

## “Non- Alcoholic Fatty Liver Disease and Its Relationship with Metabolic Syndrome Among the Adult Patients Attending in Rajshahi Medical College Hospital, Rajshahi, Bangladesh”

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### Abstract

**Background:** Metabolic syndrome describes the co-occurrence of central adiposity, hyperglycemia, hypertension, lipid abnormalities and other metabolic changes that increase risk of cardiovascular, cerebrovascular, renal diseases. This multi-system condition has adverse effects on many organs, the liver being one of them. Non-alcoholic fatty liver disease appears to be the hepatic manifestation of metabolic syndrome, and is increasingly recognized as a major contributor to the burden of chronic liver disease world-wide. Metabolic syndrome and non-alcoholic fatty liver disease appear to have a common pathogenesis, arising from insulin resistance, central adiposity and chronic low grade inflammation.

**Objective:** The aim of the study is to find out the occurrence of NAFLD and metabolic syndrome among the patient attending in RMCH.

**Materials and Methods:** This is a cross sectional descriptive study which was conducted in the Department of Medicine, Rajshahi Medical College Hospital, Rajshahi, Bangladesh. 250 patients age above 20 years nonalcoholic both male and female were included for the study. All patients were interviewed by structured questionnaire. Statistical analysis was carried out by using the Statistical Package for the Social Sciences (SPSS) software version 23.0 for windows (SPSS Inc, Chicago, Illinois, USA). Continuous data are expressed as the mean  $\pm$  standard deviation (SD) and categorical variables are expressed as percentages. Pearson correlation coefficient test and unpaired t-test were used for this study. For all statistical tests, p-value is less than 0.05 was considered as statistically significant.

**Results:** Among 250 respondents a total of 67(26.8%) cases were diagnosed as metabolic syndrome and out of the 67 metabolic syndrome patients 23(34.33%) were male and 44(65.67%) were female. Out of the 23 male metabolic

*syndrome patients 9(39.13%) were diagnosed as NAFLD and out of the 44 female metabolic syndrome patients 16(36.36%) were diagnosed as NAFLD. Among the 250 respondents 53 (21.2%) cases ultrasonographically diagnosed as NAFLD and showed 41(77.36%), 11(20.75%) and 1(1.89%) of cases had grade I, II, and III fatty liver respectively. Out of the 53 NAFLD patient's 25 patients were presented with metabolic syndrome and 28 patients were without metabolic syndrome. Patients of NAFLD with metabolic syndrome presented with high fasting plasma glucose level in 19(67.80%) cases, hypertensive in 17(68%) cases, high triglyceride in 17((68%) cases, low HDL in 16(64%) cases, waist circumference high in 18(72%) cases. The difference was significant for fasting plasma glucose, blood pressure, triglycerides, high-density lipoprotein and waist circumference ( $p<0.05$ ) between metabolic syndrome and non-metabolic syndrome patients.*

**Conclusion:** *From the study, it can be concluded that the proportion of NAFLD significantly higher in metabolic syndrome patients compare to non-metabolic syndrome patients and metabolic syndrome is higher in female compare to male. So early diagnosis of metabolic syndrome suspected cases and ultrasonographic detection of NAFLD would help not only modifying the disease course but also delaying its complication.*

**Keywords:** Nonalcoholic Fatty Liver Disease, Non Alcoholic Steatohepatitis, Metabolic Syndrome, Low Hdl, Risk of Cardiovascular.

## Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most prevalent liver disease. Non-alcoholic fatty liver disease (NAFLD) refers to a spectrum of liver damage ranging from simple steatosis to Non-alcoholic steatohepatitis (NASH), advanced fibrosis and cirrhosis (1). There are other factors and conditions that can lead to fatty liver such as lipodystrophy, Wilson's disease, primary mitochondrial disease, bariatric surgery, parenteral nutrition, medication (amiodarone, methotrexate, tamoxifen), toxins. The incidence of NAFLD varies on the geographic area and the diagnostic method. In Europe, the NAFLD incidence in the general population is 20-30% and in the USA is 27-38% (2, 3). Prevalence in the Middle East, Japan, and China is almost the same as the Western world, with a prevalence rate of 15-30%. In Asian countries, the prevalence of NAFLD varies in different regions. However, in the Indian subcontinent, prevalence of NAFLD is recorded to be 16-32% in urban population and approximately 9-16% in rural areas (4-6). Bangladesh is also experiencing an increasing trend of NAFLD due to changing dietary patterns and sedentary lifestyles (5-7). The World Health Organization (WHO) has been documented in May 2014 stating that 2.82% of total deaths in Bangladesh are due to liver diseases. It is the eighth most common cause of death in Bangladesh, and the age-adjusted death rate is 19.26 per 100 000 populations (8-10). Chronic liver diseases (CLDs) are responsible for 37-69% of liver diseases in Bangladesh, and NAFLD is a significant contributor to the burden of chronic liver diseases. However, data on the burden of NAFLD are very limited in Bangladesh. The few studies that have been conducted included hospitalized patients, and little information is available on the community-based estimation of NAFLD burden (11, 12). In low-income countries like Bangladesh, hospital-based prevalence estimates may underestimate the true burden of disease as many patients with NAFLD may never seek medical care as a result of being asymptomatic, having limited access to healthcare services, and being in fear of significant economic burden (13). NAFLD is associated with components of the Metabolic Syndrome (MS) such as abdominal obesity, insulin resistance, dyslipidemia, glucose intolerance or type 2 diabetes mellitus (T2DM). The insulin resistance was identified as a central point in pathogenetic mechanism of NAFLD, so it can be considered the liver manifestation of the MS. Insulin resistance in NAFLD is characterized by reduced whole-body, hepatic, and adipose tissue insulin sensitivity.

