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Cardiovascular disease risk assessment among adults attending HIV Clinic at Korle-Bu Teaching Hospital

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Abstract

Background: The risk of developing chronic cardiovascular diseases (CVDs) is a significant public health concern for people living with HIV (PLWH). This recognition has been in place for over a decade. The lack of resources in some settings means that most older PLWH will receive limited care, requiring further research to identify CVD risk and accurate estimation methods. Such research enables the identification of optimal models of care, improving outcomes for this population.

Objective: This study aimed to perform a CVD risk assessment (using three different assessment tools) on PLWH attending the HIV clinic at the Korle-Bu Teaching Hospital (KBTH).

Methods: A hospital-based cross-sectional study involving 311 PLWH was conducted at the HIV Clinic of the KBTH using a questionnaire adopted from the WHO STEPwise approach to chronic disease risk factor surveillance. Blood pressure, anthropometric measurements and fasting blood samples were taken for metabolic/biochemical parameters. A retrospective chart review of clinical folders for HIV and ART-related data was done. To determine the level of risk for CVD, three estimation methods were used: the 10-year Framingham risk score (FRS), the 10-year WHO/International Society of Hypertension (ISH) risk prediction chart, and the 5-year Data Collection on Adverse Effects of Anti-HIV Drugs (D:A:D) cardiovascular risk score.

Results: The estimated 10-year moderate to high risk of CVD was 20.6% using the FRS, 13.2% using the WHO/ISH risk score, and 52.4% using the D:A:D score. The majority of study participants were classified as having a low risk of CVD according to the FRS and WHO/ISH scoring systems. However, the D:A:D cardiovascular scoring system identified that over 50% of the participants were at a moderate to high risk of developing CVD.

Conclusion: This study indicates that when using the D:A:D risk assessment system, over 50% of the individuals who participated were found to have moderate-to-high risks of CVD. This underscores the importance of conducting a cardiovascular risk assessment before initiation of antiretroviral therapy as well as regular assessments to promptly identify and manage these risk factors, thereby aiding in preventing the occurrence of cardiovascular events. Additionally, the findings highlight the need for CVD management to be included in the HIV clinic.

Keywords: Cardiovascular disease, Framingham risk score, WHO/International Society of Hypertension risk prediction, D:A:D risk score

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INTRODUCTION

The chronic nature of the Human Immunodeficiency Virus (HIV) infection requires lifelong antiretroviral therapy (ART) [1] to continuously suppress viral replication, thus reducing morbidity and mortality.

However, ART is restricted by treatment barriers such as complex dosing, drug-drug interactions and associated toxicities. In addition, some HIV-positive patients still require concomitant treatment with drugs for opportunistic infections and medication to treat unrelated medical conditions and/or the metabolic complications of ART [2]. The management of co-morbidities is one of the major challenges associated with the multidrug regimens used for HIV therapy. Among the many co-morbid conditions,

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cardiovascular diseases (CVDs) are of particular concern due to antiretroviral (ARV) induced metabolic changes. Cardiovascular disease is a term used commonly to refer to a group of disorders of the heart and blood vessels which include coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, deep vein thrombosis, and pulmonary embolism [3]. Cardiovascular diseases are the number one cause of death globally, with projections indicating mortality due to CVDs will reach 23.9 million by the year 2030 [4]. Cardiovascular diseases in low and middle-income countries (LMIC) are reported to represent more than 80% of the global burden of CVDs [5].

Studies from high-income countries with large sample sizes have implicated HIV and ART as likely mediators of an observed increase in the risk of CVDs in PLWH, and reports have cited CVDs as a significant cause of morbidity and mortality in people living with HIV (PLWH) [6-8]. In 2014, a multi-centred, comparative, cross-sectional survey was conducted among HIV-infected individuals in 12 countries across five continents. The findings indicated that the prevalence of self-reported CVD risk factors was 28% among PLWH globally, while the prevalence was estimated to be 12% among PLWH in sub-Saharan Africa (SSA) [9]. The risk of developing chronic cardiovascular and pulmonary diseases is recognised as a major public health problem in PLWH [7,10,11]. Consequently, medical care for this population is focusing more intently on the control and prevention of age- and metabolic-related comorbidities [12-15]. While the risk of CVD generally tends to increase with advancing age, predicting an individual's CVD risk can allow for timely interventions aimed at reducing the likelihood of future CVD events.

