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RESEARCH ARTICLE
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THE PHYSIOLOGIC AND BIOCHEMICAL ROLE OF ALANINE AMINOTRANSFERASE IN NON-ALCOHOLIC FATTY LIVER DISEASE AND ITS ASSOCIATION WITH DIABETES MELLITUS

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) has emerged as one of the most prevalent liver disorders worldwide and is closely linked with obesity, insulin resistance, and diabetes mellitus. Among biochemical markers, Alanine Aminotransferase (ALT) plays a pivotal role in reflecting hepatocellular injury and may also indicate underlying metabolic dysfunction. Understanding the association between ALT levels and diabetes in patients with NAFLD can help in early identification of individuals at metabolic risk.

Methodology: A cross-sectional analytical study was conducted at Mercy Teaching Hospital from January 2023 to January 2024, in collaboration between the Departments of Medicine and Community Medicine. A total of 82 patients with ultrasonographically confirmed NAFLD were included and categorized into two groups 'NAFLD with diabetes mellitus (n=36) and NAFLD without diabetes mellitus (n=46)'. Detailed demographic, clinical, and biochemical data were collected using a structured proforma. Laboratory investigations included liver function tests, fasting blood glucose, HbA1c, and lipid profile. Data were analyzed using SPSS version 25.0, applying independent t-tests, Chi-square tests, and Pearson correlation where appropriate.

Results: The mean ALT level was significantly higher among diabetic NAFLD participants (71.9 ± 18.4 IU/L) compared to non-diabetic individuals (58.2 ± 15.6 IU/L; p=0.001). ALT showed a strong positive correlation with fasting blood glucose ($r = 0.512$, $p < 0.001$), HbA1c ($r = 0.484$, $p < 0.001$), BMI ($r = 0.426$, $p = 0.001$), and triglyceride levels ($r = 0.372$, $p = 0.002$). Sedentary lifestyle and high-fat dietary intake were significantly associated with NAFLD among diabetic participants.

Conclusion: Elevated ALT levels in NAFLD patients reflect both hepatic and metabolic derangements. The enzyme serves as a useful biochemical marker linking fatty liver with glycemic imbalance and insulin resistance. Routine monitoring of ALT, along with lifestyle modification and

early metabolic screening, can aid in the prevention and control of diabetes-related liver disease in the community.

Key Words: Alanine Aminotransferase, Non-Alcoholic Fatty Liver Disease, Diabetes Mellitus, Liver Enzymes, Insulin Resistance, Metabolic Syndrome

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a condition affecting close to a quarter of the adult population globally and is becoming a noticeable health issue worldwide. It can range from a mild case of simple steatosis to more serious conditions like NASH, liver fibrosis, and cirrhosis. Unlike alcoholic liver disease, NAFLD occurs in individuals who are lower or non-drinkers, and thus more metabolic factors are implicated. The growing body of literature suggests NAFLD is not simply a liver disorder, but rather a liver component of a wider metabolic syndrome which is closely linked to type 2 diabetes, obesity, dyslipidemia, and hypertension [1-3].

Alanine Aminotransferase (ALT) is one of the liver biochemical markers that garners the most attention, because it not only reflects liver cellular injury, but it also indicates possible injury related to metabolic dysfunction. Even mildly elevated ALT, levels which are only considered to be within the 'normal range,' are associated with predicting insulin resistance and the development of diabetes. Studies have demonstrated that raised ALT values are associated with increased risk of type 2 diabetes and cardiovascular disease. This reflects the growing understanding that hepatic lipid accumulation and impaired glucose metabolism are deeply interconnected [4-6].

Diabetes mellitus, in turn, exacerbates fatty infiltration of the liver by increasing free fatty acid flux, enhancing de novo lipogenesis, and reducing hepatic fat oxidation. Consequently, individuals with diabetes are more likely to develop progressive forms of NAFLD and suffer from worse metabolic profiles. Recognition of this bidirectional relationship is important for clinical management and preventive health strategies [7-9].

