Neck Circumference as an Indicator of Glycemic Status in Type 2 Diabetes Mellitus: Evidence from a Tertiary Care Hospital of Mangaluru.

Dr. K S Tushar Gowda[1], Dr. Reshma S[2], Dr. Asharani N[3*] and Dr Janice Dsa[4]

1. *House Surgeon, A J Institute of Medical Sciences, Mangaluru 575004, Karnataka, India*
2. *Associate Professor, Department of Biochemistry, A J Institute of Medical Sciences, Mangaluru 575004, Karnataka, India.*
3. *Professor & Head, Department of Biochemistry, Adichunchanagiri Institute of Medical Sciences, Adichunchanagiri University, B G Nagara-571448, Mandya, Karnataka, India.*
4. *Associate Professor, Department of Biochemistry, A J Institute of Medical Sciences, Mangaluru 575004, Karnataka, India.*

Corresponding Author: Dr. Asharani N

Professor & Head, Department of Biochemistry, Adichunchanagiri Institute of Medical Sciences, Adichunchanagiri University, B G Nagara-571448, Mandya, Karnataka, India. E-mail ID: drashanellore@bgsaims.edu.in

Abstract:

Upper body subcutaneous fat is a distinct fat depot that confer increased cardiometabolic risk in diabetes mellitus (DM). Neck circumference (NC) is an index for upper-body subcutaneous fat and related to cardiovascular events in DM. This study was designed to exploring the link between neck circumference and glycemic control in Type 2 Diabetic patients. After collecting demographic and anthropometric measurements, fasting plasma glucose (FPG), HbA1c and Insulin were measured. BMI and waist-hip ratio (WHR) was calculated. The mean waist circumference (WC), hip circumference (HC), NC and FPG increased with deterioration of glycemic control. NC correlated better with WC followed by HC, WHR, weight, FPG, HbA1c, fasting insulin and HOMA-IR. WC, HC, WHR and NC were found to be reliable predictors of glycemic control and could distinguish between those with good glycemic control (HbA1c <7%) and those that did not have (HbA1c ≥ 7%). The cut-off for neck circumference to determine inadequate or poor glycemic control is >39 cm. In conclusion NC was able to distinguish between those with good and poor glycemic control. NC is a novel, easily measured fat depot that could be considered as an indirect measure to screen the glycemic status among diabetic population in the community.

Keywords: *Diabetes, Neck circumference, Insulin, Glycemic status, Glycated haemoglobin*

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INTRODUCTION:

Diabetes Mellitus (DM) is the most common endocrine disorder characterized by hyperglycaemia, insulin resistance and or decreased secretion of insulin. According to the World Health Organization (WHO), diabetic population in the world will reach 300 million by 2025[1]. India is a diabetic capital and is worst affected by this epidemic. Increase in elderly population, rapid urbanization, sedentary lifestyle, and increased prevalence of obesity are the main environmental factors contributing to the present diabetic epidemic. Cardiovascular disease (CVD) is the major cause of high morbidity and mortality in DM. Upper body subcutaneous fat is a distinct fat depot that may confer increased cardiometabolic risk. Neck circumference (NC) is an index for upper-body subcutaneous fat distribution. [2] Some studies have shown that neck circumference is associated with cardiometabolic risk factors [3] and subclinical atherosclerosis [4]. Lee et al. found that NC was positively associated with fasting plasma glucose [5]. Further, NC was also related to cardiovascular events in diabetes of Chinese population [6], Japanese postmenopausal women [7], and other populations [8]. However, few studies reported that NC was not significantly associated with fasting plasma glucose, insulin or insulin resistance [3,9-10]. To the best of our knowledge, very few studies in Indian diabetic population has been conducted to evaluate the relation of NC with glycemic parameter among type2 diabetes mellitus (T2DM) patients. Hence this present study was designed to assess the utility of neck circumference as a glycemic status marker in diabetic patients.

