Neck circumference: a simple screening parameter for cardiovascular risk in diabetics

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Introduction
High-sensitivity C-reactive protein (hs-CRP) is considered a biomarker of cardiovascular disease (CVD). WHO has recommended waist circumference (WC), waist-to-hip ratio, and waist-to-height ratio as screening tools for CVD. Various studies used neck circumference (NC) as a method for measuring of the upper-body fat, and it was positively correlated to WC and BMI.
Aim
The aim was to investigate the correlation between NC as a screening tool for cardiovascular risk in type 2 diabetic patients and circulatory levels of hs-CRP and fibrinogen as biomarkers of inflammation in CVD.
Patients and methods
A total of 100 patients with type 2 diabetes were recruited from the diabetes clinic in Mansoura specialized medical hospital fulfilling the inclusion and exclusion criteria and were divided into two groups according to the measured circulatory levels of hs-CRP: group 1 included 46 participants whose circulatory levels of hs-CRP were less than 5, and group 2 included 54 participants whose circulatory levels of hs-CRP were greater than or equal to 5. All recruited participants were subjected to fasting blood sample to measure low-density lipoprotein, high-density lipoprotein, A1c, fibrinogen, and hs-CRP.
Results
Group 1 with hs-CRP less than 5 showed a significant increase in BMI, WC, NC, ischemic heart disease, fibrinogen, and HBA1c in relation to group 2. There was a significant positive correlation between NC and BMI, WC, and low-density lipoprotein (r=0.397, 0.520, and 0.317, respectively), with P value less than 0.05. Cutoff value of NC more than 40.50 cm is a predictor of CVD.
Conclusion
NC can be effectively used as a screening parameter for identification of cardiovascular risk factors in type 2 diabetic patients.

Keywords:
cardiovascular risk, diabetes, high-sensitivity C-reactive protein, neck circumference

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Background

Cardiovascular disease (CVD) is the leading cause of death and disability worldwide [1]. Hypertension, diabetes mellitus, smoking, and hypercholesterolemia are the main risk factors for CVD [2].

Inflammation is the cornerstone in the development and progression of coronary artery disease (CAD). A variety of biomolecules have been studied to understand their role in setting and progression of the inflammatory cascade in co-morbidities like obesity, type 2 diabetes, and CAD. Serum C-reactive protein (CRP) is the most extensively studied biomarker of inflammation in CVD. Simultaneously, standardized high-sensitivity assays (hs-CRP) can be used as a marker of inflammation on a large number of patients [3].

Till now, there is no clear evidence on the way or the mechanism that prove the correlation between CVD and the level of CRP. However, there are several facts that prove this direct correlation: first, the presence of CRP inside the atherosclerotic lesions; second, easy uptake of LDL, combined to CRP, by macrophages without any facilitated reactions; and third, induction of inflammation in humans and induction of atherosclerosis in an animal model can be done via administration of CRP [4].

Hepatocyte is the main site of synthesis of CRP. The synthesis and release of CRP are provoked by different cytokines like interleukin 6 and tumor necrosis factor-α [5].

As the adipose tissue is the richest source of inflammatory cytokines all over the body [6]. CRP level is strongly correlated to measures of obesity, such as waist circumference (WC) and BMI [7].

Value of hs-CRP is reliable and appears to be valid for all patients, even after multiple adjustments [8], in spite of the presence of some reported differences between both sexes and some ethnicities [9].

WHO has recommended WC, waist-to-hip ratio (W : H) and waist-to-height ratio (W : Ht) as a screening tool for CVD risks among general population [10]. However, the measurement of WC is variable with respiration, postprandial states, and presence heavy clothing, and it is difficult in bedridden patients. This variability makes measuring of WC not reliable in some cases [11].

On comparing the measurement of neck circumference (NC) with other measures of obesity and cardiovascular risks recommended by the WHO, it is measured easily, has fixed value over long time, and is not time consuming as other measures used to assess overweight and obese patients [12]. So, we can use NC as an indicator of central adiposity, hypertension, and other components of metabolic syndrome [13,14].

So, the measurement of NC can be a practical and economical method used for measuring of the upper-body fat. NC is positively correlated to WC and BMI in various studies [15].

Moreover, Vallianou *et al.* [16] demonstrated that NC has a negative correlation to serum high-density lipoprotein HDL and positive correlation to serum triglycerides and cholesterol in relation to the use of other parameters like to BMI and WC in men and women.

