



## A Comparative Study of Prevalence of Impaired Glucose Tolerance Test in Non Alcoholic Fatty Liver Disease Patients and Normal Controls

### KEYWORDS

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### INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD), which develops in the absence of alcohol abuse, has been recognized as a major health burden. The clinical implications of NAFLD are derived mostly from its common occurrence in the general population and its potential to progress to cirrhosis and liver failure. Estimates suggest that about 20% to 30% of adults in developed countries have excess fat accumulation in the liver, 50% among people with diabetes, and about 80% in the obese and morbidly obese. The high prevalence of NAFLD in Western countries is probably due to the contemporary epidemics of obesity and associated metabolic complications. Obesity, type 2 diabetes, and hyperlipidemia are recognized as risk factors for NAFLD. Insulin resistance is frequently detected in patients with NAFLD, as it is in those without obesity and diabetes. An increasing number of patients have been described with normal body mass index (BMI), although these individuals may have central adiposity and occult insulin resistance.<sup>6</sup> Moreover, epidemiological studies<sup>7</sup> indicate that this unique group of normal weight patients is characterized by an unhealthy dietary composition.

### AIM OF STUDY

To compare the prevalence of impaired glucose tolerance test in non alcoholic fatty liver

disease patients and normal controls.

### OBJECTIVES OF STUDY

- To find out the prevalence of impaired oral glucose intolerance test in non alcoholic fatty liver disease.
- The prevalence of prediabetes (IFG, IGT) in patients with NAFLD verses matched controls without fatty liver disease are studied.
- To compare the insulin resistance in non alcoholic fatty liver disease subjects and controls.

### PATIENTS AND METHODS

#### SOURCE OF COLLECTION OF DATA

The study shall be RETROSEPECTIVE OBSERVATIONAL STUDY, The cases for the study were selected retrospectively who were diagnosed as fatty liver by ultrasound imaging who attended the Department of General medicine and Department of Gastroenterology, Gandhi Hospital, and sex matched controls were selected randomly following which the data will be enumerated who fulfills the inclusion criteria. This study was conducted between March 2014- March 2015.

#### SAMPLE SIZE

A total of 100 patients of which 50 were diagnosed to have NAFLD on USG abdomen and remaining 50 were

age and sex matched controls were enrolled in this study

### INCLUSION CRITERIA

Age of between 20 and 50 years were taken into the study age and sex matched controls were included in the study.

Fatty liver confirmed by ultrasound imaging for cases and normal ultrasound in cases of controls

### EXCLUSION CRITERIA

People with significant alcohol consumption (more than 20gms/day)

Presence of Hepatitis B or C virus infection

Chronic liver diseases like

1. Auto immune hepatitis
2. Wilsons disease
3. Haemochromatosis

Patients on medications producing steatosis with in past 6 months

Patients on parenteral nutrition .

### RESULTS

- Out of 50 subjects,38(76%) are male patients and 12 (24%) are females, age and sex matched controls were taken, of which Sex ratio 3.16: 1
- Age range is 20-50 (mean 34.98+7.11), most patients are of 3<sup>rd</sup> and 4<sup>th</sup> decade.
- Normal BMI found in 8 patients (16%), Overweight was found in 11 patients (22%), Obese BMI was found in 31 patients (62%) in cases,with a mean BMI 26.52 ± 3.62, and that of controls is 22.74 ± 1.10 that is of statistically significant(p-value 0.000)
- Majority (38%)are having higher levels of Fasting blood glucose (>100) with a mean of 101.14 ± 17.79, compare to controls (8%),with mean of 88. 58 ± 9.05 that is proved to be statistically significant(chi square 12.70,df=1,p=0.001).
- Majority (36%)are having higher levels of Post lunch blood sugars at the end of one and half hour (>160) with a mean fasting glucose levels of 158.98 ± 31.45, compare to controls (8%),with mean of 88.137.94 ± 15.38 that is proved to be statistically significant(p=0.000).
- Majority Of the cases having higher levels of triglycerides 175.02 ± 30.76 and that of controls is of 162.12 ± 35.85 which was of not statistically significant (p-value 0.301).
- HDL levels in both cases and controls are significantly above the desired level i.e., mean of 42.50 ± 9.63 and in controls is 42.44 ± 7.33.which has a significant (p-value 0.000).
- Mean T.cholesterol (mg/dl) 175.66+22.55 is seen in cases and that of controls is 170.16 ± 34.19, which

was of statistically significant (p-value is 0.003)