MATERIALS AND METHODS

The study was carried out after obtaining ethical approval from institutional ethical committee. A Cross-Sectional Study for a period of 3 months with a sample size of 255 was considered based on a study carried out by Assyov Y. et al in 2017 [11] clinically diagnosed type 2 diabetes mellitus patients with or with-out complications of both gender and in the age group of 35years to 60 years were recruited for the present study. A simple random sampling technique was employed to recruit the participants who attended General Medicine OPD and IPD at our institute. Patients diagnosed with malignancy of neck or goitre, Cushing syndrome, on long-term corticosteroids and, pregnant women were excluded from the study. All eligible participants were explained about the aims and objectives of the study. Demographic data including age and sex of the participants were recorded. All anthropometric parameters were measured as per the standard guidelines [12-13]. All measurements were made by one investigator using standard techniques as follows: weight by digital scales to within 100g without heavy clothing; height by portable stadiometer to within 0.5 cm, while barefoot; Measurement was made to the nearest 0.5 centimetre. Hip circumference was taken as the greatest circumference at the level of greater trochanter (the widest portion of the hip) on both sides. Body Mass Index and Waist Hip ratio was calculated using standard formulas. Neck Circumference was measured at mid neck height between mid- cervical spine and mid anterior neck, to within 1mm with plastic tapes calibrated weekly. In men with laryngeal prominence, it was measured just below the prominence. All circumference were taken with the subjects standing upright and facing the investigator, having their shoulder relaxed. Body Mass Index (BMI): calculated by dividing weight in kilograms by the square of height in meters (kg/m^2).Waist Hip ratio (WHR): calculated by dividing the WC by HC, both measured in centimetre. After a 14 hour fast, 5ml blood in a plain vacutainer and 2ml in EDTA vacutainer was drawn for analyses of fasting blood glucose using glucose oxidase peroxidase method on Abbott automated clinical chemistry analyser and glycated haemoglobin using HPLC method on D10 analyzer. Serum Insulin was analyzed by the DRG Insulin ELISA kit which is a solid phase enzyme linked immunosorbent assay based on the sandwich principle on Alere AM 2100 ELISA microplate reader.

Definition of variable: As per the American Diabetes Association 2019 criteria, diagnosis of diabetes is based on the following criteria[14]:

Statistical analysis: All data analysis was done using SPSS version 20. Categorical variables was represented as frequency and percentage and continuous variables represented as Mean ± SD. Chi Square test was employed for checking association between categorical variables. Correlation between Neck circumference and glycemic parameters was done using Pearsons correlation test. The sensitivity, specificity, positive and negative predictive values was calculated for the anthropometric parameters. Statistical significance was considered at $p<0.05$.

RESULTS:

The study comprised of 255 patients with type 2 diabetes mellitus, of which 52.9% (n=135) were males and 47.1% (n=120) were females. (Figure 1)

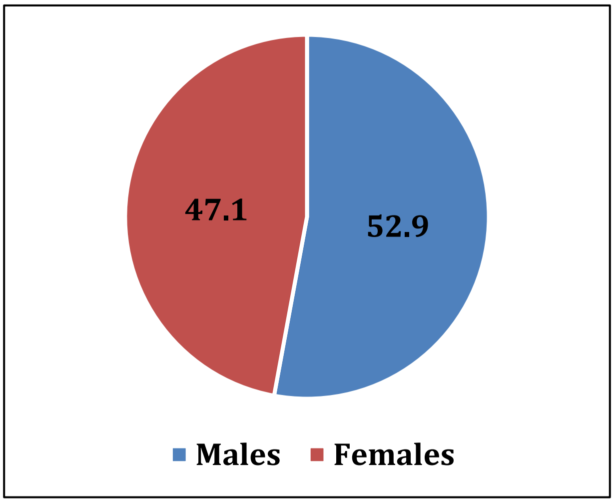

Figure 1: Distribution of study participants based on gender

The age of the participants ranged between 35 and 59 years and the mean age was 46.99 ± 6.61 years. The mean age of the male and female study participants was 47.07 ± 6.61 and 46.89 ± 6.63 years respectively. The distribution of subjects based on age groups and gender are depicted in Figure 2.