Cizza *et al.* [17] used NC to detect the correlation between cardiovascular risk, insulin resistance, and other biochemical components of MetS.

On the contrary, fibrinogen is considered as a marker of thrombosis and inflammation, so it can be used as a predictor of CVD via its role in increasing the intima and media thickness, and it is significantly associated with subclinical atherosclerosis [18].

Chuang *et al.* [19], used fibrinogen as a predictor for the incidence of ischemic stroke and incidence of hypertension.

Aim

The aim of this study was to investigate the correlation between NC as a screening tool for cardiovascular risk in type 2 diabetic patients and circulatory levels of hs-CRP and fibrinogen as biomarkers of inflammation in CVD via cross-sectional analysis.

Procedure

This is a cross-sectional study that was done in Mansoura Specialized Medicine Hospital, Mansoura University, Egypt. A total of 100 patients with type 2 diabetes were recruited from the diabetes clinic in Mansoura Specialized Medical Hospital from July 2018 to April 2019. Written consents were taken from all participants. All included participants who fulfilled the inclusion and exclusion criteria were divided into two groups according to the measured circulatory levels of hs-CRP: group 1 included 46 participants (eight men and 38 women) whose circulatory levels of hs-CRP were less than 5, and group 2 included 54 participants (21 men and 33 women) whose circulatory levels of hs-CRP more than or equal to 5.

Inclusion criteria

Patients with type 2 diabetes from 18 to 70 years with and without ischemic heart disease were included.

Exclusion criteria

The following were the exclusion criteria:

(1) Pregnancy.
(2) Critically ill diabetic patients.
(3) Diabetic patients with severe systemic diseases (such as end-stage liver or kidney disease, cancer, or heart failure).
(4) Diabetic patients on intravenous fluids or total parenteral nutrition.
(5) Presence of goiter or any other conditions that falsely increase the NC measurement.

Data collection

Data collection included age, sex, smoking, duration of diabetes mellitus, treatment of diabetes (oral or insulin), and presence or absence of hypertension, microvascular complications, and CAD.

Full examination was done, including anthropometric measures such as weight, height, BMI, WC, and NC.

Patients and methods

The presence or absence of hypertension, CAD, and microvascular complications including retinopathy, neuropathy, or nephropathy was recorded by history or Mansoura Specialized Medical Hospital registered data about patients.

Measurement of weight and height was done using calibrated instruments after removal of heavy clothes and asking participants to take off their shoes. BMI was computed as a person's weight in kilograms divided by the square of their height in meters, as weight/height^2 [kg/m^2]. According to the 1998 Clinical Guidelines, overweight was defined as a BMI of 25 to 29.9 kg/m^2 and obesity greater than 30 kg/m^2 [20].

WC was measured halfway between the upper most border of the iliac crest and the lower border of the costal margin using a tape placed around the abdomen at this point [21] (Table 1).

When measuring NC, head is straight and eyes look forward, and it was measured in the halfway between mid-cervical spine and mid anterior neck, to within 1 mm, using non-stretchable plastic tape with the participants standing upright [23].

Laboratory measurements of LDL, HDL, HBA1C, fibrinogen, and hs-CRP were done for all participants after aspiration of 5 ml of venous blood after overnight fasting.

HDL was estimated by commercially available kits supplied by Spinreact (Reactivos Spinreact, Girona, Spain). LDL was determined by Friedewald equation [LDL=TC–(HDL+TGs/5)], provided that TGs level is not above 400 mg/dl.

HBA1c was done using ion-exchange high-performance liquid chromatography technique (HPLC) visible two wavelength absorption, using Tosoh GB.

Fibrinogen was done by Siemens multifibrenu on Coatron M1 coagulometer (TECO Medical Instruments, Germany; Production + Trading GmbH, Dieselstrasse 1, D-84088 Neufahrn NB). Normal reference range for fibrinogen was 180–350 mg/dl.

Table 1 Egyptian specific values for waist circumference (cm) [22]

Sex	Men	Women
Waist circumference	≥88	≥89.6

Plasma level of hs-CRP (immuno-fluorescence assay) was assessed by Getein Biotech Inc (Nanjing, China), and was performed using Getein 1100.

The used kits for measuring hs-CRP considered level greater than or equal to 5 as nonsignificant and level less than 5 as correlated with cardiovascular risks.

