Current Science International
Volume: 12 | Issue: 02| April - June| 2023

EISSN:2706-7920 ISSN: 2077-4435
DOI: 10.36632/csi/2023.12.2.20
Journal homepage: www.curresweb.com
Pages: 209-222

Evaluation of The Role of Neck Circumference as A Predictive Value for Non-Alcoholic Fatty Liver Disease in Type 2 Diabetic Patient

Ahmed A. El Hager, Mostafa T. Yousef Gabr, Abdallah A. Elsawy and Yasser M. Hafez

Internal Medicine Department, Faculty of Medicine, Tanta University, Tanta, Egypt

Received: 26 April 2023 **Accepted:** 31 May 2023 **Published:** 10 June 2023

ABSTRACT

Background: Recently, it has been recognized that non-alcoholic fatty liver disease (NAFLD) represents an important burden of disease for patients with type 2 diabetes mellitus (DM). those individuals not only have a high prevalence of NAFLD but also seem to have increased severity of the disease. Therefore, it is very important to diagnose NAFLD early and manage it properly in a primary stage which will enhance prognosis and prevent secondary complications. **Objective:** The present study aimed to evaluate the role of neck circumference (NC) as a predictive value for NAFLD in type 2 diabetic patients. **Patients and methods:** A total of 250 individuals who fulfilled our criteria were enrolled in this cross-sectional study. Physical examination, anthropometric measurements, and abdominal ultrasonography were performed by trained staff. Blood samples for biochemical tests were also obtained after fasting for 8 hr. **Results**: as regards NC for detection of NAFLD in type 2 DM, at a cut-off value of 38.25; the area under curve (AUC) was 0.647, the sensitivity was 81%, the specificity was 64%, the positive predictive value (PPV) was 60%, and the negative predictive value (NPV) was 83.47%. NC was associated with NAFLD in type 2 diabetic patients ($p<0.0001$) and remained significant even after adjustment for possible confounding factors. It was also significantly associated with other anthropometric indices, such as systolic blood pressure, diastolic blood pressure, disease duration of diabetes, height, weight, waist to hip ratio, alanine aminotransferase, triglycerides, cholesterol, and fatty liver status. **Conclusion:** Nick circumference was significantly correlated with NAFLD in type 2 diabetic patients. In addition, it had a high predictive value for NAFLD in type 2 diabetic patients among other common anthropometric indices. Therefore, it can be used as a simple and feasible tool for screening NAFLD in a large population with type 2 DM.

Keywords: Neck circumference**,** non-alcoholic fatty liver disease, diabetes mellitus.

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is a condition of chronic hepatic fat accumulation ranging from indolent fat deposition to severe lipotoxicity-induced steatohepatitis with necroinflammation. Being one of the major health problems increasing the risk of liver cirrhosis, liver cancer, and metabolic disorders and is regarded as a metabolic syndrome (MS) exhibited by the liver (Augustin *et al.,* 2017).

Recently, it has been recognized that NAFLD represents an important burden of disease for patients with type 2 DM. Individuals with type 2 DM not only have a high prevalence of NAFLD, up to 70% but also seem to have increased severity of the disease (Targher *et al.,* 2007).

Therefore, it is very important to diagnose NAFLD early and manage it properly in a primary stage which will enhance prognosis and prevent secondary complications.

The liver biopsy is the gold standard for fatty liver diagnosis. Being invasive, it cannot be used widely in the general population and is reserved for complicated forms of the disease. Blood serum transaminase has a very low sensitivity and will fail to detect many cases since it is normal in most cases of fatty liver disease. Although radiologic investigations, such as ultrasonography (US) and

Corresponding Author: Yasser Mostafa Hafez, Internal Medicine Department, Faculty of Medicine, Tanta University, Tanta, Egypt
E-mail: drymh80@yahoo.com, yasser.hafez@med.tanta.edu.eg

magnetic resonance spectroscopy, have high sensitivity, they are not cost-effective as primary screening tests in the general population (Idilman *et al.,* 2016).

On the other hand, anthropometric indices have been widely used as simple and feasible tools for screening metabolic disorders in the general population. The traditional one, such as body mass index (BMI), is not accurate as it only reflects the total body obesity, not the fat distribution, which is assumed to be much more imperative in metabolic diseases. Waist circumference (WC) and waist-to-height and waist-to-hip ratio (WHR) as a surrogate to central obesity are strongly associated with visceral adipose tissue (Guasch-Ferré *et al.,* 2012). Recent studies have also demonstrated that subcutaneous adipose tissue in the upper body has a stronger relationship with metabolic disorders than visceral adipose tissue (Patel and Abate, 2013).

In addition, NC as a surrogate for measuring upper-body subcutaneous fat has received attention (Assyov *et al.,* 2017). Several studies have shown the relationship between NC and MS. However, few studies had demonstrated the relationship between NC and NAFLD.

The aim of our study was the evaluation the role of NC as a predictive value for NAFLD in type 2 diabetic patients.

2. Patients and Methods

Study population and study setting:

This cross-sectional study was conducted on 250 patients with type 2 DM recruited from the Endocrinology & Diabetes outpatient Clinic and inpatient wards of the Internal Medicine Department of Tanta University Hospitals from April 2021 to May 2022.

These patients were categorized into 2 study groups: Group 1: 100 type 2 diabetic patients with NAFLD.Group 2: 150 type 2 diabetic patients without NAFLD.

Inclusion criteria:

250 patients, above the age of 18 years, were diagnosed as type 2 diabetic patients according to the American Association of Diabetes (ADA) criteria ((ADAPPC, 2021). Both sexes were included.

Exclusion criteria:

Patients < 18 years old, with a history of current/previous alcohol consumption of ≥ 30 g/day for men or ≥ 20 g/day for women, with a history of regular consumption of any medication known to cause hepatic steatoses such as (estrogen, corticosteroids, amiodarone, and tamoxifen), with known liver disease for any other etiology such as (viral hepatitis, Wilsons disease, hemochromatosis, and Cushing syndrome), with thyroid or any other disease that may interfere with NC, all were excluded. Also, pregnant and lactating females were excluded.

