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Clinical Profile of Patients with Non Alcoholic Fatty Liver Disease and its Association with Metabolic Syndrome –a cross sectional study

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ABSTRACT : ***Background:*** *In India NAFLD is emerging as an important cause of liver disease. It is known to be associated with various metabolic abnormalities . This study evaluated the clinical profile of patients of NAFLD and its relationship with metabolic syndrome.* ***Methodology:*** *This was a prospective cross sectional study carried out in the OPD of a private medical college. All patients diagnosed as NAFLD were investigated for metabolic syndrome according to the NCEP ATP 3 Criteria and a relationship between NAFLD and metabolic syndrome was studied.* ***Results:*** *Out of 226 cases, 46.02%, 44.7% and 9.29% of cases had grade I, II, and III fatty liver respectively. 146(64.6%) had metabolic syndrome. All the components of metabolic syndrome was significantly associated with NAFLD (p≤0.05). 80.2% and 90.5% of grade II and III NAFLD patients suffered from metabolic syndrome respectively.* ***Conclusion:*** *There is higher prevalence of all the components of metabolic syndrome in cases of NAFLD. Early detection will help in modifying the disease course and delaying its complications .Preventive programs should be encouraged.*

Keywords - *NAFLD, Metabolic syndrome*

I. Introduction

The term NAFLD is used to describe a wide array of fatty liver changes from simple steatosis to steatohepatitis, cirrhosis and hepatocellular carcinoma (HCC), in the absence of excessive alcohol intake.[1] A disease practically unheard of three decades ago, is now considered as one of the most common causes of chronic liver disease in industrialized world.[2] Because of its potential to progress to cirrhosis and liver failure, interest in this disease is increasing among researchers and clinicians in the relevant basic and clinical science fields.[3] The overall prevalence of NAFLD in western countries varies from 15-40% and in Asian countries from 9-40%.[1,4-5] In India too, NAFLD is emerging as an important cause of liver disease. Epidemiological studies suggest the prevalence of NAFLD to be around 9-32% in general Indian population, with a higher incidence amongst overweight/obese and diabetic/ prediabetic patients.[6-10]

Metabolic syndrome and associated comorbidities like type 2 diabetes (T2DM), obesity and dyslipidemia are predisposing factors of NAFLD; and prevalence of NAFLD has increased parallel to these epidemics.[11-13] NAFLD is strongly associated with T2DM and cardiovascular disease (CVD). It is characterized by insulin resistance and mitochondrial dysfunction.[6] 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.[10]

This work was designed to study the clinical profile of patients of NAFLD with varying degrees of severity as diagnosed by ultrasonography and evaluate the relationship between the non-alcoholic fatty liver disease and the metabolic syndrome as defined by the modified NCEP ATP III criteria.

II. Materials and Methods

This was a prospective cross sectional study carried out over a period of 9 months (January 2015 to September 2015) in the OPD of a private medical college. The study was approved by the Institutional Ethics Committee. Patients attending the medicine OPD during this period were selected. Written informed consent from all patients was obtained prior to the study. Subjects 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.[14]

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

After detailed history, anthropometry and clinical examination, 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[15] and a relationship between NAFLD and metabolic syndrome was correlated.
Metabolic syndrome was diagnosed as per NCEP ATP 3 criteria (three or more of the following)
1. Elevated waist circumference (asian Indian criteria)[16]
a. Men — Equal to or greater than 90 cm
b. Women — Equal to or greater than 80 cm
2. Elevated triglycerides: Equal to or greater than 150 mg/dL (1.7 mmol/L)
3. Reduced HDL cholesterol:
a. Men — Less than 40 mg/dL (1.03 mmol/L)
b. Women — Less than 50 mg/dL (1.29 mmol/L)
4. Elevated blood pressure: Equal to or greater than 130/85 mm Hg or use of medication for hypertension
5. Elevated fasting glucose: Equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycaemia.

Inclusion criteria
• All patients diagnosed as NAFLD by abdominal ultrasonography.
• Age more than 18 years.

Exclusion criteria
• Patients less than 18 years and more than 75 years.
• Patients with history of alcohol intake more than 30 grams/day in males and more than 20 grams/ day in females.
• Patients with history of jaundice or HBsAg positive.
• Patients with history of following drug intake -steroids, synthetic oestrogens, heparin, calcium channel blockers, amiodarone, valproic acid, antiviral agents.

