OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences

Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) |ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article

"Association of *Low HDL of NAFLD Patients with or without* Metabolic Syndrome: A Study in Rajshahi Medical College Hospital, Rajshahi, Bangladesh"

Momtazul Islam NSM[1*], Md. Khalilur Rahman[2], Mohammad Mahbubur Rahman Khan[3], Mohammad Hasan Tarik[4], Mohd Harun-or-Rashid[5], Mainuddin Ahmed[6], Md. Nurul Islam[7]

[1]Assistant Registrar (Medicine), Rajshahi Medical College Hospital, Rajshahi, Bangladesh
[2]Professor & Head, Department of Medicine, MBBS, FCPS (Medicine), FACP (America), Rajshahi Medical College, Rajshahi, Bangladesh
[3]Professor, Department of Medicine, MBBS, MCPS, MD (Internal Medicine), FACP, PhD, Rajshahi Medical College, Rajshahi, Bangladesh
[4]Professor, Department of Medicine MBBS, FCPS (Medicine), Rajshahi Medical College, Rajshahi, Bangladesh
[5]Associate Professor, Department of Hepatology, MBBS, MCPS (Medicine), MD (Hepatology), PhD, FACP, Rajshahi Medical College, Rajshahi, Bangladesh
[6]Associate Professor & Head (Ex.), Department of Haematology, MBBS, MCPS (Clinical Pathology), FCPS (Haematology), Rajshahi Medical College, Rajshahi, Bangladesh
Assistant Professor, Department of Medicine, MBBS, MD (Internal Medicine), Rajshahi Medical College, Rajshahi, Bangladesh

DOI: 10.36348/sjmps.2020.v06i12.003 | **Received:** 28.11.2020 | **Accepted:** 07.12.2020 | **Published:** 14.12.2020

***Corresponding author:** N. S. M. Momtazul Islam

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. Non-alcoholic fatty liver disease (NAFLD) is associated with a substantial increased risk of cardiovascular disease (CVD), which is partly related to low HDL-C level. 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. ***Objective:*** To find out the Association of Low HDL of NAFLD Patients With or Without Metabolic Syndrome. ***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). ***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. 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 low HDL in 16(64%) cases. The difference was significant for 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. The results of this study indicate that central obesity and dyslipidemia, with low HDL cholesterol, are important associates of NAFLD in patients.

Keywords: Nonalcoholic Fatty Liver Disease, 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, and tamoxifen), and 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 [3, 5, 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, 9, 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 [11, 12], and little information is available on the community-based estimation of NAFLD burden. 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]. Metabolic Syndrome is a set of metabolic and cardiovascular risk. According to the NCEP ATP lll definition, Metabolic Syndrome is present if three or more of the following five criteria are met : abdominal obesity (waist circumference increased for the Europeans ≥ 94 cm in men and ≥ 80 cm in women; for the Americans ≥ 102 cm in men and 88 cm in women, for south Asian men≥ 90 cm and women≥80cm), elevated triglycerides ≥ 150 mg/dl or treatment for hypertriglyceridemia, low HDL cholesterol <40 mg/ dl for women or <50mg/dl for men or treatment for low HDL cholesterol, hypertension ≥ 130/85 mm Hg or treated hypertension, high fasting plasma glucose ≥ 100 mg/dl or treatment for hyperglycemia [14,15,16]. 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 [1]. 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). 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.

Operational definitions

Definition of metabolic syndrome (According To ATP lll Criteria)

Glucose	≥5.6mmol/L (≥100mg/dL) or drug treatment for elevated glucose
Blood Pressure	≥130/85 mmHg or drug treatment for elevated blood pressure
Triglycerides	≥1.7mmol/l (≥150mg/dL) or specific treatment for this
High Density Lipoprotein (HDL) Cholesterol	Men:1.03mmol/L (<40mg/dL) Women: 1.29mmol/L (<50mg/dL)
Obesity	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")

MATERIALS AND METHODS

This is a cross sectional descriptive study which was conducted in the Department of Medicine, Rajshahi Medical College Hospital, Rajshahi, Bangladesh From July 2017 to June 2019. 250 patients age above 20 years nonalcoholic both male and female were included for the study. All patients were interviewed by structured questionnaire.

