Non-Alcoholic Fatty Liver Disease in Cardiovascular Patients, Frequency, Risk Factors and Clinical Patterns in Qena Governorate

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Abstract

Background: Cardiovascular diseases (CVD) and liver disorders, like Non-Alcoholic Fatty Liver Disease (NAFLD), are major global health concerns, linked to significant morbidity and mortality.

Objectives: The study aimed to determine the prevalence of NAFLD in cardiac patients and identify risk factors contributing to its development.

Patients and methods: This cross-sectional research was conducted at Qena University Hospital, Egypt (April 2022–April 2023) on 100 cardiovascular patients. Assessments involved clinical, diagnostic, and laboratory methods, including liver function, lipid profile, abdominal ultrasonography, ECG, echocardiography, hepatitis testing, BMI, waist size, FibroScan, and NAFLD severity assessment.

Results: In a study of 24 adult NAFLD patients compared to 76 non-NAFLD cases, significant findings included NAFLD at S2 (62.5%) and S3 (37.5%) stages, all with F2 fibrosis. Significant gender distribution difference ($p=0.014$) with fewer males (33.3%). NAFLD patients were younger (60.08 vs. 63.92 years, $p=0.0053$) with higher BMI (32.62 vs. 29.66 kg/m^2, $p<0.001$). Clinical characteristics showed significant increases in hypertension, diabetes, and other conditions in NAFLD ($p<0.001$). Cardiac differences included lower ejection fraction ($p<0.001$) and larger left atrial diameter ($p=0.001$) in NAFLD. Lipid profile variations included higher total cholesterol ($p=0.034$), LDL-C ($p<0.001$), and lower HDL-C ($p<0.001$) in NAFLD. Elevated liver function markers in NAFLD ($p<0.001$), with lower NFS score ($p=0.012$). Trends indicated a non-significant increase in cirrhosis prevalence in NAFLD ($p=0.166$), higher liver stiffness ($p<0.001$), and CAP score ($p<0.001$).

Conclusion: NAFLD significantly increase in Cardiac patients and significantly associated with factors like sex, age, BMI, chronic diseases, obesity, hyperlipidemia and heart diseases.

Keywords: NAFLD, Cardiovascular events, Metabolic Syndrome, Cardiometabolic Risk

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Introduction

Cardiovascular diseases (CVDs) and liver disorders are two of the most pervasive health concerns worldwide, collectively responsible for a substantial portion of global morbidity and mortality **(Mantovani et al., 2021).** Among liver conditions, Non-Alcoholic Fatty Liver Disease (NAFLD) has emerged as a growing public health crisis, while CVDs continue to be a leading cause of death. NAFLD has been recognized as a critical player in cardiovascular health **(Younossi, 2019).**

Intrahepatic free fatty acid (FFA) buildup causes mitochondrial dysfunction, reactive oxygen species generation, and renin–angiotensin–aldosterone system (RAAS) activation, which worsens atrial fibrillation (AF), diastolic heart failure, and ASCVD **(Shroff et al., 2020).**

NAFLD has garnered increasing attention in recent years, primarily due to its alarming prevalence and the diverse spectrum of health issues it encompasses **(Perumpail et al., 2017).** With an estimated global prevalence rate of 25%, NAFLD has evolved into the most prevalent chronic liver disease, with an incidence that continues to rise steadily **(Mundi et al., 2020).**

However, NAFLD is not confined to the liver alone. It is a multifaceted condition with systemic repercussions, extending its influence beyond hepatology into the realm of cardiology. As we explore the landscape of NAFLD, it becomes evident that understanding its relationship with CVD is pivotal in our quest for comprehensive healthcare solutions **(Marques et al., 2023).**

The CVD, encompassing a broad spectrum of conditions such as coronary heart disease, stroke, and hypertension, remain the leading cause of mortality globally. While traditional risk factors for CVD, including age, sex, obesity, hypertension, dyslipidemia, diabetes, and smoking, are well-established, emerging evidence suggests that NAFLD should also be recognized as an independent risk factor for CVD. This revelation challenges our understanding of cardiovascular risk stratification, calling for a deeper exploration of NAFLD's role in shaping the cardiovascular landscape **(Kasper et al., 2021).**

Recent studies have revealed that NAFLD significantly contributes to the burden of CVD, particularly coronary heart disease, independent of traditional risk factors **(Kasper et al., 2021)**. This independence emphasizes the need to view NAFLD as more than a mere hepatic concern. It becomes evident that patients with NAFLD face an increased risk of cardiovascular events and related morbidity and mortality **(Lee et al., 2021).**

The study aimed to identify risk factors for NAFLD in cardiovascular patients, raise awareness, and establish screening guidelines for NAFLD in cardiovascular disease patients.

Patients and Methods

The research was designed as a cross-sectional inquiry and was carried out at Qena University Hospital in Egypt's Tropical Medicine & Gastroenterology Department and Clinic, as well as the internal medicine department and clinic, Qena University Hospital, Qena-Egypt. The research was carried out between April 2022 and April 2023 including 100 cardiac patients of both sex (55 were males and 45 were females) aged > 18 years and were divided into two groups: 24 patients with NAFLD and 76 patients without NAFLD. The study started after obtaining the approval from the ethical committee and written informed consent and obtained from all patients **Ethical code: SVU-MED-GIT023-1-22-2-320**

Sample size: Using Epi Info to calculate the sample size. The final sample size was 100.

