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CARDIOVASCULAR DISEASE BURDEN IN HOSPITALIZED PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE: AN OBSERVATIONAL STUDY

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ABSTRACT
Non-alcoholic fatty liver disease is a highly prevalent liver disorder in India, affecting nearly one in three individuals. It is increasingly recognized as an emerging risk factor for cardiovascular disease(CVD), with individuals diagnosed with non alcoholic fatty liver disease (NAFLD) having a 64% higher likelihood of experiencing cardiovascular events (CVE). Despite this growing concern, limited data exist on the association between NAFLD and CVD risk in the Indian population. This observational study aimed to evaluate this relationship in patients attending a tertiary care hospital. A total of 118 patients diagnosed with NAFLD were included, and relevant clinical data were obtained from medical records. Among the participants, 78.8% were male and 21.2% female, with a median age of 55.5 years. NAFLD staging showed that 39% had cirrhosis, 33% had steatosis, and 19% were diagnosed with non-alcoholic steatohepatitis (NASH). Key risk factors identified included impaired glucose regulation (37%), obesity (33%), and hypercholesterolemia (30%)—all strongly linked to elevated CVD risk. Cardiovascular risk was assessed using the Framingham Risk Score (FRS), indicated that high CVD risk in HCC(100%) followed by steatosis (96.4%), cirrhosis (80.8%). Analysis of variance (ANOVA) was employed to determine independent factors associated with NAFLD progression. The results underscore the critical need for early identification and comprehensive management of NAFLD, with a strong emphasis on cardiovascular risk evaluation. Integrated care approaches, including lifestyle interventions and routine monitoring, are essential to mitigate the risk of adverse cardiovascular outcomes and improve long-term prognosis in this patient population.

KEYWORDS: NAFLD, Cardiovascular disease, Obesity, Hypercholesterolemia and Liver disorder.

INTRODUCTION
Cardiovascular disease remains the leading cause of death globally, accounting for approximately one-third of all mortality, according to the World Health Organization. To mitigate this high mortality rate, it is essential to identify predictive risk factors that may indicate the likelihood of adverse cardiovascular outcomes, including death. Emerging evidence increasingly supports a strong association between non-alcoholic fatty liver disease and CVD.[1,2] Although a definitive causal relationship and underlying pathophysiological mechanisms between these two conditions are still under investigation, it is well recognized that they share several common risk factors—most notably obesity, type 2 diabetes mellitus, and dyslipidaemia.[3] Furthermore, both diseases affect multiple organ systems, contributing to their systemic impact. Globally, NAFLD affects an estimated 25.24% of the population, which translates to roughly 1.9 billion individuals out of a total global population of 7.6 billion.[4] While NAFLD is primarily viewed as a hepatic disorder, recent studies have revealed its systemic implications, showing that it contributes not only to liver-related morbidity and mortality but also to non-hepatic complications.[5] These findings reinforce NAFLD's status as the most prevalent cause of chronic liver disease worldwide. Interestingly, a large-scale population-based study conducted in the United States reported that among patients with NAFLD, cardiovascular disease—not liver cirrhosis—is the second most common cause of death. In fact, CVD-related mortality in this population surpasses deaths from cancers, including hepatocellular carcinoma (HCC).[6-8] Although both NAFLD and CVD individually elevate the risk of all-cause mortality compared to the general population, the precise impact of NAFLD on mortality

among patients who already have CVD remains ambiguous.[9] In 2016, two systematic reviews and meta-analyses attempted to clarify this relationship, but they yielded inconsistent conclusions regarding whether NAFLD significantly increases all-cause mortality in individuals with CVD. This inconsistency highlights the pressing need for more robust and conclusive research. A clearer understanding would facilitate the development of targeted interventions aimed at preventing premature and potentially avoidable deaths among patients with coexisting CVD and NAFLD, while also considering cost-effectiveness and resource allocation. Accordingly, the present study aims to investigate the association between non-alcoholic fatty liver disease and cardiovascular disease risk through an observational study conducted in a tertiary care hospital.

MATERIALS AND METHODS

Study Design

An observational study design was employed to explore the association between non-alcoholic fatty liver disease and cardiovascular disease risk at a Tertiary care hospital in Hyderabad.

Sample Size

A total of 118 patients were included in the study based on predefined eligibility criteria.

Eligibility Criteria

The study population was selected based on the following inclusion and exclusion parameters:

Inclusion Criteria

Patients aged above 12 years
Diagnosed with NAFLD
No history of alcohol consumption
Hospitalized (inpatients) at the study site

Exclusion Criteria

Individuals with immunodeficiency disorders such as HIV/AIDS
Neonates and infants
Pregnant or lactating women
Patients with cancers other than hepatocellular carcinoma (HCC)
Patients admitted to intensive or critical care units

Sampling Procedure

Participants were selected using a simple random sampling technique to minimize selection bias and ensure representativeness.