Insulin resistance is often associated with chronic low-grade in-

flammation, and numerous mediators released from immune cells and adipocytes may contribute liver damage and liver disease progression. In the MS the major associations of NAFLD are with obesity and with T2DM. The patients with these disorders have a 70-90% prevalence of NAFLD. Patients with NAFLD and T2DM have an additional risk of developing NASH, advanced fibrosis and cirrhosis and hepatocellular carcinoma, chronic kidney disease and retinopathy (14). Metabolic Syndrome is a set of metabolic and cardiovascular risk. According to the NCEP ATP III definition, Metabolic Syndrome is present if three or more of the following five criteria are met : abdominal obesity (waist circumference increased for the Europeans  $\geq 94$  cm in men and  $\geq 80$  cm in women; for the Americans  $\geq 102$  cm in men and 88 cm in women, for south asian men  $\geq 90$  cm and women  $\geq 80$ cm), elevated triglycerides  $\geq 150$  mg/dl or treatment for hypertriglyceridemia, low HDL cholesterol  $<40$  mg/ dl for women or  $<50$ mg/dl for men or treatment for low HDL cholesterol, hypertension  $\geq 130/85$  mm Hg or treated hypertension, high fasting plasma glucose  $\geq 100$  mg/dl or treatment for hyperglycemia (15-17). Over 90% of patients with NAFLD have at least one component of the Metabolic Syndrome and the complete diagnosis of Metabolic Syndrome is present at 55-65% of the patients with liver disease.

The weighted pooled prevalence of metabolic syndrome regardless of gender and criteria used to define metabolic syndrome was 20% with high heterogeneity observed. Weighted pooled prevalence of metabolic syndrome is higher in female (32%) compared to male (25%) though not statistically significant ( $P=0.434$ ). Prevalence was highest (37%) when modified NCEP ATP III criteria was used to define Metabolic Syndrome. Non-alcoholic fatty liver disease is common, and may contribute significantly to the burden of chronic liver disease. A study of long term follows up of NAFLD patients suggests that overall prognosis of NAFLD is good, and only a minority of patients develop NASH and cirrhosis (18). Risk factors for the development of Metabolic syndrome and NAFLD include: Increasing age - around 44% of the US population above the age of 50 years have MS, possibly due to weight gain, reduced physical activity & hormonal effects. Obesity - increased waist circumference and central adiposity is strongly linked with metabolic syndrome, with an increase of 1 cm in waist circumference increasing the risk of metabolic syndrome by around 7.4%. Physical inactivity is a potent predictor of cardiovascular mortality and morbidity, probably mediated via central adiposity, reduced high density lipoprotein (HDL) cholesterol levels and hypertension.

Female sex- women are affected by metabolic syndrome more commonly than men, particularly post menopause. Hormonal changes- low levels of testosterone and sex hormone binding globulin (SHBG), growth hormone (GH), and high levels of glucocorticoids are all associated with increased risk of Metabolic syndrome. Stress - physiological, emotional or psychological stress can be an underlying cause of MS, possibly due to imbalance of the hypothalamic-pituitary- adrenal (HPA) axis. Ethnicity - South Asians appear to be the highest risk for development of MS. Polycystic Ovarian Syndrome (PCOS)-Peripheral insulin resistance with a compensatory hyperinsulinaemia is frequently seen in PCOS, and the insulin excess leads to ovarian and adrenal androgen production. PCOS is frequently, although not always, associated with obesity and glucose intolerance. Treatment with metformin can improve insulin sensitivity and lead to ovulatory cycles (19-21). Rapid development, urbanization and consequent change in diet and physical activity levels has led to a rapid growth in obesity and prevalence of MS. The commensurate rise in NAFLD worldwide is consequent on these changes. Whilst fatty liver disease is less of a burden of total liver disease worldwide, compared to viral hepatitis and alcohol, it is likely to grow in prevalence, especially in the developing world, unless major improvements in the prevention and management of Metabolic syndrome are developed. The aim of the present study is to evaluate the association of metabolic syndrome with non- alcoholic fatty liver disease.

## Objectives

### General:

- a. To find out the metabolic syndrome and NAFLD among the patients attending in RMCH.

### Specific:

- a. To find out the metabolic syndrome patient in RMCH.
- b. To find out the occurrence of NAFLD among the patients with metabolic syndrome.
- c. To find out the occurrence of NAFLD among the patients without metabolic syndrome.
- d. To find out the socio demographic characteristics of both metabolic syndrome and non-metabolic syndrome patients.
- e. To calculation of BAAT score to find out high risk group among NAFLD who runs risk to develop fibrosis in liver.
- f. To find out the association of NAFLD between metabolic syndrome and non-metabolic syndrome.

## Literature Review

Literature reviews have been done to conduct systemic search of published work to find out what is already known about the intended research topic. This chapter provides an overview of previous research about association between NAFLD and metabolic syndrome. We made an extensive review of literature to collect information related to topic. Metabolic syndrome (MS) describes the co-occurrence of a constellation of metabolic disorders, which increase the risk of developing atherosclerotic vascular disease and Type 2 diabetes (T2D). The syndrome affects around one in five people worldwide, with the prevalence mirroring the rapid rise in obesity (22). Non-alcoholic fatty liver disease (NAFLD) is common, and increasingly recognised as a major cause of hepatic morbidity in developed and developing countries. Epidemiological evidence suggests a close link between the prevalence of MetS and NAFLD. This brief review discusses the evidence suggesting

a potential link between MS and NAFLD, and the potential pathogenic mechanisms behind this link. In 1947 Jean Vague (1947), observed that upper body obesity predisposed to diabetes, atherosclerosis and gout. Some thirty years later, Haller and colleagues, used the term “metabolic syndrome” for the association of diabetes mellitus, obesity and hepatic steatosis when describing the additive effects of risk factors on atherosclerosis. Reaven, subsequently proposed that insulin resistance was an underlying factor linking the metabolic abnormalities associated with his “syndrome X”. Metabolic Syndrome has been variously named as metabolic syndrome X, syndrome X, insulin resistance syndrome, Reaven, syndrome and CHAOS (coronary artery disease, hypertension, adult onset diabetes, obesity, and stroke (23, 24). There has been some debate over the clinical utility of the metabolic syndrome to delineate increased risk of cardiovascular disease, and whether the label of metabolic syndrome offers any benefit over and above the individual risk. A very recent position of the World Health Organization, is that the MS has limited practical utility as a diagnostic or management tool, and some authors suggest that the use of term metabolic syndrome may divert focus away from simpler and more precise risk models (25). Nevertheless, a number of major international organizations have developed definitions for MS, and in recent years, a single unified definition has been agreed, based on the presence of abdominal obesity and a number of other cardiovascular factors) (2009).