Patients with cardiovascular disorders aged 18 and above were evaluated for non-alcoholic fatty liver disease (NAFLD) using a variety of approaches, including biochemical markers, abdominal ultrasonography, and an analysis of characteristics associated with hepatic steatosis. The study excluded patients aged 18 and above with NAFLD, chronic hepatitis C, B, hepatocellular carcinoma, primary sclerosing cholangitis, or alcoholism history, as they might impair liver stiffness assessment.

Methods: All patients were subjected to:

A. Full history taking: A complete medical history was obtained, which included medical history of comorbidities such as diabetes mellitus (DM), hypertension (HTN), and heart disease. The patient's drug usage was correctly recorded in their medical history.

B. Clinical examination:

- General physical examination including the measurement of vital signs such as heart rate, blood pressure, respiratory rate, and temperature.
- Chronic liver disease signs including jaundice, tremors, swelling of the lower extremities, enlarged organs, and ascites were checked for using specialized diagnostic procedures.
- Body mass index (BMI) was determined by dividing the subject's kilogram weight by their square meter height. The cutoff for obesity was set at (BMI) of 30 kg/m2 or above. In addition, the smallest possible gap between the lower rib edge and the iliac crest was used as the measurement point for the waist **(Habib, 2013).**

C. Laboratory investigations:

- CBC for Platelet count.
- Coagulation profile: prothrombin time (PT), and international normalized ratio (INR).
- Liver function test: Aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum albumin level, and serum bilirubin level.
- Lipid profile: total cholesterol, triglyceride, low density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C).
- Hepatitis B surface antigen and Hepatitis C viral antibodies to exclude other liver diseases.

Blood sampling: 6 ml of venous blood was obtained from each participant under aseptic conditions. Samples were divided into 3 tubes, 2 ml in an EDTA tube for complete blood count (CBC) to evaluate platelet count. Plasma samples were obtained by centrifuging the sodium citrate tube at 2000 x g for 10 minutes at room temperature, with testing conducted within a two-hour timeframe. Plasma samples were used to analyze prothrombin time (PT), and international normalized ratio (INR). For serum sample collection, the blood was allowed to clot at 37°C. Serum then acquired through centrifugation of the clotted blood at 3000 x g for 10 minutes at room temperature. Serum was used to analyze lipid profile (total cholesterol, triglyceride, low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) and liver function test including Aspartate aminotransferase (AST), alanine aminotransferase

(ALT), serum albumin level, serum bilirubin level sing ELISA technique

Calculation of Liver fibrosis indices (Age, AST, ALT, and platelet count) were rigorously computed using the following equation: **Fibrosis-4 (FIB-4) = (age × AST) / (platelet count × √ALT) (Sterling et al., 2006).**

D. Imaging:

- Abdominal Ultrasonography using Logiq P7 (GE healthcare, United states) to identify NAFLD: Utilizing a high-resolution B-mode ultrasound system, they precisely measured the liver's dimensions in the midline and mid-clavicular lines, while also assessing its surface and echogenicity. The diagnosis of fatty liver was made according to the recommendations for the diagnosis and therapy of nonalcoholic fatty liver disease: I) The liver's near-field echo is diffusely enhanced, more so than the kidney's; (II) the intrahepatic duct structure is unclear; (III) the liver's far-field echo is gradually decreasing. Diagnosis of cirrhosis was based on results of liver function test and US. **(Kinner et al., 2016).**

- Echocardiographic images were obtained using GE Vivid S5 with a 3.5-MHz transducer. All subjects were examined with conventional two-dimensional echocardiography (using standard two-dimensional, pulse-wave Doppler, color flow Doppler, and M-mode echocardiographic methods) according to standardized study protocol. Echocardiographic measurements were performed in the left lateral decubitus position. All measurements were made by a single investigator using the same machine to avoid the bias by different operators and devices. Conventional echocardiography was performed. Left atrium (LA) dimension, left ventricular (LV) diameters and wall thicknesses were measured from 2D images at the level of the mitral valve tips, ensuring a measurement perpendicular to the long axis of the ventricle. And LV ejection fraction (LVEF) was calculated by two-dimensional echocardiography using the M-mode. Pulsed wave Doppler at the apical position was used to record mitral inflow between the tips of the mitral leaflets and five to ten cardiac cycles were recorded. From the mitral inflow velocities, the following variables were measured: peak velocity of early (E) and atrial (A) diastolic filling were measured. E/A was calculated. An estimate of pulmonary artery systolic pressure was calculated using the tricuspid regurgitant velocity (**Selimovic et al., 2007**).

