



## A STUDY OF CLINICAL, BIOCHEMICAL, SONOLOGICAL PROFILE OF HEPATIC STATUS IN TYPE 2 DIABETES MELLITUS IN TERTIARY CARE SETTING

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**ABSTRACT** **INTRODUCTION:** The prevalence of diabetes is increasing world over and is expected to affect 57 million adults in India by 2025. Apart from kidney, eye, heart and blood vessels, liver is also indirectly related with diabetes mellitus. Virtually the entire spectrum of liver disease is seen in patients with type 2 diabetes. This includes abnormal liver enzymes, non alcoholic fatty liver disease (NAFLD), cirrhosis, hepatocellular carcinoma, and acute liver failure. In addition, there is an unexplained association of diabetes with hepatitis C. Finally, the prevalence of diabetes in cirrhosis is 12.3–57%. Thus, patients with diabetes have a high prevalence of liver disease and patients with liver disease have a high prevalence of diabetes.

**AIM OF STUDY :** This study aims to describe clinical, biochemical, sonological profile of hepatic status in type 2 diabetes mellitus in tertiary care setting in relation with non alcoholic fatty liver disease (NAFLD).

**MATERIALS AND METHODS:** This study was done at ASRAM medical college Eluru between March 2018 and February 2019.

**Sample size :** 118

**Inclusion criteria :** Type 2 diabetic patients diagnosed according to the American Diabetic Association criteria, newly diagnosed or on follow-up were included in the study. Exclusion criteria 1. Patients with history of any chronic drug intake other than oral hypoglycemic drugs 2. Jaundice 3. History of alcohol intake 4. HBsAg positive.

**DISCUSSION:** Since clinical symptoms of fatty liver are nonspecific or silent this study does not attempt to define the clinical symptoms of fatty liver. Fatty liver most commonly affects middle-aged women with obesity, altered glucose metabolism, hyperlipidemia, and hypertension.

**RESULTS:** A total of one hundred and eighteen patients were included in the study, 71 (60.2%) females and 47 (39.8%) males. Eleven (9.3%) cases were newly diagnosed during the course of the study. Sixty six (55.9%) cases had diabetes for duration less than 5 years. Forty one (34.7%) cases had diabetes for a duration more than or equal to 5 years.

**CONCLUSIONS:** The increasing prevalence of fatty liver in diabetes is well established. It is important to acknowledge that the increased incidence of steatohepatitis and hepatic fibrosis in type 2 diabetes may translate into increased incidence of hepatocellular carcinoma. Liver biopsy though the gold standard for the diagnosis and staging of the disease, cannot be used for large scale screening.

**KEYWORDS :** Diabetes, Jaundice, Hypoalbuminemia, Hepatocellular Carcinoma, Nafld-non Alcoholic Fatty Liver Disease, Serum Albumin

### INTRODUCTION:

The prevalence of diabetes is increasing world over and is expected to affect 57 million adults in India by 2025. Apart from kidney, eye, heart and blood vessels, liver is also indirectly related with diabetes mellitus. Virtually the entire spectrum of liver disease is seen in patients with type 2 diabetes. This includes abnormal liver enzymes, non alcoholic fatty liver disease (NAFLD), cirrhosis, hepatocellular carcinoma, and acute liver failure. In addition, there is an unexplained association of diabetes with hepatitis C. Finally, the prevalence of diabetes in cirrhosis is 12.3–57%. Thus, patients with diabetes have a high prevalence of liver disease and patients with liver disease have a high prevalence of diabetes.

### NON-ALCOHOLIC FATTY LIVER DISEASE

There is renewed interest in Non alcoholic fatty liver (NAFL) recently because of its increased prevalence in diabetes. It has been shown to be a predisposing factor for insulin resistance and hyperinsulinemia, a major cause of cryptogenic cirrhosis and may even lead to hepatocellular carcinoma. There are not enough studies done on the hepatic status of diabetic patients in our country. Hence this study aims to describe the hepatic profile of type 2 diabetic patients.

**AIM OF STUDY :** This study aims to describe clinical, biochemical, sonological profile of hepatic status in type 2 diabetes mellitus in tertiary care setting in relation with non alcoholic fatty liver disease (NAFLD)

### MATERIALS AND METHODS :

This study was done at ASRAM medical college Eluru between March 2018 and February 2019.

