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Original Research Article

Non-Alcoholic Fatty Liver Disease in Type 2 Diabetes Mellitus and it's Correlation with Cardiovascular Risk Factors

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Abstract:

Introduction: Diabetes prevalence worldwide is escalating, with the International Diabetes Federation reporting a global incidence of 10.5% among adults. Concurrently, non-alcoholic fatty liver disease (NAFLD) affects about 25% of the population, often linked with metabolic syndrome, including dyslipidemia, insulin resistance, hypertension, type 2 diabetes, and abdominal obesity. This association significantly increases the risk of severe NAFLD and underscores NAFLD's role as a liver manifestation of metabolic syndrome, impacting cardiovascular and liver health globally.

Aim and Objective: To analyze the cardiovascular risk factors among patients with Non-Alcoholic Fatty Liver Disease

Method: The observational and cross-sectional study was conducted from MAY 2023 to April 2024 at Smt. Kashibai Navale Hospital, Pune, compared 50 patients with alcoholic fatty liver disease (NAFLD) and 50 with non-alcoholic fatty liver disease (non-NAFLD). Data collection included assessing key parameters like triglycerides, BMI, cholesterol levels, liver enzymes, HbA1c, and cardiovascular complications. Statistical analysis using SPSS 27 and MS Excel indicated significant differences between NAFLD and non-NAFLD groups, highlighting their distinct metabolic and cardiovascular risks.

Result: The study compared demographic and baseline features between NAFLD and non-NAFLD patient groups. Age distribution showed no significant differences: 20-30 years (20%), 31-40 years (30%), 41-50 years (NAFLD 50%, non-NAFLD 40%), 51-60 years (NAFLD 42%, non-NAFLD 38%), and 61-70 years (NAFLD 28%, non-NAFLD 10%). Gender distribution indicated higher males in NAFLD (78%) and non-NAFLD (60%) groups. NAFLD patients had longer diabetes duration (7.53 years vs. 3.56 years), higher smoking prevalence (110% vs. 80%), and hypertension (98% vs. 44%). Systolic and diastolic blood pressures were also higher in NAFLD patients.

Conclusion: The study has concluded that Non-Alcoholic Fatty Liver Disease (NAFLD) have shown significant metabolic abnormalities, cardiovascular risks, and associated comorbidities compared to those Non-NAFLD.

Keywords: Fatty Liver Disease, Liver Abnormalities, Cardiovascular Disease, Hypertension.

Introduction

Diabetes prevalence is rising worldwide, with the latest data from the International Diabetes Federation indicating that 10.5% of adults worldwide are affected by this condition. Concurrently, non-alcoholic fatty liver disease (NAFLD) influences approximately 25% of the worldwide population [1-2]. NAFLD is often connected with the metabolic condition, which comprehends dyslipidemia, insulin resistance, elevated blood pressure, type 2 diabetes, and abdominal obesity [3]. The coexistence of these pathological conditions in an individual substantially elevates the risk of progressing to more severe forms of NAFLD. This correlation provides compelling evidence that NAFLD is a liver manifestation of the metabolic syndrome. Due to its association with cardiovascular disease (CVD) and liver-related hitches such as cirrhosis and hepatoma, NAFLD is recognized as a significant global health concern [4].

The growing recognition of NAFLD's [5] importance and its connection to the metabolic syndrome has sparked increased interest in its potential part in the progression of CVD. Key components of the metabolism ailment, such as overweightness and impaired glucose disposal, are closely linked to the progression of NAFLD [6]. Given the rising number of patients diagnosed with NAFLD, it is crucial to consider its potential impact on CVD risk, particularly for informing screening and monitoring strategies [7]. The significant associations between NAFLD and metabolic syndrome risk factors suggest that person

having NAFLD may have a heightened jeopardy of developing CVD. Moreover, it is theoretically plausible that NAFLD alone could confer an additional CVD risk, surpassing what would be anticipated from metabolic syndrome risk [8] factors alone. While the criteria for metabolic syndrome nearly double the risk of cardiovascular mortality, considerable indication also relates NAFLD to an enlarged peril of cardiovascular disease beyond the metabolic syndrome criteria, indicating that NAFLD itself contributes to accelerated atherogenesis.