## Epidemiology of Metabolic Syndrome:

Prevalence of MS in Europe varies from 12-26% depending on geographical area, urbanization and ethnic mix (IDF, 2010). Studies in Asia, suggest the prevalence is 5-20%, with an overall global prevalence of around 16% of the adult population (26). Prevalence in India appears to be highest, at around 26% of the adult urban population [26, 27], and prevalence appears to be increasing as obesity rates and urbanization increase. Data from the USA National Health and Nutritional Examination Survey (NHANES) show an age adjusted prevalence increase by 23.5% in women and 22.2% in men between 1994 and 2000 (28). Overweight and obesity appears to be increasing in children and adolescents, suggesting that the prevalence of metabolic syndrome is also increasing, and likely to go on increasing for the foreseeable future. A recent study comprising of 105 obese adolescent subjects undergoing laparoscopic obesity surgery, reported a 25% incidence of Non-alcoholic steatohepatitis (NASH), and also confirms that the presence of metabolic syndrome in obese adolescents predicts impaired glucose tolerance and NAFLD (29).

## Risk Factors for the Development of Metabolic Syndrome and Nafld:

Non-alcoholic fatty liver disease is common, and may contribute significantly to the burden of chronic liver disease. It is important to note, however, that selection bias may be a factor in the study of MS in patients with NAFLD and NASH. Liver biopsy is generally only performed in selected patients, and the natural history of the disease may be completely different in subjects from the general population. A recent study of long term follow up of NAFLD patients suggests that overall prognosis of NAFLD is good, and only a minority of patients develop NASH and cirrhosis. Nevertheless, the number of people with NAFLD is large, and hence even a small number of them progressing to NASH is likely to lead to a



significant burden of chronic liver disease.

### Risk Factors for the Development of ms and Nafld Include:

1. Increasing age - around 44% of the US population above the age of 50 years have MS, possibly due to weight gain, reduced physical activity & hormonal effects.
2. Obesity - increased waist circumference and central adiposity is strongly linked with MS, with an increase of 1 cm in waist circumference increasing the risk of MS by around 7.4%.
3. Physical inactivity - is a potent predictor of cardiovascular mortality and morbidity, probably mediated via central adiposity, reduced high density lipoprotein (HDL) cholesterol levels and hypertension.
4. Female sex - women are affected by MS more commonly than men, particularly post menopause.
5. Hormonal changes – low levels of testosterone and sex hormone binding globulin (SHBG), growth hormone (GH), and high levels of glucocorticoids (Syed and Weaver, 2005) are all associated with increased risk of MetS.
6. Stress - physiological, emotional or psychological stress can be an underlying cause of MS, possibly due to imbalance of the hypothalamic-pituitary- adrenal (HPA) axis.
7. Ethnicity - South Asians appear to be the highest risk for development of MS.
8. Polycystic Ovarian Syndrome (PCOS) - Peripheral insulin resistance with a compensatory hyperinsulinaemia is frequently seen in PCOS, and the insulin excess leads to ovarian and adrenal androgen production. PCOS is frequently, although not always, associated with obesity and glucose intolerance, Treatment with metformin can improve insulin sensitivity and lead to ovulatory cycles.

### Operational Definitions:

Definition of metabolic syndrome (According To ATP III Criteria ):

<b>Glucose</b>	≥5.6mmol/L (≥100mg/dL) or drug treatment for elevated glucose
<b>Blood Pressure</b>	≥130/85 mmHg or drug treatment for elevated blood pressure
<b>Triglycerides</b>	≥1.7mmol/l (≥150mg/dL) or specific treatment for this
<b>High Density Lipoprotein (HDL) Cholesterol</b>	Men: 1.03mmol/L (<40mg/dL) Women: 1.29mmol/L (<50mg/dL)
<b>Obesity</b>	Abdominal Waist Circumference -population specific: European men: ≥ 102cm (≥40") European women ≥88cm (≥34.5") South Asian men: ≥90cm (≥35") South Asian women: ≥80cm (≥31.5")

Measure (Any 3 of 5 Criteria Constitute Diagnosis of Metabolic Syndrome) Waist Circumference Measurement procedure: - In case of non-obese - Start at the approximate midpoint between the lower margin of the last palpable rib and top of the iliac crest usually at the level of belly button. In case of obese - Stand and place

a tape measure around middle just above the iliac crest. The accuracy of waist circumference measurement depends on tightness of the measuring tape and on its correct positioning that is parallel to the floor at the level at which the measurement is made. The tape should be snug around the body, but not pulled so tight that it is constricting. The posture of the patient at the time of measurement should stand with arms at the sides, feet positioned close together and weight evenly distributed across the feet. Waist circumference should be measured at the end of a normal expiration when the lung are at their functional residual capacity. Patient should be fasted overnight or is in a fasted state (30-34).

### Materials and Methods

Study Design: Cross sectional descriptive study.

**Study Place:** Department of Medicine, Rajshahi Medical College Hospital, Rajshahi, Bangladesh.

**Study Period:** From July 2017 to June 2019.

**Study population:** Study was conducted on non-alcoholic patients in the age group of >20, attending Medicine Department of Rajshahi Medical College Hospital, Rajshahi, Bangladesh.

**Sampling Technique:** Purposive sampling

### Selection criteria:

Inclusion criteria:

1. Non-alcoholic patients.
2. Age >20 years
3. Both metabolic and non-metabolic syndrome patients.
4. Adult male and female patients equal in number.

Exclusion Criteria:

5. Alcoholic patients.
6. Drug causing obesity (Antipsychotics, Antidepressant, Anti-convulsants)
7. Disease causing obesity (Hypothyroidism, Cushing's syndrome, PCOS)
8. Age <20 year

Determination of Sample Size: According to this formula the estimated final sample size was 246

### Selection of patients and Study Procedure:

A standardized structured data collection method was used to collect necessary information of the study subjects that included: The sample consisted of 250 medical records of adult patients who were meet the inclusion criteria, which were patients of both genders, both metabolic syndrome and non-metabolic syndrome, aged >20 years, None of these patients had history of alcohol consumption. The studied variables were gender, age, biochemical parameters (fasting glucose, HDL-cholesterol, and triglycerides), abdominal ultrasound, blood pressure, and anthropometrics (weight, height, waist circumference, and BMI). Grade I obesity is those with BMI 30 to 34.99, Grade II obesity is considered in patients with BMI 35.0-39.9 kg/m<sup>2</sup>, and grade III obesity in those with BMI ≥ 40.0 kg/m<sup>2</sup>. The Western pacific Region Office Of WHO recommends that, among Asians, BMI >23.0 is overweight and >25.0 is obese.

