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ORIGINAL RESEARCH

Correlation of N-terminal pro-brain natriuretic peptide levels in non-alcoholic fatty liver disease

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ABSTRACT

Aim: To evaluate the correlation between N-terminal pro-brain natriuretic peptide (NT-proBNP) levels and the severity of hepatic steatosis in patients with non-alcoholic fatty liver disease (NAFLD), and to explore associations with key metabolic parameters. **Materials and Methods:** This cross-sectional observational study included 100 adult patients (aged 18–65 years) diagnosed with NAFLD via ultrasonography. Individuals with significant alcohol intake, cardiovascular or renal diseases, other chronic liver diseases, or medications affecting NT-proBNP levels were excluded. Comprehensive clinical, anthropometric, and biochemical evaluations were conducted, including NT-proBNP levels measured using electrochemiluminescence immunoassay. Ultrasonographic grading of hepatic steatosis was performed, and correlations between NT-proBNP levels and NAFLD severity, as well as metabolic parameters, were analyzed using appropriate statistical methods. **Results:** The mean NT-proBNP levels showed a significant stepwise increase with the severity of hepatic steatosis: Grade I (78.5 ± 25.7 pg/mL), Grade II (92.3 ± 31.2 pg/mL), and Grade III (108.9 ± 35.4 pg/mL) ($p < 0.05$). NT-proBNP levels were moderately correlated with BMI ($r = 0.35$, $p = 0.001$), and weakly but significantly correlated with fasting glucose ($r = 0.22$, $p = 0.03$), HOMA-IR ($r = 0.28$, $p = 0.01$), triglycerides ($r = 0.25$, $p = 0.02$), and negatively with HDL cholesterol ($r = -0.21$, $p = 0.04$). A mild, non-significant correlation was observed with ALT levels ($r = 0.18$, $p = 0.06$). **Conclusion:** NT-proBNP levels correlate positively with the severity of hepatic steatosis and with several metabolic risk markers in patients with NAFLD. These findings support NT-proBNP as a potential non-invasive biomarker for systemic metabolic and cardiovascular stress in NAFLD, offering additional insight for comprehensive patient risk assessment and management.

Keywords: NT-proBNP, NAFLD, hepatic steatosis, insulin resistance, metabolic syndrome

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has emerged as the most common chronic liver condition globally, affecting a significant proportion of the adult population. Characterized by the accumulation of excess fat in hepatocytes in the absence of significant alcohol consumption or other secondary causes of hepatic steatosis, NAFLD encompasses a wide clinical spectrum. This includes simple steatosis (non-alcoholic fatty liver or NAFL) and the more progressive form, non-alcoholic steatohepatitis (NASH), which can lead to fibrosis, cirrhosis, and hepatocellular carcinoma. Importantly, NAFLD is now recognized not only as a liver disease but also as a multisystem condition that is closely associated with obesity, insulin resistance, type 2 diabetes mellitus, dyslipidemia, and hypertension—collectively components of the metabolic syndrome.[1]

Given its systemic nature, NAFLD is increasingly linked with an elevated risk of cardiovascular disease (CVD), which remains the leading cause of morbidity and mortality in these patients. While liver-related complications such as cirrhosis and liver failure are important endpoints, cardiovascular complications often occur earlier and more frequently, significantly impacting clinical outcomes. This paradigm shift in the understanding of NAFLD has fueled interest in identifying biomarkers that can predict both hepatic and cardiovascular outcomes, thereby facilitating a more integrated approach to patient management.[2]

In this context, N-terminal pro-brain natriuretic peptide (NT-proBNP) has gained attention as a potential biomarker of cardiovascular stress and dysfunction. NT-proBNP is a non-active cleavage product released into the bloodstream in response to volume expansion and increased myocardial wall

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tension. It is commonly used in clinical practice as a diagnostic and prognostic marker for heart failure and is associated with subclinical cardiac dysfunction even in the absence of overt heart failure symptoms. Elevated NT-proBNP levels reflect myocardial strain, and its measurement has become a reliable tool for risk stratification in a wide range of cardiovascular conditions.[3]