All participants were divided into two groups according to their hs-CRP levels:

(1) low CRP concentration (<5 mg/l).
(2) high-level categories (CRP concentration ≥5 mg/l),

American Heart Association stated that elevated CRP level of greater than 10 mg/l may be present in acute cardiovascular events like rupture of atheromatous plaque in heart attack or stroke, after exclusion of other causes that may be associated with its elevated level like other inflammatory or infectious process [24].

This research was approved by Institutional Review Board (IRB) Mansoura Faculty of Medicine-Mansoura University (Code number R.19.12.699).

The recruited participants were divided according to hs-CRP as follows:

(1) Group 1: hs-CRP less than 5 with the possibility of CVD risk.
(2) Group 2: hs-CRP greater than or equal to 5 without possibility of CVD risk.

Results

A total of 100 type 2 diabetic patients were recruited in our study from the diabetic clinic in Mansoura Specialized Medical Hospital from July 2018 to April 2019. All included participants in the study were divided into two groups according to circulatory levels of hs-CRP: group 1 had 46 participants (eight men and 38 women), with mean age 51.24±8.19 years, whose circulatory level of hs-CRP was less than 5, and group 2 had 54 participants (21 men and 33 women), with mean age of 55.02 ±11.69 years, whose circulatory level of hs-CRP was greater than or equal to 5.

Analysis of the demographic data showed that 29 (29%) of the study population were male, 71 (71%) were female, and 12 (12%) were smokers. Mean age of the studied group was 53.28±10.35 years. Mean duration of DM was 6.5 (0.5–35). Mean BMI was

Table 2 Demographic data of recruited subjects

Clinical characteristics	The study groups (*n*=100) [*n* (%)]
Sex	
Male	29 (29)
Female	71 (71)
Age (years)	53.28±10.35
Height (cm)	161.47±8.64
Weight (kg)	97.90±18.84
BMI	37.69±7.56
Obesity	
Obese	87 (87)
Nonobese	13 (13)
Waist circumference	116.60±13.95
Neck circumference	41.48±3.27
Duration of DM [median (minimum–maximum)]	6.5 (0.5–35)
Smokers	12 (12)
Treatment of DM	
Insulin	64 (64)
Oral	36 (36)
Distal polyneuropathy	51 (51)
Diabetic nephropathy	17 (17)
Diabetic retinopathy	27 (27)
Hypertension	66 (66)
Ischemic heart disease	27 (27)
Systolic blood pressure	129.71±23.36
Diastolic blood pressure	83.00±13.52
HBA1c	8.24±1.92
Fibrinogen	287.98±35.15
Hs-CRP	
Hs-CRP (<5)	46 (46)
Hs-CRP (≥5)	54 (54)
LDL	144.23±25.56
HDL	43.69±7.65

HBA1c, hemoglobin A1c; HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein.

37.69±7.56, where 87 (87%) were obese and 13 (13%) were nonobese. Mean WC was 116.60±13.95, mean NC was 41.48±3.27, and mean LDL was 144.23 ±25.56. According to hs-CRP, 46 participants were with hs-CRP less than 5, whereas 54 (54%) were with hs-CRP greater than 5 (Table 2).

Analysis of the clinical data between both groups showed significant difference regarding BMI, WC, NC, DPN (distal polyneuropathy), ischemic heart disease (IHD), fibrinogen, and HBA1c, being significantly increased in group 1 with hs-CRP less than 5 ($P<0.05$) (Table 3).

There was a significant positive correlation between NC and BMI, WC, and LDL (r=0.397, 0.520, and 0.317, respectively), with P value less than 0.05 (Figs 1 and 2). On the contrary, there was a highly significant negative correlation with hs-CRP and HDL) (r=–0.537 and –0.486, respectively) ($P<0.001$) (Table 4 and Fig. 3).

