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ASSESSMENT OF INSULIN RESISTANCE IN NONALCOHOLIC FATTY LIVER DISEASE IN NON-DIABETIC PATIENTS

Medicine

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) refers to a spectrum of liver damage ranging from simple steatosis to nonalcoholic steatohepatitis (NASH). The ectopic accumulation of fat in the liver has been strongly associated with insulin resistance. **Aim of the study:** To explore the proportion of insulin resistance in non-diabetic NAFLD patients compared to normal healthy populations using HOMA-IR model. **Materials and Methods:** This was a hospital based case control study carried out on 100 patients diagnosed with NAFLD by ultrasound. Fasting Insulin estimation was done by Insulin IRMA (IMMUNORADIOMETRIC ASSAY) Kit. **Results:** Patients with NAFLD had a higher prevalence (33%) of metabolic syndrome than the controls (15%) with an Odds Ratio of 2.791. Insulin resistance in non-diabetic NAFLD patients was higher (36%) than the control populations (11%) (p value was <0.001). **Conclusion:** This study has shown that insulin resistance has a positive association with NAFLD.

KEYWORDS

NAFLD, Insulin Resistance, Metabolic syndrome

INTRODUCTION:

Non-alcoholic fatty liver disease (NAFLD) refers to the presence of hepatic steatosis, demonstrated by histology or imaging, in the absence of significant alcohol consumption and the other known secondary causes.[1] The identification of NAFLD risk factors such as increased BMI, insulin resistance, type 2 diabetes, metabolic syndrome, hypertension, dyslipidemia, and cardiovascular disease improves confidence in the diagnosis of NAFLD. Ultrasound of abdomen is a good first-line diagnostic test. Liver biopsy is considered the gold standard in the diagnosis of NAFLD.[2] Transient elastography (FibroScan) is a relatively new technology for assessing liver tissue elasticity and is thought to be a good predictor of higher degrees of fibrosis.[3]

Insulin is a peptide hormone that has anabolic effects on a variety of cell types, most notably liver cells, muscle cells, and adipocytes. It stimulates lipogenesis and lipid storage, glycogen and protein synthesis, and inhibits lipolysis, glycogenolysis, and protein breakdown. As a result, resistance to the hormone causes hyperglycemia and hyperlipidemia. Insulin resistance is commonly defined as a reduction in insulin-mediated glucose delivery to insulin-sensitive tissues and an increase in hepatic glucose production. Peripheral insulin resistance is defined as a reduced ability to use glucose in target tissues, primarily skeletal muscle.[4]

Insulin resistance is pivotal in the progression of NAFLD. Hepatic macrophages are the major immune cells that secrete inflammatory mediators, such as tumor necrosis factor alpha and interleukin-1 beta, leading to systemic insulin resistance and NASH. The ectopic accumulation of fat in the liver has been strongly associated with insulin resistance, an almost universal finding in NAFLD.[5,6]

The metabolic syndrome, the insulin resistance syndrome, and syndrome X are terms used to describe a constellation of metabolic derangements that includes insulin resistance, hypertension, dyslipidemia, central or visceral obesity, type 2 DM and accelerated cardiovascular disease.

The gold standard for investigating and quantifying insulin resistance is the "hyperinsulinemic euglycemic clamp". Homeostatic Model for Assessment of Insulin Resistance (HOMA-IR), which employs fasting insulin and glucose levels to calculate insulin resistance, is an alternative to clamping studies.[7]

This study was carried out with the aim to explore the proportion of insulin resistance in non-diabetic NAFLD patients compared to normal healthy populations using HOMA-IR model.

MATERIALS AND METHODS

Aim And Objective:

To study the insulin resistance in non-diabetic NAFLD patients and to compare the proportion of insulin resistance in non-diabetic NAFLD patients with healthy controls using HOMA IR model.

Study Design:

Hospital based Case Control Study carried out for one year (from 1st July, 2020 to 30th June, 2021) at department of Medicine, Assam Medical College & Hospital, Dibrugarh with a sample size of 100.

Study Population:

All patients more than 12 years of age diagnosed by abdominal Ultrasonography as NAFLD attending OPD or admitted in Department of Medicine, Assam Medical College and Hospital, Dibrugarh were included in the study. Informed written consent was taken from the participants before enrolment into the study.