NAFLD diagnosis was obtained through abdominal ultrasonography, which classifies NASH as NAFLD diagnosis was obtained through abdominal ultrasonography, which classifies NASH as Grade I (slight diffuse increase of fine echoes in the hepatic parenchyma, with normal visualization of the diaphragm and intrahepatic vessel walls), Grade II (moderate diffuse increase of fine echoes with slight difficulty in visualization of the vascular wall and diaphragm), or Grade III (significant increase of fine echoes with poor visualization of the diaphragm, vascular walls, and posterior segments of the right lobe, which could increase liver volume) The diagnosis of MS was attained using the protocol described by the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III, 2001), updated by the American Heart Association, and the National Heart, Lung, and Blood Institute (AHA / NHLBI, 2005), which considers that the patient has MS when three or more risk factors described below are associated: high waist circumference European men:  $\geq 102\text{cm}$  (40") European women  $\geq 88\text{cm}$  (34.5") South Asian men :  $\geq 90\text{cm}$  (35") South Asian women:  $\geq 80\text{cm}$  (31.5"), high triglycerides ( $\geq 150\text{ mg/dL}$  or specific treatment), reduced HDL cholesterol ( $< 40\text{ mg/dL}$  for men and  $< 50\text{ mg/dL}$  for women, or specific treatment), high blood pressure ( $\geq 130 / \geq 85\text{ mmHg}$ , or drug treatment hypertension), elevated fasting glucose ( $\geq 100\text{ mg/dL}$ , ).

### Data Analysis

Data were entered in duplicate into a SPSS and analyzed using SPSS software, version 23.0. Analyses of data consistency were initially conducted, followed by descriptive analyses. The associations of the outcome "NAFLD" with the "MS" exposure and other explanatory variables were tested using the chi-squared test and linear association, and prevalence ratios with their respective 95% confidence intervals (95% CI) was calculated. The data collected was presented in the form of percentages, frequencies and figures such as tables, charts and graphs. Statistical comparisons were made using unpaired student t-test for 2 independent variables. A P value of less than .05 was considered to be statistically significant.

### Results

Among the 250 respondents a total of 67(26.8%) cases were diagnosed as metabolic syndrome and out of the 67 metabolic syndrome patients 23(34.33%) were male and 44(65.67%) were female. Out of the 23 male metabolic syndrome patients 9(39.13%) were diagnosed as NAFLD and out of the 44 female metabolic syndrome patients 16(36.36%) were diagnosed as NAFLD. Among the 250

respondents 53 (21.2%) cases ultrasonographically diagnosed as NAFLD and showed 41(77.36%), 11(20.75%) and 1(1.89%) of cases had grade I, II, and III fatty liver respectively. Out of the 53 NAFLD patient's 25 patients were presented with metabolic syndrome and 28 patients were without metabolic syndrome. Patients of NAFLD with metabolic syndrome presented with high fasting plasma glucose level in 19(67.80%) cases, hypertensive in 17(68%) cases, high triglyceride in 17((68%) cases, low HDL in 16(64%) cases, waist circumference high in 18(72%)cases.

**Table 1: Distribution of patients according to their clinical and biochemical profiles (n=250)**

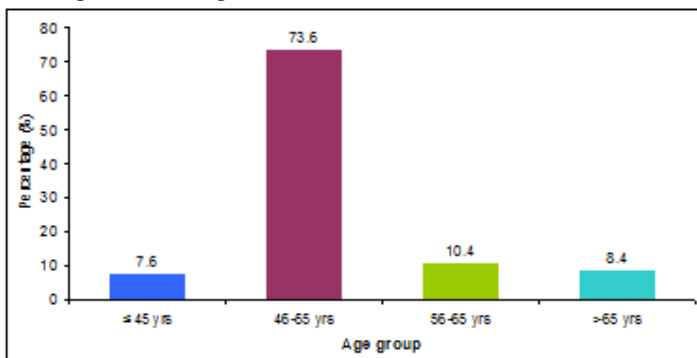
Variable	Mean± SD	Odd Ratio
Age (in year)	45.70±7.22	1.20
Body mass index (kg/m <sup>2</sup> )	20.60±4.39	3.10
Waist circumference (cm)	4.22±7.44(Women) 82.87±6.25(Men)	2.10 2.12
Diastolic blood pressure (mm Hg)	78.87±6.25	3.1
Systolic blood pressure (mm Hg)	126.0±18.17	2.20
Fasting blood sugar (mg/dl)	124.17±62.62	1.12
Total cholesterol (mg/dl)	196.16±54.59	1.00
Serum triglycerides (mg/dl)	185.13± 77.5	2.00
High density lipoprotein (mg/dl)	45.23±9.13	2.10
Serum LDL (mg/dl)	125.43±27.44	3.60
Alanine amino transferase (SGPT) (u/l)	65.33±49.02	1.30

Table 1 shows that mean age of the patient was 45.70±7.22 years. On physical examination findings showed the mean BMI was 20.6±4.39 kg/m<sup>2</sup>, mean waist circumference was 74.22±7.44 cm. Mean diastolic blood pressure (mm Hg) was 78.87±6.25 and mean systolic blood pressure (mm Hg) 126.0±18.17. The mean fasting blood sugar (mg/dl) was 124.17±62.62 and mean total cholesterol (mg/dl) was 196.16±54.59 and mean serum triglycerides (mg/dl) were 185.13±77.5.

