ARTICLE

Red cell distribution width as a cardiovascular risk predictor in adults with hypertension in sub-Saharan Africa

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Red cell distribution width (RDW) quantifies the degree of variation in erythrocyte size, is identified as a potential marker of adverse cardiovascular events, and may be a surrogate marker for assessing cardiovascular disease (CVD) risk in low-resource settings. We evaluated RDW as a predictor of CVD risk compared to the World Health Organization (WHO) CVD risk score among adults with hypertension attending primary healthcare centers (PHCs) in Ghana and Nigeria. Adults with hypertension attending selected PHCs in Ghana and Nigeria participated in a cross-sectional study. Each participant underwent blood pressure (BP) measurement and laboratory evaluation (RDW, total cholesterol, and fasting blood sugar) following standard methods. We recruited 319 adults aged 40–74 years from the study sites. The mean (standard deviation) RDW was 13.96 (1.1%). The median CVD risk score was 8.11% [interquartile range (IQR) 4.00 to 11.00]. For participants with hemoglobin (Hb) levels ≥ 12 g/dL, RDW showed positive correlations with age ($r = 0.136$; $p = 0.042$); systolic BP ($r = 0.183$; $p = 0.006$), diastolic BP ($r = 0.206$, $p = 0.002$) and WHO CVD risk scores ($r = 0.166$, $p = 0.013$). Multiple linear regression showed an independent association between RDW and WHO CVD risk scores with an upward gradient, and was most significant at 3rd quartiles. Using receiver operating characteristic curve, the C-statistic was 0.673 (95% confidence interval: 0.618 to 0.724), $p = 0.031$. With a cut-off of >14, the RDW demonstrated a sensitivity of 81.82% and specificity of 55.84%. This study shows that at Hb levels ≥ 12 g/dL, RDW modestly predicted CVD risk in adults with hypertension in sub-Saharan Africa.

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INTRODUCTION

Cardiovascular disease (CVD) continues to be the primary cause of death worldwide, resulting in approximately 17.9 million deaths in 2019 [1]. In 2019, CVDs caused over one million deaths in sub-Saharan Africa, representing approximately 5.4% of all globally CVD-related deaths and 13% of all deaths in Africa [2]. A main risk factor for CVD-related deaths is hypertension, with African countries having the highest-burden globally and the highest percentage rise over the past three decades [3, 4].

Current cardiovascular disease prevention guidelines emphasize the need to manage based on an individual's risk assessment which allows for identification of patients with high-risk CVD for more focused treatment and improved outcomes [5, 6]. Many risk assessment and prediction models have been developed over time, but only the World Health Organization (WHO) CVD risk predictor has been validated in the African sub-region [7]. The WHO CVD risk prediction charts are available in both laboratory- and non-laboratory-based charts. Despite its applicability in low-resource settings, the non-laboratory chart significantly underestimates the risk of CVD by up to 35% in men and 65% in women, particularly in patients with moderate to high CVD risk [7]. In addition, other limiting factors for laboratory-based assessment of CVD risk, included the cost of laboratory tests, lack of trained personnel, and equipment to routinely carry out some of these tests (lipid profiles) at primary and some secondary health facilities in low- and middle-income countries (LMICs) [6, 8]. Therefore, there is a need to develop an alternative approach that is easily applicable to our environment, and red cell distribution withdth (RDW) may be found to be such a biomarker.

The RDW is a biomarker that is reported as part of routine full blood counts (FBC) and has been found to independently predict adverse CVD events [9]. It is inexpensive and remains the most common test requested by clinicians in both clinical and community settings [10]. RDW is a simple assessment of red blood cell (RBC) size variability (anisocytosis) and is involved in the pathogenesis of cardiovascular disorders [11–13]. Researchers have evaluated RDW as a promising biomarker in predicting CVD such as arteriosclerosis, stroke, myocardial infarction, and heart

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failure [11, 14–16]. In low-resource settings, the role of RDW in predicting CVD risk in hypertensive adults remains unknown and may be a plausible surrogate marker for assessing CVD risk in the sub-population [9]. Therefore, we hypothesized that RDW would independently predict CVD risk among patients with hypertension attending primary healthcare centers (PHCs) in sub-Saharan Africa (Ghana and Nigeria) when compared with the WHO CVD risk score. Thus, we sought to evaluate RDW as a predictor of CVD risk compared to the WHO CVD risk score among adults with hypertension attending PHC centers.

MATERIALS AND METHODS

Study design

This study was cross-sectional and involved hypertensive participants attending primary healthcare facilities in Ghana and Nigeria.

