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Original article

Non alcoholic fatty liver disease in patients with type 2 diabetes mellitus

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ABSTRACT

Background and Objective: Nonalcoholic fatty liver disease (NAFLD) has emerged as the most common cause of chronic liver disease worldwide.Type2Diabetes mellitus (DM) is a risk factor for progressive liver disease and mortality in patients with NAFLD, whereas NAFLD is a marker of cardiovascular risk and mortality in patients with type 2diabetes. Hence, the diagnosis and evaluation of fatty liver is an important part of management of diabetes. We conducted a study to determine anthropometric and metabolic parameters in diabetic patients with NAFLD. Anthropometric and metabolic parameters in diabetic patients with fatty liver were compared with diabetic patients without fatty liver. Research Design and Methods: 44 patients with type 2 diabetes mellitus attending diabetic clinic of a tertiary care hospital participated in the study. 30 diabetic patients had fatty liver and 14 diabetic patients without fatty liver acted as controls. History and thorough clinical examination including anthropometry (waist hip ratio and body mass index (BMI)) and lab investigations were done.Ultrasound abdomen was done to detect fatty liver. Anthropometric and metabolic parameters in diabetic patients with fatty liver was compared with diabetic patients without fatty liver. Results : In our study diabetic patients with fatty liver had high body mass index (BMI), high waist hip ratio ,elevated SGPT /SGOT ratio(>1) and deranged lipid profile when compared to diabetic patients without fatty liver. This was found be statistically significant. Conclusions: Increased waist hip ratio and BMI would act as early anthropometric indicators in prediction of NAFLD in type 2 diabetic patients. SGPT / SGOT ratio>1could act as biochemical marker for prediction of development of fatty liver in diabetic patients.

1.Introduction:

When hepatosteatosis is present in the absence of excessive alcohol consumption, it is termed non-alcoholic fatty liver disease(NAFLD). NAFLD encompasses a spectrum of disorders ranging from simple steatosis to inflammatory steatohepatitis (NASH) and cirrhosis.

Non-alcoholic fatty liver disease has emerged as the most common cause of chronic liver disease worldwide [1]. NAFLD can lead to hepatocellular carcinoma. NAFLD is an independent determinant of cardiovascular disease (CVD) [2]. NAFLD is therefore a complex problem with implications far beyond the liver. The pathogenesis of diabetes and NAFLD are intimately related to insulin resistance and hyperinsulinemia [3].

Type 2DM increases the risk of liver-related death by up to 22-fold in patients with NAFLD [4]. In patients with Type 2 diabetes, the prevalence of NAFLD is as high as 75% [5]. Diabetes mellitus is frequently observed in patients with NAFLD, being present in 18-45% of cases[6,7]. Type 2DM is a risk factor for progressive liver disease and mortality in patients with NAFLD, whereas NAFLD is a marker of cardiovascular risk and mortality in patients with diabetes. Hence, the diagnosis and evaluation of fatty liver is an important part of management of diabetes.

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We conducted a study to determine the anthropometric and metabolic parameters in NAFLD patients with type 2 diabetes. Anthropometric and metabolic parameters in diabetic patients with fatty liver was compared with diabetic patients without fatty liver.

2. Materials and Methods

This cross sectionalstudy was conducted at a tertiary care hospital in mangalore. The study subjects were 44 patients with type 2 diabetes mellitus. 30 Diabetic patients had fatty liver and 14 diabetic patients without fatty liver acted as controls. Approval of Ethics committee of the hospital was sought prior to starting the study. Written informed consent was taken from all the study subjects. Exclusion Criteria were : patients consuming alcohol, patients with congestive cardiac failure and renal failure patients on hepatotoxic drugs, patients with history of of jejunoileal bypass or extensive small bowel resection and patients on insulin.

History and thorough clinical examination including anthropometry (waist hip ratio and BMI) was done.

Fasting blood sugar(FBS), Fasting Lipid Profile,blood Urea, serum creatinine, serum uric acid, serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT) ,Gamma glutamyltransferase (GGT) were done for all patients.

USG abdomen was done to detect fatty liver. Those patients who had increased echogenicity of liver as compared to kidney by USG were considered to have fatty liver [8].

Anthropometric and metabolic parameters in diabetic patients with fatty liver was compared with diabetic patients without fatty liver.

Statistical methods

Statistical analysis was done by comparing diabetic patients with fatty liver and diabetic patients without fatty liver .Z test was done and $p < 0.05$ was considered to be significant.

3. Results

A total of 44 patients participated in the study.Data of 30 diabetic patients with fatty liver was compared with 14 diabetic patients without fatty liver. The results are as follows-

1.Sociodemographic profile and anthropometry:

Diabetic patients with fatty liver (Table 1)

In this group 18 were males and 12 were females. Mean BMI was 27.26 ± 6.69 (Kg/m^2). Mean Waist Hip ratio was 0.93 ± 0.162.Waist hip ratio was abnormal in 60% of the cases.

Diabetic patients without fatty liver (Table 1)

In this group 3 were females and 11 males. Mean BMI was23.7± 2.38(Kg/m^2). Mean Waist Hip ratio was 0.82 ±0.05. Waist hip ratio was normal in all controls.

2. Comparison of Biochemical Parameters:

Diabetic patients with fatty liver SGPT /SGOT ratio was >1 in 60% of the cases. GGT>64 in 90% of the cases.Mean HDL, LDL and TG was 31.16 ± 10.2 mg/dl, 170.83± 20.5 mg/dl and 224 ± 71.58 mg/dl (Table 2).

