Original Article

Association between Insulin Resistance and Nonalcoholic Fatty Liver Disease

***Joha F[1], Nargis S[2], Roy HL[3], Rahman MB[4]**

Abstract :

Background: *Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide.The growing body of evidence has demonstrated that insulin resistance is an independent risk factor for nonalcoholic fatty liver disease. Limited evidence is available regarding the association between insulin resistance and NAFLD.* ***Aims and Objectives:*** *The aim of this study was to investigate the association of insulinresistance with non-alcoholic fatty liver disease.* ***Materials and Methods:*** *A cross-sectional observational study carried out in the Department of Biochemistry, Sylhet MAG Osmani Medical College, Sylhet in collaboration with the Department of Hepatology, Sylhet MAG Osmani Medical College, Hospital during the period between July 2017 and June 2018. Fifty cases of NAFLD and 50 age and sex matched healthy subjects were selected. Fasting blood glucose & fasting insulin level of the participants was measured.* ***Results:*** *The mean serum insulin level (µIU/ml) was 9.36 (inter quartile range, 5.94-14.05) in non-alcoholic fatty liver disease and was 4.69(inter quartile range, 3.44-6.72) in control subjects. The serum insulin level of the non-alcoholic fatty liver disease was significantly higher compared to control subjects (p<0.001).* ***Conclusion:*** *It may be concluded that insulin resistance is strongly associated with non-alcoholic fatty liver disease*

Keywords: Insulin resistance, Nonalcoholic fatty liver disease, Steatohepatitis

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Introduction

Nonalcoholic fatty liver disease (NAFLD), characterized by increased fat accumulation in the hepatocytes of the liver parenchyma, is today one of the most common causes of chronic liver disease worldwide[1]. Nonalcoholic fatty liver disease (NAFLD), develops in the absence of alcohol abuse. When nonalcoholic fatty liver disease is accompanied with liver cell injury and inflammation it is called nonalcoholic steatohepatitis. About 30% nonalcoholic fatty liver disease progress to nonalcoholic steatohepatitis, if untreated it can be lead to fibrosis, cirrhosis or even hepatocellular carcinoma (HCC)[2].The prevalence of NASH may be underestimated, as the diagnosis requires histological confirmation. It is considered that at least 5% of the population may have NASH[3].

Several studies showed that nonalcoholic fatty liver disease is almost associated with obesity, hypertension, dyslipidemia, and glucose intolerance, a cluster of disorders now recognized as metabolic syndrome[4,5]. The proportion nonalcoholic fatty liver disease is higher in people with type 2 diabetes (60%-70%), and in those who are obese or morbidly obese (75%-92%) compared to the general population[6,7,8]. It seems that insulin resistance (IR) related to obesity is central to the pathogenesis of NAFLD. In addition, oxidative stress and cytokines are important contributing factors, together resulting in steatosis and progressive liver damage in genetically susceptible individuals. Key histological components of NASH are steatosis, hepatocellular ballooning, and lobular inflammation[9].

Therefore metabolic derangement based on insulin resistance is the most acknowledged cause of fat accumulation9 and metabolic syndrome is

1. FarhanJoha, Assistant Professor, Department of Biochemistry, Monno Medical college, Manikganj.
2. SusmitaNargis, Associate Professor, Department of Biochemistry, Ad-din Sakina Womens' Medical College, Jashore.
3. HeeraLal Roy, Associate Professor, Department of Biochemistry, Khulna City Medical College, Khulna.
4. Md. Bazlur Rahman, Lecturer, Department of Biochemistry, Jalalabad RagibRabeya Medical College, Sylhet.

***Correspondence:** taslima.anne92@gmail.com

considered to be a crucial mediator from simple over-nutrition to severe body lesion by promoting inflammation10 and are hypothesized to explain the complex pathogenesis and progression of nonalcoholic fatty liver disease[11]. Nonalcoholic fatty liver disease is potential to progress to severe liver disease and association with serious cardio-metabolic abnormalities including type-2 diabetes mellitus, metabolic syndrome and coronary heart disease1. For this reason, nonalcoholic fatty liver disease has been considered as the hepatic manifestation of metabolic syndrome[12]

