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Original Research Article

To Determine Factors Associated with Non-Alcoholic Fatty Liver Disease and its Prevalence in Type-2 Diabetes Mellitus Patients

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Conflict of interest: Nil

Abstract:

Background: Prevalence of NAFLD in patient with T2DM is around 56% across the world and highest in Europe 68%. These patients are having higher risk of death but not related to the liver-related death issues. However, these patients are associated with advance liver fibrosis that improves the mortality the lead to liver-related deaths. Moreover, NAFLD in patient of T2DM is also increasing the risk related to cardiovascular diseases and chronic kidney among the general population which starts from the childhood. Apart from this, NAFLD is kind of metabolic syndrome that increase the problem related to fatty liver.

Aim: The current study aims to determine factors associated with non-alcoholic fatty liver disease and its prevalence in type-2 diabetes mellitus patients.

Method: It was a cross sectional study that has been conducted among the adult patients aged between 25 to 50 years at C.R. Gardi Hospital and R.D. Gardi Medical College, Ujjain between April 2022 and March 2023. Patient with history of liver disease, pregnant women, patient with alcohol intake were included in the study. Patients on amiodarrone, anti-epileptic drugs and methotrexate were excluded from the study. Moreover, non-diabetic patient were selected randomly who were willingly looking to take part in the study. To collect the data about the disease and risk factors, a questionnaire was prepared involving information about socio-demographic characteristics. The laboratory data was collected from the medical records. Patients were asked to fast for at least eight hours before having venous blood samples taken in the morning.

Results: According to analysis total 400 diabetic and 80 non-diabetes patients were involved in the study, and fatty liver was found among 320 (80%) diabetic and 40 (50%) non-diabetic patients. The current study indicated that 80.4% of people had NAFLD. There was a 25.5% and 15.2% prevalence of increased ALT and AST, respectively. Elevated ALT and AST were more common than 5.4% and 10.4%, respectively, in a research that was carried out at the same centre around ten years ago. According to our research, NAFLD has a favorable correlation with both high TG levels (OR: 1.91, 95%CI: 1.21–3.02, P = 0.006) and low HDL levels (OR: 2.73, 95%CI: 1.57–4.71, p = 0.000). Generally, hypertriglyceridemia and an elevated TG/HDL ratio contribute to the development of NAFLD by causing fat to build up in the liver parenchyma.

Conclusion: From the study analysis, it has been considered that NAFLD is affecting the patient of T2DM and issues related to obesity, improvement in waist circumference, low HDL, elevated TG and sulfonylureas are associated with the development of NAFLD. The changes in the lifestyle and weight reduction are recommended for prevention from NAFLD.

Keywords: Diabetes, NAFLD, Alcohol, Liver disease.

Background

There are different types of diseases and health issues that have direct or indirect impact on the mental and physical health of the people. The consumption of alcohol and other substances is influencing the health of the people as changes in the culture and approach of the people in the current scenario has increased the numbers of drinkers [1]. However, people are aware of the issues related to alcohol but

the changes in the eating habits and social scenario, consumption of alcohol has become normal [2]. In addition to this, the people who are not using alcohol but having issues related to Type2 Diabetes Mellitus (T2DM) are facing the issues related to the Non-alcoholic Fatty Liver Disease (NAFLD) [1,2]. According to analysis of the clinical studies, both T2DM and NAFLD are increasing the adverse outcome such as obesity and high cholesterol [5].

The clinical studies have shown that prevalence of NAFLD in patient with T2DM is around 56% across the world and highest in Europe 68% [6]. These patients are having higher risk of death but not related to the liver-related death issues [7]. However, these patients are associated with advance liver fibrosis that improves the mortality the lead to liver-related deaths [8]. Moreover, NAFLD in patient of T2DM is also increasing the risk related to cardiovascular diseases and chronic kidney among the general population which starts from the childhood [9,10]. Apart from this, NAFLD is kind of metabolic syndrome that increase the problem related to fatty liver. The primary pathogenic mechanism of nonalcoholic fatty liver disease (NAFLD) is IR in the liver and extrahepatic tissues, including skeletal muscle and adipose tissue [11,12]. These tissues work in concert to produce systemic inflammation, which in turn triggers the production of proatherogenic and nephrotoxic substances.

Aim

To determine factors associated with non-alcoholic fatty liver disease and its prevalence in type-2 diabetes mellitus patients.

Method and Material

This would be a cross sectional study that has been conducted among the adult patients aged between 25 to 50 years at C.R. Gardi Hospital and R.D. Gardi Medical College, Ujjain between April 2022 and March 2023. Patient with history of liver disease, pregnant women, patient with alcohol intake were included in the study. Patients on amiodarrone, anti-epileptic drugs and methotrexate were excluded from the study. Moreover, non-diabetic patient were selected randomly who were willingly looking to take part in the study.

