International Journal of Clinical Science and Medical Research

ISSN(print): 2770-5803, ISSN(online): 2770-582X

Volume 06 Issue 01 January 2026

DOI: https://doi.org/10.55677/IJCSMR/V6I1-06/2026, Impact Factor: 8.005

Page No : 23-29

Association between Neck Circumference and Vitamin D amongst Patients with Type 2 Diabetes in Nigeria

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ABSTRACT

Background: Neck circumference and vitamin D have been linked with risk of development of chronic disorders especially those with cardiovascular implications, including type 2 diabetes mellitus. This study aimed to examine the relationship between neck circumference and vitamin D among persons with type 2 diabetes.

Method: The design of the research work was comparative cross-sectional, which included a total of 180 persons, comprising 120 patients with type 2 diabetes and 60 healthy controls. Neck circumference of subjects with type 2 diabetes and controls was measured, alongside determination of vitamin D levels for both categories of individuals. Data obtained was analyzed with Statistical Package for Social Sciences, version 22.

Results: The mean neck circumference of subjects with type 2 diabetes compared with controls showed no statistical difference (34.30 ± 3.09 cm vs 34.81 ± 2.61 cm; $p>0.05$). Neck circumference of male subjects with type 2 diabetes was higher than their female counterparts and this was statistically significant (37.46±2.97 cm vs 33.05±2.09 cm; $p=0.01$). The mean serum vitamin D of the subjects with type 2 diabetes was significantly lower than the controls (35.84 ± 11.65ng/ml vs 44.71 ± 20.12ng/ml; $p< 0.001$). However, there was no correlation between neck circumference and vitamin D amongst individuals with diabetes (rho= -0.07; $p=0.46$).

Conclusion: Neck circumference was not associated with vitamin D among subjects with type 2 diabetes in this study population. Further local and intercontinental studies may be required to fully elucidate on the existence of relationship between neck circumference and vitamin D amongst individuals with diabetes mellitus.

Published Online: January 20, 2026

KEYWORDS:
Neck circumference, Vitamin D, Type 2 diabetes mellitus, chronic diseases

INTRODUCTION

Vitamin D (Vit. D) is a fat-soluble vitamin and hormone, that is principally synthesized in the skin under the influence of ultraviolet light and is commonly known for regulation of calcium and phosphate homeostasis with promotion of bone health but extra-skeletal effects of vitamin D have been highlighted in recent studies [1, 2]. In the past few years, different research endeavours have elucidated on the role of vitamin D in the development of many chronic diseases, especially those with cardiovascular implications including type 2 diabetes mellitus (T2DM) [2-4]. Vitamin D has been linked with insulin resistance, obesity and consequent cardiometabolic complications in some studies [3,5,6]. Insulin resistance, obesity and physical inactivity have been identified as risk factors for T2DM and this is notably linked with markers of obesity such as waist circumference (WC), waist-hip ratio (WHR) and body mass index (BMI) [7,8]. In recent times, neck circumference (NC), which is a measure of upper body subcutaneous fat, has also been associated with insulin resistance and cardiovascular risk factors such as BMI, WC and WHR [9,10]. However, studies on the relationship between NC and Vitamin D are very few especially as it relates to T2DM and results are at variance as these have produced mixed outcomes, with some reporting a direct correlation while others yielded no relationship [11,12]. In addition, research endeavours on this subject between NC and Vitamin D are lacking in predominant black

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****Cite this Article: Emuze, M.E. (2026). Association between Neck Circumference and Vitamin D amongst Patients with Type 2 Diabetes in Nigeria. International Journal of Clinical Science and Medical Research, 6(1), 23-29. https://doi.org/10.55677/IJCSMR/V6I1-06/2026***

population, and Nigeria specifically.

Type 2 diabetes is a chronic disease that has witnessed increasing prevalence globally and has been designated as a disease of global public health concern, considering that currently, more than half a billion people live with diabetes worldwide [13]. Hence, research into this complex and heterogenous disease continues to generate interest in the scientific world in order to halt this progression. This study aimed to evaluate the relationship between NC and vitamin D among T2DM patients in a tertiary health facility in Nigeria. This would expand on the body of knowledge regarding NC and vitamin D in sub-Saharan Africa and could help draw some inferences on their role in the manifestation of T2DM and other cardiovascular disorders.

