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Mediating effect of fasting blood glucose and peripheral arterial disease on the relationship between sexual functioning and health-related quality of life among Nigerians with type 2 diabetes

Olufemi O. Oyewole[1,2*], Ayotunde O. Ale[3], Ayanbola I. Adepoju[4], Grace M. Emmanuel[1], Michael O. Ogunlana[2,5], Olufunmilayo O. Oyewole[6] and Olatunde Odusan[3]

Abstract

Background Poor glycemic control and sexual dysfunction have been shown to impair health-related quality of life (HRQoL) of individuals with diabetes. However, mediators underlying this relationship have not been evaluated. This study aimed/sought to assess the effect of fasting blood glucose (FBG) and peripheral arterial disease (PAD) on the relationship between sexual functioning (SeF) and HRQoL among Nigerians with type 2 diabetes mellitus (T2DM).

Methods This cross-sectional study consecutively recruited 210 participants diagnosed with T2DM. The recent FBG and lipid profiles were gleaned from the medical records of the participants. We assessed the ankle-brachial index by 8 MHz handheld vascular Doppler. Participants completed the Changes in Sexual Functioning Questionnaire and Short Form 12 (SF-12) questionnaire to assess SeF and HRQoL, respectively.

Results Significant differences exist in HRQoL of participants with good and poor glycemic control (mean rank = 111.02 vs. 93.64, $p = 0.035$) but none between participants with and without PAD (mean rank = 101.39 vs. 107.60, $p = 0.483$). There was a significant correlation between SeF and HRQoL ($r = 0.181$, CI = 0.043–0.313, $p = 0.008$), and a significant negative correlation between HRQoL and FBG ($r = -0.149$, CI = -0.284 - -0.008, $p = 0.033$). There is a significant indirect effect of impact of SeF on HRQoL through FBG (b = -0.027, t = -0.899) and PAD (b = 0.034, t = 1.246). Furthermore, the direct effect of SeF on HRQoL in the presence of the mediators was also significant (b = 0.483, $p = 0.001$). This shows that PAD and FBG mediates the relationship between SeF and HRQoL.

Conclusion Good glycemic control and the absence of PAD mediate the relationship between SeF and HRQoL in Nigerians with T2DM.

Clinical trial number Not applicable.

*Correspondence:
Olufemi O. Oyewole
oyewoleye@gmail.com; OyewoleO1@ukzn.ac.za

Full list of author information is available at the end of the article

Keywords Glycemic control, Peripheral arterial disease, Sexual function, Health-related quality of life, Type 2 diabetes mellitus, Nigerian

Introduction

Type 2 diabetes mellitus (T2DM) remains a major public health issue globally. It is estimated to affect 476 million people globally in 2017 and projected to increase to 693 million by 2045 [1, 2]. This translates to 6059 cases per 100,000 in 2017 with increase to 7079 cases per 100,000 [3] by 2030. The vital proportion of these affected individuals reside in sub-Saharan Africa and is estimated to increase from 25 million people in 2021 to 55 million by 2045 [4]. In Nigeria, T2DM is estimated to affect 4.7 million in 2015 and 3.6 million in 2021 [4, 5]. T2DM and its complications have imposed a great burden not only on the afflicted but the society at large. To mitigate these burden, focus has shifted from a biomedical model of health to a biopsychosocial model of health in offering adequate treatment for T2DM [6]. One of such biopsychosocial aspect is the improvement in health-related quality of life (HRQoL) of people with type 2 diabetes.

Uncontrolled blood glucose and other complications of T2DM negatively impact HRQoL of people with T2DM [7–9]. The more the number of diabetes complications, the poorer the HRQoL [7, 10]. Literature search suggests that individuals with T2DM who have good glycemic control demonstrated better HRQoL than those who have poor glycemic control [10–13]. The mechanism by which controlled blood glucose translates to a better quality of life has been attributed to reduction in diabetes complications [7, 10].

