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Original Research Article

Assessment of Insulin Resistance and Lipid Profile in Alcoholic and Non-Alcoholic Chronic Liver Disease

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Conflict of interest: Nil

Abstract

Introduction: Chronic liver disease (CLD) is commonly associated with insulin resistance and dyslipidemia, especially in non-alcoholic CLD due to its association with obesity and metabolic syndrome. Early identification of these abnormalities is important to reduce disease progression and cardiovascular risk.

Materials and Method: This comparative cross-sectional study included 80 CLD patients divided into alcoholic CLD (n=40) and non-alcoholic CLD (n=40) groups. Fasting blood sugar, fasting serum insulin, HOMA-IR, total cholesterol, triglycerides, HDL-C, LDL-C, and VLDL-C were assessed and compared between the groups.

Result: Non-alcoholic CLD patients had significantly higher fasting blood sugar (118.7 ± 24.9 mg/dL vs 101.6 ± 18.4 mg/dL), fasting insulin (15.1 ± 4.6 µU/mL vs 9.8 ± 3.2 µU/mL), and HOMA-IR (4.39 ± 1.52 vs 2.46 ± 0.91) than alcoholic CLD patients. Total cholesterol, triglycerides, LDL-C, and VLDL-C were higher, while HDL-C was lower in the non-alcoholic CLD group. HOMA-IR showed positive correlation with lipid abnormalities.

Conclusion: Non-alcoholic CLD patients had greater insulin resistance and dyslipidemia than alcoholic CLD patients, highlighting the need for early metabolic screening and management.

Keywords: Chronic liver disease, Insulin resistance, HOMA-IR, Lipid profile, Alcoholic liver disease, Non-alcoholic liver disease, Dyslipidemia.

Introduction

Chronic liver disease (CLD) is a major global health problem and contributes substantially to morbidity and mortality worldwide [1]. The most common etiologies of CLD include alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD), both of which may progress to fibrosis, cirrhosis, liver failure, and hepatocellular carcinoma. Although alcohol consumption remains a major cause of liver injury, the prevalence of NAFLD has increased rapidly in recent years due to the rising burden of obesity, diabetes mellitus, insulin resistance, and metabolic syndrome [2].

Insulin resistance is considered one of the central mechanisms involved in the development and progression of chronic liver disease, particularly in NAFLD. In patients with insulin resistance, the ability of insulin to suppress hepatic glucose production and regulate lipid metabolism becomes impaired, leading to increased hepatic fat accumulation, enhanced lipolysis, and progression of steatosis [3]. Persistent insulin resistance also contributes to oxidative stress, inflammation, fibrosis, and worsening liver injury [4]Dyslipidemia is another important metabolic abnormality frequently associated with CLD. Patients with liver disease often exhibit altered lipid metabolism characterized by elevated serum triglycerides, increased low-density lipoprotein cholesterol (LDL-C), increased total cholesterol, and reduced high-density lipoprotein cholesterol (HDL-C).

Such abnormalities are more pronounced in NAFLD because hepatic steatosis is closely linked to insulin resistance and disturbed lipid handling by the liver.[5,6]NAFLD is now recognized as the hepatic manifestation of metabolic syndrome and is strongly associated with obesity, type 2 diabetes mellitus, hypertension, insulin resistance, and atherogenic dyslipidemia [7]. Studies have shown that elevated triglycerides, LDL-C, and total cholesterol, along with decreased HDL-C, are significantly associated with the severity of fatty liver disease and worsening insulin resistance. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) is commonly

used as a simple and reliable tool for estimating insulin resistance in such patients [8].

Alcoholic liver disease also has significant effects on glucose and lipid metabolism. Chronic alcohol consumption alters hepatic lipid oxidation and promotes triglyceride accumulation within hepatocytes, resulting in fatty liver and dyslipidemia [9]. Alcohol-related liver injury may further impair insulin signaling pathways and contribute to insulin resistance, although the metabolic profile of ALD differs from that of NAFLD [10].

