RESEARCH ARTICLE

"CLINICAL PROFILE WITH NON-ALCOHOLIC FATTY LIVER DISEASE AND METABOLIC SYNDROME PATIENTS"

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Manuscript Info

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Abstract

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Background: The 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. The rising incidence of obesity is associated with health complications. Currently, a liver biopsy is the gold standard method for diagnosing NAFLD. Ultrasonography is relatively inexpensive and widely available in clinical settings. NAFLD is considered to be an integral part of the metabolic syndrome. Objective: To find out the clinical profile with non-alcoholic fatty liver disease and metabolic syndrome patients. Methods: A cross-sectional study was conducted by Department of Cardiology, Enam Medical College and Hospital, Savar, Bangladesh. A total of 100 cases during the study period of February 2019 to January 2020 were included and investigated for metabolic syndrome according to the NCEP ATP 3 Criteria. Results: Total of 100 cases ultrasonographically diagnosed as NAFLD were included in the study and showed 49%, 38% and 13% of cases had grade I, II, and III fatty liver respectively. On physical examination mean BMI was 27.6 ± 4.39 kg/m^2. Mean diastolic blood pressure was 92.87 ± 6.25 and mean systolic blood pressure (mm Hg) 132.0 ± 18.17. Out of the 100, patients with NAFLD with metabolic syndrome were 57% and without metabolic syndrome were 43%. The correlation was significant for fasting plasma glucose, diastolic blood pressure, triglycerides, high-density lipoprotein and waist circumference ($p<0.05$).
Conclusions: From the study, it can be concluded that symptoms and signs of NAFLD are non-specific and occur later in the course of the

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disease hence the physician should have a high index of suspicion in order to detect NAFLD early in the course of the disease. Early detection would help not only in modifying the disease course and delaying its complications.

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Introduction:-

Non-alcoholic fatty liver disease (NAFLD) is the accumulation of lipid, primarily in the form of triacylglycerols Non in individuals alcoholic fatty who liver do not disease consume (NAFLD significant) is the amounts accumulation of alcohol of lipid, and primarily other known in the causes form of steatosis, such as certain drugs and toxins, have been excluded.Non-alcoholic fatty liver disease (NAFLD) is defined as the accumulation of lipid, primarily in the form of triacylglycerols in individuals who do not consume significant amounts of alcohol (<20 g ethanol/d).[1] The rising incidence of obesity in today's environment is associated with many obesity-related health complications, including cardiovascular disease, diabetes, hyperlipidemia, hypertension, and nonalcoholic fatty liver disease.[2]This combination is also recognized as the metabolic syndrome and is characterized by underlying insulin resistance.[3] 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.[4]The overall prevalence of NAFLD in western countries varies from 15-40% and in Asian countries from 940%.[5,6] 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.[7,8] Published literature on NAFLD from Bangladesh is sparse. This may be related to the fact that the condition was recognized fairly recently, a presumption that the condition is benign and has a no progressive course, a large burden of viral hepatitis in Bangladesh tends to reduce the priority accorded to this condition. 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.[9,10]The pathologic picture of the non-alcoholic fatty liver disease, ranging from simple steatosis to steatohepatitis, advanced fibrosis, and cirrhosis, resembles that of alcohol-induced liver disease, but it also occurs in patients who do not abuse alcohol.[10] Nonalcoholic steatohepatitis that is characterized by hepatic steatosis, liver cell injury, hepatic inflammation, fibrosis, and necrosis is believed to be an intermediate stage of the non-alcoholic fatty liver disease.4 Even in the absence of alcohol intake, patients who have one or more components of the metabolic syndrome with insulin resistance, develop hepatic steatosis due to increased lipolysis and increased delivery of fatty acids from adipose tissue to liver.[4] Fatty liver disease is defined as more than 5% of the hepatocytes containing fat or more than 5% of the liver weight due to fat.[11] Currently a liver biopsy is the gold standard method for diagnosing NAFLD. Compared to invasive biopsy and expensive MRS and CT, ultrasonography (USG) is relatively inexpensive and widely available in clinical settings, although it is unable to detect less than 10% steatosis of hepatocytes.[12] The third report of the national cholesterol education programme expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III [ATP III]) recommended the use of five variables for diagnosing the metabolic syndrome, namely waist circumference, serum triglyceride level, serum high-density lipoprotein (HDL) cholesterol level, blood pressure, and fasting plasma glucose level.[13] Currently, NAFLD is considered to be an integral part of the metabolic syndrome with insulin resistance as a central pathogenic factor. Metabolic syndrome is characterized by the presence of insulin resistance in association with other metabolic abnormalities such as obesity, diabetes, dyslipidemia and hypertension. According to adult treatment panel III (ATP III) criteria, metabolic syndrome is defined by the presence of at least 3 of the 5 criteria, namely obesity, diabetes mellitus, hypertension, low HDL, high triglycerides.[14] The present study was designed to study the clinical Profile of patients with NAFLD with varying degrees of severity as diagnosed by Ultrasonography and evaluate the cross-sectional relationship between the non-alcoholic fatty liver disease and the metabolic syndrome along with its individual components, as defined by the modified NCEP ATP III criteria.