**Table- 2: Socio-demographic characteristics of the study patients (n=250)**

Variables	Frequency	Percentage (%)
Age		
≤45 years	19	7.6
46-55 years	184	73.6
56-65 years	26	10.4
>65 years	21	8.4
Mean± SD	45.70±7.22	
Sex		
Male	125	50.0
Female	125	50.0
Smoking History		
Present	58	23.2
Absent	192	76.8
Occupation		
Farmer	74	29.6
Businessman	59	23.6
Housewife	88	35.2
Others	29	11.6
Religion		
Muslim	227	90.8
Non Muslim	23	9.2
Education		
Below primary	113	45.2
Up to HSC	113	45.2
Graduate	24	9.6
Monthly income		
<10000 Tk.	58	23.2
>10000 -20000 Tk.	161	64.4
>20000 Tk	31	12.4
Marital status		
Married	228	91.2
Unmarried	22	8.8

Table-2: shows that maximum number of patients were in between 46-55 years of age and mean was 53.70±7.22. Male female ratio was 1:1. Most of the patients (76.8%) were non-smoker, 90.8% patient were Muslim, 91.2% patient were married, 64.4% patient had monthly income >10000 -20000 taka, 29.6% patient were farmer, 35.2% patient were housewife and 23.6% were businessman, 45.2% patient were graduate.



**Figure-1: Bar diagram showing the age distribution of the study**

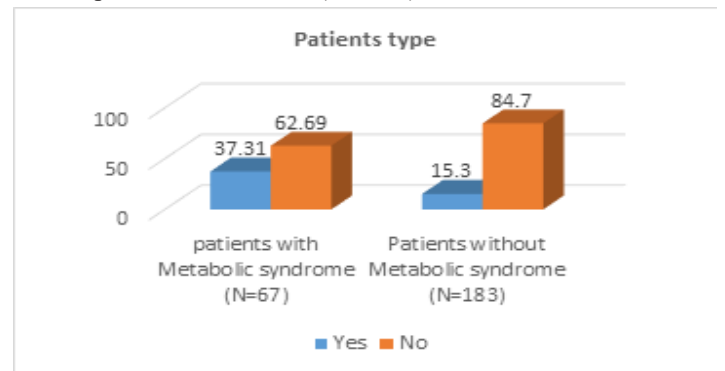
patients

**Table-3: Association of NAFLD with /without Metabolic Syndrome (n=250)**

NAFLD	Patients with Metabolic syndrome (N=67)	Patients without Metabolic syndrome (N=183)	P-value
Yes	25 (37.31%)	28 (15.30%)	0.011*
No	42 (62.69%)	155 (84.70%)	
Total	67 (100.0%)	183 (100.0%)	

P-value measured by Chi-square test, \*significant

Analysis of the above table indicated that the proportion of NAFLD significantly higher (37.31%) in patients with MS compare to normal patients without MS (15.30%).



**Figure-2: Bar diagram showing the NAFLD patients relation to MS syndrome (n=250)**

**Table-4: Association of NAFLD with /without Metabolic Syndrome relation to sex (n=250)**

NAFLD	Male (N=125)		Female (N=125)	
	With Metabolic syndrome (n=23)	Without Metabolic syndrome (n=102)	With Metabolic syndrome (n=44)	Without Metabolic syndrome (n=81)
Yes	9(39.13%)	16(15.69%)	16(36.36%)	12(14.81%)
No	14(60.87%)	86(84.31%)	28(63.64%)	69(85.19%)
Total	23 (100%)	102 (100%)	44(100%)	81(100%)
p-value	0.029s		0.178ns	

P-value measured by Chi-square test, ns= not significant

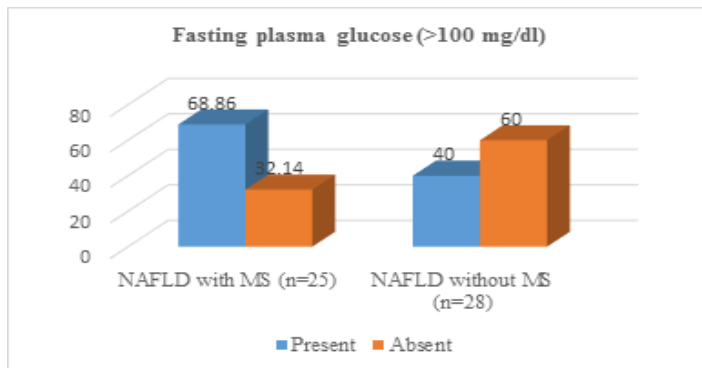
Analysis of the above table indicated that the proportion of NAFLD significantly higher in metabolic syndrome in male patients compare to non-metabolic syndrome and no significant difference of NAFLD with or without MS in female patients.

**Table-5: Association of impaired fasting plasma glucose of NAFLD patients with/without Metabolic Syndrome (n=53)**

Fasting plasma glucose ( $\geq 100$ mg/dl)	NAFLD with Metabolic syndrome (N= 25)	NAFLD without Metabolic syndrome (N=28)	Total	P-value
Present	19 (67.86%)	10 (40%)	29(54.72%)	0.036*
Absent	9(32.14%)	15(60%)	24(45.28%)	
Total	28(100.0%)	25(100.0%)	53(100.0%)	

P-value measured by Chi-square test, \*significant

Table-5 shows that out of 53 patients, impaired fasting plasma glucose level significantly higher (67.86%) in NAFLD with metabolic syndrome group compare to without metabolic syndrome.



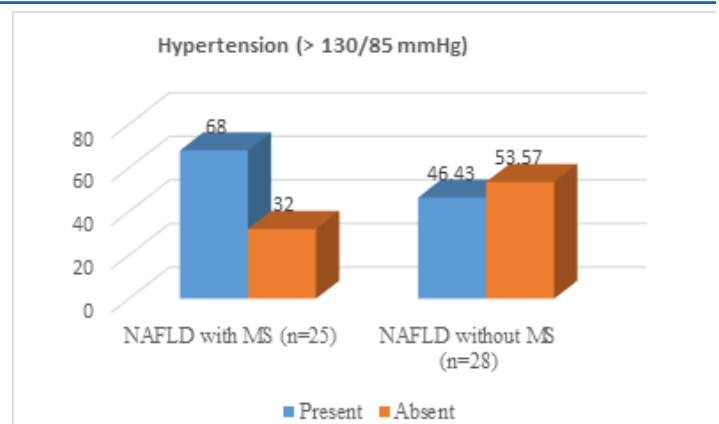
**Figure-3:** Bar diagram showing the impaired fasting plasma glucose of NAFLD patients relation to Metabolic Syndrome.