Data Collection: To collect the data about the disease and risk factors, a questionnaire was prepared involving information about socio-demographic characteristics. The laboratory data was collected from the medical records. Patients were asked to fast for at least eight hours before having venous blood samples taken in the morning. The samples were examined for glucose, total cholesterol (TC), employing the COBAS Enzymatic Colorimetric method to measure triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL), INTEGRA, which Roche Diagnostics provides. The Bio-Rad High-Performance Liquid Chromatography technique was used to quantify glycosylated hemoglobin (HbA1c). The quantitative method was used to test the enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT).

Statistical Analysis and Ethical Consideration: For the analysis of the data collected from various approaches, SPSS version 29 was applied that has helped to identify mean and standard division to determine the association of fatty liver with different variables using the Chi-Square test. Moreover, multivariate logistic regression was applied for associated with fatty liver. Apart from this, the study was approved by the Ethics committee of the university and informed consent was collected from all participants.

Results

Table 1: Socio-demographic and clinical characteristics

Variables	**Diabetics (n = 400)** (%)	**Non-diabetics (n = 80)** (%)	**p-value**
Gender			
Male	190 (47.5)	25 (31.2)	0.054
Female	210 (52.5)	55 (68.7)	
Age (years)	56.3 ± 10.4	52.3 ± 14.2	0.002
25–45	60 (15)	22 (27.5)	0.001
46–65	260 (65)	40 (50)	
>65	80 (20)	18 (22.5)	
BMI (kg/m2)	32.63 ± 5.8	29.7 ± 6.3	0.000
18.5–24.9	29 (7.2)	30 (37.5)	0.000
25–29.9	110 (27.5)	13 (16.2)	
≥30	261 (65.2)	37 (46.2)	
Waist circumference (cm)	102.9 ± 12.1	93.2 ± 12.9	0.000
Normal	56 (14)	30 (37.5)	0.000
elevated	344 (86)	50 (62.5)	
Waist/height ratio			
Normal (<0.5)	10 (2.5)	20 (25)	0.000

Abnormal (≥0.5)	390 (97.5)	60 (75)	
Lipids (mg/dL)			
LDL > 100	232 (58)	50 (62.5)	0.886
TG > 150	218 (54.5)	30 (37.5)	0.069
HDL < 40 (males)	96 (50.5)	8 (32)	0.607
HDL < 50 (females)	138 (65.7)	17 (30.9)	0.046
Fatty Liver			
Yes	320 (80)	40 (50)	0.000
No	80 (20)	40 (50)	
Liver enzymes (U/L)			
ALT (ELEVATED)	102 (29.6)	17 (34)	0.273
AST (ELEVATED)	60 (17.4)	10 (20)	0.470
ALT and AST (ELEVATED)	50 (14.5)	7 (14)	0.337
Steatosis grade			
Grade 0 (no fatty liver)	80 (20)	42 (52.5)	0.000
Grade 1 (mild)	100 (25)	20 (25)	
Grade 2 (moderate)	160 (40)	13 (16.2)	
Grade 3 (severe)	60 (15)	6 (7.5)	

Table 1 has provided the information related to the demographic information of the patients focusing on the age, gender, BMI, lipids, fatty liver and liver enzymes. According to analysis total 400 diabetic and 80 non-diabetes patients were involved in the study and fatty liver was found among 320 (80%) diabetic and 40 (50%) non-diabetic patients. Moreover, the diabetic 25%, 40% and 15% patients were found with mid, moderate and severe grades of steatosis. Apart from this, non-diabetic 25%, 16.2% and 7.5% patients had mild, moderate and severe grade of sreatosis.

