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ORIGINAL ARTICLE

Risk Factor Analysis and Prevalence of the Non-Alcoholic Fatty Liver Disease in Patients with Type-II Diabetes Mellitus

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ABSTRACT

Though non-alcoholic fatty liver disease (NAFLD) is associated strongly with type-II diabetes mellitus (T2DM), the NAFLD analysis in patients with Type-II DM remainders an issue.

Aim: This analysis was designed to examine the pervasiveness and NAFLD risk factors in T2DM patients.

Study Design: A retrospective, cross-sectional study

Place and duration: In the department of Medicine, Mardan Medical Complex and Northwest General Hospital & Research Centre Hayatabad, Peshawar for six-months duration from May 2021 to October 2021.

Methods: This study includes 420 patients with DM2 presented and treated for glycaemic control. Targeted patients were selected and separated using strict exclusion criteria. Patients with NAFLD (study group) and patients without NAFLD (control group) were divided into two groups. Then, comparison of thirty-four factors amid the 2 groups were done. In addition, NAFLD risk factors multivariate analysis was executed by means of logistic regression. Lastly, the combined predictive indicator (CPI) as well as the analytical significance of the biochemical predictors for NAFLD were assessed by receiver operational characteristic curve (ROC) analysis.

Results: The general incidence of NAFLD in this study among DM2 patients was 53.6%. 17 patient target factors were recognised using univariate analysis NAFLD analysis, and eight factors turned out to be important forecasters of NAFLD by means of a binary logistic regression model. Moreover, C-peptide and CPI have augmented analytical importance for NAFLD in patients with T2DM. **Conclusion:** This analysis delivers a thorough analysis of NAFLD risk factors in subjects with DM2. This information can be cast-off to ensure the effective treatment and timely analysis of NAFLD.

Keywords: NAFLD, metabolism, routine examination, obesity, screening, type-II diabetes

INTRODUCTION

Non-alcoholic fatty liver disease is definite by the occurrence of fatty liver disease in the absenteeism of subordinate reasons, and presently documented widely as the communal reason of CLD globally, with an incidence of 27%[1-2]. The NAFLD prevalence in Pakistan has crumpled in the last twenty years. Though, this is often ignored in clinical exercise. The patients of NAFLD are often symptomless Clinically, have smoking history and are in poor health. Several current analyses are held to evaluate the relationship amid metabolic syndromes (MetS) and NAFLD, counting abdominal obesity, elevated plasma glucose levels, hyperlipidaemia, hypertension and diabetes mellitus, and have shown that MetS is suggestively related with Non-alcoholic fatty liver[3-4]. Amongst these ailments, type-II DM is supposed to be the chief forecaster of progression of NAFLD. The incidence of NAFLD has increased in proportion to the increase in DM2 cases worldwide[5-6]. The T2DM existence seems to quicken the sequence of disease of liver in NAFLD[7]. The augmented incidence in DM2 patients with NAFLD and its grave clinical consequences are of apprehension. Earlier discoveries exhibited that the NAFLD incidence and non-alcoholic steatohepatitis (NASH) in T2DM subjects reaches up to 63%, though the NAFLD incidence amongst Type-II DM patients was 45.4%. Based on earlier studies, NAFLD is an autonomous causing factor for cardiovascular diseases and T2DM, which suggests that the relationship between NAFLD and T2DM may be bi-directional[8-9]. Currently, several laboratory tests and serum biomarkers for NASH are projected to evade unnecessary liver biopsies. These biomarkers include hormone markers and liver fibrosis, as well as markers of oxidative stress, insulin resistance (IR), apoptosis and inflammation[10]. However, these markers can be expensive to test and therefore have limited broad use[11]. So, the advancement of dependable NAFLD risk factors turn out to be necessary guide for treatment in T2DM patients. Although various analysis has recognised DM as a main NAFLD risk factor, few studies have identified risk factors for NAFLD events in patients with DM2[12]. Therefore, this study was designed to examine the pervasiveness and NAFLD risk factors in T2DM patients.

MATERIALS AND METHODS

This retrospective cross-sectional study in the department of Medicine, Mardan Medical Complex and Northwest General Hospital & Research Centre Hayatabad, Peshawar for six-months duration from May 2021 to October 2021among 420 treated DM2 patients admitted for glycaemic control. Specific cases were selected conferring to the criteria of exclusion. Based on the 1998 WHO analytical standards for diabetes mellitus, the following criteria of diagnosis were used: typical diabetes mellitus symptoms with fasting glucose ≥ 7.0 mmol / L or RBS ≥ 11.1 mmol / L or two-hour OGTT shows blood sugar ≥11.1 mmol / L.

