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Original Research Article

To Evaluate the Prevalence of Fatty Liver and Liver Stiffness in Persons with Metabolic Syndrome in a North-Eastern State of India

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Abstract

Introduction: The significance of metabolic syndrome and its implications in cardiovascular and cerebrovascular diseases has been proved beyond doubt. Particularly in India and more specifically in Eastern part of our country where carbohydrate constitutes major part of the meal, the problem seems to be even graver. The present cross sectional study was done to assess the relationship between metabolic syndrome with its hepatic manifestation namely fatty liver and liver stiffness.

Aim and Objective: Of the study is to find out the prevalence of fatty liver and grades of liver stiffness/fibrosis in patients with metabolic syndrome and also to evaluate the association of various cumulative risk factors in this cohort of patients.

Materials and Methods: After fulfilling inclusion and exclusion and as per sample size one hundred haemodynamically stable diagnosed cases of metabolic syndrome (MetS) as defined by International Diabetes Federation (IDF) and Consensus definition for Asian Indians, were recruited in the study. Ultrasonography to assess fatty liver and transient elastography for liver stiffness were done in fasting state.

Results: The mean liver stiffness measurement (LSM) was 8.3 kilopascal (kPa). 54% of study cohort had 4 risk factors, 27% had 3 risk factors and 19% had all 5 risk factors of metabolic syndrome. 46% had Grade II fatty liver, 22% had Grade I and 17% had Grade III fatty liver. Most of the study population (31%) were in Stage F2 fibrosis while the least number of study population (8%) were in stage F4 fibrosis. Liver stiffness was significantly higher in persons having 5 risk factors compared to 3 or 4 risk factors. There was significant positive correlation with fasting plasma glucose, waist circumference (WC), Aspartate Aminotransferase-to-Platelet-Ratio Index (APRI) and fibrosis - 4 (FIB-4) values with liver stiffness.

Conclusion: It is evident that persons with metabolic syndrome are at higher risk of development of fatty liver and liver fibrosis which if unchecked can lead to cirrhosis. Therefore it is imperative to evaluate these high risk individuals at regular intervals for fatty liver and liver fibrosis as this disease is a dynamic process.

Keywords: Metabolic syndrome (MetS), WC (waist circumference), APRI score (Aspartate Aminotransferase-to-Platelet-Ratio Index), FIB-4 scores (Fibrosis-4).

Introduction

Metabolic Syndrome or syndrome X is associated with increased risk of developing insulin resistance, cardiovascular events and it affects the liver in many ways. Non-alcoholic fatty liver disease (NAFLD) is considered the hepatic manifestation of metabolic syndrome and is characterized by triglyceride accumulation and a variable degree of hepatic injury, inflammation and repair. [1,2] Persons with metabolic syndrome are twice likely to die of cardiovascular diseases compared to those individuals who do not have those risk factors. It is also shown that the overall risk of an acute myocardial or stroke is threefold higher. [3] A strong association between NAFLD and metabolic syndrome is known, patients with metabolic syndrome are at a higher risk of NAFLD as well as liver fibrosis. [4-7] Moreover, there was evidence showed that about 29% of non-obese NAFLD patients were diagnosed with significant fibrosis. [8]

Aim and Objectives

The study was done to find out the prevalence of fatty liver and grades of liver stiffness/fibrosis in patients with metabolic syndrome and also to evaluate the association of various cumulative risk factors in this cohort of patients

Method

This was a cross sectional study comprising of 100 adult patients of more than 18 years with diagnosed cases of metabolic syndrome attending the outpatient department or endocrinology clinic in the Department of Medicine, Tripura Medical College & DR BRAM Teaching Hospital, and Agartala from January 2020 to July 2021. History included standard set of questionnaires which included duration and types of various risk factors of metabolic syndrome, any past history of viral hepatitis, drug induced hepatitis, family history of any chronic liver disease, duration and amount of alcohol intake if present or any past history of decompensated liver disease. Fibroscan 402 manufactured by Echosens, was used to estimate liver stiffness and fibrosis. Patients were grouped into grade 0, grade1, grade 2, and grade 3 and grade 4 fibrosis depending upon the fibroscan value. APRI and FIB-4 values were also calculated.

Inclusion Criteria

- Age more than18 years.
- Subjects diagnosed as Metabolic Syndrome by International Diabetes Foundation and consensus definition for Indians.

Exclusion Criteria

1. Other causes of chronic liver disease like Viral Hepatitis, Drug induced Hepatitis, Autoimmune Hepatitis and Alcohol related Chronic Liver Disease.
2. All haemodynamically unstable patients.
3. Decompensated liver disease.
4. Patients with congestive heart failure.
5. Patients with other significant co-morbid illness.
6. The Patients who are not willing to participate.

