

A STUDY OF SPECTRUM OF LIVER DYSFUNCTION IN TYPE 2 DIABETES MELLITUS*Chandrashekar¹, Avinash Patil², Ishwar S. Hasab³, Chetan K. Ganteppanavar⁴, Basavaraj D. Baligar⁵*¹Assistant Professor, Department of Medicine, Karnataka Institute of Medical Sciences, Hubballi.²Senior Resident, Department of Medicine, Karnataka Institute of Medical Sciences, Hubballi.³Professor and HOD, Department of Medicine, Karnataka Institute of Medical Sciences, Hubballi.⁴Junior Resident, Department of Medicine, Karnataka Institute of Medical Sciences, Hubballi.⁵Assistant Professor, Department of Medicine, Karnataka Institute of Medical Sciences, Hubballi.**ABSTRACT****BACKGROUND**

India is popularly known as diabetic capital of the world. Every day, hundreds of new diabetics are added to the existent pool of the diabetics. The bulk and prevalence of diabetics is increasing every day at an alarming rate. Unlike many other organs affected like eyes, kidneys and nerves, liver is also one of the major organ affected. The spectrum of disorder ranges from simple abnormal liver enzyme status to frank cirrhosis. Liver has also major role in maintaining body sugar homeostasis as it is the site of glycogenolysis and gluconeogenesis. In this study, we would like to know more about the spectrum of abnormalities associated with hepatic metabolism as very few studies have been done previously.

MATERIALS AND METHODS

The study is a prospective and cross-sectional study done with 350 cases attending the KIMS, Hubballi Hospital. The population is aged more than 40 years and are diagnosed case of type 2 diabetes. Ultrasonography, liver function tests and many other relevant investigations are done. Alcoholics and patients with hepatocellular carcinoma, etc. are excluded from study.

RESULTS

350 cases were included in the study and 46% of cases (161) had fatty liver. Among them, 54.6% were males and 45.3% were females. It was also noticed that HbA1c was >9 gm% in patients with fatty liver. Obesity is a frequent association with fatty liver. ALT and AST, both were elevated and ALT being more elevated than AST. Triglycerides, total cholesterol, HDL cholesterol and LDL cholesterol was also higher when compared with non-alcoholic fatty liver group.

CONCLUSION

Non-alcoholic fatty liver disease is higher in patient with type 2 diabetes mellitus. Insulin resistance is also having a positive correlation with NAFLD. Better glycaemic control results in prevention of early disease progression and complications.

KEYWORDS

Diabetes Mellitus, Non-Alcoholic Fatty Liver Disease, Ultrasonography, Insulin Resistance, Glycaemic Control.

HOW TO CITE THIS ARTICLE: Chandrashekar, Patil A, Hasabi IS, et al. A study of spectrum of liver dysfunction in type 2 diabetes mellitus. J. Evid. Based Med. Healthc. 2018; 5(1), 1-3. DOI: 10.18410/jebmh/2018/1

BACKGROUND

The diabetes mellitus is a rapidly spreading non-infectious epidemic affecting at least 422 million people as of the year 2016.¹ Developing countries are worst hit and it accounts for around 2/3rd of cases.² It is also seen that diabetes affects the majority of population who are in economically productive age group. India has 69.2 million diabetics as per WHO statistics of the year 2015. In the last 3 to 4 decades, diabetes has become one of the major cause of morbidity and mortality. It is estimated that every 5th Indian is a diabetic.

Financial or Other, Competing Interest: None.
Submission 21-12-2017, Peer Review 24-12-2017,
Acceptance 28-12-2017, Published 01-01-2018.
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DOI: 10.18410/jebmh/2018/1



Rapid urbanisation, industrialisation, changing food habits and trendy lifestyle all have resulted in rapid surge of the disease. The real burden of the disease is not because of its presence, but due to the complications it produces like myocardial infarction, neuropathy, nephropathy and even complete blindness.