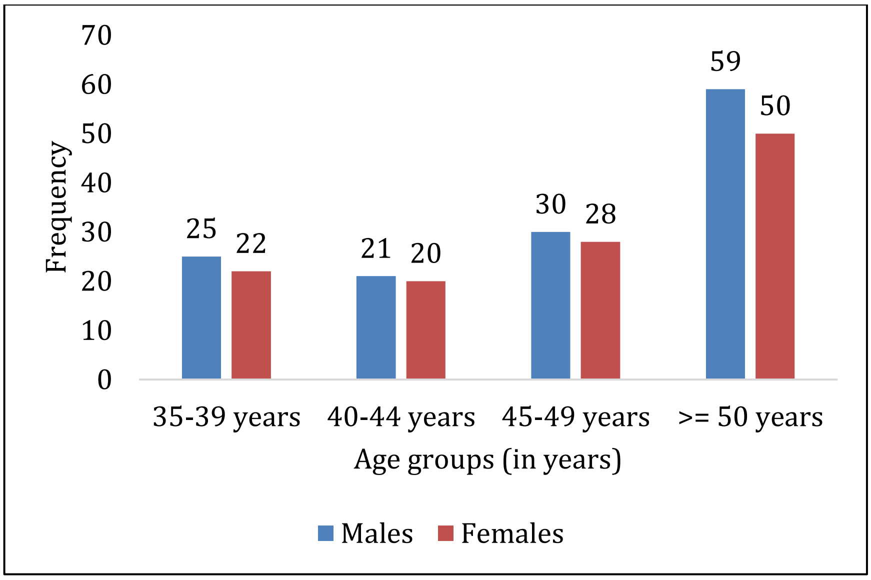

Figure 2: Distribution of study participants based on age group and gender

The anthropometric parameters, biochemical parameters and HOMA-IR are mentioned in Table 1. The parameters were compared between males and females. The mean height, weight, BMI, WC, HC, WHR and neck circumference values were higher in males compared to females. ($p<0.01$)

Fasting insulin and HOMA -IR were found to be lower in males compared to females. (p<0.01) The mean fasting blood glucose and glycated haemoglobin levels showed no significant difference between male and female study participants.

Table 1: Anthropometric and biochemical parameters among the study participants

Parameters	All study participants (n=255)	Male study participants (n=135)	Female study participants (n=120)	p value (Comparison between males & females)
	Mean ± SD (Min – Max)			
Age (years)	46.99 ± 6.61 (35 - 59)	47.07 ± 6.61 (35 -58)	46.89 ± 6.63 (35 – 59)	0.826
Height (meters)	1.58 ± 0.04 (1.46-1.72)	1.61 ± 0.04 (1.52 – 1.72)	1.54 ± 0.03 (1.46 – 1.62)	<0.001*
Weight (kilogram)	64.28 ± 10.08 (42.8 – 87.4)	70.13 ± 7.88 (50.6 – 87.4)	57.71 ± 8.03 (42.8 – 75.4)	<0.001*
BMI (kg/m2)	25.66 ± 3.32 (18.5 – 32.1)	27.13 ± 2.85 (19.2 – 32.1)	24.00 ± 3.03 (18.5 – 31)	<0.001*
Waist circumference (cm)	77.11 ± 16.23 (55 – 108)	87.69 ± 12.26 (62 – 108)	65.21 ± 11.1 (55 – 99)	<0.001*
Hip circumference(cm)	89.86 ± 8.41 (77– 118)	93.61 ± 9.76 (77 – 118)	85.64 ± 3.12 (81 – 99)	<0.001*
Waist-Hip ratio	0.86 ± 0.15 (0.53 – 1.18)	0.94 ± 0.12 (0.53 – 1.18)	0.76 ± 0.11 (0.64 – 1.05)	<0.001*
Neck circumference (cm)	37.52 ± 2.24 (32.00 – 42.50)	39.06 ± 1.36 (35.20 – 42.50)	35.79 ± 1.71 (32.00 – 39.90)	<0.001*
Fasting blood glucose (mg/dL)	157.05 ± 66.64 (57– 482)	161.96 ± 72.69 (57 – 466)	151.53 ± 58.92 (74 – 482)	0.213
Fasting insulin (microIU/mL)	30.44 ± 26.82 (1.85 – 95.08)	25.28 ± 26.64 (1.85 – 93.94)	36.25 ± 25.90 (2.14 – 95.08)	0.001*
HOMA -IR	11.52 ± 11.62 (0.39 – 56.28)	9.23 ± 9.99 (0.39 – 52.19)	14.09 ± 12.76 (0.69 – 56.28)	0.001*
Glycated haemoglobin (%)	7.47 ± 2.11 (4.80 -15)	7.56 ± 2.12 (4.80 – 13.60)	7.38 ± 2.09 (5.10 – 15)	0.502

