categorical and discrete variables, whereas mean and standard deviation were used for continuous variables. Other statistical tools like logistic regression analysis and Pearson correlation coefficient were used in interpretation of the data.

Ethical considerations

Study was conducted after obtaining institutional ethical clearance. No additional financial burden was put on the study subject and informed consent was obtained before the data collection from all study subjects.

Results

In this study, a total of 168 consecutive asymptomatic apparently healthy subjects attending the routine health check-up clinic at a tertiary care academic centre during the study period were included. Out of this 111(66.07%) were males and 57(33.93%) were females. Study subjects mainly consisted of those with officejobs (41.07%) followed by those who were unemployed/housewives (27.98%). 17.26% of the study population consisted of manual labourers and 13.69% were working in the service sector. As per the information obtained 80.95% of the subjects were engaged in moderate physical activity and 14.28% had sedentary lifestyle. Only 4.76% of the study subjects had vigorous physical activity routinely. 95.24% of subjects were following non-vegetarian diet and only 4.76% had the habit of smoking. Table 1 shows the clinical characteristics and biochemical investigation reports of the study participants.

Table 2: Clinical and biochemical characteristics of the study population

Variable	Mean	Standard Deviation
Age (in yrs)	47.11	10.30
Height (in cm)	163.97	8.56
Weight (in Kg)	69.95	11.13
BMI	26.00	3.61
Waist circumference (in cm)	97.14	8.71
Systolic BP (mm of Hg)	129.17	13.00
Diastolic BP (mm of Hg)	80.48	7.71
Fasting blood sugar (mg/dl)	103.80	38.12
S Cholesterol (mg/dl)	208.36	40.35
Triglyceride (mg/dl)	136.55	76.37
S LDL (mg/dl)	114.23	27.30
S HDL (mg/dl)	41.02	10.39
S Bilirubin (mg/dl)	0.88	0.64
AST (IU)	31.25	13.72
ALT (IU)	39.98	28.35

Non-Alcoholic Liver Disease [NAFLD]

Among the 168 study subjects; 75.60% (127) have NAFLD whereas 24.40% (41) were devoid of any fatty changes in the liver. The comparison of the clinical characteristics among subjects with and without NAFLD is represented in Table 2.

Table 2: Comparison between clinical characteristics among patients with and without NAFLD

Characteristics	Non Alcoholic Fatty Liver Disease		P value
	Present	Absent	
Weight	71.92 ± 10.18	63.83 ± 11.81	<0.001*
Height	164.18 ± 8.72	163.32 ± 8.14	0.576
BMI	26.69 ± 3.36	23.85 ± 3.56	<0.001*
Waist circumference	98.38 ± 8.26	93.30 ± 9.05	0.001*
Systolic BP	129.98 ± 13.24	126.66 ± 12.04	0.155
Diastolic BP	81.12 ± 7.57	78.51 ± 7.89	0.060
Fasting blood sugar	106.60 ± 39.62	95.15 ± 31.95	0.095
S Cholesterol	205.91 ± 38.09	215.93 ± 46.39	0.168
Triglyceride	145.14 ± 79.04	109.95 ± 60.92	0.010*

S LDL	112.90 ± 25.51	118.34 ± 32.23	0.268
S HDL	40.79 ± 10.81	41.73 ± 9.05	0.614
S Bilirubin	0.84 ± 0.47	1.01 ± 0.98	0.135
SGOT	33.33 ± 13.86	24.80 ± 11.16	<0.001*
SGPT	45.01 ± 29.51	24.41 ± 16.86	<0.001*

*Statistically significant difference (p<0.05)

The clinical characteristics compared between these two groups of subjects showed that weight, BMI, waist circumference, serum triglycerides, SGOT and SGPT were having statistically significant differences.

Metabolic Syndrome (MS)

Among the 168 study subjects; 80 [47.62%] had metabolic syndrome according to IDF 2009 criteria. Individual baseline characteristics of patients with and without metabolic syndrome, namely age, gender, occupation, NRI status, physical activity, diet and smoking status when compared showed no statistically significant difference.

Table 3 : Clinical characteristics of patients with and without MS

Characteristics	Metabolic Syndrome		P value
	Present	Absent	
Weight	72.36 ± 10.67	67.75 ± 11.14	0.007*
Height	163.69 ± 9.67	164.23 ± 7.47	0.688
BMI	27.05 ± 3.62	25.04 ± 3.35	<0.001*
Waist circumference	99.97 ± 6.58	94.56 ± 9.60	<0.001*
Systolic BP	132.80 ± 14.54	125.88 ± 10.46	0.001*
Diastolic BP	82.51 ± 8.59	78.64 ± 6.30	0.001*
Fasting blood sugar	117.60 ± 46.17	91.26 ± 22.80	<0.001*
S Cholesterol	201.00 ± 35.50	215.05 ± 43.43	0.023*
Triglyceride	171.28 ± 82.60	104.99 ± 53.70	<0.001*
S LDL	111.88 ± 26.62	116.36 ± 27.89	0.289
S HDL	36.31 ± 7.07	45.30 ± 11.09	<0.001*
S Bilirubin	1.02 ± 0.85	0.75 ± 0.30	0.008*
SGOT	33.25 ± 14.72	29.43 ± 12.55	0.072
SGPT	43.69 ± 29.49	36.61 ± 27.00	0.106

*Statistically significant difference (p<0.05)

Metabolic syndrome and NAFLD

Among the 80 study subjects with Metabolic syndrome; 69 (86.25%) subjects had NAFLD and among the 88 study subjects without Metabolic syndrome only 58 (65.91%) had NAFLD. There is a significant difference between the prevalence of NAFLD among subjects with and without metabolic syndrome (p=0.002).

