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Association of Non-Alcoholic Fatty Liver Disease with Metabolic Syndrome: A Single Center Study

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Abstract

Background: NAFLD is a condition defined by excessive fat accumulation in the form of triglycerides (steatosis) in the liver (> 5% of hepatocytes histologically). Non-alcoholic fatty liver disease is increasingly being recognized as a major cause of liver-related morbidity and mortality among 15-40% of the general population. Aim of the study: To evaluate the clinical profile of patients with non-alcoholic fatty liver disease and its association with metabolic syndrome. **Methods:** The present cross-sectional, retro-spective study was conducted as outdoor patient basis in the Department of Medicine, Jashore medical college hospital & a private diagnostic centre, Jashore.. A total of 74 cases were included for the study. All patients in the study underwent routine investigations including complete blood counts, blood sugar, liver function tests, HBsAg, anti-HCV, lipid profile andUSG of whole abdomen. The data was collected during OPD treatment and was recorded in predesigned and pretested proforma and analyzed. **Results:** Mean age of the patient was 53.70±7.22 years. On physical examination findings showed the mean BMI was 27.6±4.39 kg/m2, mean waist circumference was 74.22±7.44 cm. Mean diastolic blood pressure (mm Hg) was 92.87±6.25 and mean systolic blood pressure (mm Hg) 132.0±18.17. Maximum 52% patients had triglycerides >150 mg/dl while low serum HDL level was seen in 37% patients and increased waist circumference was found in 32% patients. Altered ALT ≥41 IU was observed in 10 (62.50%) of Grade II of patients with NAFLD with metabolic syndrome. Central obesity was observed in 12 (75.00%) of Grade II patients with NAFLD with metabolic syndrome. While 14 (87.50%) Grade II of patients with NAFLD with metabolic syndrome showed impaired fasting glucose (>110 mg/dl). Hypertriglyceridemia (>150 mg/dl) in 12 (70.58%) seen in Grade I of patients with NAFLD without metabolic syndrome. **Conclusion:** Higher prevalence of all the components of metabolic syndrome in cases of NAFLD was observed. It can be concluded that symptoms and signs of NAFLD are non-specific and occur later 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.

Keywords:- Metabolic Syndrome, NAFLD, Clinical Profile, Liver, Disease.

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INTRODUCTION

NAFLD is a condition defined by excessive fat accumulation in the form of triglycerides (steatosis) in the liver (> 5% of hepatocytes histologically). A subgroup of NAFLD patients have liver cell injury and inflammation in addition to excessive fat (steatohepatitis). Most cases of NAFLD are discovered in the fourth to sixth decades of life, although NAFLD is also described, with increasing frequency, in obese children and adolescents, as well as in older adults. The reasons for racial and ethnic disparities in the prevalence of NAFLD is not known but may be related, at least in part, to racial differences in body fat distribution and the prevalence of the metabolic syndrome, which is greatest in people of Hispanic descent. Most patients who come to medical attention with NAFLD are identified as a result of incidentally discovered elevated liver enzymes (ALT, AST). When patients are symptomatic, symptoms include fatigue or a vague right upper quadrant discomfort. ALT is generally higher than AST, and aminotransferases are only mildly (1.5–2 times the upper limit of normal) elevated. Non-alcoholic fatty liver disease is increasingly being recognized as a major cause of liver-related morbidity and mortality among 15-40% of the general population.[1] Epidemiological studies suggest the prevalence of NAFLD be around 9-32% in general Indian population, with a higher incidence amongst overweight/obese and diabetic/pre-diabetic patients.[2,3] The absence of signs and symptoms and a lack of sensitive and specific diagnostic tests limit the ability to estimate the prevalence of NAFLD. The current epidemics of obesity and diabetes among adults and children residing in both developed and developing countries suggest that prevalence of NAFLD is expected to increase further in future.[4,5] USB-mode imaging allows to subjectively estimate the degree of fatty infiltration in the liver. The grading of liver steatosis is usually obtained using some US features that include liver brightness, contrast between the liver and the kidney, US appearance of the intrahepatic vessels, liver parenchyma and diaphragm. Steatosis is graded as follows: Absent (score 0) when the echotexture of the liver is normal; mild (score 1), when there is a slight and diffuse increase of liver echogenicity with normal visualization of the diaphragm and of the portal vein wall; moderate (score 2), in case of a moderate increase of liver echogenicity with slightly impaired appearance of the portal vein wall and the diaphragm; severe (score 3), in case of marked increase of liver echogenicity with poor or no visualization of portal vein wall diaphragm and posterior part of the right liver lobe.[4,5,6] The performance of US B-mode imaging for the detection of mild steatosis (fat content >5%) is low, with reported sensitivity of 60.9%-65%.[6,7] A meta-analysis has assessed that, for the detection of moderate-severe fatty liver (>20%-30% steatosis), B-mode US has a performance similar with computed tomography or magnetic resonance imaging (MRI). Compared to histology as reference standard, the overall sensitivity and specificity of B-mode US were, respectively, 84.8% and 93.6%, with 0.93 (0.91-0.95) area under the ROC curve (AUROC).[8] Abdominal gas or obesity may decrease the applicability of B-mode US. Moreover, in patients with liver fibrosis the accuracy of the technique for diagnosing hepatic steatosis may decrease.[9,10] On the other hand, a significant intra- and inter-

