



Impact of Non-Alcoholic Fatty Liver Disease (NAFLD) on Biochemical Parameters of Patients

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Abstract: *Background:* Non-Alcoholic Fatty Liver Disease (NAFLD) is a growing health concern globally, with varying prevalence and severity. This study aimed to investigate the demographic distribution, severity grading, associated risk factors, and biochemical profiles in patients with NAFLD. *Methods:* This cross-sectional study was conducted at Comilla Medical College and Hospital, involving 50 adult patients diagnosed with NAFLD. The study assessed demographic characteristics, NAFLD grading through ultrasound, and the association of risk factors and biochemical markers with NAFLD severity. *Result:* The study cohort had a higher representation of older adults (56% aged 55 years or older) and females (64%). The majority of participants (54%) were diagnosed with Grade 1 NAFLD, while Grades 2 and 3 were observed in 32% and 14% of participants, respectively. Significant associations were found between higher NAFLD grades and risk factors such as hypertension, BMI ≥ 23 kg/m², and a weight-to-height ratio >0.8 . Elevated levels of total cholesterol, ALT, AST, and ALP were significantly associated with higher NAFLD grades, whereas HDL-C, LDL-C, and triglycerides levels did not show a significant correlation with disease severity. *Conclusion:* This study underscores the prevalence of NAFLD in older adults and females, with a higher occurrence of less severe disease forms. The progression of NAFLD severity is closely linked with specific risk factors and biochemical markers. These findings highlight the importance of considering demographic characteristics and individual risk profiles in the management and treatment of NAFLD.

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Article at a glance:

Study Purpose: To explore the demographic distribution, severity, risk factors, and biochemical profiles in NAFLD patients.

Key findings: NAFLD is more common in older adults (56%) and females (64%). Higher severity is linked to hypertension, BMI ≥ 23 , and elevated cholesterol, ALT, AST, and ALP levels.

Newer findings: This study emphasizes the correlation between specific risk factors and biochemical markers with NAFLD severity, offering insights for more targeted management.

Abbreviations: NAFLD - Non-Alcoholic Fatty Liver Disease, BMI - Body Mass Index, ALT - Alanine Aminotransferase, AST - Aspartate Aminotransferase, ALP - Alkaline Phosphatase.



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INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) has emerged as the most prevalent form

of chronic liver disease globally, intricately linked with metabolic syndromes such as obesity and diabetes.^{1,2} Characterized by excessive fat

accumulation in hepatocytes, NAFLD represents a spectrum of liver conditions ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), potentially progressing to cirrhosis and hepatocellular carcinoma.^{2,3} The global burden of NAFLD is a reflection of the rising prevalence of obesity and sedentary lifestyles, particularly in Western populations.^{2,4} The pathophysiology of NAFLD is complex and multifactorial, involving genetic predisposition, insulin resistance, oxidative stress, and lipid metabolism abnormalities.⁵ This complexity is further compounded by the disease's association with other metabolic disorders, including type 2 diabetes mellitus (T2DM) and cardiovascular diseases, positioning NAFLD not only as a liver-specific ailment but also as a systemic condition.^{3,6}

The progression from NAFL to NASH and further stages remains a critical area of research, with the transition mechanisms still not fully understood.^{2,7} Biochemical parameters play a pivotal role in the diagnosis, grading, and monitoring of NAFLD. Traditional liver function tests, such as serum levels of aminotransferases (ALT and AST), gamma glutamyl transferase (GGT), and bilirubin, are commonly used, albeit with limitations in sensitivity and specificity.⁸ Recent studies have highlighted the potential of novel biomarkers, including lipid droplet-associated proteins and inflammatory markers, in providing a more accurate assessment of NAFLD severity and progression (1,9). For instance, the ratio of mitochondrial AST to total AST has been suggested as a differential diagnostic tool between alcoholic fatty liver disease and NAFLD (10). The clinical significance of these biochemical markers extends beyond mere diagnostic utility. They offer insights into the metabolic derangements associated with NAFLD and its comorbid conditions. Elevated aminotransferase levels, for instance, have been linked to insulin resistance and increased cardiovascular risk (11). Furthermore, the interplay between NAFLD and other systemic conditions, such as the impact of COVID-19 on liver function and the role of the gut microbiome in metabolic diseases, underscores the need for a holistic approach in managing NAFLD (6,12,13). Despite advancements in understanding NAFLD, several gaps remain in the literature, particularly concerning the correlation between NAFLD grades

and specific biochemical parameters. While some studies have explored the relationship between dietary patterns and NAFLD progression, the direct impact of these patterns on liver biochemistry is not fully elucidated (4,5). Additionally, the role of emerging biomarkers in differentiating between NAFLD stages and their prognostic value in clinical practice requires further investigation (9). The current study aims to address these gaps by examining the impact of NAFLD grade on various biochemical parameters in patients. By doing so, it seeks to contribute to a more nuanced understanding of NAFLD pathophysiology and to aid in the development of more targeted therapeutic strategies. The findings of this study are expected to have significant implications for the clinical management of NAFLD, offering a more comprehensive approach to diagnosis, grading, and monitoring of this increasingly prevalent disease.