Data Collection

Following approval from the Institutional Ethics Committee (IEC), the study commenced with data collection. This involved a retrospective review of case records to gather patient demographics, medical and medication history, laboratory results, clinical diagnoses, current pharmacotherapy, and progress notes. A structured data collection form was used to document relevant information. The data collection process adhered to a medical record review protocol.

Statistical Analysis

Collected data were compiled and analyzed using descriptive statistics (simple percentages) and inferential statistics, specifically Analysis of Variance (ANOVA), to identify significant associations and trends.

RESULTS AND DISCUSSION

In this study, the highest proportion of patients (27.9%) were aged 56–65 years, while the lowest was in the 15–25 age group (0.84%), with a median age of 55.5 years, indicating a higher prevalence of NAFLD in middle-aged individuals. A total of 118 patients were included in this study, with a predominance of male patients (78.8%) compared to females (21.2%) that lies in line with previous studies.[10] The observed male predominance and median age of 55.5 years align with epidemiological trends suggesting a higher prevalence of NAFLD and its complications in middle-aged males, though NAFLD is increasingly recognized across all demographics.

Among the 118 subjects, 39% had cirrhosis, 33% had steatosis, 19% were diagnosed with non-alcoholic steatohepatitis (NASH), 6% had fibrosis, and 2% were found to have hepatocellular carcinoma (HCC) (Figure 1). Veeral ajmera et al. study found that prevalence of NAFLD, advanced fibrosis and cirrhosis was 65%, 14% and 6%, respectively. The distribution of NAFLD staging, with a substantial proportion exhibiting cirrhosis and non-alcoholic steatohepatitis (NASH)[11], indicates that a significant number of participants had advanced liver disease. This is particularly concerning given the well-established link between advanced NAFLD and increased morbidity and mortality, including cardiovascular events.

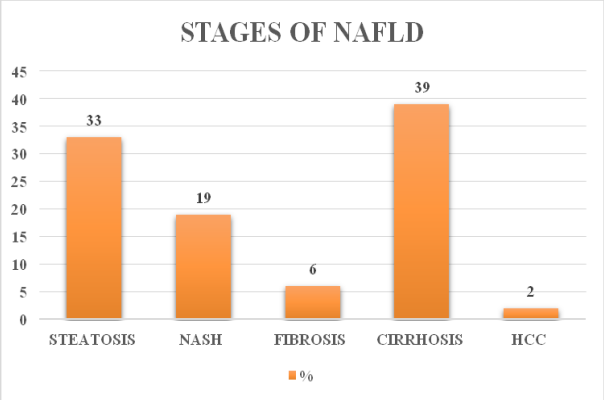
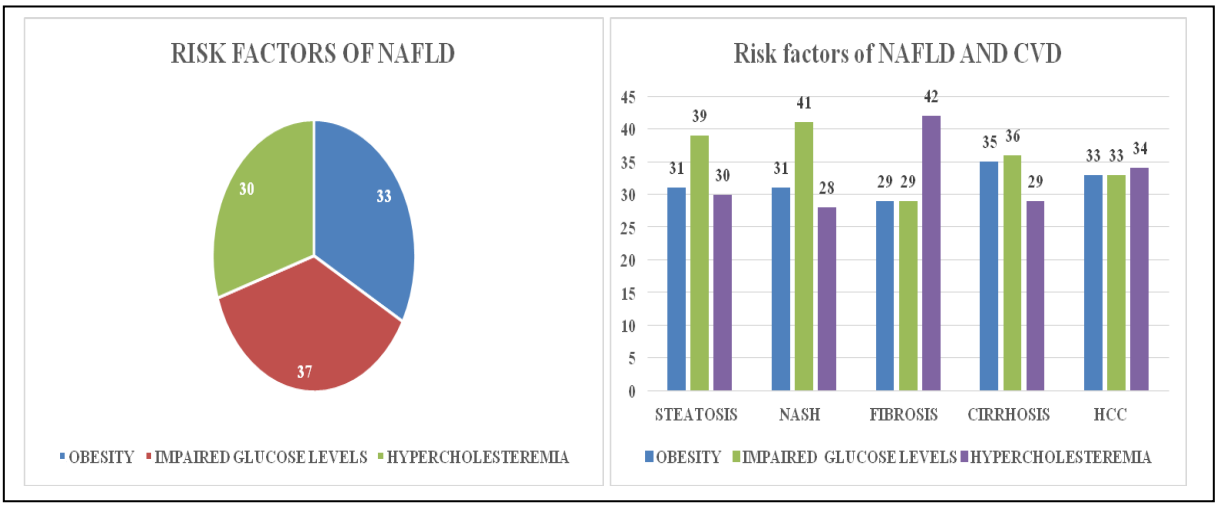


Figure 1: Percentage distribution of Stages of NAFLD.