One of the T2DM complications that impacted HRQoL is sexual dysfunction. Evidence suggests that people with T2DM have lower sexual functioning compared with the general population [14–17]. This reduction in sexual functioning has been reported to impact the quality of life of individuals with diabetes negatively [18, 19]. A negative relationship between sexual dysfunction and quality of life exists among people with diabetes [18–21]. It therefore becomes imperative to find a way of improving the sexual functioning of individuals with diabetes in order to better their quality of life.

HRQoL among individuals with T2DM has been shown to be impacted by microvascular and macrovascular complications [8, 9] one of which is peripheral arterial disease (PAD). People with T2DM who have developed PAD experience significant reduction in their HRQoL and walking distance [22]. T2DM with PAD has been suggested to be at risk of impaired functional capacity, reduced general health and greater social isolation [22].

Several studies have determined the HRQoL and its correlates or determinants and reported that a significant impact of these correlates impaired the HRQoL in the T2DM population [9–12, 23–27]. There are few studies on factors that may mediate or moderate these correlates. It is essential to elucidate factors that can mediate these correlations for optimal glycemic control and quality of life. As mentioned above both poor glycemic control and presence of PAD independently impacted HRQoL. Thus, both FBG and PAD were chosen as mediators that may likely mediate association between sexual functioning and HRQoL. Therefore, this study assessed the relationship between sexual functioning and health-related quality of life and its mediators among Nigerians with type 2 diabetes.

Methods

Design and population

This cross-sectional study consecutively recruited participants diagnosed with type 2 diabetes mellitus using WHO criteria [28] sourced from the endocrinology clinic of Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria. Inclusion criteria are that study participants must have been attending clinic and receiving treatment for diabetes for at least four weeks, give informed consent and be able to communicate and complete the questionnaires. Prior to the study, a standard formula was used to estimate sample size with an error margin set at 0.05, 95% confidence level Z scores at 1.959964, $p=0.5$, and diabetes population attendees at a clinic set at 414 [29]. A minimum of 199 participants was required to power the study.

Informed written consent was obtained from all the participants prior to recruitment whilst Olabisi Onabanjo University Teaching Hospital Health Research and Ethics Committee approved the study (Approval no: OOUTH/HREC/472/2021AP).

Measurement

Sociodemographic data including age, sex, marital and occupation were obtained from the participants. The recent fasting blood glucose and lipid profiles were gleaned from the medical records of the participants. Fasting blood glucose (FBG) < 7.0 mmol/L (< 126 mg/dl) was set as achieving blood glucose control [28].

Ankle-brachial index (ABI) was assessed with a standard method using 8 MHz handheld vascular Doppler (Dopplex Doppler, LUS-D900-P-VP8KIT, Arjo Inc), Sphygmomanometer (DEKAMET MK3 ACCOSON), and Stethoscope (3M™ Littmann®Classic II S.E. Stethoscope) [30] as a ratio of ankle systolic pressure and brachial systolic pressure. The ABI is assessed during the clinic visit in the morning hours after the patient rests for

five minutes in a supine position on a plinth in a private room. Both arms were measured simultaneously then followed by both ankles. The arm with the highest brachial systolic pressure was used for ABI calculation. Brachial pressure was measured with the patient in the supine position. An appropriate blood pressure cuff linked to a sphygmomanometer was wrapped around the arm, with the arm at the level of the heart. The stethoscope was placed on the antecubital fossa over the participant's brachial pulse. The cuff was inflated to about 180 mmHg. Then slowly deflate the cuff, not faster than 3 mmHg/sec. The first Korotkoff sound was recorded as the brachial systolic pressure. Ankle pressure was assessed placing the appropriate cuff linked to the sphygmomanometer just above the ankle or immediately proximal to the malleoli. Ultrasound gel was placed on the skin overlying the dorsalis pedis (DP) artery in the foot. We locate the Doppler signal of the DP slightly lateral to the midline of the dorsum of the foot with a handheld 8 MHz vascular Doppler. We slowly move the Doppler until the strongest signal is heard. The cuff was inflated until the signal disappeared. Then the cuff was slowly deflated until the Doppler signal reappeared. This was recorded as the ankle systolic pressure measurement. ABI was used to determine the presence or absence of arterial disease for both legs. ABI value < 0.90 was set as the presence of peripheral arterial disease (PAD) [31]. Both legs were used for analysis by categorizing it as the presence of PAD in at least one limb or both and no PAD. For mediation analysis, the continuous variable of ABI was used, and the mean values of both legs were used in addition to the right and left leg separately.