Study site

The study was conducted at the Okelele PHC, Ilorin, North-Central Nigeria, and St. Anthony Ann Hospital, Donyina, Ashanti region, both being primary healthcare facilities in Nigeria and Ghana, respectively. The Okelele PHC has an average clinic attendance of 250 patients with hypertension monthly, whereas St. Anthony Ann Hospital has an average of 172 patients attending the hypertension clinic monthly.

Study participants

The study participants were patients with hypertension attending the general outpatient departments of selected PHCs in Nigeria and Ghana.

We included patients aged 40–74 years with hypertension who consented to participate in the study. Hypertension was defined as those already on treatment (controlled or uncontrolled), treatment-naïve with a blood pressure ≥ 140/90 mmHg, and newly diagnosed with three resting blood pressure measurements (BP ≥ 140/90 mmHg).

We excluded patients with evidence of CVDs (stroke, heart failure, peripheral artery disease and ischemic heart disease), pregnant women, hematological disorders (e.g., leukemia, sickle cell disease), clinical paleness, history of renal failure and liver disease, and those taking vitamin supplements 24 h before the study.

Sample size estimation

Using Andrew Fischer's formula, we estimated a minimum sample size of 316 from a 71% prevalence of elevated RDW among hypertensive adults in a previous study [17] at a 5% level of precision and 95% confidence interval.

Sampling, recruitment procedure and data collection

We consecutively recruited participants who met the study inclusion criteria between July and December 2023. A total of 160 participants (160) were recruited from Nigeria and 159 were recruited from Ghana. We used a pretested questionnaire to gather relevant sociodemographic and cardiovascular risk factors from participants. Each participant underwent physical measurements, and blood sampling for biochemical and hematological measurements was performed among the study participants. We employed a modified version of the WHO's STEP-wise non-communicable disease risk factor surveillance tool to gather pertinent CVD history from the study participants.

Physical measurements

Anthropometric measurements were carried out according to the WHO guidelines. The weight was measured using an Omron HN286 electronic human weighing scale with an accuracy of 0.1 kg. Each participant's height was measured with a "Seca 213" mobile stadiometer with accuracy of 0.1 cm. Body mass index (BMI) was calculated using the following formula: BMI (kg/m2) = weight (kg)/height (m^2).

'Omron M7 Intelli IT,' a validated upper-arm blood pressure (BP) monitor was used to measure participants BP. In brief, each participant sat quietly with their feet on the floor and their clothes loosened around the arm for at least five minutes before the BP readings were taken. We placed a correct-sized cuff (bladder width 80% of the arm circumference) on the exposed arm, approximately 2 cm above the elbow, and positioned the tube in front and at the center of the arm. The BP reading was recorded some minutes after pressing the start button, and the reading was displaced and documented. We took three serial BP measurements, three minutes apart, and used the average of the last two readings for data analysis.

Blood sample collection

Each participant also had blood samples taken for analysis (biochemical and hematologic analyses). Blood samples were analyzed using the EasyRa Chemistry Analyzer and a fully automated assay hematology analyzer to determine the serum cholesterol and full blood count (FBC), respectively. The system automatically determined the RDW from the FBC results.

Cardiovascular disease risk score assessment

We calculated the cardiovascular disease risk scores of participants using the WHO cardiovascular risk (laboratory-based) prediction charts (2019 revised edition) [7]. Each participant 's WHO CVD risk score was calculated based on age, gender, smoking status, presence or absence of diabetes, systolic BP, and total cholesterol.

Outcomes

The level of prediction of cardiovascular risk using RDW in adults with hypertension attending PHC centers in Ghana and Nigeria.

Data analysis

We analyzed the data from the study proforma using IBM SPSS version 29. Descriptive statistics were used to summarize the participants' sociodemographic variables and were compared across the RDW quartiles. The WHO CVD risk scores did not follow a normal distribution, and as such, were log-transformed before analysis, and the RDW (%) was stratified into four quartiles. Pearson and Spearman's rank correlation coefficients, and multiple linear regression were used to evaluate the relationship between the RDW and CVD risk score. To determine the cut-off RDW that predicted a high CVD risk (WHO CVD risk score > 20%) C-statistics was used. The *p*-value for the level of statistical significance was set at $p < 0.05$.