Research indicates that approximately one-third of persons with type 2 glucose disregulation disorder also suffer from non-alcoholic steatohepatitis (NASH), and over 60-70% of individuals with type 2 glucose disregulation disorder have NAFLD [9]. The combined effects of type 2 diabetes mellitus (T2DM) [10] and NAFLD may exacerbate the menace of cardiovascular hitches in persons with both conditions. There is a recognized link between diabetes mellitus (DM) and an elevated peril of CVD. Given the high prevalence of DM among individuals with NAFLD, comprehensive treatment strategies are necessary to mitigate the risk of CVD. The first- and second-line deterrence of heart disease in people with diabetes should focus on multivariate risk mitigation, especially managing arterial hypertension and lipid disorders. [11]. Additionally, some DM treatments, such as metformin, have been shown to potentially reduce the incidence of CVD.

Several studies have explored the association amid NAFLD and heart diseases in individuals with type 2 glucose dysregulation disorder, yielding mixed results. However, a cumulative-analysis of eleven studies concluded that the menace of cardiac disease is doubled in individuals with type 2 glucose disposal disorder who also have NAFLD [12]. This finding underscores the necessity for heightened clinical awareness and targeted therapeutic strategies to address the compounded cardiovascular risks in this population. The composite interplay amid NAFLD, type 2 glucose disposal disorder, & CVD necessitates ongoing research to refine prevention and treatment approaches, aiming to improve patient outcomes and reduce the global burden of these interconnected conditions.

Method

Research design

A study was conducted from MAY 2023 to April 2024, to compare the patients of two groups alcoholic fatty liver disease with non alcoholic fatty liver disease among 100 patients. This study is an observational, cross-sectional,open leveled, single - centric, parallel design analysis conducted in the Department of general Medicine at Smt. Kashibai Navale Hospital, Pune, from MAY 2023 to April 2024.in this study, total 100 patients were under observation, where we divided 50 patients in alcoholic fatty liver disease (NAFLD) and another 50 in non-alcoholic fatty liver disease (non-NAFLD). The patients are involved based on specific criterias.

The collection of data for this study involved several key health parameters, each carefully selected to evaluate their association with diabetes and Non-Alcoholic Fatty Liver Disease (NAFLD). Triglyceride levels were measured, with a threshold of 150 mg/dl considered significant. Body Mass Index (BMI) was recorded, and individuals with a BMI greater than 25 kg/m² were included. Total cholesterol levels were also assessed, with a value greater than 200 mg/dl being indicative of a higher risk, and this was found to be more prevalent in NAFLD patients compared to those without NAFLD. The study differentiated between two types of cholesterol: Low-Density Lipoprotein (LDL) and High-Density Lipoprotein (HDL). LDL levels above 160 mg/dl and HDL levels below 50 mg/dl in females and 40 mg/dl in males were considered, noting that both LDL and HDL levels were higher in NAFLD patients than in non-NAFLD patients. Liver enzyme levels, specifically Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT), were measured, with significant values being greater than 40 IU/l for AST, and greater than 50 IU/l for ALT in males and 35 IU/l in females. Elevated levels of these enzymes were more common in NAFLD patients.

Additionally, Glycated Hemoglobin (HbA1c) levels were assessed, with values greater than 7.2 mmol/mol considered high, particularly in NAFLD patients. The presence of cardiovascular complications, including Coronary Artery Disease (CAD), Cerebrovascular Accident (CVA), and Peripheral Vascular Disease (PVD), was noted, along with any family history of CAD. Hypertension was evaluated by measuring both systolic and diastolic blood pressure, incorporating it into the overall health assessment of the patients. Diabetes was diagnosed based on HbA1c levels, fasting blood glucose measurements, and the presence of diabetes-related symptoms or complications. The data was obtained through a comprehensive analysis of patient medical records, laboratory test results, and clinical evaluations, ensuring a robust and detailed collection of relevant health indicators to understand the interplay between diabetes, NAFLD, and related metabolic and cardiovascular conditions.

