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Risk Factors of Cardiovascular Disease as Predictors of Cardiomotor Profiles in Hispanic-Latinos Living with HIV

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Abstract: Background: People living with HIV are at increased risk of developing cardiovascular disease. Risk factors associated with cardiovascular disease negatively impact cardiovascular and muscular function. Therefore, this study aims to determine if cardiovascular disease risk factors are predictors of cardiomotor profiles in Hispanic-Latinos living with HIV. **Subjects:** A total of 176 participants were enrolled in this study. There were 134 males and 42 females with a mean age of 53.34 +/- 10.31 years old. **Methods:** Data was collected retrospectively from people living with HIV in San Juan, Puerto Rico from 2000-2020. Cardiovascular disease risk factors were collected by interview. In addition, the cardiovascular and locomotor components were collected using the Ross submaximal exercise test. **Results:** Hyperlipidemia was a significant predictor of treadmill time (B= -1.882, p=.034) and heart rate (B= -6.878, p<.001), whereas hypertension was a predictor of heart rate (B= -12.903, p=.026) and systolic blood pressure (B=12.263, p<.001). Hyperlipidemia was also a significant predictor of inclination (B= -1.707, p=.034). In addition, 57.4 % of the sample had at least one cardiovascular disease risk factor. **Conclusion:** Hyperlipidemia and hypertension should be considered in managing people living with HIV. This study indicated that hyperlipidemia and hypertension negatively affect cardiovascular and locomotor performance during exercise. Clinicians should be aware that exercise tolerance may be reduced in people with HIV and CVD risk factors; therefore, exercise prescription should be tailored and monitored accordingly.

Keywords: HIV, Cardiovascular Disease, Exercise, Hyperlipidemia, Hypertension

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1. Introduction

As of 2020, 37.7 million people worldwide were living with the human immunodeficiency virus (HIV) [1]. Antiretroviral therapies have improved the treatment of HIV and reduced mortality rates in this population, allowing people with HIV to live close to average lifespans [1]. However, it is estimated that by 2030, 73% of people living with HIV (PLHIV) will be 50 years of age or older [2]. As a result, this population is developing non-communicable diseases such as cardiovascular disease (CVD) [2]. A recent systematic review and meta-analysis found that PLHIV are two times more likely to develop CVD than their non-infected counterparts and increased mortality [3]. Therefore, PLHIV are at greater risk of experiencing debilitating complications of CVD such as stroke, myocardial infarction, heart failure, pulmonary hypertension, and venous thrombosis [4, 5].

The exact mechanism for developing CVD in PLHIV is not well understood. However, it is likely due to chronic inflammation from the virus, dyslipidemia secondary to antiretroviral medications, metabolic dysfunction, and modifiable lifestyle factors [4].What is concerning is that research has found that in the United States, PLHIV has less access to antiplatelet therapy, statins, and aspirin, thus increasing the risk of developing CVD [6].

Therefore, screening for CVD risk factors is crucial in PLHIV due to the high prevalence and severe complications associated with the disease [7]. According to the American Heart Association overall rate of CVD hospitalization was 11 per 1000 person-years among HIV positive and 6 per 1000 person-years among uninfected individuals [5]. It has been recommended that PLHIV consult with a physician before starting an exercise program to ensure participant's safety and to make appropriate modifications as needed [8]. When screening PLHIV for CVD, common risk factors are hypertension, hyperlipidemia, diabetes mellitus, visceral fat accumulation, sedentary behaviors, and smoking [9]. It is estimated that 8.9 million PLHIV have hypertension, with a higher prevalence in North America, (including Puerto Rico and Latino Hispanic population) than in other parts of the world [10]. In addition, dyslipidemia and metabolic dysfunction are commonly seen in PLHIV secondary to the use of antiretroviral therapies, sedentary lifestyles, and the presence of obesity. A combination of CVD risk factors and HIV negatively influence the cardiovascular system (heart and blood vessels), making PLHIV more prone to developing CVD [9]. Therefore, cardiovascular and muscular function are negatively impacted by the mechanisms that contribute to CVD, secondary complications of the disease, and limited access to proper treatment of CVD in PLHIV [9,11].