Despite extensive research worldwide, local data on the biochemical behavior of ALT among NAFLD patients with and without diabetes remain limited, particularly in community-based hospital settings [10-12]. 'to assess the physiologic and biochemical role of Alanine Aminotransferase in patients with non-alcoholic fatty liver disease and to examine its association with diabetes mellitus'. The collaborative nature of this research between Medicine and Community Medicine departments was intended to bridge clinical insight with public health relevance. By identifying the metabolic correlates of ALT elevation, this study aims to emphasize the importance of early detection and lifestyle intervention in reducing the growing burden of fatty liver disease and diabetes in the population.

METHODOLOGY

This research was conducted as a cross-sectional analytical study. Although this research was conducted jointly by the Departments of Medicine and Community Medicine, the findings hold significant endocrinological relevance. Alanine Aminotransferase (ALT) serves not only as a hepatic enzyme but also as a marker of endocrine metabolic dysfunction associated with insulin resistance and type 2 diabetes mellitus. Future studies may benefit from collaboration with the Department of Endocrinology to further explore hormonal mechanisms underlying these associations. The study period extended from January 2023 to January 2024. The hospital was chosen as the study site because it serves a diverse population from both urban and rural areas, offering a suitable setting for assessing the clinical and biochemical profile of NAFLD and 'its association with diabetes mellitus'.

A total of 82 adult participants were enrolled in the study. All participants were diagnosed with NAFLD through ultrasonographic examination and were categorized into two groups 'NAFLD without Diabetes Mellitus (n = 46) and NAFLD with Diabetes Mellitus (n = 36)'

All participants were outpatients or inpatients from the Department of Medicine who consented to participate. The study included 'both male and female participants aged between 25 and 65 years'.

Inclusion Criteria
- Adults aged 25–65 years.
- Ultrasonographically confirmed non-alcoholic fatty liver disease.
- Patients with or without type 2 diabetes mellitus (diagnosed based on fasting blood glucose and HbA1c).
- Individuals who provided written informed consent to participate.

Exclusion Criteria
- History of alcohol consumption in any quantity.
- Presence of viral hepatitis (A, B, C, or E) confirmed by serological testing.
- Patients on hepatotoxic drugs (such as steroids, methotrexate, or anti-tubercular drugs).
- Individuals with autoimmune liver diseases, Wilson's disease, or hemochromatosis.
- Pregnant women and individuals with severe systemic illness.

After obtaining institutional ethical approval, participants were recruited consecutively from the Medicine outpatient and inpatient departments. Each participant was interviewed and examined using a pre-designed structured proforma that included demographic details, clinical history, anthropometric measurements, and biochemical investigations.
Demographic data included age, sex, residence, socioeconomic status, and occupation. Clinical information comprised dietary habits, physical activity, family history of diabetes or liver disease, and smoking status. Anthropometric measurements such as height, weight, body mass index (BMI), and waist circumference were recorded following standard procedures.
Fasting venous blood samples were collected under aseptic conditions after an overnight fast of at least 8 hours. The following investigations were performed:
- Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) using the standard kinetic method.
- Fasting Blood Glucose (FBG) measured by the glucose oxidase-peroxidase method.
- Glycated Hemoglobin (HbA1c) determined by high-performance liquid chromatography (HPLC).
- Lipid profile, including total cholesterol, HDL, LDL, and triglycerides.
- Serum bilirubin and albumin were also measured to assess overall liver function.

All biochemical tests were carried out in the hospital's central diagnostic laboratory using automated analyzers under strict quality control protocols.
Ultrasonography of the abdomen was performed for all participants to confirm the diagnosis of NAFLD and assess the grade of hepatic steatosis. Grading was done according to standard radiological criteria:
- Grade I: Mild increase in echogenicity of liver parenchyma.
- Grade II: Moderate increase with partial obscuration of intrahepatic vessels.
- Grade III: Marked increase with poor visualization of the diaphragm and vessels.

All ultrasounds were interpreted by a senior radiologist blinded to the biochemical data to minimize bias.
Data were entered and analyzed using SPSS version 25.0. Continuous variables such as ALT, AST, BMI, and fasting glucose were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages.
The independent sample t-test was used to compare means between groups, and the Chi-square test was applied for categorical variables. Pearson's correlation coefficient (r) was calculated to determine the relationship between ALT levels and metabolic parameters such as BMI, fasting glucose, HbA1c, and lipid levels. 'A p-value less than 0.05 was considered statistically significant'.