The interplay between NT-proBNP and NAFLD, however, remains complex and not fully understood. Traditionally, lower levels of NT-proBNP have been observed in obese individuals and those with metabolic syndrome, likely due to the suppressive effect of adiposity on natriuretic peptide production or clearance mechanisms. In patients with NAFLD, the interaction becomes more nuanced, as the disease is often accompanied by insulin resistance, systemic inflammation, endothelial dysfunction, and increased cardiac workload—all of which can influence NT-proBNP levels.[4]

Emerging evidence suggests that NT-proBNP may serve as a bridge marker linking hepatic pathology with cardiovascular strain. Some studies have proposed that patients with more advanced forms of NAFLD, particularly those with NASH or fibrosis, may exhibit altered NT-proBNP profiles. This may be due to shared pathogenic mechanisms such as increased oxidative stress, chronic low-grade inflammation, and dysregulated lipid metabolism, all of which can contribute to both hepatic and cardiac injury. Furthermore, NT-proBNP may serve as an early indicator of subclinical cardiac remodeling in patients with NAFLD, providing a valuable non-invasive marker for identifying high-risk individuals before the onset of overt cardiovascular disease.[5]

At the same time, it is important to recognize the limitations and challenges in interpreting NT-proBNP levels in the context of NAFLD. Factors such as obesity, age, renal function, and gender can all influence natriuretic peptide levels, potentially confounding their diagnostic and prognostic utility. Moreover, the dynamic nature of NAFLD progression—from simple steatosis to steatohepatitis and fibrosis—means that the relationship with NT-proBNP may vary depending on the stage of liver involvement and the presence of comorbidities.[6]

Therefore, a clearer understanding of the correlation between NT-proBNP levels and the severity of NAFLD could provide critical insights into the systemic effects of the disease and its cardiovascular implications. Identifying whether NT-proBNP levels rise in parallel with hepatic steatosis or whether they reflect an inverse association due to metabolic suppression could significantly enhance clinical decision-making. In particular, it may help clinicians identify NAFLD patients who are at heightened risk for cardiovascular complications, thereby justifying more intensive monitoring and early therapeutic intervention.[7]

In light of this, the current study aims to explore the relationship between NT-proBNP levels and varying degrees of hepatic steatosis in patients with NAFLD. By correlating NT-proBNP levels with ultrasonographic grading of steatosis and key metabolic parameters, this study seeks to determine whether NT-proBNP can serve as a meaningful biomarker not only for cardiovascular stress but also for NAFLD severity. Such findings could contribute to a more holistic approach to managing NAFLD, reinforcing the importance of cardiovascular evaluation in the routine assessment of patients with fatty liver disease.

MATERIAL AND METHODS

This cross-sectional observational study was conducted at tertiary care hospital, after obtaining approval from the Institutional Ethics Committee. A total of 100 adult patients (aged 18–65 years) with a diagnosis of non-alcoholic fatty liver disease (NAFLD) were enrolled after obtaining written informed consent.

Inclusion Criteria

- Patients diagnosed with NAFLD based on ultrasonographic evidence of hepatic steatosis.
- Age between 18 and 65 years.
- Body mass index (BMI) between 25 and 40 kg/m².
- No history of significant alcohol consumption (defined as <20 g/day for men and <10 g/day for women).

Exclusion Criteria

- History of alcohol consumption exceeding defined limits.
- Known cardiovascular diseases, including heart failure or ischemic heart disease.
- Chronic kidney disease (eGFR < 60 mL/min/1.73 m²).
- Hepatitis B, hepatitis C, or other chronic liver diseases.
- Use of medications known to affect NT-proBNP levels (e.g., diuretics, ACE inhibitors, beta-blockers).
- Pregnancy.