Study approval and Ethical consideration:

Permission was obtained from Research Ethics Committee as a part of the Quality Assurance Unit in the Faculty of Medicine at Tanta University to conduct this study and to use the facilities in the hospital. Informed written consent was obtained from all study participants after explaining the study design, anticipated benefits, and possible risks. Patients' privacy was ensured by coding the patients' data with a special number for each patient that included all of his investigations.

Methodology:

All the study participants were subjected to:

History taking:

As regards age, gender, cigarette smoking, alcohol consumption, duration of DM, any medications, and known liver or any other diseases.

Clinical examination:

All the study participants were subjected to measurement of the systolic and diastolic blood pressure. Chest, cardiac, and abdominal examination was performed excluding subjects with any abnormal findings. Furthermore, Anthropometric measurements (height, weight, hip circumference,

waist circumference, neck circumference) were also performed. Mathematical algebraic calculation of waist-to-hip ratio and body mass index.

Laboratory investigation:

Under quality control and safety procedure for sample collection, the blood samples (4 ml of venous blood) were collected in plain vacutainer tubes, after fasting overnight for 8 hr. Serum was separated from all specimens using centrifugation at 3000 rpm for 15 min. serum sample for assayed for Fasting plasma glucose (FPG), 2-hour postprandial plasma glucose (2h-PG), and glycosylated hemoglobin (HbA1c)., lipid profile, liver function tests, and Hepatitis B surface antigen (HBsAg) and hepatitis C virus antibody (HCV Ab) virology.

All biochemical parameters were determined by THERMO FISHER SCIENTIFIC Konelab Prime 60i and virology assessment with Roche Cobas E601 Immunology Analyzer.

Radiological assessment:

Abdominal ultrasonography: was performed using Philips Affiniti 50 Ultrasound Machine equipped with a convex probe 2 - 6 MHz (C6-2), and the radiologist was blinded to clinical and laboratory data of the patients. The fatty liver disease was reported based on (1) parenchymal brightness (echogenicity), (2) liver-to-kidney or liver-to-spleen contrast, (3) deep beam attenuation, (4) bright vessel walls, and (5) gallbladder wall and diaphragm definition. Its severity is categorized in a semi-quantitated manner according to Graif's criteria (Graif *et al.*, 2000).

Statistical analysis of the collected data:

Data were analyzed using the IBM SPSS software package version 23.0. (SPSS Inc., Chicago, IL, USA). Qualitative data were described using numbers and percentages. Quantitative data were described as mean and standard deviation for numerical variables with normal distribution, and median and interquartile range (IQR) for numerical variables with abnormal distribution. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Chi-square test: for categorical variables, to compare between different groups. Fisher's Exact or Monte Carlo correction: correction for chi-square when more than 20% of the cells have an expected count of less than 5. Student's t-test: for normally distributed quantitative variables, to compare two studied groups. Mann-Whitney test: for abnormally distributed quantitative variables, to compare two studied groups. Correlations between variables: were analyzed using (Pearson's) and (Spearman's rho) methods. Univariate and multivariate logistic regression analyses: were used to adjust for variables. Receiver operating characteristic curve (ROC): was used to compare the ability of variables to distinguish between specific groups of patients. The significance of the obtained results was considered at a P-value ≤ 0.05.

3. Results

As presented in table 1 and table 2, there was a statistically significant increase between DM patients with NAFLD and DM patients without NAFLD group as regards SBP, DBP, and disease duration (P-value ≤ 0.05). While, there was no significant difference between DM patients with NAFLD and DM patients without NAFLD group as regards age, gender, and smoking status (P-value > 0.05).

There was a statistically significant increase between DM patients with NAFLD and DM patients without NAFLD group as regards Wt, BMI, WC, WHR, and NC (P-value ≤ 0.05). While, there was no significant difference between DM patients with NAFLD and DM patients without NAFLD group as regards Ht, and HC (P-value > 0.05) as shown in table 3.

There was a statistically significant increase between DM patients with NAFLD and DM patients without NAFLD group as regards AST and ALT (P-value ≤ 0.05) in table 4. Furthermore, in table 5 there was a statistically significant increase between DM patients with NAFLD and DM patients without NAFLD group as regards FPG, 2h-PG, and HbA1c (P-value ≤ 0.05).

In table 6, a statistically significant increase between DM patients with NAFLD and DM patients without NAFLD group was detected as regards TGs, cholesterol, and LDL. Also, there was a statistically significant decrease between DM patients with NAFLD and DM patients without NAFLD group as regards HDL (P-value ≤ 0.05). Moreover, there was a statistically significant difference

between DM patients with NAFLD and DM patients without NAFLD group as regards fatty liver status (P-value ≤ 0.05) as detected in table 7.

In table 8, the NC was positively correlated with SBP, DBP, disease duration, Ht, Wt, WHR, ALT, TGs, cholesterol, and fatty liver status. Also; the neck circumference was negatively correlated with gender and smoking status.

Logistic regression analysis in table 9 revealed that disease duration, HBA1c, TGs, cholesterol, and HDL were significantly associated with affecting DM patients with NAFLD and DM patients without NAFLD.

Table 10 shows the univariate analysis which revealed that NC was significantly associated with NAFLD when adjusted with age. While table 11 shows the multivariate analysis revealed that neck circumference was significantly associated with NAFLD when adjusted with age, BMI, WC, and WHR.

Table 12 and figure 1 showed Receiver operating characteristic (ROC) curves analysis of NC, BMI, WC, HC, and WHR in the diagnosis of DM patients with NAFLD: according to NC for the detection of DM patients with NAFLD, at the cut-off value of 38.25; the area under the curve was 0.647, the sensitivity was 81%, the specificity was 64%, the PPV was 60%, and the NPV was 83.47%. As regards BMI for the detection of DM patients with NAFLD, at the cut-off value of 28.67; the area under the curve was 0.608, the sensitivity was 77%, the specificity was 59.33%, the PPV was 56.11%, and the NPV was 80.18%.