Ethical approval

Ghana Health Service Ethics Review Committee (Ghana) and Kwara State Ethical Review Committee (Nigeria) approved this study. We also sought permission from the appropriate authorities at both primary healthcare facilities. A detailed explanation of what the study entails in information sheets, including study procedures, was made available to all the participants in the language they best understood, and written informed consent was obtained. The data collected were coded to ensure the anonymity of the study participants and were stored in a password-encrypted computer.

RESULTS

General characteristics

This study included 319 adults aged 40 to 74 years from study sites in Ghana (159) and Nigeria (160). The mean (standard deviation) age of participants was 59.10 (10.2) years. Based on the age group, the highest category was those aged 70–74 (66;20.7%), followed by 60–64 (55;17.2%), 65–69 (48;15.0%); 55–59 (45;14.1%), 50–54 (43;13.5%), 45–49 (29;9.1%) and 40–44 (33;10.3%). There were more females (259;81.2%) (Table 1).

Based on the RDW quartile stratification, the variables that were significantly different across the subgroups included educational level ($p < 0.001$), diabetes mellitus ($p = 0.011$), systolic BP ($p = 0.017$), hemoglobin ($p = 0.007$), MCV ($p < 0.001$), study sites ($p < 0.001$), and alcohol consumption ($p = 0.002$) (Table 1).

The mean [standard deviation (SD)] RDW was 13.96 (1.1%), with a range of 11.50% to 21.70%. The mean (SD) RDW in Ghana was 13.63 (1.3%) vs 14.28 (0.8%) in Nigeria ($p < 0.001$). The CVD risk score median (interquartile range [IQR]) was 8.11% (4.00 to 11.00] with a minimum of 1.0% and a maximum of 30.0%. The median (IQR) CVD risk scores were comparable between the two countries (Ghana 7.0% (4.0 to 11.0) vs Nigeria 7.5% (4.0 to 13.0), $p = 0.577$); Table 1.

Table 1. General characteristic of the study participants.

Variables	Total $n = 319$ (%)	Q1 11.50 to 13.19% $n = 74$	Q2 13.20 to 13.99% $n = 85$	Q3 14.00 to 14.49% $n = 67$	Q4 14.50 to 21.70% $n = 93$	*P* value
Age-Mean (SD)	59.10 (10.2)[a]	58.11 (9.4)	58.75 (10.7)	60.02 (11.3)	59.53 (9.4)	0.682
Sex						
Male	60 (18.8)	22	10	15	13	0.015
Female	259 (81.2)	52	75	52	80	
Educated	186 (63.9)	60	47	32	47	<0.001
Diabetes	23 (7.2)	10	4	3	6	0.011
Smoker	5 (1.6)	2	0	2	1	0.393
BMI	26.51 (5.6)	26.57 (4.8)	26.40 (5.8)	26.30 (5.9)	26.72 (5.6)	0.965
Systolic BP	142.80 (24.4)[a]	136.02 (21.8)	142.22 (22.0)	143.84 (24.6)	147.97 (27.2)	0.017
Diastolic BP	86.38 (13.1)[a]	84.15 (12.7)	85.2 (11.4)	86.89 (13.6)	88.84 (14.3)	0.102
Total cholesterol	5.22 (1.1)[a]	5.08 (1.1)	5.19 (1.1)	5.06 (1.1)	5.44 (1.2)	0.113
Serum Glucose	5.37 (2.2)[a]	5.90 (2.9)	5.04 (1.4)	5.10 (1.2)	5.43 (2.6)	0.069
Hemoglobin (mg/dl)	12.69 (1.3)[a]	13.07 (1.6)	12.73 (1.2)	12.66 (1.1)	12.69 (1.3)	0.007
MCV (fL)	85.25 (6.7)[a]	88.90 (5.4)	86.49 (5.1)	85.10 (6.6)	81.32 (7.1)	<0.001
Ghana	159 (49.8)	65	39	22	33	<0.001
Nigeria	160 (50.2)	9	46	45	60	
Alcohol	(19; 6.0%)	10	7	0	2	0.002
CVD risk scores[b]	7.00 (4.00 to 11.00)	6.00 (4.0 to 10.00)	7.00 (4.00 to 10.25)	9.00 (3.25 to 13.00)	7.00 (4.00 to 11.00)	0.337

SD standard deviation, *CVD* cardiovascular diseases, *BP* blood pressure, *BMI* body mass index, *MCV* mean corpuscular volume.
[a]Mean with standard deviation.
[b]Values in median with interquartile range.

