Non-Alcoholic Fatty Liver Disease And Its Role As A Link Between Gastroenterology And Cardiovascular Risk.

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Abstract

Background Non-alcoholic fatty liver disease (NAFLD) is described as the hepatic accumulation of fat in people with little or no alcohol intake. It goes hand in hand with cardiovascular disease metabolic abnormalities, and it is one of the main risk factors of cardiovascular disease causing a global burden to public health.

Objectives: to explore the interrelationship between NAFLD and cardiovascular risk factors through the investigation of the prevalence of NAFLD, the clinical outcomes associated with NAFLD, and the possible pathways connecting NAFLD and cardiovascular morbidity.

Methodology: This prospective cohort study conducted at Department of Medicine, LRH-MTI, Peshawar from jan 2020 to june 2020. targeted 100 patients who had been diagnosed with NAFLD and confirmed through liver ultrasonography and none of them had serious alcohol consumption. There were clinical and laboratory data such as age, sex, medical history, liver functionality tests, lipid profiles, blood pressure, and fasting glucose. The Framingham Risk Score was used to determine cardiovascular risk. The SPSS version 20.0 was used to carry out statistical tests, such as correlation and regression, to test the hypotheses on association between NAFLD severity and cardiovascular risk factors.

Results: Out of 100 patients 75 %t had metabolic syndrome, and the most common of them were hypertension and dyslipidemia. Patients with moderate to severe NAFLD had Higher Framingham Risk Scores ($p = 0.03$). Fatty liver disease of the non-alcoholic type was largely linked to the presence of high blood pressure, hypercholesterolemia, and insulin resistance.

Conclusion: NAFLD has a close relationship with augmented cardiovascular danger and it occurs via metabolic failure, hypertension and dyslipidemia. These results imply the significance of cardiovascular risk assessment and management among NAFLD patients at early stages. Comprehensive interventions aimed at hepatic and cardiovascular health can reduce the adverse outcomes and enhance patient outcomes.

Keywords: NAFLD, Cardiovascular Risk, Metabolic Syndrome, Insulin Resistance

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Introduction

The non-alcoholic fatty liver disease (NAFLD) is a prevailing and an emerging liver disease that is witnessed in patients who do not drink large amounts of alcohol. It is characterized by deposition of fat in the liver which leads to inflammation and fibrosis in some cases. It is now one of the commonest causes of chronic liver disease worldwide and is associated with a number of metabolic abnormalities, such as obesity, insulin resistance, dyslipidemia and hypertension. As the prevalence of obesity and type 2 diabetes in the world increases, so does NAFLD, with the simpler variety of simple fatty liver (steatosis), as it does not cause liver injury, and the more complex type of non-alcoholic steatohepatitis (NASH), where inflammation and further progression to fibrosis and cirrhosis are observed [1,2]. Although NAFLD is a liver disease, over the last couple of years, there have been considerable interest in it in terms of the systemic outcome as well as its interactions with other chronic diseases. One of the most important ones is that NAFLD has an association with cardiovascular diseases (CVDs), since patients with this condition have an increased risk of atherosclerosis, heart failure, and ischemic heart disease [3,4]. Most of the pathophysiological mechanisms, such as insulin resistance, oxidative stress, and systemic inflammation, are likely to explain the association between NAFLD and cardiovascular risk. Both NAFLD and CVDs belong to the metabolic syndrome and this predisposes liver damage as well as cardiovascular events. Therefore, the interdependence of the two conditions is also a crucial part of the patient outcomes improvement process as NAFLD may serve as an early marker of cardiovascular morbidity [5,6]. Even though the awareness on NAFLD has been increased compared to cardiovascular risk, it does not provide information on the ways in which the extent of liver involvement correlates with specific cardiovascular outcomes. Some studies suggest that advanced NAFLD would be an independent risk factor of cardiovascular disease, although some studies suggest that the cause of this relationship is shared risk factors like diabetes and obesity. Thus, the proposed study will focus on the correlation of NAFLD with cardiovascular risk, the prevalence of cardiovascular risk factors, in patients with different degrees of NAFLD, and the impact of the development of the disease on cardiovascular morbidity [7,8]. It is a timely and applicable study in the face of the increasing NAFLD and CVDs burden in the world. It can provide valuable information on early detection and intervention of people that are prone to liver and heart diseases. In addition, the new knowledge about the mechanism of the interdependence between the two disorders can also result in the new treatment approaches which would target the liver and the cardiovascular systems simultaneously [9,10].