Consequently, cardiovascular and locomotor functions are lower in PLHIV [12-17]. Locomotor function declines faster in PLHIV secondary to antiretroviral medications showing signs of early onset of age-related comorbidities [12]. The virus impacts lower extremity muscle function, creates side effects of HIV medications, and promotes sedentary behaviors [17]. One study found that a decline in muscle strength was positively correlated with a decline in cardiorespiratory fitness in PLHIV [18]. Cardiorespiratory fitness measures cardiovascular function and is a predictor of CVD [19]. Cardiorespiratory fitness measures the ability and the capacity in which the heart, lungs, and muscles work together during physical activity [20]. Low levels of cardiorespiratory fitness are associated with increased risk for mortality and CVD [21]. In addition, previous studies have found that cardiorespiratory fitness is lower in PLHIV and inversely related to age, exposing PLHIV to greater health complications [14-17, 22].

Physical activity has improved cardiovascular function in PLHIV [22-25]. For example, Orozco and Rosario (2020) found that Hispanic- Latinos living with HIV who participated in a community-based exercise program for one year demonstrated improved CD4 count and heart rate achieved during a submaximal test [16]. Similarly, a randomized control trial by Ezema et al. (2014) found that individuals with HIV who participated in a moderate-intensity exercise program demonstrated significant improvements in cardiovascular function compared to the group of individuals with HIV who only underwent counseling and antiretroviral therapy [26]. Furthermore, physical activity and exercise intervention is recommended in PLHIV to reduce the mortality rate and CVD risk factors in this population [24-26].

While many studies have investigated how physical activity and exercise can improve cardiovascular function in PLHIV, it is poorly understood how the presence of CVD risk factors can influence cardiorespiratory and locomotor performance in this population [16,17, 25, 26]. One study utilized a submaximal treadmill test to determine how cardiovascular risk factors impacted exercise performance in PLHIV [17]. However, the study only investigated how age and body mass index were correlated with cardiorespiratory fitness. In addition, the study did not investigate if other comorbidities and lifestyle factors contributed to cardiovascular and locomotor performance during exercise [17]. Therefore, our study aims to determine if risk factors of cardiovascular disease are predictors of cardiomotor profiles in Hispanic-Latinos living with HIV. It is hypothesized that CVD risk factors will significantly predict cardiovascular and locomotor performance during a submaximal exercise test in Hispanic-Latinos living with HIV.

2. Methods

The current examination is a retrospective study where data was collected at La Perla de Gran Precio (LPGP), a nonprofit organization in San Juan, Puerto Rico, from 2000 to 2020. LPGP serves the Hispanic-Latino population living with HIV, focusing on promoting wellness and improving the quality of life through exercise and other clinical services. This study adhered to all privacy and confidentiality standards established by LPGP and was approved by Texas Woman's University Institutional Review Board (#FY2022-210).

Records of participants who met the following criteria were included in the current study: 1) between the ages of 18-65, 2) had a CD4 count greater than 200 cells per cubic millimeter, 3) were a community ambulators, and 4) actively participating in an antiretroviral therapy protocol. A cut-off age of 65 was used in this study because previous studies have found that age is inversely related to cardiorespiratory fitness [17, 22]. Participants were excluded from the study for the following reasons: if the participant 1) was pregnant, 2) reported a history of hospitalization within the last six months, 3) reported a history of musculoskeletal injury or surgery in the past six months, and 4) had an HIV dementia diagnosis.

Fitness Center Requirements: To participate in the organization's exercise and clinical services, various requirements were requested to be met by each participant. The requirements included obtaining a signed release form from a primary doctor to ensure the participant was safe to participate in the LPGP activities. After informed consent was obtained, the participant underwent an evaluation by a licensed physical therapist to collect demographic information, review the participant's medical history, identify physical impairments, and provide approval of a fitness evaluation with or without modifications. In addition, participants were instructed to bring a copy of their most recent blood work to determine and record their CD4 count. Also, cardiovascular risk factors (hyperlipidemia, hypertension, obesity, smoking, and sedentary lifestyle) were collected during the interview portion of the physical therapy evaluation. Finally, if the participant was cleared (by a medical doctor and Physiotherapist) then he was guided through the Ross Test by a certified personal trainer. During the process mentioned above, information related to CD4, cardiovascular risk factors, and medical history were gathered, added to a database, and included in the current study.