METHODS

This cross-sectional was conducted at the Department of Medicine, Comilla Medical College and Hospital (CoMCH), Comilla, over a period of six months from July to December 2012. The study included 50 adult patients purposively, both male and female, diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD) and admitted to the Department of Medicine at CoMCH. Inclusion criteria were patients diagnosed with NAFLD and admitted to the Department of Medicine at Comilla Medical College and Hospital during the specified study period, and patients willing to provide informed consent. Exclusion criteria included history of alcohol consumption, presence of known hepatic diseases other than NAFLD, positive test results for Hepatitis B surface antigen (HBsAg) and Anti-Hepatitis C virus (Anti-HCV), history of ingestion of hepatotoxic drugs, and unwillingness to provide informed consent. NAFLD diagnosis was confirmed through ultrasound examination of the liver. Sonographic findings were graded based on severity into three grades. Grade 1 was identified by a slight diffuse increase in fine echoes in the liver parenchyma with normal visualization of the diaphragm and intrahepatic blood vessel borders. Grade 2 was characterized by a moderate diffuse increase in fine echoes with slightly impaired visualization of the diaphragm and intrahepatic blood vessel borders. Grade 3 was

marked by a significant increase in fine echoes with poor or non-visualization of the diaphragm, intrahepatic blood vessel borders, and the posterior

lobe of the liver. Data were collected retrospectively from hospital information system (HIS).

RESULTS

Table 1: Distribution of participants by demographic characteristics (N=50)

Variables	Frequency	Percentage
Age		
<55 years	22	44%
≥ 55 years	28	56%
Gender		
Male	18	36%
Female	32	64%

The demographic characteristics of the study participants (N=50) are presented in Table 1. The age distribution of the participants revealed that a majority, 28 (56%), were aged 55 years or older, while 22 (44%) were under 55 years. Regarding

gender distribution, the study had a higher representation of females, with 32 (64%) of the participants being female, compared to 18 (36%) male participants.

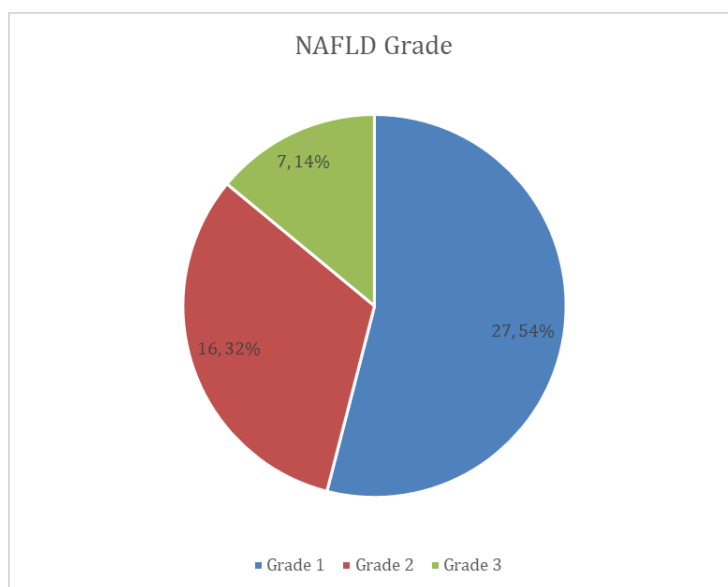


Figure 1: Distribution of participants by grade of Non-Alcoholic Fatty Liver Disease (NAFLD) (N=50)

Figure 1 illustrates the distribution of the study participants (N=50) according to the grade of Non-Alcoholic Fatty Liver Disease (NAFLD) they were diagnosed with. The majority of the participants, 27 (54%), were diagnosed with Grade 1 NAFLD. This

was followed by 16 (32%) participants who were classified as having Grade 2 NAFLD. The smallest group consisted of 7 (14%) participants who were diagnosed with Grade 3 NAFLD.