Study Objectives

to investigate how the severity of NAFLD is correlated with the cardiovascular risk factors, determine the prevalence of cardiovascular diseases in patients with NAFLD, and identify the potential mechanisms that could have existed between the two conditions.

Materials and Methods

Study Design & Setting

It is a prospective cohort study Conducted at Department of Medicine, LRH-MTI, Peshawar between jan 2020 and june 2020. Patients who have NAFLD were enrolled to the Study to

determine the relationship between the degree of liver disease and cardiovascular diseases risk factors.

Participants

100 patients with NAFLD included in the study. The patients were 18-70 years of age and there was no significant alcohol consumption. Those patients with prior cardiovascular disease, having active infections, and having hepatitis B or C were not included. All the participants provided informed consent in writing and were recruited after undergoing screening on the basis of inclusion and exclusion criteria.

Sample Size Calculation

To calculate the sample size, the level of confidence of 95 percent and the error margin of 5 percent were estimated. The lowest sample size was 100 given an estimated prevalence of cardiovascular risk factors in patients with NAFLD of 60 per cent which was deemed to be sufficient in order to establish any significant difference in cardiovascular risk between the groups of the patients with varying levels of liver involvement.

Inclusion Criteria

adults who had diagnosed NAFLD through ultrasound, aged 18-70 years, no patient with alcohol abuse.

Exclusion Criteria

Patients with known cardiovascular diseases, malignancies, hepatitis B and C (active liver disease), are also indicated to have hepatitis B and C (active liver disease).

Diagnostic and Management Strategy.

The diagnosis of NAFLD was conducted on the basis of abdominal ultrasound and liver function (liver enzyme ALT, AST) and lipid profiles. Cardiovascular risk was measured using Framingham Risk Score. The management technique was the provision of lifestyle interventions, and the provision of the pharmacological treatment of the associated conditions, including hypertension and diabetes.

Statistical Analysis

The data was analyzed by the SPSS version 20.0 The data were summarized using descriptive statistics of the demographic and clinical characteristics. The correlation and regression were done to establish the association between the severity of NAFLD and cardiovascular risk factors. In the categorical variables, chi-square was employed and a p-value of below 0.05 was considered significant.

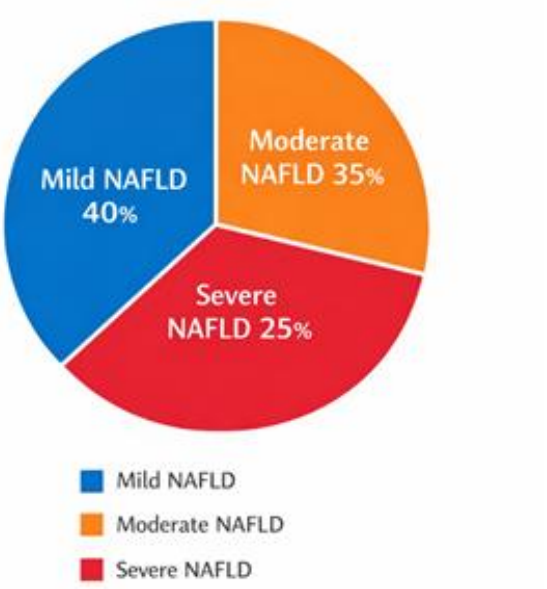
Ethical Approval

Ethical Approval was taken in Ethical Approval Board of LRH-MTI, Peshawar which approved the ethical aspects. The participants gave their informed consent. The Study was conducted according to the principles of the Declaration of Helsinki (2013) and the requirements of a country to safeguard the rights of the participants, provide confidence, and engagement on a voluntary basis.