*Highly significant, BMI-Body Mass Index

Correlation between neck circumference and various parameters are shown in Table 2. Among the biochemical parameters, neck circumference showed significant correlation with all the parameters. (p<0.001) Among the anthropometric parameters, neck circumference correlated better with waist circumference (r=0.839, p<0.001), followed by hip circumference (r=0.762, p<0.001), waist-hip-ratio (r= 0.636, p<0.001) and weight (r=0.616, p<0.001). Neck circumference correlated better with fasting blood glucose (r=0.251), followed by HbA1c (r=0.250), fasting insulin (r=-0.187) and HOMA-IR (r=-0.136).

Table 2: Correlation of neck circumference with various parameters

Neck circumference v/s Parameters	All participants (n=255)		Males (n=135)		Females (n=120)	
	r value	p value	r value	p value	r value	p value
Age (yrs)	0.174	0.005	0.281	0.001*	0.205	0.025*
Height (meters)	0.466	<0.001*	-0.195	0.024*	0.211	0.021*
Weight (kilogram)	0.616	<0.001*	0.120	0.167	0.480	<0.001*
BMI (kg/m2)	0.553	<0.001*	0.217	0.012*	0.464	<0.001*
Waist Circumference (cm)	0.839	<0.001*	0.499	<0.001*	0.869	<0.001*
Height Circumference (cm)	0.762	<0.001*	0.847	<0.001*	0.755	<0.001*
Waist Hip Ratio	0.636	<0.001*	-0.106	0.222	0.824	<0.001*
Fasting plasma glucose (mg/dL)	0.251	<0.001*	0.276	0.001*	0.307	0.001*
Fasting Insulin (microIU/mL)	-0.187	0.003*	-0.150	0.082	0.031	0.736
HOMA-IR	-0.136	0.030*	-0.086	0.322	0.103	0.262
HbA1c (%)	0.250	<0.001*	0.407	<0.001*	0.247	0.007*

The glycemic control was categorized as good glycemic control (HbA1c < 7%), inadequate glycemic control (HbA1c 7-8%) and poor glycemic control (HbA1c >8%) based on the ADA guidelines. Distribution of study participants based on glycemic control is shown in Figure 3. The percentages of study participants with good, inadequate and poor glycemic control were 52.5% (n=134), 17.3% (n=44) and 30.2% (n=77) respectively.