RESULTS

The participants ranged in age from 25 to 65 years, with a mean age of 41.6 ± 9.8 years among non-diabetic NAFLD individuals and 48.9 ± 8.6 years among those with diabetes. The difference in age between the two groups was statistically significant (p = 0.002), indicating that NAFLD associated with diabetes was more common among older adults.

Gender distribution showed no marked difference; males were slightly predominant in both groups (28 males and 18 females in non-diabetic NAFLD; 22 males and 14 females in diabetic NAFLD), with a p-value of 0.965, which was not statistically significant.

Body mass index (BMI) was notably higher among diabetic NAFLD subjects (30.1 ± 3.7 kg/m²) compared to the non-diabetic group (27.2 ± 3.5 kg/m²), and this difference was highly significant (p = 0.001). Similarly, the mean waist circumference was greater in diabetic individuals (98.4 ± 9.2 cm) than in non-diabetic counterparts (91.8 ± 10.6 cm), with a p-value of 0.010.

No significant association was found between residence (urban or rural) or socioeconomic status and the presence of diabetes among NAFLD patients.

Table 1. Demographic Characteristics of Study Participants (n = 82)

Variable	NAFLD without Diabetes (n=46)	NAFLD with Diabetes (n=36)	p-value
Age (years, mean ± SD)	41.6 ± 9.8	48.9 ± 8.6	0.002*
Gender (Male/Female)	28 / 18	22 / 14	0.965
BMI (kg/m², mean ± SD)	27.2 ± 3.5	30.1 ± 3.7	0.001*
Waist circumference (cm, mean ± SD)	91.8 ± 10.6	98.4 ± 9.2	0.010*
Residence (Urban/Rural)	30 / 16	25 / 11	0.851
Socioeconomic status (Low/Medium/High)	10 / 28 / 8	7 / 20 / 9	0.723

***p < 0.05, statistically significant**

Physical activity showed a clear difference between the two groups. Most diabetic NAFLD participants were sedentary (80.5%), while in the non-diabetic group, only 65.2% were sedentary. 'This difference was statistically significant (p = 0.045)' highlighting the contribution of physical inactivity to metabolic dysfunction.

Dietary patterns revealed that 75% of diabetic NAFLD subjects consumed a high-fat diet compared to 54.3% among non-diabetic individuals (p = 0.048). Smoking habits were comparable in both groups, showing no significant association.

A strong positive family history of diabetes was seen in 61.1% of diabetic NAFLD cases versus 26.1% among non-diabetic participants (p = 0.002), confirming the genetic predisposition. Family history of liver disease was not significantly different between groups.

Table 2. Clinical and Lifestyle Profile of Participants

Variable	'NAFLD without Diabetes (n=46)'	'NAFLD with Diabetes (n=36)'	p-value
Physical activity (Sedentary/Active)	30 / 16	29 / 7	0.045*
Dietary pattern (High-fat diet)	25 (54.3%)	27 (75%)	0.048*
Smoking (Yes/No)	9 / 37	10 / 26	0.405
Family history of diabetes	12 (26.1%)	22 (61.1%)	0.002*
Family history of liver disease	8 (17.4%)	9 (25%)	0.403

***p < 0.05, statistically significant**

Biochemical parameters showed clear metabolic alterations in diabetic NAFLD participants. The mean Alanine Aminotransferase (ALT) level was 71.9 ± 18.4 IU/L in diabetic subjects compared to 58.2 ± 15.6 IU/L in non-diabetics, a statistically significant difference ($p = 0.001$).

Aspartate Aminotransferase (AST) also showed higher mean levels among diabetics (52.8 ± 13.1 IU/L) than in non-diabetics (45.3 ± 11.2 IU/L) with $p = 0.018$. Although the ALT/AST ratio was slightly higher in diabetics (1.36 ± 0.28) than non-diabetics (1.28 ± 0.31), this difference was not statistically significant.