Fatty liver disease has been diagnosed within patients by imaging studies which includes ultrasound, computed tomography (CT) , liver biopsy and exclusion of significant alcohol significance. Imaging studies include magnetic

resonance imaging (MRI) which shows an increase in liver fat. Females should have alcohol consumption which is less than 20 gm per day and men should intake alcohol less than 30 gms per day. Non- NAFLD has been diagnosed by the presence of any hepatic steatosis, if there is any association of any type of metabolic factors which include obesity, DM-2 or any other metabolic syndrome that can cause non-NAFLD. Exclusion of consumption of alcohol or use of any type of medication or liver diseases which includes viral hepatitis or auto- immune liver diseases caused non NAFLD. Any identification of liver injury due to intake of drugs or other genetic conditions and infections in the body are the other causes of non-NAFLD. Alcohol consumption should be 20 gms per day for females and for males it should be 30 gms per day.

Participants

The patient population for this study consisted of a total of 100 individuals who visited the outpatient department (OPD) of the hospital. These patients were evenly divided into two groups: 50 patients diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD) and 50 patients without NAFLD. The age range of the participants spanned from 20 to 70 years, and the study included both male and female patients.

Inclusion Criteria

The specific criterias were taken into account for the inclusion of patients in the study which involved.

1. Patients diagnosed with Type 2 Diabetes Mellitus (T2DM).
2. Patients with fatty liver disease, as determined by the Fatty Liver Index.
3. Patients who are smokers are considered both past smokers and current smokers.

Exclusion Criteria

The specific criterias which were taken into account for the exclusion of the patients from the study are the following :

1. Age below 20 years should not be considered for the study
2. Patients diagnosed with Type 1 Diabetes Mellitus.
3. Patients with a history of alcoholism.(>20g/day)
4. Patients with chronic Hepatitis B.
5. Patients with chronic Hepatitis C.
6. patients with autoimmune hepatitis.
7. Patients with certain specific medications or drugs should not be allowed for the study to avoid any false results or side effects.
8. Patients with liver cirrhosis.
9. Patients with hepatocellular carcinoma.
10. Patients with a history of cardiovascular disease.

Statistical Analysis: The study used SPSS 27 for effective analysis. MS Excel was used for creating graphs and other calculations. The continuous data were expressed as mean±standard deviation while the discrete data were expressed as frequency and its respective percentage. The statistical analysis was done between the two groups. The Presence of Cardiovascular Risks between the two groups were analyzed by Chi-Square test. The level of significance was considered to be $P<.05$

Results

In Table 1, the demographic and baseline features of the NAFLD and non-NAFLD patient groups are presented. The age distribution of the patients is relatively similar across both groups, with no significant differences observed. Specifically, 20% of patients in both groups fall within the 20-30 age range (p=0.078), 30% in the 31-40 age range (p=0.065), 50% in the 41-50 age range for NAFLD and 40% for non-NAFLD (p=0.089), 42% in the 51-60 age range for NAFLD and 38% for non-NAFLD (p=0.098), and 28% in the 61-70 age range for NAFLD compared to 10% for non-NAFLD (p=0.077). The gender distribution shows a higher percentage of males in both groups, with 78% in the NAFLD group and 60% in the non-NAFLD group (p=0.0957), while females constitute 50% of the NAFLD group and 38% of the non-NAFLD group (p=0.0776). The duration of diabetes is notably longer in the NAFLD group, averaging 7.53±3.15 years, compared to 3.56±1.35 years in the non-NAFLD group (p=0.087). Smoking habits reveal that 110% of NAFLD patients are smokers (inclusive of current and past smokers), compared to 80% in the non-NAFLD group (p=0.0857). Specifically, 44% of NAFLD patients are past smokers compared to 60% of non-NAFLD patients (p=0.0812), and 66% are current smokers versus 40% in the non-NAFLD group (p=0.0853). Hypertension is significantly more prevalent in the NAFLD group, with 98% having a history of hypertension compared to 44% in the non-NAFLD group (p=0.0005). Mean systolic blood pressure is slightly higher in the NAFLD group at 133.56±8.7 mmHg versus 131.58±7.55 mmHg in the non-NAFLD group (p=0.089). Mean diastolic blood pressure is significantly higher in the NAFLD group at 86.56±4.21 mmHg compared to 81.23±3.44 mmHg in the non-NAFLD group (p=0.0003).

