TAJ December 2015; Volume 28 Number-2

ISSN 1019-8555
The Journal of
Teachers Association
RMC, Rajshahi

Original Article

Nonalcoholic Fatty Liver Disease and Metabolic Syndrome among patients attending in a tertiary care center in Bangladesh.

Khan MMR[1], MK Rahman[1], Sana NK[2], PM Basak[3], BC Sarker[3], M Akhtarul Islam[3], Nure Alam Siddiqui[3] KI Jahan[4], MHO Rashid[5], A Sarker[6], CK Das[7], SC Majumder[8]

Abstract

Non-alcoholic fatty liver disease (NAFLD) is an emerging chronic liver disease and may lead to liver cirrhosis and hepatocellular carcinoma. It is now the most common chronic liver disease in many developed as well as developing countries. This hospital based study was done to see the prevalence of non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome among patients attending in a tertiary care center in Bangladesh. Here, 334 nonalcoholic subjects of both sex and age were included. Metabolic syndrome was assessed by modified ATP III criteria and fatty liver diagnosis was based on ultrasound findings. 27.2% had the metabolic syndrome and was more common in female. Prevalence of NAFLD was 44% and was more common in female. Metabolic syndrome was found in 61.5% with NAFLD.

Keyword: metabolic syndrome, nonalcoholic fatty liver disease, NCEP ATP III.

TAJ 2015; 28: No-2: 44-51

Introduction

Non-alcoholic fatty liver disease (NAFLD) affects a substantial proportion of the general population and is frequently associated with many features of the metabolic syndrome. Non-alcoholic fatty liver disease (NAFLD) is an emerging chronic liver disease and may lead to liver cirrhosis and hepatocellular carcinoma. It is now the most common chronic liver disease in many developed countries[1,2] . NAFLD is closely associated with obesity and cardiovascular disease[3,4]. Patients with NAFLD have a higher rate of MetS than those without NAFLD[2,5,6,7] and Metabolic syndrome (MetS) is a cluster of metabolic abnormalities that is a precursor to cardiovascular disease. Some researchers have proposed that NAFLD can be regarded as a hepatic manifestation of MetS[8,14]. Moreover, NAFLD has also been reported to be independent of the traditional risk factors cardiovascular disease (CVD)[9,10] and MetS[11] and to increase the risk of mortality[12,13]. NAFLD is increasingly recognized as a major contributor to the burden of hepatic morbidity world-wide. The aim was to assess the potential association between metabolic syndrome and NAFLD.

[1] Associate Professor, Department of Medicine, Rajshahi Medical College, Rajshahi.
[2] Professor, department of biochemistry and molecular biology, Rajshahi University, Rajshahi.
[3] Assistant Professor, Department of Medicine, Rajshahi Medical College, Rajshahi.
[4] Lecturer, Department of Biochemistry, Rajshahi Medical College, Rajshahi.
[5] Assistant Professor, Department of Hepatology, Rajshahi Medical College, Rajshahi.
[6] Emergency Medical Officer, Rajshahi Medical College Hospital, Rajshahi.
[7] Associate Professor, Department of Community Medicine, Rajshahi Medical College, Rajshahi.
[8] Associate Professor, Department of Respiratory Medicine, Rajshahi Medical College, Rajshahi.

Material and Methods

This hospital based study done on 334 nonalcoholic subjects of both sex and age of 20 years. All of the participants completed detailed surveys that included standardized questionnaires. All subjects were prospectively assessed. The exclusion criteria's was subjects with alcohol user and chronic liver diseases (including chronic hepatitis, autoimmune, drug-induced, vascular and inherited hemochromatosis and Wilson disease). History taking, clinical examination and necessary laboratory investigations were performed. Prevalence of the metabolic syndrome was defined by using modified (waist circumference: men 90 cm and women 80 cm) National Cholesterol Education Program - Adult Treatment Panel III criteria. Fatty liver diagnosis was based on the ultrasound examination of liver.