Methodology

All patients underwent a comprehensive clinical evaluation that included a detailed medical history, physical examination, and assessment of anthropometric parameters such as height, weight, and body mass index (BMI), along with blood pressure measurement. Laboratory investigations were carried out for each participant and included fasting blood glucose, lipid profile, liver function tests (including alanine aminotransferase [ALT], aspartate aminotransferase [AST], and gamma-glutamyl transferase [GGT]), renal function tests, serum insulin, and calculation of the homeostatic model

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assessment for insulin resistance (HOMA-IR). Serum N-terminal pro-brain natriuretic peptide (NT-proBNP) levels were measured using the [electrochemiluminescence immunoassay] method on a [Roche Elecsys] analyzer, with values expressed in picograms per milliliter (pg/mL). All laboratory analyses were conducted in the same facility to ensure methodological consistency and reduce inter-assay variability. In addition to biochemical evaluation, all patients underwent abdominal ultrasonography performed by an experienced radiologist to confirm the presence of hepatic steatosis. The severity of fatty liver was graded according to standard ultrasonographic criteria into Grade I, Grade II, or Grade III steatosis.

Statistical Analysis

Statistical analysis was carried out using [e.g., SPSS version 25.0]. Descriptive statistics were presented as mean ± standard deviation (SD) for continuous variables and as frequencies and percentages for categorical variables. The correlation between NT-proBNP levels and NAFLD severity, as well as with metabolic parameters, was assessed using Pearson or Spearman correlation coefficients, as appropriate. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population (N = 100)

The study population consisted of 100 patients diagnosed with non-alcoholic fatty liver disease (NAFLD). The mean age of the participants was 45.2 ± 9.8 years, with a higher proportion of males (58%) compared to females (42%). The body mass index (BMI) of the participants had a mean of 31.4 ± 3.7 kg/m², indicating that the majority of the study group were overweight or obese, which is a typical characteristic of NAFLD patients. Systolic blood pressure (BP) was measured at 132.5 ± 14.1 mmHg, while the diastolic BP was 84.7 ± 9.6 mmHg. Hypertension was observed in 36% of the participants, and 40% had a history of type 2 diabetes mellitus (T2DM).

Table 2: Distribution of Hepatic Steatosis Grades Based on Ultrasound Findings

Ultrasonographic evaluation revealed varying degrees of hepatic steatosis among the study participants. Grade I hepatic steatosis (mild) was found in 42% of the participants, while Grade II (moderate) and Grade III (severe) steatosis were observed in 38% and 20% of the participants, respectively. This distribution suggests that the majority of the patients had moderate to mild hepatic steatosis, with a smaller portion presenting with severe steatosis. The proportion of patients with severe hepatic steatosis (Grade III) is relatively low compared to Grade I and Grade II, which is in line with the typical spectrum of NAFLD progression.

Table 3: Laboratory Parameters of Study Participants

The laboratory findings in this cohort revealed several metabolic disturbances. The mean fasting blood glucose level was 112.4 ± 28.3 mg/dL, suggesting impaired glucose regulation in the population. The lipid profile showed a mean total cholesterol of 192.8 ± 38.6 mg/dL and triglycerides of 180.5 ± 45.2 mg/dL, both of which are elevated and commonly associated with NAFLD. The mean high-density lipoprotein (HDL) was 42.1 ± 9.5 mg/dL, which is lower than the recommended value of >60 mg/dL, contributing to a higher cardiovascular risk. The low-density lipoprotein (LDL) level was 120.3 ± 32.8 mg/dL, which is also considered elevated and contributes to the lipid dysregulation observed in NAFLD. Liver enzymes, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT), were elevated, with mean values of 58.6 ± 25.1 U/L, 49.3 ± 20.6 U/L, and 61.7 ± 28.9 U/L, respectively, indicating liver injury or inflammation. Serum insulin levels averaged 16.8 ± 7.4 μIU/mL, and the mean HOMA-IR was 4.2 ± 1.9, indicating the presence of insulin resistance, a hallmark of NAFLD.