Cardiovascular risk scoring systems give an estimate of the probability that an individual will develop CVD within a specified length of time. Cardiovascular risk scoring systems are useful tools both to individual patients and to attending clinicians in helping decide on when to initiate appropriate lifestyle modifications and preventive medical treatment. Several cardiovascular risk-scoring systems on individuals have been developed in different study populations targeted at different ethnic groups. The most popular and widely used of these cardiovascular risk assessment scores is the Framingham risk score (FRS), which was modelled from the Framingham Heart Study [16]. Another commonly used cardiovascular risk assessment tool is The World Health Organisation/International Society of Hypertension (WHO/ISH) risk prediction chart developed for the assessment and prediction of cardiovascular risk in different populations [17], which is regionally based and thus can be used for LMIC. Except for the Data Collection on Adverse Events of anti-HIV Drugs (D:A:D) 5-year cardiovascular risk scoring system meant for the HIV-positive population, the rest of the cardiovascular scoring systems are designed for the general population. However, with the HIV-positive subpopulation, issues on the effect of

HIV itself and the administration of ART on the risk of CVD have raised the appropriateness of the use of general cardiovascular risk scores in PLWH. A commentary by D'Agostino [18] reviewed the use of FRS and D:A:D cardiovascular risk equation in HIV-positive population and suggested that whilst FRS can be used for general CVD risk assessment in PLWH, more specific assessment tools like the D:A:D must be developed for the HIV-positive population.

Although there are increasing worldwide concerns of comorbidity in PLWH, and there is considerable research into the commonly occurring non-communicable diseases and CVDs among PLWH in resource-rich settings, less is known about the burden in resource-limited settings. Available data suggests that in SSA, chronic cardiovascular and pulmonary diseases are increasing in HIV-positive patients [19,20]. As the dual burden of HIV and CVDs continues to rise in Sub-Saharan Africa (SSA), the relationships between these conditions and our understanding of them will gain heightened public health significance. In resource-limited settings, additional research is needed to better understand the risk and impact of CVD and identify optimal models of care to address this challenge in the areas where the majority of older PLWHs will be receiving care. This study aimed to perform a CVD risk assessment (using FRS, WHO/ISH and D:A:D) on adults attending the HIV clinic at the Korle-Bu Teaching Hospital (KBTH), Accra, Ghana.

MATERIALS AND METHODS

Study design and sites

A hospital-based cross-sectional study was conducted at the HIV clinic of KBTH from February 2016 to May 2016. The HIV clinic is located in the Fever Unit under the Department of Medicine. The KBTH is a 2,000-bed-capacity hospital, and it is currently the third-largest hospital in Africa and the leading national referral centre in Ghana. Currently, the KBTH HIV Clinic has a 24-bed capacity and runs the largest cohort of HIV patients in Ghana. The study population was made up of about 20,000 HIV-positive patients who attend the HIV clinic, and the sampling frame was the electronic register of patients. Each patient was scheduled to attend the clinic at least once every three months for both clinical assessment and dispensing of medication for patients on ARV. The study included individuals aged ≥ 18 years who have been attending the HIV clinic for at least six months and are not pregnant (females). The study excluded patients who had less than 95% adherence to HIV clinic follow-up visits or ART medication, as measured using the Proportion of Days Covered method described by Ankrah et al. [21]. Additionally, patients who were hospitalized or diagnosed with AIDS were also excluded from the study.

Sample size and sampling technique

The minimum sample size was calculated by estimating a population parameter for cross-sectional studies [22], using

a prevalence of 31.1% for CVD PLWH from a prior study [23]. Including a 14% attrition rate, the calculated minimum sample size was 311. A total of 311 adult patients attending the HIV clinic at KBTH were recruited as study participants for this study. A simple random sampling technique was used to recruit potential study participants based on routine HIV clinic attendance. Trained research assistants (who were clinical staff from the HIV Clinic) administered an interviewer-administered questionnaire to study participants in their preferred language. The questionnaire aimed to collect data on socio-demographic characteristics, lifestyle characteristics, and family history of CVD. Additionally, blood pressure and anthropometric measurements were taken, and fasting blood samples were collected for metabolic/biochemical parameters. The baseline variables of each study participant were obtained through a retrospective chart review of their clinical folders. HIV and ART-related data, including baseline CD4+ T-cell count, Nadir CD4+ T-cell count, and cumulative exposure to ART, were extracted from the clinical folders of the study participants. The study estimated the risk level of CVD