The criteria of exclusion were as follows:

1 Subjects over 74 years of age;
2 Patients who consume alcohol excessively or do not have data on their consumption of alcohol
3 subjects with alcoholic hepatitis, viral hepatitis, autoimmune hepatitis or drug-induced hepatitis;
4 Subjects who consumed drugs to regulate their hormone or lipid levels within the previous three-months;
5 Cases of gallstones or cholecystitis;
6 Patients with a recent surgery, infection, diabetic ketoacidosis, tumor or any other diseases of the blood;
7 Patients with hypothyroidism or hyperthyroidism;
8 Hypoproteinaemia, hyperuricemia, gestational diabetes, gout, chronic gastritis or chronic kidney disease;
9 Patients with missing data of laboratory tests, physical examination, ultrasound or CT of the liver. The Ethical Committee accepts the analysis. The 420 specific patients were alienated into 2 groups: patients without NAFLD (control group) and NAFLD patients (study group). A total of 34 NAFLD-related factors were included in this study as independent variables, and demographics, body measurements, and biochemistry were obtained from patients' medical histories. The demographic data comprised gender, age, diabetes extent, history of drug use,

history of drug use, alcohol consumption and smoking. Smoking was categorized as a current smoker or a non-smoker. Physical evaluation encompassed weight in kg, height in cm, circumference of hip and waist, BP and heart rate. The laboratory tests counting liver and renal chemistry, diabetes tests and serum lipid levels were compiled from discharge and admission data and precisely, serum biochemical factors embrace HbA1c, fasting insulin, fasting plasma glucose (FPG), fasting C-peptide, triglycerides (TG), total cholesterol (TC), serum uric acid (SUA), HDL, ALT and AST. All the data was collected from the hospital records. An overnight fasting blood levels was done for analysis. HbA1c, fasting samples for C-Peptide and FINS were analyzed and collected. The glucose oxidase method was used for FPG levels analysis. The chemistry of the liver, renal, and blood lipids were assessed with an automatic biochemical analyser. Also, body mass index (BMI); the waist to height ratio (WHtR) was determined as: WHtR = waist circumference (m) / height (m); WHR = waist circumference (m) / hip circumference (m); the score of the homeostasis model assessment- IR (HOMA-IR) was designed according to the given formula: [FINS (mIU / mL) FPG (mmol / L)] / 22.5.

SPSS 22.0 was applied for analysis of data. Continuous variables are articulated as mean ± SD and independent samples are accessed by Student's t-test. One-dimensional analysis ($p < 0.05$ considered statistically significant) was applied to select variables which are independent related to the occurrence of NAFLD. Finally, all estimators were evaluated using ROC (receiver working character) curves.

RESULTS

420 total patients with DM2 participated in the study. According to ultrasound or computed tomography, the frequency of NAFLD was over 53.6%. Patients with NAFLD (study group) and patients without NAFLD (control group) were divided into two groups. The clinical characteristics and demographic profile of the patients in the control and study groups are given in Table 1. The 7 factors were included for continuous variables as; serum creatinine, AST, TG, GGT, ALP, HOMA-IR and fasting insulin. After that these factors are applied with log transformation. 17 parameters were analyzed by Univariate analysis that were significantly associated ($P < 0.05$) with NAFLD at admission and binary logistic regression model was used for entry of these factors. The results exhibited that Type-II DM patients with NAFLD were younger than patients not having NAFLD (mean age 53.63 ± 11.21 years and 58.21 ± 8.96 years). Remarkably, a substantial relationship between NAFLD and age was found as 78.37% of patients <40 years of age had NAFLD ($P < 001$). Stronger relationship between NAFLD and T2DM was noticed. Additionally, patients with T2DM and NAFLD had high WHR, BMI, diastolic blood pressure, WHtR, TG, SUA, AST, ALT, TP, GGT, peptide Higher C fasting, albumin and lower fasting insulin levels - cholesterol lipoprotein density (LDL-c) than not having NAFLD.