- The FibroScan 502 (Echosens, France) was used to assess the liver stiffness measurement (LSM) and the controlled attenuation parameter (CAP). (**Fig.1,2).** Steatosis Grade based on CAP Score: S0 had CAP score of 150-238 dB/m, S1 had CAP score of 238-260 dB/m, S2 had CAP score of 260-290 dB/m ans S3 had CAP score of ≥ 290 dB/m **(Myers et al., 2012),** Fibrosis Grade based on LSM Score: F0-F1 stage had LSM value of < 7 kPa, F2 had LSM value of 7-8.6 kPa, F3 stage had LSM value of 8.7-10.2 kPa and F4 stahe had LSM value of ≥ 10.3 kPa **(Chan et al., 2009)**, and NAFLD severity **(López-Riera et al., 2018)** were evaluated.

E. ECG:

- Electrocardiography (ECG) (FUKUDA, United states) to examine the heart's electrical activity from different angles. This allowed for the detection of various cardiac conditions, including arrhythmias, atrial enlargement, and myocardial ischemia, among others. Echocardiography was used to assess the size of the heart, the contraction and relaxation of the heart muscle, and the operation of the valves. **(Hutyra et al., 2018).**

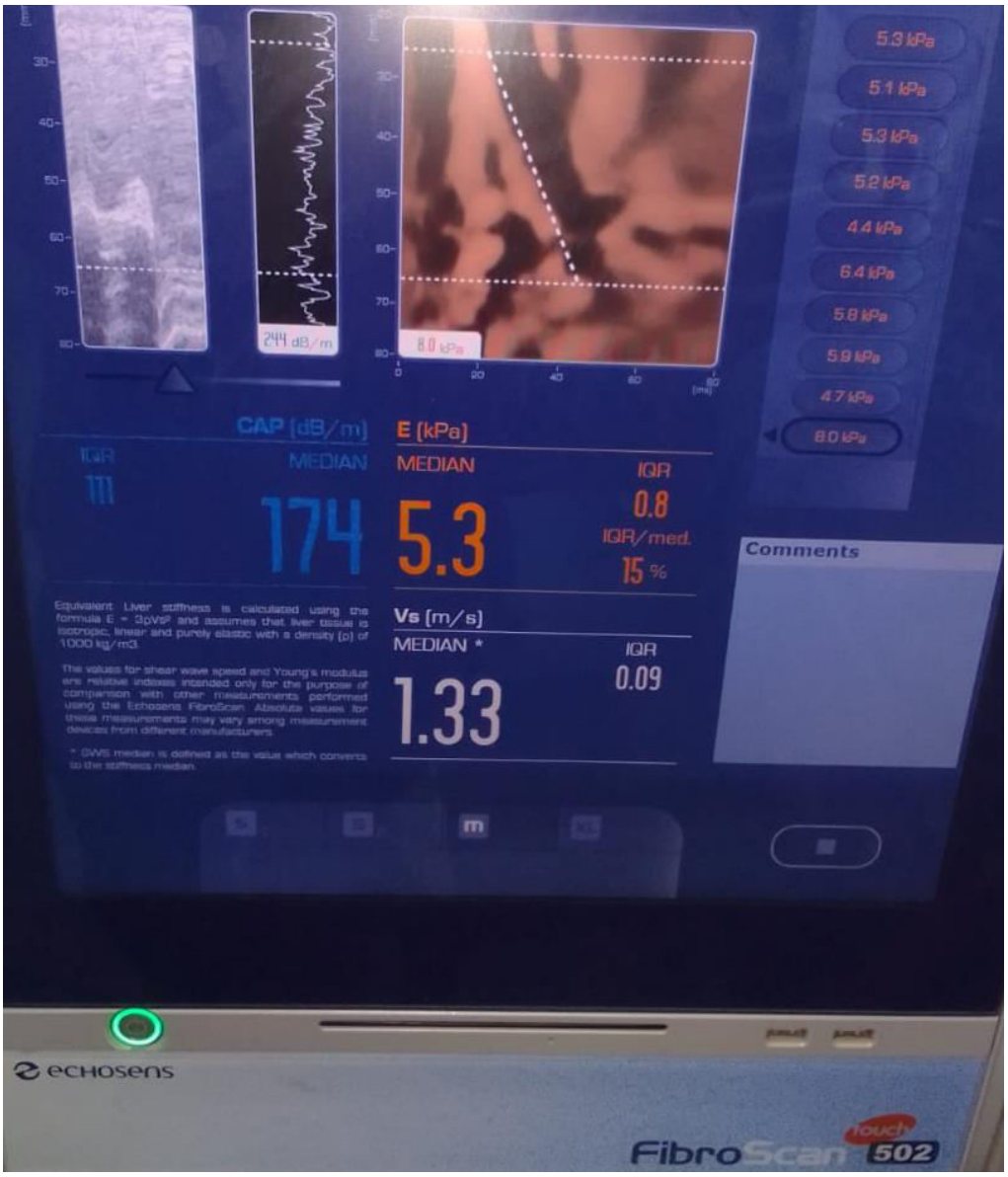

Fig.1. Fibro-Scan results. The device computer interprets data obtained from any measurement and generates an output like the depicted one, showing and printing results. The most important are the 'shear wave speed' (m/s) and the 'liver equivalent stiffness' (kPa) **(Deorsola et al., 2016).**