Table 2: Distribution of risk factors among different grade of NAFLD (N=50)

Variables	Grade 1 (n=27)		Grade 2 (n=16)		Grade 3 (n=7)		p-value
	n	%	n	%	n	%	
Smoking	11	40.74%	8	50.00%	4	57.14%	>0.05
Hypertension	17	62.96%	11	68.75%	7	100.00%	<0.05

BMI ≥ 23kg/m ²	15	55.56%	16	100.00%	7	100.00%	<0.001
Weight: Height ration >0.8	23	85.19%	16	100.00%	7	100.00%	<0.01
Family history of CVD	13	48.15%	9	56.25%	5	71.43%	>0.05

Among the 27 individuals classified as Grade 1 NAFLD, 40.74% were smokers, 62.96% had hypertension, 55.56% had a BMI ≥ 23 kg/m², 85.19% had a weight-to-height ratio > 0.8, and 48.15% had a family history of CVD. In comparison, among the 16 individuals with Grade 2 NAFLD, 50.00% were smokers, 68.75% had hypertension, 100.00% had a BMI ≥ 23 kg/m², 100.00% had a weight-to-height ratio > 0.8, and 56.25% had a family history of CVD. Finally, among the 7 individuals with Grade 3 NAFLD, 57.14% were smokers, 100.00% had hypertension, 100.00% had a BMI ≥ 23 kg/m², 100.00% had a weight-to-height ratio > 0.8, and

71.43% had a family history of CVD. Statistical analysis revealed significant differences in the prevalence of hypertension and BMI ≥ 23 kg/m² across the different grades of NAFLD (p < 0.05 and p < 0.001, respectively). Additionally, the weight-to-height ratio > 0.8 differed significantly across the grades (p < 0.01). However, no significant differences were found in smoking status and family history of CVD among the different grades of NAFLD (p > 0.05). These findings suggest a potential association between hypertension, elevated BMI, and weight-to-height ratio with the severity of NAFLD.

Table 3: Distribution of abnormal biochemical Profile among different grades of NAFLD (N=50)

Variables	Grade 1 (n=27)		Grade 2 (n=16)		Grade 3 (n=7)		p-value
	n	%	n	%	n	%	
Elevated Total Cholesterol	6	22.22%	8	50.00%	5	71.43%	<0.001
Decreased HDL-C	25	92.59%	14	87.50%	7	100.00%	>0.05
Elevated LDL-C	23	85.19%	15	93.75%	7	100.00%	>0.05
Elevated Triglyceride	20	74.07%	14	87.50%	7	100.00%	>0.05
Elevated ALT	3	11.11%	10	62.50%	7	100.00%	<0.001
Elevated AST	4	14.81%	9	56.25%	6	85.71%	<0.001
Elevated ALP	1	3.70%	2	12.50%	4	57.14%	<0.001

Table 3 presents the distribution of abnormal biochemical profiles among different grades of non-alcoholic fatty liver disease (NAFLD) in a sample size of 50 individuals. The variables examined include elevated total cholesterol, decreased HDL-C (High-Density Lipoprotein Cholesterol), elevated LDL-C (Low-Density Lipoprotein Cholesterol), elevated triglycerides, elevated ALT (Alanine Aminotransferase), elevated AST (Aspartate Aminotransferase), and elevated ALP (Alkaline Phosphatase). Among the 27 individuals classified as Grade 1 NAFLD, 22.22% had elevated total cholesterol, 92.59% had decreased HDL-C, 85.19% had elevated LDL-C,

74.07% had elevated triglycerides, 11.11% had elevated ALT, 14.81% had elevated AST, and 3.70% had elevated ALP. In comparison, among the 16 individuals with Grade 2 NAFLD, 50.00% had elevated total cholesterol, 87.50% had decreased HDL-C, 93.75% had elevated LDL-C, 87.50% had elevated triglycerides, 62.50% had elevated ALT, 56.25% had elevated AST, and 12.50% had elevated ALP. Finally, among the 7 individuals with Grade 3 NAFLD, 71.43% had elevated total cholesterol, 100.00% had decreased HDL-C, 100.00% had elevated LDL-C, 100.00% had elevated triglycerides, 100.00% had elevated ALT, 85.71% had elevated AST, and 57.14% had elevated ALP.

Statistical analysis revealed significant differences in the prevalence of elevated total cholesterol, elevated ALT, elevated AST, and elevated ALP across the different grades of NAFLD ($p < 0.001$ for all). However, no significant differences were found in the prevalence of decreased HDL-C, elevated LDL-C, and elevated triglycerides among the different grades of NAFLD ($p > 0.05$ for all). These findings suggest a notable association between elevated total cholesterol, ALT, AST, and ALP with the severity of NAFLD, while other lipid parameters remain relatively consistent across the grades.