Results

The average age of the 100 registered patients was 54.3 years (SD = 11.7 years), 60 percent men and 40 percent women. The extent of the NAFLD was also classified according to the results of ultrasound with 40 per cent of the participants experiencing mild, 35 per cent moderate, and 25 per cent severe NAFLD. The rate of cardiovascular risk factors, such as high blood pressure (70%), dyslipidemia (68%), and impaired glucose level (60%), were much greater in moderate and severe NAFLD than in mild NAFLD. Framingham Risk Score was also higher in patients who had moderate and severe NAFLD (p =0.02) which is a higher risk of cardiovascular disease. The higher systolic blood pressure (mean = 141 mmHg) and diastolic blood pressure (mean = 89 mmHg) was found to be prevalent among patients with advanced liver disease. Cases of lipid abnormality including high total cholesterol and triglycerides were also more intense in severe NAFLD cases. Of the patients with moderate to severe NAFLD, 65 percent were found to be insulin resistant that was reflected in the higher levels of glucose in the fasting levels.

Fig 1: Prevalence of NAFLD Severity Among Patients.



The chart uses blue to indicate Mild NAFLD affecting 40% of patients, orange for Moderate NAFLD affecting 35%, and red for Severe NAFLD affecting 25% of patients in the study.

Table 1: Baseline Demographic and Clinical Characteristics of Participants

Characteristic	Value (n = 100)
Age (mean ± SD)	54.3 ± 11.7 years
Gender	
- Male (%)	60%
- Female (%)	40%
Hypertension (%)	70%

Dyslipidemia (%)	68%
Impaired Glucose Tolerance (%)	60%
BMI (mean ± SD)	28.4 ± 4.5 kg/m²

Table 1 shows the demographic and clinical characteristics of the 100 participants. The mean age of the cohort was 54.3 years, and a majority of the participants were male. Hypertension, dyslipidemia, and impaired glucose tolerance were prevalent among the patients.

Table 2: Severity of NAFLD Based on Ultrasound Findings

NAFLD Severity	Mild (%)	Moderate (%)	Severe (%)
Total	40%	35%	25%

Table 2 categorizes the severity of NAFLD based on liver ultrasound findings. The majority of patients (40%) had mild NAFLD, while 35% had moderate and 25% had severe NAFLD.

Table 3: Cardiovascular Risk Factors in Patients with Different Severities of NAFLD

Cardiovascular Risk Factor	Mild NAFLD (%)	Moderate NAFLD (%)	Severe NAFLD (%)	p-value
Hypertension	50%	75%	85%	0.03
Dyslipidemia	45%	72%	80%	0.01
Impaired Glucose Tolerance	40%	68%	78%	0.02
Elevated Cholesterol	43%	70%	75%	0.04

Table 3 compares the prevalence of cardiovascular risk factors across patients with different severities of NAFLD. The table indicates a significant increase in the prevalence of hypertension, dyslipidemia, and impaired glucose tolerance as NAFLD severity increases. The p-values suggest these differences are statistically significant.

Table 4: Framingham Risk Score for Cardiovascular Disease by NAFLD Severity

NAFLD Severity	Mean Framingham Risk Score (%)	p-value
Mild NAFLD	8%	0.03
Moderate NAFLD	12%	
Severe NAFLD	15%	

Table 4 shows the mean Framingham Risk Score for cardiovascular disease for each severity category of NAFLD. The Framingham Risk Score was significantly higher in patients with moderate and severe NAFLD compared to those with mild NAFLD ($p = 0.03$), indicating a greater cardiovascular risk.