III. Results

Total of 226 cases ultrasonographically diagnosed as NAFLD were included in the study and showed 46.02%, 44.7% and 9.29% of cases had grade I, II, and III fatty liver respectively. Mean age of the patients was 45.4±7.39 years and male : female ratio was 3:2. One twenty three out were symptomatic. Abdominal pain was the presenting symptom in 63.91 % of the patients. Clinical and biochemical parameters of all the cases of NAFLD are shown in Table 1. The mean BMI of the patients was 27.24±3.68 kg/m2 while 168 (74.3%) patients had increased waist circumference. Out of all the NAFLD patients, 146(64.6%) had metabolic syndrome as per NCEP ATP III criteria using asian indian criteria for waist circumference and all the components of metabolic syndrome was significantly associated with NAFLD($p \leq 0.05$) (Tables 1, 2). 109 (48.23%) of total patients were hypertensive. Percentage of hypertensive patients increased as grade of NAFLD increased in patients with metabolic syndrome i.e. 12.5%, 51.5% and 66.7% in grade I, II and III respectively (Table 5). Fasting glucose > 100mg/dl was found in 55.75% of patients. 61.9 % patient of grade III fatty liver had impaired fasting glucose (Table 5). ALT and AST levels were elevated in 51.8% and 45.13% of patients and ALT/AST ratio was > 1.0 in all the patients. Hypertriglyceridaemia was seen in 64.6 % patients. 83.56 % patients of fatty liver with metabolic syndrome had hypertriglyceridaemia (Table 2) and 85.7% patients of grade III fatty liver with metabolic syndrome had hypertriglyceridaemia (Table 5). Low serum HDL level were seen in 54.4 % patients (Table 2). When comparing the mean of variables of metabolic syndrome in patients of NAFLD with and without metabolic syndrome, statistical significance was found with all except diastolic blood pressure(Table 3). 80.2% and 90.5% of grade II and III NAFLD patients suffered from metabolic syndrome respectively (Table 4).

IV. Discussion

NAFLD has emerged as the most common cause of chronic liver disease worldwide. NAFLD can lead to hepatocellular carcinoma. NAFLD is an independent determinant of cardiovascular disease(CVD).NAFLD is therefore a complex problem with complications far beyond the liver.64.6% of NAFLD cases had metabolic syndrome according to the NCEP ATP III modified criteria using asian indian standards for waist circumference. Ajay Duseja et al (50%) and Deepa Uchil et al (47.1%) have had similar findings.[6,9] 123(84.2 %) of those having NAFLD with metabolic syndrome had increased waist circumference (male > 90cms, female > 80cms) and this observation was statistically significant (Table2). 58.7% and 47.1% of cases had increased waist circumference as reported by Ajay Duseja et al and Bajaj et al respectively.[17,18] Type 2 diabetes mellitus is a major component of metabolic syndrome and is associated with both obesity and NAFLD. Diabetes is not only associated with NAFLD but may also be a risk factor for development of progressive fibrosis. Mean fasting plasma glucose (mg/dl) of patients with NAFLD and metabolic syndrome was 132.6±39.3 12 mg/dl (Table 3). 45(30.8%) were having diabetes (> 126 mg/ dl) as compared to 9% described by Kaushal et al in those having metabolic syndrome.[19] 92(63.01%) cases had impaired fasting glucose (>100 mg/dl) and was found to be statistically significant when compared to NAFLD without metabolic syndrome. 72.4% and 28% patients had impaired fasting glucose as reported by Ajay Duseja et al and Bajaj et al respectively.[17,18] 54.1% patients had blood pressure ≥ 130/85 mm Hg with a mean of139.63 ± 16.34 /82.13 ± 6.89 mm Hg which was similar to that reported by Bajaj et al(48.72%).[17]In patients of NAFLD with metabolic syndrome 122(83.56%) had hypertriglyceridaemia (>150 mg/dl) with a mean of 282.84± 94.03 which is significantly higher than those reported by Deepa Uchil et al (43.6%) and Bajaj et al (23.1%). [9,18] 90(54.8%) patients had low HDL levels (< 40 mg/ dl in males and < 50 mg/dl in females) with a mean of 38.78±5.6 mg/dl as compared to 66.7% described by Bajaj et al. Dyslipidaemia between the two groups i.e., NAFLD with and without metabolic syndrome was significant both for prevalence as well as the respective means. The incidence of impairment of various parameters in grade II and III fatty liver is consistently higher in cases of NAFLD with metabolic syndrome when compared with those without metabolic syndrome (Table 5). Therefore a conclusion can be drawn that there is a greater association of metabolic syndrome with increasing severity of fatty liver disease.

V. Conclusion

As symptoms and signs of NAFLD are non specific and occur later in the course of the disease it can be inferred from the above observations that a clinician should have a high index of suspicion in order to detect NAFLD early in the course of the disease. Our study also reveals that there is higher prevalence of all the components of metabolic syndrome in cases of NAFLD. Liver biopsy is considered the gold standard for diagnosing NAFLD but is not practical and most patients shy away from getting it done. Thus patients must be evaluated for the presence of NAFLD by abdominal ultrasonography. Early detection would help not only in modifying the disease course and delaying its complications .Preventive programs should be launched to encourage people to adopt healthy life style ie do regular exercise, take low calorie - high fibre diet, and avoid over indulgence in alcohol.