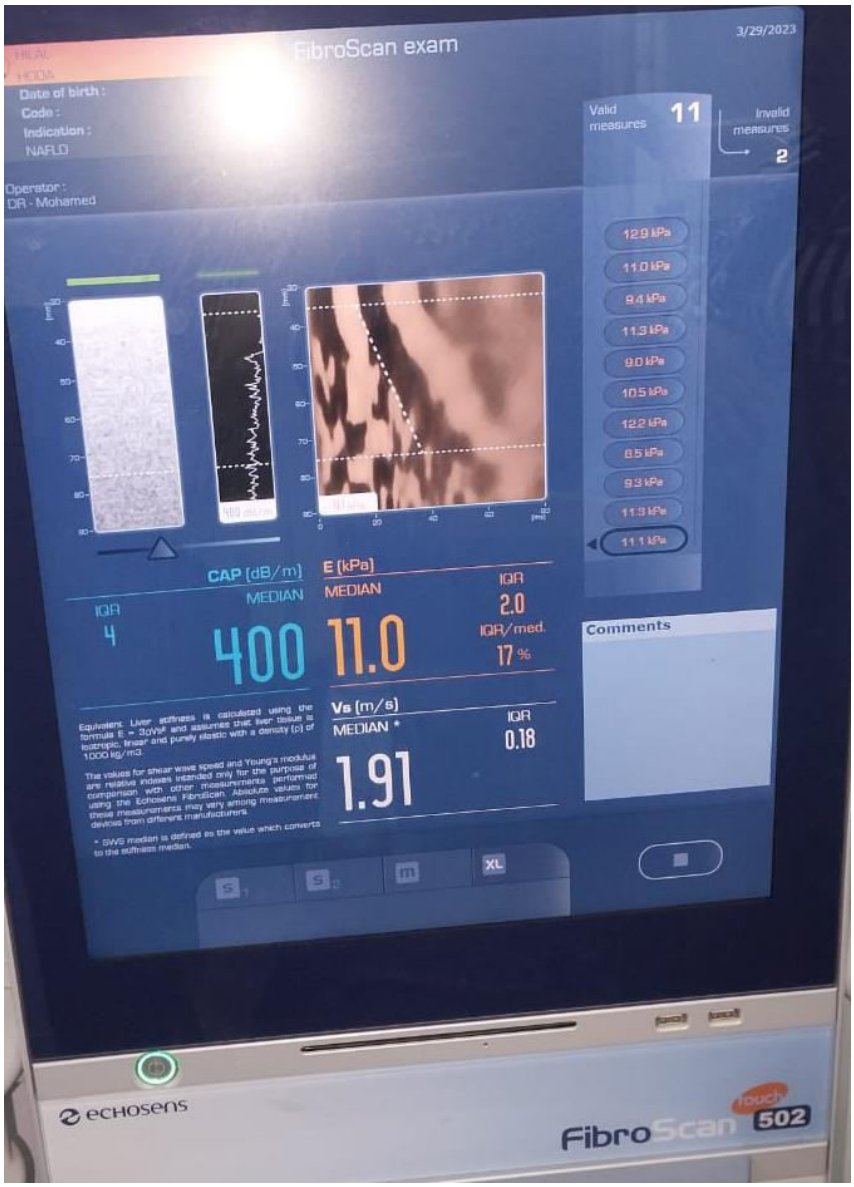

Fig.2.Controlled Attenuation Parameter using fibroscan indicated in blue. The interquartile range (IQR), which is a quality parameter, is displayed as well **(Berzigotti et al., 2018).**

Statistical analysis

IBM SPSS version 20.0 was used to input and analyze the data. Qualitative descriptive statistics used numbers and percentages Quantitative data included mean, standard deviation. t-test and Chi square were used to compare data between groups. Linear regression was used for regression analysis to determine risk factors. Results were significant at < 0.05.

Results

The study assessed 24 adult NAFLD patients, with 62.5% having stage S2 and 37.5% having stage S3, with 100% exhibiting fibrosis at the F2 stage, 37.5% at Grade 3, and 62.5% classified as Grade 4 NAFLD.

Table 1.Demographic data and Clinical characteristics in cases with and without NAFLD

Variables	NAFLD				P- Value
	No (n = 76)		Yes (n = 24)		
	No.	%	No.	%	
Demographic data					
Sex					
• **Male**	47	61.8	8	33.3	0.014 * x
• **Female**	29	38.2	16	66.7	
Age (years) (Mean ±SD)	63.92 ± 5.50		60.08 ± 6.50		0.0053 t
BMI (kg/m^2) (Mean ±SD)	29.66 ± 1.55		32.62 ± 0.49		<0.001 * t
Clinical characteristics					
• **Hypertension**	42	55.3	24	100.0	<0.001 * x
• **Ischemic heart disease**	59	77.63	23	95.83	0.043 x
• **Diabetes mellitus**	16	21.1	24	100.0	<0.001 * x
• **Obesity (BMI>30 kg/m2)**	29	38.2	24	100.0	<0.001 * x
• **Atrial fibrillation**	21	27.6	7	29.2	0.884 x
• **Dyslipidemia**	29	38.2	24	100.0	<0.001 * x
• **Heart Failure**	75	98.68	23	95.83	0.384
• **Valvular disease**	29	38.2	24	100.0	<0.001 * x
• **Statin use**	13	17.1	24	100.0	<0.001 * x