**Sample size :** 118

**Inclusion criteria :** Type 2 diabetic patients diagnosed according to the American Diabetic Association criteria, newly diagnosed or on follow-up were included in the study.

### Exclusion criteria :

1. Patients with history of any chronic drug intake other than oral hypoglycemic drugs
2. Jaundice
3. History of alcohol intake
4. HBsAg positive

The type of oral hypoglycemic drug intake, height and weight were recorded and Body Mass Index (BMI) calculated. Patients were subjected to biochemical investigations to detect the liver enzyme levels, serum bilirubin, serum albumin, serum globulin, serum total proteins and total cholesterol.

Fifty two patients were subjected for ultrasonographic examination by a qualified radiologist who was masked from the patient's diagnosis or the indication for ultrasound, to assess the liver parenchyma, liver size, gall bladder, biliary and portal system.

The echo texture of the liver was graded as follows :

**Grade 1:** A slight diffuse increase in fine echoes in the hepatic parenchyma with normal visualization of the diaphragm and intrahepatic vessel borders.

**Grade 2:** A moderate diffuse increase in fine echoes with slightly impaired visualization of the intrahepatic vessels and diaphragm.

**Grade 3:** A marked increase in fine echoes with poor or no visualization of the intrahepatic vessel borders, diaphragm and

posterior portion of the right lobe of the liver.

#### ANALYSIS OF RESULTS :

A total of one hundred and eighteen patients were included in the study, 71(60.2%) females and 47(39.8%) males.

Eleven (9.3%) cases were newly diagnosed during the course of the study. Sixty six (55.9%) cases had diabetes for duration less than 5 years. Forty one (34.7%) cases had diabetes for a duration more than or equal to 5 years.

The total serum proteins were within the normal range for all the patients with a mean value of 7.03 +/- 0.4. low albumin levels, taken as less than 3.5 mg% were found in 4 (3.4%) patients and low globulin level, taken as less than 2 mg% in 2 (1.7%) patients.

Age-wise and Sex-wise comparison of the liver function tests revealed no significant difference between the various age classes or between sexes as depicted in tables 1 and 2.

**Table 1**

Test	30-39	40-49	50-59	60-69	70-79
Serum Total Protein	7.0	7.0	7.0	7.1	7.0
S. Albumin	4.0	4.3	4.0	4.0	4.3
S. Globulin	2.9	2.9	2.9	2.9	2.9
S. Bilirubin	0.9	0.9	0.8	1.0	1.2
AST	23	22	22	23	31
ALT	19	19	19	20	25
ALP	110	127	110	109	119

**Table 2**

Investigation	Female	Male
Serum Total Protein	7.0	7.1
S. Albumin	4.1	4.2
S. Globulin	2.9	3.0
S. Bilirubin	0.8	1.0
AST	22	24
ALT	19	20
ALP	114	114

Among the patients whose recent fasting and 2 hr postprandial blood glucose values were available, 47 percent had a fasting glucose more than 130 mg% and 61% had a 2 hr post prandial glucose more than 180mg%. There was no significant difference between mean values across gender or age classes. Body mass index measurements revealed that 25 (35.2%) women were overweight (BMI>25) and 5 (7.0%) were obese (BMI>30). The numbers of overweight men were 12 (25.5%). No male patient was found to be obese.

Ultrasonographic examination was done in 52 patients, fatty liver was found to be more common in females. Overall 23 patients (42.3%) had fatty liver out of the 52 patients screened. Sex wise and BMI class wise distribution is given in tables 3 and 4. Hepatomegaly was identified in 5 (9.6%) patients of whom 4 were males. Asymptomatic gallstones were found in 5 (9.6%) patients, 3 females and 2 males. Bile duct was found to be dilated (>5mm) in 6 patients, portal vein was normal (<12mm) in size in all the patients.