Table 3 Analysis of the clinical data between both groups

	Hs-CRP <5 (*n*=46) [*n* (%)]	Hs-CRP ≥5 (*n*=54) [*n* (%)]	*P* value
Sex			
Male	8 (17.4)	21 (38.9)	0.018*
Female	38 (82.6)	33 (61.1)	
Age (years)	51.24±8.19	55.02±11.69	0.069
BMI	40.46±8.73	35.34±5.46	0.001*
WC	121.0±13.23	112.85±13.55	0.003*
NC	42.82±2.73	40.33±2.29	<0.001*
Duration of DM			
Median (minimum–maximum)	7.0 (0.5–30)	5.5 (0.5–35)	0.841
Smokers	4 (8.7)	8 (14.8)	0.566
DPN	29 (63)	22 (40.7)	0.026*
DN	9 (19.6)	8 (14.8)	0.529
DR	13 (28.3)	14 (25.9)	0.793
HTN	32 (69.6)	34 (63)	0.487
IHD	20 (37)	7 (15)	0.014*
SBP	132.39±19.68	127.43±26.05	0.292
DBP	84.13±11.26	82.04±15.21	0.443
HBA1c	8.83±2.02	7.73±1.68	0.004*
Fibrinogen	296.83±28.18	280.44±38.83	0.019*
LDL	141.51±26.12	146.54±25.08	0.330
HDL	43.58±7.87	43.78±7.54	0.902

DBP, diastolic blood pressure; DN, diabetic nephropathy; DPN, diabetic peripheral neuropathy; DR, diabetic retinopathy; hs-CRP, high-sensitivity C-reactive protein; IHD, ischemic heart disease; NC, neck circumference; SBP, systolic blood pressure.

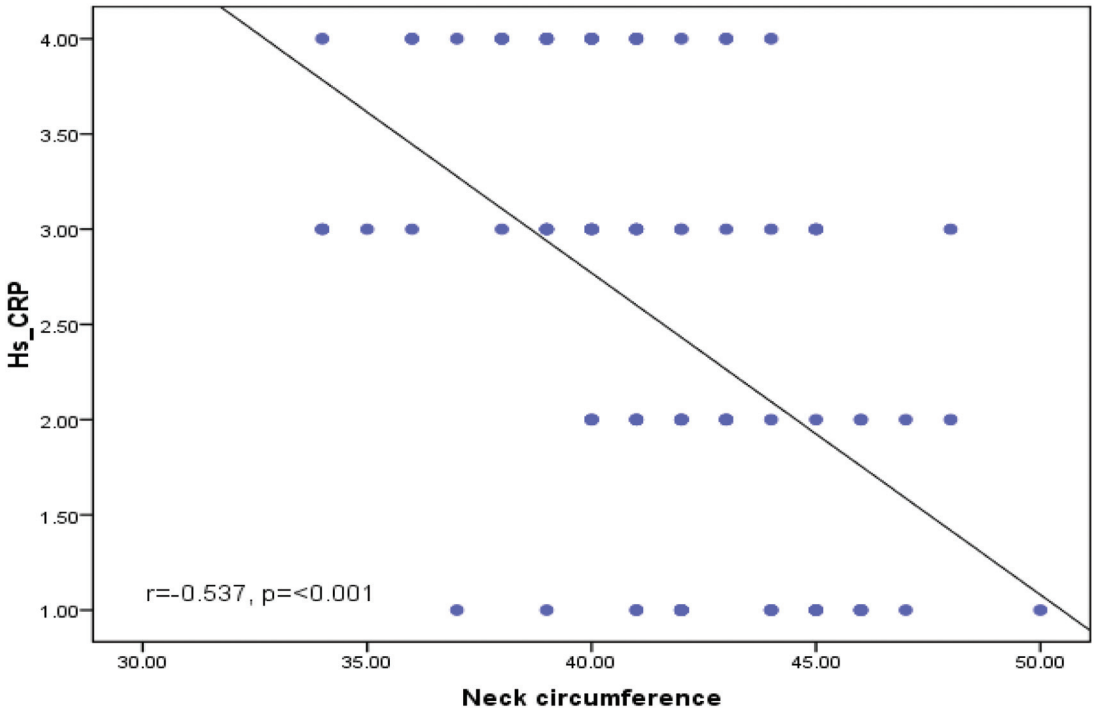
After univariate logistic regression analysis, the independent predictors of hs-CRP less than 5 were BMI, WC, NC DPN, IHD, HBA1c, and fibrinogen. (OR=1.11, 1.05, 1.32, 2.48, 3.28, 1.38, 1.02, respectively). On the contrary, after multivariate regression analysis and adjusting the confounding factors, the independent predictors of hs-CRP less than 5 were NC, DPN, IHD, and HBA1c (OR=1.01, 3.85, 4.99, and 1.01, respectively) (Table 5).

