Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Serum Aminotransferase Level among Non-Alcoholic Fatty Liver Disease/Metabolism-Associated Steatotic Liver Disease Patients of North East India

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Abstract

Introduction: Non alcoholic fatty liver disease or Metabolism associated steatotic liver disease is emerging as an increasingly common liver disease worldwide, especially in association with obesity, diabetes and metabolic syndrome.

Aim of the Study: This study aims at assessing serum aminotransferase enzymes: aspartate aminotransferase (AST) and alanine aminotransferase (ALT)

Methods: The study was conducted in 628 patients with NAFLD diagnosed by abdominal ultrasonography. The patients were categorized into three grades based on the extent of liver fat accumulation. The patients were divided into Grade I (mild fat accumulation of 5-33%), Grade II (moderate fat accumulation of 34-66%), and Grade III (severe fat accumulation of more than 66%). Result : the work conducted showed that serum AST and ALT concentrations rose in proportion to the severity of NAFLD. In Grade I, the mean AST was 35.06 U/L and mean ALT was 39.17 U/L, while in Grade III the levels increased to 248.00 U/L of AST and 286.00 U/L of ALT, which shows severe liver inflammation. Further it was observed that, aminotransferase alterations were higher amongst male patients in all grades while the female patients' results were relatively low.

Discussion: Aminotransferase levels was normal in many grade I patients arguing the fact that normal AST and ALT levels may not effectively rule out early NAFLD. It reflects that though aminotransferase level may not increase in early NAFLD, but in later stage aminotransferase level increases invariably and requiring further noninvasive diagnostic evaluation.

Conclusion: Aminotransferase level may vary in different area or community and standardization and validation is very much required . Though aminotransferase is single independent marker of inflammation of liver but confirmation by other associated non invasive marker is required.

Key words: Non-Alcoholic Fatty Liver Disease (NAFLD), Aminotransferases, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Liver Biomarkers, Metabolism Associated Steatotic Liver Disease (MSLD)

INTRODUCTION

The liver, the major internal organ in the human body, is a vigorous organ accountable for numerous metabolic, excretory, and synthetic functions. Structurally, it is a spongy mass composed of two lobes, situated in the upper right quadrant of the abdomen. The liver is pivotal in maintaining homeostasis and metabolic regulation, including the metabolism of fats, carbohydrates, and proteins (Sherwood, 2015). In addition, it detoxifies the blood, produces bile necessary for digestion, stores glycogen for energy, and synthesizes critical proteins such as albumin and clotting factors (Guyton and Hall, 2016).[1-5]

Access this article online

www.ijss-sn.com

Month of Submission : 10-2024
Month of Peer Review : 11-2024
Month of Acceptance : 12-2024
Month of Publishing : 12-2024

Non-alcoholic fatty liver disease (NAFLD) is characterized by the accumulation of fat in liver cells, accounting for more than 5% of liver mass, in the absence of significant

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alcohol drinking (Chalasani *et al*., 2018). NAFLD represents a spectrum of liver disorders vacillating from simple steatosis (non-alcoholic fatty liver or NAFL) to more severe forms such as non-alcoholic steatohepatitis (NASH), which can grow to fibrosis, cirrhosis, or even hepatocellular carcinoma (Adams *et al*., 2017).[6-10]

The global prevalence of NAFLD is appraised to be about 25%, but it varies significantly across different populations and geographical regions (Younossi *et al*., 2016). Factors such as ethnicity, lifestyle, genetic predisposition, and socioeconomic status influence these variations. For instance, studies show higher NAFLD rates in populations with increased incidences of obesity, diabetes, and metabolic syndrome, especially in Western countries and developing regions where sedentary lifestyles and high-calorie diets are prevalent (Younossi *et al*., 2018).

The development of NAFLD is intricately related to metabolic dysfunction, particularly insulin resistance and obesity. Insulin resistance promotes lipolysis, leading to an increased influx of free fatty acids into the liver. These fatty acids are then re-esterified to triglycerides, causing hepatic steatosis (Friedman *et al*., 2018). In addition, oxidative stress, inflammation, and mitochondrial dysfunction play significant roles in the development of simple steatosis to NASH (Friedman *et al*., 2018).