While as regard WC for the detection of DM patients with NAFLD, at the cut-off value of 95.50; the area under the curve was 0.649, the sensitivity was 66%, the specificity was 52%, the PPV was 57.34%, and the NPV was 83.17%. According to HC for the detection of DM patients with NAFLD, at the cut-off value of 105.5; the area under the curve was 0.569, the sensitivity was 66%, the specificity was 52%, the PPV was 47.82%, and the NPV was 63.93%. According to the WHR for the detection of DM patients with NAFLD, at the cut-off value of 0.9043; the area under the curve was 0.727, the sensitivity was 83%, the specificity was 82%, the PPV was 75.45%, and the NPV was 87.85% also found in table 12 and figure 1.

Table 1: Demographic characteristics of DM patients with NAFLD and DM patients without NAFLD

Groups / **Parameters**	**Group A NAFLD (n=100) (40%)**	**Group B Non-NAFLD (n=150) (60%)**	**Test of sig.**	**P-value**
Age (years)				
Mean ± SD	52.85±9.29	52.27±8.78		
Min.–Max.	28-74	30-71		
Gender				
Male	58(42.33%)	79(57.66%)	X^2= 0.690	0.406(b)
Female	42(37.2%)	71(62.8%)		
Smoking				
Smoker	22(22%)	30(20%)	X2= 3.263	0.196(b)
Ex-Smoker	13(13%)	10(6.66%)		
Non-Smoker	65(65%)	110(73.33%)		
Disease duration(years)				
Median (IQR)	8(5)	5(4)	H= 2460.5	0.000**(c)
Min.–Max.	3-25	1-25		

Group A: DM patients with NAFLD, **Group B:** DM patients without NAFLD, **NAFLD:** non-alcoholic fatty liver disease, **n:** number, **IQR**: interquartile range, **(a):** Independent-Sample T-Test, **(b):** Chi-Square Test, **(c):** Mann-Whitney U, *: Statistically significant at P ≤ 0.05, **: Statistically significant at P ≤ 0.001.

Table 2: Demographic and clinical characteristics of DM patients with NAFLD and DM patients without NAFLD:

Parameters	Groups	Group A NAFLD (n=100) (40%)	Group B Non-NAFLD (n=150) (60%)	Test of sig.	P-value
SBP (mmHg)					
Mean ± SD		129.2±15.8	122.53±13.61	t= 3.553	**0.000**(a)**
Min.–Max.		110-170	90-150		
DBP (mmHg)					
Mean ± SD		82.7±13.98	78±8.74	t= 3.268	**0.001**(a)**
Min.–Max.		60-180	60-100		

Group A: DM patients with NAFLD, **Group B:** DM patients without NAFLD, **NAFLD:** non-alcoholic fatty liver disease, **n:** number, **IQR**: interquartile range, **(a):** Independent-Sample T-Test, *: Statistically significant at P ≤ 0.05, **: Statistically significant at P ≤ 0.001

Table 3: Demographic characteristics of DM patients with NAFLD and DM patients without NAFLD:

Parameters	Groups	Group A NAFLD (n=100) (40%)	Group B Non-NAFLD (n=150) (60%)	Test of sig.	P-value
Ht (cm)					
Mean ± SD		172.14±7.19	171.28±7.046	t= 0.938	0.349(a)
Min.–Max.		155-190	155-190		
Wt (Kg)					
Mean ± SD		92.44±12.81	82.39±10.64	t= 6.736	**0.000**(a)**
Min.–Max.		62-125	55-110		
BMI (Kg/m^2)					
Mean ± SD		30.26±3.36	29.31±3.17	t= 2.262	0.025*(a)
Min.–Max.		21.5-39.89	21.19-39.7		
WC (cm)					
Mean ± SD		104.78±10.011	98.9±12.15	t= 4.171	**0.000**(a)**
Min.–Max.		75-132	75-132		
HC (cm)					
Mean ± SD		111.09±10.32	108.41±12.27	t= 1.802	0.073(a)
Min.–Max.		80-135	84-142		
WHR					
Median (IQR)		0.9307 (0.0372)	0.9142 (0.147)	H= 4090.5	**0.000**(c)**
Min.–Max.		0.85-1.15	0.882-0.995		
NC (cm)					
Mean ± SD		41.21±3.22	39.38±3.61	t= 4.098	**0.000**(a)**
Min.–Max.		33-46.5	30-46		

Group A: DM patients with NAFLD, **Group B:** DM patients without NAFLD, **NAFLD:** non-alcoholic fatty liver disease, **n:** number, **BMI:** body mass index, **WC:** waist circumference**, HC:** hip circumference, **WHR:** waist to hip ratio, **NC:** neck circumference, **IQR**: interquartile range, **(a):** Independent-Sample T-Test, **(c):** Mann-Whitney U Test *: Statistically significant at P ≤ 0.05, **: Statistically significant at P ≤ 0.001

Table 4: Results of liver enzymes of DM patients with NAFLD and DM patients without NAFLD

Groups / Parameters	Group A NAFLD (n=100) (40%)	Group B Non-NAFLD (n=150) (60%)	Test of sig.	P-value
AST(U/L)				
Mean ± SD	38.71±11.27	29.59±9.87	t= 6.759	**0.000**(a)**
Min.–Max.	18-67	12-58		
ALT(U/L)				
Mean ± SD	45.88±13.66	32.59±8.91	t= 8.582	**0.000**(a)**
Min.–Max.	18-78	14-58		

Group A: DM patients with NAFLD, **Group B:** DM patients without NAFLD, **NAFLD:** non-alcoholic fatty liver disease, **n:** number, **AST:** aspartate aminotransferase, **ALT:** alanine transaminase, **U/L:** unit/ liter, **(a):** Independent-Sample T-Test, *: Statistically significant at P ≤ 0.05, **: Statistically significant at P ≤ 0.001

Table 5: Results of glucose levels of DM patients with NAFLD and DM patients without NAFLD