Conflict of interest

All authors declare no conflicts of interest.

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Table-1: Clinical and biochemical profiles of all cases of NAFLD

Variable	NAFLD (n=226) Mean ± SD
Age(yr)	45.4±7.39
Systolic blood pressure (mm Hg)	136.0±14.76
Diastolic blood pressure (mm Hg)	79.17±8.52
Body mass index (kg/m2)	27.24±3.68
Waist circumference (cm)	88.18±8.97
Fasting blood sugar (mg/dl)	119.85±47.81
Total cholesterol (mg/dl)	234.74±37.53
Serum triglycerides (mg/dl)	268.88±89.8
High density lipoprotein (mg/dl)	41.64±5.58
serum LDL (mg/dl)	128.06+38.12
serum VLDL (mg/dl)	25.28+8.95
Aspartate amino transferase (u/l)	52.14±29.78
Alanine amino transferase (u/l)	76.74±49.07

Table-2: Comparison of prevalence of variables in patients of NAFLD with metabolic syndrome and NAFLD without metabolic syndrome

Variable	Nafld With Metabolic syndrome (N=146) No. (%)	Nafld Without metabolic syndrome(N=80) No. (%)	p value
Fasting Plasma Glucose >100 mg/dl	92 (63.01%)	34 (42.5%)	≤ 0.05
Hypertension > 130/85 mmHg	79 (54.1%)	30 (37.5%)	≤ 0.05
Triglycerides > 150 mg/dl	122 (83.56%)	24 (30%)	≤ 0.05
HDL M < 40mg/dl F < 50mg/dl	90 (54.8%)	33 (41.25%)	≤ 0.05
Waist Circumference M > 90cm F > 80 cm	123 (84.2%)	45(56.25%)	≤ 0.05

Table-3: Comparison of means of all the components of metabolic syndrome in patients of NAFLD with and without metabolic syndrome

Variable	Nafld With Metabolic syndrome (N=146)	Nafld Without metabolic syndrome(N=80)	p value
Fasting Plasma Glucose	132.6±39.3	91.2±19.8	≤ 0.05
Hypertension			
SBP	139.63 ± 16.34	124.65 ± 15.17	≤ 0.05
DBP	82.13 ± 6.89	77.35 ± 6.16	≥0.05
Triglycerides (mg/dl)	282.84± 94.03	201±78.92	≤ 0.05
HDL	38.78±5.6	43.34±5.8	≤ 0.05
Waist Circumference(in cm)	92.56±46	84.23±37	≤ 0.05

Table-4: Distribution of prevalence of metabolic syndrome in different grades of Fatty liver

Metabolic syndrome	Grade I NAFLD (n=104)	Grade II NAFLD (n=101)	Grade III NAFLD (n=21)
present(%)	46(44.2)	81(80.2)	19(90.5)
absent(%)	58(55.8)	20(19.8)	2(9.5)

Table-5: Distribution of grades of NAFLD with and without metabolic syndrome

Variables	Grade I NAFLD (n=104)		Grade II NAFLD (n=101)		Grade III NAFLD (n=21)	
	metabolic syndrome		metabolic syndrome		metabolic syndrome	
	yes	no	yes	no	yes	no
Symptomatic	28(26.9%)	37(35.6%)	24(23.7%)	20(19.8%)	11(52.4%)	2(9.5%)
ALT ≥ 41IU	34(32.7%)	47(45.2%)	68(67.3%)	17(16.8%)	15(71.4%)	2(9.5%)
AST ≥ 38IU	30(28.4%)	28(26.9%)	55(54.5%)	30(29.7%)	17(80.9%)	1(4.8%)
Central Obesity (WC) (> 90 cm - M,> 80 cm -F)	45(43.2%)	18(17.3%)	62(61.4%)	25(24.7%)	16(76.2%)	2(9.5%)
Impaired fasting glucose (> 100 mg/dl)	29(27.9%)	12(11.5%)	50(49.5%)	22(21.8%)	13(61.9%)	0
Hypertension (130/85 mmHg)	13(12.5%)	12(11.5%)	52(51.5%)	17(16.8%)	14(66.7%)	1(4.8%)
Low HDL (< 50 mg/dl-F, < 40 mg/dl-M)	18(17.3%)	19(18.3%)	58(57.4%)	13(12.9%)	14(66.7%)	1(4.8%)
Hypertriglyceridaemia (>150 mg/dl)	26(25.0%)	10(9.6%)	78(77.2%)	14(13.7%)	18(85.7%)	0