Diabetes is an important public health disease because it accounts for huge economic burden over an individual person, family, society and even the government of the nation, which needs to maintain the health of its citizens.

MATERIALS AND METHODS

The study is a single centre cross-sectional study with 350 cases. The study is done over a period of 1.5 years. The sample population for the study was collected from Karnataka Institute of Medical Sciences, Hubballi, using random sampling methods.

All the cases were aged >40 years. All cases either male or female with history of alcohol consumption of any quantity were excluded from the study. History of jaundice,

ascites, signs of liver cell failure, hepatitis B and hepatitis C infection were also excluded from study. History of intake of glucocorticoids, hormones like oestrogen, antitubercular therapy and antiretroviral therapy were excluded from study.

Complete haemogram, fasting blood sugar, postprandial blood sugar, HbA1c, HIV serology, liver function test, HBV serology, anti-HCV antibodies, fasting lipid profile and ultrasonography was done. Ultrasonography was used to rule out cirrhosis and non-alcoholic fatty liver disease.

Statistical analysis was done using mean values with standard deviation and Chi-square test and proportion test. Student's t-test was used to calculate the statistical significance.

RESULTS

Of the total 350 cases, 44.6% of cases (156) were from age group of 50-59 years with mean age of 56.34 ± 6.7 years. Males formed the majority of 62.85% cases. 102 were males and 54 were females in the age group of 50-59 years. Majority of patients, i.e. 53.7% of cases (188) were with diabetes mellitus for 6-10 years. 31% cases (109) were suffering from diabetes for a period of 1-5 years. 57.14% cases (200) were overweight with BMI of 25-29.9 kg/m². 86.6% (303) cases had a waist circumference of 81-90 cm and 87.7% (307) cases had hip circumference of 91-100 cm.

52.3% (183) cases were prehypertensive with BP of 120-140 mmHg. FBS was between 151-200 mg/dL in 45.7% (160) cases. PPBS was in range of 201-300 mg/dL in 44.3% (155) cases. 34% of cases had HbA1c of 7.1-8 mg% and 22.9% cases had HbA1c of 8.1-9 gm%. 40.3% of cases had AST of 40-60 U/L with mean of 32.46 ± 16.99 . Similarly, ALT was 61-80 U/L in 35.7% cases with mean of 45.75 ± 29.46 .

72.6% had triglycerides level in range of 152-200 mg/dL. HDL cholesterol was between 41-50 in 81.4% cases. Total cholesterol was in range of 201-240 mg/dL in 54% cases. LDL cholesterol was in range of 130-159 mg/dL in 42.3% of cases. Ultrasound had showed fatty liver in 46% (161) cases and non-fatty liver in 54% (189) cases.

In patients with diabetes of 6-10 years duration, fatty liver was seen in 99 cases and non-fatty liver was in 89 cases. There were no patients in non-fatty liver group with duration of diabetes of >11 years. The correlation between diabetes mellitus, fatty liver and non-fatty liver was statistically significant with 'p' value of 0.0011.

18% cases with fatty liver were obese with BMI of >30 kg/m². 74 cases of fatty liver were having HbA1c of >9.1. It was observed that the duration of diabetes was directly proportional to HbA1c level. This was indication that insulin resistance increases with duration of diabetes with statistical significance of 'p' value 0.0001.

DISCUSSION

Non-alcoholic fatty liver disease is a common hepatic disorder characterised by accumulation of fat in hepatocytes who is non-alcoholic. The spectrum of NAFLD ranges from simple steatosis, steatohepatitis and fibrosis to frank cirrhosis. The association of NAFLD is high with insulin resistance, obesity, type 2 diabetes, dyslipidaemia and metabolic syndrome.