t: t-test, x: Chi square, *: Statistically significant at $p \leq 0.05$

(Table.1) provides a comprehensive overview of demographic data and clinical characteristics in individuals with and without non-alcoholic fatty liver disease (NAFLD). The data, derived from a comparison of 76 cases without NAFLD and 24 cases with NAFLD, reveal several significant differences. Notably, there was a significant decrease in the proportion of males with NAFLD (33.3%) compared to females (66.7%), with a p-value of 0.014, indicating a gender-based discrepancy in NAFLD prevalence. Moreover, individuals with NAFLD exhibited a significant decrease in mean age (60.08 ± 6.50 years) compared to those without NAFLD (63.92 ± 5.50 years), as reflected by a p-value of 0.0053. Additionally, there was a significant increase in BMI among those with NAFLD (32.62 ± 0.49 kg/m2) compared to those without NAFLD (29.66 ± 1.55 kg/m2), with a p-value of less than 0.001. In terms of clinical characteristics, individuals with NAFLD showed significant increases in the prevalence of hypertension (100.0%), ischemic heart disease (95.83%), diabetes mellitus (100.0%), obesity (100.0%), dyslipidemia (100.0%), valvular disease (100.0%), and statin use (100.0%) compared to those without NAFLD, all with p-values of less than 0.001. However, there were no significant differences in the prevalence of atrial fibrillation (29.2%) and heart failure (95.83%) between the two groups, with p-values of 0.884 and 0.384, respectively.

Table 2.Echocardiography and Cardiac Dysfunctions in cases with and without NAFLD

Variables	NAFLD				P-Value
	No (n = 76)		Yes (n = 24)		
Echocardiography					
• **Ejection fraction (Mean ±SD)**	64.33 ± 0.96		62.82 ± 2.41		<0.001 * t
• **Left atrial diameter (Mean ±SD)**	44.76 ± 1.23		46.67 ± 2.41		0.001 * t
• **RVSP (Mean ±SD)**	42.45 ± 4.60		43.63 ± 3.85		0.260 t
• **Aortic Root Diameter (Cm) (Mean ±SD)**	3.85 ± 0.32		3.91 ± 0.34		0.4369 t
• **Right Ventricle Size (Cm) (Mean ±SD)**	4.47 ± 0.37		4.52 ± 0.38		0.56 t
• **IVSD (Cm) (Mean ±SD)**	0.98 ± 0.12		0.99 ± 0.12		0.7819 t
• **LVEDD (Cm) (Mean ±SD)**	5.43 ± 0.38		5.45 ± 0.4		0.7887 t
• **LVESD (Cm) (Mean ±SD)**	4.2 ± 0.3		4.23 ± 0.31		0.7184 t
• **LVPWD (Cm) (Mean ±SD)**	1.08 ± 0.12		1.09 ± 0.12		0.7819 t
Dysfunctions	**No**	%	**No**	%	
• **Diastolic dysfunction** • **(grade 0–1 or indeterminate)**	28	36.8	11	48.8	0.431 x
• **Diastolic dysfunction (Grade ≥ 2)**	48	63.16	13	54.17	
• **RV systolic dysfunction**	21	27.6	8	33.3	0.592 x
• **Motion abnormalities**	45	59.21	14	58.33	0.94 x

t: t-test, x: Chi square, *: Statistically significant at $p \leq 0.05$

(**Table 2**) provides an overview of echocardiographic findings and cardiac dysfunctions in cases with and without non-alcoholic fatty liver disease (NAFLD). Among the 76 cases without NAFLD and 24 cases with NAFLD, several significant differences were observed. Notably, there was a significant decrease in ejection fraction in individuals with NAFLD (62.82 ± 2.41) compared to those without NAFLD (64.33 ± 0.96), with a p-value of less than 0.001. Additionally, the left atrial diameter was significantly larger in the NAFLD group (46.67 ± 2.41) compared to the non-NAFLD group (44.76 ± 1.23), with a p-value of 0.001. On the other hand, there were no significant differences in right ventricular systolic pressure (RVSP), aortic root diameter, right ventricle size, interventricular septal thickness (IVSD), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), and left ventricular posterior wall thickness (LVPWD) between the two groups, as indicated by the non-significant p-values. In terms of cardiac dysfunctions, there was no significant difference in the prevalence of diastolic dysfunction (grades 0-1 or indeterminate) between the NAFLD (48.8%) and non-NAFLD (36.8%) groups, with a p-value of 0.431. Similarly, there was no significant difference in the prevalence of diastolic dysfunction (Grade ≥ 2), RV systolic dysfunction, and motion abnormalities between the two groups, with p-values of 0.592, 0.94, and 0.7819, respectively.