using the following cardiovascular risk score assessment tools: the 10-year FRS, the 10-year WHO/ISH risk prediction chart for fatal or non-fatal cardiovascular events, and the 5-year D:A:D cardiovascular risk score. A questionnaire adapted from the WHO STEPwise approach to chronic disease risk-factor surveillance [24] was used for the collection of study participants' data. In addition, other relevant clinical characteristics, including the presence of co-morbidities, were obtained from the medical history record of the study participants.

Data management and statistical analysis

All analyses were performed using STATA Statistical Software (Version 16, StataCorp LLC, College Station, Texas, USA) and $p < 0.05$ was deemed significant. Continuous variables were reported as mean \pm standard deviation or median with interquartile range if not normally distributed. Continuous variables were modelled in class or after log transformation. Data were analysed to estimate the 10-year general FRS, the 5-year D:A:D cardiovascular risk score, and the 10-year WHO/ISH cardiovascular risk prediction score of study participants. The FRSs were classified as low risk ($< 10\%$), moderate risk (10% to $< 20\%$) and high risk ($\geq 20\%$) [25]. The D:A:D CVD risk scores were classified as low risk ($< 1\%$), moderate risk (1% to $< 5\%$) and high/very high risk ($\geq 5\%$) [26]. The WHO/ISH cardiovascular risk prediction scores were classified as low risk ($< 10\%$), moderate risk (10% to $< 20\%$) and high risk ($\geq 20\%$) [27]. Comparisons of the cardiovascular risk scoring systems were determined using Cohen's Kappa coefficient (K) with a 95% confidence interval. Kappa was interpreted as perfect agreement (> 0.80), substantial agreement (0.6 - 0.8), moderate agreement (0.4 - 0.6), fair agreement (0.2 - 0.4) and poor agreement (≤ 0.2) [23,28]. For the comparison of the D:A:D 5-year score with the FRS and the WHO/ISH scores, it was assumed that the 5-year D:A:D prediction was constant over 10 years.

RESULTS

Table 1 shows the socio-demographic and lifestyle characteristics of study participants. A total of 311 PLWH were recruited as study participants. This was made up of 76.2% females, and most (73.0%, $n = 227$) of the study participants were aged > 40 years (Table 1). The majority of study participants did not smoke tobacco (95.8%, $n = 298$) or drink alcohol (68.5%, $n = 213$) (Table 1). A total of 114 (36.7%) study participants were hypertensive. The blood pressure levels, as well as the anthropometric and biochemical indices of the study participants, are displayed in Table 2. A total of 10% of the study participants had elevated fasting plasma glucose of ≥ 7.0 mmol/L, whilst 15.4% had a reduced estimated glomerular filtration rate of < 60 min/mL/1.73 m² (Table 2). Table 3 shows the HIV/ART-related characteristics of study participants. Most of the study participants (73.6%) had a current CD4+ T-cell count of > 350 cells/ μ L (Table 3). The median duration of HIV infection for the study participants was 7.9

Table 1: Socio-demographic and life-style characteristics of study participants

Characteristics	Freq (%) n =311
Age, median (Interquartile range) (years)	44.0 (39.0-51.0)
Age group	
< 40 years	84 (27.0)
≥ 40 years	227 (73.0)
Sex	
Female	237 (76.2)
Male	74 (23.8)
Highest educational level attained	
None	44 (14.2)
Basic	163 (52.4)
Secondary	95 (30.5)
Tertiary/Professional	9 (2.9)
Marital status	
Single	57 (18.3)
Married/Co-habiting	134 (43.1)
Widowed/Divorced/Separated	120 (38.6)
Employment status	
Unemployed	38 (12.2)
Employed	273 (87.8)
Present	39 (12.5)
Absent	272 (87.5)
Tobacco smoking status	
Ever smoker	13 (4.2)
Never smoker	298 (95.8)
Alcohol drinking status	
Ever drinker	98 (31.5)
Abstainer	213 (68.5)
Fruit intake	
Rare/Never	99 (31.8)
Most at times	212 (68.2)
Engagement in physical activity/exercising	
Rare/Never	216 (69.5)
Most at times	95 (30.5)

n, number of respondents per characteristic; Freq, frequency; %, percentage.