- Mean LDL (mg/dl)  $98.22 \pm 23.68$  in cases and that of controls is  $85.88 \pm 16.15$ , which was of not statistically significant (p-value 0.892)
- Mean of TC/HDL in cases is  $4.40 \pm 1.32$  and that of controls is  $4.11 \pm 1.00$ , which was of statistically significant (p-value is 0.004)
- Mean Total serum bilirubin in cases is of  $0.94 \pm 0.03$  and that of controls is  $0.76 \pm 0.15$ , that is proved to be statistically significant (p=0.003).
- Elevated SGOT is seen in 19 cases (38%) in majority with a mean value of  $36.70 \pm 10.16$  and that of controls is  $42.48 \pm 12.51$  which is not statistically significant.
- Elevated SGPT is seen in 38 cases (76%) in majority with a mean value of  $47.68 \pm 12.41$  and that of controls is  $61.28 \pm 15.23$  which is of not statistically significant.
- Majority (36%) of cases are having impaired glucose tolerance test in at the end of second (>140) with a mean glucose levels  $144.12 \pm 20.25$ , compare to controls (8%), with mean of  $113.36 \pm 14.37$  that is proved to be statistically significant (chi square- 11.422, df-1 p-0.000).
- Majority (42%) of cases are having HOMA-IR values of more than 2 with a mean value of  $2.14 \pm 1.07$ , compare to controls (23%), with mean of  $0.99 \pm 0.44$  that is proved to be statistically significant (chi square- 20.384, df-1 p-0.000).

## DISCUSSION

There is compelling evidence that abnormal glucose tolerance, and NAFLD originate from shared pathophysiological mechanisms. In fact, a continuous increase of hepatic fat accumulation has been reported in parallel with the deterioration of glucose tolerance from NGT to isolated IFG, isolated IGT, and combined IFG/IGT. In addition, it has been suggested by a number of studies that future type 2 diabetes may be predicted from the presence of NAFLD, or on the basis of liver biomarkers and hepatic pro-inflammatory and anti-inflammatory molecule levels. Because of the increasing prevalence of T2DM in the INDIA and its close relation with NAFLD, we felt compelled to examine the prevalence of pre-diabetes in this population. This was also important because fatty liver may carry serious metabolic and liver related complications (i.e., cirrhosis, hepatocellular carcinoma). In the current cross-sectional study, we observe that individuals with NGT, whose 2 h post load plasma glucose is  $\geq 140$  mg/dL, have an increased risk to have NAFLD assessed by ultrasonography as compared with NGT individuals with 2 h post load plasma  $< 140$  mg/dL. The pathophysiological mechanisms underlying the associations between NAFLD and 2nd hour post load hyperglycemia are unsettled. A greater degree of IR in NGT 1 h-high individuals as compared with NGT 2h-low participants is one of the possible explanations for the development of NAFLD. Higher BMI is also a known risk factor for IFG, IGTT. In our study higher BMI independently predicted the risk for the presence of hyperglycemia among patients with non-alcoholic fatty liver disease<sup>73</sup>. More than half of our study population had a BMI below the threshold of 30 kg/m<sup>2</sup> though. Therefore, our findings should not be interpreted as if only obese patients with non-alcoholic fatty liver disease have IGTT. Serum levels of HDL-C were also lower in the subgroup of patients with IGTT in the non-alcoholic fatty liver disease patients evaluated in our study. Low HDL-C is a characteristic finding in diabetic dyslipidemia and is also associated with prediabetes, insulin resistance,

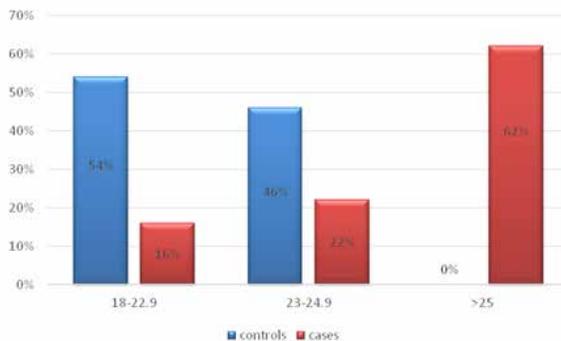
metabolic syndrome, and non-alcoholic fatty liver disease. The elevated levels of serum triglycerides, another feature of diabetic dyslipidemia, seem to differ between the non-alcoholic fatty liver disease patients who had IGTT compared with controls, in our study. Also, comparison of the two groups on the basis of the ratio triglycerides/HDL-C, a parameter that has been associated with insulin resistance and atherogenicity, showed only a marginal difference. Screening for hyperglycemia could be considered in patients with non-alcoholic fatty liver disease given the strong association of this disorder with IGT, including diabetes mellitus. There are known risk factors for type 2 diabetes to guide the selection of patients to screen. Age above 35 years and the association of a BMI above 25 kg/m<sup>2</sup> with HDL-C below 35mg/dL are among the indicators for screening for type 2 diabetes proposed by the American Diabetes Association. In our study, Age, BMI, and HDL were independent indicators for the presence of impaired glucose regulation in patients with non-alcoholic fatty liver disease who had no known derangement in glucose metabolism. In our study Fasting blood glucose levels were elevated in (38%) of cases and (8%) of controls in, Impaired Glucose Tolerance test is seen in (36%) of cases and (4%) of controls. We also found that NAFLD was strongly associated with metabolic syndrome even after adjusting for age, gender and waist circumference. Indeed, some authors suggest that NAFLD should be included as a feature of the metabolic syndrome. The mechanism of "liver-related" insulin resistance may be via fatty acid-induced hepatocyte inflammation with the subsequent release of systemic pro-inflammatory cytokines including TNF  $\alpha$  and IL-6. A recent clinic based study has showed that Asian Indian subjects with NAFLD had lower BMI, lower prevalence of diabetes and metabolic syndrome compared to that reported in the west. Indeed, it has been shown that programs aimed at modifying lifestyle and pharmacological interventions are extremely effective in preventing or delaying type 2 diabetes onset in participants at high risk for the disease. It is notable that these treatments are also capable of reducing fat liver content and improving biomarkers of NAFLD. The observation that NGT 2 hour-high individuals are at increased risk for type 2 diabetes and NAFLD suggests that the value of a 2 hour OGTT glucose  $\geq 140$ mg/dl may be suitable for identifying a subset of NGT individuals potentially harboring an increased risk of developing type 2 diabetes in whom it would be helpful to perform liver ultrasonography, not routinely carried out, because they could be targeted by these effective prevention programs.