Results

It is seen that the maximum proportion of patients (34%) belonged to the age group of 30-40 years, while the lowest proportion (5%) were in the age group of <30 years. In this study population a larger proportion of participants were females (54%) compared to male (46%). Most of the patients in the present study were Obese (95%), followed by Overweight (3%) and the least number

of patients were of normal BMI (2%) (Table1).

Table1: Distribution of study population based on BMI (Asia Pacific classification) (n=100)

Category	Frequency	Percent
Normal	2	2
Overweight	3	3
Obese	95	95
Total	100	100

The mean Waist circumference (WC) in males was 90.9cms, while that in females was 90.1cms.

The mean FBS was 170.4 mg/dL, the mean TG levels were ≥ 281.8 mg/dL. The mean HDL levels were 37.5mg/dL in males and 42.9 mg/dl in males and females respectively. The mean SBP was147.3mmHg and the mean DBP was87.7mmHg (Table 2).

Table2: Mean and standard deviation of variables related to Metabolic Syndrome (n=100)

Variables	Levels	Categorical cut points	Mean	Standard deviation(±SD)
WC(in cm)	Male	≥ 90cm	90.9	7.9
	Female	≥ 80cm	90.1	7.7
FBS		≥100mg/dL	170.4	76.4
Triglyceride		≥150mg/dL(1.7mmol/L)	281.8	49.4
HDL	Male	≤40mg/dL(1.03mmol/L)	37.5	7.1
	Female	≤50mg/dL(1.3mmol/L)	42.9	5.7
SBP		≥130mmHg	147.3	18.6
DBP		≥85mmHg	87.7	9.6

In this study population we evaluated the mean and standard deviation of liver function test (AST, ALT) and platelet count. The mean AST was 54.2 with SD of 26.6, mean ALT was 72.5 with SD of 26 and mean platelet count was$192.3*10^6$ with a SD 34.5(Table 3).

Table 3: Mean and standard deviation of hematological and biochemical parameters

Parameters	Mean	Standard deviation(±SD)
AST	54.2	26.6
ALT	72.5	26.0
Platelet count	192.3	34.5

FIB-4 scores and Liver stiffness in Kpa of the study population were evaluated (Table 4).

Table 4: Table shows the mean FIB-4 and Liver stiffness (kPa scores) (n=100)

Parameters	Mean	Standard deviation(±SD)
FIB-4	1.6	1.0
Liver stiffness(KPa)	8.3	3.3

Most patients in the present study had 4 risk factors (54%), followed by 3 risk factors (27%) and 5 risk factors (19%).(Table5).

Table 5: Distribution of study subjects according to no of risk factors (n=100)

Nos of Risk factor	Frequency	Percentage (%)
3	27	27.0
4	54	54.0
5	19	19.0
Total	100	100.0

According to the based on grades of fatty liver, the highest proportion of patients in the present study had Grade II (46%) followed by grade I (22%) and Grade III (17%) (Table 6).

Table 6: Distribution of study subjects according to grades of fatty liver (n=100)

Grades of Fatty Liver	Frequency	Percentage (%)
0	15	15.0
I	22	22.0
II	46	46.0
III	17	17.0
Total	100	100.0

The distribution of study subjects based on the stage of fibrosis were evaluated and among them the highest proportion of patients (31%) were in Stage F2 of fibrosis while then lowest proportion (8%) of patients were in stage F4 of fibrosis.(Table 7).

Table 7: Distribution of study subjects according to fibrosis stage (n=100)

Stage of Fibrosis	Frequency	Percentage (%)
F0	11	11.0
F1	29	29.0
F2	31	31.0
F3	21	21.0
F4	8	8.0
Total	100	100.0

The association of fatty liver with age group were compared and the percentage of patients with fatty liver is highest in patients in age group 31-40 years of age.(Table 8).

Table 8: Association between Fatty liver and Age groups in the study population (n=100)

Age group	Fatty Liver		Total	Chi Square	P value
	No	Yes			
≤ 30	1(20)	4(80)	5(100)	3.194	0.526
31-40	7(20.6)	27(79.4)	34(100)		
41-50	4(16.7)	20(83.3)	24(100)		
51-60	1(4.2)	23(95.8)	24(100)		
≥ 60	2(15.4)	11(84.6)	13(100)		
Total	15(15)	85(85)	100(100)		

In the present study there were significant positive correlation found between fasting glucose, waist circumference, APRI, FIB-4 with liver stiffness but statistically not significant with triglyceride and HDL.(Table 9).