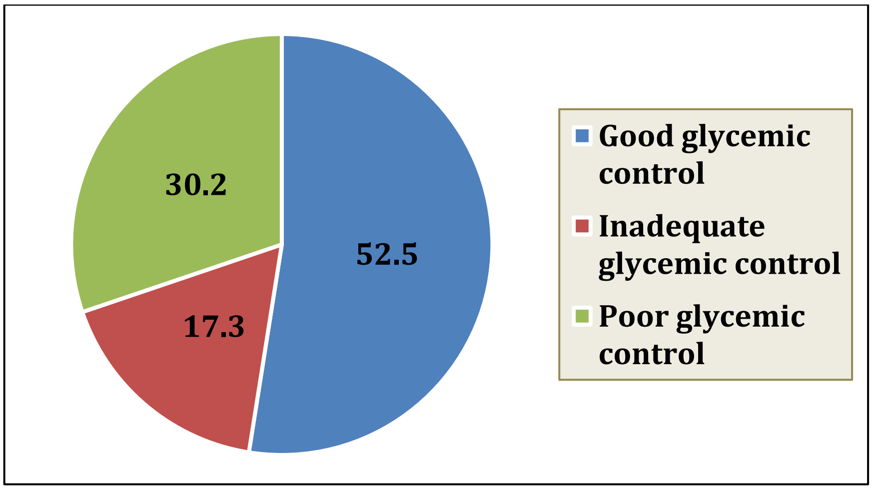

Figure 3: Distribution of study participants based on glycemic control

The anthropometric measurements including neck circumference along with various parameters were compared based on glycemic control. (Table 3). The mean waist circumference, hip circumference, neck circumference and fasting blood glucose increased with deterioration of glycemic control. ($p<0.01$) The mean waist circumference, hip circumference and neck circumference were significantly higher in those with poor glycemic control compared to those with good control. ($p<0.05$) There was no difference in the neck circumferences obtained between those with good and inadequate glycemic control or inadequate and poor glycemic control.

Table 3: Comparison of anthropometric measurements and biochemical parameters based on glycemic control

Parameters	Good glycemic control (n=134)	Inadequate glycemic control (n=44)	Poor glycemic control (n=77)	p value
Height (meters)	1.58 ± 0.04 (1.47 – 1.71)	1.58 ± 0.04 (1.50 – 1.68)	1.59 ± 0.05 (1.46 – 1.72)	0.379
Weight (kilogram)	63.61 ± 9.71 (43.5 – 77.4)	64.01 ± 10.93 (45.0 – 82.9)	65.62 ± 10.21 (42.8 – 87.4)	0.373
BMI (kg/m2)	25.50 ± 3.15 (18.90 – 31.20)	25.52 ± 3.98 (18.50 – 31.60)	26.02 ± 3.21 (19.40 – 32.10)	0.530
Waist circumference (cm)	73.58 ± 14.89 (55.00 – 108.00)	78.39 ± 15.62 (58.00 – 108.00)	82.52 ± 17.36[a**] (56.00 – 107.00)	<0.001
Hip circumference (cm)	87.46 ± 5.78 (77.00 – 118.00)	90.55 ± 8.25 (81.00 – 118.00)	93.65 ± 10.70[a**] (83.00 – 118.00)	<0.001
Waist Hip Ratio	0.84 ± 0.14 (0.53 – 1.17)	0.86 ± 0.14 (0.68 – 1.18)	0.88 ± 0.15 (0.63 – 1.17)	0.141
Neck circumference (cm)	37.02 ± 2.05 (32.00 – 40.90)	37.76 ± 2.14 (33.80 – 41.20)	38.27 ± 2.41[a*] (33.20 – 42.50)	<0.001
Fasting blood glucose (mg/dL)	124.99 ± 39.59 (71.00 – 324.00)	158.05 ± 40.33 [b*] (79.00 – 253.00)	212.27 ± 79.23 [a**c**] (57.00 – 482.00)	<0.001
Fasting insulin (microIU/mL)	31.84 ± 26.29 (2.21 – 93.55)	29.31 ± 27.00 (2.14 – 95.08)	28.65 ± 27.81 (1.85 – 91.43)	0.676
HOMA -IR	10.35 ± 10.24 (0.39 – 56.28)	11.37 ± 11.39 (0.69 – 52.19)	13.63 ± 13.68 (0.78 – 50.23)	0.143
Glycated haemoglobin (%)	5.95 ± 0.49 (4.80 – 6.90)	7.42 ± 0.33[b**] (7.00 – 8.00)	10.13 ± 1.77[a**c**] (8.10 – 15.00)	<0.001

a=comparison between good glycemic control and poor glycemic control; b=comparison between good glycemic control and inadequate glycemic control; c=comparison between inadequate glycemic control and poor glycemic control; *, $p<0.05$; **, $p<0.001$

ROC analysis was performed to determine the best predictor of glycemic control. Among the anthropometric parameters, waist circumference, hip circumference, waist-hip-ratio and neck circumference were found to be reliable predictors of glycemic control and could distinguish between those with good glycemic control (HbA1c <7%) and those that did not have. (HbA1c ≥ 7%). 7%).