Methods:-

The present cross-sectional study was conducted by Department of Cardiology, Enam Medical College and Hospital, Savar, Bangladesh. A total of 100 cases were included in the study, during the study period of February 2019 to January 2020. The patients diagnosed as NAFLD on USG seeking treatment were included and investigated for metabolic syndrome according to the NCEP ATP 3 criteria. The data was collected during OPD/IPD treatment and was recorded in predesigned and pretested proforma and analyzed.

Inclusion criteria
1. All patients diagnosed as NAFLD by abdominal Ultrasonography
2. Age more than 18 years.

Exclusion criteria
1. Patients with a history of alcohol intake more than 30 grams/day in males and more than 20 grams/day in females
2. Patients with a history of jaundice or HBsAg positive
3. Patients with history of following drug intake steroids, synthetic estrogens, heparin, and calcium channel blockers, amiodarone, valproic acid, antiviral agents.[15]
4. Unwilling patients.

Patients were included in the study according to the standard criteria accepted by the American Gastroenterology Association i.e., an increase in hepatic echogenicity as a reference, the presence of enhancement and lack of differentiation in the periportal intensity and the vascular wall due to great hyperechogenicity in the parenchyma.[15]

Grade 1: Slight diffuse increase in the fine echoes. Liver appears bright as compared to the cortex of the kidney. Normal visualization of the diaphragm and intrahepatic vessel borders.
Grade 2: Moderate diffuse increase in the fine echoes. Slightly impaired visualization of the intrahepatic vessels and diaphragm
Grade 3: Marked increase in the fine echoes. Poor or no visualization of intrahepatic vessel borders, diaphragm, and the vessels.

Detailed history, anthropometry, and clinical examinations were carried out after taking informed consent of the patient. All patients in the study underwent routine investigations including complete blood counts, blood sugar, liver function tests, HBsAg, anti-HCV, and lipid Profile. All patients diagnosed as NAFLD were investigated for metabolic syndrome according to the NCEP ATP III criteria and a relationship between NAFLD and metabolic syndrome was correlated. [10] Metabolic syndrome was diagnosed as per NCEP ATP 3 criteria (three or more of the following):

Elevated waist circumference (Asian criteria)
1. Men: Equal to or greater than 90 cm
2. Women: Equal to or greater than 80 cm
3. Elevated triglycerides: Equal to or greater than 150 mg/dL (1.7 mmol/L).
4. Reduced HDL cholesterol
5. Men: Less than 40 mg/dL (1.03 mmol/L)
6. Women: Less than 50 mg/dL (1.29 mmol/L)
7. Elevated blood pressure: Equal to or greater than 130/85 mm Hg or use of medication for hypertension
8. Elevated fasting glucose: Equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycaemia.

Results:-
A total of 100 cases ultrasonographically diagnosed as NAFLD were included in the study and showed 49%, 38% and 13% of cases had grade I, II, and III fatty liver respectively. [Table 1] shows that 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/m^2, 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 2] shows that out of 100, patients with NAFLD with metabolic syndrome were 57% and without metabolic syndrome were 43%. The study shows that 53% patients had fasting plasma glucose >100 mg/dl while 38% patients were hypertensive. Maximum 70% patients had triglycerides >150 mg/dl while low serum HDL level was seen in 51% patients and increased waist circumference was found in 44% patients. The difference was statistically significant ($p<0.05$). [Table 3] shows that altered ALT ≥ 41 IU was observed in 14 (63.63%) of Grade II of patients with NAFLD with metabolic syndrome. Central obesity was observed in 16 (72.72%) of Grade II patients with NAFLD with metabolic syndrome. 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 16 (69.56%) seen in Grade I of patients with NAFLD without metabolic syndrome.