Anthropometric and metabolic data were collected by routine physical examinations. Waist circumference (WC) was measured at the mid-level between the costal margins and the iliac crests. Fasting plasma glucose (FPG), total cholesterol (TCH), high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C), and triglycerides (TG) were measured after an 8-hour overnight fast. Metabolic syndrome was defined as modified (ethnic specific) NCEPATP III criteria. The diagnosis required at least three of the following metabolic factors: 1) a WC of ≥90 cm for men or ≥80 cm for women; 2) a systolic blood pressure ≥130 mmHg, or a diastolic blood pressure ≥85 mmHg, or the use of medications for hypertension; 3) hyperglycemia (FPG ≥ 100 mg/dL) or the use of medications for diabetes; 4) hypertriglyceridemia (TG ≥ 150 mg/dL) or the use of medications for hyperlipidemia; and 5) low HDL-C (≤40 mg/dL in men and ≤50 mg/dL in women).

Results

A total of 334 participants including 161 (48.2%) men and 173 (51.8%) women were recruited. Table-1 showed that the participants mean age was 40.1±12.2 years. The mean age of the male patients was 41.7±12.1 years and the female patients was 38.6±12.2 years and the mean difference was statistically significant ($p<0.05$) indicating the mean age of the male patients were a little bit higher than the female patients. Among the male patients highest percentage were in the age group 30-39 years (24.2%) followed by 40-49 years (23.6%), less than 30 years (23.0%), 50-59 years (19.3%) and lowest in the age group 60 years and above (9.9%). However, among the female patients, highest percentage were in the age group less than 30 years (28.3%) followed by 30-39 years (25.4%), 40-49 years (22.0%), 50-59 years (17.3%) and lowest in the age group 60 years and above (6.9%).

Table 1. Age and sex distribution of the patients

Age in years	Sex				Total(n=334)		p value
	Male(n=161)		Female (n=173)				
	No.	%	No.	%	No.	%	
<30	37	23.0	49	28.3	86	25.7	
30-39	39	24.2	44	25.4	83	24.9	
40-49	38	23.6	38	22.0	76	22.8	
50-59	31	19.3	30	17.3	61	18.3	
≥60	16	9.9	12	6.9	28	8.4	
Mean ± SD	**41.7±12.1**		**38.6±12.2**		**40.1±12.2**		**0.020**

Table 2. Socio-demographic characteristics of the patients (n=334)

Variables	Frequency	Percent	Mean ± SD
Age in years			
<30	86	25.7	40.1±12.2 years
30-39	83	24.9	Range=20-75 years
40-49	76	22.8	
50-59	61	18.3	
≥60	28	8.4	
Sex			
Male	161	48.2	Male : Female
Female	173	51.8	0.9 : 1.0
Martial Status			
Married	306	91.6	
Unmarried	28	8.4	
Educational status			
Illiterate	83	24.9	
Primary	99	29.6	
Secondary	85	25.4	
Higher secondary	48	14.4	
University	19	5.7	
Monthly family income(Tk.)			
≤4000	92	27.5	Median =Tk.6000
4001-6000	102	30.5	Range=1000 to 80000
6001-8000	68	20.4	
≥8001	72	21.6	

The mean age of the patients was 40.1±12.2 years ranging from 20 to 75 years. Data shows that highest percentage were in the age group less than 30 years(25.7%) followed by 30-39 years (24.9%), 40-49 years (22.8%), 50-59 years (18.3%) and lowest in the age group 60 years and above (8.4%). Among the studied patients more than half of the patients were female (51.8%) and the rest were male (48.2%) and the male and female ratio was 0.93: 1.0. Majority of the patients were married (91.6%) and only 8.4% were unmarried. Considering the level of education, highest percentage had primary level of education (29.6%) followed by secondary level of education (25.4%), higher secondary (14.4%) and 5.7% had university degree. However, one fourth (24.9%) of the patients were illiterate. The median family income of the patients was Taka 6000 ranging from Tk. 1000 to Tk.80000. About one third (30.5%) of the patients monthly family income ranges from Taka 4001 to 6000 followed by taka 1000-4000 (27.5%), Tk. 8001 - 80000 (21.6%) and lowest in the range of Tk.6001-8000(20.4%).