Diabetic and pre-diabetic patients; patients consuming >21 standard drinks per week [(or) >30 g/day)] in males and >14 standard drinks per week [(or) >20 g/day)] in females over a periods of 2 years as required by international associations for diagnosis of NAFLD[1,8]; positive HBsAg or anti HCV antibody or HIV status, and known cirrhotics were excluded.

Data Collection:

A detailed clinical history, thorough physical examination, and biochemical parameters were obtained. Body Mass Index (BMI), waist circumference, and hip circumference were measured.

Ultrasound whole abdomen was done to detect steatosis in liver. Liver function tests, fasting blood sugar, post prandial blood sugar, glycosylated haemoglobin, and fasting lipid profile were done in **all patients. Fasting Insulin estimation was done by** Insulin IRMA (IMMUNORADIOMETRIC ASSAY) Kit.

Statistical Analysis:

The statistical analysis of data was performed using the computer program, Statistical Package for Social Sciences and Microsoft Excel

2010. Results on continuous measurements are presented as mean ± standard deviation and compared using student t test. Discrete data are expressed as number (%) and are analysed using Chi square test and Fischer's exact test. For all analyses, the statistical significance was fixed at 5% (p value <0.05).

Results:

In both the NAFLD and control population, age and gender were matched. The most common age group of our study population was 31-40 years (32%). The mean age was 40.96 ± 10.87 years in NAFLD patients and 40.65 ± 10.97 years in controls. The maximum age was 67 and the minimum was 17 years. In both the case and control populations, 58 were male (58%) and 42 were female (42%). The male: female ratio was 1.38: 1. Patients with NAFLD had significantly higher mean body weight (61.66±6.82 vs. 59.17±5.65, p=0.005), BMI (25.00±2.39 vs.23.89±2.28, p=0.001), waist circumference (90.05±4.76 vs. 85.33±5.16, p<0.001), hip circumference (98.35±3.55 vs. 95.11±4.19, p<0.001) and Waist Hip ratio (0.92±0.04 vs. 0.89±0.05, p =0.001) than control. Patients with NAFLD had significantly higher mean serum Total Cholesterol, Triglyceride, LDL cholesterol than the control group, p value being <0.001, <0.001, and 0.002 respectively. Serum HDL cholesterol was lower in NAFLD patients than controls, p value 0.001. The mean AST and ALT were significantly higher in the NAFLD group (41.43±14.32 vs. 27.72±5.40 U/L and 58.43±27.08 vs. 31.63±4.87 U/L) than the control group, p value being <0.001 and <0.001 respectively.

The mean systolic blood pressure in NAFLD group was 129.34±12.62 mm Hg and in the control group it was 124.48±10.70 mm Hg. The mean diastolic blood pressure in NAFLD group was 79.54±7.13mm Hg and in the control group it was 76.28 ±6.32 mm Hg. The differences between the two in the NAFLD and control groups were statistically significant (p=0.001). The mean fasting blood glucose of NAFLD patients was 82.76 ±7.12 mg/dl and controls was 81.90 ± 6.70 mg/dl (p value 0.38). The mean fasting insulin level in NAFLD patients was 10.68 ± 3.87 and controls was 8.75 ± 2.68 (p=<0.001). The mean HOMA-IR value in NAFLD patients was 2.18± 0.77 and controls was 1.77±0.55 (p<0.001).

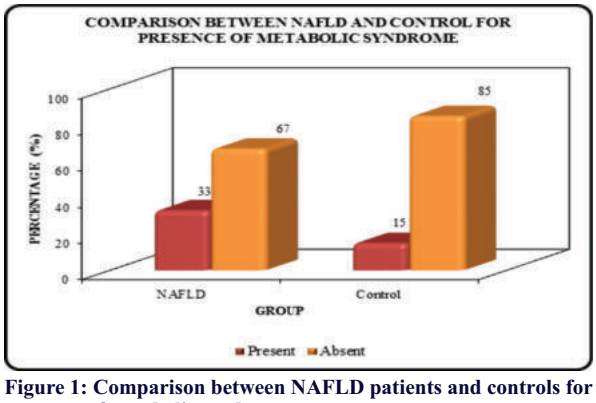

Figure 1: Comparison between NAFLD patients and controls for presence of metabolic syndrome.