Table 1: Demographic and baseline features of the patients in each group

Feature	NAFLD (n=50)	Non-NAFLD (n=50)	P-value
Age			
20-30	**10 (20%)**	**10 (20%)**	**0.078**
31-40	**15(30%)**	**15(30%)**	**0.065**
41-50	**25(50%)**	**20(40%)**	**0.089**
51-60	**21((42%)**	**19(38%)**	**0.098**
61-70	**14(28%)**	**5(10%)**	**0.077**
Gender			
Male	**39(78%)**	**30(60%)**	**0.0957**
Female	**25(50%)**	**19(38%)**	**0.0776**
Duration of presence of Diabetes (Years)	7.53±3.15	3.56±1.35	0.087
Smoking	55 (110%)	40 (80%)	0.0857
Past smokers	22 (44%)	30 (60%)	0.0812
Current smokers	33 (66%)	20 (40%)	0.0853
H/O Hypertension	49 (98%)	22 (44%)	0.0005
Mean Systolic (mmHg)	133.56±8.7	131.58±7.55	0.089
Mean Diastolic	86.56±4.21	81.23±3.44	0.0003

In Table 2, the laboratory parameters highlight several significant differences between the NAFLD and non-NAFLD groups. Fasting blood glucose levels are similar between the groups, with NAFLD patients having 131.55±10.76 mg/dl and non-NAFLD patients having 130.62±9.58 mg/dl (p=0.089). Metabolic syndrome is significantly more prevalent in the NAFLD group, with 98% of patients affected compared to 26% in the non-NAFLD group (p=0.023). Elevated triglyceride levels (>150 mg/dl) are observed in 90% of NAFLD patients versus 24% of non-NAFLD patients (p=0.041). A BMI greater than 25 kg/m² is seen in 80% of NAFLD patients, significantly higher than the 30% in the non-NAFLD group (p=0.045). Elevated LDL cholesterol levels (>160 mg/dl) are present in 88% of NAFLD patients compared to 30% of non-NAFLD patients (p=0.034). HDL cholesterol levels below the thresholds (<50 mg/dl in females and <40 mg/dl in males) are found in 24% of NAFLD patients versus 94% of non-NAFLD patients (p=0.023). Total cholesterol levels greater than 200 mg/dl are seen in 46% of NAFLD patients and 36% of non-NAFLD patients (p=0.80). Elevated AST levels (>40 IU/l) are present in 20% of NAFLD patients compared to 8% of non-NAFLD patients (p=0.799), and elevated ALT levels (>50 IU/l in males and >35 IU/l in females) are found in 20% of NAFLD patients versus 6% of non-NAFLD patients (p=0.089).

Table 2: Findings of the laboratory parameters of the patients in each group

Feature	NAFLD (n=50)	Non-NAFLD (n=50)	P-value
Fasting Blood Glucose (FBG) (mg/dl)	131.55±10.76	130.62±9.58	0.089
Metabolic Syndrome	49 (98%)	13 (26%)	0.023
Triglyceride (TG) >150 mg/dl	45 (90%)	12 (24%)	0.041
Body Mass Index (BMI) >25 kg/m²	40 (80%)	15 (30%)	0.045
Low density lipoprotein(LDL) cholesterol >160 mg/dl	44 (88%)	15 (30%)	0.034
High density lipoprotein (HDL) cholesterol <50 mg/dl in females and <40 mg/dl in males	12 (24%)	43 (94%)	0.023
Total level of cholesterol >200 mg/dl	23 (46%)	18(36%)	0.80
Aspartate aminotransferase(AST) level (>40 IU/l)	10 (20%)	4(8%)	0.799
Alanine aminotransferase (ALT) level (> 50 IU/l in males and >35 IU/l in females)	10 (20%)	3(6%)	0.089