Table 3. Distribution of the patients by known life style factors (n=334)

Variables	Frequency	Percent
Leisure time exercise		
Inability to work	14	4.2
≤60 minute/week	182	54.5
>60 minute /week	138	41.3
Physical activity at work/home		
Low	81	24.3
Moderate	236	70.7
High	17	5.1
Nature of work		
Non-sedentary job	322	96.4
Sedentary job	12	3.6
Smoking habit		
Non smoker	230	68.9
Past smoker	18	5.4
Current smoker	86	25.7
Alcohol consumption		
None	332	99.4
Moderate	2	.6
Carbohydrate diet		
Moderate	69	20.9
High	264	79.0
Peri-menopausal status (n=173)		
Pre-menopausal	129	74.6
Postmenopausal	44	25.4

Data of Table revealed that more than half of the patients (54.5%) had history of leisure time exercise less than 60 minutes and two fifths (41.3%) had history of leisure time exercise more than 60 minute per week. However, 4.2% of the patients were unable to do exercise. Considering the physical activity, 70.7% of the patients were habituated to moderate physical activity followed by 24.3% had low physical activity and 5.1% had extraneous physical activity. Majority of the patients were their job which was non-sedentary in nature and only 3.6% had habituated with sedentary job. Among the studied patients, one fourth (25.7%) were current smokers and 5.4% were past smokers and 68.9% were non-smokers. Regarding dietary habit, four fifths (79.0%) of the respondents had habit of taking high carbohydrate diet and 20.7% had history of taking low carbohydrate diet and two patients had history of taking alcohol.

Table 4. Mean distribution of selected parameters of studied parameters by sex (n=334)

Parameters	Mean ± SD			p value
	Male (n=161)	Female (n=173)	Total (n=334)	
Weight (kg)	70.71±15.2 (44.00-124.00)	56.70±11.7 (30.00-96.00)	63.45±15.2 (30.00-124.00)	.000
Height (m)	1.68±0.1 (1.20-1.82)	1.55±0.1 (1.34-1.74)	1.61±0.1 (1.20-1.82)	.000
Body Mass Index	25.06±5.2 (16.77-42.36)	23.60±4.4 (10.94-40.48)	24.31±4.9 (10.94-42.36)	.006
Hip circumference (cm)	103.13±12.2 (71.00-141.00)	97.20±10.7 (70.00-121.00)	100.06±11.8 (70.00-141.00)	.000
Waist circumference (cm)	91.55±13.2 (58.00-130.00)	85.07±12.8 (54.00-140.00)	88.19±13.4 (54.00-140.00)	.000
Waist-Hip ratio	0.89±0.0 (.750-.990)	0.87±0.1 (.720-1.176)	0.88±0.1 (.720-1.176)	.039
Systolic blood pressure (mmHg)	121.18±10.3 (100-170)	121.36±17.3 (70-200)	121.28±14.3 (70-200)	.907
Diastolic blood pressure (mmHg)	79.10±7.2 (60-110)	79.56±9.6 (34-110)	79.34±8.5 (34-110)	.621
Triglyceride (mg/dl)	156.57±61.3 (38-393)	142.46±67.3 (38-589)	149.26±64.8 (38-589)	.046
High density lipoprotein (mg/dl)	38.51±4.7 (19-58)	37.90±6.9 (19-93)	38.19±5.9 (19-93)	.349
Total cholesterol (mg/dl)	184.71±38.9 (102-318)	177.36±39.7 (102-306)	180.90±39.4 (102-318)	.088
Low density lipoprotein (mg/dl)	114.87±36.6 (34-246)	116.52±37.0 (26-234)	115.73±36.8 (26-246)	.682
Fasting plasma glucose (mmol/l)	5.67±1.6 (3.80-16.20)	5.41±1.2 (3.20-14.50)	5.53±1.4 (3.20-16.20)	.088

p value reached from unpaired student's t test
Figure in parenthesis indicate range