Assessment of insulin resistance and lipid profile in patients with alcoholic and non-alcoholic CLD is therefore important not only for understanding disease pathogenesis but also for predicting cardiovascular risk and disease progression. Early identification of abnormal lipid parameters and insulin resistance may facilitate timely lifestyle modification, pharmacological intervention, and prevention of long-term complications [11,12].

In view of the above, the present study was conducted to assess insulin resistance and lipid profile among patients with alcoholic and non-alcoholic chronic liver disease and to compare the metabolic alterations between the two groups.

Materials and Methods

Study Design: This hospital-based cross-sectional observational study was conducted in the Department of General Medicine

Study Population: A total of 80 patients diagnosed with chronic liver disease were included in the study.

Grouping of Study Population

The study population was divided into two groups:

- Group A: Alcoholic chronic liver disease (n = 40)
- Group B: Non-alcoholic chronic liver disease (n = 40)

Inclusion Criteria

- Patients aged more than 18 years
- Patients with clinical, biochemical, radiological, or histopathological evidence of chronic liver disease
- Patients with alcoholic chronic liver disease having a significant history of chronic alcohol consumption
- Patients with non-alcoholic chronic liver disease without significant alcohol intake and with evidence of fatty liver disease or other non-alcohol-related liver pathology
- Patients willing to provide informed consent

Exclusion Criteria

- Patients with acute liver failure
- Patients with viral hepatitis
- Patients with hepatocellular carcinoma
- Patients with chronic kidney disease
- Pregnant women
- Patients with known diabetes mellitus on insulin therapy
- Patients with thyroid disorders
- Patients on corticosteroid therapy
- Patients taking lipid-lowering drugs
- Patients with severe systemic illness

Data Collection: Detailed demographic and clinical history was obtained from all patients, including:

- Age
- Sex
- Body mass index
- Duration of illness
- Alcohol intake
- Smoking history
- Comorbidities
- Family history

A detailed general physical examination and systemic examination were performed in all patients.

Laboratory Investigations

The following investigations were carried out in all patients:

- Fasting blood sugar
- Fasting serum insulin
- Liver function tests
- Serum bilirubin
- Serum albumin
- Serum transaminases
- Alkaline phosphatase
- Prothrombin time
- Fasting lipid profile
- Ultrasonography of abdomen

Lipid Profile Parameters

The fasting lipid profile included:

- Total cholesterol
- Triglycerides
- High-density lipoprotein cholesterol (HDL-C)
- Low-density lipoprotein cholesterol (LDL-C)
- Very low-density lipoprotein cholesterol (VLDL-C)

Assessment of Insulin Resistance: Insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR):

$$HOMA\text{-}IR = \frac{\text{Fasting Insulin}\,(\mu U/mL) \times \text{Fasting Glucose}\,(mg/dL)}{405}$$

Higher HOMA-IR values indicated greater insulin resistance.

Statistical Analysis: The collected data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) software version 25.0.

- Continuous variables were expressed as Mean ± SD
- Categorical variables were expressed as frequency and percentage
- Independent t-test was used to compare continuous variables between the two groups
- Chi-square test was used to compare categorical variables
- Pearson's correlation coefficient was used to assess the relationship between insulin resistance and lipid profile parameters
- A p-value of less than 0.05 was considered statistically significant

Results

Demographic Characteristics: A total of 80 patients with chronic liver disease were included in the study, of whom 40 patients had alcoholic chronic liver disease and 40 patients had non-alcoholic chronic liver disease. The demographic characteristics of both groups are shown in Table 1. The mean age of patients in the alcoholic CLD group was 49.8 ± 8.6 years, whereas in the non-alcoholic CLD group it was 47.3 ± 9.2 years. The difference in age between the two groups was not statistically significant ($p = 0.214$), indicating that both groups were comparable with respect to age distribution. Male predominance was observed in both groups, although it was more marked in the alcoholic CLD group. Among alcoholic CLD patients, 34 patients (85.0%) were male and 6 patients (15.0%) were female, whereas in the non-alcoholic CLD group, 24 patients (60.0%) were male and 16 patients (40.0%) were female. This difference in gender distribution was statistically significant ($p = 0.012$). The mean BMI was significantly higher in the non-alcoholic CLD group (28.1 ± 4.2 kg/m^2) compared to the alcoholic CLD group (23.9 ± 3.4 kg/m^2), and this difference was highly significant ($p < 0.001$) (Table 1).