Impaired glucose levels were the most common risk factor, present in 37% of the 118 subjects. Obesity and hypercholesterolemia were also significant risk factors, affecting 33% and 30% of patients, respectively. These findings suggest that all three risk factors—impaired glucose levels, obesity, and hypercholesterolemia—play a significant role throughout the progression of NAFLD,

from Steatosis to HCC. A study highlighted that Steatosis, the hallmark of NAFLD, is closely linked to obesity, with increased fat accumulation in the liver correlating with higher body mass index (BMI).[12] NAFLD is associated with a 2- to 3-fold increased risk of developing type 2 diabetes (T2D), especially in patients with more severe liver disease.[13] A study found that 44% of NAFLD patients had hypercholesterolemia, and in NASH patients, the prevalence ranged from 60% to 90%.[14] These risk factors are not only central to the pathogenesis and progression of NAFLD but are also independently and synergistically associated with elevated CVD risk. The strong correlation identified between these metabolic derangements and cardiovascular risk in our cohort further emphasizes the systemic nature of NAFLD, extending beyond hepatic pathology to impact overall cardiovascular health. Impaired glucose, obesity, and hypercholesterolemia were prevalent across all NAFLD stages. Steatosis and NASH patients had similar rates of these risk factors, while fibrosis was more linked to hypercholesterolemia. Cirrhosis patients commonly had all three, and one-third of HCC cases showed all risk factors, highlighting their role in disease progression.



The FRS analysis showed high CVD risk in HCC (100%) followed by steatosis (96.4%), cirrhosis (80.8%), NASH (45.5%), and fibrosis (25.0%). stages .This finding is particularly salient, as it directly quantifies the heightened cardiovascular vulnerability in individuals with advanced NAFLD. It suggests that HCC, steatosis and cirrhosis may serve as a powerful independent predictor or amplifier of cardiovascular risk, necessitating aggressive risk stratification and preventative interventions in this subgroup.

Table 1: CVD Vs stages of NAFLD.

CVD Type	Steatosis (%)	NASH (%)	Fibrosis (%)	Cirrhosis (%)	HCC (%)
Hypertension (HTN)	64	44	63	69	100
Coronary Artery Calcification (CAC)	6	0	0	0	0
Unstable Angina	6	0	0	0	0
Cardiomyopathy	0	0	0	2	0
Atherosclerosis	3	0	0	0	0
Coronary Artery Disease (CAD)	14	38	13	18	0
Stable Ischemic Heart Disease (IHD)	3	0	0	0	0
Heart Failure (HF)	0	6	13	2	0
Myocardial Infarction (MI)	3	0	13	4	0
Ventricular Tachycardia	0	0	0	2	0
Sinus Tachycardia	3	0	0	0	0
Left Ventricular Dysfunction (LV Dysfunction)	0	12	0	2	0

Table 1 showed that Hypertension was the most frequent CVD, particularly in cirrhosis (69%), steatosis (64%), and NASH (44%). CAD, heart failure, and MI were also observed.

The results of this study strongly advocate for the early identification and comprehensive management of NAFLD, with an explicit emphasis on cardiovascular risk evaluation. Given the silent progression of NAFLD in its early stages and the high prevalence of co-existing

metabolic risk factors, routine screening for both liver disease progression and cardiovascular risk factors is paramount. Integrated care approaches, encompassing lifestyle interventions (e.g., dietary modifications, increased physical activity) and routine monitoring of both hepatic and cardiovascular parameters, are essential. Such a holistic strategy is crucial to mitigate the risk of adverse cardiovascular outcomes and ultimately improve the long-term prognosis and quality of life in patients with NAFLD.