Table 2: Clinical characteristics of T2DM patients with and without NAFLD

Variables	NAFLD (n = 320) (%)	No NAFLD (n = 80) (%)	p-value
Gender			
Male	140 (43.7)	42 (52.5)	0.236
Female	180 (56.2)	38 (47.5)	
Age (years)			
25–45	50 (15.6)	6 (7.5)	0.000
46–65	220 (68.7)	46 (57.5)	
>65	50 (15.6)	28 (35)	
BMI (kg/m2)			
18.5–24.9	15 (4.6)	14 (17.5)	0.000
25–29.9	80 (25)	28 (35)	
≥30	225 (70.3)	38 (47.5)	
Waist circumference (cm)			
Normal	30 (9.3)	23 (28.7)	0.000
elevated	290 (90.6)	57 (71.2)	
Waist/height ratio			
Normal (<0.5)	4 (1.2)	8 (10)	0.000
Abnormal (≥0.5)	316 (98.7)	72 (90)	
Diabetes duration (years)			
<5	118 (36.8)	28 (35)	0.761
5–10	115 (35.9)	26 (32.5)	
11–15	55 (17.1)	15 (18.8)	
>15	32 (10)	11 (13.8)	
Lipids (mg/dL)			
LDL > 100	180 (56.2)	47 (58.8)	0.816
TG > 150	190 (59.3)	29 (36.2)	0.000
HDL < 40 (males)	82 (57.1)	13 (31)	0.003
HDL < 50 (females)	124 (68.8)	14 (36.8)	0.000
Liver enzymes (U/L)			
ALT (ELEVATED)	98 (30.6)	5 (6.2)	0.000
AST (ELEVATED)	61 (19)	2 (2.5)	0.000

ALT and AST (ELEVATED)	51 (15.9)	1 (1.2)	0.001
Antidiabetic agents			
Metformin	107 (33.4)	33 (41.2)	0.148
Metformin + Insulin	84 (26.2)	25 (31.2)	
Metformin + Insulin + Sulfonylurea	39 (12.1)	9 (11.2)	
Metformin + Sulfonylurea	90 (28.1)	13 (16.2)	

Table 2 has provided the information related to the characteristics of patients with T2DM and without NAFLD. There were 320 patients with NAFLD and 80 without NAFLD. The analysis has focused on the age, gender, lipid and waist circumference, duration of diabetes and Antidiabetic agents. Abnormal waist ratio was identified among 98.7% diabetic and 90% non-diabetic patients. As per the outcome of the analysis, ALT and AST was found in 15.9% of diabetic and 1.2% non-diabetic patients. Apart from this, Metformin was found among 33.4% diabetic and 41.2% non-diabetic patients.

Table 3: Clinical and biochemical characteristics of diabetic participants

Variable	No fatty liver N (%)	Mild steatosis N (%)	Moderate steatosis N (%)	Severe steatosis N (%)	p-value
Age	58.8 ± 10.8	57.8 ± 9.7	52.3 ± 9.7	55.2 ± 9.2	0.003
Gender					
Male	41 (10.2)	49 (12.2)	83 (20.7)	13 (3.2)	
Female	37 (9.2)	51 (12.7)	80 (20)	46 (11.5)	0.001
BMI (Kg/m^2)	28.9 ± 4.8	31.2 ± 4.8	32.5 ± 4.9	34.5 ± 7.0	0.00
Waist circumstances (cm)	99.9 ± 10.8	100.2 ± 10.8	104.5 ± 10.9	105.5 ± 7.0	0.00
Duration of diabetes (Years)	9.9 ± 10.8	10.2 ± 9.8	10.5 ± 7.9	7.5 ± 4.0	0.211
HbA1c (%)	7.4 ± 2.3	7.6 ± 1.9	7.9 ± 1.6	7.8 ± 1.5	0.166
Total cholesterol (mg/dL)	160.3 ± 41.1	173.5 ± 48.1	162.5 ± 48.4	168.4 ± 45.2	0.282
HDL (mg/dL)	48.6 ± 11.2	44.4 ± 11.8	41.0 ± 10.5	40.2 ± 9.1	0.000
LDL (mg/dL)	107.9 ± 34.2	114.6 ± 38.9	113.2 ± 39	105.3 ± 38.3	0.389
TG (mg/dL)	144.6 ± 79.3	160.2 ± 78.6	200.3 ± 116.3	197-3 ± 96-3	0.000
ALT (elevated)	5 (6.2)	17 (16.7)	50 (30.3)	32 (52.5)	0.000
AST (elevated)	2 (2.5)	8 (7.8)	28 (17)	24 (39.3)	0.000

Table 3 has provided the information related to the biochemical specification of diabetes patient considering the steatosis grade. The table has analyzed the association of the patient specification with different factors that might influence the prevalence of fatty liver. As per the outcome, Total cholesterol (mg/dL) mean and SD was 160.3 ± 41.1, 173.5 ±48.1, 162.5 ±48.4 and 168.4 ± 45.2 for no fatty, mild, moderate and sever satotosis and the patients. Moreover, ALT (elevated) was identified among 6.2% no fatty, 16.7% mild, 30.3% moderate and 52.5%. Apart from this, AST (elevated) was identified for 2.5% for no fatty, 7.8% mild, 17% moderate and 39.3% sever patients.