Short Form 12 (SF-12) questionnaire was used to assess health-related quality of life. It consists of 12 items, six each from physical and mental summary measures. The score ranges from 0 (the worst) to 100 (the best), with higher scores associated with the highest levels of quality of life. Its validity has been established among the Nigerian population [32].

A standardized validated questionnaire, a short form of the Changes in Sexual Functioning Questionnaire (CSFQ-14) was utilized to evaluate the sexual functioning of the participants. It consists of 14 items rated on a five-point Likert scale of frequency (1 = never to 5 = every day/always) to assess behavior or problems during phases of the sexual response cycle. This instrument had been validated in ill health and among healthy people with Cronbach's alphas coefficient of 0.87 [33, 34].

Data analysis

Data was tested for normal distribution. Shapiro-Wilk test of normality indicated that sexual functioning, quality of life, fasting blood sugar, and peripheral arterial disease data were not normally distributed ($p < 0.001$). IBM Statistical Package for Social Science (SPSS) version 28 (SPSS Inc., Chicago, IL) was used to analyze the data. The p-value was set at 0.05.

Descriptive statistics of mean, mean rank, standard deviation, and percentage were used to summarize the data. Mann-Whitney U test was used to assess differences in sexual functioning and quality of life between participants with good and poor glycemic control as well as differences in sexual functioning and quality of life between the presence and absence of PAD.

Spearman's correlation was used to assess the relationship between sexual functioning, quality of life, FBG, and PAD. Model 4 of Hayes PROCESS Macro was used to assess the mediating effect of FBG and PAD on the relationship between sexual functioning and quality of life. The model has a continuous dependent variable as HRQoL, a continuous independent variable as sexual functioning, continuous mediators of FBG, and PAD.

Results

Two hundred and ten (210) subjects participated in the study. There were more females (71.4%), mostly married (70%) with mean age of 59.7 ± 11.6 years. About half of study participants achieved good glycemic control (49.5%) while 71 (33.8%) have PAD in at least one limb (Fig. 1).

Table 1 shows the health-related quality of life (HRQoL) and sexual functioning stratified by glycemic control and PAD. A significant difference was demonstrated among participants who have good and poor glycemic control in overall quality of life (mean rank = 111.02 vs. 93.64, $p = 0.035$) and its mental composite domain (mean rank = 111.53 vs. 93.11, $p = 0.026$). This indicates that participants with good glycemic control have better HRQoL than those with poor glycemic control. There were no significant differences in the mean ranks of sexual functioning and HRQoL of participants with and without PAD ($p > 0.05$). However, participants with no PAD demonstrated insignificant higher values or better HRQoL and sexual functioning than those with PAD.

Table 2 shows correlation matrixes between sexual functioning, quality of life, FBG, and PAD. There was a significant correlation between sexual functioning and quality of life ($r = 0.181$, CI = 0.043–0.313, $p = 0.008$). A significant negative correlation exists between quality of life and FBG ($r = -0.149$, CI = -0.284 - -0.008, $p = 0.033$).