Table 4: Prevalence of NAFLD among patients with and without MS

METABOLIC SYNDROME	NAFLD Present	NAFLD Absent
MS Present (80)	69 (86.25%)	11(13.75%)
MS Absent (88)	58 (65.91%)	30 (34.09%)

Body Mass Index (BMI) in Metabolic syndrome and NAFLD

BMI when compared among patients identified as metabolic syndrome and those who do not have metabolic syndrome showed significant difference among the two groups. Mean BMI among those who had metabolic syndrome was 28.51 ± 9.67 whereas mean BMI in those who are not categorised as metabolic syndrome was 25.04 ± 3.35 (p =0.005).When patients were categorized based on BMI as obese groups (BMI≥25) and non-obese groups (BMI<25), proportion of obese individuals having NAFLD was 85.71% compared to those with normal body weight which was 58.73% (p<0.001).

Predictors of NAFLD

A logistic regression analysis was performed to assess the ability of components of metabolic syndrome to predict the occurrence of NAFLD in an individual. Out of the predictor variables only waist circumference is found to have significant contribution in model predicting occurrence of NAFLD. The unstandardised beta weight of the predictor variable waist circumference is B=0.07 with SE=0.02, Wald=7.89 and p=0.005. The estimated odds ratio favoured an increase in 7% for NAFLD for every unit increase in waist circumference [Exp(B)=1.07, 95% CI (1.02,1.12)].

Logistic regression on individual predictor variable BMI was done to assess its ability in predicting NAFLD and result suggested significant contribution of BMI in predicting the occurrence of NAFLD. The unstandardised beta weight of the predictor variable weight is B=0.26 with SE=0.06, Wald=17.02 and p<0.001. The estimated odds ratio favoured an increase in 29% for NAFLD for every unit increase in BMI [Exp(B)=1.29, 95% CI (1.14,1.46)].

Discussion

In this study with a total of 168 consecutive asymptomatic apparently healthy subjects attending the routine health check-up clinic in a tertiary care academic centre 80 (47.62%) subjects satisfied IDF 2009 criteria for metabolic syndrome. No significant difference was noted in the baseline characteristics of subjects with and without metabolic syndrome regarding their age, gender, occupation, NRI status, diet and smoking status. An association was noted regarding body weight with higher body weight significantly associated with the metabolic syndrome group. This percentage of MS in our study is higher than most other studies done in Asian population. In other studies, conducted in Asian population report a prevalence ranging from 11.11% to 25.8% [6-10]. This increase in the proportion of metabolic syndrome patients may be attributed to the characteristics of the study population in our study. Most of the study subjects were otherwise healthy adults undergoing routine health check-up. Most of them were engaged with office jobs and having either sedentary habits or having much less physical activity. Prevalence of NAFLD among patients

with and without metabolic syndrome in our study was found to be 86.25% and 65.91% respectively. This is also higher than previously reported studies. In Chen SH et al, it was 62.78% and 12.97% respectively [7]. It was noted that NAFLD was of far higher proportion in our population even in those who were not having metabolic syndrome. It points to the fact metabolic syndrome and obesity even though have a strong influence in the development of NAFLD, there may be other factors that may be responsible for this overall higher prevalence of NAFLD in our population. There is enough documentation about specific genotypes which are more prone to develop NAFLD with no direct relation to existence of metabolic syndrome [11]. So, it is imperative that studies to be done in our population in ascertaining the existence of other factors including genetic peculiarity that gives rise to increased prevalence of NAFLD. Also, NAFLD can be considered as an early indicator of the development of the MS even before the other diagnostic criteria were fully developed. In this regard presence of NAFLD in an asymptomatic individual can be considered as a risk factor for developing Metabolic Syndrome and warrant the need for aggressive life style modification. In this study among the parameters studied it was noted that groups of participants with and without NAFLD had a significant difference in their mean body weight, BMI, waist circumference, serum triglycerides, SGOT (AST) and SGPT (ALT). Out of the various component factors used in the diagnostic criteria of metabolic syndrome only waist circumference was significantly associated to the occurrence of NAFLD. Other factors that were significantly associated with NAFLD were body weight and BMI. So, considering the above factors with a significant association to waist circumference, body weight and BMI; our study results were clearly suggestive that obesity, especially abdominal obesity is an important predictor in development of NAFLD which is in accordance with previous conclusions [11][12]. So even without any invasive blood investigations subjects with higher BMI, body weight and waist circumference can be considered as at higher risk of underlying NAFLD.Among the metabolic parameters studied only serum triglycerides and liver enzymes (SGOT and SGPT) were having significant differences between the groups with and without NAFLD. There was no significant difference in mean values of other parameters like fasting blood sugar, total cholesterol, LDL and HDL cholesterol levels. Previous studies also have inferred that serum triglycerides and liver enzymes were important indicators of progressive liver disease [13][14]. But unlike our results, many previous studies have data suggesting significant differences in fasting blood sugar and HbA1c values between patients with and without NAFLD [15][16]. Since insulin resistance is one of the major pathophysiologic mechanisms in development of NAFLD, we definitely expect such a metabolic profile in NAFLD patients [13]. But the data from the current study only showed significant differences between the mean values of triglycerides in the two groups and no difference among values of other biochemical parameters.

Conclusion

Metabolic syndrome and NAFLD are two coexisting conditions with common pathophysiological mechanisms. Prevalence of NAFLD in those with metabolic syndrome is considerably higher than those who do not satisfy the criteria for metabolic syndrome. The prevalence of both NAFLD and Metabolic syndrome will be increasing in the coming decades because of the change in the life style and increasing number of people with abdominal obesity. The study points to the importance of screening and aggressive life style intervention in patients with abdominal obesity to prevent the development of NAFLD and Metabolic Syndrome.

Conflict of Interest: Nil

Source of support:Nil

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