A Cross Sectional Study to Assess Liver Fibrosis in Patients with Diabetes and Metabolic Syndrome

Syed Safiullah Ghorī2,3*, Hafsa Khalid1,3, Mohammed Alim1, Mohammed Abdul Quddus3

1Department of Endocrinology, Osmania General Hospital, Afzalgunj, Hyderabad, Telangana, India.
2Pharmacology Research Lab, Anwar-ul-Uloom College of Pharmacy, New Mallepally, Hyderabad 500016, Telangana, India.
3Department of Hospital and Clinical Pharmacy, Anwar-ul-Uloom College of Pharmacy, New Mallepally, Hyderabad 500016, Telangana, India.

ABSTRACT
The present study was conducted in Osmania General Hospital, Hyderabad. The study included evaluation of liver fibrosis in patients with diabetes and metabolic syndrome. Liver fibrosis is now being considered as a reversible process which is characterized by excessive accumulation of extracellular matrix. The use of non-invasive methods to assess liver fibrosis in patients with HCV, Non-Alcoholic Fatty Liver Disease (NAFLD) and alcohol abuse has been well validated. However, use of these non-invasive methods in patients with diabetes mellitus and metabolic syndrome assessed might develop fibrosis during asymptomatic stages. Hence we tried to use these non-invasive methods in patients with diabetes and metabolic syndrome who are at high risk of developing NAFLD or liver fibrosis in routine clinical practice. This was a single-center prospective study. 50 patients with diabetes and metabolic syndrome attending the endocrinology department of Osmania General Hospital were assessed for fatty liver and enrolled in to the study. NAFLD fibrosis score was used to assess liver fibrosis and BARD score was used for staging of fibrosis as per metavir classification. The mean age of the patients was 50.8 ± 8.2 with 22 males and 28 females. 90% of the population was found to have some degree of fibrosis. 56% of the patients were at advance fibrosis stage as per the BARD score. Patients with diabetes and metabolic syndrome should be constantly evaluated for liver fibrosis apart from development of diabetes and other complications and to prevent any adverse effects due to waning of liver functions.

Keywords: liver fibrosis, enhanced liver fibrosis, non-alcoholic fatty liver disease, cirrhosis, NAFLD fibrosis score, BARD score.

INTRODUCTION
Liver fibrosis is a reversible process, due to chronic tissue damage characterized by excessive accumulation of extracellular matrix. It is the first stage of liver scarring, this scar tissue slowly builds up and takes over most of the liver, diminishing the normal activities of liver1. If untreated liver fibrosis may lead to cirrhosis which is the final stage of liver fibrosis2. The onset of liver fibrosis is usually insidious and mostly related to morbidity and mortality after development of cirrhosis. Liver fibrosis has been associated with diabetics, metabolic syndrome, cardiovascular problems and portal hypertension. Obesity is found in 35-100% of liver fibrosis patients and diabetics in 5-55%3. The non-alcoholic fatty liver disease patient is an obese middle aged individual with diabetics. Liver fibrosis is a common consequence of almost all chronic liver diseases. Asian countries have a higher prevalence of type II diabetes and fatty liver as well as increased rates of hyperinsulinemia and insulin resistance4. Epidemiological studies suggest prevalence of Liver Fibrosis in around 9% to 32% of general population in India with higher prevalence in those with overweight or obesity and those with diabetes or prediabetes. The prevalence of Liver Fibrosis has increased over the past two decades to become the commonest disease in Indians. Indians have a high prevalence of insulin resistance and the metabolic syndrome5. Liver fibrosis actually represents an emerging disease of clinical interest. The advanced liver fibrosis may lead to development of cirrhosis, hepatocellular carcinoma, portal hypertension, ascites and end stage liver disease. Assessing fibrosis with coexistence disease condition may prevent further progression of fibrosis and advanced liver diseases and also control other diseases progression.

Treatment strategies for liver fibrosis aim to improve insulin sensitivity, modify underlying metabolic risk factors, or to protect the liver from further damage by reducing oxidative stress. Multiple pharmacological interventions have been attempted with variable success. Insulin sensitizing agents such as metformin, thiazolidinedione’s and lipid lowering agents have yielded promising results. The removal of the causative agent is the most effective intervention in the treatment of liver fibrosis.

*Author for Correspondence: safiullahghori@gmail.com
Thus, identifying the presence of liver fibrosis in patients with diabetes and metabolic syndrome is of major importance in management of liver fibrosis. This study aims to assess liver fibrosis in type 2 diabetic and metabolic syndrome patients.