Fasting Blood Sugar, Serum Insulin, and HOMA-IR: The comparison of fasting blood sugar, fasting serum insulin, and HOMA-IR between the two groups is presented in Table 2. The mean fasting blood sugar level in alcoholic CLD patients was 101.6 ± 18.4 mg/dL, while it was significantly higher in non-alcoholic CLD patients at 118.7 ± 24.9 mg/dL ($p = 0.001$). Similarly, the mean fasting serum insulin level was significantly higher in the non-alcoholic CLD group (15.1 ± 4.6 μU/mL) compared to the alcoholic CLD group (9.8 ± 3.2 μU/mL), with a highly significant difference ($p < 0.001$). The mean HOMA-IR value in alcoholic CLD patients was 2.46 ± 0.91, whereas in non-alcoholic CLD patients it was 4.39 ± 1.52. This difference was highly significant ($p < 0.001$), indicating that insulin resistance was substantially greater in patients with non-alcoholic chronic liver disease (Table 2).

Lipid Profile Comparison between Alcoholic and Non-Alcoholic CLD Patients: The lipid profile findings of the two groups are summarized in Table 2. Patients with non-alcoholic CLD had significantly more deranged lipid profiles compared to alcoholic CLD patients. The mean total cholesterol level was 162.5 ± 28.3 mg/dL in the alcoholic CLD group and 198.6 ± 34.1 mg/dL in the non-alcoholic CLD group, with a highly significant difference between the groups ($p < 0.001$). Similarly, mean triglyceride levels were significantly higher in non-alcoholic CLD patients (189.8 ± 46.7 mg/dL) compared to alcoholic CLD patients (141.2 ± 39.6 mg/dL) ($p < 0.001$).

The mean HDL-C level was significantly lower in the non-alcoholic CLD group (36.4 ± 6.8 mg/dL) compared to the alcoholic CLD group (42.8 ± 7.9 mg/dL), with a statistically significant difference ($p < 0.001$). On the other hand, LDL-C levels were significantly higher in non-alcoholic CLD patients (124.2 ± 28.5 mg/dL) compared to alcoholic CLD patients (92.6 ± 21.7 mg/dL) ($p < 0.001$).

Similarly, mean VLDL-C levels were significantly higher in the non-alcoholic CLD group (37.9 ± 9.3 mg/dL) compared to the alcoholic CLD group (28.2 ± 7.9 mg/dL), and the difference was statistically significant ($p < 0.001$) (Table 2).

Correlation of HOMA-IR with Lipid Profile Parameters: The correlation between HOMA-IR and various lipid profile parameters is shown in Table 3. HOMA-IR showed a significant positive correlation with total cholesterol ($r = +0.48$, $p < 0.001$), indicating that higher insulin resistance was associated with higher total cholesterol levels. A similar positive correlation was observed with triglycerides ($r = +0.56$, $p < 0.001$), LDL-C ($r = +0.51$, $p < 0.001$), and VLDL-C ($r = +0.53$, $p < 0.001$). In contrast, HDL-C showed a significant negative correlation with HOMA-IR ($r = -0.42$, $p = 0.001$), suggesting that increasing insulin resistance was associated with lower HDL-C levels (Table 3).Overall, the study demonstrated that patients with non-alcoholic chronic liver disease had significantly greater insulin resistance and more severe dyslipidemia compared to patients with alcoholic chronic liver disease. The significantly higher fasting blood sugar, fasting insulin, HOMA-IR, total cholesterol, triglycerides, LDL-C, and VLDL-C levels, along with lower HDL-C levels, suggest that metabolic abnormalities are more pronounced in non-alcoholic CLD patients. These findings indicate that insulin resistance plays a major role in the

pathogenesis and progression of metabolic disturbances in chronic liver disease.