Blood glucose parameters reflected expected differences: fasting blood glucose and HbA1c were significantly elevated in diabetic participants ($p < 0.001$ for both). Lipid profile assessment showed significantly higher triglyceride and LDL levels and lower HDL levels among diabetics, all indicating increased cardiovascular and hepatic risk.

Table 3. Biochemical Profile of Study Participants

Parameter	'NAFLD without Diabetes (n=46)'	'NAFLD with Diabetes (n=36)'	p-value
ALT (IU/L, mean ± SD)	58.2 ± 15.6	71.9 ± 18.4	0.001*
AST (IU/L, mean ± SD)	45.3 ± 11.2	52.8 ± 13.1	0.018*
ALT/AST ratio	1.28 ± 0.31	1.36 ± 0.28	0.211
Fasting Blood Glucose (mg/dL)	95.7 ± 9.3	148.4 ± 22.6	<0.001*
HbA1c (%)	5.6 ± 0.4	7.8 ± 0.6	<0.001*
Triglycerides (mg/dL)	162.5 ± 34.8	188.7 ± 45.1	0.008*
HDL (mg/dL)	45.2 ± 6.7	39.8 ± 5.5	0.002*
LDL (mg/dL)	123.6 ± 22.1	139.4 ± 25.6	0.007*

***p < 0.05, statistically significant**

Correlation analysis demonstrated a significant positive relationship between ALT levels and several metabolic risk factors. ALT showed a moderate positive correlation with BMI ($r = 0.426$, $p = 0.001$), fasting glucose ($r = 0.512$, $p < 0.001$), HbA1c ($r = 0.484$, $p < 0.001$), and triglycerides ($r = 0.372$, $p = 0.002$).

A negative correlation was noted between ALT and HDL cholesterol ($r = -0.288$, $p = 0.009$), suggesting that higher ALT levels were associated with a less favorable lipid profile. Elevated ALT levels represent more than just a liver enzyme abnormality. ALT fluctuations connote more extensive metabolic disturbances including insulin resistance and dyslipidemia.

Table 4. Correlation Between ALT Levels and Metabolic Parameters

Parameter	Correlation coefficient (r)	p-value
ALT vs BMI	0.426	0.001*
ALT vs Fasting Glucose	0.512	<0.001*
ALT vs HbA1c	0.484	<0.001*
ALT vs Triglycerides	0.372	0.002*
ALT vs HDL	-0.288	0.009*

***p < 0.05, statistically significant**

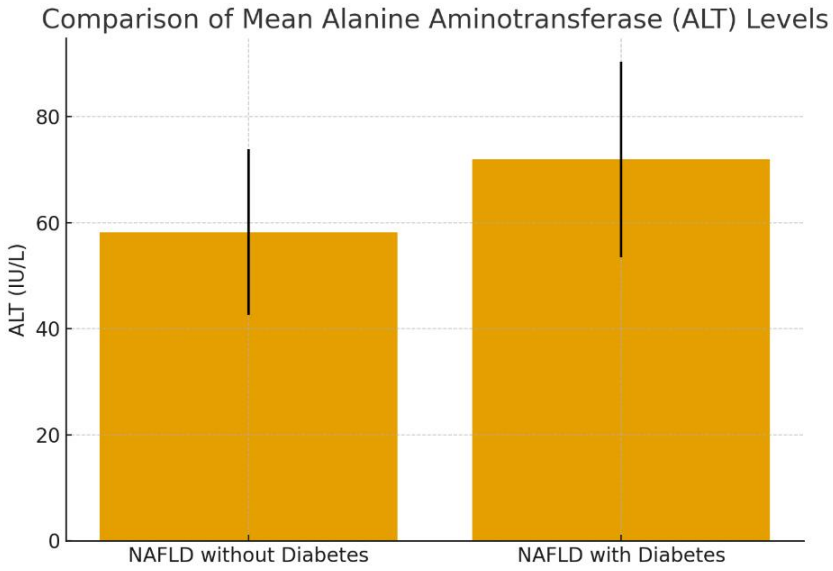

Figure 1: Graph comparing the mean ALT levels between participants with and without diabetes mellitus in NAFLD.