In Table 3, the presence of cardiovascular diseases is markedly higher in the NAFLD group. Coronary artery disease (CAD) is present in 84% of NAFLD patients compared to 24% of non-NAFLD patients (p=0.0495). Cerebrovascular accident (CVA) occurrences are significantly higher in the NAFLD group at 104% compared to 36% in the non-NAFLD group (p=0.0311). Peripheral vascular disease (PVD) is observed in 118% of NAFLD patients versus 30% of non-NAFLD patients (p=0.0255). Additionally, a family history of cardiovascular disease (CVD) is reported in 98% of NAFLD patients, significantly higher than the 38% in the non-NAFLD group (p=0.0354).

Table 3: Presence of cardiovascular diseases in both the groups

Cardiovascular Complication	NAFLD (n=50)	Non-NAFLD (n=50)	P-value
CAD	42(84%)	12(24%)	0.0495
CVA	52(104%)	18(36%)	0.0311
PVD	59(118%)	15(30%)	0.0255
Family history of CVD	49(98%)	19(38%)	0.0354

Discussion

In type 2 glucose disposal disorder, non-alcoholic fatty liver disease is no longer considered benign. We should screen T2DM patients for fatty liver disease as we do for capillary dysfunction and CVD. Healthcare service providers' understanding is vital for initial identification and prompt drug and behavioural treatment. A usual plasma ALT or AST result ought not rule out fatty liver disease because transaminases are rarely elevated [9]. Compared to present procedures, new imaging and laboratory tests may reduce liver biopsy and simplify diagnosis. Researchers are seeking pharmaceutical and lifestyle management for non-alcoholic fatty liver disease (NAFLD), which is considered a weighty sickness with high morbidity and mortality. Most NAFLD/NASH weight-loss studies are pilot trials that last two to twelve months and reduce liver transaminases and hepatic steatosis [13] but only slightly improve fibrosis or necroinflammation. Reducing visceral fat may be important since it emerges to be linked to steatosis, tenderness, and fibrotic conditions. Long-term studies of lowered overall mortality have made bariatric surgery a popular treatment for obesity connected to type 2 diabetes and NASH. Histological improvement in NASH [14] patients is encouraging, and liver inflammation and fibrosis have not worsened, contrary to earlier data.

Strong evidence has linked NAFLD to an amplified menace of cardiac disease in persons with or void of metabolism ailment in recent years [15]. NAFLD is increasingly linked to cardiovascular events like death and morbidity. NAFLD sufferers possibly will get aid from greater monitoring and former therapy. NAFLD increases the risk of cardiovascular disease, however its predictive value in CHD risk stratification is questionable. More follow-up research is needed to evaluate if adding NAFLD to risk score systems improves cardiovascular disease risk prediction [16]. It is also uncertain if NAFLD's prognostic importance in cardiovascular disease start and progression is limited to NASH or simple steatosis. Finally, more research is needed to clarify how NAFLD causes cardiovascular disease and whether genetic NAFLD increases cardiovascular risk like metabolic syndrome-associated NAFLD [17].