years, and the median duration of ART administration for the ART-exposed group was 6.8 years. Most of the study participants were on ART (81.0%) (Table 3). Table 4 shows the various cardiovascular risk score assessment classified as low, medium, or high. In the 10-year FRS, 79.4% of the study participants were classified as low risk for CVD, while in the 10-year WHO/ISH prediction chart, 86.8% were classified as low risk. The study found that a larger much larger proportion (52.4%) of participants had moderate to high risk of CVD according to the 5-year D:A:D cardiovascular risk score. In contrast, the 10-year general FRS and 10-year WHO/ISH risk prediction charts showed 20.6% and 13.2% of participants having moderate to high risk, respectively.

Table 2. Blood pressure levels, anthropometric and biochemical indices of study participants

Characteristics	Freq (%) n = 311
Current systolic blood pressure (median IQR in mmHg)	130 (113-144)
Current diastolic blood pressure (median IQR in mmHg)	80 (70-91)
Current blood pressure category	
Non-hypertensive	197 (63.3)
Hypertensive	114 (36.7)
Current body mass index	
< 25.0 (kg/m ²)	189 (60.8)
≥ 25.0 (kg/m ²)	122 (39.2)
Abdominal obesity (WHR)	
Absent (WHR < 0.85 for women; WHR < 0.90 for men)	196 (63.0)
Present (WHR ≥ 0.85 for women; WHR ≥ 0.90 for men)	115 (37.0)
Abdominal obesity (WC)	
Absent (WC ≤ 88 for women; WC ≤ 102 for men)	254 (81.7)
Present (WC > 88 for women; WC > 102 for men)	57 (18.3)
Fasting plasma glucose	
Normal FPG (FPG < 7.0 mmol/L)	280 (90.0)
Elevated FPG (FPG ≥ 7.0 mmol/L)	31 (10.0)
Total cholesterol	
Normal total cholesterol (TC < 5.17 mmol/L)	148 (47.6)
Hypercholesterolemia (TC ≥ 5.17 mmol/L)	163 (52.4)
High-density lipoprotein cholesterol	
Normal (HDL-C ≥ 1.03 mmol/L)	280 (90.0)
Abnormal (HDL-C < 1.03 mmol/L)	31 (10.0)
Low-density lipoprotein cholesterol	
Normal (LDL-C < 3.36 mmol/L)	195 (62.7)
Elevated (LDL-C ≥ 3.36 mmol/L)	116 (37.3)
Triglycerides	
Normal (TG < 2.26 mmol/L)	300 (96.5)
Elevated (TG ≥ 2.26 mmol/L)	11 (3.5)
Estimated glomerular filtration rate	
Normal eGFR (eGFR ≥ 60 min/mL/1.73 m ²)	263 (84.6)
Reduced eGFR (eGFR < 60 min/mL/1.73 m ²)	48 (15.4)

Freq, frequency of respondents per characteristic; n, total number of study participants; IQR, interquartile range; WHR, waist-to-hip ratio; WC, waist circumference; FPG, fasting plasma glucose; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; eGFR, estimated glomerular filtration rate.

DISCUSSION

In this study, 311 HIV-positive patients with no previous history of CVD and attending the HIV Clinic in KBTH were assessed for their 10-year FRS, 5-year D:A:D risk score, and 10-year WHO/ISH risk score. The FRS and the WHO/ISH risk score showed estimated 10-year moderate to high risks of CVD at 20.6% and 13.2%, respectively. However, the D:A:D score indicated a risk of 52.4%. Cardiovascular disease is a leading cause of death in most populations and has been recognized as an important cause of morbidity and mortality among PLWH [29]. In North America and Europe, CVD ranks as the second most prevalent cause of death among HIV-infected individuals, following AIDS-related mortality. As a result, there is a need to shift the long-term care approach for PLWH to incorporate a greater emphasis on cardiovascular risk assessment, prevention, and suitable management [30,31]. Using the FRS and WHO/ISH cardiovascular scoring systems, most study participants in this study were classified as having a low risk of CVD. Nevertheless, the D:A:D cardiovascular scoring system identified over 50% of the participants in the study as being at a moderate to high risk of developing CVD. Despite the comparable results of low CVD risk obtained from the FRS and WHO/ISH scoring systems, which align with previous studies reporting rates of 72.3% in Slovenians [32], 60.3% in Germans [29], 93.3% in South Africans [23], and 88.3% in Nigerians [28], there are debates regarding the suitability