The prevalence of fatty liver in our study was 46% (161) cases in ultrasonography. Ashutosh M Somalwar et al in their study of association of T2DM with NAFLD was showing a prevalence of 56.6%.³ Ganesh Bhat et al in their study had prevalence of 76% with 76% being males and 18% females.⁴ Shivanand Pai et al in their study showed prevalence of 68.18%, out of them, 60% were males and 40% females.⁵

Liver is an organ of production and consumption of glucose. Diabetes may itself cause liver disease of metabolic origin called NAFLD.⁶ It is also associated with dyslipidaemia, obesity and hypertension. In a study done with 103 patients where serial liver biopsy are done, the cases with diabetes and low initial fibrosis were associated with faster progression rates towards cirrhosis.⁷ Patients with diabetes with increased BMI are at increased risk of fibrosis.

Liver contributes significantly to morbidity and mortality in patients with diabetes.⁸

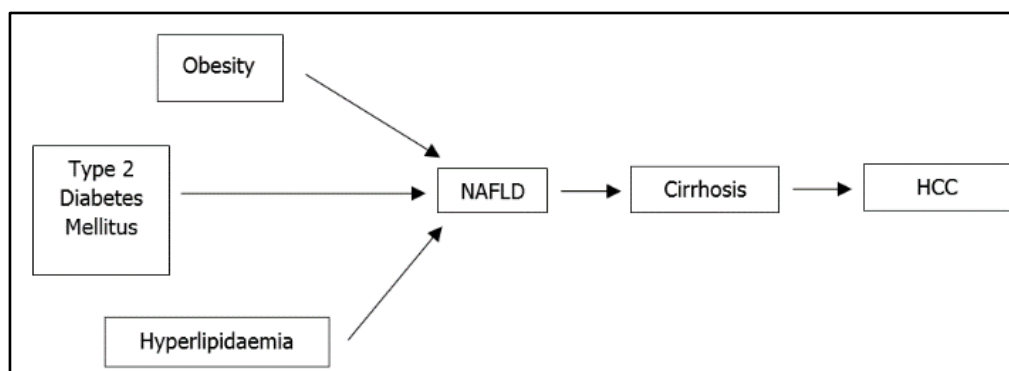


Figure 1. Liver Contributes Significantly to Morbidity and Mortality in Patients with Diabetes⁸

Fatty liver is most benign manifestation of NAFLD. The fatty liver has mainly triglycerides in the hepatocytes in presence of insulin resistance and it is also a part of metabolic syndrome.

Multiple risk factors are for NAFLD like diabetes, female gender, hyperlipidaemia, obesity and total parenteral nutrition. Prevalence of NAFLD is 30-98% with obesity, 21-60% with hyperlipidaemia and 21-33% with diabetes

mellitus. It is observed that NAFLD, type 2 diabetes mellitus and hyperlipidaemia, all share a common pathogenesis.

Insulin resistance is the key factor in NASH and NAFLD. There is a direct relation between duration of type 2 diabetes mellitus with NASH. The fatty liver changes are due to de novo lipogenesis and at the same time decrease in hepatic secretion of very low-density lipoprotein. There also exists associated hepatic damage from increased mitochondrial oxidative stress and generation of free radicals and peroxisomes.

The multi-hit process in pathogenesis of NAFLD begins with first hit from insulin resistance and second hit being alteration in cytokine and oxidative stress. A study showed that Asians had 2- to 3-fold increase in insulin resistance and 2-fold increase in hepatic triglyceride content.⁹ The

association between severe obesity with diabetes mellitus and prevalence of NAFLD is 100%.

A study by Peterson et al showed that Asian Indians had higher insulin resistance. Increased resistance was due to increased hepatic triglyceride content and plasma interleukin-6 concentration.¹⁰ Aminotransferases are the indicators of hepatocellular health. ALT is found in liver only and hence more specific. Liver is also a major organ in maintaining normal glucose and also a major site of insulin clearance. Many studies showed that abnormal hepatocellular function is associated with obesity and insulin resistance.

Insulin deficiency is also an important cause implicated in liver damage especially when the sugar controls are poor.