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

1. Alcoholic patients.
2. Drug causing obesity (Antipsychotics, Antidepressant, Anticonvulsants)
3. Disease causing obesity (Hypothyroidism, Cushing's syndrome, PCOS)
4. Age <20 year

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 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. 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 low HDL in 16(64%) cases. The difference was significant for high-density lipoprotein and waist circumference ($p<0.05$) between metabolic syndrome and non-metabolic syndrome patients.

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/m2)	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/m2, 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.

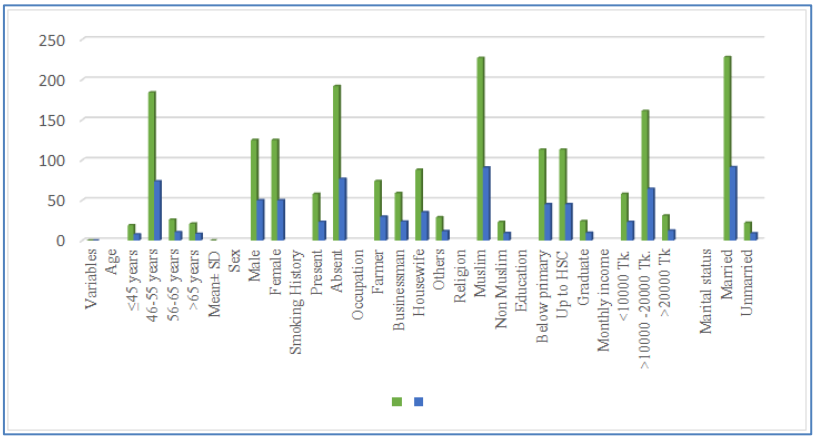

Fig-1: Socio-demographic characteristics of the study patients (n=250)

[Figure-1] shows that maximum number of patients was 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.

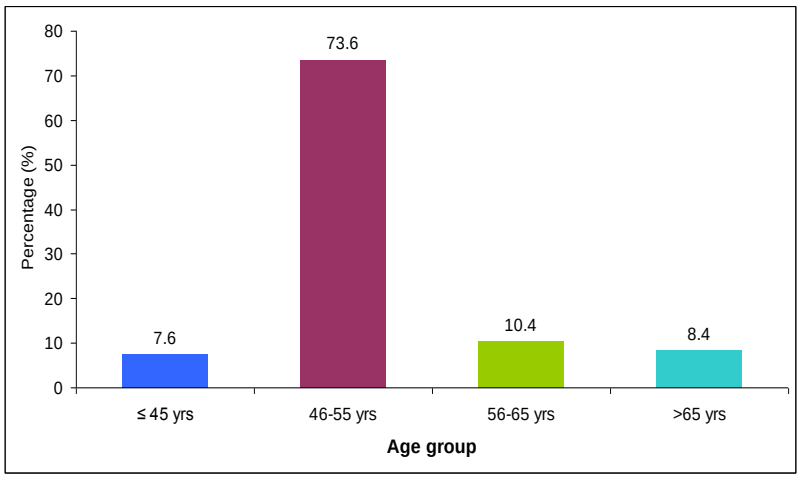

Fig-2: Bar diagram showing the age distribution of the study patients

Table-2: 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%) shows in [Table-2].

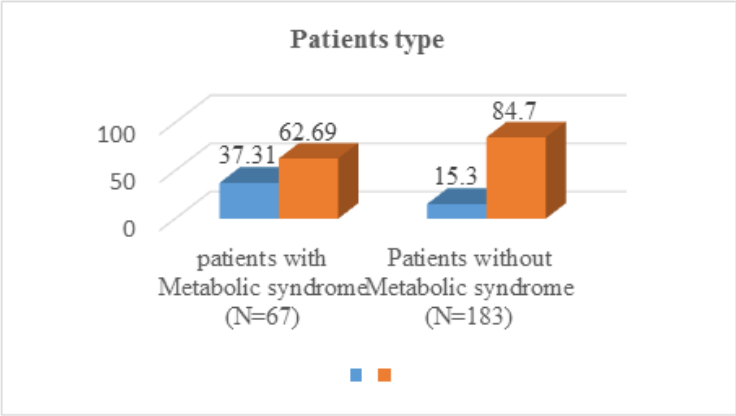

Fig-3: Bar diagram showing the NAFLD patients relation to MS syndrome (n=250)

Table-3: 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	0.029^{s}		0.178^{ns}	
P-value measured by Chi-square test, ns= not significant				

Table-3 shows 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-4: 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 Absent	16(64%) 9(36%)	16 (57.14%) 12 (42.86%)	32(60.38%) 21(39.62%)	0.009*
Total	25(100.0%)	28(100.0%)	53(100.0%)	
P-value measured by Chi-square test, *significant				

Table-4 shows that out of 53 patients, low HDL level significantly higher (64%) in NAFLD with metabolic syndrome group compare to without metabolic syndrome.