Groups / Parameters	Group A NAFLD (n=100) (40%)	Group B Non-NAFLD (n=150) (60%)	Test of sig.	P-value
FPG (mg/dL)				
Mean ± SD	190.99±39.33	175.32±31.51	t= 3.334	**0.001**(a)**
Min.–Max.	121-295	70-267		
2h-PG (mg/dL)				
Mean ± SD	302.01±64.18	267.03±51.34	t= 4.563	**0.000**(a)**
Min.–Max.	176-425	148-424		
HbA1c (%)				
Mean ± SD	8.78±1.61	7.78±0.918	t= 5.599	**0.000**(a)**
Min.–Max.	6.5-14	6.2-12.5		

Group A: DM patients with NAFLD, **Group B:** DM patients without NAFLD, **NAFLD:** non-alcoholic fatty liver disease, **n:** number, **FPG:** fasting blood glucose, **2h-PG:** postprandial blood glucose, **L:** liter, **HbA1c:** hemoglobin A1C, **(a):** Independent-Sample T-Test, *: Statistically significant at P ≤ 0.05, **: Statistically significant at P ≤ 0.001

Table 6: Results of the lipid profile of DM patients with NAFLD and DM patients without NAFLD:

Groups / Parameters	Group A NAFLD (n=100) (40%)	Group B Non-NAFLD (n=150) (60%)	Test of sig.	P-value
TGs (mg/dL)				
Mean ± SD	173.39±28.15	133.77±23.44	t= 11.637	**0.000**(a)**
Min.–Max.	110-245	70-189		
Cholesterol (mg/dL)				
Mean ± SD	219.76±29.76	186.26±21.06	t= 9.746	**0.000**(a)**
Min.–Max.	90-288	110-230		
LDL (mg/dL)				
Mean ± SD	121.13±35.39	94.97±22.92	t= 6.535	**0.000**(a)**
Min.–Max.	45-215	34-138		
HDL (mg/dL)				
Mean ± SD	45.02±15.27	65.61±20.45	t= -8.594	**0.000**(a)**
Min.–Max.	13-98	35-154		

Group A: DM patients with NAFLD, **Group B:** DM patients without NAFLD, **NAFLD:** non-alcoholic fatty liver disease, **n:** number, **TGs:** triglycerides, **LDL:** low-density lipoproteins**, HDL:** low-density lipoproteins, **L:** liter, **(a):** Independent-Sample T-Test, *: Statistically significant at P ≤ 0.05, **: Statistically significant at P ≤ 0.001

Table 7: Results of ultrasound of DM patients with NAFLD and DM patients without NAFLD

Groups Parameters	Group A NAFLD (n=100) (40%)	Group B Non-NAFLD (n=150) (60%)	Test of sig.	P-value
Ultrasound Fatty liver status				
Not NAFLD	0(0%)	150(100%)	X^2=	**0.000**(b)**
Mild	37(37%)	0(100%)	336.506	
Moderate	30(30%)	0(100%)		
Sever	33(33%)	0(100%)		

Group A: DM patients with NAFLD, **Group B:** DM patients without NAFLD, **NAFLD:** non-alcoholic fatty liver disease, **n:** number, **(b):** Chi-Square Test, *: Statistically significant at P ≤ 0.05, **: Statistically significant at P ≤ 0.001.

Table 8: Correlation between NC and other parameters

Variables	Neck circumference (NC) r	p
Age	0.004	0.951
Gender	**-0.519**	**0.000****
Smoking status	**-0.249**	**0.000****
SBP	**0.213**	**0.001****
DBP	**0.267**	**0.000****
Disease duration	**0.157**	**0.013***
Ht	**0.366**	**0.000****
Wt	**0.268**	**0.000****
BMI	0.075	0.235
WC	0.019	0.767
HC	-0.074	0.242
WHR	**0.266**	**0.000****
NC	1	---------
AST	0.114	0.072
ALT	**0.187**	**0.003***
FPG	0.046	0.466
2h-PG	-0.003	0.960
HbA1c	0.039	0.537
TGs	**0.306**	**0.000****
Cholesterol	**0.231**	**0.000****
LDL	0.026	0.677
HDL	-0.044	0.485
Fatty liver status	**0.251**	**0.000****

BMI: body mass index, **WC:** waist circumference**, HC:** hip circumference, **WHR:** waist to hip ratio, **NC:** neck circumference, **AST:** aspartate aminotransferase, **ALT:** alanine transaminase, **FPG:** fasting blood glucose, **2h-PG:** postprandial blood glucose, **L:** liter, **HbA1c:** hemoglobin A1C, **LDL:** low-density lipoproteins**, HDL:** low-density lipoproteins. *: Statistically significant at P ≤ 0.05, **: Statistically significant at P ≤ 0.001

Table 9: Logistic regression for predictor factors affecting DM patients with NAFLD and DM patients without NAFLD

Independent variables	Odds Ratio (95%) CI	P- value
Disease duration	0.751 (0.664 – 0.849)	**0.000****
SBP	0.988 (0.927 – 1.052)	0.699
DBP	0.969 (0.869 – 1.081)	0.576
Wt	1.032 (0.966 – 1.103)	0.351
BMI	1.186 (0.950 – 1.481)	0.131
WC	1.046 (0.973 – 1.124)	0.223
WHR	0.000 (0.000 – 222.902)	0.158
NC	0.925 (0.789 – 1.084)	0.333
AST	0.980 (0.922 – 1.041)	0.508
ALT	0.940 (0.880 -1.005)	0.070
FPG	1.023 (1.000 – 1.047)	0.053
2h-PG	1.011 (0.993 – 1.030)	0.240
HBA1c	0.255 (0.103 -0.636)	**0.003***
TGs	0.948 (0.922 – 0.975)	**0.000****
Cholesterol	0.967 (0.944 -0.992)	**0.009***
LDL	1.010 (0.986 – 1.035)	0.421
HDL	1.047 (1.002 – 1.095)	**0.041***