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observer variability for the assessment of the US findings of liver steatosis has been reported.[11,12] However, it should be emphasized that US B-mode imaging is widely available, noninvasive, repeatable because there is no exposition to ionizing radiation, it has low cost and is well-accepted by patients. Indeed, the technique has been recommended as the preferred first-line diagnostic procedure for imaging of NAFLD in adults by the clinical practice guidelines of the European Association for the Study of the Liver released together with the European Association for the Study of Diabetes and the European Association for the Study of Obesity.[13] An A1 score, i.e., a high quality of evidence with a strong strength, has been assigned to this recommendation. The aim of the study was to evaluate the clinical profile of patients with non-alcoholic fatty liver disease and its association with metabolic syndrome.

MATERIAL AND METHODS

The present cross-sectional, retro-spective study was conducted as outdoor patient basis in the Department of Medicine, Jashore medical college hospital & a private diagnostic centre, Jashore. A total of 74 cases were included for the study. All patients in the study underwent routine investigations including complete blood counts, blood sugar, liver function tests, HBsAg, anti-HCV, lipid profile andUSG of whole abdomen. The data was collected during OPD treatment and was recorded in predesigned and pretested proforma and analyzed.

Inclusion Criteria

- All patients diagnosed as NAFLD by abdominal Ultrasonography
- Age more than 18 years.

Exclusion Criteria

- Patients with a history of alcohol intake more than 30 Unit/day in males and more than 20 Unit/day in females
- Patients with a history of jaundice or HBsAg positive
- Patients with history of following drug intake - steroids, synthetic estrogens, heparin, and calcium channel blockers, amiodarone, valproic acid, antiviral agents.
- Unwilling patients.

RESULTS

Mean age of the patient was 53.70±7.22 years. On physical examination findings showed the mean BMI was 27.6±4.39 kg/m2, mean waist circumference was 74.22±7.44 cm. Mean diastolic blood pressure (mm Hg) was 92.87±6.25 and mean systolic blood pressure (mm Hg) 132.0±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 1]. Out of 74, patients with NAFLD with metabolic syndrome were 42 (56.75%) and without metabolic syndrome were 32 (43.24%). The study shows that 25 (59.64%) patients had fasting plasma glucose >100 mg/dl while 18 (42.10%) patients were hypertensive. Maximum 32 (75.43%) patients had triglycerides >150 mg/dl while low serum HDL level was seen in 27 (64.91%) patients and increased waist circumference was found in

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21(50.87%) patients. The difference was statistically significant ($p<0.05$) [Table 2]. Altered ALT ≥60 IU was observed in 10(62.50%) of Grade II of patients with NAFLD with metabolic syndrome. Central obesity was observed in 12 (75.00%) of Grade II patients with NAFLD with metabolic syndrome. While 14 (87.50%) Grade II of patients with NAFLD with metabolic syndrome showed impaired fasting glucose (>100 mg/dl). Hypertriglyceridemia (>150 mg/dl) in 12 (70.58%) seen in Grade I of patients with NAFLD without metabolic syndrome [Table 3]. Mean Fasting plasma glucose (mg/dl) 132.62±45.35 was observed in patients with NAFLD with metabolic syndrome, while mean SBP 134.21±17.56 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 correlation was significant for fasting plasma glucose, diastolic blood pressure, triglycerides, high-density lipoprotein and waist circumference ($p<0.05$) [Table 4].

Table 1: Distribution of patients according to their clinical and biochemical profiles (n=74).

Variable	**Mean± SD**
Age (in year)	53.70±7.22
Body mass index (kg/m2)	27.60±4.39
Waist circumference (cm)	74.22±7.44
Diastolic blood pressure (mm Hg)	92.87±6.25
Systolic blood pressure (mm Hg)	132.0±18.17
Fasting blood sugar (mg/dl)	124.17±62.62
Total cholesterol (mg/dl)	196.16±54.59
Serum triglycerides (mg/dl)	185.13± 77.5
High density lipoprotein (mg/dl)	45.23±9.13
Serum LDL (mg/dl)	125.43±27.44
Serum VLDL (mg/dl)	22.14±6.09
Aspartate amino transferase (u/l)	53.12±31.33
Alanine amino transferase (u/l)	65.33±49.02

Table 2: Distribution of patients according to the prevalence of variables in patients of NAFLD with metabolic syndrome and NAFLD without metabolic syndrome.

Variables	**NAFLD with Metabolic syndrome N= 42(56.76%)**	**NAFLD without Metabolic syndrome N=32(43.24%)**	**Total**	**P-value**
Fasting plasma glucose >100 mg/dl	25 (59.64%)	14 (44.18%)	39	<0.05
Hypertension > 140/90 mmHg	18 (42.10%)	10 (32.55%)	28	<0.05
Triglycerides > 150 mg/dl	32 (75.43%)	20 (62.79%)	52	<0.05

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HDL M < 40mg/dl F < 50mg/dl	27 (64.91%)	10 (32.55%)	37	<0.05
Waist circumference M > 90cm F > 80 cm	21 (50.87%)	11 (34.88%)	32	<0.05

Table 3: Distribution of patients according to the grades of NAFLD.