Hip circumference was found to be a better indicator of glycemic control (AUC = 0.643, p<0.001), followed by waist circumference (AUC = 0.642, p<0.001), neck circumference (AUC = 0.638, p<0.001) and waist-hip-ratio (AUC = 0.576, p=0.036).

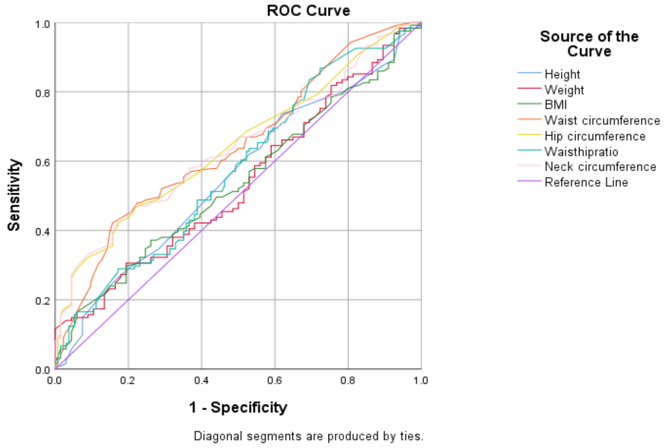

Figure 4: ROC analysis of glycemic control among diabetic patients

Table 4: Area under the curve for anthropometric parameters as the best predictor for glycemic control

Area Under the Curve					
				Asymptotic 95% Confidence Interval	
Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Lower Bound	Upper Bound
Height	0.555	0.036	0.130	0.484	0.626
Weight	0.537	0.036	0.313	0.465	0.608
BMI	0.538	0.036	0.293	0.467	0.610
Waist circumference	0.642	0.035	<0.001	0.574	0.710
Hip circumference	0.643	0.035	<0.001	0.575	0.711
Waist-hip-ratio	0.576	0.036	0.036	0.506	0.646
Neck circumference	0.638	0.035	<0.001	0.569	0.707

a. Under the nonparametric assumption, b. Null hypothesis: true area = 0.5

The sensitivity, specificity, positive predictive value and negative predictive value of the anthropometric measurements are shown in Table # 5. The cut-off for neck circumference to determine inadequate or poor glycemic control is >39 cm.

Table 5: Sensitivity, specificity, positive predictive value, negative predictive value and cut-off for anthropometric measurements to determine inadequate or poor glycemic control in diabetic patients

Parameter	Cut-off	Sensitivity	Specificity	PPV	NPV
BMI	>28.1	37.2%	73.9%	56.3%	56.6%
Waist circumference (cm)	>89	42.2%	84.3%	70.8%	61.7%
Hip circumference (cm)	>90	42.2%	82.8%	68.9%	61.3%
Waist Hip Ratio	>0.69	86.8%	27.6%	52.0%	69.8%
Neck circumference (cm)	>39	42.9%	82.8%	69.3%	61.7%

PPV: Positive Predictive value, NPV: Negative Predictive Value

DISCUSSION

Cardiovascular disease (CVD) is the major cause of high morbidity and mortality in Diabetes Mellitus. Upper body subcutaneous fat is a distinct fat depot that may confer increased cardiometabolic risk. Waist circumference has been used as the standard method to define central obesity, according to the NCEP ATP III guideline. However, measurement of WC has substantial variability and certain limitations. Neck circumference (NC) is an index for upper-body subcutaneous fat distribution.

The present study provides insightful data on the anthropometric differences between males and females, as well as the relationship between these measures and glycemic control. The findings demonstrate that the mean height, weight, BMI, WC, HC, WHR and neck circumference values were higher in males compared to females ($p<0.01$). This gender difference in anthropometric parameters could be attributed to inherent biological and physiological differences between the genders, which is consistent with existing literature. Xuhong Wang et al. [15] examined the general Chinese population aged 20-65 years and reported that NC positively correlated with BMI and WC in both genders. In the present study, among the anthropometric parameters, neck circumference correlated better with waist circumference ($r=0.839$, $p<0.001$), followed by hip circumference ($r=0.762$, $p<0.001$), waist-hip-ratio ($r= 0.636$, $p<0.001$) and weight ($r=0.616$, $p<0.001$).