Genetic factors also contribute to NAFLD susceptibility. For example, variations in the PNPLA3 gene (patatin-like phospholipase domain-containing protein 3) are related to increased fat accretion in the liver and a greater risk of fibrosis (Romeo *et al*., 2008). These genetic predispositions, combined with environmental issues, emphasize the complexity of NAFLD pathogenesis.[11-13]

NAFLD Grading and Classification

Imaging techniques such as ultrasonography play a critical role in identifying and grading NAFLD (Dasarathy *et al*., 2011). Ultrasonography is a non-invasive, extensively existing, and cost-effective diagnostic tool used to detect hepatic steatosis and classify NAFLD into the following grades:

- Grade I (mild): Fat accumulation of 5–33%
- Grade II (moderate): Fat accumulation of 34–66%
- Grade III (severe): Fat accumulation >66%.

This grading system is vital for measuring the severity of the disease and determining the appropriate clinical management approach. While ultrasonography provides a preliminary assessment, liver biopsy remains the gold standard for identifying and differentiating between simple steatosis and NASH. However, due to their invasive nature and potential complications, non-invasive biomarkers such as serum aminotransferases (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) are usually used as screening tools (European Association for the Study of the Liver, 2016).

Serum aminotransferases, namely AST and ALT, are enzymes that play a crucial role in amino acid metabolism. They are primarily found in the liver, and their levels in the blood increase when liver cells are spoiled or inflamed (Botros and Sikaris, 2013). ALT is considered more liver-specific than AST, as AST is also present in other tissues such as the heart and skeletal muscles. Elevated levels of these enzymes can specify liver injury and are commonly used in the screening and monitoring of liver diseases, with NAFLD (Kim *et al*., 2015).

These tests are widely available and provide crucial insights into liver function and damage. However, it is important to note that normal AST and ALT levels do not necessarily eliminate NAFLD, as some individuals with NAFLD or even NASH may present with normal enzyme levels. Studies have shown that a significant amount of NAFLD patients, particularly those with mild disease, may have normal serum aminotransferase values (Miele *et al*., 2017).

The occurrence of NAFLD has been rising globally, reflecting the growing incidence of obesity and metabolic syndrome. In North America and Europe, the occurrence is estimated to be around 24–32%, whereas in Asia, it ranges from 15 to 30% (Eslam *et al*., 2020). This upward trend is driven by lifestyle changes such as improved intake of high-calorie foods and reduced physical activity. As urbanization and economic development progress in many countries, these factors contribute to a sedentary lifestyle, leading to higher rates of obesity and metabolic disorders, which are closely linked to NAFLD (Wong *et al*., 2018).

Ultrasonography is widely used for the diagnosis and grading of NAFLD due to its non-invasive nature, accessibility, and cost-effectiveness. It allows clinicians to detect liver fat and evaluate its extent, providing a reliable method for NAFLD screening. Studies indicate that ultrasonography has a high sensitivity (89%) and specificity (93%) for sensing moderate-to-severe fatty liver when liver fat content is above 20% (Hernaez *et al*., 2011).

In cases where further differentiation between simple steatosis and NASH is required, more advanced imaging techniques such as magnetic resonance imaging or transient elastography, and invasive methods, such as liver biopsy, are employed (Hamaguchi *et al*., 2007).

In patients with NAFLD, elevated ALT levels are often more pronounced than AST, a pattern that is typically reversed in advanced liver diseases such as cirrhosis (Chalasani *et al*., 2018).

Research indicates that although elevated aminotransferase levels correlate with the presence of NAFLD, they are not exclusively specific to this condition and may also rise due to other factors such as muscle injury, medication use, and other liver conditions (Neuman *et al*., 2014). While aminotransferase levels provide valuable insights into liver health, they are not entirely accurate in predicting the severity or presence of NAFLD, particularly NASH. Normal levels of AST and ALT can exist in a significant amount of NAFLD patients, especially in those with metabolic syndrome or early-stage disease (Kim *et al*., 2017).