Table 1: Demographic Characteristics of the Study Population

Parameter	Alcoholic CLD (n=40)	Non-Alcoholic CLD (n=40)	p-value
Age (years)	49.8 ± 8.6	47.3 ± 9.2	0.214
Male	34 (85.0%)	24 (60.0%)	0.012
Female	6 (15.0%)	16 (40.0%)	
BMI (kg/m²)	23.9 ± 3.4	28.1 ± 4.2	<0.001

Table 2: Comparison of Fasting Blood Sugar, Serum Insulin, HOMA-IR, and Lipid Profile Between Alcoholic and Non-Alcoholic CLD Patients

Parameter	Alcoholic CLD (n=40)	Non-Alcoholic CLD (n=40)	p-value
Fasting Blood Sugar (mg/dL)	101.6 ± 18.4	118.7 ± 24.9	0.001
Fasting Serum Insulin (µU/mL)	9.8 ± 3.2	15.1 ± 4.6	<0.001
HOMA-IR	2.46 ± 0.91	4.39 ± 1.52	<0.001
Total Cholesterol (mg/dL)	162.5 ± 28.3	198.6 ± 34.1	<0.001
Triglycerides (mg/dL)	141.2 ± 39.6	189.8 ± 46.7	<0.001
HDL-C (mg/dL)	42.8 ± 7.9	36.4 ± 6.8	<0.001
LDL-C (mg/dL)	92.6 ± 21.7	124.2 ± 28.5	<0.001
VLDL-C (mg/dL)	28.2 ± 7.9	37.9 ± 9.3	<0.001

Table 3: Correlation of HOMA-IR with Lipid Profile Parameters

Lipid Parameter	Correlation Coefficient (r)	p-value
Total Cholesterol	+0.48	<0.001
Triglycerides	+0.56	<0.001
HDL-C	−0.42	0.001
LDL-C	+0.51	<0.001
VLDL-C	+0.53	<0.001

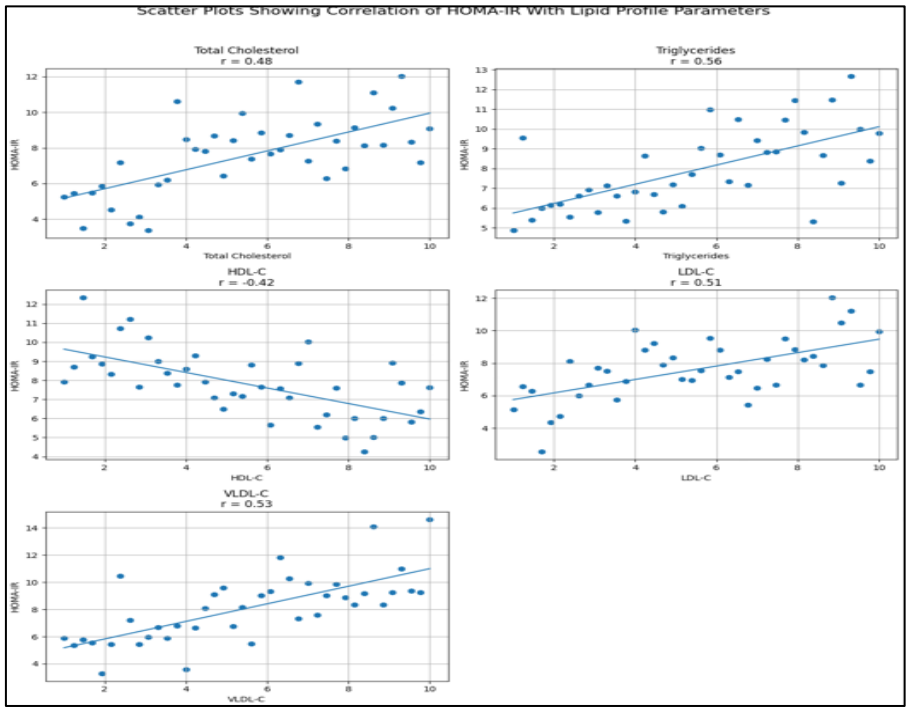

Figure 1:

Discussion

In the present study, fasting blood sugar, fasting serum insulin, and HOMA-IR were significantly higher in the non-alcoholic CLD group than in the alcoholic CLD group. Mean fasting blood sugar was 118.7 ± 24.9 mg/dL in non-alcoholic CLD patients compared to 101.6 ± 18.4 mg/dL in alcoholic CLD patients. Mean fasting insulin was 15.1 ± 4.6 µU/mL versus 9.8 ± 3.2 µU/mL, while mean HOMA-IR was

4.39 ± 1.52 versus 2.46 ± 0.91, indicating greater insulin resistance in non-alcoholic CLD patients.

These findings are supported by Neschen et al. [13], who reported that GPAT1 knockout mice had 59% lower hepatic triglyceride content and 74% lower diacylglycerol content than controls and remained protected from hepatic insulin resistance despite high-fat feeding.

Similarly, Jornayvaz et al. [14] found that DGAT2-overexpressing mice showed only 0.8 ± 41.8% suppression of endogenous glucose production compared to 87.7 ± 34.3% in wild-type mice, along with an almost 12-fold increase in hepatic diacylglycerol content and marked worsening of insulin sensitivity. Choi et al. also reported that suppression of DGAT2 reduced hepatic triglyceride accumulation and improved insulin sensitivity.

In the present study, non-alcoholic CLD patients had significantly more deranged lipid profiles than alcoholic CLD patients. Mean total cholesterol was 198.6 ± 34.1 mg/dL in the non-alcoholic CLD group compared to 162.5 ± 28.3 mg/dL in the alcoholic CLD group. Mean triglycerides were 189.8 ± 46.7 mg/dL versus 141.2 ± 39.6 mg/dL. LDL-C and VLDL-C were also significantly higher in non-alcoholic CLD patients, while HDL-C was lower (36.4 ± 6.8 mg/dL vs 42.8 ± 7.9 mg/dL).Stone et al. [15] demonstrated that DGAT2 promotes triglyceride synthesis and hepatic fat accumulation, thereby contributing to steatosis.

Similarly, Jornayvaz et al. [14] observed marked hepatic triglyceride accumulation and an almost 12-fold rise in hepatic diacylglycerol content in DGAT2-overexpressing mice. Choi et al. [16] further reported that mice with lower DGAT2 expression had nearly fivefold lower hepatic triglyceride levels and 1.5-fold lower diacylglycerol levels than DGAT2-overexpressing mice. Kaczocha et al. [17] also suggested that increased intracellular fatty acid transport contributes to hepatic steatosis and dyslipidemia.

In the present study, HOMA-IR showed positive correlation with total cholesterol (r = +0.48), triglycerides (r = +0.56), LDL-C (r = +0.51), and VLDL-C (r = +0.53), while it showed negative correlation with HDL-C (r = −0.42). This suggests that worsening insulin resistance is associated with greater dyslipidemia in CLD patients. These findings are comparable to those of Neschen et al. [13], who observed 59% lower hepatic triglycerides and 74% lower diacylglycerol content in GPAT1 knockout mice, with preservation of insulin sensitivity. Choi et al. also found that reducing DGAT2 expression lowered hepatic lipid accumulation and improved insulin signaling.

Conclusion

Non-alcoholic chronic liver disease patients had significantly higher insulin resistance and more severe lipid abnormalities than alcoholic chronic liver disease patients. Fasting blood sugar, serum insulin, HOMA-IR, total cholesterol, triglycerides, LDL-C, and VLDL-C were significantly higher, while HDL-C was lower in the non-alcoholic group. HOMA-IR showed positive correlation with cholesterol, triglycerides, LDL-C, and VLDL-C and negative correlation with HDL-C. Overall findings suggested that non-alcoholic CLD patients were metabolically more compromised and required early screening and management.

Limitations

The study had a relatively small sample size and was conducted at a single center, which may limit the generalizability of the findings. Its cross-sectional design did not permit assessment of temporal changes in insulin resistance and lipid profile. Liver biopsy and advanced imaging for hepatic fat quantification were not performed in all patients. In addition, factors such as diet, physical activity, obesity severity, and medication use were not evaluated in detail.