The study assessed the mediating role of FBG and PAD on the relationship between sexual functioning and HRQoL. Table 3 shows the mediation analysis for the mean values of ABI to report PAD and also provides a summary of the overall model with $R^2 = 7.99\%$ ($p < 0.001$). The results revealed a significant indirect effect of impact of sexual functioning on HRQoL through FBG (b = -0.027, t = -0.899). This indicates that FBG mediates the

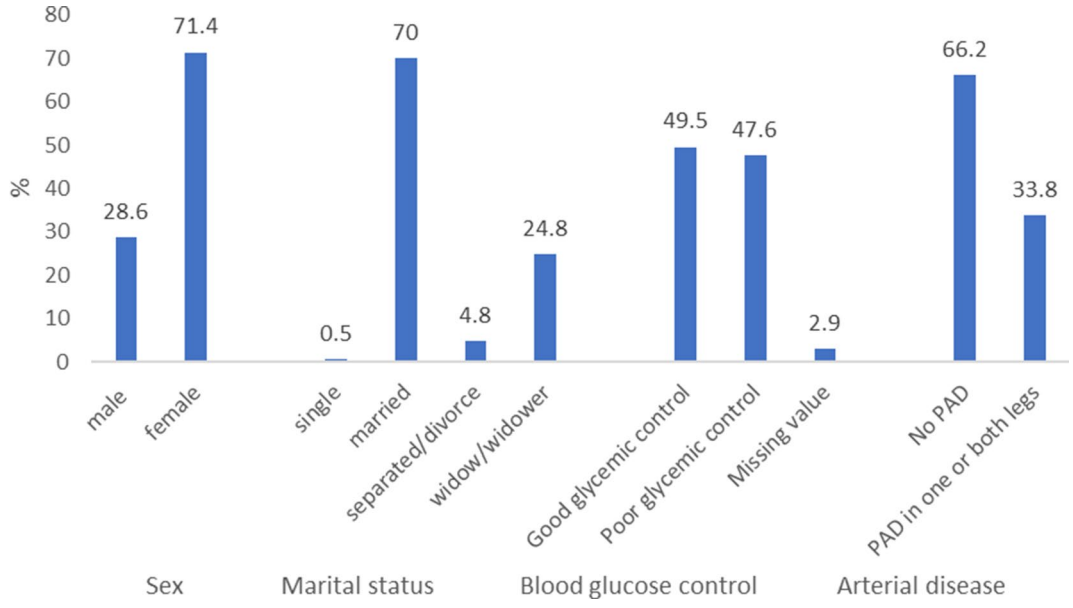

Fig. 1 Sociodemographic and clinical characteristics of the participants (N = 210)

relationship between sexual functioning and HRQoL. The study also found a significant indirect effect of impact of sexual functioning on HRQoL through PAD (b = 0.034, t = 1.246). This indicates that PAD mediates the relationship between sexual functioning and HRQoL. Furthermore, the direct effect of sexual functioning on HRQoL in the presence of the mediators was also found to be significant (b = 0.483, p = 0.001). Hence, both FBG and PAD partially mediated the relationship between sexual functioning and HRQoL (Table 3). The results were similar when using ABI values for each of right and left leg (Table S1 and Table S2).

The FBG (b = -0.071, t = -1.325) and PAD (b = 0.033, t = 0.846) independently mediate (indirect effect) the relationship between sexual functioning and HRQoL among females when the data was stratified by sex (Table S3). Also, the direct effect of sexual functioning on HRQoL in the presence of the mediators was significant among females (b = 0.601, p = 0.002). Comparable results were demonstrated for the right and left legs (Table S4 and Table S5).