**Table 3**

Fatty liver	Female (%)	Male (%)
Grade I Fatty liver	13 (50)	8(30.8)
Grade II Fatty liver	2 (7.7)	0(0)
no fatty change	11(42.3)	18(69.2)

**Table 4**

Fatty liver	Underweig ht	Normal	Overweight	Obese	morbid Obese
Grade I Fatty liver	0%	25%	31.3%	100%	0%
Grade II Fatty liver	0%	0%	6.3%	0%	0%
No fatty change	100%	75%	62.5%	0%	0%

#### DISCUSSION :

Since clinical symptoms of fatty liver are nonspecific or silent this study does not attempt to define the clinical symptoms of fatty liver. Fatty liver most commonly affects middle-aged women with obesity, altered glucose metabolism, hyperlipidemia, and hypertension.

#### Age, Gender and Obesity :

As reported by Kelly et al there was no difference in the mean age of patients with fatty liver as compared to those with normal liver. Sixty five percent of the patients with fatty liver in this study were females but no significant difference(p value>0.05) in proportion based on gender was found in those with grade 1 fatty liver compared to those without evidence of fatty liver. Obesity was found to have a significant association with fatty liver, in the current study 70% of patients with grade 1 fatty liver had a BMI more than 25 and both patients with grade 2 fatty liver were overweight.

#### Liver enzymes :

Reid et al and Dixon et al found elevated AST levels in patients with NASH. Laboratory abnormalities identified included a 2-4-fold elevation of serum aminotransferase levels while other liver function test results were normal. Agarwal et al and Kelly et al documented elevation of ALT as the biochemical abnormality in patients with NASH. A recent study found that patients with NASH and those with higher grade of histological inflammation had increment of transaminases and albumin levels. The same study showed a correlation of fibrosis with AST and ALT levels. Elariny et al showed that while ALT was associated with NASH and advanced fibrosis, the majority of the patients with either NASH or advanced fibrosis had normal AST. An AST/ALT ratio >1.0 was yet another finding in a study on NASH. Contrary to all these a study in 2003 found liver enzymes to be insensitive and unreliable to confirm the diagnosis or stage the extent of fibrosis. Older age, obesity and diabetes were shown to be predictive of fibrosis. Our study also did not find a significant elevation of any of the liver enzymes. There was no statistically significant difference (p value >0.05) between the parameters among patients with grade 1 fatty liver and those without fatty liver. Eighty five percent of the patients in this study had AST/ALT ratio more than one, but it was not found to have any association with fatty liver as shown in table 5.

**Table 5**

Enzyme	Grade I fatty liver	Grade II fatty liver	No fatty change
AST	22	21	21
ALT	19	17	18
AST/ALT	1.2	1.2	1.2
ALP	121	77	110

**Insulin resistance :** Obesity, insulin resistance, and increased concentrations of plasma fatty acids are considered to increase the risk for fatty liver, and each of these metabolic factors is also characteristic of type 2 DM. It has been reported that fatty liver in turn influences severity of hepatic insulin resistance in type 2 DM. The present study did not measure insulin resistance. The fasting blood glucose in grade 1 fatty liver was 132, grade 2 fatty liver was 130 and in patients with no fatty liver 134. The 2 hour postprandial blood glucose was 186 in grade 1 fatty liver, 230 in grade 2 fatty liver and 216 in patients with normal liver. By comparing the mean blood glucose values between those with or without fatty liver it did not reveal any significant difference (p value >0.05)

**Hyperlipidaemia:** Hypertriglyceridemia is more severe in individuals with fatty liver. Only the total cholesterol levels were assayed in our study. A comparison of the mean total cholesterol levels between the fatty liver group and the rest did not reveal any statistically significant difference.

#### CONCLUSIONS :

The increasing prevalence of fatty liver in diabetes is well established. There is an increasing understanding about its etio pathogenesis, and its various pathological stages have been well defined. It is important to acknowledge that the increased incidence of steatohepatitis and hepatic fibrosis in type 2 diabetes may translate into increased incidence of hepatocellular carcinoma. Liver biopsy though the gold standard for the diagnosis and staging of the disease, cannot be used for large scale screening. More non invasive methods are the need of the hour for early and wide screening to detect this disease. Liver enzymes were thought to be a potential non invasive strategy for early detection of this disease, but the present study did not find any correlation of the level of liver enzymes and the degree of fatty liver in Indian patients.

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