## SUMMARY

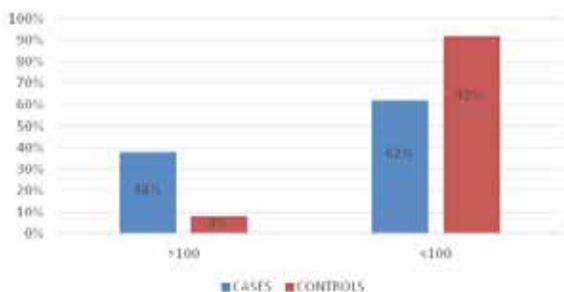
In conclusion, the current study brings to our attention that abnormal glucose metabolism is much more common than previously appreciated in patients with NAFLD. These patients are insulin resistant in all target tissues, with adipose tissue IR playing a major role in the severity of NAFLD. The clinical implication is that some patients with NAFLD may benefit from early screening for Pre diabetes to prevent the long-term complications of hyperglycemia and the progression to steatohepatitis (NASH) and cirrhosis. Our study has important implications. Since about a third of the general population has NAFLD, this would translate to nearly 200–300 million people in India with NAFLD even using conservative estimates, given India's population of 1.1 billion people even assuming lower prevalence of NAFLD in rural India. In our study of patients with non-alcoholic fatty liver disease, older age, higher BMI, and lower serum levels of HDL-C independently predicted the presence of hyperglycemia (defined

as IFG, IGT,) that was primarily identified through an oral glucose tolerance test. Conclusively, we suggest that oral glucose tolerance testing should be considered for patients with non-alcoholic fatty liver disease with one or more of the above-mentioned predictor factors for hyperglycemia to readily diagnose and manage disorders of glucose metabolism. Thus NAFLD/NASH could cause significant morbidity and its early detection, as well as steps to prevent the condition through lifestyle modification, is urgently needed.

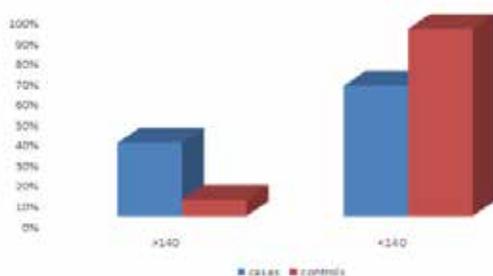
**B M I IN CASES AND CONTROLS**



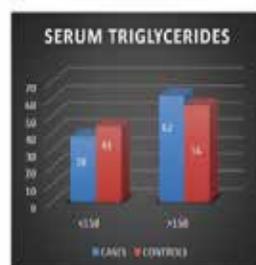
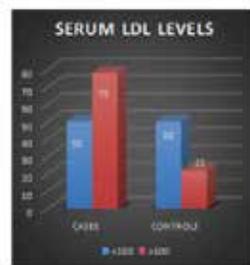
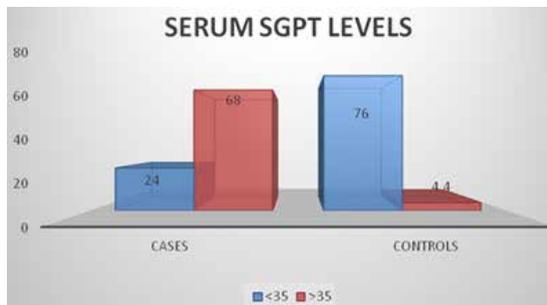
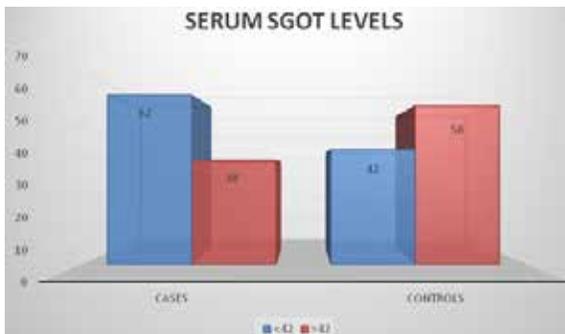
**FASTING BLOOD GLUCOSE LEVELS**



**OGTT LEVEL AT THE END OF 2ND HOUR**



**SERUM SGOT LEVELS**



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