Cardio-motor components: The cardio-motor components were collected with the Ross test. The Ross test is a submaximal aerobic exercise test performed using a treadmill. This test was used to assess cardiorespiratory fitness and locomotor performance. Before beginning the test, heart rate and blood pressure were obtained to establish baseline values for each participant. A heart rate monitor was worn throughout the test using a chest strap. The test began with the participant walking at a speed of 2.0 mph. After three minutes passed, the speed was increased to 3.4 mph for the remainder of the test. The incline began at 0%, increased to 3s% after the first three minutes of the test, and increased by 3% every three minutes after that. If the participant was physically able, the test would continue for 21 minutes and six intervals. Heart rate, blood pressure, and time completed (cardiovascular component) were recorded upon the termination of the test. Blood pressure was obtained manually by the personal trainer using a sphygmomanometer. The level of inclination (locomotor component) achieved at the end of the test was also recorded. Variables related to cardiovascular (heart rate, blood pressure, and time completed) and motor components (treadmill level of inclination) were input into a database and included in the current study.

Data Encoding System: Once the data was collected during the above process, it was de-identified using a numerical coding system and stored in an extensive database on a password-protected computer at LPGP. A total of 426 records were reviewed for data completeness. Participants' records were excluded if there were any missing values from the completed Ross Test or if the cardiovascular risk factors were not addressed in the interview as denoted by a blank value in the database.

2.1 Data Analysis

This study aimed to determine whether CVD risk factors predicted cardiomotor profiles in Hispanic-Latinos living with HIV. Descriptive statistics were calculated for demographic, cardiovascular, and locomotor data. Frequency statistics were performed to determine the prevalence of each CVD risk factor in the given sample. In addition, frequency statistics were performed to determine how many comorbidities were present in each of our participants. A multiple regression analysis was performed for each cardiovascular component (treadmill time, heart rate, systolic blood pressure, and diastolic blood pressure) and the locomotor component (inclination) using SPSS version 28. The significance level was set at $p \leq 0.05$.

3. Results

Table 1 depicts descriptive statistics for all cardiovascular and locomotor data collected at the termination of the Ross Test. Data from 176 out of 426 records were selected due to the completeness of all variables mentioned above. Table 1 also presents the demographic characteristics of HIV participants. The majority of the participants were male with an average age of 53.34 +/- 10.31 years old. In addition, the average years with the HIV diagnosis for this sample was 18.94 +/- 8.44 years. The results of the frequency statistics revealed that hypertension (25.6%), smoking (22.7%), and hyperlipidemia (21.6%) were among the top three cardiovascular risk factors found in the sample. In addition, while 42.6% of participants had no history of cardiovascular disease risk factors, 57.4% of the participants had at least one or more risk factors (Table 2).

Table 1. Descriptive Statistics for Demographic, Cardiovascular, and Locomotor Data.

Characteristics	Participant data
Age (yrs)	53.34 +/- 10.31
Years with diagnosis	18.94 +/- 8.44
Gender (n=176)	Male = 134 Female = 42
Female = 42	636.79 +/- 344.65
CD4 count (cells per cubic millimeter)	
Cardiovascular component	10.72 +/- 4.72
Treadmill time (minutes)	138. 66 +/- 17.83
Heart Rate (bpm)	124.63 +/- 17.33
Systolic blood pressure (mmhg)	74.69 +/- 11.30
Diastolic blood pressure (mmhg)	
Locomotor component	5.90 +/- 4.29

Table 2. Frequency table for cardiovascular risk factors and the number of risk factors

Risk factor	Frequency	%
Hypertension	45	25.6
Hyperlipidemia	38	21.6
Obesity	23	13.1
Smoker	40	22.7
Sedentary lifestyle	24	13.6
Number of risk factors	Frequency	%
0	75	42.6
1	59	33.5
2	23	13.1
3	11	6.3
4	8	4.5
5	0	0

Table 3. Results of multiple regressions analyses for all cardiovascular and locomotor components. Significance level set at p≤0.05.