Discussion

In this cross-sectional study of 210 subjects with T2DM, individuals with good glycemic control have better HRQoL and mental health than those with poor glycemic control. This was consistent with previous studies which reported that poor glycemic control impaired HRQoL [10–12]. This suggests that maintaining good glycemic control is essential for better HRQoL among individuals with T2DM. Therefore, health professionals involved in diabetes management should strive to formulate and promote management that enhances glycemic control for optimum HRQoL. This is necessary as about half (50.5%) of present study participants have not achieved optimum glycemic control. Generally, about 65% of Nigerians with diabetes have been reported to attain optimum glycemic control [35, 36]. HRQoL was not significantly different whether there was the presence or absence of PAD in our subjects. However, individuals without PAD showed better HRQoL than those who have PAD though not significant. Studies have suggested that individuals with PAD are at increased risk of poorer HRQoL and that PAD is an independent predictor of poor quality of life [9, 22]. About one-third of participants in the present study have PAD which corroborates the previous findings among Nigerians with diabetes, reporting prevalence ranges between 22% and 40% of PAD [37–39].

Our data indicates no significant differences in sexual functioning between individuals with good and or poor glycemic control. This was at variance with previous studies which reported that people with poor glycemic have greater odds of sexual dysfunction [40–43]. The present study relied on FBG to stratify good or poor glycemic control while all those previous studies used glycated hemoglobin (HbA1c) to assess the participants. This may account for differences in our findings, as the HbA1c has shown high sensitivity in screening sexual dysfunction in high-risk individuals [42]. The presence or absence of PAD in the present study participants indicated no significant difference in sexual functioning. Although not significant, individuals without PAD exhibited higher sexual function values than those who have PAD. Literature search suggests that presence of PAD impaired sexual function among individuals with T2DM and that the presence of PAD is an independent predictor of sexual

Table 1 Health-related quality of life and sexual functioning by glycemic control and peripheral arterial disease

Variable	All sample	Glycemic control (N = 204)						Peripheral arterial disease (PAD) (N = 210)					
		Good glycemic control		Poor glycemic control		U	*P*	No PAD		PAD in at least one leg		U	*P*
	Mean ± SD	Mean ± SD	Mean Rank	Mean ± SD	Mean Rank			Mean ± SD	Mean Rank	Mean ± SD	Mean Rank		
Quality of life													
Physical composite summary	57.30 ± 26.08	59.98 ± 27.09	108.51	54.71 ± 25.20	96.25	4574.5	0.137	58.93 ± 25.81	109.19	54.11 ± 26.51	98.27	4421.5	0.218
Mental composite summary	67.95 ± 23.21	71.85 ± 21.91	111.53	64.21 ± 24.45	93.11	4260.5	0.026*	68.09 ± 22.89	105.67	67.69 ± 23.98	105.17	4911.0	0.955
Total quality of life	62.63 ± 22.28	65.91 ± 22.46	111.02	59.46 ± 22.18	93.64	4313.5	0.035*	63.51 ± 21.99	107.60	60.90 ± 22.90	101.39	4642.5	0.483
Sexual functioning													
Desire phase of sexual functioning	10.20 ± 4.73	9.75 ± 4.24	99.80	10.48 ± 5.14	105.31	4919.5	0.501	10.30 ± 4.84	106.42	9.99 ± 4.52	103.69	4806.0	0.755
Arousal phase of sexual functioning	5.87 ± 3.23	5.88 ± 2.96	105.47	5.83 ± 3.52	99.42	4891.5	0.445	6.08 ± 3.46	107.86	5.46 ± 2.71	100.88	4606.5	0.412
Orgasm phase of sexual functioning	5.80 ± 3.18	5.63 ± 3.04	100.62	5.89 ± 3.32	104.46	5004.5	0.624	5.90 ± 3.22	107.17	5.59 ± 3.11	102.23	4702.5	0.557
Total sexual functioning	32.74 ± 10.49	32.26 ± 9.68	102.17	32.97 ± 11.35	102.84	5166.0	0.935	33.23 ± 11.01	107.40	31.77 ± 9.37	101.79	4671.0	0.524

U: Mann-Whitney U; P: P-value; *Significant at 0.05

Table 2 Spearman's correlation matrixes between sexual functioning, health-related quality of life, fasting blood glucose and peripheral arterial disease (N = 210)

