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Frequency of Metabolic Risk Factors and Association with Demographic Characteristics in Patients with Non-alcoholic Fatty Liver Disease

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ABSTRACT

Non-alcoholic fatty liver disease is a rapidly growing public health concern worldwide and is closely associated with metabolic and cardiovascular risk factors. **Objectives:** To determine the frequency and demographic associations of metabolic and cardiovascular risk factors among patients with NAFLD. **Methods:** This analytical cross-sectional study was conducted at the Department of Medicine, Fazaia Ruth Pfau Medical College, Base Faisal, Karachi, from June 2025 to December 2025. A total of 121 patients with NAFLD were enrolled through consecutive sampling. Diagnosis was based on elevated alanine aminotransferase levels and ultrasonographic evidence of fatty liver. Patients with significant alcohol intake, viral hepatitis, or other chronic liver diseases were excluded. **Results:** The mean age of the patients was 37.18±10.30 years, with a mean BMI of 27.27±4.27 kg/m^2, and a predominance of males (80.2%). Diabetes mellitus was present in 16.5% of patients, hypertension in 15.7%, and ischemic heart disease in 5.8%. Dyslipidemia was frequently observed, with hypertriglyceridemia in 47.1% and hypercholesterolemia in 27.3%, while obesity was identified in 31.4% of cases. A significant association was observed between age greater than 40 years and the presence of diabetes, hypertension, and ischemic heart disease ($p<0.001$). **Conclusion:** NAFLD is strongly associated with metabolic risk factors, particularly dyslipidemia and obesity, with a significant clustering of cardiovascular comorbidities in older individuals.

INTRODUCTION

The liver disease associated with excess fat in the liver cells is called non-alcoholic fatty liver disease (NAFLD) [1] and is a spectrum of liver diseases characterized by the presence of excessive fat in the liver cells, but no significant alcohol consumption. It is the most common chronic liver disease in the world and is often diagnosed as a coincidence during imaging of unrelated diseases [2]. The condition ranges from the mildest steatosis to the more complicated non-alcoholic steatohepatitis (NASH), after fibrosis, cirrhosis, and hepatocellular carcinoma (HCC) [3]. NAFLD is highly associated with metabolic dysfunction, and hence becomes more than a liver-related condition but also emerges as a system-related illness with tremendous cardiovascular as well as overall health effects [4]. Various metabolic and cardiovascular comorbidities are risk factors for NAFLD, the strongest being diabetes mellitus [5]. Insulin resistance is directly responsible for fat accumulation and inflammatory changes in the liver as well

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as the progression of steatosis to NASH [6]. NAFLD is a common problem in patients with hypertension and IHD because there are similarities in the pathophysiological pattern in metabolic syndrome and liver disease [7]. The co-morbidities stem from the fact that NAFLD is a systemic disease, in which liver lesions are associated with endothelial dysfunction, chronic inflammation and oxidative stress, and these conditions are linked to cardiovascular mortality and morbidity [8]. The risk and the size of NAFLD are maintained by obesity and dyslipidaemia [9]. Other factors such as central obesity increase the flux of free fatty acids into the body through the liver, and hyperlipidaemia, high triglycerides, and low HDL increase the buildup of fat and liver damage [10]. The coagulation of the factors generates metabolic dysfunction cycle that puts one at risk of hepatic as well as extrahepatic manifestations [11]. Therefore, it is important to diagnose the risk factors in patients with incidental NAFLD when a scan is performed, as intervention through lifestyle modification and targeted medication, if required, and measures reducing the cardiovascular risk, are valuable and prevent the progression of the liver disease and potential long-term consequences [12]. It was reported by Tunio *et al.* that among the patients with NAFLD, 33.9% were suffering from diabetes mellitus, 48.1% were suffering from hypertriglyceridemia, 28.1% were suffering from hypercholesterolemia, and 50.9% were obese [13]. A prevalence of around 30-33 % of NAFLD has been recently reported globally, and there was a significant association with the metabolic risk factors, obesity, diabetes, and dyslipidaemia [14].

Non-alcoholic fatty liver disease has been known to have a close association with metabolic risk factors like diabetes, hypertension, obesity, and dyslipidaemia, but little regional evidence exists in the Pakistani population, especially in cases where the disease comes incidentally on ultrasound. Previous studies are largely concentrated on advanced or symptomatic cases, thus missing out on the early metabolic profile and demographic distribution of the incidental diagnosis of NAFLD. Further, the age- and gender-based associations of these risk factors have not been adequately studied in urban environments such as Karachi, where the disease patterns might be altered by fast lifestyle changes. Hence, the present study aimed to assess the prevalence of major metabolic and cardiovascular risk factors in patients with incidentally detected NAFLD and their relationship with demographic factors to enable early risk stratification of the disease and to plan preventive measures.