Table 1:-Distribution of patients according to their clinical and biochemical Profiles (n=100).

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= 57)	NAFLD without Metabolic syndrome (N=43)	Total	P value
Fasting plasma glucose>100 mg/d1	34 (59.64%)	19 (44.18%)	53	<0.05
Hypertension > 130/85 mmHg	24 (42.10%)	14 (32.55%)	38	<0.05
Triglycerides > 150 mg/dl	43 (75.43%)	27 (62.79%)	70	<0.05
HDL M < 40mg/dl F < 50mg/dl	37 (64.91%)	14 (32.55%)	51	<0.05
Waist circumference M > 90cm F > 80 cm	29 (50.87%)	15 (34.88%)	44	<0.05

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

Variables	NAFLD with Metabolic syndrome (N= 57)			NAFLD without Metabolic syndrome (N=43)		
	Grade I	Grade II	Grade III	Grade I	Grade II	Grade III
	n= 26	n= 22	n= 9	n= 23	n= 16	n=4
ALT ≥ 41 IU	8 (30.76%)	14 (63.63%)	6 (66.66%)	15 (65.21%)	7 (43.75%)	1 (25%)
AST ≥ 38 IU	8 (30.76%)	8 (36.36%)	6 (66.6%)	9 (39.13%)	4 (25.00%)	1 (25%)
Central obesity (WC) (> 90 cm - M, > 80 cm - F)	9 (34.61%)	16 (72.72%)	4 (44.44%)	9 (39.13%)	5 (31.25%)	1 (25%)
Impaired fasting glucose (>100 mg/dl)	9 (34.61%)	20 (90.90%)	5 (55.55%)	10 (43.47%)	7 (43.75%)	2 (50%)
Hypertension (130/85 mmHg)	6 (23.07%)	14 (63.63%)	4 (44.44%)	10 (43.47%)	3 (18.75%)	1 (25%)
Low HDL (<50 mg/dl- F, <40 mg/dl- M)	11 (42.30%)	19 (86.36%)	7 (77.77%)	9 (39.13%)	4 (25.00%)	1 (25%)
Hypertriglyceridemia	16	19 (86.36%)	8 (88.88%)	16 (69.56%)	9 (56.25%)	2 (50%)

(>150 mg/dl)	(61.53%)					

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

Variables	NAFLD with Metabolic syndrome (N= 57)	NAFLD without Metabolic syndrome (N=43)	P value
Fasting plasma glucose (mg/dl)	132.62±45.35	101.24±27.28	<0.05
Blood pressure (mm of Hg)			
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

Shows that 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].

Discussion:-
A total of 100 cases ultrasonographically diagnosed as NAFLD were included in the study and showed 49%, 38% and 13% 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 by RakeshGaharwar et al and Animesh Deb et al.[17,18] 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 Shivaram Prasad Singh et al and Kwon YM et al.[19,20]In the present study, it was observed that out of 100, patients with NAFLD with metabolic syndrome were 57% and without metabolic syndrome were 43%. The study shows that 53% patients had fasting plasma glucose >100 mg/dl, while 38% patients were hypertensive similar to studies by RakeshGaharwar et al and Animesh Deb et al.[17,18] Maximum 70% patients had Triglycerides >150 mg/dl while low Serum HDL level was seen in 51% patients and increased waist circumference was found in 44% patients which were also observed by Yang KC et al and the difference was statistically significant.[21] In the present study, it was observed that altered ALT ≥41 IU was observed in 14 (63.63%) Grade II NAFLD patients with metabolic syndrome. Central obesity was observed in 16 (72.72%) Grade II NAFLD patients with metabolic syndrome. These findings are consistent with the study by Vendhan R et al and Andrade GC, while 20 (90.90%) Grade II of patients with NAFLD with metabolic syndrome showed impaired fasting glucose (>100 mg/dl).[22,23]Hypertriglyceridaemia (>150 mg/dl) in 16 (69.56%) Grade I of patients with NAFLD without metabolic syndrome. These results are consistent with studies by Gaharwar R et al and Deb A et al.[17,18] In the present study, it was observed that 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. These results are consistent with studies by Gaharwar R et al, Deb A et al and Younossi ZM et al.[17,18,24]

Conclusion:-
From our study, 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.

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.

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