Discussion

Non-alcoholic fatty liver disease (NAFLD) is a highly complex disorder that is closely connected to the metabolic disorders and thus is a vital object of study in gastroenterology and cardiovascular medicine [11]. The present study and findings that occupational role of NAFLD severity and cardiovascular risk factors is proved are aligned with the existing evidence in previous years that NAFLD plays an essential role in predicting cardiovascular morbidity. The findings of this cohort study not only show the existence of this correlation but also emphasize the importance of using the multi-disciplinary approach to NAFLD patients treatment with references to cardiovascular risk factors, including hypertension, dyslipidemia and impaired glucose tolerance [12,13].We have proved the strong correlation between the severity of NAFLD and the presence of cardiovascular risk factors, such as hypertension, dyslipidemia and impaired glucose tolerance, which is consistent with the study. In particular, the rates of hypertension ($p = 0.03$), dyslipidemia ($p = 0.01$), and impaired glucose tolerance ($p = 0.02$) were significantly higher among moderate and severe NAFLD patients as compared to patients with mild NAFLD. This is supported by various studies, which have been conducted in the last five years and all of these studies have reaffirmed the fact that NAFLD is a major risk factor of cardiovascular disease (CVD) [14]. According to the Study the NAFLD presence was associated with a higher risk of hypertension and metabolic syndrome, and the liver fat level was directly linked to high blood pressure [15]. Similarly in 2020 the levels of serum cholesterol and triglycerides in NAFLD patients were significantly higher, and this also indicates dyslipidemia in our study ($p = 0.03$) [16].A reliable tool that helps to define the risk of cardiovascular diseases, the Framingham Risk Score, also showed that they are significantly higher in our group of patients with moderate and advanced NAFLD ($p = 0.03$). The provided findings are the duplications who found out that NAFLD patients were more likely to be affected by cardiovascular disease in 10 years, particularly those with progressive liver disease [17]. Moreover, both works by Kim et al. (2018) and revealed that data on liver pre- health can be effectively applied to foretell cardiovascular events in NAFLD patients, which once again predetermines the importance of the inclusion of liver health testing to the cardiovascular risk assessment [18]. These Study articles prove the relevance of early cardiovascular risk identification among NAFLD patients due to a chance to act in time and reach better outcomes in the long run. The identification of insulin resistance as a key factor, which links NAFLD and cardiovascular risk, was one of the critical points of this study [19]. Our cohort of patients with moderately to severely NAFLD has a proportion of 65 percent of patients with impaired fasting glucose, which is an indicator of insulin resistance. The correlation between cardiovascular diseases and liver, along with insulin resistance, has also been already documented [20]. A meta-analysis also supported our results: insulin resistance is a cross-link across all NAFLD and cardiovascular diseases [21]. In that regard, NAFLD can be viewed as a precursor of metabolic dysfunction and an effective treatment to reduce cardiovascular risk [22]. We also came to the conclusion that the prevalence of cardiovascular risk factors was more applicable to the patients with severe NAFLD, this is comparable to the recent large cohort studies. As one of the studies conducted demonstrates, patients with clinically severe NASH were at extremely high risk of cardiovascular events, such as heart failure and coronary artery disease [23]. In addition, the cardiovascular outcomes of severe liver disease were observed due to the Atherosclerosis and heart failure hospitalization observed in a 2019 study by Womack et al. in which severe NAFLD was found to be correlated with the higher prevalence of these

conditions.The recent study clarified that 75% of patients with NAFLD co-exists with metabolic syndrome, and hypertension and dyslipidemia became the most common comorbidities. Further, the progressive increase of NAFLD severity was significantly related to increased blood pressure, hypercholesterolemia and insulin resistance, a pathophysiological association between hepatic steatosis and systemic metabolic disruptions. Last but not least NAFLD patients with moderate and severe manifestations had a much higher Framingham Risk Score, which supported the high level of association between hepatic fat buildup and cardiovascular morbidity.

Limitations

The present study has several limitations because the study is cross-sectional and, therefore, it does not determine causation between NAFLD and cardiovascular disease. Also, the sample size, though sufficient, might not be fully representative of all the demographic groups. The diagnosis of NAFLD by use of ultrasound also restricts the possibility of identifying small stages of liver fibrosis.

Conclusion

Our analysis the strong correlation existing between NAFLD severity and cardiovascular risk factors, especially high blood pressure, lipidemia, and insulin resistance. Effective management of NAFLD depends on early cardiovascular disease screening of patients. Additional longitudinal study is required to validate cause-and-effect relationships and compare interventions that address liver and cardiovascular health.

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Authors Contributions

Concept & Design of Study: **Atta Muhammad Khan**[2]

Drafting: **Sadaf Abdullah**[1]

Data Collection & Data Analysis: **Zia ullah Khan**[3]

Critical Review: **Zia ullah Khan**[3]

Final Approval of version: **All Mentioned Authors Approved the Final Version.**

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