BMI: body mass index, **WC:** waist circumference, **WHR:** waist to hip ratio, **NC:** neck circumference, **AST:** aspartate aminotransferase, **ALT:** alanine transaminase, **FPG:** fasting blood glucose, **2h-PG:** postprandial blood glucose, **HbA1c:** hemoglobin A1C, **LDL:** low-density lipoproteins, **HDL:** low-density lipoproteins, *: Statistically significant at $P \leq 0.05$ **: Statistically significant at $P \leq 0.001$

Table 10: Regression analysis of NAFLD by quartile of NC adjusted by age

Variable		NAFLD (%)	Model 1	P-value
Groups			**OR (95% CI)**	
NAFLD	Q1(26.5-33)	1 (1.0%)	1.00	
	Q2(33.1-37.7)	14 (14%)	0.457(0.05-4.165)	**0.002***
	Q3(37.8-42.4)	45 (45%)	0.267(0.031-2.297)	
	Q4(42.5-50)	40 (40%)	0.121(0.014-1.066)	

Model 1: Age-adjusted, NAFLD**:** non-alcoholic fatty liver disease

Table 11: Regression analysis of NAFLD by quartile of NC adjusted by age, BMI, WC, and WHR:

Variable		NAFLD (%)	Model 1	P-value
Groups			**OR (95% CI)**	
NAFLD	Q1(26.5-33)	1 (1.0%)	1.00	
	Q2(33.1-37.7)	14 (14%)	1.838(0.175-19.339)	**0.022***
	Q3(37.8-42.4)	45 (45%)	0.996(0.103-9.606)	
	Q4(42.5-50)	40 (40%)	0.478(0.049-4.688)	

Model 2: Age, BMI, WC, and WHR adjusted, **NAFLD:** non-alcoholic fatty liver disease, **BMI:** body mass index, **WC:** waist circumference**, HC:** hip circumference, **WHR:** waist to hip ratio, **NC:** neck circumference.

Table 12: Receiver operating characteristic (ROC) curves analysis of NC, BMI, WC, HC, and WHR in the diagnosis of DM patients with NAFLD

parameters	AUC	P-value	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
NC	0.647	**0.000****	(0.578-0.716)	38.25	81 %	64 %	60 %	83.47 %
BMI	0.608	**0.004***	(0.537-0.680)	28.67	77 %	59.33 %	56.11 %	80.18 %
WC	0.649	**0.000****	(0.582-0.716)	95.50	82 %	59.33 %	57.34 %	83.17 %
HC	0.569	0.066	(0.498-0.640)	105.50	66 %	52 %	47.82 %	63.93 %
WHR	0.727	**0.000****	(0.654-0.800)	0.9043	83 %	82 %	75.45 %	87.85 %

AUC: Area Under a Curve, **P-value:** Probability value, **CI:** Confidence Intervals, **NPV:** Negative predictive value, **PPV:** Positive predictive value, **NC:** neck circumference, **BMI:** body mass index, **WC:** waist circumference**, HC:** hip circumference, **WHR:** waist to hip ratio, *: Statistically significant at P ≤ 0.05, **: Statistically significant at P ≤ 0.001

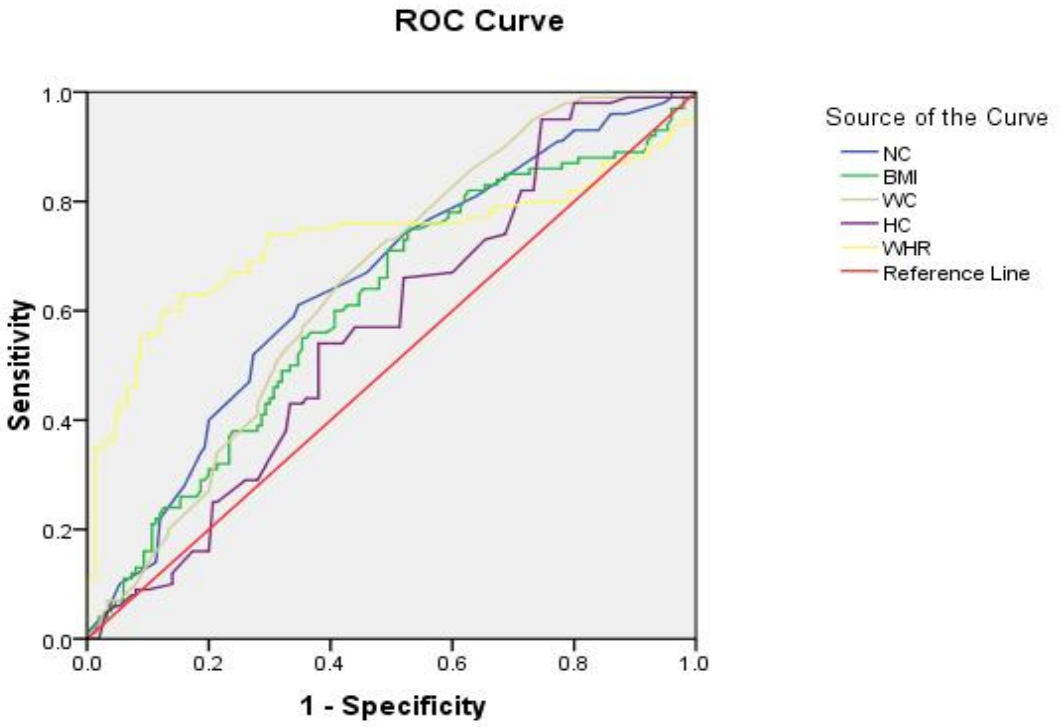

Fig. 1. ROC curve for detection of DM patients with NAFLD.

4. Discussion

In this study, there was no significant difference between the NAFLD group and the non-NAFLD group as regards age. It was in agreement with Almobarak *et al.* (2015) a Sudanese study conducted on 167 outpatients with type 2 DM and fatty liver diagnosed based on the US, the overall prevalence of fatty liver among participants was about 50.3% with no significant difference reported between the age in studied patients with and without fatty liver with P-value > 0.05

In contrast to our study, Zhao *et al.* (2018) a Chinese study conducted on 629 patients with type 2 DM, it was found that patients with hepatic steatosis and fibrosis were significantly older than those without steatosis and fibrosis, but in this result, alcohol consumption was not excluded in the participants which may have an impact on the result.