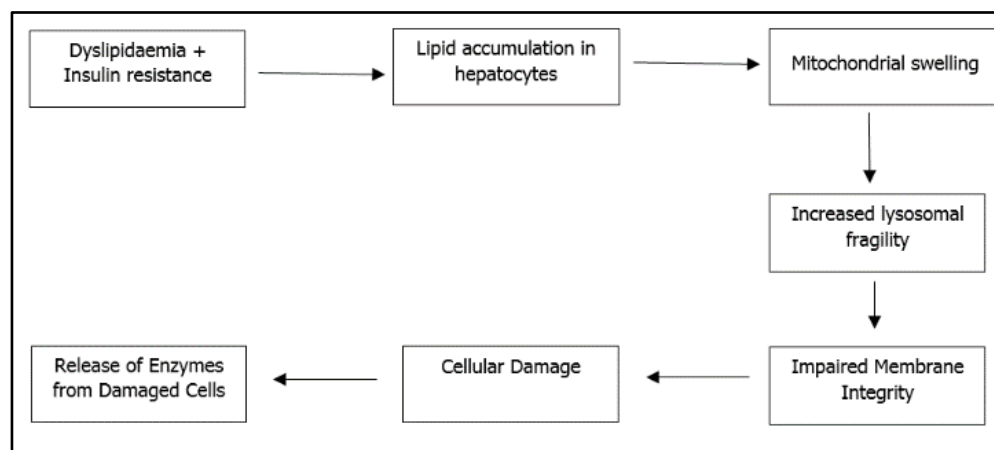


Figure 2. Insulin Deficiency is also an Important Cause Implicated in Liver Damage Especially when the Sugar Controls are Poor

CONCLUSION

The study has concluded that prevalence of NAFLD is higher among type 2 diabetes mellitus patients. The high mortality associated with the NAFLD should be remembered. Hence, the aggressive action should be taken to prevent the complication. Measures are needed at early stage to prevent morbidity and mortality.

REFERENCES

- [1] Huizinga MM, Rothman RL. Addressing the diabetes pandemic: a comprehensive approach. *Indian J Med Res* 2006;124(5):481-484.
- [2] Wild S, Roglic G, Green A, et al. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004;27(5):1047-1053.
- [3] Bhat G, Baba CS, Pandey A, et al. Insulin resistance and metabolic syndrome in non-obese Indian patients with non-alcoholic fatty liver disease. *Tropical Gastroenterology* 2013;34(1):18-24.
- [4] Hedley AA, Ogden CL, Johnson CL, et al. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999-2002. *JAMA* 2004;291(23):2847-2850.
- [5] Bellentani S, Saccoccio G, Masutti F, et al. Prevalence of and risk factors for hepatic steatosis in Northern Italy. *Ann Intern Med* 2000;132(2):112-117.
- [6] Moscatiello S, Manini R, Marchesini G. Diabetes and liver disease: an ominous association. *Nutr Metab Cardiovasc Dis*. 2007;17(1):63-70.
- [7] Adams LA, Sanderson S, Lindor KD, et al. The histological course of nonalcoholic fatty liver disease: a longitudinal study of 103 patients with sequential liver biopsies. *J Hepatol* 2005;42(1):132-138.
- [8] Fassio E, Alvarez E, Dominguez N, et al. Natural history of nonalcoholic steatohepatitis: a longitudinal study of repeat liver biopsies. *Hepatology* 2004;40(4):820-826.
- [9] Petersen KF, Dufour S, Feng J, et al. Increased prevalence of insulin resistance and nonalcoholic fatty liver disease in Asian-Indian men. *Proc Natl Acad Sci USA* 2006;103(48):18273-18277.
- [10] Marchesini G, Brizi M, Bianchi G, et al. Nonalcoholic fatty liver disease: a feature of the metabolic syndrome. *Diabetes* 2001;50(8):1844-1850.