Table 3: HIV/ART-related characteristics of study participants.

Characteristics	Freq (%) n = 311
Baseline CD4+ T-cell count	
≤ 350 cells/μL	176 (56.6)
> 350 cells/μL	135 (43.4)
Current CD4+ T-cell count	
≤ 350 cells/μL	82 (26.4)
> 350 cells/μL	229 (73.6)
Nadir CD4+ T-cell count	
≤ 350 cells/μL	220 (70.7)
> 350 cells/μL	91 (29.3)
Duration since HIV-positive diagnosis (median IQR in years)	7.9 (4.5-10.6)
HIV-type	
Type I only	228 (73.3)
Type II only	7 (2.3)
Mixed (Type I and II)	76 (24.4)
Presence of co-morbidities (excluding hypertension)	
Absent	243 (78.1)
Present	68 (21.9)
ART exposure status	
ART-naive	59 (19.0)
ART-exposed	252 (81.0)
Cumulative exposure to ART (median IQR in years, n = 252)	6.8 (5.9-7.5)

ART, antiretroviral therapy; IQR, interquartile range; n, total number of study participants; n, number of respondents per characteristic

Table 4. Cardiovascular disease risk assessment score

Cardiovascular risk scoring system	Freq (%) n = 311	Comparison with D: A: D score		
		Kappa	p-value	Agreement
Modified FRS				
Low	247 (79.4)	0.34	<0.001	64.0%
Moderate	47 (15.1)			
High	17 (5.5)			
WHO/ISH risk prediction score				
Low	270 (86.8)	0.10	<0.001	50.2%
Moderate	19 (6.1)			
High	22 (7.1)			
D:A:D risk score				
Low	148 (47.6)	-	-	-
Moderate	148 (47.6)			
High	15 (4.8)			

D: A: D, Data Collection on Adverse events of anti-HIV Drugs; FRS, framingham risk score; ISH, International Society for Hypertension; WHO, World Health Organization; %, percentage; n, number.

of utilizing the FRS to assess the cardiovascular risk in HIV-positive individuals. In general, there have been suggestions that the FRS tends to overestimate the risk of CVD in Europeans who are not infected with HIV [18,33]. This overestimation of the FRS has also been observed in HIV-infected Thais [34], Brazilians [35] and Europeans [36]. This has raised the issue of the appropriateness of the use of the FRS in HIV-infected populations. However, the present study points to an underestimation of the risk of CVD using the FRS compared with the D:A:D score in this group of HIV-infected Ghanaian population. The current study's estimation of a 20.6% moderate to high risk of CVD using the FRS is consistent with findings published by Mashinya et al., in 2015 [23], who observed that despite the level of agreement between the FRS and the D:A:D score in HIV-infected South Africans, the FRS still underestimates the risk of CVD among PLWH. This current study highlights the importance of addressing the underestimation of CVD risk to avoid excluding individuals who could benefit from aggressive prevention or management of their condition. It has also been observed that the FRS underestimates the risk of CVD in the general population of South Africans who are not infected with HIV [37]. These observations clearly show the inappropriateness of using the FRS in SSA populations, particularly HIV-infected individuals in this sub-region.