Table 4 shows the mean distribution of selected parameters of the studied patients. Analysis revealed that a statistically significant mean difference of weight, height and body mass index, waist and hip circumference and waist and hip circumference ($p<0.05$) was found between male and female patients with male preponderance. However, no statistically significant mean difference was found male and female patients in terms of systolic and diastolic blood pressure ($p>0.05$). Considering the lipoprotein profiles, no statistically significant mean difference was found between male and female patients($p>0.05$) except triglycerides ($p<0.05$) which was significantly high among the male patients. It was also noted that no statistically significant mean difference was found between male and female patients in terms of fasting plasma glucose level ($p>0.05$).

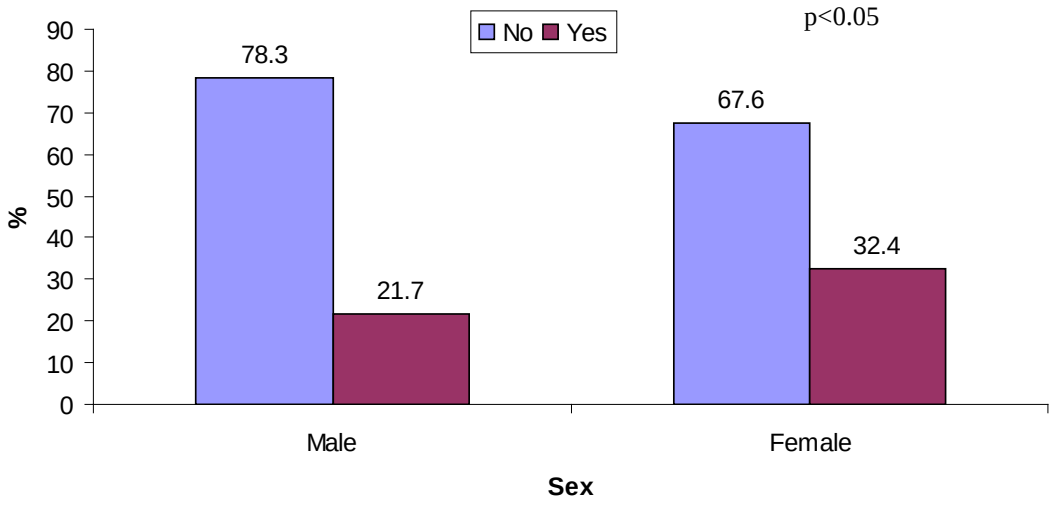

Figure 1. Distribution of patients by metabolic syndrome and sex (n=334)

* p value reached from chi square test (p<0.05)

Analysis of the above table indicated that the proportion of metabolic syndrome was higher among the female patients (32.4%) compared to male patients (21.7%) and the difference was statistically significant (p<0.05).

Table 5. Prevalence of metabolic syndrome and NAFLD among general population

	Male N (%)	Female N (%)	Total N=334 N (%)
Metabolic syndrome (N=91)	35(38.5%)	56(61.5%)	91(27.2%)
NAFLD (N=148)	68(45.9%)	80(54.1%)	148(44.0%)

Discussion

Among 334 studied subjects 27.2% (n 91) had the metabolic syndrome and was more commonly seen in women than in men (32.4% vs 21.7%, P < 0.05). Majority of the patients (59.3%) were in the age group 40-60 years. Overall frequencies of components of metabolic syndrome were in the order of abdominal obesity (97.8%) > low high density lipoprotein (83.5%) > hypertension (71.4%) > triglycerides (67%) > fasting plasma glucose (44%).