Treadmill time	**b**	**SE**	**P-value**
constant	12.221	0.463	<.001
Hypertension	-1.578	0.809	.053
Hyperlipidemia	-1.882	0.880	.034
Obesity	-1.872	1.118	.096
Smoked	-1.394	0.839	.099
Sedentary lifestyle	-0.943	1.068	.378
Heart Rate	**b**	**SE**	**P-value**
constant	143.406	1.758	<.001
Hypertension	-12.903	3.343	<.001
Hyperlipidemia	-6.878	3.072	.026
Obesity	4.869	4.247	.253
Smoked	-4.451	3.188	.165
Sedentary lifestyle	1.311	4.057	.747
Systolic blood pressure	**b**	**SE**	**P-value**
constant	122.212	1.739	<.001
Hypertension	12.263	3.038	<.001
Hyperlipidemia	-0.153	3.306	.963
Obesity	-2.036	4.199	.628
Smoked	-0.031	3.153	.992
Sedentary lifestyle	-3.009	4.011	.454
Diastolic blood pressure	**b**	**SE**	**P-value**
constant	73.185	1.173	<.001
Hypertension	2.496	2.049	.225
Hyperlipidemia	2.051	2.229	.359
Obesity	2.432	2.832	.392
Smoked	1.275	2.126	.550
Sedentary lifestyle	-1.323	2.705	.625
% Inclination	**b**	**SE**	**P-value**
constant	7.239	0.421	<.001
Hypertension	-1.419	0.735	.055
Hyperlipidemia	-1.707	0.800	.034
Obesity	-1.838	1.016	.072
Smoked	-1.227	0.763	.109
Sedentary lifestyle	-0.668	0.971	.492

A series of multiple regression analyses were performed to assess if the CVD risk factors obtained during the interview predicted any of the outcome variables collected during the Ross submaximal treadmill test (Table 3). The first multiple regression analysis revealed that the model was a significant predictor of treadmill time, $F(5,170) = 5.305$, $p = <.001$, and hyperlipidemia was a significant predictor of the model (B= -1.882, p=.034). Additionally, there was an inverse relationship between the presence of hyperlipidemia and treadmill time, as denoted by the beta coefficient. The second multiple regression analysis showed that the model was a significant predictor of heart rate, F (1,170) = 4.792, p = <.001. Hyperlipidemia (B= -6.878, p.026), and hypertension (B= -12.903, p=<.001) were significant predictors of the model. Both risk factors (hypertension and hyperlipidemia) also had an inverse relationship with heart rate. The third multiple regression analysis found that the model was a significant predictor of systolic blood pressure, F (5,170) = 3.466, p =.005, and in this model, hypertension was a significant predictor of systolic blood pressure (B=12.263, p<.001). The relationship between hypertension and systolic blood pressure was positive. The fourth regression analysis showed no significant predictors of diastolic blood pressure, F (5,170) = 1.012, p=.412. Lastly, the fifth regression analysis revealed that the model was a significant predictor of inclination, F (5,170) = 5.233, p<.001, and hyperlipidemia (B= -1.707, p=.034) was a significant predictor of inclination achieved during the Ross test. In addition, the presence of hyperlipidemia was inversely related to the level of inclination.

4. Discussion

This study aimed to discover which CVD risk factors were predictors of cardiomotor profiles as determined by performance on the Ross submaximal treadmill test. This study found that hyperlipidemia and hypertension were predictors of cardiomotor profiles; however, the other three risk factors collected (obesity, smoking, and sedentary lifestyle) were not. The results of this study were partially aligned with the hypothesis that the presence of cardiovascular risk factors predicts cardiovascular and locomotor performance on the Ross test; therefore, the hypothesis was partially accepted.

Cardiovascular component: The first outcome of this study found that hyperlipidemia and hypertension were predictors of the cardiovascular components of the Ross submaximal exercise test. Specifically, hyperlipidemia was a predictor of heart rate and treadmill time achieved during the Ross test. In addition, the presence of hyperlipidemia was inversely associated with heart rate and treadmill time, resulting in a lower heart rate and less time completed during the submaximal exercise test. Like hyperlipidemia, hypertension predicted heart rate and was inversely associated with heart rate; however, this study found that hypertension was also a predictor of systolic blood pressure (SBP), and the presence of hypertension generally resulted in a higher SBP at the termination of the test.