Future research aims to identify more accurate and specific biomarkers that can reliably differentiate between the stages of NAFLD and predict the risk of development to advanced liver diseases. Biomarkers such as cytokeratin-18, adipokines, and genetic markers (e.g., PNPLA3 polymorphisms) are currently under investigation for their potential use in diagnosing and monitoring NAFLD (Neuman *et al*., 2014)

Aim and Objectives

1. To evaluate serum aminotransferase (AST and ALT) levels among NAFLD patients in North East India
2. To review the scope of serum aminotransferase as a predictor/biomarker of NAFLD.

MATERIALS AND METHODS

Adults of both sexes, ages ranging from 18 years to 60 years, with ultrasonography findings of NAFLD, and who had given their written consent were selected for the study. A total of 655 male and female patients were selected for the study. The study was conducted between October 2022 and March 2024 at Agartala, Tripura, a small state in the Northeast Region of India. The height was measured in meters (mt) and weight in kilograms (kg) and blood samples were collected for further laboratory investigation. In the laboratory tests were performed in a full auto biochemistry analyzer. Blood sugar, urea, S. creatinine, bilirubin, AST, and ALT were estimated along with viral marker tests (HBsAg, Anti HCV, and HIV). All the results were recorded properly. After applying exclusion criteria 628 patient samples were considered for the study. Results of AST and ALT (modified IFCC method) were tabulated and analyzed. Normal value of AST and ALT generally followed is <40 U/L

RESULTS

Table 1 illustrates the distribution of 628 NAFLD patients across different age groups and genders, revealing key demographic patterns. It categorizes patients into four age ranges: 18–30, 31–40, 41–50, and 51–60 years. The highest concentration of patients is in the 51–60 years group (29.46%), followed by 41–50 years (27.39%), indicating that NAFLD is more prevalent among older individuals. Gender-wise, males comprise the majority, making up 63.38% of the total patient population, with the highest percentage (31.16%) also in the 51–60 years category. Females account for 36.62% overall, showing a similar trend of higher prevalence in the older age group (26.52% in the 51–60 years bracket). The data highlights a gender and age-related pattern, with older males being more affected by NAFLD, suggesting the need for age and gender-specific medical attention and intervention.

Table 2 presents the distribution of NAFLD patients (totaling 628) based on the severity of their condition (Grades I, II, and III) and their corresponding AST and ALT levels.

The majority of patients fall under Grade I (71.34%), with an AST range of 19–106 U/L and a mean AST level of 35.06 U/L. The ALT range for this grade is 23–119 U/L, with a mean of 39.17 U/L, indicating mild enzyme elevation. Grade II accounts for 27.71% of patients, showing a wider AST range of 31–229 U/L and a higher mean value of 62.78 U/L. ALT levels in this group range from 36 to 271 U/L, with a mean of 75.65 U/L, reflecting more significant liver enzyme elevation. Grade III, the most severe category, includes only 0.95% of patients, with AST levels ranging from 92 to 314 U/L and an exceptionally high mean AST of 248 U/L. ALT levels for this grade vary between 102 and 403 U/L, with a mean of 286 U/L, indicating severe liver damage. This table highlights how increasing NAFLD severity correlates with elevated AST and ALT levels, underscoring their role as indicators of liver damage (Figure 1).