The area under the receiver operating characteristic curve for prediction of hs-CRP less than 5 by NC was 0.715 (95% confidence interval: 0.62–0.82). By using receiver operating characteristic curve, sensitivity, specificity, PPV, NPV, and accuracy at cutoff value of NC more than 40.50 were 80.4, 52.9, 58.7, 75.7, and 77%, respectively (Table 6 and Fig. 4).

Discussion

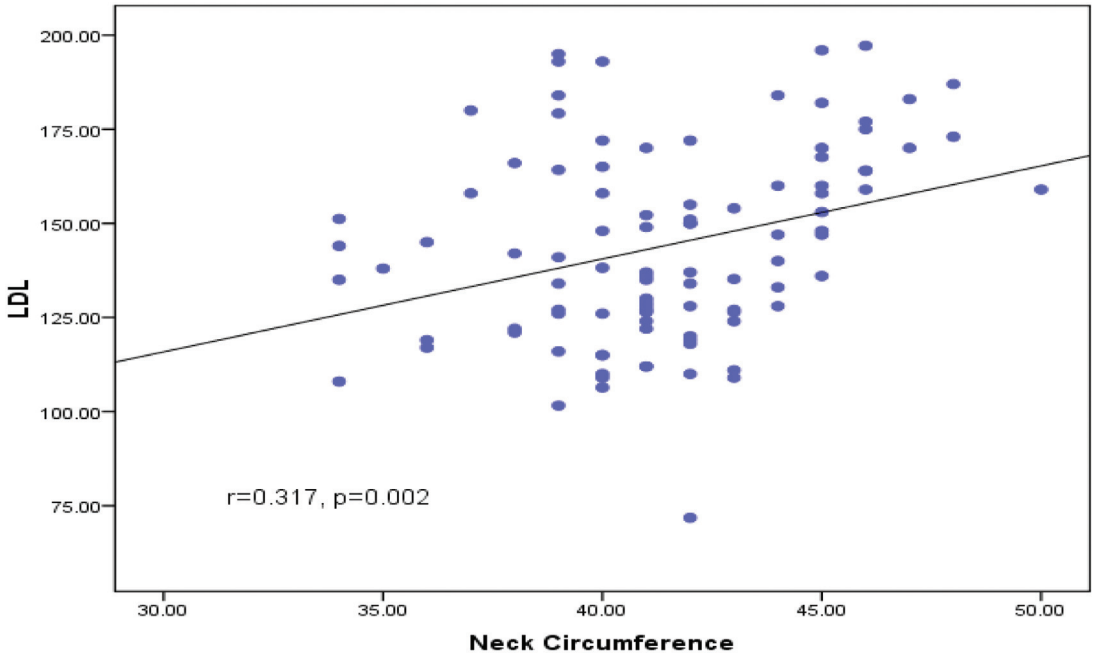
This cross-sectional Study investigated the correlation between NC as a screening parameter for cardiovascular risk in type 2 diabetic patients and circulatory levels of hs-CRP and fibrinogen, which

Figure 1



Scatter diagram for negative correlation between neck circumference and high-sensitivity C-reactive protein.

Figure 2



Scatter diagram for positive correlation between neck circumference and low-density lipoprotein.

are already approved as biomarkers of inflammation in CVD.

The effect of adipose tissue on cardiovascular system varies according to body fat distribution (such as visceral fat, upper-body subcutaneous fat, and lower body subcutaneous fat), and this distribution could be a risk factor for CVD [25]. According to the data from current results, NC is considered as a marker of central adiposity in diabetic patients.

NC is an easy and practical method but is rarely used in clinical practice. BMI and WC have been traditionally used as first steps in detecting the cardiovascular risks via their relation to body fat distribution either general by BMI or central by WC.

However, there are different factors that influence normal values of BMI and WC like age, sex, and ethnicity. Moreover, measurement of BMI does reflect the body fat distribution and cannot distinguish between lean and fat mass [26].

There are some precautions during measuring of WC such as participants should be with minimal dressing, empty stomach before the measurement, and an empty bladder. Furthermore, NC measurements are less agonizing for patients compared with WC. There are some social limitations during WC measurement for patients like feeling shameful on removing of clothes and for healthcare providers from feeling uncomfortable on performing waist measurements as their patients might feel embarrassed [27].