Abdominal obesity appeared to be the highest frequent components of the metabolic syndrome in both sexes (men 100% and women 96.4%). Most of those with metabolic syndrome had three components (48.3%), 38.4% had four and 13% had five components. Prevalence of NAFLD among studied subjects (n 334) was 44% (n 148). Metabolic syndrome was found in 61.5% of cases with NAFLD and was more commonly seen in men than in women (54% vs 46%).

As mentioned previously, many studies have shown the cross-sectional associations between the metabolic syndrome and this disease [15-19]. Another study showed that participants with the metabolic syndrome, as defined by the modified ATP III

criteria, have a 4 to 11 time's higher risk for future nonalcoholic fatty liver disease. In addition, if nonalcoholic fatty liver disease and the metabolic syndrome coexist, disease regression is less likely. The effect of sex on the prevalence of nonalcoholic fatty liver disease has been variously reported [20-22]. We found a higher incidence of the disease in women than in men in our study sample.

Conclusion

Metabolic syndrome and NAFLD are common in general population in Bangladesh. Female are more sufferer than male.

Limitations

Ultrasonography has relatively high sensitivity (82% to 94%) and specificity (66% to 95%) in detecting fatty liver [23-28]. it may give an incorrect diagnosis in 10% to 30% of cases.

References

1. Farrell, G. C., Wong, V. W.-S. & Chitturi, S. NAFLD in Asia-as common and important as in the West. *Nat Rev Gastroenterol Hepatol* **10**, 307–318 (2013).
2. Younossi, Z. M. *et al*. Global Epidemiology of Non-Alcoholic Fatty Liver Disease-Meta-Analytic Assessment of Prevalence, Incidence and Outcomes. *Hepatology*, doi: 10.1002/hep.28431 (2015).
3. Lonardo, A. *et al*. Epidemiological modifiers of non-alcoholic fatty liver disease: Focus on high-risk groups*. Dig Liver Dis*. **47**, 997–1006 (2015).
4. Lonardo, A., Sookoian, S., Pirola, C. J. & Targher, G. Non-alcoholic fatty liver disease and risk of cardiovascular disease. *Metabolism*, doi: 10.1016/j.metabol.2015.1009.1017 (2015).
5. Shen, Y.-H. *et al*. Bright liver and alanine aminotransferase are associated with metabolic syndrome in adults. *Obes Res*. **13**, 1238–1245 (2005).
6. FAN, J.-G. *et al.* Fatty liver and the metabolic syndrome among Shanghai adults. *J Gastroenterol Hepatol* **20**, 1825–1832 (2005).
7. Ballestri, S. *et al.* Nonalcoholic fatty liver disease is associated with an almost two-fold increased risk of incident type 2 diabetes and metabolic syndrome. Evidence from a systematic review and meta-analysis. *J Gastroenterol Hepatol*, doi: 10.1111/jgh.13264 (2015).
8. FAN, J.-G. *et al.* Fatty liver and the metabolic syndrome among Shanghai adults. *J Gastroenterol Hepatol* **20**, 1825–1832 (2005).
9. Pisto, P., Santaniemi, M., Bloigu, R., Ukkola, O. & Kesäniemi, Y. A. Fatty liver predicts the risk for cardiovascular events in middle-aged population: a population-based cohort study. *BMJ open* **4**, e004973 (2014).
10. Targher, G., Day, C. P. & Bonora, E. Risk of cardiovascular disease in patients with nonalcoholic fatty liver disease. *N Engl J Med*. **363**, 1341–1350 (2010).
11. Arulanandan, A. *et al.* Association Between Quantity of Liver Fat and Cardiovascular Risk in Patients With Nonalcoholic Fatty Liver Disease Independent of Nonalcoholic Steatohepatitis. *Clin Gastroenterol Hepatol* **13**, 1513–1520.e1511 (2015).
12. Younossi, Z. M., Otgonsuren, M., Venkatesan, C. & Mishra, A. In patients with non-alcoholic fatty liver disease, metabolically abnormal individuals are at a higher risk for mortality while metabolically normal individuals are not. *Metabolism* **62**, 352–360 (2013).
13. Ong, J. P., Pitts, A. & Younossi, Z. M. Increased overall mortality and liver-related mortality in non-alcoholic fatty liver disease. *J Hepatol* **49**, 608–612 (2008).
14. Vanni, E. *et al.* From the metabolic syndrome to NAFLD or vice versa? *Dig Liver Dis.* **42**, 320–330 (2010).
15. Bellentani S, Saccoccio G, Masutti F, Crocè LS, Brandi G, Sasso F, *et al.* Prevalence of and risk factors for hepatic steatosis in Northern Italy. *Ann Intern Med*. 2000; 132: 112-7.
16. Akbar DH, Kawther AH. Nonalcoholic fatty liver disease in Saudi type 2 diabetic subjects attending a medical outpatient clinic: prevalence and general characteristics [Letter]. *Diabetes Care.* 2003; 26: 3351-2.
17. Gupte P, Amarapurkar D, Agal S, Baijal R, Kulshrestha P, Pramanik S, *et al.* Non-alcoholic steatohepatitis in type 2 diabetes mellitus. *J Gastroenterol Hepatol.* 2004; 19: 854-8.
18. Assy N, Kaita K, Mymin D, Levy C, Rosser B, Minuk G. Fatty infiltration of liver in hyperlipidemic patients. *Dig Dis Sci*. 2000; 45: 1929-34.
19. Donati G, Stagni B, Piscaglia F, Venturoli N, Morselli-Labate AM, Rasciti L, *et al.* Increased prevalence of fatty liver in arterial hypertensive patients with normal liver enzymes: role of insulin resistance. *Gut.* 2004; 53: 1020-3.