Table 1: The clinical characteristics and Demographic of patients with T2DM with or without NAFLD

Parameter	Overall (n=420)	With NAFLD (n=225)	Without NAFLD (n=195)	P- value
Features				
Age in years	54.81 (±9.31)	53.63 (±11.21)	58.21 (±8.96)	0.004
<40	41 (100)	32 (78.1)	9 (21.9)	
41–50	76 (100)	42 (55.3)	34 (44.7)	
51–60	153 (100)	79 (51.6)	74 (48.4)	
>60	150 (100)	69 (46)	81 (54)	
Duration of Diabetes in year	5.92 (±7.01)	5.48 (±6.52)	8.10 (±7.11)	0.002
Sex (male/female)	226/194	118/96	108/98	0.390
Smoking status (yes/no)	68/420	39/225	29/195	0.529
Body measurement				
Diastolic Pressure (mmHg)	83.05 (±10.50)	85.67 (±11.50)	80.42 (±9.41)	0.002
Systolic Pressure (mmHg)	130.11 (±16.10)	131.70 (±18.15)	130.66 (±15.81)	0.59
WHtR	58.5 (±7.85)	58.92 (±56.55)	55.41 (±58.11)	< 0.001
Heart rate (beats/min)	80.11 (±9.23)	80.80 (±8.99)	79.41 (±9.46)	0.152
≧25	222 (52.8)	139 (62.6)	83 (37.4)	
<25	198 (47.2)	68 (34.34)	130 (65.66)	
BMI (kg/m2)	24.78 (±3.48)	25.11 (±4.11)	24.44 (±2.85)	< 0.001
WHR	92.96 (±7.21)	94.68 (±68.12)	91.24 (±60.30)	< 0.001
Renal chemistry				
Blood uric acid (mmol/L)	289.17 (±73.11)	308.99 (±68.11)	269.34 (±78.11)	< 0.001
Serum creatinine	58.51 (±27.51)	59.88 (±26.80)	57.14 (±28.22)	0.911
Blood urea nitrogen	5.55 (±2.14)	5.11 (±1.68)	5.98 (±2.60)	0.523
Liver chemistry				
AST (IU/L)	19 (±8.33)	22.88 (±11.83)	15.12 (±4.82)	< 0.001
ALT (IU/L)	23.12 (±14.67)	28.77 (±19.22)	17.47 (±10.12)	< 0.001
ALP (IU/L)	97.97 (±38.99)	100.15 (±35.31)	95.79 (±42.67)	0.155
GGT (IU/L)	34.59 (±39.36)	40.55 (±35.81)	28.64 (±42.91)	< 0.001
Direct bilirubin (mmol/L)	3.88 (±1.85)	3.92 (±1.95)	3.84 (±1.74)	0.821
Indirect bilirubin (mmol/L)	9.44 (±4.96)	9.22 (±6.56)	9.65 (±3.35)	0.602
Total bilirubin (mmol/L)	12.72 (±6.84)	11.44 (±7.62)	13.99 (±6.05)	0.742
Albumin (g/L)	42.44 (±4.46)	44.21 (±4.12)	40.67 (±4.80)	<0.001
Globulin (g/L)	28.13 (±4.27)	28.29 (±4.21)	27.96 (±4.33)	0.472
Total protein (g/L)	67.78 (±6.45)	68.67 (±5.98)	66.88 (±6.91)	0.007
Albumin to globulin ratio	1.67 (±0.34)	1.74 (±0.39)	1.59 (±0.28)	0.361
Blood lipids				
Cholesterol (mmol/L)	4.93 (±1.44)	4.96 (±1.22)	4.89 (±1.65)	0.071
Triglyceride (mmol/L)	2.34 (±2.35)	2.99 (±3.21)	1.68 (±1.46)	<0.001
LDL-cholesterol (mmol/L)	2.70 (±0.54)	2.44 (±0.74)	2.96 (±0.33)	0.164
HDL-cholesterol (mmol/L)	1.23 (±0.37)	1.29 (±0.34)	1.17 (±0.40)	<0.001
Diabetes tests				
FPG (mmol/L)	9.16 (±3.39)	9.33 (±3.32)	8.99 (±3.47)	0.90
HbA1c (%)	8.40 (±2.66)	8.64 (±2.67)	8.15 (±2.64)	0.820
Fasting insulin (mIU/mL)	9.98 (±10.76)	13.16 (±14.71	6.79 (±6.80)	<0.001
Fasting C-peptide (ng/mL)	2.33 (±1.12)	2.98 (±1.22)	1.68 (±0.89)	<0.001
HOMA-IR	4 (±7.32)	5.89 (±8.74)	2.71 (±2.11)	<0.001

We executed a logistic binary regression analysis to identify the clinical and personal factors related with NAFLD. As exhibited in Table-II, NAFLD risk factors were WHR, BMI while length of diabetes was a protecting factor (95% CI 0.911-0.980; odds ratio 0.940 p=0.002).