Relationship between cardiovascular risk factors, WHO CVD risk scores, and RDW

Correlations of RDW with cardiovascular risk factors and WHO CVD risk scores. For all recruited participants, there was a significant positive correlation between RDW and the following variables: alcohol consumption ($r = 0.193$, $p < 0.001$), systolic BP ($r = 0.159$, $p = 0.004$), and diastolic BP ($r = 0.149$; $p = 0.013$). For Hemoglobin levels ≥ 12 g/dL, RDW was positively correlated with age ($r = 0.136$; $p = 0.042$), alcohol consumption ($r = 0.312$, $p < 0.001$), systolic BP ($r = 0.183$; $p = 0.006$), diastolic BP ($r = 0.206$, $p = 002$), and WHO CVD risk scores ($r = 0.166$, $p = 0.013$). For participants with hemoglobin levels < 12 g/dL, there was no significant correlation between RDW, cardiovascular risk factors, and WHO CVD risk scores (Table 2).

Multiple linear regression of RDW as a predictor of CVD risk. The multiple linear regression model showed an independent association between RDW and WHO CVD risk scores with an upward gradient. WHO CVD scores increased with increasing RDW quartile and most significant at 3rd quartiles (Table 3).

ROC curve of RDW as a predictor of CVD risk. The CVD risk scores were dichotomized into high-risk (20.0% or more) and those with CVD risk scores of less than 20.0% versus RDW. Using ROC analysis, the C-statistics (area under the curve) was 0.673 (95% CI 0.618–0.724), $p = 0.031$. At a cut-off of >14, the RDW had a sensitivity of 81.82%, specificity of 55.84%, and Youden index of 0.377 (Fig. 1 and Table 4).

DISCUSSION

African countries have the highest global burden of hypertension, a leading risk factor for adverse CVD outcomes. This study examines the role of RDW, an inexpensive parameter in full blood counts in assessing CVD risk among cohort of adults with hypertension in Ghana and Nigeria. This study showed that RDW correlated with systolic and diastolic BP. These finding are consistent with other studies that demonstrated a similar correlation between RDW and blood pressure (systolic and diastolic) [18–21]. However, a study in Turkey only observed a positive correlation between systolic BP and RDW [22]. The differences in our findings compared with the Turkey study may be relative higher mean age of our cohort (59 years) vs 50 years in Turkey study. Younger adults, especially those with diastolic hypertension, tend to have less inflammatory biomarkers, which may impact RDW findings [22]. The association between RDW and BP in hypertensive patients in this study provides additional evidence for the use of RDW as a biomarker for cardiovascular disorders [11]. RDW is a marker of increased inflammation and oxidative stress, which are equally implicated in the development and progression of hypertension. This inflammation leads to endothelial dysfunction, reduced compliance of arteries leading to high vascular resistance which worsens hypertension [23].

The present study showed that, for participants with Hb ≥ 12 g/dL, there was a correlation between a high RDW and a higher WHO CVD risk score. A large cohort study in Brazil also showed that RDW was positively correlated with increased CVD risk using the Framingham risk score [24]. Our study further reinforces the role of RDW in cardiovascular diseases, including hypertension. This study showed that RDW is independently associated with the WHO CVD risk score and is most significant at Q3. A large cohort study in Brazil revealed that RDW was independently associated with the CVD risk score as assessed using the Framingham risk score [24]. Whereas we observed an independent association at the 3rd RDW quartile; the study in Brazil was most significant at the four quartiles. The differences between our study and the

Table 2. Correlations of RDW with cardiovascular risk factors.

Variable	Total ($n = 319$)		Hb < 12 g/dL ($n = 94$)		Hb 12 g/dL & above ($n = 225$)	
	r	*p*	*r*	*p*	*r*	*p*
Age	0.057	0.311	−0.092	0.380	0.136	0.042
Sex	0.105	0.062	0.129	0.216	0.063	0.348
Diabetes	−0.084	0.132	−0.047	0.652	−0.120	0.073
Smoking	0.019	0.739	—	—	0.005	0.940
Alcohol	0.193	<0.001	0.171	0.100	0.312	<0.001
Body mass index	0.030	0.598	−0.073	0.485	0.035	0.599
Systolic blood pressure	0.159	0.004	0.122	0.241	0.183	0.006
Diastolic blood pressure	0.140	0.013	0.012	0.912	0.206	0.002
Total cholesterol	0.069	0.216	0.038	0.715	0.091	0.171
Glucose	−0.033	0.559	−0.024	0.818	−0.041	0.540
CVD risk Scores	0.088	0.116	−0.035	0.740	0.166	0.013

CVD cardiovascular diseases.