**Table-6: Association of hypertension of NAFLD patients with/without metabolic syndrome (n=53)**

Hypertension ( $\geq 130/85$ mmHg)	NAFLD with Metabolic syndrome (N= 25)	NAFLD without Metabolic syndrome (N=28)	Total	P-value
Present	17 (68%)	13 (46.43%)	30(56.60%)	0.039*
Absent	8(32%)	15(53.57%)	23(43.40%)	
Total	25(100.0%)	28(100.0%)	53(100.0%)	

P-value measured by Chi-square test, \*significant

Table-6 shows that out of 53 patients, hypertension was significantly higher (68%) in NAFLD with metabolic syndrome group compare to without metabolic syndrome.



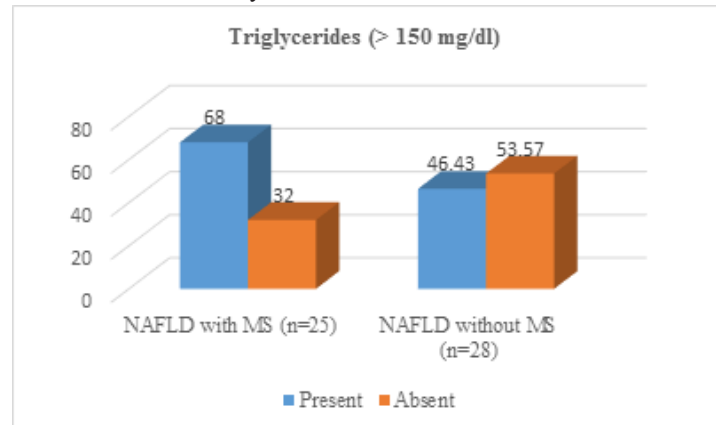
**Figure-4:** Bar diagram showing the hypertension of NAFLD patient's relation to metabolic syndrome.

**Table-7: Association of high TG of NAFLD patients with/without Metabolic Syndrome (n=53)**

Tri-glycerides ( $\geq 150$ mg/dl)	NAFLD with Metabolic syndrome (N= 25)	NAFLD without Metabolic syndrome (N=28)	Total	P-value
Present	17 (68%)	15(53.57%)	32(60.79%)	0.010*
Absent	8(32%)	13(46.43%)	21(39.21%)	
Total	25(100.0%)	28(100.0%)	53(100.0%)	

p-value measured by Chi-square test, \*significant

Table-7 shows that out of 53 patients, high TG was significantly higher (68%) in NAFLD with metabolic syndrome group compare to without metabolic syndrome.



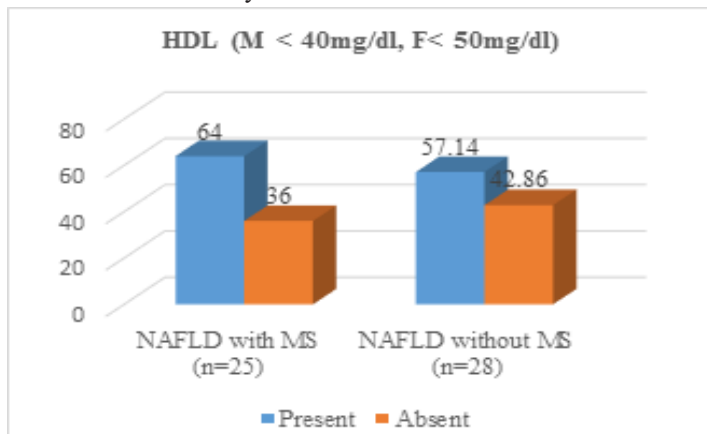
**Figure-5:** Bar diagram showing the high TG of NAFLD patients relation to Metabolic Syndrome.

**Table-8: Association of Low HDL of NAFLD patients with/without Metabolic Syndrome (n=53)**

HDL (M < 40mg/dl, F < 50mg/dl)	NAFLD with Metabolic syndrome (N= 25)	NAFLD without Metabolic syndrome (N=28)	Total	P-value
Present	16(64%)	16 (57.14%)	32(60.38%)	0.009*
Absent	9(36%)	12 (42.86%)	21(39.62%)	
Total	25(100.0%)	28(100.0%)	53(100.0%)	

P-value measured by Chi-square test, \*significant

Table-8 shows that out of 53 patients, low HDL level significantly higher (64%) in NAFLD with metabolic syndrome group compare to without metabolic syndrome.



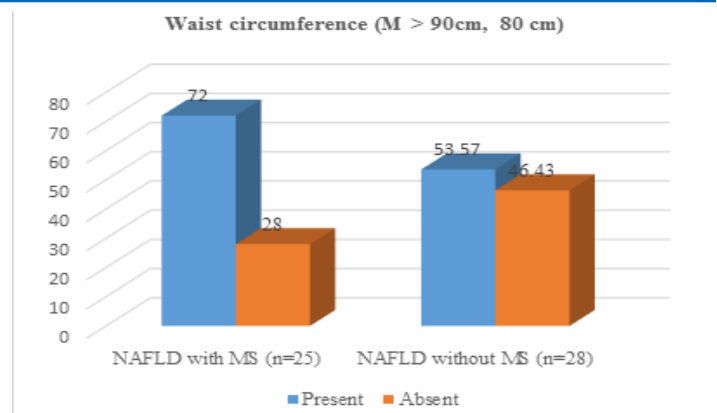
**Figure-6:** Bar diagram showing the low HDL of NAFLD patients relation to Metabolic Syndrome.

**Table-9: Association of increased WC of NAFLD patients with/without Metabolic Syndrome (n=53)**

Waist circumference (M ≥ 90cm, F ≥ 80 cm)	NAFLD with Metabolic syndrome (N= 25)	NAFLD without Metabolic syndrome (N=28)	Total	P-value
Present	18 (72%)	15(53.57%)	33(62.26%)	0.041*
Absent	7(28%)	13(46.43%)	20(37.74%)	
Total	25(100.0%)	28(100.0%)	53(100.0%)	

p-value measured by Chi-square test, \*significant

Table-9 shows that out of 53 patients, increased level of WC was significantly higher (72%) in NAFLD with metabolic syndrome group compare to without metabolic syndrome.