Table 2: The clinical and Personal factors related with NAFLD amongst patients with T2DM

Parameter	B coefficient	Odds ratio	95% CI	P-value
Diabetic duration (year)	- 0.059	0.940	0.911–0.980	0.002
Age (year)	- 0.018	0.978	0.959–1.009559	0.229
WHR (%)	0.075	1.081	1.015–1.124	0.005
Diastolic (mm Hg)	0.019	1.019	1.022–0.991	0.072
BMI (kg/m2	0.220	1.239	1.120–1.380	<0.001
WHtR (%)	- 0.002	0.982	0.940–1.070	0.979

Table 3: Routine blood biochemical factors related with NAFLD amongst patients with T2DM

Parameter	B coefficient	S.E.	Wald	ODD Ratio	95% CI	P-value
ALT (IU/L)	0.045	0.011	14.641	1.034	1.12–1.066	<0.001
TG (mmol/L)	2.280	0.562	16.822	9.542	3.305–27.951	<0.001
HOMA-IR1	0.781	0.362	4.712	2.170	1.082–4.360	0.029
C-peptide (ng/mL)	0.301	0.145	3.800	1.452	0.921–1.763	0.049
SUA (mmol/L)	0.004	0.003	4.115	1.010	1.000–1.008	0.039

DISCUSSION

NAFLD perceived by CT or ultrasound is communal in type 2 diabetic patients. This analysis presented NAFLD in 53.6%. In addition, we gathered biochemical and clinical information from subjects with type 2 diabetic patients and inspected important NAFLD risk factors[12-13]. We noticed that that significant NAFLD risk factors in multivariate and univariate analyses were WHR, BMI, UA, TG, IR or ALT. Moreover, the diabetes mellitus duration in patients with NAFLD was briefer than in patients not having NAFLD[14-15]. Logistic analysis of regression showed that diabetes duration was a defensive NAFLD factor. These outcomes are comparable to the study by Takeuchi Y, demonstrating that the incidence of NAFLD rises with the progress of Type-II DM. There has been a durable relation amid NAFLD and obesity, especially given rising obesity rates[16]. This study outcomes are chiefly in line with those previously testified showing that WHR, WHtR and BMI are commonly used anthropometric measures to assess the paraphernalia of obesity on NAFLD in comparison to the group of control, WHR, BMI and WHtR were higher significantly in subjects with T2DM and NAFLD. Also, ROC and LOC analyses showed that WHR and BMI are operative predictors[17-18]. The results of this analysis did not contain WHtR as an important factor of prognosis, but Lin et al. He found a durable relationship between the NAFLD severity and WHtR in children[19-20]. Moreover, it was found that an increase in WHtR is significantly associated with an increase in hypertension risk, mortality and cardiometabolic risk factors[21]. One new analysis institute that people with NAFLD have better progresses in insulin sensitivity and liver function after reasonable loss of weight with diet than those not having NAFLD. This study displayed that it is related with several biochemical factors counting liver chemistry (ALT), kidney chemistry (SUA), and diabetic effects (HOMA-IR and C-peptide), serum lipids (TG) signifying a mixture of these aspects are much important in forecasting NAFLD in DM2 subjects[22-23]. This study showed that the NAFLD pathogenesis is the consequence of many factors that make value of CPI clinically relevant in the treatment and diagnosis of NAFLD in T2DM patients. As formerly described, SUA levels in NAFLD and T2DM were associated positively with abnormal liver enzymes, central obesity, abnormal glucose metabolism and lipid metabolism, indicating the clinical significance of SUA in NAFLD and DM2 patients.

CONCLUSION

NAFLD is relatively communal in DM2 patients. This study presents the utmost significant factors for NAFLD in patients with T2DM (triglycerides, IR homeostasis model assessment, waist-to-hip ratio, body weight, duration of diabetes, alanine aminotransferase, C-peptide, CPI and serum uric acid. These data can be used to rapidly diagnose and effectively treat NAFLD, and to lessen liver-related mortality and morbidity in patients with diabetes.

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