METHODS

This analytical cross-sectional study was performed from June 2025 to December 2025 at the Department of Medicine, Fazaia Ruth Pfau Medical College, Base Faisal, Karachi, under the reference no FRPMC-IRB-2023-14, dated 18 December 2024. The study comprised 121 patients diagnosed with non-alcoholic fatty liver disease (NAFLD). The sample size was determined using a 95% confidence level and an 8% margin of error, considering an anticipated frequency of hypertriglyceridemia of 28.1% among patients with NAFLD [14], calculated through the WHO sample size calculator. Patients were selected using a non-probability consecutive sampling technique. Participants were selected if they were males or females aged 18-75 who had high levels of alanine aminotransferase (ALT) and the presence of fatty liver as seen on ultrasound. Patients with significant alcohol intake, positive serology for hepatitis B or hepatitis C virus, as well as those with other known chronic liver diseases (autoimmune, metabolic, drug-induced), were excluded. Demographic and clinical data were gathered, informed consent obtained, and included age, sex, and body mass index (BMI). Laboratory tests were performed, including fasting and random blood sugar, fasting lipid profile (triglycerides and cholesterol), and liver function tests. Obesity was considered if the body mass index (BMI) was ≥30 kg/m^2. Diabetes mellitus was identified by any of the following parameters: fasting blood glucose ≥126 mg/dL, random blood glucose ≥200 mg/dL, and/or by the use of antidiabetic medications. Hypertension was defined as a double blood pressure measurement ≥140/90 mmHg or if the patient was taking anti-hypertensive therapy. Hypertriglyceridemia was defined as a fasting triglyceride level of ≥150 mg/dL, while hypercholesterol was defined as a level of ≥200 mg/dL of fasting cholesterol. A history of angina or myocardial infarction recorded in the patient's medical history, or if the patient was prescribed an IHD medication, was considered ischemic heart disease (IHD).

IBM SPSS version 27.0 was used for data analysis. Data for continuous variables like age, BMI, blood sugar, and lipid values were presented as mean ± SD. Categorical variables like sex, diabetes, hypertension, IHD, hypertriglyceridemia, hypercholesterolemia, and obesity were reported as frequencies and percentages. The Chi-square test was used for the analysis of categorical variables, but Fisher's exact test was used when the expected cell count was less than 5. A p-value of <0.005 was considered to be statistically significant.

RESULTS

The study comprised 121 patients with a mean age of 37.18 ± 10.30 years and body mass index (BMI) of 27.27 ± 4.27 kg/m^2. Laboratory results revealed increased liver enzymes, with alanine transaminase (ALT) at 51.14 ± 16.17 U/L, aspartate transaminase (AST) at 45.31 ± 14.56 U/L, gamma-glutamyl transferase (GGT) at 52.28 ± 20.96 U/L, and alkaline

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phosphatase (ALP) at 98.82 ± 28.71 U/L. Glycemic status, as measured by hemoglobin A1c (HbA1c), was 5.79 ± 0.94%. Lipid profile results revealed triglycerides at 161.36 ± 70.43 mg/dL and total cholesterol at 185.34 ± 30.41 mg/dL (Table 1).

Table 1: Patient Demographics

Demographics	Mean ± SD / n (%)
Age (years)	37.18 ± 10.30
BMI (kg/m^2)	27.27 ± 4.27
ALT (U/L)	51.14 ± 16.17
AST (U/L)	45.31 ± 14.56
GGT (U/L)	52.28 ± 20.96
AP (U/L)	98.82 ± 28.71
HbA1c (%)	5.79 ± 0.94
Sr. Triglycerides level (mg/dL)	161.36 ± 70.43
Total Cholesterol (mg/dL)	185.34 ± 30.41
Gender	
Male	97 (80.2%)
Female	24 (19.8%)

Analysis of the risk factors showed that there were differential prevalence rates among the study subjects, where diabetes mellitus was found in 20 subjects (16.50%), hypertension in 19 subjects (15.70%), and ischemic heart disease in 7 subjects (5.80%). Lipid abnormalities were also common among the subjects, where hypertriglyceridemia was found in 57 subjects (47.10%), hypercholesterolemia in 33 subjects (27.30%), and obesity in 38 subjects (31.40%) (Table 2).