Table 3 provides an analysis of AST and ALT levels among NAFLD patients, categorized by disease grade (I, II, and III) and gender. In Grade I, males make up 58.71% (263 patients) and females 41.29% (185 patients). Males in this group exhibit AST levels ranging from 22 to 106 U/L (mean: 35.96 U/L) and ALT levels from 25 to 119 U/L (mean: 40.54 U/L), whereas females show slightly lower ranges and means for both AST (19–102 U/L, mean: 33.78 U/L) and ALT (23–106 U/L, mean: 37.22 U/L). In Grade II, the majority are males (74.14%, 129 patients) with AST levels ranging from 35 to 228 U/L (mean: 63.83 U/L) and ALT from 36 to 269 U/L (mean: 74.28 U/L). Females in this grade represent 25.86% (45 patients) with slightly lower mean values for AST (59.77 U/L) and ALT (69.79 U/L). Grade III only includes six male patients (100%), showing markedly elevated AST (92–354 U/L, mean: 248.00 U/L) and ALT (102–403 U/L, mean: 286.00 U/L), with no female patients in this category. This pattern indicates higher severity and enzyme levels in males across all grades (Figure 2).

Table 1: Total male and female patients – 628: Age group-wise percentage

Age group	18–30 years		31–40 years		41–50 years		51–60 years		Total	
Sex	Number of Pt.	%	Number of Pt.	%	Number of Pt.	%	Number of Pt.	%	Number of Pt.	%
Male	64	16.08	95	23.87	115	28.89	124	31.16	398	63.38
Female	54	23.48	58	25.22	57	24.78	61	26.52	230	36.62
Total	118	18.79	153	24.36	172	27.39	185	29.46	628	

Table 2: Grade-wise AST and ALT level and mean value: Total patients 628

NAFLD grade	Number of patients	%	AST range (U/L)	Mean AST (U/L)	ALT range (U/L)	Mean ALT (U/L)
Grade I	448	71.34	19–106	35.06	23–119	39.17
Grade II	174	27.71	31–229	62.78	36–271	75.65
Grade III	06	0.95	92–314	248.00	102–403	286.00

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, NAFLD: Non-alcoholic fatty liver disease

Table 3: Grade-wise male and female AST and ALT level and mean value

Grade	Sex	Number of patients	%	AST range (U/L)	Mean AST (U/L)	ALT range (U/L)	Mean ALT (U/L)
I	Male	263	58.71	22–106	35.96	25–119	40.54
	Female	185	41.29	19–102	33.78	23–106	37.22
II	Male	129	74.14	35–228	63.83	36–269	74.28
	Female	45	25.86	31–229	59.77	34–268	69.79
III	Male	06	100.00	92–354	248.00	102–403	286.00
	Female	00	00.00	-	-	-	-

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

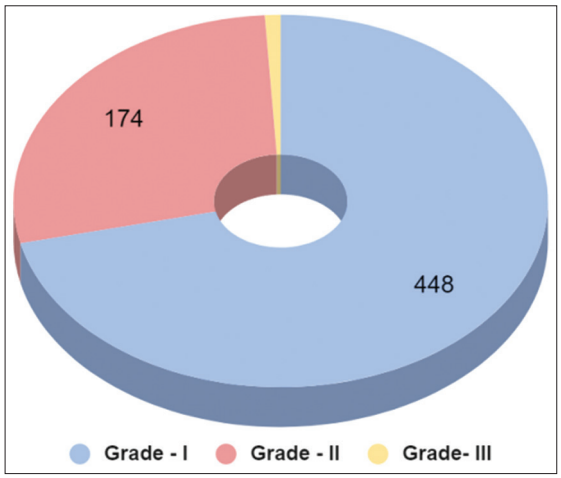

Figure 1: Grade-wise aspartate aminotransferase, and alanine aminotransferase level and mean value: Total patient 628

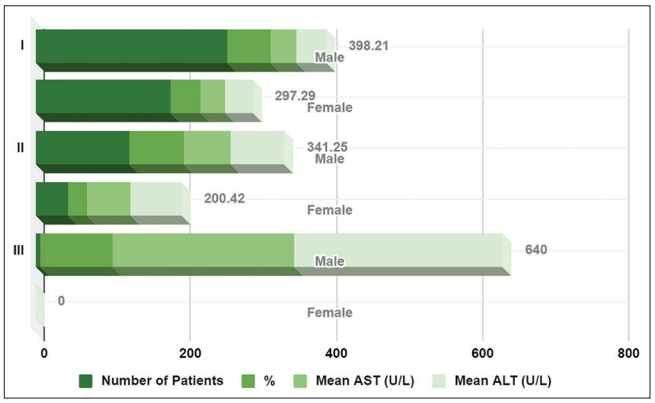

Figure 2: Grade-wise male and female aspartate aminotransferase and alanine aminotransferase level and mean value