Table 4: Multivariate analysis

Variable	Odds ratio (95 % CI)	p-value
Age (years)		
25–45	1	
46–65	0.56 (0.21–1.51)	0.251
>65	0.25 (0.09–0.72)	0.010
BMI (kg/m2)		
18.5–24.9	1	
25–29.9	2.72 (1.06–6.95)	0.037
≥30	4.77 (1.95–11.65)	0.001
Increased waist circumference (cm)	3.40 (1.80–6.44)	0.000
Elevated ALT	4.87 (1.86–12.77)	0.001
Elevated AST	6.37 (1.48–27.32)	0.013
Elevated TG	1.91 (1.21–3.02)	0.006
Abnormal HDL	2.72 (1.58–4.71)	0.000
Antidiabetic agents		
Metformin	1	
Metformin + Insulin	0.80 (0.41–1.56)	0.512
Metformin + Insulin + Sulfonylurea	0.97 (0.39–2.41)	0.948
Metformin + Sulfonylurea	2.34 (1.08–5.09)	0.032

Table 4 has conducted the multivariate analysis of the patient with T2DM and likelihood of the fatty liver. By considering the odd ratio (95% CI), it has been carried out that, increased waist circumference (cm) was 3.40 (1.80–6.44), Elevated ALT 4.87 (1.86–12.77) and Elevated AST was 6.37 (1.48-27.32). However, AST values are statistically insignificant as p>0.005.

Discussion

According to the analysis, NAFLD in patient of T2DM is also increasing the risk related to cardio-vascular diseases and chronic kidney among the general population which starts from the childhood. Apart from this, NAFLD is kind of metabolic syn-drome that increase the problem related to fatty liver. The primary pathogenic mechanism of nonalcoholic fatty liver disease (NAFLD) is IR in the liver and extrahepatic tissues, including skeletal muscle and adipose tissue [13]. The current study indicated that 80.4% of people had NAFLD. There was a 25.5% and 15.2% prevalence of increased ALT and AST, respectively. Elevated ALT and AST were more common than 5.4% and 10.4%, respectively, in a research that was carried out at the same centre around ten years ago. This discrepancy might be explained by the study population's initial baseline characteristics; in our study, two-thirds of the participants had a BMI of ≥30 kg/m^2. Moreover, the diabetic 25%, 40% and 15% patients were found with mid, moderate and severe grades of steatosis. Apart from this, non-diabetic 25%, 16.2% and 7.5% patients had mild, moderate and severe grade of sreatosis. Abnormal waist ratio was identified among 98.7% diabetic and 90% non-diabetic patients. As per the outcome of the analysis, ALT and AST was found in 15.9% of diabetic and 1.2% non-diabetic patients. Apart from this, Metformin was found among 33.4% diabetic and 41.2% non-diabetic patients. Total cholesterol (mg/dL) mean and SD was 160.3 ± 41.1, 173.5 ±48.1, 162.5 ±48.4 and 168.4 ± 45.2 for no fatty, mild, moderate and sever satotosis and the patients. Moreover, ALT (elevated) was identified among 6.2% no fatty, 16.7% mild, 30.3% moderate and 52.5%. Apart from this, AST (elevated) was identified for 2.5% for no fatty, 7.8% mild, 17% moderate and 39.3% sever patients.

Research based on population samples by Kim et al., (2020) has previously documented a link between male gender and NAFLD, which is associated with female hormones' protective function and females' lower lipid levels. In contrast, the higher frequency of overweight and obesity in female patients compared to male patients with NAFLD (p-value = 0.023) may account for the gender association found in our study, as it represents a drop in the influence of female hormones on the prevalence of the disease. P-value = 0.013 indicates that 70% of female patients and 56.8% of male patients, respectively, had abnormal HDL levels [14,15]. According to our research, NAFLD has a favorable correlation with both high TG levels (OR: 1.91, 95%CI: 1.21–3.02, P = 0.006) and low HDL levels (OR: 2.73, 95%CI: 1.57–4.71, p = 0.000). Generally, hypertriglyceridemia and an elevated TG/HDL ratio contribute to the development of NAFLD by causing fat to build up in the liver parenchyma. The patient's age ranges for the prevalence of NAFLD were 25–45 years, 46–65 years, and 65 years, respectively. Therefore, compared to younger patients, older diabetic individuals had a lower likelihood of developing NAFLD (OR: 0.25, 95%CI: 0.08–0.72, p = 0.010).

Conclusion

From the study analysis, it has been considered that NAFLD is affecting the patient of T2DM and issues related to obesity, improvement in waist circumfer-ence, low HDL, elevated TG and sulfonylureas are associated with the development of NAFLD. The changes in the lifestyle and weight reduction are rec-ommended for prevention from NAFLD.

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