Variable	Fasting blood glucose (N = 204)§ *r* (95% CI)	Quality of life (SF) *r* (95% CI)	Sexual functioning *r* (95% CI)
Quality of life	-0.149* (-0.284 – -0.008)		
Sexual functioning	0.016 (-0.125–0.157)	0.181** (0.043–0.313)	
Peripheral arterial disease	-0.132 (-0.268–0.010)	-0.048 (-0.187–0.091)	-0.044 (-0.182–0.096)

*. Correlation is significant at the 0.05 level (2-tailed)

**. Correlation is significant at the 0.01 level (2-tailed)

§ 204 sample was used for fasting blood glucose

CI: Confidence interval

r: Correlation matrix

dysfunction [44, 45]. PAD is reported as a modifiable risk factor for erectile dysfunction in men [44]. Therefore, efforts should be directed at mitigating the occurrence of PAD among individuals with T2DM for optimum care and improved sexual function.

One of the key findings of the present study is the significant relationship between sexual functioning and quality of life in our subjects. The better the sexual function, the better the quality of life of individuals with diabetes. The mediation analysis further confirmed this positive relationship. Lower sexual functioning significantly impacts HRQoL of the participants. This is in tandem with previous studies that reported a positive correlation between sexual functioning and HRQoL and that erectile dysfunction predicted poor HRQoL [18, 20, 21]. Again, this serves as pointer that all health professionals involved in the management of people with diabetes should strive to engage patients in sexual health for optimum HRQoL. This study also observes a significant negative correlation between FBG and HRQoL. This suggests the higher the FBG the poorer the HRQoL. This is in tandem with a previous study in multi-linear regression reporting a negative correlation and reported uncontrolled FBG as predicting poor HRQoL [12].

One of the principal aims of this study is to assess the mediating effect of FBG and PAD on the relationship between sexual functioning and HRQoL. Results from this study suggest that PAD mediates the relationship between sexual functioning and HRQoL. This suggests that if PAD, a modifiable risk factor can be delayed in individuals with T2DM, it can enhance better HRQoL in the presence of sexual dysfunction. FBG also mediates the relationship between sexual functioning and HRQoL suggesting the need for optimal glycemic control.

This study results also indicate that the interaction of both PAD and FBG mediated the relationship between

Table 3 Mediating effect of fasting blood glucose and peripheral arterial disease (mean of both legs) on sexual functioning and health-related quality of life (N = 204)

Variable	Coefficient	SE of Coefficient	t-value	*p*-value	Lower Limit of Confidence Interval	Upper Limit of Confidence Interval
Constant	36.310	10.464	3.470	0.001	15.675	56.945
Sexual functioning (SeF)	0.483	0.147	3.290	0.001	0.194	0.773
Fasting blood glucose (FBG)	-0.049	0.026	-1.864	0.064	-0.100	0.003
Mean of both legs peripheral arterial disease (PAD)	17.917	9.820	1.825	0.070	-1.447	37.280
Model Summary						
R	R-sq	MSE	F	df1	df2	p
0.2827	0.0799	472.8667	5.7892	3.0000	200.0000	0.0008
Total effect (SeF → HRQoL)	**Direct effect (SeF → HRQoL)**	**Relationship**	**Indirect effect**	**Confidence interval**	**t-statistics**	**Conclusion**
				Lower - upper		
0.490(0.001)	0.483(0.001)	SeF → FBG → HRQoL	-0.027	-0.010–0.013	-0.899	Partial mediation
		SeF → PAD →HRQoL	0.034	-0.008–0.097	1.246	Partial mediation

Model: 4

Dependent or outcome variable Y(continuous): Health-related quality of life (HRQoL)

Independent variable X(continuous): Sexual functioning (SeF)

Mediator W(continuous): Fasting blood glucose (FBG)