As regards gender, male patients with and without NAFLD were represented by 42.33% and 57.66% respectively. Female patients with and without NAFLD were represented by 37.2% and 62.8% respectively with no significant difference regarding gender in the prevalence of hepatic steatosis with a P-value > 0.05. It was in agreement with Herath, *et al.* (2019) study that examined 233 patients with type 2 DM, followed up at a diabetes center in Southern Sri Lanka with an overall prevalence of fatty liver based on the US was 62.6% with no significant gender difference (P-value > 0.05). On the other hand, the Sudanese study conducted by Almobarak *et al.* (2015) revealed a statistically significant higher prevalence of fatty liver in women than in men with a P-value < 0.05.

As regards smoking status, the participants of our study with NAFLD were found to be 22% smokers, 13% ex-smokers, and 65% non-smokers. Also, participants without NAFLD were found to be 20% smokers, 6.66% ex-smokers, and 73.33% non-smokers with no significant difference between the two groups as regards smoking status. The same was found in Brazil, Leite *et al.* (2009) examined 180 patients with type 2 DM, and there was no impact of smoking status on the prevalence of fatty liver. While in China, Zhao *et al.* (2018) study revealed that smoking can promote hepatic fibrosis in patients with type 2 DM but with no statistical significance (P-value > 0.05).

In our study, the SBP of the participants with NAFLD ranged between 110 - 170 (mmHg) with Mean ± SD 129.2 ± 15.8 and for the participants without NAFLD ranged between 90-150 (mmHg) with Mean ± SD 122.53 ± 13.61. Also, the DBP of the participants with NAFLD ranged between 60 - 180 (mmHg) with Mean ± SD 82.7 ± 13.98 and for participants without NAFLD ranged between 60 - 100 (mmHg) with Mean ± SD 78 ± 8.74. These findings indicate a statistically significant difference between the two groups as regards SBP and DBP.

In our study, the disease duration as regards DM in participants with NAFLD ranged between 3 - 25 years with a median of 8 and for those without NAFLD ranged between 1 - 25 years with a median of 5. This finding reveals a statistically significant increase between the NAFLD and non-NAFLD groups as regards disease duration. It was in agreement with Chandel *et al.* (2016) an Indian study conducted on 185 type 2 diabetic patients with 55.67% of them found to have fatty liver based on the US and the mean duration of DM in the fatty liver group was 10.3 years with statistically significant correlation between diabetic duration, prevalence, and severity of fatty liver with P-value < 0.05.

Also, Banerjee *et al*. (2008), who examined 47 patients with type 2 DM for the prevalence of hepatic steatosis and fibrosis using liver biopsy, found a significant correlation between the longer duration of type 2 DM and the prevalence of hepatic steatosis and fibrosis with P-value <0.05.

Against our study, in Chen *et al.* (2020) study that was conducted on 449 patients with type 2 DM with 78.72% of the patients had increased CAP suggestive of hepatic steatosis, there was no significant correlation between the prevalence of hepatic steatosis and the duration of DM with P-value > 0.05 which may be due to narrow spectrum of diabetic duration in study participants than in our study.

In our study, there was no statistically significant difference between the two patient groups, and the Ht ranged between 155 - 190 cm with a Mean ± SD of 172.14 ± 7.19 and 171.28 ± 7.046 for patients with NAFLD and patients without NAFLD respectively. Our study revealed that there was a statistically significant increase between the NAFLD group and the non-NAFLD group as regards Wt which ranged between 62 - 125 Kg with Mean ± SD 92.44 ± 12.81 and 55 - 110 Kg with Mean ± SD 82.39 ± 10.64 for patients with NAFLD and patients without NAFLD respectively.

Our study revealed that there was a statistically significant increase between the NAFLD group and the non-NAFLD group as regards BMI that ranged between 21.5-39.89 Kg/m2 with Mean ± SD 30.26 ± 3.36 and 21.19 - 39.7 Kg/m2 with Mean ± SD 29.31 ± 3.17 for the patient groups respectively. Also, we found that there was a statistically significant increase between the NAFLD group and the non-NAFLD group as regards WC that ranged between 75 - 132 cm with Mean ± SD 104.78 ± 10.011 and 98.9 ± 12.15 for the two patient groups respectively.

In agreement with our study, Chen *et al.* (2020) conducted a cross-sectional study in Singapore and enrolled 436 type 2 diabetic patients, TE was done as screening for hepatic steatosis and fibrosis

and it was found that higher BMI and WC were significantly correlated with subjects with increased liver stiffness and also higher BMI, WC was significantly higher in patients with hepatic steatosis. The same was in Portillo-Sanchez *et al.* (2015) study that was conducted on 103 patients with type 2 DM examined by H-MRS for the prevalence of hepatic steatosis and fibrosis. the results revealed a statistically significant correlation between higher BMI and the prevalence of hepatic steatosis and fibrosis (P-value < 0.05).

Also, in Brazil, Ferreira *et al.* (2010) examined 78 type 2 diabetic patients diagnosed with NAFLD by the US, and almost half of the patients were found to have fatty liver, and they had significantly elevated BMI (P-value < 0.05). Also, the prevalence of NAFLD is significantly associated with higher BMI and WC in a Chinese study conducted by Lu *et al.* (2009) on 560 patients with type 2 DM, 75.18% of them were diagnosed with NAFLD based on the US.

In contrast to our study, Seetlani, *et al.* (2016) a Pakistanian study enrolled 262 patients with type 2 DM of more than 5 years duration having raised transaminases level and fatty liver on the US then liver biopsy was performed with 56.49% showed NASH. However, the risk and severity of NASH are not significantly correlated with BMI.