DISCUSSION

This study examined the physiological and biochemical role of ALT in NAFLD patients and its association with diabetes mellitus. For patients with NAFLD and diabetes mellitus, the study stated, 'ALT levels were significantly higher. Increased ALT levels reflect hepatic injury and underline metabolic dysfunction.'

From a demographic perspective, older and overweight people were more likely to have diabetes associated with NAFLD. This is consistent with the literature as older age and obesity are the key determinants of hepatic fat accumulation. Obesity, diabetes, and the concomitant central fat distribution syndrome significantly increase risks. Mechanistically, central obesity is a driver of insulin resistance and therefore promotes the deposition of hepatic lipids. This likely stems from the NAFLD and type 2 diabetes metabolic overlap, with insulin resistance, dysfunctional adipose tissue, and chronic low-grade inflammation as key triggers for both [13, 14].

A notable finding was the significant association between sedentary lifestyle and high-fat dietary intake among diabetic NAFLD patients. These observations are consistent with the studies emphasized that lifestyle factors play a decisive role in the development and progression of fatty liver disease [15, 16]. The presence of a family history of diabetes among most diabetic participants also mirrors evidence from studies highlighting genetic predisposition as an additional contributing factor. This suggests that lifestyle modification and targeted family-based preventive strategies could have a substantial impact on disease control [17].

Biochemical analysis revealed significantly higher ALT and AST levels in diabetic NAFLD patients. This aligns with the observations of studies described elevated aminotransferases as surrogate markers of hepatic inflammation and steatosis in metabolic disorders. The close relationship between raised ALT and glycemic indices such as fasting blood glucose and HbA1c in this study reinforces the hypothesis that ALT can serve as an early indicator of metabolic stress, even before overt hepatic decompensation occurs. The positive correlations found between ALT, BMI, triglycerides, and fasting glucose in this study further support the role of ALT as a biochemical bridge between hepatic and systemic metabolic dysfunction [18].

In contrast to some earlier studies, where no significant association between ALT and lipid fractions was reported, this study observed a significant positive correlation between ALT and triglyceride levels, along with a negative correlation with HDL cholesterol. This difference may reflect population-specific dietary patterns and differences in glycemic control across study groups. The lower HDL and higher triglyceride levels in the diabetic NAFLD group suggest that hepatic fat

accumulation parallels the degree of dyslipidemia, contributing to the overall metabolic syndrome burden [19].

ALT's diagnostic potential in ascertaining metabolic risk remains significant. An increased ALT – even within the upper-normal range may suggest a greater propensity for developing type 2 diabetes mellitus. This further reinforces the need for clinicians to view liver enzymes not merely as indicators of liver damage, but as potential markers of metabolic discordance that warrant further investigation [20].

Finding the intersection of chronic diseases like diabetes and fatty liver disease as they develop in certain regions points to possible shifts in eating habits, urbanization, and inactivity in those regions. Valuing the collaboration of both the Medicine and Community Medicine departments as well as the integration of clinical and lifestyle factors, will aid in the biochemical reasoning while also coming from the perspective of avoidance.

Future studies will help combine community health frameworks with the utilization of biochemical markers such as ALT. The findings illustrate that NAFLD should be approached with strategies that transcend mere liver-centric care and call for a comprehensive metabolic and lifestyle framework. This understanding will likely inform future interventions that will be community-centered and address early screening and modification of metabolic health.

CONCLUSION

This research verified that elevated levels of ALT correlate with non–alcoholic fatty liver disease in patients with type 2 diabetes mellitus. There was a strong correlation ALT with body mass index, fasting glucose, HbA1c, and triglyceride levels, which confirms that ALT is a biochemical parameter that reflects liver and multi system metabolic disorders.

From a preventive perspective, this research urges the adoption of lifestyle changes, routine exercise, and dietary changes to reduce the accumulation of fat in the liver and the glycemic load. This suggests that the integration of clinical medicine and community–based health education is critical in addressing the diabesity and fatty liver syndromes.