MATERIALS AND METHODS

The study was a comparative cross-sectional study among 120 persons with T2DM attending the Diabetes clinic of a tertiary hospital in Southern Nigeria and 60 apparently healthy control subjects.

Ethical approval for the study was obtained from the Research Ethics Committee and informed consent was obtained from each study participant. The study period spanned 6 months.

Sample size determination

The sample size for the study was determined using the Leslie Kish formula (Kish 1949) [14].

$$N = \frac{Z\alpha^2 [pq]}{d^2}$$

Zα = standard deviation (SD) set at 1.96

P = Prevalence of Vit. D deficiency among patients with T2DM = 92.4% (Fondjo et al) [15]

q = 1 – P

d = degree of accuracy required = 0.05

$$N = \frac{(1.96)^2 (0.924)(1-0.924)}{(0.05)^2}$$

$$= \frac{3.8416 \times 0.070224}{0.0025}$$

$$N = 107.9$$

Assuming an attrition rate of 10%

$$N = 107.9 + 10.79 = 118.7 \approx 119$$

The ratio of control to T2DM subjects of 1:2 was utilized. Therefore, 120 subjects with T2DM and 60 healthy adults as controls were recruited into the study, resulting in a total number of 180 participants.

Patients with T2DM, aged 30-65 years and who were on oral glucose lowering agents and consented to participate in the study were recruited for the study.

Apparently healthy members of staff and relatives of patients in the hospital served as controls. These were individuals greater than or equal to 30 years of age who did not have a history of diabetes mellitus, had a normal fasting plasma glucose (FPG <110mg/dl) and gave consent to participate in the study.

Pregnant women, patients with thyroid disease, goiter or previous neck surgery, patients with history or clinical features in keeping with chronic kidney disease, chronic liver disease, tuberculosis, chronic diarrhoea, malabsorption, patients with malignancy, patients on medications that could affect serum vitamin D levels and patients on vitamin D or calcium supplements were all excluded from the study.

Socio-demographic characteristics of the participants were obtained with the use of a pretested structured questionnaire. Neck circumference (NC) and other anthropometric measures such as weight (kg), height (m) and waist circumference (cm) were obtained following standard techniques and analyzed.

Neck circumference was measured with the tape measure, which was held perpendicular to the long axis of the neck with the superior border of the tape measure placed just below the laryngeal prominence [16,17]. Normal value: in males < 37cms and in females < 34 cms [16].

Levels of serum vitamin D were determined using enzyme linked immunosorbent assay (ELISA) method (Calbiotech , Inc. 1935 Cordell Ct., El Cajon, CA 92020, USA; intra-assay and inter-assay coefficients of variations was 8.35% and 8.78% respectively). 25-hydroxyvitamin D [25(OH)D] was used to classify vitamin D status with Vitamin D deficiency defined as a level of 25(OH)D less than 20ng/ml. Concentrations between 21- 29ng/ml was taken as vitamin D insufficiency and values >30ng/ml were considered as normal levels of 25(OH)D [18, 19]. Both vitamin D deficiency and insufficiency constitute hypovitaminosis D.

Fasting plasma glucose was analyzed by glucose oxidase method. Fasting plasma insulin levels were determined using the Calbiotech Human Insulin ELISA kit (intra-assay and inter-assay coefficients of variations was 8.58% and 9.13% respectively). Insulin resistance was calculated using the Homeostatic Model Assessment-Insulin Resistance (HOMA-IR) model, as derived from the formula [20,21].

$$\text{HOMA-IR} = \frac{\text{fasting glucose (mmol/L) X fasting insulin (mU/L)}}{22.5}$$

Data Analysis

Statistical analysis was done using Statistical Package for Social Sciences version 22. Categorical variables such as sociodemographic characteristics, lifestyle variables and medical history were presented using frequency tables, and histograms while quantitative variables were presented as means ± standard deviation and median (interquartile range) where appropriate. The comparison of means between patients with T2DM and control subjects was done using the student t-test. Chi-square, Fisher's exact test and spearman's correlation analysis were utilized as applicable; p-value <0.05 was considered statistically significant.