As regards HC, our study revealed no significant difference between the NAFLD group and the non-NAFLD group. The HC ranged between 80 -135 cm with Mean ± SD 111.09 ± 10.32 and 84 - 142 cm with Mean ± SD 108.41 ± 12.2 for the two patient groups respectively. In our study, the WHR ranged between 0.85 - 1.15 with a median of 0.9307 and 0.882 - 0.995 with a median of 0.9142 for the NAFLD group and non-NAFLD group respectively. This finding indicates a statistically significant increase between the NAFLD group and the non-NAFLD group as regards WHR (P-value < 0.05).

In our study, NC ranged between 33 - 46.5 cm with a Mean ± SD of 41.21 ± 3.22 and 30 - 46 cm with a Mean ± SD of 39.38 ± 3.61 for patients with NAFLD and patients without NAFLD respectively. These results show a statistically significant increase between the NAFLD group and the non-NAFLD group as regards NC (P-value < 0.05).

In our study, there was a statistically significant increase between the NAFLD group and the non-NAFLD group as regards AST and ALT (P-value ≤ 0.05). It was in agreement with the Indian study conducted by Somalwar and Raut (2014) that proved that ALT and AST levels were significantly higher in type 2 diabetic patients with fatty liver diagnosed by the abdominal US.

On the contrary, the Turkish study conducted by Demir *et al.* (2019) showed that ALT levels were within the normal range in patients with TE-defined cirrhosis and did not distinguish between different grades of hepatic steatosis.

Also, the Indian study conducted by Paruk *et al.* (2011) on 100 type 2 diabetic patients, 49% of them had evidence of fatty liver on the abdominal US, showed no significant difference in the transaminase levels between the NAFLD group and non-NAFLD group.

Our study revealed that There was a statistically significant increase between the NAFLD group and the non-NAFLD group as regards FBG, 2h-PG, and HbA1c (P-value < 0.05). In agreement with our study, in the Chandel *et al.* (2016) study that include 185 Indian type 2 diabetic patients with 55.67% of them found to have fatty liver, it was observed that raised FBS and 2h-PG levels were significantly associated with fatty liver in patients with type 2 DM (P-value < 0.05).

Also, in the Heidari and Gharebagh (2017) study that include 255 Iranian type 2 diabetic patients with 86.66% of them having fatty liver on US examination, HbA1c was significantly associated with risk and severity of fatty liver. On the other hand, Dvorak *et al.* (2015) study in which there was no significant difference in fasting glycemia between the NAFLD group and the non-NAFLD group (P-value > 0.05). Also, HbA1c levels appeared to have no significant impact on the fatty liver prevalence in the Sudanese study conducted by Almobarak *et al.* (2015).

Dyslipidemia is considered a risk factor for developing ASCVD and mainly CHD which is a leading cause of mortality in type 2 DM. In our study, dyslipidemia defined by elevated total cholesterol, TGs, LDL, and decreased HDL in participants, was associated with a significant risk of development of hepatic steatosis and fibrosis and their severity in type 2 diabetic patients (P-value < 0.05).

The same was proved in the Sudanese study conducted by Almobarak *et al.* (2015) which stated that high TGs levels and low HDL levels are possible risk factors for fatty liver.

However, in China, Zhan *et al.* (2012) who examined 363 type 2 diabetic patients with 56% of them having fatty liver on US examination, found that patients with fatty liver had higher TGs (P-value < 0.05), lower HDL (P-value < 0.05) than patients without fatty liver with no difference between the two groups as regard total cholesterol and LDL cholesterol.

In our study, at a cut-off point (38.25) NC had a high PPV (60%), NPV (83.47%), sensitivity (81%), and specificity (64%) for the detection of NAFLD in type 2 diabetic patients compared with BMI, HC, and WC. The WHR had the highest PPV (75.45%), NPV (87.85%), sensitivity (83%), specificity (82%), with AUC (0.727) at cut off point (0.904).

Neck circumference (NC) was positively correlated with SBP, DBP, disease duration, Ht, Wt, WHR, ALT, TGs, cholesterol, and fatty liver status in patients with type 2 DM.

The same was proved by the Iranian study conducted by Salmanroghani *et al.* (2019) on 590 subjects and revealed a positive correlation between NC and SBP, DBP, Ht, Wt, WHR, ALT, TGs, cholesterol, and fatty liver status. But the study included a community-based population (both diabetic and non-diabetic). The same was also proved by the study conducted by Lin *et al.* (2018) in China on 1000 subjects (234 were found to have NAFLD and type 2 DM).

5. Conclusion

Nick circumference was significantly correlated with NAFLD in type 2 diabetic patients. In addition, it had a high predictive value for NAFLD in type 2 diabetic patients among other common anthropometric indices. Therefore, it can be used as a simple and feasible tool for screening NAFLD in a large population with type 2 DM being more feasible, accessible, and had lower limitations as compared to BMI, which cannot account for fat distribution, and WC, which can be affected by external factors, such as abdominal bloating or clothing, whereas NC has excellent repeatability and minimal variance during the day.

Limitations

Our study had several limitations. First, a small number of patients were recruited from a single center. The second is the short period of the study. Third, it was a cross-sectional study, which has its limitation, such as a lack of study of the causality between factors. Finally, the use of US for the evaluation of NAFLD and was better to evaluate with liver biopsy as the gold standard or MRI as a highly sensitive modality. On the other hand, these techniques are of limited use because of ethical issues being invasive techniques or because of their high cost.

Funding

No fund received from any organizations.

Conflict of interest

No conflict of interest.

References

Almobarak, A.O., S. Barakat, E.A. Suliman, et al., 2015. Prevalence of and predictive factors for nonalcoholic fatty liver disease in Sudanese individuals with type 2 diabetes: Is metabolic syndrome the culprit? Arab Journal of Gastroenterology, 1;16(2):54–8.

American Diabetes Association Professional Practice Committee (ADAPPC), 2021. Classification and diagnosis of diabetes: Standards of medical care in diabetes-2021. Diabetes Care, 41(supplement 1):S15–33.