Table 3. Multiple regression models for the association between RDW and WHO cardiovascular risk by quartiles.

CVD risk scores[a]				
Model	**Q1 [11.50 to 13.19%. $n = 58$]**	**Q2 [13.20 to 13.99%. $n = 64$]**	**Q3 [14.00 to 14.49%. $n = 51$]**	**Q4 [14.50 to 21.70%. $n = 52$]**
	Reference			
e^{β}		0.975	1.179	1.163
95% CI		0.879, 1.099	1.006, 1.274	0.996, 1.259
P value		0.753	0.039	0.059

CI confidence interval.
[a]$n = 225$ (with hemoglobin ≥ 12 g/dL); Regression coefficients (β) were log-transformed. e^{β} exponential of Beta Coefficient.

Brazil study may be due to the CVD risk assessment used with the participants in our study having the highest median score of WHO CVD risk score (9.00 (IQR–3.25, 13.00)] at 3rd quartiles.

In our study, at an RDW > 14%, the RDW had modest C-statistics of 0.673, sensitivity of 82%, and specificity of 56% in predicting CVD adverse outcomes in the study cohort. RDW has been demonstrated to predict outcomes in various cardiovascular diseases [11]. Among the cohort of 1971 admitted with chest pain in a regional hospital in Italy, at a cut-off of 13.7%, RDW has an area under curve (AUC) of 0.61 with a sensitivity of 75% and a specificity of 52.0% [25]. In China, RDW at a cut-off of 14.1% predicted a 90-day cardiovascular event (cardiac death or readmission for heart failure) for patients with acute heart failure and has a sensitivity of 87%, specificity of 54.9%, and area under the curve of 0.728 [26]. Although with a modest level of specificity (56%), the RDW has a high sensitivity (82%) in our study, suggesting it may be a good screening tool to identify adults with hypertension in the sub-Saharan population at high risk of adverse CVD outcomes, especially when there is limited access to advance laboratory and diagnostic investigations.

This study also shows that at hemoglobin less than 12 g/dL, the RDW was not associated with demographics, BMI, blood pressure, or CVD risk scores. The inability to find a significant association at this low hemoglobin in this study may be due to the exclusion of patients who were clinically pale from our study and those on multivitamins and iron supplements. The clinical conditions associated with iron deficiency, folic acid deficiency, and vitamin B12 deficiency are usually associated with high anisoscytosis and subsequent high RDW [11]. This observation in our study further supports the need to cautiously interpret RDW in patients who are anemic from various causes in our clinical settings

Study limitations

This study's strengths include being multi-country and comparing RDW with the WHO CVD risk score, which has been validated for the assessment of CVD risk in the sub-Saharan African population. However, this study has some limitations, as it was a cross-sectional study, which means that a cause-effect relationship could not be established. In addition, we did not test for other inflammatory markers, such as c-reactive protein and erthrocytes sedimentation rate to reduce cofounders in our analysis, and participants were not followed up to see how many will later develop adverse cardiovascular outcomes.

CONCLUSIONS

In a cross-sectional multi-center study among adults with hypertension in sub-Saharan Africa, RDW correlated significantly with the WHO CVD risk score for adults with Hb ≥12 g/dL or more with a modest predictive ability for CVD risk. For patients with Hb ≥ 12 g/dl or more, RDW, a cheap and readily available biomarker, maybe a good screening tool for low-resource settings to identify patients with hypertension who may be at high risk of adverse CVD outcomes. We recommend further evaluation of the strength of the association in a larger population.

SUMMARY TABLE

What is known

- Researchers have evaluated RDW as a promising biomarker of CVD risk in conditions such as arteriosclerosis, heart failure, and ischemic stroke; however, its role in predicting CVD risk in hypertensive adults in low-resource settings remains unknown