Table 4 Correlation between neck circumference and other variables

Variables	NC		Hs-CRP	
	r	*P*	*r*	*P*
Hs-CRP	−0.537	<0.001*	–	–
BMI	0.397	<0.001*	0.229	0.022*
WC	0.520	<0.001*	0.241	0.016*
Duration of DM	−0.020	0.843	−0.030	0.766
SBP	0.114	0.257	0.151	0.133
DBP	0.165	0.100	0.189	0.060
HBA1c	−0.005	0.959	0.265	0.008*
Fibrinogen	0.099	0.326	0.273	0.006*
LDL	0.317	0.002*	−0.058	0.566
HDL	−0.486	<0.001*	−0.016	0.872

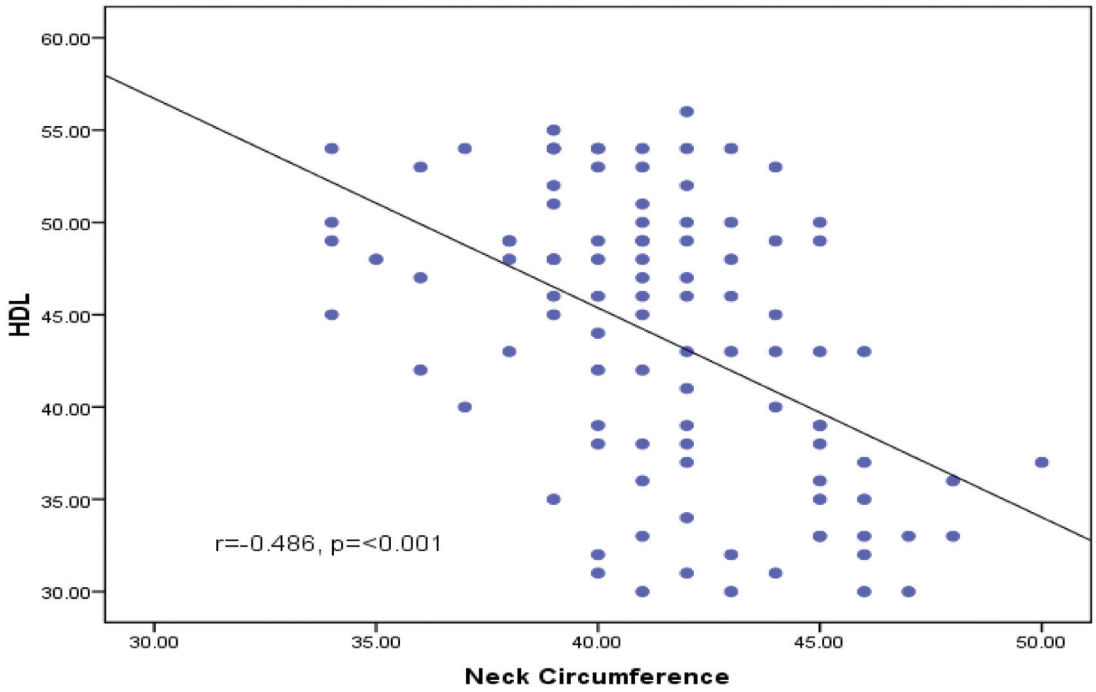
DBP, diastolic blood pressure; HBA1c, hemoglobin A1c; HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; *r*, Spearman correlation; SBP, systolic blood pressure.

In this study, mean NC was found significantly higher in study participants having CVD risk defined as hs-CRP less than 5 when compared with the participants who do not have CVD ($P<0.001$). Similar findings were reported in the studies by Preis *et al.*, Vallianou *et al.*, Zhou *et al.*, Limpawattana *et al.*, Baena *et al.* [15,28–31].

NC was positively correlated with BMI and WC ($r=0.397$ and 0.520, respectively) ($P<0.05$), matching an Egyptian community based cross-sectional survey done by Din *et al.* [32] on 6718 adult Egyptian, which found a strong positive correlation of NC with BMI and WC in both male ($r=0.587$ and 0.538, respectively) and female ($r=0.420$ and 0.369, respectively) participants.

NC had also a positive and significant relationship with LDL but a negative relationship with HDL ($r=0.317$ and −0.486, respectively) ($P<0.05$), which is in agreement with a cross-sectional study performed on 300 men and woman

Figure 3



Scatter diagram for negative correlation between neck circumference and high-density lipoprotein.