DISCUSSION

The study reveals that the prevalence of NAFLD upsurges significantly with age, with the majority of patients falling into the 51–60 years age group (29.46%), followed closely by the 41–50 years group (27.39%). This is consistent with the literature, indicating that the incidence of NAFLD rises with age, as older individuals tend to accumulate more hepatic fat due to factors such as metabolic syndrome and insulin confrontation (Younossi *et al*., 2016). Furthermore, males represent 63.38% of the total patient population, suggesting that gender may play a significant role in NAFLD prevalence, which aligns with findings that men are more predisposed to NAFLD due to differences in fat distribution and hormonal influences (Yki-Järvinen, 2014).[14-16]

Table 2 provides insights into the biochemical profiles of these patients, categorized by NAFLD grades. Grade I accounts for the majority (71.34%), with AST and ALT levels generally within mild-to-moderate elevation ranges (mean AST: 35.06 U/L; mean ALT: 39.17 U/L). These levels indicate that while liver damage is present, it is less severe in the early stages of

NAFLD. Grade II, comprising 27.71% of the patient sample, shows a significant increase in mean AST (62.78 U/L) and ALT (75.65 U/L) levels, suggesting that as the disease progresses, enzyme levels elevate due to worsening liver inflammation and fibrosis (Neuman *et al*, 2014).[17-19]

The most severe category, Grade III, involves only 0.95% of patients, but these individuals exhibit dramatically elevated enzyme levels (mean AST: 248.00 U/L; mean ALT: 286.00 U/L). This suggests extensive liver damage, likely indicating advanced fibrosis or cirrhosis. The small number of Grade III cases is consistent with the understanding that only a minority of NAFLD patients develop severe liver disease (Schwenger *et al*., 2018). However, the marked elevation in enzyme levels underscores the need for close monitoring and early intervention in patients showing rising AST and ALT values.

The overall correlation between higher NAFLD grades and increased AST and ALT levels supports the role of these enzymes as biomarkers for liver damage and disease progression in NAFLD. This finding is also supported by other studies that recommend using aminotransferase levels for initial screening and monitoring of liver function in suspected NAFLD cases (Chalasani *et al*., 2018).[20-22]

CONCLUSION

NAFLD is a progressively widespread liver disease, closely related to metabolic syndrome, obesity, and diabetes. The disease spectrum ranges from simple steatosis to severe stages such as NASH, fibrosis, and cirrhosis, highlighting the need for effective diagnostic and monitoring strategies. Ultrasonography remains a primary diagnostic tool due to its non-invasive, accessible, and cost-effective nature, allowing for grading based on fat accumulation levels. However, while serum aminotransferases (AST and ALT) serve as common biomarkers for assessing liver function and damage, they have limitations. Normal levels of these enzymes do not entirely rule out NAFLD, as some patients, especially those with mild disease, may present with values within the normal range. To address these limitations, further research is needed to identify more sensitive and specific biomarkers for early detection and differentiation of NAFLD stages. In addition, given the rising global burden of NAFLD, targeted lifestyle interventions, including dietary modifications and increased physical activity, are essential for managing and preventing disease progression. Understanding the demographic and biochemical patterns associated with NAFLD will aid in developing more effective screening programs and therapeutic approaches to mitigate the long-term impact of this condition on global health.

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How to cite this article: Bhaumik R, Bhat SA, Bhaumik P. Serum Aminotransferase Level among Non-Alcoholic Fatty Liver Disease/ Metabolism-Associated Steatotic Liver Disease Patients of North East India. Int J Sci Stud 2024;12(9):49-54.

Source of Support: Nil, **Conflicts of Interest:** None declared.