RESULTS

Socio-demographic characteristics of the participants is presented in Table 1. Subjects with T2DM included 86 females and 34 males, with 52.5% of T2DM subjects in the 51-60 year age group. The biochemical profiles of subjects with T2DM and controls is shown in Table 2 and this demonstrated that the mean serum vitamin D,
(25-(OH)D) of the T2DM study subjects (35.84 ± 11.65ng/ml) was significantly lower than that obtained for the controls (44.71 ± 20.12ng/ml), p< 0.001. Furthermore, T2DM subjects had a higher proportion of hypovitaminosis D when compared to the controls (31.7% versus 15.0%); p =0.02. The median HOMA-IR among T2DM study subjects was significantly higher than that of the controls, p= 0.002.
The mean ± SD NC among subjects with T2DM was 34.30 ± 3.09 and this was found to be slightly lower than the value obtained for controls (34.81 ± 2.61) but not statistically significant, p>0.05 (Table 3). The male participants with T2DM had higher NC compared to their female counterparts and this was statistically significant (p =0.01). A similar pattern was observed among the controls but without statistical significance.
The relationship between NC and HOMA-IR was examined as well as Vitamin D and HOMA-IR as reflected in Table 4 and Figure 1 respectively. While no significant relationship existed between NC and HOMA-IR, it was discovered that there was significant negative correlation of vitamin D with HOMA-IR among subjects with T2DM (r=-0.32, p<0.001).
Table 5 shows the relationship between NC and vitamin D among T2DM and controls. There was no relationship observed between NC and vitamin D among T2DM (rho= -0.07; p=0.46) and controls (rho=0.20, p=0.12).
The relationship of both neck circumference and vitamin D levels with cardiometabolic factors is revealed in Table 6. A moderate significant relationship existed between NC and BMI (rho = 0.30; p = 0.001), waist circumference (rho = 0.48; p <0.001) and WHR (rho = 0.26; p= 0.004). However, no statistically significant relationship was observed between vitamin D and the various cardiometabolic factors.

DISCUSSION

Type 2 diabetes has witnessed astronomical increase in terms of prevalence for many decades, with consequences for cardiovascular health, economy and social lives of people in different parts of the world [13].
This study was targeted at answering the question of existence of any connection between neck circumference and vitamin D, both of which have been linked with development of chronic disorders including T2DM and cardiometabolic disorders [2-4,10, 16, 22]
The study showed that the mean serum vitamin D for patients with T2DM was significantly lower than in control subjects, similar to findings by Abbiyesuku et al in Nigeria [23], Fondjo et al in Ghana [24], Kostoglou- Athanassiou et al in Greece [25], and Bachali et al in India [26]. Furthermore, the frequency of low vitamin D levels (vitamin D deficiency and insufficiency) among study subjects with T2DM was also significantly higher than that obtained for the controls similar to results from previous studies [23, 25].
It has been suggested that the higher prevalence of hypovitaminosis D in patients with diabetes compared to healthy controls could be explained by insulin resistance mediating such association, providing a probable reason for correlation of vitamin D with HOMA-IR in this study, and hence may indicate a role for vitamin D deficiency in the pathogenesis of T2DM [25].
With regards to neck circumference, the male participants with T2DM had higher NC than the female participants, which agrees with the study done by Dada et al in Nigeria [10], Cho et al in Korea [27] and Lucas et al in Brazil [28] with the extent of obesity suggested as a possible explanation [27, 28].
In addition, this study revealed no relationship between neck circumference and vitamin D among participants with T2DM. Similar outcome was reported by Chen et al in Taiwan among elderly individuals from the Healthy Aging Project with different comorbidities, including diabetes, where no correlation was found between the serum vitamin D level and neck circumference [12]. Contrary to this result, Fu et al in the BCAMS (Beijing Child and Adolescent Metabolic Syndrome) study discovered a negative correlation between NC and vitamin D, though their subjects were young adults and adolescents with no prior diagnosis of diabetes mellitus [11]. Looking closely at this index study, it could be seen that while vitamin D correlated with insulin resistance (HOMA-IR), such relationship did not exist between NC and insulin resistance among subjects with T2DM. Despite the fact that vitamin D had negative correlation with insulin resistance (HOMA-IR) similar to findings by Bachali et al [26] and Zhao et al [29], and NC correlated with cardiovascular risk factors such as BMI, WC and WHR amongst individuals with T2DM as previously documented by Dada et al [10] and Gowda et al [9], no correlation was observed between NC and vitamin D amongst patients with T2DM in this study. Hence this heterogenous result of vitamin D and NC with regards to insulin resistance may explain why there was no correlation between NC and vitamin D, considering that insulin resistance is an important currency in T2DM [7,8].
From the foregoing, it appears the relationship between NC and vitamin D among individuals with T2DM could be heterogenous and complex. Considering the paucity of data in literature, more studies may be necessary to give further and deeper insights into this area, which could have a bearing on chronic diseases, including T2DM.