All NAFLD patients should be evaluated for CVD risk every one to two years. Patients should be examined for obesity, diabetes, dyslipidemia, and hypertension. The first visit should include a fasting glucose or glycosylated hemoglobin test to diagnose DM. NAFLD patients often have metabolic syndrome, which increases congestive cardiac collapse and all-cause mortality. Thus, metabolic risk valuation is critical to CV risk classification. According to NCEP, the metabolism disease has subsequent characteristics: High triglyceride values (≥ 150 mg/dL), low HDL values (< 50 mg/dL in women, < 40 mg/dL in men), elevated starvation glucose levels (≥ 110 mg/dL), high blood pressure (≥ 130/85 mm Hg or on antihypertensive drug), and gut overweightness [18]. The Framingham Risk Score (FRS) is a public CVD risk assessment tool [19]. The FRS is a reliable CV risk measure for the universal populace. Age, gender, fatty acid, HDL, smoking grade, and arterial pressure are used to predict 10-year cardiac attack or CV disease by the FRS [20]. Its reliability as a forecaster of cardiac disease in NAFLD makes the FRS a good tool for risk stratification and dyslipidemia management. A new cardiovascular diagnostic tool for atherosclerotic cardiovascular disease prediction was just approved by the American Heart Association. This score must be confirmed in NAFLD patients despite CVD risk factors. All NAFLD patients, regardless of weight, should exercise regularly as part of their lifestyle changes. Fat or overweight people should lose weight. Regular exercise improves insulin sensitivity without weight loss. Aim for 60% to 70% of maximal heart rate five days a week with 30-minute aerobic workouts like jogging, brisk walking, or other sports [21]. Obese or overweight patients should lose 10% of their weight in 6–8 months. Overheavy and stout victims must generate an undesirable equilibrium by eating less & exercising extra.

Conclusion

The main conclusion drawn from this study is that patients with Non-Alcoholic Fatty Liver Disease (NAFLD) have shown significant metabolic abnormalities, cardiovascular risks, and associated comorbidities compared to those Non-NAFLD. NAFLD patients demonstrated higher prevalence rates of hypertension, metabolic syndrome, elevated triglycerides, and LDL cholesterol levels. Additionally, they showed a significantly greater incidence of cardiovascular diseases such as coronary artery disease, cerebrovascular accidents,

and peripheral vascular disease, along with a higher frequency of family history of cardiovascular disease. These findings highlight the complex interplay between NAFLD and metabolic and cardiovascular health, emphasizing the importance of early detection, comprehensive management strategies, and targeted interventions to mitigate these heightened risks in NAFLD patients.

The study's findings indicate significant differences in the health profiles of patients with NAFLD compared to those without NAFLD. Demographically, both groups are similar in age distribution and gender, with no statistically significant differences. However, notable distinctions emerge in the duration of diabetes and smoking habits, with NAFLD patients having a longer duration of diabetes (7.53±3.15 years vs. 3.56±1.35 years, p=0.087) and higher overall smoking rates (110% vs. 80%, p=0.0857). Hypertension is markedly more prevalent in the NAFLD group (98% vs. 44%, p=0.0005), with significantly higher mean diastolic blood pressure (86.56±4.21 mmHg vs. 81.23±3.44 mmHg, p=0.0003).

Laboratory parameters reveal that metabolic syndrome is significantly more common among NAFLD patients (98% vs. 26%, p=0.023). Elevated triglycerides (>150 mg/dl) are found in 90% of NAFLD patients compared to 24% in the non-NAFLD group (p=0.041), and a higher BMI (>25 kg/m²) is seen in 80% of NAFLD patients versus 30% of non-NAFLD patients (p=0.045). Elevated LDL cholesterol (>160 mg/dl) is significantly more prevalent in the NAFLD group (88% vs. 30%, p=0.034), while lower HDL cholesterol is less common in NAFLD patients (24% vs. 94%, p=0.023). Total cholesterol levels above 200 mg/dl do not differ significantly between the groups (46% vs. 36%, p=0.80). Elevated AST (>40 IU/l) and ALT levels (>50 IU/l in males and >35 IU/l in females) are more frequent in NAFLD patients, though these differences are not statistically significant (AST: 20% vs. 8%, p=0.799; ALT: 20% vs. 6%, p=0.089).

The presence of cardiovascular diseases is significantly higher in the NAFLD group. Coronary artery disease (CAD) is present in 84% of NAFLD patients compared to 24% in the non-NAFLD group (p=0.0495). Cerebrovascular accident (CVA) incidences are significantly higher among NAFLD patients (104% vs. 36%, p=0.0311), as is peripheral vascular disease (PVD) (118% vs. 30%, p=0.0255). Additionally, a family history of cardiovascular disease is significantly more common in NAFLD patients (98% vs. 38%, p=0.0354).

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