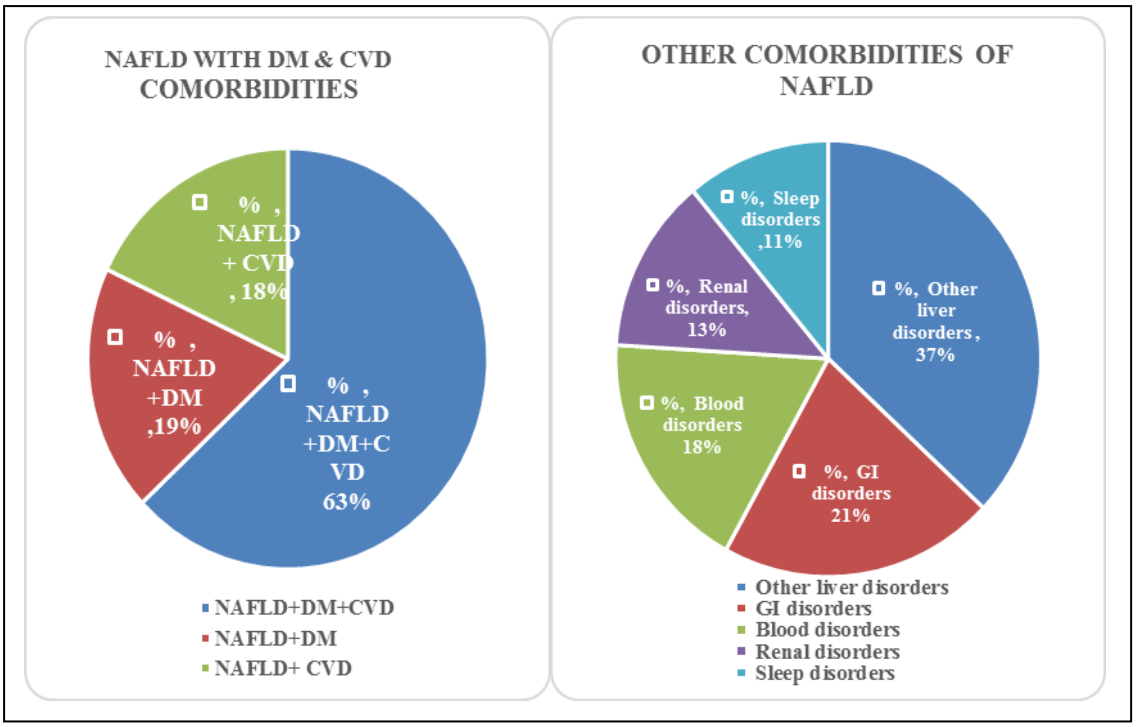


Figure 4: Co-existence of NAFLD with DM, CVD and other Co morbid conditions.

Figure 4 highlights the substantial overlap between NAFLD and Co morbid conditions. A significant majority of NAFLD patients presented with both CVD and diabetes, underscoring the strong interrelationship between these conditions. Furthermore, a notable proportion had either diabetes alone or CVD alone, indicating that each of these comorbidities frequently co-occurs with NAFLD. These findings reinforce the concept that NAFLD often exists within a cluster of metabolic and cardiovascular risk factors, necessitating a comprehensive approach to patient management. Beyond the well-established associations with obesity, diabetes, and dyslipidaemia, a considerable percentage of our NAFLD cohort exhibited other comorbidities. Among these, liver disorders were the most prevalent, which is expected given the study population. However, the significant presence of gastrointestinal, blood, renal, and sleep disorders suggests a broader spectrum of systemic involvement in individuals with NAFLD. These findings emphasize the need to consider and screen for a wider range of extra hepatic manifestations and co-existing conditions in patients with NAFLD, as they may impact disease progression, treatment strategies, and overall prognosis. The high prevalence of these diverse comorbidities further supports the notion of NAFLD as a multisystemic disease rather than solely a liver-centric condition.

While this study provides valuable insights, it is important to acknowledge certain limitations. The cross-sectional nature of the data limits the ability to infer causality or track disease progression over time. Furthermore, the specific methodology for diagnosing and staging NAFLD (e.g., biopsy, imaging, non-invasive markers) was not detailed, which could influence the staging prevalence. Future longitudinal studies with larger and more diverse cohorts, utilizing standardized diagnostic criteria and incorporating detailed cardiovascular imaging, would further elucidate the complex relationship between NAFLD progression and cardiovascular outcomes.

CONCLUSION

This study strongly confirms the established link between NAFLD and increased CVD risk. NAFLD patients showed a higher prevalence of traditional CVD risk factors (obesity, impaired glucose metabolism, dyslipidemia) across all liver disease stages. Notably, advanced NAFLD (Steatosis, Cirrhosis, HCC) was associated with a greater risk of cardiovascular events, evidenced by progressively higher Framingham Risk Scores with worsening liver pathology. The co-occurrence of hypertension, CAD, and HF in NAFLD patients further emphasizes this interconnectedness. These findings underscore the critical need for integrated screening and management strategies addressing both hepatic and cardiovascular health to mitigate long-term

complications and improve outcomes, especially given the rising prevalence of NAFLD.

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