Table 3. Laboratory data in cases with and without NAFLD

Variables	NAFLD		P-Value
	No (n = 76)	Yes (n = 24)	
Total cholesterol (mg/dL)	157.70 ± 9.71	162.50 ± 8.89	0.034 *t
Triglycerides (mg/dL)	115.05 ± 4.44	113.33 ± 10.74	0.452 t
LDL-C (mg/dL)	64.04 ± 5.69	85.36 ± 6.21	<0.001 *t
HDL-C (mg/dL)	46.29 ± 2.71	41.80 ± 2.68	<0.001 *t
Platelets (x10^9/L)	247.46 ± 20.60	240.04 ± 19.35	0.122 t
AST (U/L)	29.84 ± 6.45	49.13 ± 4.55	<0.001 *t
ALT (U/L)	32.97 ± 4.90	46.54 ± 5.77	<0.001 *t
INR	1.14 ± 0.10	1.06 ± 0.09	<0.001 *t
Total bilirubin (mg/dL)	0.57 ± 0.10	0.53 ± 0.05	0.008 *t
Albumin (g/L)	3.79 ± 0.44	3.33 ± 0.05	<0.001 *t
FIB-4	2.07 ± 0.22	2.09 ± 0.17	0.64 t
NFS	1.12 ± 0.37	0.90 ± 0.34	0.012 *t

t: t-test, *: Statistically significant at $p \leq 0.05$

(**Table.3**) displays the laboratory data for cases with and without non-alcoholic fatty liver disease (NAFLD). In a comparison between 76 cases without NAFLD and 24 cases with NAFLD, several notable differences were observed. There was a significant increase in total cholesterol levels among individuals with NAFLD (162.50 ± 8.89 mg/dL) compared to those without NAFLD (157.70 ± 9.71 mg/dL), with a p-value of 0.034. Conversely, there were no significant differences in triglyceride levels, platelet counts, and the FIB-4 index between the two groups, as indicated by non-significant p-values. LDL-C levels were significantly higher in the NAFLD group (85.36 ± 6.21 mg/dL) than in the non-NAFLD group (64.04 ± 5.69 mg/dL), with a p-value of less than 0.001. Additionally, HDL-C levels were significantly lower in individuals with NAFLD (41.80 ± 2.68 mg/dL) compared to those without NAFLD (46.29 ± 2.71 mg/dL), with a p-value of less than 0.001. Furthermore, there were significant increases in AST, ALT, INR, total bilirubin, and albumin in individuals with NAFLD, with p-values less than 0.001, indicating potential liver function and coagulation profile abnormalities. On the other hand, the NFS score was significantly lower in the NAFLD group (0.90 ± 0.34) compared to the non-NAFLD group (1.12 ± 0.37) with a p-value of 0.012.

Table 4. Relation between NAFLD and different parameters

Variables	NAFLD				P-Value
	No (n = 76)		Yes (n = 24)		
	No.	%	No.	%	
Cirrhosis by imaging	29	38.2	13	54.2	0.166 x
Post NAFDL	14	18.4	4	16.7	1.000 x
Post cardiac	15	19.7	9	37.5	0.076 x
LSM score \ kPa	4.70 ± 0.51		8.09 ± 0.17		<0.001 *t
CAP score \dB/m	217.8 ± 8.09		292.62 ± 25.09		<0.001 *t

t: t-test, x: Chi square, *: Statistically significant at $p \leq 0.05$

(**Table.4**) explores the relationship between non-alcoholic fatty liver disease (NAFLD) and various parameters. In a comparison between 76 cases without NAFLD and 24 cases with NAFLD, some noteworthy trends emerged. Notably, while there was no significant difference in the prevalence of cirrhosis by imaging between the two groups, there was a slight increase in the percentage of individuals with cirrhosis in the NAFLD group (54.2%) compared to the non-NAFLD group (38.2%), although this difference did not reach statistical significance, with a p-value of 0.166. Furthermore, there were no significant differences in the prevalence of post-NAFDL and post-cardiac conditions between the two groups, with p-values of 1.000 and 0.076, respectively. However, the liver stiffness measurement (LSM) score was significantly higher in individuals with NAFLD (8.09 ± 0.17 kPa) compared to those without NAFLD (4.70 ± 0.51 kPa), with a p-value of less than 0.001. Similarly, the controlled attenuation parameter (CAP) score was significantly higher in the NAFLD group (292.62 ± 25.09 dB/m) than in the non-NAFLD group (217.8 ± 8.09 dB/m), with a p-value of less than 0.001.