Table 9: Correlation between liver stiffness with fasting plasma glucose, waist circumference, APRI, FIB-4, triglyceride and HDL

	Components of Metabolic syndrome(MetS)	Pearson correlation co-efficient		Statistically significant
		r	P value	
Liver stiffness	Fasting plasma glucose	0.707	<0.00001	yes
	Waist cicumference	0.372	<0.00013	yes
	APRI	0.647	<0.00001	yes
	FIB-4	0.662	<0.00001	yes
	Triglyceride	0.138	0.171	no
	LDL	-0.082	0.4173	No

The association between the number of risk factors and the stage of fibrosis in the study population were evaluated. It is evident that fibrosis increases with increase in the number of risk factors and the observation is statistically significant. (Table 10.)

Table 10: Association between the number of risk factors and the stage of fibrosis in the study population(n=100)

No of risk factors	Fibrosis stage(%)					Total (%)
	F0	F1	F2	F3	F4	
3	1(3.7)	13(48.1)	6(22.2)	6(22.2)	1(3.7)	27(100)
4	10(18.5)	12(22.2)	19(35.2)	11(20.4)	2(3.7)	54(100)
5	0(0.0)	4(21.1)	6(31.6)	4(21.1)	5(26.3)	19(100)
Total	11(11.0)	29(29.0)	31(31.0)	21(21.0)	8(8.0)	100(100)

Figure 1 shows that 85.2 % of patients with 3 risk factors have fatty liver, 81.5 % patients have fatty liver who have 4 risk factor and 94.7% patients have fatty liver having all the 5 risk factors.

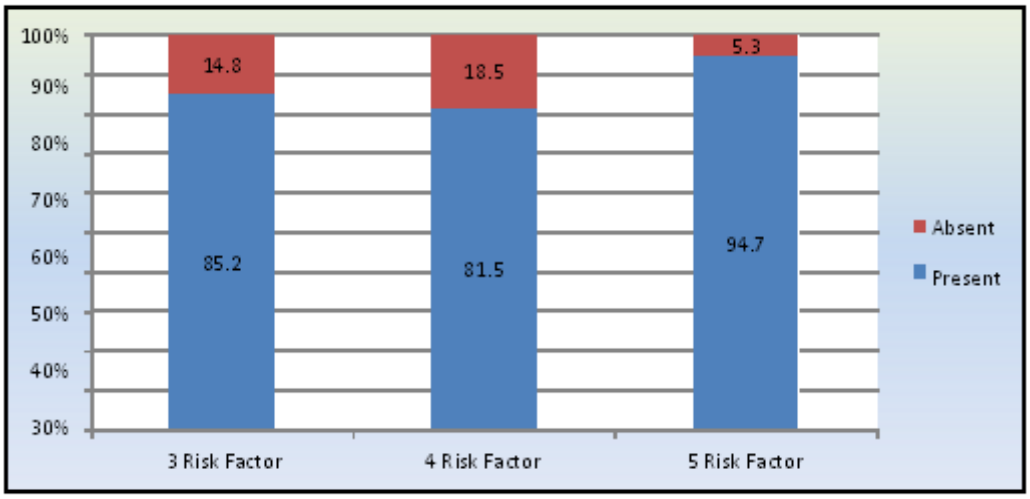

Figure 1: Figure showing percentage of people having fatty liver with cumulative risk factors (n=100)

Discussion

NAFLD is a clinicopathologic entity that is widely recognized as a major public health problem. It encompasses a wide range of liver damage, from simple steatosis to non-alcoholic steatohepatitis (NASH), advanced fibrosis, and may progress to cirrhosis. [9]

Components of Metabolic syndrome:

The waist circumference (WC) of the men and women participants in this study was 90.9and 90.1 cm, respectively. Larger waist circumference of the participants of 106 cm was seen in a study conducted by Goyal et al. [10] However, a lower level of WC was reported by Fan et al [11] in South China. He found the mean WC of the participants as 85.5cm much lower than findings of this study, though the central obesity was seen in more than half of the participants in his study. The average fasting blood glucose level of the participants in this study was 170.4 mg/dl. Amuch lower fasting glucose was seen in the study by Romanowski et al, [12] where fasting blood sugar level was 95.6 mg/dl in the participants with metabolic syndrome. This higher fasting blood sugar level in our study in contrast to other Western studies can be explained by the preferential carbohydrate intake in our part of the country and also probably due to poor glycemic control.

The triglyceride (TG) level in this study was 281.8mg/dl which much higher than the participants in the study by Romanowski et al [12] and the study done in China where the TG level in participants were 103.3 and 118.6 mg/dl, respectively. Whereas Goyal et al,[10] found the triglyceride level in metabolic syndrome participants was comparable to this study. The average HDL level in the present study participants was 40.2 mg/dl. Higher level of average HDL (45.6 mg/dl) in participants with metabolic syndrome was seen in the study by Romanowski et al.12 and a study by Fan et al.[11]where the HDL was found as 52.5 mg/dl in the participants. This higher triglyceride level and lower LDL levels in our study and also in other Indian studies compared to Western studies are probably due to distinct Indian phenotype of dyslipidemia.