CONCLUSION

In this study, neck circumference was not associated with vitamin D among individuals with T2DM, though varied relationship was observed with each entity as regards insulin resistance. Reports on association between these two parameters in the setting of T2DM is very scarce and considering the impact of T2DM on global health, more research activities could be undertaken to elaborate further on the subject.

ACKNOWLEDGEMENTS
The author appreciates the members of the Endocrine unit, University College Hospital, Ibadan, Nigeria, including Dr. J.O. Adeleye and Dr. A. Esan for their encouragement and support during the period of the study.

Table 1: Socio-demographic characteristics of study subjects and controls

Sociodemographic Characteristics	Cases; N=120 f (%)	Controls; N=60 f (%)	X^2	p-value
Age (Years)				
≤40	5 (4.2)	3 (5.0)	0.17	0.98
41-50	22 (18.3)	12 (20.0)		
51-60	63 (52.5)	31 (51.7)		
>60	30 (25.0)	14 (23.3)		
Mean ± SD	**55.22 ± 6.94**	**54.22 ± 8.03**		**0.39**
Sex				
Female	86 (71.7)	43 (71.7)	0.00	1.00
Male	34 (28.3)	17 (28.3)		
Educational Status				
Tertiary	54 (45.0)	52 (86.7)	33.20#	<0.001**
Secondary	39 (32.5)	8 (13.3)		
Primary	15 (12.5)	0 (0.0)		
No Education	12 (10.0)	0 (0.0)		
Alcohol Use				
Does not drink alcohol	101 (84.2)	49 (81.7)	0.65#	0.13
Drank but stopped at least 1 year ago	9 (7.5)	0 (0.0)		
Still drinking alcohol	10 (8.3)	11 (18.3)		
Smoking History				
Non-smoker	119 (99.2)	58 (96.7)	1.53#	0.26
Ex-smoker	1 (0.8)	2 (3.3)		
Current smoker	0 (0.0)	0 (0.0)		

****p-value <0.001, *p-value < 0.05 #Fisher Exact X^2 Pearson Chi Square**
SD: Standard deviation

Table 2: Biochemical Parameters of Study subjects and controls

Laboratory Variables	Cases; N=120 (mean ± SD)	Control; N=60 (mean ± SD)	*t-test*	p-value
Serum 25-(OH)D (ng/ml)	35.84 ± 11.65	44.71 ± 20.12	18.23	<0.001**
Hypovitaminosis; n (%)	38 (31.7)	9 (15.0)		0.02*
Deficiency; n (%)	4 (3.3)	2 (3.3)		0.04*
Insufficient; n (%)	34 (28.3)	7 (11.7)		
Sufficient; n (%)	82 (68.3)	51 (85.0)		
FPG (mg/dl)	133.70 ± 39.78	94.50 ± 12.20	7.45	<0.001**
FPG (mmol/L)	7.43 ± 2.21	5.25 ± 0.70	7.43	<0.001**
HbA1c (%)	7.70 ± 2.20	5.00 ± 0.60	9.44	<0.001**
Plasma Insulin (μU/ml)	10.23 ± 7.23	9.58 ± 6.10	0.26	0.82
HOMA-IR; median (IQR)	2.26 (2.57)	1.59 (1.53)	1.40	0.002*

**** p-value <0.001, * p-value <0.05**

25-(OH)D= 25-hydroxyvitamin D, FPG= Fasting Plasma Glucose, HbA1c= Glycated Haemoglobin, IQR= Interquartile range