Discussion

NAFLD is the most common liver disease, affecting 25% of the worldwide population. NASH affects 2–7% of the population and may lead to cirrhosis or hepatocellular carcinoma if ignored **(Angona et al., 2020).** According to **Younossi et al. (2016),** liver-related complications and CVD account for at least 40% of NAFLD deaths. NAFLD is a risk factor for CVD and CHD even after controlling for age, sex, family history of CVD, obesity, hypertension, dyslipidemia, diabetes, and smoking **(Targher et al., 2016).** NAFLD increases CVD and CHD risk in several studies. Radiographic identification of NAFLD increases the risk of fatal and nonfatal CVD events such as coronary heart disease (CHD) and cerebrovascular accidents **(Przybyszews et al., 2021).**

A critical pathological link between atherogenic lipoprotein patterns and vascular immune activation and inflammation in NAFLD patients is the activation of Toll-like receptors (TLRs) by apolipoprotein-B containing lipoproteins, notably those containing apolipoprotein C3 (ApoC3). This activation, in turn, triggers the NLRP3 inflammasome, which is involved in the development of vascular inflammation and atherosclerotic cardiovascular disease. Additionally, saturated fatty acids like palmitic acid can induce vascular inflammation by activating TLRs 2 and 4, further contributing to vascular damage and atherosclerosis in NAFLD patients. Abnormal glucose metabolism and hepatic insulin resistance are also hallmark features in both NAFLD and CVD pathogenesis. Insulin resistance and impaired insulin signaling affect various processes linked to atherogenesis, enhanced atherosclerotic lesion progression, and plaque vulnerability. Persistent hyperglycemia and postprandial glucose spikes promote oxidative stress, inflammasome activation, vascular inflammation, and dysregulation of lipoprotein metabolism (**Kasper et al., 2021**).

In **Ismael et al. (2020)**, The average age of participants was 48 years (±8 SD), with 30% being female. 52% smoked, 30% had type 2 diabetes, and 36% had essential hypertension.

In our research, 24 (24%) participants had NAFLD. Contrary to the finding of **Ajmal et al., 2014**, who detected NAFLD in 69.2% (72/104) using ultrasonography (USG), with 50% (36/72) having grade 1 NAFLD and the remainder grade 2 NAFLD.

A primary cause of NAFLD mortality is CVD. Metabolic risk worsens liver disease with obesity, insulin resistance, T2DM, and

NAFLD. 25% of NAFLD patients develop NASH and fibrosis, and 7% develop cirrhosis and end-stage liver disease. Fibrosis severity affects long-term outcomes such as CVD **(Pais and Maurel, 2021).**
NAFLD patients had higher AF recurrence, subclinical atherosclerosis, and high-risk plaques than controls **(Donnellan et al., 2020).** NAFLD and CVD/CKD are not linked to obesity or T2DM **(Papademetriou et al., 2018).**

The research connected NAFLD to HTN, DM, obesity (BMI>30 kg/m2), dyslipidemia, valvular disease, and statin usage. Increased left atrial diameter and decreased EF with NAFLD.
The meta-analysis by **Wu et al. (2016)** confirmed that NAFLD is associated with an increased risk of incident CVD (HR 1.37; 95% CI 1.10–1.72). NAFLD patients are also more likely to develop hypertension (HR 1.16; 95% CI 1.06–1.27). The severity of NAFLD, particularly the presence of NASH, significantly increases the risk of CVD (HR 2.97; 95% CI 1.03–8.52).
Furthermore, several trials have indicated that NAFLD is linked to the presence of aortic-valve sclerosis and mitral annulus calcification, factors that could promote the development of functionally relevant valve diseases in this population **(Bonapace et al., 2014; Mantovani et al., 2015).**

There is a growing body of evidence suggesting that metabolic dysregulation serves as the common factor explaining the observed associations of NAFLD with conditions like hypertension, coronary artery disease, and structural heart disease. Consequently, a group of experts recently proposed the term "metabolic (dysfunction) associated fatty liver disease" or "MAFLD" as a more suitable and inclusive term, better reflecting the pathogenesis of NAFLD **(Eslam et al., 2020).**

We found no association between NAFLD and atrial fibrillation. Our results were inconsistent with **Targher et al. (2013)** prospective cohort study of 400 patients with T2DM, they observed a significantly higher incidence of atrial fibrillation over a 10-year follow-up period in diabetic patients with concurrent NAFLD compared to diabetic individuals without NAFLD (OR 4.49; 95% CI 1.6–12.9; $p < 0.005$). These findings were corroborated by a Finnish prospective cohort study of 958 subjects conducted by **Käräjämäk et al. (2015),** which also revealed that NAFLD independently predicted the occurrence of atrial fibrillation, regardless of the presence of T2DM.

Individuals with NAFLD exhibited significantly higher levels of total cholesterol, LDL-C, AST, ALT, INR, and lower levels of HDL-C, total bilirubin, and albumin compared to those without NAFLD. However, Triglycerides, platelets, FIB-4, and NFS were not associated with NAFLD.Liver disease predicts CV events in NAFLD patients independent of type 2 diabetes and obesity **(Younossi et al., 2016).** After multiple risk factor adjustments, NAFLD patients showed a higher rate of left ventricular hypertrophy (82% vs. 18%; $p = 0.01$). LVD quadrupled, affecting more cardiac functions **(Mantovani et al., 2015).**
In the SHIP study, NAFLD patients had a higher prevalence of aortic valve sclerosis (36.8% vs. 28.4%; $p < 0.001$) **(Markus et al., 2013).** NAFLD diabetics exhibit aortic sclerosis **(Bonapace et al., 2014).**

Leaking valves, larger hearts, and exhausted pumping are linked to NAFLD. An Italian research found that older NAFLD patients hospitalized for acute heart failure had a higher mortality risk (adjusted-HR 1.82, 95% confidence intervals 1.22-2.81, p 0.005). The study indicated that heart failure patients with maintained ejection fraction had higher NAFLD fibrosis (**Yoshihisa et al., 2018**).