Diabetic patients without fatty liver

Elevated GGT levels, SGPT/SGOT ratio >1 was seen in only 20% of cases. Mean HDL, LDL and TG was 40.5 ± 4.23 mg/dl, 114± 16.54 mg/dl and 123.92± 25.25 mg/dl (Table 2).

Table 1- Comparison of anthropometric variables in diabetic patients with and without fatty liver

	Diabetic patients with fatty liver (Mean ± SD)	Diabetic patients without fatty liver (Mean±SD)	P Value
Weight (kg)	68.9±11.11	66.92±7.85	.511
Height (cm)	160.26±13.54	167.85±9.55	.037
Waist Hip ratio	0.9312±.162	0.82±.057	.022
BMI((Kg/m2)	27.2±6.69	23.78±2.38	.023

Table 2- Comparison of biochemical variables in diabetic patients with and without fatty liver

	Diabetic patients with fatty liver (Mean ± SD)	Diabetic patients without fatty liver (Mean± SD)	P Value
SGPT/ SGOT ratio	1.01± .289	835±.148	.021
GGT(units/ ml)	79.3± 5.3	62±4.36	.013
Uric acid (mg %)	6.39±1.181	3.7±1	.001
HBa1c (%)	9.46± 4.66	7.6±0.76	.211
Cholesterol (mg%)	249.93±37.05	172.64±32.62	.001
TG*(mg%)	224.96±71.58	123.92±25.25	.001
HDL** (mg%)	31.16±10.22	40.05±4.23	.001
LDL*** (mg%)	170.83±20.51	114±16.54	.001

TG-Triglyceride,**HDL- High density lipoprotein,LDL-Low density lipoprotein**

4. Discussion

In our study we found that anthropometric parameters like BMI and waist hip ratio had significant association with occurrence of NAFLD. In our study SGPT / SGOT ratio>1 was associated with increased incidence of fatty liver there by implying its role as a screening test in detection of fatty liver. Deranged lipid parameters particularly hypertriglyceridemia was seen in diabetic patients with fatty liver.

NASH was first described in 1980 in a series of patients of the Mayo Clinic[9].In 1980, Ludwig et al. described an alcoholic hepatitis-like pattern of injury in the liver of non-alcoholic patients. They introduced the term 'non-alcoholic steatohepatitis' (NASH) to describe this disease entity. The histologic features characteristic of steatohepatitis in the absence of significant alcohol consumption can be seen in a wide variety of conditions like drugs and toxins exposure, jejunoilealbypass , extensive small bowel resection and Wilsons disease.

Obesity and in particular central obesity has been described as one of the strongest risk factors for NAFLD and fibrosis, with NASH being prevalent in 18.5% of the obese patients [10]. Goland et al have showed that patients with NAFLD had a significantly higher BMI[11]. Marchesani et al showed that 80% of patients with NAFLD were obese[12]. In our study BMI and waist hip ratio were high in diabetic patients with NAFLD thereby implying role of abdominal obesity and hence BMI in pathogenesis of fatty liver in diabetic patients and need of weight control in the these patients.

NAFLD is commonly characterized by elevated levels markers of liver injury like alanine aminotransferase (ALT),aspartate aminotransferase (AST) and Gamma glutamyltransferase (GGT). Of these liver enzymes, ALT is most closely related to liver fat accumulation, and is often used in epidemiological studies as a surrogate marker for NAFLD [13]. It is now clearly known that the whole spectrum of histological findings of fatty liver and NASH may exist without elevation of transaminases[14]. In our study 60% of diabetic patients with fatty liver had SGPT /SGOT ratio was >1. The ratio of AST/ALT is usually less than 1 in patients who have either no or minimal fibrosis, although this ratio may be greater than 1 with the development of cirrhosis [15].

Gamma-glutamyltransferase (GGT) in the serum is frequently elevated in patients with NAFLD, and it has been reported to be associated with increased mortality [16]. GGT > 64 was seen in 90% of diabetes patients with fatty liver with the mean of 79.3 units/ ml . Although GGT is a marker of alcoholic liver disease, our study showed that in addition to SGPT and SGPT/SGOT ratio persistent elevation of GGT also would act as a marker of NAFLD. We found that there was no statistical correlation of HBA1c with NAFLD, reason for this observation could be due to the smaller sample size

Dyslipidemia has been reported in 20 to 92% of patients with NAFLD [5].Elevated triglycerides, increased LDL and decreased HDL was seen in diabetic patients with NAFLD in our study. Accordoing to Williamson et al independent predictors of NAFLD in diabetic patients are BMI, HbA1c and triglycerides [17].

Our study had some limitations. The important limitation of this study is the selection bias associated with the inclusion of patients from a tertiary care hospital. Another limitation of this study is that subjects did not have a liver biopsy and histological examination, the gold standard technique for identifying steatosis. Performance of this invasive procedure was not feasible as we conducted the study in patients attending outpatient clinics. We used ultrasound to detect fatty liver in our study. USG has a sensitivity of 89% and specificity of 93% in detecting steatosis and a sensitivity and specificity of 77% and 89% respectively in detecting increased fibrosis. Other tests like hepatitis B and C antibody, antinuclear antibody(ANA), antismooth muscle antibody, antimitochondrial antibody and ferritin were not done in our study.

5. Conclusion

Increased waist hip ratio and BMI would act as early Anthropometic indicators in prediction of NAFLD in type 2 diabetic patients. SGPT / SGOT ratio >1,GGT levels > 64 could act as biochemical markers for prediction of development of fatty liver in diabetic patients during follow up.

Deranged lipid profile parameters (increased LDL, TG, and decreased HDL) predispose to occurrence of fatty liver in diabetic patients, hence substantiating the necessity of aggressive lipid control among these patients to prevent fatty liver.

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