One possible explanation for the above results is that hyperlipidemia and hypertension occur in PLHIV secondary to side effects of antiretroviral therapies and the virus, leading to narrowing and stiffening of the arteries [27-29]. As a result, blood flow to the heart and muscles is impeded [30, 31]. Therefore, when considering how hyperlipidemia and hypertension affect heart rate, the results of this study showed that the presence of either condition negatively affected the heart rate achieved during the Ross test. While increased resistance within the arteries often leads to a higher resting heart rate, a lower heart rate observed in participants with hyperlipidemia and hypertension can be explained by reducing blood flow to the heart and muscles [31]. As a result, participants with hypertension and hyperlipidemia likely experienced fatigue, resulting in early termination of the Ross test before the participant's submaximal heart rate was achieved.

While there is limited evidence to describe the relationship between hyperlipidemia and cardiorespiratory fitness, one study by LaMonte et al. (2005) found an inverse relationship between metabolic syndrome and cardiorespiratory fitness in the general population as measured by a maximal treadmill test [32]. This study is consistent with our findings that treadmill time is inversely related to the presence of hyperlipidemia. Similarly, previous studies have found a reduction in submaximal exercise capacity due to the long-term use of beta-blockers in the general population with hypertension [33-35]. Furthermore, during exercise, systolic blood pressure rises in response to an increase in heart rate, thus, explaining the surge in blood pressure in participants with hypertension in our study [35]. Therefore, monitoring blood pressure during aerobic exercise combined with utilizing the Borg Rating of Percieved Exertion Scale is crucial in people with HIV and hypertension to prevent adverse cardiovascular events.

One weakness of this study was that the use of beta-blockers was not collected during the interview process. Therefore, further research is needed to determine if the consumption of beta-blockers strengthened the inverse relationship between heart rate and treadmill time with the presence of hyperlipidemia and hypertension. Another limitation of this study was not considering how the presence of both hypertension and hyperlipidemia impacted cardiovascular components of the Ross Test. Future studies should consider if hypertension and hyperlipidemia strengthen the prediction of cardiovascular components during the submaximal test versus each CVD risk factor alone. Knowing this information will provide clinicians with a better understanding of exercise response in PLHIV and help guide exercise prescription in individuals with hypertension and hyperlipidemia. Additionally, based on the results of this study, cardiovascular exercises and testing needs to be adjusted accordingly since the cardio components were lessened in this group. Therefore a "one size fits all" protocol is an inadequate approach for those living with HIV.

Locomotor component: In addition to being a predictor of cardio profiles, hyperlipidemia was a predictor of the level of inclination achieved during the Ross Test. The presence of hyperlipidemia was inversely related to the level of inclination. Since the level inclination increases with time during the Ross test, a lower level of inclination is associated with the earlier termination of the test. Additionally, an increase in inclination is also associated with an increased workload for the musculoskeletal and cardiovascular systems [36, 37]. The inverse relationship found between the inclination and hyperlipidemia can be explained by the impedance of blood flow to the heart, lungs, and muscles from plaque build-up, thus limiting the participants' ability to tolerate increased physical exertion. In addition, previous research has reported that deficits in cardiovascular function are accompanied by a reduction in motor output that is often portrayed as muscle weakness [18]. One study by Raso et al. (2013) found that muscle strength was positively correlated with cardiorespiratory fitness in PLHIV [18]. Evidence suggests that the virus causes an alteration in oxygen kinetics, thus limiting the withdrawal and utilization of oxygen in the muscles [38]. Also, the plaque build-up secondary to hyperlipidemia likely impedes the withdrawal of oxygen from arteries. Therefore, lactate production increases, and muscle output decreases, leading to quicker onset of fatigue [38]. Finally, another possible explanation for the previous finding could be related to poor lower limb circulation provoking pain and resulting in early termination of the Ross test. Rosario and Orozco (2022) studied a similar population as the current study and found reduced treadmill time and inclination in those presenting with chronic pain. The authors concluded that chronic pain is common among those living with HIV and is associated with gait abnormalities [39]. Based on this research and the current study, future examinations should focus on a cardio-motor variation on various surfaces to understand gait alterations in everyday scenarios, the role of muscle fatigue, and how those deficiencies impact their quality of life [39].