The average blood pressure level in this study was much higher than the study by Fan et al. [11] and Romanowski et al. [12] This study found mean SBP as 147.3 mm Hg and DBP as 87.7 mm Hg,whereas the average BP in the study by Fan et al. was 136.7 and 81.5-mm Hg, respectively. Romanowski et al. reported SBP and DBP as 116 and 74 mmHg, respectively. Among the participants in this study, more than half (54%) presented with four components of metabolic syndrome, 27% presented with three risk factors and 19% presented with all five risk factors. In a study by Uchil et al. [13] showed that about one third of the NAFLD patients in the study had all the risk factors for metabolic syndrome.

Prevalence of Fatty Liver by Age, Gender, and BMI:

The prevalence of fatty liver in this study was high(85%).In the study of Goyal et al. [10] the prevalance of fatty liver was found as73%.In contrast to this study, a study by Uchil et al. [13]found the prevalence of NAFLD was 22%. Individuals with Metabolic Syndrome (MetS) are more likely to develop NAFLD over time. In a study by Hamaguchi M et al, it was discovered that patients with Metabolic syndrome at the baseline had a much higher chance of developing NAFLD over the next 414 days than those without MetS. [14] 46% of the participants in this study had grade II or moderate fatty liver, 22% had grade I and17% had grade III fatty liver.

In the present study, participants above 50 years had the highest prevalence of fatty liver around 34%. In the study by Duseja et al. [15] the mean age of patients with NAFLD was 49 years, which was comparable to the present study. The prevalence of fatty liver in the present study was 100% in the overweight and 85.3% in the obese patients according to the BMI Asia-Pacific classification. However, 1 participant with normal BMI also had fatty liver. But there is no significant difference p=0.293 in the proportion of fatty liver based on the BMI for Asia-pacific of the study population. The APRI score (aspartate aminotransferases (AST) to platelet ratio index and Fibrosis-4 (FIB-4) are the simple and cost-effective non-invasive markers of liver fibrosis. The

APRI had a sensitivity of 60% and a specificity of 73.3% for detecting fibrosis in the NAFLD group. [16] The current study found a FIB-4 value of 1.6(SD=1.0) showing moderate risk of fibrosis.

Liver stiffness in Metabolic Syndrome

In this study, the liver stiffness measurement (LSM) was 8.3kilopascal (kPa). 31% which comprises most of the participants had stage 2 fibrosis. A 11 years long prospective study by Lallukka et al. [17] found the median liver stiffness was 10.4 kPa.

Individual Risk Factors in Metabolic Syndrome

In the present study there exists a significant positive correlation between waist circumference and liver stiffness (Pearson Correlation Coefficient: r= 0.372, p value= 0.00013). Similarly, there exists a strong positive correlation between fasting plasma glucose and liver stiffness in the present study, with correlation coefficient r=0.707 and p value<0.00001. Similarly a prospective study done in Northern India by Kuchay, Mohammad Shafi, et al [18] on 601diabetic adults found that 84.2% with T2DM had NAFLD detected by USG. And among them 28.2% had LSM >8 Kpa which was taken as clinically relevant liver fibrosis (CRLF) for that particular study. The present study demonstrated a mild or minimal positive correlation (r=0.138) between Triglyceride level and liver stiffness which is statistically insignificant. [19]

Fatty liver and liver stiffness with cumulative Risk Factors of Metabolic syndrome

Participants with all the risk factors for metabolic syndrome had a significantly higher liver stiffness compared to those with 3 or 4 risk factors. These findings are comparable to the study by Lallukka et al. [17] Our study also shows that, presence of fatty liver of various grades are present in 94.7% population having all the five risk factors of metabolic syndrome whereas fatty liver is present in 85.2 % and 81.5% patients with 3 and 4 risk factors respectively. However, the difference among the group is not statistically significant (p=0.379).

Conclusion

In our study fatty liver (I -III) was seen in 85% of the patients while Liver Fibrosis (F1-F4) was seen in 89%. Significant correlation was also seen between Liver stiffness and waist circumference, BMI and number of risk factors of metabolic syndrome. Liver stiffness is significantly higher in patients with 4 or 5 risk factors. APRI and FIB-4 values too correlate significantly with liver stiffness. Thus, it is found that persons associated with metabolic syndrome are at greater risk of development of fatty liver and liver fibrosis which ultimately lead to cirrhosis.

Limitation of the study

The study size is small and is a cross sectional study.

Large scale analytical study with adequate follow up period is required as liver fibrosis is a dynamic process.

The duration of individual risk factors of metabolic syndrome is not taken into account.

Difficulty in performing fibroscan of very obese individuals even with XL probe.MR elastography is more accurate way of assessing liver stiffness than fibroscan.

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