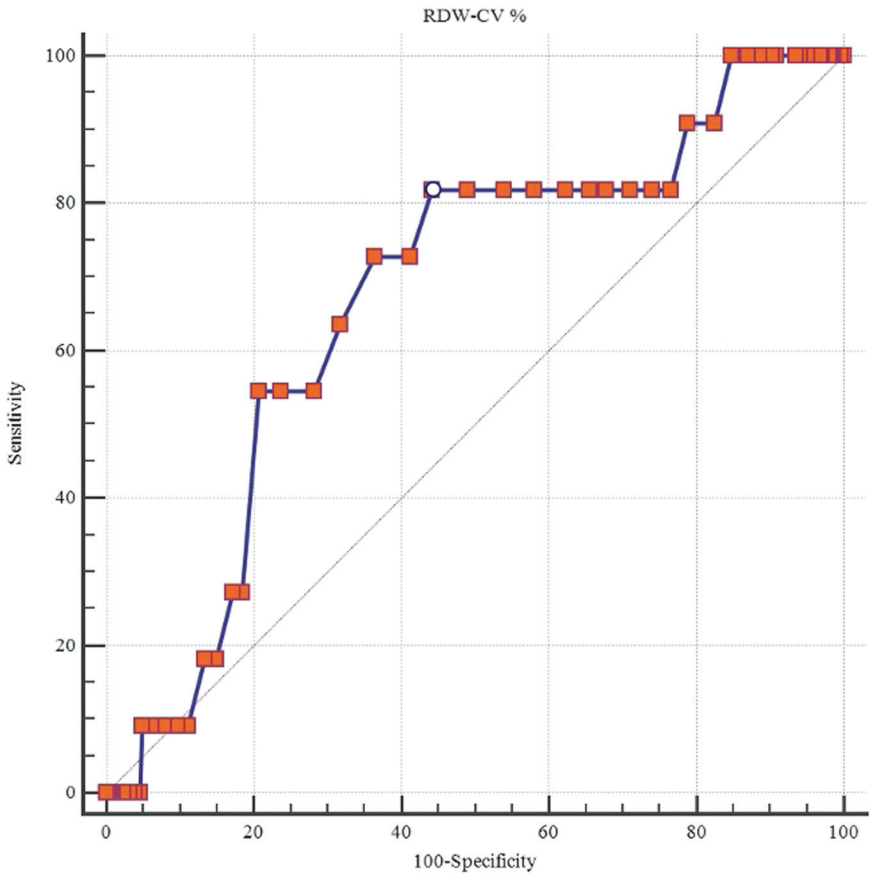

Fig. 1 ROC for red cell distribution width [RDW] as a predictor of CVD risk. RDW-CV red cell distribution width coefficient of variation.

Table 4. Summary of the ROC curve of RDW to predict a high risk for CVD based on WHO risk scores.

Characteristics	Values
Sample size	$n = 319$
Area under the ROC curve	0.673
95% CI for area under the ROC curve	0.618 to 0.724
P value for Area = 0.5	0.0310
Youden index J	0.377
Associated criterion	>14
Sensitivity	81.82
Specificity	55.54

ROC receiver operating characteristic curve, *CI* confidence interval.

What the study adds

- In sub-Saharan Africa, this study shows that RDW plays a role in predicting CVD risk among hypertensive patients in our sub-region and may be incorporated as part of routine tests for adults with hypertension in our environment, improving CVD risk stratification and subsequent management in LMICs.

DATA AVAILABILITY

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

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AUTHOR CONTRIBUTIONS

ORI conceptualized the work, literature review, data collection, analysis, draft and appraished the manuscript. KAH conceptualized the work, literature review, data collection, analysis, draft and appraished the manuscript. FTA conceptualized the work, literature review, data collection, analysis, draft and appraished the manuscript GBN conceptualized the work, literature review, data collection, analysis, draft and appraished the manuscript. AMN conceptualized the work, literature review, data collection, analysis, draft and appraished the manuscript. AYN was inlvolved in literature review, data collection, data visualization, draft and appraished the manuscript. AO was invloved in the conceptualization, literature review, data visualization and analysis, draft and critically appraished the manuscript. DO was invloved in the conceptualization, literature review, data visualization and analysis, draft and critically appraished the manuscript. OA was invloved in the conceptualization, literature review, data visualization and analysis, draft and critically appraished the manuscript. BSA was invloved in the conceptualization, literature review, data visualization and analysis, draft and critically appraished the manuscript. DS was invloved in the conceptualization, literature review, data visualization and analysis, draft and critically appraished the manuscript. OAM was invloved in the conceptualization, literature review, data visualization and analysis, draft and critically appraished the manuscript

COMPETING INTERESTS

The authors declare no competing interests.

ETHICS APPROVAL

Ghana Health Service Ethics Review Committee (Ghana) and Kwara State Ethical Review Committee (Nigeria) approved this study. We also sought permission from the appropriate authorities at both primary healthcare facilities. A detailed explanation of what the study entails in information sheets, including study procedures, was made available to all the participants in the language they best understood, and written informed consent was obtained. The data collected were coded to ensure the anonymity of the study participants and were stored in a password-encrypted computer.

ADDITIONAL INFORMATION

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