Table 2: Frequency of Risk Factors Among Patients with Non-Alcoholic Fatty Liver Disease

Risk Factors	Category	n (%)
Diabetes Mellitus	Yes	20 (16.5%)
	No	101 (83.5%)
Hypertension	Yes	19 (15.7%)
	No	102 (84.3%)
Ischemic Heart Disease	Yes	7 (5.8%)
	No	114 (94.2%)
Hypertriglyceridemia	Yes	57 (47.1%)
	No	64 (52.9%)
Hypercholesterolemia	Yes	33 (27.3%)
	No	88 (72.7%)
Obesity	Yes	38 (31.4%)
	No	83 (68.6%)

Diabetes mellitus showed a strong association with age, with no cases occurring in patients ≤40 years (0.0%) compared to 20 cases (45.5%) in those >40 years (p<0.001). Gender differences in diabetes prevalence were not statistically significant, with 18 males (18.6%) and 2 females (8.3%) affected (p=0.358). Hypertension exhibited similar age dependency, occurring in only 1 patient ≤40 years (1.3%) versus 18 patients >40 years (40.9%) (p<0.001), while gender distribution showed 18 males (18.6%) and 1 female (4.2%) with hypertension (p=0.117). Ischemic heart disease exclusively affected patients >40 years, with 7 cases (15.9%) in this age group and none in younger patients (p<0.001), with minimal gender variation between 6 males (6.2%) and 1 female (4.2%) (p=1.000) (Table 3).

Table 3: Association of Metabolic and Cardiovascular Characteristics with Demographic Factors

Variables	Category	≤40 Years, n (%)	>40 Years, n (%)	p-value	Male, n (%)	Female, n (%)	p-value
Diabetes Mellitus	Yes	0 (0.0%)	20 (45.5%)	<0.001*	18 (18.6%)	2 (8.3%)	0.358*
	No	77 (100.0%)	24 (54.5%)		79 (81.4%)	22 (91.7%)	
Hypertension	Yes	1 (1.3%)	18 (40.9%)	<0.001*	18 (18.6%)	1 (4.2%)	0.117*
	No	76 (98.7%)	26 (59.1%)		79 (81.4%)	23 (95.8%)	
Ischemic Heart Disease	Yes	0 (0.0%)	7 (15.9%)	<0.001*	6 (6.2%)	1 (4.2%)	1.000*
	No	77 (100.0%)	37 (84.1%)		91 (93.8%)	23 (95.8%)	
Hypertriglyceridemia	Yes	37 (48.1%)	20 (45.5%)	0.783**	45 (46.4%)	12 (50.0%)	0.751**
	No	40 (51.9%)	24 (54.5%)		52 (53.6%)	12 (50.0%)	
Hypercholesterolemia	Yes	21 (27.3%)	12 (27.3%)	1.000**	30 (30.9%)	3 (12.5%)	0.078*
	No	56 (72.7%)	32 (72.7%)		67 (69.1%)	21 (87.5%)	
Obesity	Yes	21 (27.3%)	17 (38.6%)	0.195**	31 (32.0%)	7 (29.2%)	0.792**
	No	56 (72.7%)	27 (61.4%)		66 (68.0%)	17 (70.8%)	

DISCUSSION

The present study aimed to investigate the risk factors for NAFLD, as well as the relationship between NAFLD risk factors and demographic factors, revealing some clinically significant patterns that are consistent with the pathophysiological mechanisms for NAFLD. Male predominance 97 (80.2%) in the present study might be attributed to higher prevalence of NAFLD among men which can be attributed to fat deposition and distribution in men, the role of hormones in men and women and lifestyle factors which include the role of testosterone, known to increase the risk for NAFLD by increasing visceral adiposity, and the role of estrogen which is known to exert protective effects through increasing insulin sensitivity and regulating lipid metabolism. Given that