Table 5 Logistic regression analysis for independent predictors of high-sensitivity C-reactive protein less than 5

Independent predictors	Univariate regression analysis			Multivariate regression analysis		
	P value	OR	95%CI	*P* value	OR	95%CI
BMI	0.002*	1.11	1.04–1.18	0.088	1.09	0.98–1.22
WC	0.006*	1.05	1.01–1.08	0.800	1.01	0.95–1.07
NC	<0.001*	1.32	1.13–1.54	0.01*	1.24	1.05–1.47
DPN	0.028*	2.48	1.11–5.56	0.014*	3.85	1.31–11.3
IHD	0.017*	3.28	1.23–8.69	0.012*	4.99	1.42–17.5
HBA1c	0.005*	1.38	1.10–1.73	0.01*	1.41	1.08–1.82
Fibrinogen	0.023*	1.02	1.002–1.03	0.245	1.01	0.99–1.02

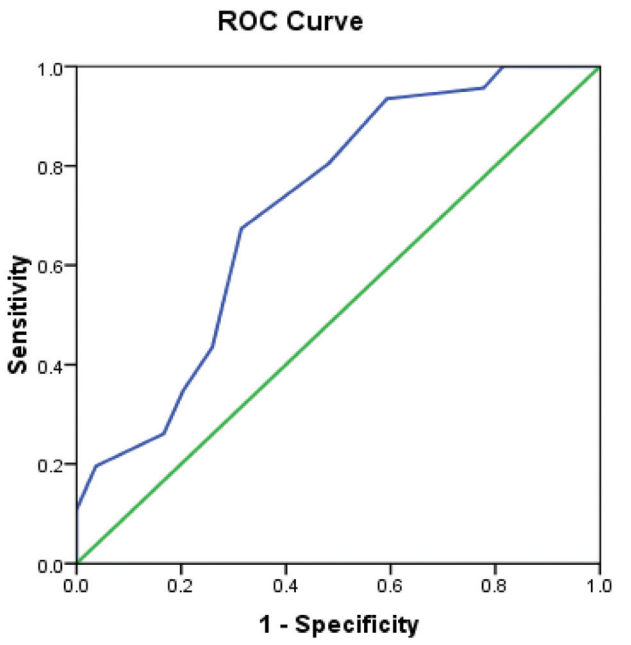
CI, confidence interval; DPN, distal polyneuropathy; IHD, ischemic heart disease; NC, neck circumference; OR, odds ratio; WC, waist circumference.

Table 6 Receiver operating characteristic curve of diagnostic accuracy of neck circumference in prediction of high-sensitivity C-reactive protein less than 5

	95% CI		Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
	Lower	Upper						
0.715	0.62	0.82	>40.50	80.4	52.9	58.7	75.7	77%

AUC, area under the curve; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

Figure 4



Roc curve of diagnostic accuracy of neck circumference in prediction of high-sensitivity C-reactive protein less than 5.

with CAD aged 18–60 years by Arjmand *et al.* [33] (r=0.256 and −0.470, respectively) (P<0.05).

On the contrary, a study done by Ben-Noun and Laor [34] on 236 men and 342 women found no significant correlation between NC and HDL in their study (r=−0.09 and −0.07, respectively) (P>0.05).

This current study reported a cutoff of more than 40.50 cm of NC as a risk factor of CAD based on AUC of 0.715, with sensitivity and specificity of 80.4 and 52.9%, respectively. This finding was stronger than the study of Arjmand *et al.* [33], which reported a cutoff of more than or equal to 38.25 cm of NC as a risk factor of CAD based on AUC of 0.711, with sensitivity and specificity of 70.6 and 33.8%, respectively.

Conclusion

NC which is an index of upper-body obesity can be effectively used as a screening parameter for identification of cardiovascular risk factors in type 2 diabetic patients. A cohort study is needed to further explore the relationship between NC and cardiovascular risks to detect higher sensitivity and specificity when compared with other risk factors.

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Rania Bahriz gave the idea of the research and design of the work, did statistical analysis, and performed data reviewing and interpretation. Mostafa Mansour was responsible for the laboratory part of the research [CRP, low-density lipoprotein (LDL), high-density lipoprotein (HDL)] and contributed in writing and data interpretation; Ahmed Albehairy contributed in writing (main role), shared in clinical part and follow up of patients in Specialized Medical Hospital in Mansoura University, was responsible for statistical analysis, and performed data reviewing and interpretation.

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Conflicts of interest
There are no conflicts of interest.

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