DISCUSSION

The demographic distribution of our study, with a higher representation of older adults and females (56% aged 55 years or older and 64% female), aligns with the growing body of evidence indicating a potential age and gender-related pattern in the occurrence or diagnosis of Non-Alcoholic Fatty Liver Disease (NAFLD) (14,15). This demographic trend is consistent with findings from other studies, which have also reported a higher prevalence of NAFLD in older populations and a potential gender disparity (16,17). The increased prevalence in older adults may be attributed to cumulative exposure to risk factors over time, while hormonal factors could play a role in the gender differences observed. Our study's finding that the majority of participants (54%) were diagnosed with Grade 1 NAFLD, with lower prevalence of Grade 2 and Grade 3 (32% and 14%, respectively), is reflective of the disease's progression pattern. This distribution is in line with other studies that have reported a higher prevalence of milder forms of NAFLD (18,19). The progression from Grade 1 to more severe forms of NAFLD is a critical area of research, as it provides insights into the natural history of the disease and potential intervention points. The significant associations found between higher grades of NAFLD and certain risk factors, such as hypertension, $\text{BMI} \geq 23 \text{ kg/m}^2$, and a weight-to-height ratio >0.8 , are corroborated by other studies (20,21). These findings highlight the importance of these risk factors in the progression of NAFLD severity. In contrast, our study did not find a significant increase in smoking and family history of CVD with advancing NAFLD severity, which suggests that these factors may not be as strongly

associated with the disease's progression as the other mentioned risk factors. This observation is particularly interesting and warrants further investigation, as it deviates from some of the established perceptions about NAFLD risk factors.

The observed association in our study between higher grades of Non-Alcoholic Fatty Liver Disease (NAFLD) and elevated levels of total cholesterol, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), and Alkaline Phosphatase (ALP) is a pivotal finding that aligns with existing literature (14,15,17). This trend underscores the clinical significance of these biochemical markers in not only diagnosing NAFLD but also in evaluating its progression and severity. The elevation of liver enzymes such as ALT and AST is indicative of hepatocellular injury, which is a hallmark of advancing NAFLD, particularly as it progresses towards Non-Alcoholic Steatohepatitis (NASH) and fibrosis (15,17). Similarly, the rise in ALP levels could be reflective of the biliary pathology often associated with more advanced stages of NAFLD. The increase in total cholesterol levels with advancing NAFLD grades observed in our study is also noteworthy, as it suggests a potential link between dyslipidemia and the progression of liver disease, which has been corroborated by other researchers (14). However, our study presents an intriguing deviation from some previous studies regarding the lipid profile, specifically High-Density Lipoprotein Cholesterol (HDL-C), Low-Density Lipoprotein Cholesterol (LDL-C), and triglycerides (16,18). The lack of a significant correlation between these lipid parameters and the severity of NAFLD in our cohort is particularly notable. While altered lipid profiles are a recognized feature in NAFLD patients, their direct correlation with disease severity is not as clear-cut as previously thought. These findings challenge some of the conventional understanding of NAFLD pathophysiology and suggests that while dyslipidemia is a common comorbidity, its role in the progression of NAFLD might be more complex than a simple linear relationship. It raises questions about the interplay between hepatic fat accumulation, lipid metabolism, and liver damage in NAFLD. The fact that HDL-C, LDL-C, and triglycerides levels did not significantly correlate with NAFLD severity in our study might indicate that other factors, possibly

genetic, lifestyle, or metabolic, play a more substantial role in the disease's progression than previously understood (16,18).

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

This study highlights significant demographic trends and associations in Non-Alcoholic Fatty Liver Disease (NAFLD), with a predominant occurrence in older adults and females. The majority of the participants presented with Grade 1 NAFLD, indicating a higher prevalence of the less severe form of the disease. Notably, the progression of NAFLD severity was significantly associated with certain risk factors, such as hypertension, increased BMI, and a higher weight-to-height ratio. Furthermore, the study identified a clear correlation between higher grades of NAFLD and elevated levels of key biochemical markers, including total cholesterol, ALT, AST, and ALP, underscoring their importance in assessing the disease's severity. These findings contribute to a deeper understanding of NAFLD, emphasizing the need for targeted screening and personalized management strategies based on demographic characteristics, risk factor profiles, and biochemical markers to effectively address this increasingly prevalent condition.

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Ethical approval: The study was approved by the Institutional Ethics Committee.

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