Table 3: Neck circumference between T2DM and controls

Variables	T2DM; N=120 (mean ± SD)			Controls; N=60 (mean ± SD)			*t-test*	p-value
NC	34 .30 ± 3.09			34.81 ± 2.61			-1.11	0.09
	Male	Female	P-value	Male	Female	P-value		
	37.46±2.97	33.05±2.09	0.01*	37.21±2.46	33.87±2.01	0.24		

*** p-value < 0.05**

NC= Neck circumference

HOMA-IR: Homeostatic model assessment-insulin resistance

Table 4: Relationship between neck circumference and HOMA-IR among T2DM

Cardio-metabolic parameters	T2DM NC	
	rho	p-value
HOMA-IR	0.13	0.16

*** p-value < 0.05**

HOMA-IR: Homeostatic model assessment-insulin resistance

Table 5: Relationship between neck circumference and Vitamin D among patients with type 2 diabetes mellitus and controls

Parameter	T2DM NC		Control NC	
	rho	**p-value**	**rho**	**p-value**
Vitamin D	- 0.07	0.46	0.20	0.12

Table 6: Neck circumference and Vitamin D relationship with Cardiometabolic factors among patients with type 2 diabetes mellitus

Cardiometabolic parameters	NC		Vitamin D	
	rho	p-value	rho	p-value
BMI (kg/m^2)	0.30	0.001*	0.01	0.92
Waist Circumference (cm)	0.48	<0.001*	0.02	0.85
WHR	0.26	0.004*	0.12	0.20
Systolic Blood Pressure (mmHg)	-0.003	0.97	-0.14	0.13
Diastolic Blood Pressure (mmHg)	0.15	0.10	-0.15	0.10
HDL-C (mg/dl)	-0.05	0.59	0.10	0.26
LDL-C (mg/dl)	-0.15	0.10	0.19	0.06
Triglyceride (mg/dl)	0.38	0.68	-0.15	0.10
Total Cholesterol (mg/dl)	-0.15	0.10	0.18	0.06

*** p-value < 0.05**

BMI: Body Mass Index WHR: Waist-hip-ratio

HDL-C= High density Lipoprotein Cholesterol LDL-C= Low density Lipoprotein Cholesterol

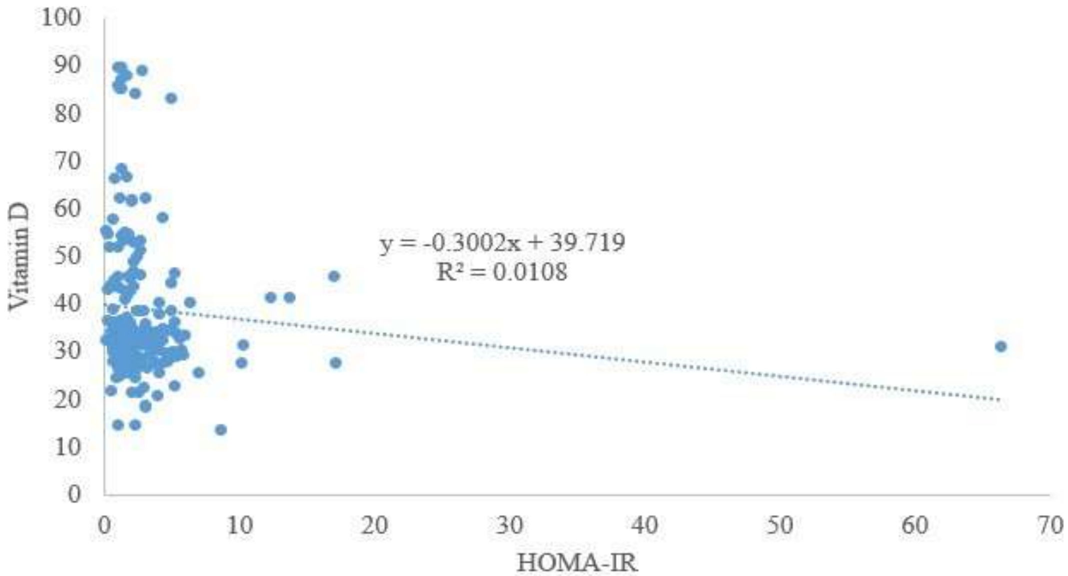

Figure 1: Linear relationship between vitamin D and HOMA-IR among T2DM subjects

Funding: Self-funded

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