A recent meta-analysis of two cross-sectional studies and three cohort studies encompassing 238,129 people found that NAFLD increases the incidence of AF. Comparing healthy livers to individuals without liver disease led to this finding. Relative risk (RR) was 2.06 and 95% CI was 1.10 to 3.85 in the pooled study. Remember that the included studies were heterogeneous **(Wijarnpreecha et al., 2018).**

ALT and AST showed significant positive correlation with NAFLD, while total bilirubin and albumin showed negative correlation with NAFLD. Uneven plasma LDL-C levels in CVD and NAFLD. LDL-C may signify liver disease or lipid-lowering medication. This at-risk population needs NAFLD-specific CVD risk assessments. Patients with steatosis exhibited higher BMIs, hyperglycemia, total cholesterol, triglycerides, and mean uCRP concentrations (4.5 vs. 2.79 mg/L; $P < 0.001$) **(Lizardi-Cervera et al., 2007)**

Corey et al. (2016) found that NAFLD CVD is independently predicted by a higher Model for End-Stage Liver Disease scores, lower albumin, and lower salt. Later prospective studies in biopsy-proven NAFLD patients found that advanced biopsy fibrosis and higher scores independently predicted CVD.

Current estimates from the World Health Organization (WHO) indicate that approximately 54% of all strokes and 47% of ischemic heart disease cases directly result from high blood pressure **(Sepanlou et al., 2020; Brouwers et al., 2021).** Furthermore, arterial hypertension heightens the likelihood of heart failure, peripheral arterial occlusive disease, and cardiac arrhythmias, particularly atrial fibrillation **(Kjeldsen, 2018; Brouwers et al., 2021).**
Within the population of individuals with NAFLD, the prevalence of arterial hypertension varies between 40% and 70%. Emerging evidence underscores a strong association between NAFLD and an increased risk of developing prehypertension (i.e., systolic blood pressure: 120–139 mmHg, diastolic blood pressure: 80–89 mmHg) and hypertension **(Ryoo et al., 2014; Aneni et al., 2015).** Prospective epidemiological studies conducted in France and Germany over 9- and 5-year observation periods, respectively, revealed a two- to three-fold rise in the incidence of arterial hypertension **(Lau et al., 2012;Bonnet et al., 2017).**

Among participants in the OPERA study in Finland, whether hypertensive or normotensive, those with hepatic steatosis observed on ultrasound displayed significantly higher 24-hour, daytime, and nighttime mean values of systolic and diastolic blood pressure compared to those without NAFLD **(Mantovani et al., 2021).** Notably, an association with a non-dipping blood pressure pattern exhibited a trend (30.9% vs. 24.6%; p=0.057) **(Vasunta et al., 2012).** In a group of hypertensive patients, ultrasonography revealed fatty liver more frequently when non-dipping or reverse dipping patterns were observed in 24-hour ambulatory blood pressure monitoring. Additionally, baroreceptor sensitivity was reduced in NAFLD patients with increased blood pressure variability **(Latea et al., 2013; Singh et al., 2017).**
As we found an association between valvular diseases and NAFLD, similar findings by **(Mari et al., 2019)** as they reported that the prevalence of aortic stenosis, aortic insufficiency, mitral stenosis, and mitral insufficiency was significantly higher in NAFLD patients compared to the control group (1.2% vs. 0.22%, 1.32% vs. 0.32%, 0.66% vs. 0.27%, and 1.87% vs. 0.41%, respectively; $P<0.001$). In the multivariate logistic regression analysis, NAFLD was found to be an independent risk factor for VHD (OR 2.39, 95% CI 2.17-2.78, $P<0.001$).

Study recommendation: More prospective studies are recommended to identify the exact role of NAFLD in the pathophysiology of CVD. The strong association between CVD and NAFLD underlines the need for early identification and adequate treatment of cardiometabolic risk factors. More studies regarding used drugs in cardiac patients with NAFLD are recommended.

Study limitations: The present study had limited sample size with only 24 (24%) patients suffering from NAFLD and was a single center experience. The study included patients from Qena governorate only while different risk factor maybe different across the country. Additionally, the diagnosis of NAFLD was based on ultrasound imaging but was not confirmed by liver biopsy.

Conclusion

We found a 24% incidence of NAFLD existing in patients with cardiovascular conditions, with significant correlations with factors like sex, age, BMI, hypertension, diabetes, obesity, dyslipidemia, statin usage, ejection fraction, left atrial diameter, total cholesterol, LDL-C, AST, ALT, INR, and lower levels of HDL-C, total bilirubin, and albumin, LSM score, and CAP score.

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