To our knowledge, this is the first study to consider the influence hyperlipidemia may have on the level of inclination as a measure of locomotor function during a submaximal treadmill test. This study is consistent with previous research that PLHIV demonstrates locomotor deficits that are often accompanied by a decline in cardiovascular function [18]. This phenomenon is likely due to long-term complications of the virus and side effects of antiretroviral medications that have contributed to a decline in muscle strength and led to a more sedentary lifestyle over time. Therefore, it has been recommended that PLHIV participate in resistance training in conjunction with aerobic exercise training at least three times a week to improve cardiorespiratory fitness and muscle strength [40].

A limitation of this study is that it is unknown whether peripheral artery disease was present in the sample of PLHIV. Since individuals with hyperlipidemia are more prone to acquiring PAD, the level of inclination achieved during the Ross test could have been limited by pain in the lower extremities and exercise intolerance secondary to poor perfusion [41]. Further research is needed to determine if the presence of PAD strengthens the inverse relationship between hyperlipidemia and level of inclination during a submaximal exercise treadmill test. Clinicians should also screen for PAD in this population prior to performing aerobic exercise and resistance training to reduce adverse effects of poor perfusion in the lower extremities secondary to PAD.

Additional findings: While this study did not aim to determine the frequency of CVD risk factors in this sample, we found that hypertension and hyperlipidemia were among the top three risk factors collected during the interview process. In addition, more than half of the sample reported at least one CVD risk factor. In previous studies Pierre et al. (2019) found that in a cohort of 397 individuals with HIV, 74% of the sample had at least one CVD risk factor [42]. While this number is more significant than the results of our study, it supports that the prevalence of CVD risk factors remains high in this population.

Hyperlipidemia has been estimated in 70-80% of PLHIV receiving antiretroviral medications [28]. The mechanism for acquiring hyperlipidemia is secondary to alterations in lipid metabolism, with a greater risk of developing this condition while using certain HIV medications like protease inhibitors and nucleoside reverse transcriptase inhibitors [28, 29]. Hyperlipidemia is a modifiable risk factor for CVD that can be addressed through changes in antiretroviral medications, lipid-lowering medications, and lifestyle factors [43]. Regular participation in physical activity has been associated with high levels of HDL cholesterol, low levels of LDL, and low levels of total cholesterol in PLHIV [24, 43]. Since our study was a retrospective analysis, specific information regarding physical activity levels was not obtained. Future studies should consider collecting information about physical activity levels before completing submaximal tests to determine if the level of physical activity influences the relationship between hyperlipidemia and cardiovascular performance. Additionally, clinicians should be aware of how hyperlipidemia negatively influences cardiovascular performance and adjust the exercise intensity accordingly.

Finally, the specific ART cocktail was not determined in the current study; as suggested by Rosario et al., the combination of different medications might be causing distinct cardio-motor alterations in this group [44]. Therefore, future inquiries should gather the specific ART cocktail and correlate these medications to cardio-motor issues.

5. Conclusion

This study revealed that hyperlipidemia and hypertension are predictors of cardiovascular performance, while hyperlipidemia is also a predictor of locomotor performance in PLHIV. In addition, this study found that more than half the sample had at least one CVD risk factor, with hyperlipidemia and hypertension being amongst the top three CVD risk factors collected during the interview process. These findings imply that CVD risk factors can negatively affect cardiorespiratory fitness and locomotor function, thus impeding functional mobility and increasing sedentary behaviors. However, it remains unclear if the quantity of CVD risk factors is a predictor of cardiorespiratory fitness and locomotor function. Therefore, further analysis is needed to determine if the quantity of risk factors influences the relationship between CVD risk factors and cardiomotor profiles. Due to the high prevalence of CVD in PLHIV and its effects on cardiorespiratory and locomotor function, clinicians should screen all PLHIV for CVD before starting an exercise program in order to make the appropriate modifications to exercise prescription. It is essential to consider that people living with HIV, hyperlipidemia, and hypertension may present with lower cardiorespiratory levels and decreased exercise tolerance. Therefore, exercise may need to begin at a low intensity and progress based on the individual's tolerance. Additionally, exercise intensity should be measured using the Borg Rating of Perceived Exertion scale due to the possible effects beta-blockers have on heart rate.

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MR supervised the work and performed data collection. EO organized the data, performed the analysis, drafted the manuscript, and designed the tables. All authors commented on the manuscript. EO wrote the manuscript, and MR edited the final draft.

Conflict of interest
No conflicts were reported by the authors.

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