Table 4: NT-proBNP Levels According to NAFLD Severity

NT-proBNP levels increased with the severity of hepatic steatosis. The mean NT-proBNP level in patients with Grade I steatosis (mild) was 78.5 ± 25.7 pg/mL, while patients with Grade II and Grade III steatosis had higher mean NT-proBNP levels of 92.3 ± 31.2 pg/mL and 108.9 ± 35.4 pg/mL, respectively. The analysis of variance (ANOVA) test revealed a statistically significant increase in NT-proBNP levels with more severe hepatic steatosis, with a p-value of < 0.05.

Table 5: Correlation Between NT-proBNP and Metabolic Parameters

The correlation analysis revealed several statistically significant relationships between NT-proBNP levels and various metabolic parameters. There was a moderate positive correlation between NT-proBNP levels and BMI ($r = 0.35$, $p = 0.001$), suggesting that higher body weight and obesity are associated with elevated NT-proBNP levels in NAFLD patients. Similarly, NT-proBNP levels showed a weak positive correlation with fasting glucose ($r = 0.22$, $p = 0.03$) and HOMA-IR ($r = 0.28$, $p = 0.01$), indicating that insulin resistance and impaired glucose metabolism are linked to higher NT-proBNP concentrations. The correlation between NT-proBNP and triglycerides was also positive ($r = 0.25$, $p = 0.02$), while the correlation with HDL cholesterol was negative ($r = -0.21$, $p = 0.04$), which suggests that lower HDL levels are associated with higher NT-proBNP levels in these patients. There was also a mild positive correlation

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with ALT levels (r = 0.18, p = 0.06), although this did not reach statistical significance.

Table 1: Baseline Demographic and Clinical Characteristics

Variable	Mean ± SD / n (%)
Age (years)	45.2 ± 9.8
Gender (Male/Female)	58 (58%) / 42 (42%)
BMI (kg/m²)	31.4 ± 3.7
Systolic BP (mmHg)	132.5 ± 14.1
Diastolic BP (mmHg)	84.7 ± 9.6
Hypertension	36 (36%)
Type 2 Diabetes Mellitus	40 (40%)

Table 2: Distribution of Hepatic Steatosis Grades Based on Ultrasound Findings

Steatosis Grade	Number of Patients (n)	Percentage (%)
Grade I	42	42%
Grade II	38	38%
Grade III	20	20%

Table 3: Laboratory Parameters of Study Participants

Parameter	Mean ± SD
Fasting Blood Glucose (mg/dL)	112.4 ± 28.3
Total Cholesterol (mg/dL)	192.8 ± 38.6
Triglycerides (mg/dL)	180.5 ± 45.2
HDL (mg/dL)	42.1 ± 9.5
LDL (mg/dL)	120.3 ± 32.8
ALT (U/L)	58.6 ± 25.1
AST (U/L)	49.3 ± 20.6
GGT (U/L)	61.7 ± 28.9
Serum Insulin (μIU/mL)	16.8 ± 7.4
HOMA-IR	4.2 ± 1.9

Table 4: NT-proBNP Levels According to NAFLD Severity

Steatosis Grade	NT-proBNP (pg/mL), Mean ± SD
Grade I	78.5 ± 25.7
Grade II	92.3 ± 31.2
Grade III	108.9 ± 35.4
p-value	**< 0.05** (ANOVA)

Table 5: Correlation Between NT-proBNP and Metabolic Parameters

Parameter	Correlation Coefficient (r)	p-value
BMI	0.35	0.001
Fasting Glucose	0.22	0.03
HOMA-IR	0.28	0.01
ALT	0.18	0.06
Triglycerides	0.25	0.02
HDL	-0.21	0.04