Article, O., 2016. Frequency of Non-Alcoholic Steatohepatitis on Histopathology in Patients of Type 2 Diabetes Mellitus with Duration of More than 5 Years. 2016;26(Cvd):643–6.

Assyov, Y., A. Gateva, A. Tsakova, et al., 2017. A comparison of the clinical usefulness of neck circumference and waist circumference in individuals with severe obesity. Endocrine Research, 42(1):6–14.

Augustin, S., I. Graupera, J. Caballeria, 2017. Non-alcoholic fatty liver disease: A poorly known pandemic. Medicina Clínica (English Edition). 149(12):542–8.

Banerjee, S., U.S. Ghosh, S. Dutta, 2008. Clinicopathological Profile of Hepatic Involvement in Type-2 Diabetes Mellitus and Its Significance [Internet]. Available from: www.japi.org593

Chandel K, Kumar S, Farooqui W, et al. A study of prevalence of non-alcoholic fatty liver disease in type 2 Diabetes Mellitus Related papers. Panacea Journal of Medical Sciences. 2016 Sep;6(3):147–50.

Chen, K., W.K. Sng, J.H.M. Quah, et al., 2020. Clinical spectrum of non-alcoholic fatty liver disease in patients with diabetes mellitus. PLoS ONE. 1;15(8 August 2020).

Demir, M., O. Deyneli, Y. Yılmaz, 2019. Screening for hepatic fibrosis and steatosis in Turkish patients with type 2 diabetes mellitus: A transient elastography study. Turkish Journal of Gastroenterology, 1;30(3):266–70.

Dvorak, K., R. Hainer, J. Petrtyl, et al., 2015. The prevalence of nonalcoholic liver steatosis in patients with type 2 diabetes mellitus in the Czech Republic. Biomedical Papers, 1;159(3):442–8.

Ferreira, V.S.G., R. B. Pernambuco, E. P. Lopes, et al., 2010. Frequency and risk factors associated with non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus, Arq Bras Endocrinol Metabol . 2010 Jun;54(4):362-8. doi: 10.1590/s0004-27302010000400004.

Graif, M., M. Yanuka, M. Baraz, et al., 2000. Quantitative estimation of attenuation in ultrasound video images: correlation with histology in diffuse liver disease. Invest Radiol., 35:319–24.

Guasch-Ferré, M., M. Bulló, M.Á. Martínez-González, et al., 2012. Waist-to-height ratio and cardiovascular risk factors in elderly individuals at high cardiovascular risk. PLoS ONE. 7(8):5–10.

Heidari, Z. and A. Gharebagh, 2017. Prevalence of non alcoholic fatty liver disease and its association with diabetic nephropathy in patients with type 2 diabetes mellitus. Journal of Clinical and Diagnostic Research. 2017 May 1;11(5):OC04–7.

Herath, H.M.M., I. Kodikara, T.P. Weerarathna, et al., 2019. Prevalence and associations of non-alcoholic fatty liver disease (NAFLD) in Sri Lankan patients with type 2 diabetes: A single center study. Diabetes and Metabolic Syndrome: Clinical Research and Reviews, 1;13(1):246–50.

Idilman, I.S., O. Keskin, A. Celik, et al., 2016. A comparison of liver fat content as determined by magnetic resonance imaging-proton density fat fraction and MRS versus liver histology in non-alcoholic fatty liver disease. Acta Radiologica, 57(3):271–8.

Leite, N.C., G.F. Salles, A.L.E. Araujo, et al., 2008. Prevalence and associated factors of non-alcoholic fatty liver disease in patients with type-2 diabetes mellitus. Journal of Evidence-Based Medicine, 113–9. https://doi.org/10.1111/j.1478-3231.2008.01718.x

Lin, S., Y. Xian, Y. Liu, et al., 2018. Risk factors and community intervention for nonalcoholic fatty liver disease in community residents of Urumqi, China. Medicine (United States). 1;97(9).

Lu, H., L. Zeng, B. Liang, et al., 2009. High Prevalence of Coronary Heart Disease in Type 2 Diabetic Patients with Non-alcoholic Fatty Liver Disease. Archives of Medical Research, 40(7):571–5.

Paruk, I.M., F.J. Pirie, A.A. Motala, et al., 2011. High prevalence of abnormal liver enzymes in South African patients with type 2 diabetes mellitus attending a diabetes clinic. Journal of Endocrinology, Metabolism and Diabetes of South Africa, 16(1):43–7.

Patel, P. and N. Abate, 2013. Role of subcutaneous adipose tissue in the pathogenesis of insulin resistance. Journal of Obesity, J Obes., 2013: 489187. doi: 10.1155/2013/489187

Portillo-Sanchez, P., F. Bril, M. Maximos, et al., 2015. High prevalence of nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus and normal plasma aminotransferase levels. Journal of Clinical Endocrinology and Metabolism, 1;100(6):2231–8.

Salmanroghani, H., R. Salmanroghani, M. Nourian, et al., 2019. Evaluation of neck circumference as an easy and reliable predictor for non-alcoholic fatty liver disease. Turkish Journal of Gastroenterology, 1;30(2):163–70.

Somalwar, A. and A. Raut, 2014. Study of association of non alcoholic fatty liver disease (NAFLD) with micro and macrovascular complications of type 2 diabetes mellitus (T2DM). International Journal of Research in Medical Sciences, 2014;2(2):493.

Targher, G., L. Bertolini, R. Padovani, et al., 2007. Prevalence of nonalcoholic fatty liver disease and its association with cardiovascular disease among type 2 diabetic patients. Diabetes Care., 30(5):1212–8.

Zhan, Y.T., C. Zhang, L. Li, et al., 2012. Non-alcoholic fatty liver disease is not related to the incidence of diabetic nephropathy in Type 2 diabetes. International Journal of Molecular Sciences, 13(11):14698–706.

Zhao, H., X. Song, Z. Li, et al., 2018. Risk factors associated with nonalcohol fatty liver disease and fibrosis among patients with type 2 diabetes mellitus. Medicine (United States), 1;97(37).