Interestingly, the study found that fasting insulin levels and HOMA-IR (a measure of insulin resistance) were lower in males compared to females ($p<0.01$). This observation could suggest that females in the study might have had higher insulin resistance, a condition often associated with central obesity and an increased risk of type 2 diabetes. Neck circumference correlated better with fasting blood glucose (r=0.251), followed by HbA1c (r=0.250), fasting insulin (r=-0.187) and HOMA-IR (r=-0.136). Qun Yan et al. [16] investigated a Chinese elderly population with T2DM and found that a larger neck circumference (NC) was significantly associated with an increased risk of T2DM in men (OR 1.18, 95% CI 1.07–1.30, p = 0.001) and women (OR 1.25, 95% CI 1.13–1.38, $p < 0.001$).

The mean waist circumference, hip circumference, neck circumference and fasting blood glucose increased with deterioration of glycemic control ($p<0.01$) The mean waist circumference, hip circumference and neck circumference were significantly higher in those with poor glycemic control compared to those with good control ($p<0.05$). Recently Heng Wan et al. [17] conducted a study on Chinese patients with T2DM and concluded that neck circumference was linked to the prevalence of carotid artery plaque. They suggested that it could be a convenient and valuable anthropometric measure for the early prevention of cardiovascular disease and Laura Boemke et al. [18] studied patients with non-alcoholic fatty liver disease (NAFLD) and found that NC is associated with the HOMA-IR index in these patients. This suggests that neck circumference could be a convenient and reliable measure of central obesity, which is a known risk factor for insulin resistance and type 2 diabetes. Further this highlights the potential of neck circumference as a simple screening tool for assessing the risk of poor glycemic control in individuals.

ROC analysis showed waist circumference, hip circumference, waist-hip-ratio and neck circumference were reliable predictors of glycemic control and could distinguish between those with good glycemic control (HbA1c <7%) and those that did not have. (HbA1c ≥ 7%). Hip circumference was found to be a better indicator of glycemic control (AUC = 0.643, $p<0.001$), followed by waist circumference (AUC = 0.642, $p<0.001$), neck circumference (AUC = 0.638, $p<0.001$) and waist-hip-ratio (AUC = 0.576, p=0.036). The cut-off for neck circumference to determine inadequate or poor glycemic control is >39 cm with 82.2% specificity and 42.9% sensitivity. Although the sensitivity is relatively low, the high specificity indicates that neck circumference could effectively rule in poor glycemic control when the cut-off is exceeded. Xuhong Wang [15] and colleagues reported the NC cut-offs of ≥38.5 cm for men and ≥34.5 cm for women. Additionally, Anothaisintawee T et al [19] found that, even after adjusting for factors like BMI, neck circumference remained strongly correlated with waist circumference in prediabetic patients. They identified neck circumference cut-offs of ≥32 cm for females and ≥38 cm for males as the most effective for identifying central obesity in this group.

This study offers novel insights into the metabolic pathways linking increased neck circumference with glycemic control in diabetes. To further substantiate these findings, additional prospective studies involving larger diabetic populations are recommended to validate the observed relationship between neck circumference and glycemic status in diabetic patients.

Limitation: It was a single centric study and no control group was included.

CONCLUSION

Neck circumference (NC) is a simple, novel, practical and efficient anthropometric measurement which can be used in larger population. It represents upper body subcutaneous fat content and also an index of central obesity and insulin resistance. NC though not or less used can be an equally effective alternative to assess glycemic status in patients with Type 2 diabetes mellitus in a resource limited setting and can be used as an indirect marker to screen the glycemic status among T2DM.

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Conflicts of Interest: Nil

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Ethical Aspects: Ethical approval [**Letter no AJEC/REV/243/2022**] for the conduction of study was obtained from Institutional Ethics Committee on **10/01/2023**.

The manuscript with above mentioned title has been read and approved by all the authors, that the requirements for authorship as stated have been met, and that each author believes that the manuscript represents honest work.

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