	NAFLD with metabolic syndrome			**NAFLD without metabolic syndrome**		
	Grade I	**Grade II**	**Grade III**	**Grade I**	**Grade II**	**Grade III**
	n=19 (25.68%)	n=16 (21.62%)	n=7 (9.46%)	n=17 (23.94%)	n=12 (16.21%)	n=3 (4.05%)
ALT ≥ 60 IU	6 (31.57%)	10 (62.50%)	5(71.42%)	11 (64.70%)	5 (41.67%)	1 (25%)
AST ≥ 38 IU	6 (31.57%)	6 (31.25%)	5(71.42%)	7 (41.17%)	3 (25.00%)	1 (25%)
Central obesity (WC) (> 90 cm - M, > 80 cm - F)	7 (36.84%)	12 (75.00%)	3(42.85%)	7 (41.17%)	4 (33.33%)	1 (25%)
Impaired fasting glucose (>100 mg/dl)	7 (36.84%)	14 (87.50%)	4(57.14%)	7 (41.17%)	5 (41.67%)	2 (50%)
Hypertension (130/85 mmHg)	4 (21.05%)	10 (62.50%)	3(42.85%)	7 (41.17%)	2 (16.67%)	1 (25%)
Low HDL (<50 mg/dl- F, <40 mg/dl- M)	8 (42.10%)	14 (87.50%)	5(71.42%)	7 (41.17%)	3 (25.00%)	1 (25%)
Hypertriglyceridemia (>150 mg/dl)	12 (63.15%)	14 (87.50%)	6(85.71%)	12 (70.58%)	7 (58.33%)	2 (50%)

Table 4: Distribution of patients according to the components of metabolic syndrome in NAFLD patients

Variables	**NAFLD with metabolic syndrome**	**NAFLD without metabolicsyndrome**	**P-value**
Fasting plasma glucose (mg/dl)	132.62±45.35	101.24±27.28	<0.05
Blood pressure (mm of Hg)			

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Systolic blood pressure	134.21±17.56	129.14±15.82	> 0.05
Diastolic blood pressure	87.21±9.15	86.35±8.14	<0.05
Triglycerides (mg/dl)	233.12±118.47	165.12±73.56	<0.05
High density lipoprotein (mg/dl)	35.10±9.12	41.99±4.76	<0.05
Waist circumference (cm)	86.67±10.22	79.55±7.55	<0.05

DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease since its prevalence is estimated to be 20-30% in general population of Western countries. It has been shown that NAFLD is strongly associated to the features of metabolic syndrome. Insulin resistance is a key pathogenic factor in both NAFLD and metabolic syndrome. NASH is frequently seen in conjunction with other components of the metabolic syndrome (hypertension, diabetes mellitus, elevated lipids, and obesity), with NAFLD being considered the hepatic manifestation of this syndrome. Insulin resistance is the underlying link between these various disorders and numerous studies have shown that virtually all patients with NASH have insulin resistance. A total of 74 cases ultrasonographically diagnosed as NAFLD with metabolic syndrome and. were included in the study and showed 19 (25.68%), 16 (21.62%), 7 (9.46%) and NAFLD without metabolic syndrome were 17 (23.94%), 12 (16.21%), 3 (4.05%) 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 27.6±4.39 kg/m2 while mean waist circumference was 74.22±7.44 cm. Mean Diastolic blood pressure (mm of Hg) was 92.87±6.25 and mean Systolic blood pressure (mm Hg)132.0±18.17. These results are consistent with studies.[9,10] 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 study11, 12.In the present study, it was observed that out of 74 patients with NAFLD, associated metabolic syndrome were 42% and without metabolic syndrome were 32%. The study shows that 39% patients had fasting plasma glucose >110 mg/dl, while 28% patients were hypertensive similar to studies.[9,10] Maximum 52% patients had Triglycerides >150 mg/dl while low Serum HDL level was seen in 37% patients and increased waist circumference was found in 32% patients which were also observed and the difference was statistically significant.[13] In the present study, it was observed that altered ALT ≥60 IU was observed in 10 (62.50%) Grade II NAFLD patients with metabolic syndrome. Central obesity was observed in 12 (75.00%) Grade II NAFLD patients with metabolic syndrome. These findings are consistent with the study while 14 (87.50%) Grade II of patients with NAFLD with metabolic syndrome showed impaired fasting glucose (>100 mg/dl).[14,15] Hypertriglyceridemia (>150 mg/dl) in 12 (70.58%) Grade I of patients with NAFLD without metabolic syndrome. These results are consistent with studies.[9,10] In the

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Limitations of the study

This study was conducted only one hospital. Sample size was small and follow-up period were short in comparison to other studies. So, the result of the study may not reflect the exact scenario of the whole country.

CONCLUSIONS

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. It can be concluded that symptoms and signs of NAFLD are non-specific and occur later 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.

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