**MATERIAL AND METHODS**

This study was a single center, prospective cross sectional observational study. Patients with diabetes and metabolic syndrome were evaluated for fatty liver by ultrasound imaging and out of 68 screened, 50 patients with fatty liver were enrolled in the study visiting to endocrinology department of Osmania General Hospital. At enrollment patient’s case details were obtained in CRF. The clinical profile consisted of age, initial diagnosis, social habits, life style and medication used. The patients were enrolled based on the inclusion criteria and exclusion criteria. The inclusion criteria was patient’s age should be above 18 years and patients must have type 2 diabetics and metabolic syndrome. Exclusion criteria were patients with NYHA class III-IV and patients suffering with neurological disease was avoided. This study was conducted for a total period of 6 months (November 2015 to April 2016) out which enrolment of patients was completed in 2 months and study duration was 5 months. This study was approved by the institutional ethics committee and is registered at clinical trial registry of India (CTRI/2014/07/004725).

**Physical examination**

Diabetes was confirmed with patient’s medical history and fasting blood glucose. Modified national cholesterol education program adult treatment panel III9 was used to define metabolic syndrome. The criteria involved is patients with waist circumference ≥ 94cm for men and ≥ 80cm for women. Increased TGs and low HDL cholesterol. High blood pressure (>130/85 mmHg or treatment of previously diagnosed hypertension). Raised fasting blood glucose (FBG) ≥ 110 mg/dL, known diabetic. Metabolic syndrome was defined by the presence of three or more of these criteria1 out of which central obesity is mandatory variable.

**Anthropometric measurements**

Physical examination weight, height, and body mass index waist circumference were measured. BMI was calculated as body weight (kg) divided by the square of height (m2) (BMI=\(\frac{weight}{height^2}\)). Waist circumference was measured, during expiration, at the narrowest point between the lower rib and the iliac crest. Overweight and obesity were defined according to the International Obesity Task Force criteria8.

**Biochemical Estimations**

**Serum lipid profile**

Low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), total cholesterol and triglycerides were measured by using common standard laboratory techniques (LDL-C, HDL-C, CHOL [plus 2nd generation]) and TG assay.

**Hematological parameters**

Fasting blood glucose, hemoglobin, platelet count and HBA1C were measured according to international guidelines9.

**Liver Function Tests**

Serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), gamma-glutamyl transferase (GGT), serum bilirubin and total protein were measured by EASL Clinical Practice Guidelines.

**Blood Pressure Measurements**

Blood pressure monitoring was obtained according to Guidelines of the International Society of Hypertension. Blood pressure readings are recorded, around three readings are obtained at 2-5 minute intervals and average reading of second and third systolic blood pressure and diastolic blood pressure is recorded and further used in the analyses10.

**Noninvasive diagnosis of liver fibrosis**

The NAFLD Fibrosis score

NAFLD score is calculated through a formula which includes six variables: age, presence of diabetes, BMI, AST/ALT ratio, platelet count, and albumin11. NAFLD fibrosis score was calculated using online calculator (http://www.nafldscore.com).

The BARD score

The BARD score includes the following 3 variables: body mass index [BMI], aspartate aminotransferase [AST]/alanine aminotransferase [ALT] ratio, and presences of diabetes for calculation. The BARD score was calculated using online calculator (http://gihep.com/calculators/hepatology/bard).

**RESULTS AND DISCUSSION**

**Physical examination**

The mean age of the population was 50.8±1.15 with 22 men and 28 women participants. The mean age of men and women was 52.1±1.76 and 49.7±1.53 respectively. The mean height and weight of the population was 156±1.076 cm for men and 152±1.76 cm for women. Increased TGs and low HDL cholesterol. High blood pressure (>130/85 mmHg or treatment of previously diagnosed hypertension). Raised fasting blood glucose (FBG) ≥ 110 mg/dL, known diabetic. Metabolic syndrome was defined by the presence of three or more of these criteria1 out of which central obesity is mandatory variable.

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Earlier studies have shown that males have a higher prevalence of fibrosis than females. However, some studies have shown that the prevalence of fibrosis is higher in females than males. The cut-off point for determining the presence of fibrosis is the same for both sexes. In this study, the prevalence of fibrosis was 21% in females and 17% in males. The mean NAFLD fibrosis score was 44.42 ± 4.33 for total population, with the mean A:G ratio being 0.26 ± 0.06 for the total population. The mean of total protein was 4.092 ± 0.125 for total population, with the mean of albumin being 0.267 ± 0.06 for the total population. The mean BMI of total population was 27.59 ± 4.33, with the mean of total protein being 4.092 ± 0.125 for total population. The mean BMI of total population was 27.59 ± 4.33, with the mean of total protein being 4.092 ± 0.125 for total population.
future liver fibrosis among type 2 diabetic individuals and the metabolic syndrome. Future research of multi centred study in larger cohorts of patients is needed to understand the association of liver fibrosis with diabetic and metabolic syndrome and how potential treatment of liver fibrosis will decrease the risk of type 2 diabetics and metabolic syndrome. Development of new therapeutic strategies will definitely lead to prevention and treatment of liver fibrosis.
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REFERENCES