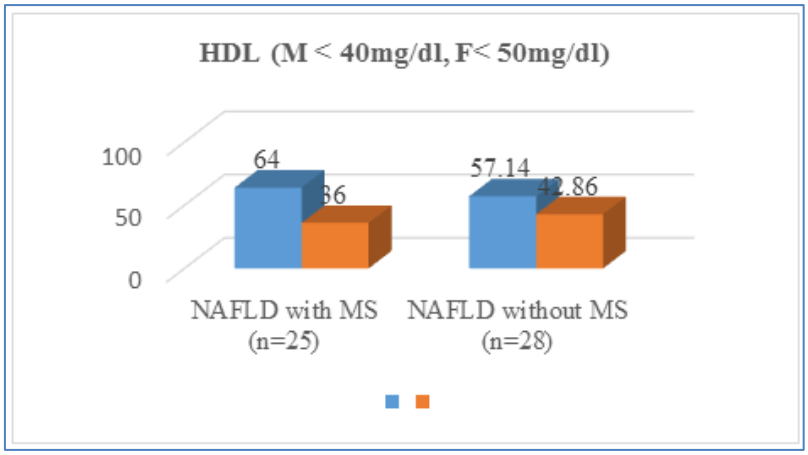

Fig-4: Bar diagram showing the low HDL of NAFLD patients' relation to Metabolic Syndrome

DISCUSSION

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/m2 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. 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*. [17], 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%. 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. [18], 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 results are consistent with studies by Rakesh Gaharwar *et al*. [19]; Animesh Deb *et al*. [20] and Younossi *et al*. [21]. Considering the MS biochemical components, hypertriglyceridemia and HDL-C low concentrations are the lipid profile impairments usually associated with the presence of NAFLD [23]. In the present study, HDL-c serum concentrations, as assessed in stages of liver disease, showed significant changes. Boza and coworkers [22], 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 [22], 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. 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. 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*. [24], 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 norm glycaemia 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.

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 high-density lipoprotein ($p<0.05$) 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.

REFERENCES

1. Genel, S., Aurelia, C., Donca, V., Emanuela, F. (2005). Is the Non-Alcoholic Fatty Liver Disease Part of Metabolic Syndrome? Journal of Diabetes & Metabolism. Apr; 1:6(4).
2. Prashanth, M., Ganesh, H.K., Vima, M.V., John, M., Bandgar, T. (2009). Prevalence of nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus. J Assoc Physicians India; 57: 205-210.
3. Rahman, M.M., Kibria, G.M., Begum, H. (2015). Prevalence and risk factors of nonalcoholic fatty liver disease in a rural community of South Asia. *Gastroenterology*; 148: S1045–6.
4. Rahman, S., Ahmed, M.F., Alam, M.J. (2014). Distribution of liver disease in Bangladesh: a cross-country study. *Eurasian J. Hepatogastroenterol*; 4: 25–30.
5. Loomba, R., Sanyal, A.J. (2013). The global NAFLD epidemic. Nat Rev. Gastroenterol. Hepatol; 10:646-90.
6. Das, K., Das, K., Mukherjee, P.S. (2011). Nonobese population in a developing country has a high prevalence of nonalcoholic fatty liver and significant liver disease. *Hepatology*; 51: 1593–602
7. Alam, S., Fahim, S.M., Chowdhury, M.A., Hassan, M.Z., Azam, G., Mustafa, G., Ahsan, M., Ahmad, N. (2018). Prevalence and risk factors of non-alcoholic fatty liver disease in Bangladesh. JGH Open: An open access journal of gastroenterology and hepatology; 2: 39–46.
8. Alam, S., Mustafa, G., Alam, M., & Ahmad, N. (2016). Insulin resistance in development and progression of nonalcoholic fatty liver disease. *World journal of gastrointestinal pathophysiology*, *7*(2), 211.
9. Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., ... & AlMazroa, M. A. (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *The lancet*, *380*(9859), 2095-2128.
10. Simmons, R. K., Alberti, K. G. M. M., Gale, E. A. M., Colagiuri, S., Tuomilehto, J., Qiao, Q., ... & Reaven, G. (2010). The metabolic syndrome: useful concept or clinical tool? Report of a WHO Expert Consultation. *Diabetologia*, *53*(4), 600-605.
11. Alam, S., Noor-E-Alam, S. M., Chowdhury, Z. R., Alam, M., & Kabir, J. (2013). Nonalcoholic steatohepatitis in nonalcoholic fatty liver disease patients of Bangladesh. *World Journal of Hepatology*, *5*(5), 281.
12. Rahman, S., Ahmed, M. F., & Alam, M. J. (2014). Distribution of liver disease in Bangladesh: a cross-country study. *Euroasian journal of hepato-gastroenterology*, *4*(1), 25.
13. Kotronen, A., Peltonen, M., Hakkarainen, A., Sevastianova, K., Bergholm, R., Johansson, L. M., ... & Orho–Melander, M. (2009). Prediction of non-alcoholic fatty liver disease and liver fat using metabolic and genetic factors. *Gastroenterology*, *137*(3), 865-872.
14. Dowman, J. K., Tomlinson, J. W., & Newsome, P. N. (2010). Pathogenesis of non-alcoholic fatty liver disease. *QJM: An International Journal of Medicine*, *103*(2), 71-83.
15. Fabbrini, E., Sullivan, S., & Klein, S. (2010). Obesity and nonalcoholic fatty liver disease: biochemical, metabolic, and clinical implications. *Hepatology*, *51*(2), 679-689.