**Figure-7:** Bar diagram showing the increased WC of NAFLD patients relation to Metabolic Syndrome.

**Table-10: Distribution of patients according to the grades of NAFLD (n=53)**

Variables	NAFLD without metabolic syndrome (n=28)			NAFLD with metabolic syndrome (n=25)	
	Grade I n= 22	Grade II n=5	Grade III n= 1	Grade I n=19	Grade II n=6
ALT ≥ 41 IU	12 (32.4%)	8 (61.5%)	1 (100%)	14 (63.6%)	4 (57.1%)
Central obesity (WC) (≥90 cm - M, ≥ 80 cm - F)	13 (35.1%)	9 (69.2%)	1 (100%)	8 (36.4%)	3 (42.8%)
Impaired fasting glucose (≥100 mg/dl)	12 (32.4%)	10 (43.3%)	1 (100%)	12 (62.3%)	4 (57.1%)
Hypertension (≥130/85 mmHg)	9 (24.3%)	8 (61.5%)	1 (100%)	10 (45.5%)	2 (28.6%)
Low HDL (<50 mg/dl- F, <40 mg/dl- M)	16 (43.2%)	11 (84.6%)	1 (100%)	9 (40.9%)	3 (42.8%)
Hypertriglyceridemia (≥150 mg/dl)	23 (62.2%)	11 (84.6%)	1 (100%)	15 (68.2%)	5 (71.4%)

Table-10 shows that altered ALT ≥41 IU was observed in 14 (63.6%) of Grade I of patients with NAFLD with metabolic syndrome. Central obesity was observed in 8 (36.4%) of Grade I patients and 3(42.8%) in Grade II with NAFLD with metabolic syndrome. While 9(69.2%) Grade II of patients with NAFLD without metabolic syndrome. Impaired fasting glucose (≥100 mg/dl) in 12 (62.3%) Grade I Patient with metabolic syndrome, Hypertriglyceridemia (≥150 mg/dl) in 15 (68.2%) seen in Grade I of patients with NAFLD with metabolic syndrome.



**Table-11: Distribution of patients according to the components of metabolic syndrome in patients of NAFLD.**

Variables	NAFLD with metabolic syndrome (n=25) Mean±SD	NAFLD without metabolic syndrome (n=28) Mean±SD	P-value
Fasting plasma glucose (mg/dl)	132.62±45.35	101.24±27.28	0.001*
Blood pressure (mm of Hg)			
Systolic blood pressure	126.0±18.17	120.14±15.82	0.202ns
Diastolic blood pressure	78.87±6.25	72.35±8.14	0.041*
Triglycerides (mg/dl)	233.12±118.47	165.12±73.56	<0.001*
High density lipoprotein (mg/dl)	35.10±9.12	41.99±4.76	0.001*
Waist circumference (cm)	82.67±10.22	76.55±7.55	0.023*

Unpaired t-test was done, \*significant, ns= not significant

Table-11 shows that mean Fasting plasma glucose (mg/dl) 132.62±45.35 was observed in patients with NAFLD with metabolic syndrome, while mean SBP 126.00±18.17 was observed in patients with NAFLD with metabolic syndrome and the difference was not significant. Mean Hypertriglyceridemia (mg/dl) 233.12±118.47 was observed in patients with NAFLD with metabolic syndrome. The relation was significant for fasting plasma glucose, blood pressure, triglycerides, high-density lipoprotein and waist circumference (p<0.05) between metabolic and non-metabolic syndrome patients.

**Table-12: Association of BAAT score of NAFLD patients with/without metabolic syndrome (n=80)**

BAAT score	NAFLD with Metabolic syndrome (N= 25)	NAFLD without Metabolic syndrome (N=28)	Total	P-value
No fibrosis (0-1)	16 (64%)	13(46.43%)	29(54.72%)	0.641ns
Possible fibrosis (≥2)	9 (36%)	15(53.57%)	24 (45.28%)	
Total	25(100.0%)	28(100.0%)	53(100.0%)	

p-value measured by Chi-square test, ns=significant

Table-12 shows that regarding the BAAT Score (one of the early predictive scores developed to assess risk of fibrosis in overweight patients with NAFLD. It is a composite score utilizing four variables (BMI, Age, ALT and Triglycerides) that were found to independently correlate with septal fibrosis on liver biopsy). The BAAT score is the weighted sum of BMI (≥23 = 1, <23 = 0), age (≥50 years = 1; <50 = 0), ALT (≥2N = 1, ≤2N = 0) and serum triglycerides (≥150 mg/dl = 1, <150 mg/dl = 0), with a score ranging from 0 to 4. Analysis indicate that there is no significant difference of BAAT score in NAFLD with metabolic syndrome group compare to without metabolic syndrome.