Med1ator Z(continuous): Peripheral arterial disease (PAD)

sexual functioning and HRQoL. This may suggest that delayed onset of PAD in addition to good glycemic control may confer better HRQoL on individuals with T2DM even though there is sexual dysfunction. While the presence of PAD and poor glycemic control have been shown to be independent predictors of sexual dysfunction and poor HRQoL, poor glycemic control can result in macrovascular complications like PAD and sexual dysfunction which can subsequently impact HRQoL [9, 22, 46, 47]. These results reinforce the need for a strategy to formulate effective management among individuals with T2DM who are experiencing sexual dysfunction for optimal glycemic control to delay PAD and in effect mitigate the negative outcome of sexual dysfunction on their HRQoL. Another observation from the present study is that the total and direct effects of mediators on the relationship between sexual functioning and HRQoL are stronger among women. This may suggest that optimal glycemic control in the absence of PAD may improve sexual function and confer better HRQoL among women.

To our knowledge, this study seems to be the first to assess the mediating effect of FBG and PAD on the relationship between sexual functioning and HRQoL among Nigerians with T2DM. This study has suggested that these modifiable factors (FBG and PAD) can mediate the influence of sexual dysfunction on HRQoL. This may open a new focus of target of management among patients with diabetes who have sexual dysfunction complications. Management that delays the onset of PAD and optimum glycemic may confer better HRQoL in the presence of sexual dysfunction. However, the results of the present study must be interpreted with caution as some limitation exists. The study was conducted in a single center which may limit the generalizability of the results. The cross-sectional nature of the study limited causal relationship. Despite these limitations, the results may serve as preliminary and point the attention of health professionals involved in the management of diabetes to the possible risk factors that can be mitigated to improve HRQoL and optimum care outcomes.

In conclusion, good glycemic control and absence of PAD mediates the relationship between sexual functioning and quality of life of Nigerians with T2DM. In effect, good glycemic control and delayed onset of PAD may confer better quality of life even in presence of sexual dysfunction.

Abbreviations

HRQoL	Health-Related Quality of Life
FBG	Fasting Blood Glucose
PAD	Peripheral arterial disease
SF-12	Short Form 12
SeF	Sexual Functioning
T2DM	Type 2 diabetes mellitus
ABI	Ankle-brachial index
CSFQ-14	Changes in Sexual Functioning Questionnaire
HbA1c	Glycated hemoglobin

Supplementary Information

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Supplementary Material 1

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Author contributions
Olufemi Oyewole, Ayotunde Ale, and Olatunde Odusan contributed to the concept of this study. Olufemi Oyewole, Ayotunde Ale, Olatunde Odusan, Ayanbola Adepoju and Grace Emmanuel made substantial contributions to the design and acquisition of data. Olufemi Oyewole performed the statistical analysis and drafted the article. Olufemi Oyewole, Ayotunde Ale, Olatunde Odusan, Ayanbola Adepoju, Olufunmilayo Oyewole, Michael Ogunlana and Grace Emmanuel contributed to its critical revision. All authors approved the final manuscript for publication.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Informed consent was obtained from all the participants prior to recruitment and those who consented gave written informed consent. Olabisi Onabanjo University Teaching Hospital Health Research Ethics Committee approved the study (Approval no: OOUTH/HREC/472/2021AP). The study was conducted in adherence to the ethical principles of the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Physiotherapy, Olabisi Onabanjo University Teaching Hospital, PMB 2001, Sagamu, Nigeria
[2]College of Health Sciences, University of KwaZulu-Natal, Private Bag X54001, Durban, South Africa
[3]Department of Medicine, Olabisi Onabanjo University, Sagamu Campus, Sagamu, Nigeria
[4]Department of Medicine, Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria
[5]Physiotherapy Department, Federal Medical Centre, Abeokuta, Nigeria
[6]Nursing Department, Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria

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