Patients with NAFLD had a higher prevalence (33%) of metabolic syndrome than the controls (15%) with an Odds Ratio of 2.791 at 95% Confidence Interval (p value = 0.0035).

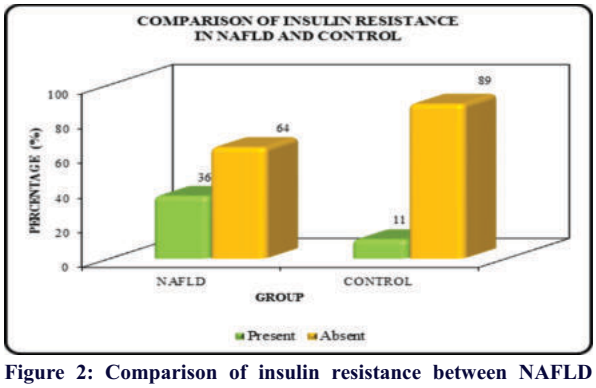

Figure 2: Comparison of insulin resistance between NAFLD patients and controls.

Insulin resistance in non-diabetic NAFLD patients was higher (36%) than the control populations (11%) (p value was <0.001).

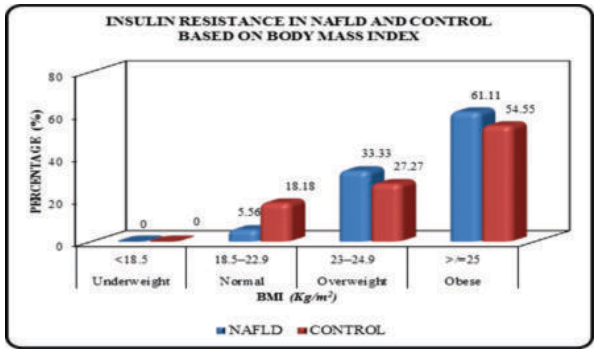

Figure 3: Comparison of insulin resistance between NAFLD patients and controls based on body mass index.

In NAFLD patients with insulin resistance, 61.11% were obese, 33.33% were overweight, and 5.56% had normal BMI. In control group with insulin resistance, 54.55% were obese, 27.27% were overweight and 18.18% had normal BMI.

DISCUSSION:

The most common age group of our study population was 31-40 years (32%). The mean age was 40.96 ± 10.87 years in NAFLD patients and 40.65 ±10.97 years in controls. In both the case and control populations, 58% were male and 42% were female. The mean waist circumference, waist hip ratio, and mean BMI were significantly higher in the NAFLD patients than the controls which is in concordance with the study by Lankarani K.B. *et al* (2013)[9]. In the present study we found that the patients with NAFLD had significantly higher mean serum Total Cholesterol, Triglyceride, LDL cholesterol than the controls, and lower mean serum HDL cholesterol in NAFLD patients than controls which is in concordance with a study by Minrui Li *et al* (2015)[11]. The mean AST and ALT were significantly higher in the NAFLD group than the control group which is in agreement with the study by V. Mohan *et al* (2008)[12]. The mean systolic and diastolic blood pressures in NAFLD group were significantly higher than the control group. The mean fasting insulin level was significantly higher in NAFLD patients than controls (10.68± 3.87 µU/mL vs. 8.75 ± 2.68 µU/mL, p<0.001) and the mean HOMA-IR value was higher in NAFLD patients than controls (2.18± 0.77 vs. 1.77 ± 0.55, p<0.001) which is in agreement with the study by Minrui Li *et al* (2015)[11]. Patients with NAFLD had a higher prevalence of metabolic syndrome (Odd Ratio= 2.791, p=0.0035) than the controls which is in agreement with the study by Lankarani K. B. *et al* (2013)[9]. Insulin resistance in non-diabetic NAFLD patients was higher (36%) than controls (11%) which is in agreement with a study by Golam Azam *et al* (2016)[8]. Most of the patients in both the NAFLD and control groups with insulin resistance had BMI more than 25. This is in concordance with a study by Singh S. P *et al* (2014)[13] which found that 74.86% of NAFLD patients were obese.

CONCLUSION:

In our study we found that insulin resistance was significantly higher in non-diabetic patients with NAFLD than controls. Despite being conducted in a single center with a relatively small sample size, findings of this clinical investigation can provide significant context for conducting larger-scale, and intervention-based trials of NAFLD.

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