The WHO/ISH prediction chart score is an alternative risk score developed by the WHO for epidemiological sub-regions but has seldom been used in general and in HIV-infected populations. The current study's report of 86.7% of study participants with a low risk of CVD, as determined by the WHO/ISH prediction chart, is similar to a study conducted in Nigeria, which reported a rate of 87.2% [28]. Nevertheless, the level of agreement between the FRS and the WHO/ISH score, which exceeds 75.0% (data not shown), suggests that there is a high likelihood that the WHO/ISH score may also underestimate the risk of CVD among PLWH in sub-Saharan Africa (SSA). However, due

to the limited amount of literature in this specific area, this argument remains open to debate. In the current study, although all three cardiovascular scoring systems displayed relatively similar scores for individuals with a high risk of CVD, the most notable disparity among the systems lies in scoring individuals with low or moderate risk of CVD. The D:A:D scoring system tends to assign more individuals to the moderate risk category compared to the FRS and the WHO/ISH risk prediction chart, which aligns with findings from other studies [35]. An important aspect of this group of patients in the moderate risk category is their relatively shorter time to progress to the high-risk group if not appropriately managed, due to factors such as HIV infection and ART. This makes the D:A:D risk scoring system more appropriate to be used in HIV-infected individuals and especially in patients on ART. Indeed, the D:A:D score revealed that 93.3% and 87.8% of individuals classified as high risk or moderate risk of CVD, respectively, were receiving ART (data not shown).

Several studies have also highlighted the efficacy of utilizing the D:A:D risk score to identify HIV-positive individuals with a high risk of CVD. However, for a comprehensive review of this literature, refer to the discussion by D'Agostino et al. [38]. The prevalence of hypertension and other cardiovascular risk factors is likely to increase among PLWH in Ghana, particularly in those receiving antiretroviral therapy, as the population ages. While the currently estimated risk score for cardiovascular events in this study was low to moderate in most patients, the increasing CD4+ T cell count threshold for initiating antiretroviral therapy, combined with the ageing of the population of PLWH, suggests that most patients will eventually fall into the high-risk group for these events and will require management. Overall, HIV care provides a good opportunity for the management of hypertension and other chronic cardiovascular events with regular assessment. Regular blood pressure measurement, which is currently routine in the HIV clinic, should be considered an

essential element of HIV care. Furthermore, studies conducted in South Africa have demonstrated that integrating non-communicable disease care into HIV care leads to improved functional ability and health status among patients receiving ART [39,40]. The increasing prevalence of comorbidities, specifically CVDs among PLWH, necessitates health policies and interventions that integrate chronic disease management into HIV care [19,41]. While data on the cost-benefit analysis of this approach is limited, integrating chronic disease management into existing HIV care has been suggested to potentially be more cost-effective in the long run compared to the traditional vertical approach and single disease management [20]. This standpoint is supported by findings from a pilot study conducted at a secondary health facility in Nigeria. The study concluded that integrating cardiovascular screening and management into HIV care is both feasible and necessary to enhance life expectancy and maintain the progress achieved in HIV care during the era of ART [42].

Conclusion

The results of this study indicate that over 50% of study participants had a moderate to high risk of CVD when using the D:A:D risk assessment system. This emphasizes the importance of performing cardiovascular risk assessments before initiating antiretroviral therapy and regularly afterwards to detect and manage risk factors promptly, thereby preventing cardiovascular events. While the existing guidelines of the National AIDS Control Programme recognize the possibility of drug-drug interactions between administered antiretroviral therapy and certain antihypertensive drugs, as well as the need to monitor for metabolic abnormalities, there is a lack of guidance on systematically screening, preventing and managing CVDs among PLWH. As PLWH grow older, the occurrence of cardiovascular events has not yet become a major concern. This provides a valuable chance to control the risk of cardiovascular problems among individuals with HIV before the situation worsens.

DECLARATIONS

Ethical considerations

The study was given ethical clearance [Protocol Identification Number: MS-Et/M.3-P 4.4/2015-2016] by the Ethical and Protocol Review Committee of the College of Health Sciences, University of Ghana. Permission was obtained from the clinician-in-charge of the Fevers Unit at the KBTH, and informed consent was sought and obtained from each study participant.

Consent to publish

All authors agreed on the content of the final paper.

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Competing Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Author contributions

ETN and RAT conceived and designed the study. RMA, WK, FA and BS gave conceptual advice. RMA, WK and RAT assisted in funding acquisition. ETN, WK, RAT, RMA and BS did the statistical analysis and drafted the manuscript. RMA, WK, RAT, FA and BS reviewed and edited the manuscript. All authors read and approved the final version of the manuscript.

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Availability of data

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

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