## Discussion

Among 250 respondents a total of 53 cases ultrasonographically diagnosed as NAFLD were included in the study and showed 41(77.36%), 11(20.75%) and 1(1.89%) of cases had grade I, II, and III fatty liver respectively. In the present study, it was observed that mean age of the patient was 53.70±7.22 years. On physical examination mean BMI was 20.6±4.39 kg/m<sup>2</sup> while mean waist circumference was 74.22±7.44 cm. Mean Diastolic blood pressure (mm of Hg) was 78.87±6.25 and mean Systolic blood pressure (mm Hg) 126.0±18.17. These results are consistent with studies by, and Animesh Deb et al. (36). The mean Fasting blood sugar (mg/dl) was 124.17±62.62 and mean total cholesterol (mg/dl) was 196.16±54.59 while mean Serum triglycerides (mg/dl) were 185.13±77.5 these findings are similar to study by Shiva ram Prasad Singh et al, and Kwon YM et al. (37, 38). In present study it is shown that the proportion of NAFLD higher in female patients compare to male patients with or without MS. Analysis indicated that the proportion of NAFLD higher in female patients compare to male patients with or without MS. Among 102 normal male patients without metabolic syndrome 16(15.65%) had NAFLD and out 81 female patients without MS 12(14.8%) patients had NAFLD. Among 23 male patients with MS 9(39.13%) patients had NAFLD and among 44 female patients with MS 16(36.36%) patients had NAFLD. A study by Khan et al. (2011) reported that the prevalence of NAFLD was 44%, with majority (54%) of cases found in male. Majority of cases (59.3%) presented at the age of 40 to 60 years and MS was present in 61.5% of cases. In the present study, it was observed that out of 53 patients with NAFLD with metabolic syndrome were 37.31% and without metabolic syndrome were 15.30%. The study shows that 54.72% patients had fasting plasma glucose >100 mg/dl, while 56.60% patients were hypertensive similar to studies by Rakesh Gaharwar et al, and Animesh Deb et al. Maximum 60.79% patients had Triglycerides >150 mg/dl while low Serum HDL level was seen in 60.38% patients and increased waist circumference was found in 62.26% patients which were also observed by Yang et al. and the difference was statistically significant. In the present study, it was observed that altered ALT ≥41 IU was observed in 14(63.6%) Grade II NAFLD patients with metabolic syndrome. Central obesity was observed in 9(69.2%) Grade II NAFLD patients with metabolic syndrome. These findings are consistent with the study by Vendhan R et al. and Andrade , while 20(90.90%) Grade II of patients with NAFLD with metabolic syndrome showed impaired fasting glucose (>100 mg/dl). Hypertriglyceridemia (>150 mg/dl) in 15 (68.20%) Grade I of patients with NAFLD without metabolic syndrome. These results are consistent with studies by Rakesh Gaharwar et al and Animesh Deb et al. (39-

41). In the present study, it was observed that mean Fasting plasma glucose (mg/dl)  $132.62 \pm 45.35$  was observed in patients with NAFLD with metabolic syndrome while mean SBP  $126.0 \pm 18.17$  was observed in patients with NAFLD with metabolic syndrome and the difference was not significant. Mean hypertriglyceridemia (mg/dl)  $233.12 \pm 118.47$  was observed in patients with NAFLD with metabolic syndrome. These results are consistent with studies by Rakesh Gaharwar, et al. Animesh Deb et al. and Younossi et al. (42). Considering the MS biochemical components, hypertriglyceridemia and HDL-C low concentrations are the lipid profile impairments usually associated with the presence of NAFLD (43). In the present study, HDL-c serum concentrations, as assessed in stages of liver disease, showed significant changes. Boza and co-workers, have observed significantly HDL-c lower means in class III obese individuals with NAFLD in comparison to the group without the disease, and this variable was the only lipid fraction associated with the diagnosis of NAFLD. Similarly, a study developed by Chaves and co-workers (2012) reported that the only lipid fraction related to the presence of steatosis was HDL-C, showing significantly lower median in patients with NAFLD. In the study of Dias and coworkers, which assessed possible predictors of NAFLD in obese individuals, no correlation for lipid fractions was observed occurring in the most advanced stages of the liver disease. Several panel markers have been created, using combinations of clinical and biochemical parameters in order to generate clinical models of fibrosis. One of the early scoring systems developed is called BAAT score and combines four clinical variables: The BAAT score is the weighted sum of BMI ( $\geq 23 = 1$ ,  $< 23 = 0$ ), age at liver biopsy ( $\geq 50$  years = 1;  $< 50 = 0$ ), ALT ( $\geq 2N = 1$ ,  $\leq 2N = 0$ ) and serum triglycerides ( $\geq 1.7$  mmol/L = 1,  $< 1.7 = 0$ ), with a score ranging from 0 to 4. In present study analysis indicate that there is no significant difference of BAAT score in NAFLD with metabolic syndrome group compare to without metabolic syndrome. Possible fibrosis ( $\geq 2$ ) was found 78.4% in NAFLD with MS group and 82.8% in NAFLD patients without MS group. Ratziu et al. reported patients with fibrotic liver disease of different etiology is noteworthy. In alcoholic liver disease, excess weight was a risk factor for cirrhosis, whereas in patients with chronic hepatitis C, a higher BMI was related to severity of fibrosis. This suggests that being overweight is an independent risk factor of liver injury and might contribute to liver fibrosis either alone or in association with other liver diseases. Marchesini et al. have pointed that NAFLD, in its whole spectrum ranging from pure fatty liver to non-alcoholic steatohepatitis (NASH), might represent another feature of MS. 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. 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 (44-46).

## Conclusion

From our study, it can be concluded that the proportion of NAFLD

significantly higher in metabolic syndrome patients compare to non-metabolic syndrome patients and metabolic syndrome is higher in female compare to male. The difference was significant for fasting plasma glucose, blood pressure, triglycerides, high-density lipoprotein and waist circumference ( $p < 0.05$ ) between metabolic syndrome and non-metabolic syndrome patients. As the patients of NAFLD remain asymptomatic in the course of the disease hence the physician should have a high index of suspicion in order to detect NAFLD early in the course of the disease. Higher prevalence of all the components of metabolic syndrome in cases of NAFLD was observed. Liver biopsy is considered the gold standard for diagnosing NAFLD but is not practical and most patients are not willing to undergo the test. Thus, patients must be evaluated for the presence of NAFLD by abdominal Ultrasonography. Early detection would help in modifying the disease course and delaying its complications.

## Limitations of the Study

Following were the limitation of this study:

1. It was a single centered study. So the findings and conclusions of the study may not be representative of all the medical college hospital as well as of the country.
2. Time and resource were limited.
3. Small number of sample was not sufficient to generate the findings.

## Recommendations

This is a small sized study, so it is difficult to draw inference from it. Further multicenter study with large sample size is needed for more reliable evidence in future. Diagnostic work-up in patients with NAFLD should include -

1. The assessment of severity of liver disease at the onset in addition to exclusion of other causes of fatty liver and raised transaminases.
2. A highly individualized approach for the lifestyle modifications based on a thorough assessment of individual metabolic and nutritional status is recommended as the first line of treatment.
3. Pharmacological treatment in NAFLD is still evolving and requires randomized controlled trials with histological end points in a large number of patients. Of the various drugs, pioglitazone and vitamin E are recommended for the non-diabetic patients who has biopsy-proven NASH.

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