16. Cohen, J. C., Horton, J. D., & Hobbs, H. H. (2011). Human fatty liver disease: old questions and new insights. *Science*, *332*(6037), 1519-1523.
17. Khan, M. M. R., Rahman, M. K., Sana, N. K., Basak, P. M., Sarker, B. C., Islam, M. A., ... & Das, C. K. (2015). Nonalcoholic Fatty Liver Disease and Metabolic Syndrome among patients attending in a tertiary care center in Bangladesh. *TAJ: Journal of Teachers Association*, *28*(2), 44-51.
18. Kwon, Y. M., Oh, S. W., Hwang, S. S., Lee, C., Kwon, H., & Chung, G. E. (2012). Association of nonalcoholic fatty liver disease with components of metabolic syndrome according to body mass index in Korean adults. *American journal of gastroenterology*, *107*(12), 1852-1858.
19. Talbott, E. O., Guzick, D. S., Sutton-Tyrrell, K., McHugh-Pemu, K. P., Zborowski, J. V., Remsberg, K. E., & Kuller, L. H. (2000). Evidence for association between polycystic ovary syndrome and premature carotid atherosclerosis in middle-aged women. *Arteriosclerosis, thrombosis, and vascular biology*, *20*(11), 2414-2421.
20. McKeigue, P. M., Shah, B., & Marmot, M. G. (1991). Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. *The Lancet*, *337*(8738), 382-386.
21. Kwon, Y. M., Oh, S. W., Hwang, S. S., Lee, C., Kwon, H., & Chung, G. E. (2012). Association of nonalcoholic fatty liver disease with components of metabolic syndrome according to body mass index in Korean adults. *American journal of gastroenterology*, *107*(12), 1852-1858.
22. Kwon, Y. M., Oh, S. W., Hwang, S. S., Lee, C., Kwon, H., & Chung, G. E. (2012). Association of nonalcoholic fatty liver disease with components of metabolic syndrome according to body mass index in Korean adults. *American journal of gastroenterology*, *107*(12), 1852-1858.
23. Singh, S. P., Kar, S. K., Panigrahi, M. K., Misra, B., Pattnaik, K., Bhuyan, P., & Swain, M. (2014). Profile of patients with incidentally detected nonalcoholic fatty liver disease (IDNAFLD) in coastal eastern India. *Tropical Gastroenterology*, *34*(3), 144-152.
24. Yang, K. C., Hung, H. F., Lu, C. W., Chang, H. H., Lee, L. T., & Huang, K. C. (2016). Association of non-alcoholic fatty liver disease with metabolic syndrome independently of central obesity and insulin resistance. *Scientific reports*, *6*, 27034.