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hypertriglyceridemia plays a significant role in the pathogenesis of nonalcoholic fatty liver disease, it is not surprising that nonalcoholic fatty liver disease was more common in this patient population, 57(47.1%). The association of hypertriglyceridemia with NAFLD is through the effects on insulin resistance on the liver, which results in increased synthesis of VLDL and decreased activity of lipoprotein lipase, which results in decreased clearance of triglycerides. The insulin-resistant nature of diabetes mellitus, hypertension, and ischemic heart disease is highlighted by the strong age associations. In older people, these complications are increased due to greater atherosclerotic change and a greater loss of pancreatic beta-cell function. The current findings show significant consistency with published studies on the risk factors of NAFLD, and highlight some unique demographic trends. The current cohort mean age of 37.18 ± 10.30 years was younger than most studies, including those by Kannan *et al.* (43-48 years) and Amini-Salehi *et al.* (48.4 years), which may be due to lifestyle factors, genetic predisposition, or better diagnostic tools in our population, which led to an earlier detection of the disease [15, 16]. Differing from Wang *et al.* who reported the highest prevalence at 60 years in women, this is a younger age group, suggesting possible regional differences in age at presentation [17]. The sex ratio of our study was 80.2% male, which was the opposite of that of several regional studies where female predominance was observed, as Huh *et al.* [18] (63% female), Bano *et al.* [19] (80% female), and Mahmood *et al.* [20] (62.9% female). This gender imbalance could be due to cultural, occupational or referral patterns specific to our study population as compared to the world, in which NAFLD occurs at a similar rate in both sexes. The current result, however, is more similar to the study by Losasso *et al.* [21] that reported 74% male participants, which could indicate that the study was conducted at a healthcare facility that was more prone to such gender predispositions or that there is a trend of risk exposure to be more common among males [21]. In the current cohort, the prevalence of diabetes mellitus was 16.5%, much lower than in many studies such as Huh *et al.* [18] (34%), Bano *et al.* [19] (48.6%), Tunio *et al.* [13] (33.9%), and especially lower than in the diabetic population as reported by Wang *et al.* (55.5%) [17]. This discrepancy could be due to the younger age of our study population since diabetes is known to increase with age, or perhaps due to the fact that we identified them with advanced detection of NAFLD before metabolic decompensation occurs [20]. The strong age-related association we observed ($p<0.001$) corroborates those of Amini-Salehi *et al.* (OR 2.12) and Wang *et al.* further supporting the progressive nature of metabolic dysfunction [16, 17]. The prevalence of hypertriglyceridemia, 57 (47.1%) in the current study, was similar to several investigations, e.g., Bano *et al.* 18 (48%) [19] and Tunio *et al.* [13] (48.1%), and was within the wide range of 20-80% quoted by Akter [22]. This cross-covariate resemblance among various populations further highlights the crucial contribution of lipid dysregulation in the pathogenesis of NAFLD and reinforces the mechanistic link between hepatic fat accumulation and triglyceride metabolism dysfunction. The non-significant association between age and hypertriglyceridemia, as well as between gender and hypertriglyceridemia, in our study is contrary to some of the literature, but could be explained by the fact that this metabolic disturbance is common among all age groups and genders within the NAFLD patients. The prevalence of obesity (31.4%) in the current study was significantly lower than most of the comparative studies, such as Kannan *et al.* [15] (66%), Huh *et al.* [18] (65.2%), and Tunio *et al.* [13] (80-90%).

This study also has several limitations. First of all, it is a study based on one center, so it may not be generalized to the rest of the population. Secondly, the sample size in this study is small, which is 121 subjects, so it may be inadequate for this study. Finally, being a cross-sectional study, the study might restrict the ability to draw cause-effect conclusions about the multiple risk factors for non-alcoholic fatty liver disease. Furthermore, the lack of a histopathological diagnosis could reduce the diagnostic accuracy. Large-scale, multicenter, prospective studies are needed to enhance generalizability and the ability to make causal inferences regarding the relationship between metabolic risk factors and disease progression from the early stages of incidental detection to the later stages of steatohepatitis and cirrhosis in future studies on non-alcoholic fatty liver disease. In addition to ultrasound, there is a need for more precise diagnostic methods such as FibroScan or MRI, and to obtain a histological diagnosis. Other factors like genetic, dietary, physical activity, and socioeconomic factors should be studied further to determine additional risk factors, performing multivariate analyses to determine independent risk factors and to create risk stratification models. Furthermore, there is a need for interventional research to assess lifestyle and pharmacological interventions, particularly in early-stage or incidentally discovered NAFLD, to assess long-term metabolic and cardiovascular outcomes and inform preventative healthcare policies, given the younger profile seen.

CONCLUSIONS

It is concluded that non-alcoholic fatty liver disease was frequently associated with metabolic risk factors, particularly hypertriglyceridemia, obesity, diabetes mellitus, and hypertension. Significant associations were observed between age greater than 40 years and the presence of diabetes, hypertension, and ischemic heart disease, indicating clustering of cardiovascular comorbidities in older patients. Early identification of

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these metabolic abnormalities in patients with NAFLD may support timely risk stratification and preventive management.

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Authors' Contribution

Conceptualization: TG
Methodology: TG, SSK
Formal analysis: TG
Writing and Drafting: TG, SSK, MK, HAB, AI, MU
Review and Editing: TG, SSK, MK, HAB, AI, MU

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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