Materials and Methods

This cross-sectional observational study was carried out in the Department of Biochemistry, Sylhet MAG Osmani Medical College, Sylhet in collaboration with the Department of Hepatology, Sylhet MAG Osmani Medical College & Hospital during the period from July 2017 to June 2018 with a view to compare serum uric acid level between non-alcoholic fatty liver disease and healthy subjects. In this study 50 cases of NAFLD and another 50 age and sex matched healthy subjects were selected and grouped as group-A and group-B respectively.Informed written consent was taken before taking any interview. Anthropometric measurements including height, weight, waist circumference, and blood pressure were recorded. BMI was calculated as weight in kg divided by the height in meter square. Fatty liver was diagnosed based on the findings of abdominal ultrasonography without alcohol consumption, viral, or autoimmune liver disease. Fasting plasma glucose (FPG) and fasting insulin was collect for biochemical analysis. Relevant information was recorded in a pre-formed data collection sheet designed for the study.

Result

The mean age of the participants of non-alcoholic fatty liver disease (Group-A) was40.04 ± 9.37 years and control subjects (Group-B) was40.90 ± 12.37 years. The mean age of the participants did not differ significantly between two groups (t=0.519; p=0.605) (Table-I).

The mean BMI of the non-alcoholic fatty liver disease was 26.08 ± 1.41 (range 23.44-30.10) Kg/M2; whereas the mean BMI of the control subjects was 23.89 ± 2.31 (range 17.82-30.10) Kg/M2. The mean BMI of non-alcoholic fatty liver disease was significantly higher than that of control subjects (t=5.718; p<0.001) (Table-I).

Table-I: Distribution of the participants according to baseline characteristics

Parameters	Case (n=50)	Control (n=50)	Test value	p-value
Age in years Mean ± SD	40.04 ± 9.37	40.90 ± 12.37	t=0.519	*p=0.605
Sex				
Male	28 (56.0%)	32 (64.0%)	p=0.667	p=0.414
Female	22 (44.0%)	18 (36.0%)		
BMI in Kg/M2 Mean ± SD	26.08 ± 1.41	23.89 ± 2.31	t=5.718	*p<0.001

*unpaired't' test and †Chi-Square (χ2) testwere employed to analyze the data. P<0.05 was the level of significance.

Distribution of patients by serum insulin level:

The meanserum insulin level (µIU/ml) was 9.36 (inter quartile range, 5.94-14.05) in non-alcoholic fatty liver disease and was 4.69(inter quartile

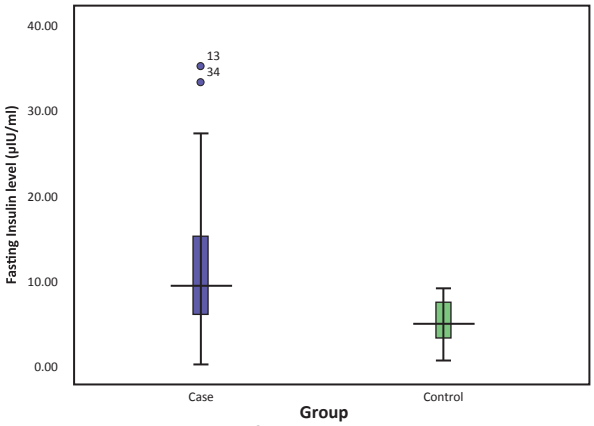

Figure 1. Distribution of patients by serum insulin level

range, 3.44-6.72) in control subjects. The serum insulin level of the non-alcoholic fatty liver disease was significantly higher compared to control subjects (p<0.001) (Figure-1).

* Mann-Whitney U test was employed to analyse the data.

Distribution of patients by fasting plasma glucose level :

The mean fasting plasma glucose level (mg/dl) was 130.54 ± 41.06 (range, 75.0-195.0) in non-alcoholic fatty liver disease and was 87.94 ± 17.38(range, 66.0-161.0) in control subjects. The mean serum insulin level of the non-alcoholic fatty liver disease was significantly higher compared to control subjects (t=6.810; p<0.001) (Figure-2)

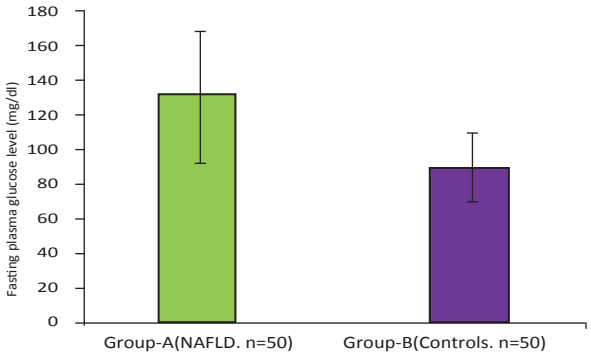

Figure 2. Distribution of patients by fasting plasma glucose level

*unpaired t test was employed to analyse the data.