20. Angulo P. Nonalcoholic fatty liver disease. *N Engl J Med*. 2002;346:1221-31.

21. Sanyal AJ.AGA technical review on nonalcoholic fatty liver disease. *Gastroenterology.* 2002;123:1705-25.

22. Neuschwander-Tetri BA, Caldwell SH. Nonalcoholic steatohepatitis: summary of an AASLD Single Topic Conference. *Hepatology.* 2003;37:1202-19.

23. Saverymuttu SH, Joseph AE, Maxwell JD. Ultrasound scanning in the detection of hepatic fibrosis and steatosis. *Br Med J (Clin Res Ed).* 1986;292:13-5.

24. Steinmaurer HJ, Jirak P, Walchshofer J, Clodi PH. [Accuracy of sonography in the diagnosis of diffuse liver parenchymal diseases—comparison of sonography and liver histology]. *Ultraschall Med*. 1984;5:98-103.

25. Needleman L, Kurtz AB, Rifkin MD, Cooper HS, Pasto ME, Goldberg BB. Sonography of diffuse benign liver disease: accuracy of pattern recognition and grading. *AJR Am J Roentgenol*. 1986;146:1011-5.

26. Joseph AE, Saverymuttu SH, al-Sam S, Cook MG, Maxwell JD. Comparison of liver histology with ultrasonography in assessing diffuse parenchymal liver disease. *Clin Radiol.* 1991; 43: 26-31.

27. Mendler MH, Bouillet P, Le Sidaner A, Lavoine E, Labrousse F, Sautereau D, *et al.* Dual-energy CT in the diagnosis and quantification of fatty liver: limited clinical value in comparison to ultrasound scan and single-energy CT, with special reference to iron overload. *J Hepatol.* 1998;28:785-94.

28. Graif M, Yanuka M, Baraz M, Blank A, Moshkovitz M, Kessler A, *et al.* Quantitative estimation of attenuation in ultrasound video images: correlation with histology in diffuse liver disease*. Invest Radiol*. 2000; 35: 319-24.

All corresponds to
Dr. Mohammad Mahbubur Rahman Khan
Associate Professor,
Department of medicine
Rajshahi Medical College, Bangladesh.
Email: khan.mahbubrahman@yahoo.com
Web: www.khanmmr.com