References

1. Bugianesi E, McCullough AJ, Marchesini G. Insulin resistance: a metabolic pathway to chronic liver disease. Hepatology. 2005;42(5):987-1000.
2. Mehta M, Choudhary P, Sharma D, Sharma S. Understanding insulin resistance in NAFLD: a systematic review. Cureus. 2024;16(9):e70276.
3. Manco M, Dallapiccola B. Insulin resistance and NAFLD: a dangerous liaison beyond the genetics. Pediatrics. 2017;4(8):74.
4. Jung I, Cho YK, Kang YM, Lee SE, Lee WJ, Park JY, et al. Insulin resistance, non-alcoholic fatty liver disease and cardiovascular risk. Diabetes Metab J. 2024;48(2):169-181.
5. Rajendra S, Vaishnavi S, Hamsavakini N, Nalini R, Aravnithan M, Shathana P. Lipid profile, insulin resistance and non-alcoholic fatty liver disease among type 2 diabetes patients getting treatment in Jaffna. Endocr Metab Sci. 2024; 15:100166.
6. Cao W, Li M, Xie Y, et al. Lipid-related insulin resistance indices for the diagnosis of non-alcoholic fatty liver disease with metabolic abnormalities. Biomed Environ Sci. 2025;38(1):1-12.
7. Tian J, Zhang Y, Wang H, et al. The potential of insulin resistance indices to predict non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus. BMC Endocr Disord. 2024; 24:179.
8. Kim SS, Cho HJ, Kim HJ, Kang DR, Berry JR, Kim JH, et al. Screening and prediction of nonalcoholic fatty liver disease using insulin

resistance markers. Clin Mol Hepatol. 2022;28(3):497-509.
9. Marchesini G, Brizi M, Bianchi G, Tomassetti S, Bugianesi E, Lenzi M, et al. Nonalcoholic fatty liver disease: a feature of the metabolic syndrome. Diabetes. 2001;50(8):1844-1850.
10. Bugianesi E, Gastaldelli A, Vanni E, Gambino R, Cassader M, Baldi S, et al. Insulin resistance in non-diabetic patients with non-alcoholic fatty liver disease: sites and mechanisms. Diabetologia. 2005;48(4):634-642.
11. Byrne CD, Targher G. NAFLD: a multisystem disease. J Hepatol. 2015;62(1 Suppl):S47-S64.
12. Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology. 2012;55(6):2005-2023.
13. Neschen S, Morino K, Hammond LE, Zhang D, Liu ZX, Romanelli AJ, et al. Prevention of hepatic steatosis and hepatic insulin resistance in mitochondrial acyl-CoA:glycerol-sn-3-phosphate acyltransferase 1 knockout mice. Cell Metab. 2005;2(1):55-65.
14. Jornayvaz FR, Birkenfeld AL, Jurczak MJ, Kanda S, Guigni BA, Jiang DC, et al. Hepatic insulin resistance in mice with hepatic overexpression of diacylglycerol acyltransferase 2. Proc Natl Acad Sci U S A. 2011;108(14):5748-5752.
15. Stone SJ, Levin MC, Zhou P, Han J, Walther TC, Farese RV Jr. The endoplasmic reticulum enzyme DGAT2 is found in mitochondria-associated membranes and has a mitochondrial targeting signal that promotes its association with mitochondria. J Biol Chem. 2009;284 (8):5352-5361.
16. Choi CS, Savage DB, Kulkarni A, Yu XX, Liu ZX, Morino K, et al. Suppression of diacylglycerol acyltransferase-2 (DGAT2), but not DGAT1, with antisense oligonucleotides reverses diet-induced hepatic steatosis and insulin resistance. J Biol Chem. 2007;282(31):22678-22688.
17. Kaczocha M, Vivieca S, Sun J, Glaser ST, Deutsch DG. Fatty acid-binding proteins transport N-acylethanolamines to nuclear receptors and are targets of endocannabinoid transport inhibitors. J Biol Chem. 2012;287(5): 3415-3424.