DISCUSSION

The current study provides a comprehensive evaluation of NT-proBNP levels in patients with non-alcoholic fatty liver disease (NAFLD) and highlights significant correlations with disease severity and associated metabolic dysfunctions. By examining both hepatic and cardiometabolic profiles, the findings offer insights into the evolving understanding of NAFLD as not only a liver-specific condition but also a systemic metabolic disorder with implications for cardiovascular health.The demographic profile of the study cohort reflects the typical population affected by NAFLD. The mean age of 45.2 years and the predominance of males (58%) are consistent with epidemiological patterns reported in the literature (Younossi et al., 2018).6 A high mean BMI (31.4 kg/m²) confirms the association between obesity and NAFLD, further substantiated by the presence of hypertension (36%) and type 2 diabetes mellitus (40%). These findings emphasize the central role of metabolic syndrome components in the pathophysiology of NAFLD and align with global

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data describing the disease burden and its link with cardiometabolic risk factors.[6,7]

The distribution of steatosis grades revealed that most patients had either Grade I or Grade II NAFLD, with only 20% presenting with severe steatosis (Grade III). This distribution mirrors the disease progression spectrum observed in community and clinical settings, where early-stage fatty liver is often more prevalent due to subclinical presentation and opportunistic diagnosis via imaging (Leoni et al., 2018).[7]While ultrasonography is limited in detecting early fibrosis, it remains an effective tool for grading hepatic steatosis noninvasively, as supported by Takeda et al. (2006).[8]

Laboratory findings in this cohort revealed hallmark features of metabolic syndrome. Elevated fasting glucose, triglycerides, and LDL cholesterol, coupled with low HDL levels, highlight dyslipidemia and insulin resistance—core contributors to both NAFLD and cardiovascular disease. Elevated liver enzymes (ALT, AST, GGT) point toward hepatic inflammation or injury, commonly seen in patients progressing toward non-alcoholic steatohepatitis (NASH) (Arvaniti et al., 2008).[9] The raised HOMA-IR (mean = 4.2) further reinforces insulin resistance as a central pathogenic mechanism, consistent with findings from Mikolasevic et al. (2016).[10]

A significant and progressive rise in NT-proBNP levels was observed with increasing grades of hepatic steatosis ($p < 0.05$). Interestingly, these results diverge from some previous studies that reported lower NT-proBNP levels in advanced NAFLD due to impaired cardiac secretion or peptide clearance (Sanchez et al., 2016; Qiao et al., 2020).[11,12]However, our findings may be interpreted in the context of increasing cardiac strain and subclinical cardiovascular stress as hepatic steatosis worsens, thereby stimulating NT-proBNP secretion. This aligns with earlier research identifying NT-proBNP as a sensitive marker of myocardial stress and early heart failure (Hunt et al., 1997) It is also plausible that in obese patients with NAFLD, elevated NT-proBNP reflects compensatory neurohormonal activation, particularly in those with concurrent hypertension and insulin resistance.[13]

The positive correlations between NT-proBNP and BMI ($r = 0.35$), fasting glucose ($r = 0.22$), and HOMA-IR ($r = 0.28$) are notable and suggest a relationship between NT-proBNP levels and metabolic dysregulation. This appears contrary to earlier findings by Sanchez et al. (2016), who reported lower NT-proBNP in individuals with hepatic steatosis, but it supports the view that increasing metabolic burden and inflammatory stress may provoke NT-proBNP release, particularly in early-stage cardiac remodeling. Additionally, the inverse correlation with HDL ($r = -0.21$, $p = 0.04$) is indicative of atherogenic dyslipidemia—a critical link between liver disease and cardiovascular pathology.[11]

While ALT showed only a borderline correlation with NT-proBNP ($r = 0.18$, $p = 0.06$), the trends suggest that NT-proBNP may also reflect hepatic metabolic stress and cellular injury. These correlations collectively support the hypothesis that NT-proBNP levels could serve as a bridge marker between liver disease and cardiovascular health, offering utility in holistic risk stratification.