Comparison of HOMA and insulin resistance between NAFLD and control subjects:

The mean HOMA level (mg/dl) was 3.29 ± 1.97 (range, 0.45-7.65) in non-alcoholic fatty liver disease and was 1.07 ± 0.40 (range, 0.38-1.95) in control subjects. The mean HOMA level of the non-alcoholic fatty liver disease was significantly higher compared to control subjects (t=7.803; p<0.001) (Figure-8).

The frequency of insulin resistance and sensitive subjects were 56.0% and 44.0% in the group of NAFLD whereas none was insulin resistance and all were insulin sensitive in the without NAFLD group. Insulin resistance was significantly more in non-alcoholic fatty liver disease compared to control subjects (χ2=38.889; p<0.001).

Table II. Comparison of HOMA and insulin resistance between NAFLD and control subjects

Parameters	Case (n=50)	Control (n=50)	Test value	p-value
HOMA	3.29 ± 1.97	1.07 ± 0.40	t=7.803	*p<0.001
Insulin				
Resistance	28 (56.0%)	0 (0.0%)	p=38.889	p<0.001
Sensitive	22 (44.0%)	50 (100.0%)		

*unpaired t test and Chi-square (χ2) Test were employed to analyse the data.

Discussion:

NAFLD has been recognized as a major health burden and the prevalence is increasing year by year. In western countries, NAFLD has also become one of the most liver diseases, affecting 20% to 40% of the general population. NAFLD is considered as a multifactorial chronic disease that is associated with genetic, environmental, and metabolic factors[13].

This study showed that the mean serum insulin level was 9.89 ± 4.71 µIU/ml in non-alcoholic fatty liver disease and was 5.00 ± 1.87µIU/ml in control subjects. The mean serum insulin level of the non-alcoholic fatty liver disease was significantly higher compared to control subjects (p<0.001). This result was supported by Gad, 2018) that patients with NAFLD (11.21 ± 6.81 microunit/ml) had significantly increased values of fasting serum insulin compared to the control group (7.79 ± 3.21 microunit/ml). In agreement with this study[14] also demonstrated that fasting serum insulin level was

significantly higher in NAFLD patients than in control subjects. [15] enforced this result as it was found that patients with NAFLD had higher serum insulin levels than the control group. Several other studies also supported these findings[16-19].

In the present study the mean fasting plasma glucose level (mg/dl) was 130.54 ± 41.06 in non-alcoholic fatty liver disease and was 87.94 ± 17.38 in control subjects. The mean serum fasting plasma glucose level of the non-alcoholic fatty liver disease was significantly higher compared to control subjects ($p<0.001$). These findings were supported by several other studies that mean fasting plasma glucose level of the non-alcoholic fatty liver disease was significantly higher compared to control subjects[20,16,18].

NAFLD subjects in the Bangladeshi population have previously been shown to have insulin resistance; however, the underlying mechanism(s) of this defect is still unclear. In this settings, we found significantly higher ($p<0.001$) levels of HOMA in NAFLD subjects (3.29 ± 1.97)compared to the controls (1.07 ± 0.40). This result was consistent with the study of Hossain et al., (2018)[19] where they found that HOMA level was significantly higher ($p=0.001$) in NAFLD subjects (2.21 ± 1.01)compared to the controls (1.79 ± 0.51). This observation was also in agreement with a number of studies[21,18].

In this study 56.0% patients were insulin resistance in non-alcoholic fatty liver disease group and none in control subjects; insulin resistance was significantly more in non-alcoholic fatty liver disease compared to control subjects ($p<0.001$)[17]. Found that the frequency of insulin resistance subjects were 42.9% in the group of NAFLD whereas 28.2% in the group of without NAFLD.

Conclusion :

This study revealed that the mean serum insulin level, HOMA and insulin resistance were significantly higher non-alcoholic fatty liver disease compared to control subjects. From the findings of this study, it may be concluded that insulin resistance has strong association in non-alcoholic fatty liver disease.

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