REFERENCES

1. Moriles, K.E. and S.A. Azer, *Alanine amino transferase.* 2020.
2. Cuomo, P., et al., *Role of branched-chain amino acid metabolism in type 2 diabetes, obesity, cardiovascular disease and non-alcoholic fatty liver disease.* 2022. **23**(8): p. 4325.
3. Ndrepepa, G.J.J.o.L. and P. Medicine, *Aspartate aminotransferase and cardiovascular disease—a narrative review.* 2021. **6**.
4. Kelardeh, B.M., et al., *Effects of non-linear resistance training and curcumin supplementation on the liver biochemical markers levels and structure in older women with non-alcoholic fatty liver disease.* 2020. **24**(3): p. 154-160.
5. Zhu, W., et al., *Higher serum uric acid to HDL-cholesterol ratio is associated with onset of non-alcoholic fatty liver disease in a non-obese Chinese population with normal blood lipid levels.* 2022. **22**(1): p. 196.
6. Zhang, Y. and H.J.B.o. Liu, *Cross-sectional association between prolactin levels and non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus: a retrospective analysis of patients from a single hospital in China.* 2022. **12**(10): p. e062252.
7. Bahrami, M., et al., *The effect of melatonin on treatment of patients with non-alcoholic fatty liver disease: a randomized double blind clinical trial.* 2020. **52**: p. 102452.
8. Pouwels, S., et al., *Non-alcoholic fatty liver disease (NAFLD): a review of pathophysiology, clinical management and effects of weight loss.* 2022. **22**(1): p. 63.
9. Savic, D., et al., *The importance of the fatty acid transporter L-carnitine in non-alcoholic fatty liver disease (NAFLD).* 2020. **12**(8): p. 2178.
10. Seth, A., et al., *Severe obesity is associated with liver disease severity in pediatric non-alcoholic fatty liver disease.* 2020. **15**(2): p. e12581.

11. Mirhafez, S.R., et al., *The effect of curcumin phytosome on the treatment of patients with non-alcoholic fatty liver disease: a double-blind, randomized, placebo-controlled trial*, in *Pharmacological properties of plant-derived natural products and implications for human health*. 2021, Springer. p. 25-35.
12. Yasmin, T., et al., *Metformin treatment reverses high fat diet-induced non-alcoholic fatty liver diseases and dyslipidemia by stimulating multiple antioxidant and anti-inflammatory pathways.* 2021. **28**: p. 101168.
13. Dong, Y., et al., *Assessment of left ventricular function in type 2 diabetes mellitus patients with non-alcoholic fatty liver disease using three-dimensional speckle-tracking echocardiography.* 2020. **23**(1).
14. Wang, W., X. Zhong, and J.J.I.J.o.M.M. Guo, *Role of 2-series prostaglandins in the pathogenesis of type 2 diabetes mellitus and non-alcoholic fatty liver disease.* 2021. **47**(6): p. 114.
15. Lin, H., et al., *Pharmacokinetic and metabolomic analyses of Mangiferin calcium salt in rat models of type 2 diabetes and non-alcoholic fatty liver disease.* 2020. **21**(1): p. 59.
16. Chen, L., et al., *Critical overview of hepatic factors that link non-alcoholic fatty liver disease and acute kidney injury: physiology and therapeutic implications.* 2022. **23**(20): p. 12464.
17. Yang, T., et al., *Amelioration of non-alcoholic fatty liver disease by sodium butyrate is linked to the modulation of intestinal tight junctions in db/db mice.* 2020. **11**(12): p. 10675-10689.
18. Elkattawy, H.A., et al., *Rho-kinase inhibition ameliorates non-alcoholic fatty liver disease in type 2 diabetic rats.* 2022. **71**(5): p. 615.
19. Monserrat-Mesquida, M., et al., *Oxidative stress and pro-inflammatory status in patients with non-alcoholic fatty liver disease.* 2020. **9**(8): p. 759.
20. Musazadeh, V., et al., *Effect of probiotics on liver enzymes in patients with non-alcoholic fatty liver disease: an umbrella of systematic review and meta-analysis.* 2022. **9**: p. 844242.