CONCLUSION

This study highlights a significant positive correlation between NT-proBNP levels and the severity of hepatic steatosis in patients with NAFLD, along with key metabolic risk factors such as BMI, insulin resistance, and dyslipidemia. These findings suggest that NT-proBNP may serve as a valuable non-invasive biomarker reflecting both hepatic and cardiovascular stress in NAFLD. Elevated NT-proBNP levels, particularly in patients with more advanced steatosis, underscore the systemic nature of the disease. Incorporating NT-proBNP into routine evaluation may aid in early risk stratification and comprehensive management.

REFERENCES

1. Choi H-I, Lee MY, Oh BK, Lee SJ, Kang JG, Lee SH, et al. Fatty liver is associated with low N-terminal pro-B-type natriuretic peptide in a healthy population. J Clin Med. 2021;10(7):1402. doi:10.3390/jcm10071402
2. Johansen ML, Schou M, Rasmussen J, Rossignol P, Holm MR, Chabanova E, et al. Low N-terminal pro-brain natriuretic peptide levels are associated with non-alcoholic fatty liver disease in patients with type 2 diabetes. Diabetes Metab. 2019;45(5):429-35. doi:10.1016/j.diabet.2018.11.003
3. Metwaly A, Khalik AA, Nasr FM, Sabry AI, Gouda MF, Hassan M. Brain natriuretic peptide in liver cirrhosis and fatty liver: correlation with cardiac performance. Electron Physician. 2016;8(2):1984-93. doi:10.19082/1984
4. Asati P, Jain N, Punekar P, Gupta R, Golchha A. Correlation of N-terminal pro-brain natriuretic peptide levels in non-alcoholic fatty liver disease. Int J Health Clin Res. 2022;5(3):856-9. Available from: https://ijhcr.com/index.php/ijhcr/article/view/5156
5. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67(1):328-57.
6. Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, et al. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. *Nat Rev Gastroenterol Hepatol*. 2018;15(1):11-20.
7. Leoni S, Tovoli F, Napoli L, Serio I, Ferri S, Bolondi L. Current guidelines for the management of non-alcoholic fatty liver disease: a systematic review with comparative analysis. *World J Gastroenterol*. 2018;24(30):3361-73.
8. Takeda J, Yasuda T, Kimura M, Nakaya M, Fujii H, Nakayama Y, et al. Noninvasive diagnosis of nonalcoholic steatohepatitis using elastometry. *Hepatology*. 2006;44(Suppl 1):652A.
9. Arvaniti VA, Thomopoulos KC, Tsamandas A, Makri M, Psyrogiannis A, Vafiadis G, et al. Serum adiponectin levels in different types of non alcoholic

DOI: 10.69605/ijlbpr_14.1.2025.143

liver disease: correlation with steatosis, necroinflammation and fibrosis. *Acta Gastroenterol Belg*. 2008;71(4):355-60.

10. Mikolasevic I, Milic S, Orlic L, Stimac D, Franjic N, Targher G. Factors associated with significant liver steatosis and fibrosis as assessed by transient elastography in patients with one or more components of the metabolic syndrome. *J Diabetes Complications*. 2016;30(7):1347-53.
11. Sanchez O, Lazo-Elizondo M, Zeb I, Tracy R, Bradley R, Duprez D, et al. Computerized tomography measured liver fat is associated with low levels of N-terminal pro-brain natriuretic protein (NT-proBNP): Multi-Ethnic Study of Atherosclerosis. *Metabolism*. 2016;65(5):728-35.
12. Qiao Z, Zheng K, Zhu P, Gao F, Ma H, Li G, et al. Lower levels of plasma NT-proBNP are associated with higher prevalence of NASH in patients with biopsy-proven NAFLD. *NutrMetab Cardiovasc Dis*. 2020;30(10):1820-5.
13. Hunt PJ, Richards AM, Nicholls MG, Yandle TG, Doughty RN, Espiner EA. Immunoreactive amino-terminal pro-brain natriuretic peptide (NT-proBNP): a new marker of cardiac impairment. *Clin Endocrinol (Oxf)*. 1997;47(3):287-96.