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PREVALENCE OF CORONARY ATHEROSCLEROSIS, EVALUATED FROM MULTISLICE TOMOGRAPHY, IN HYPERTENSIVE AFRO DESCENDANTS

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ABSTRACT

The occurrence of atherosclerosis and associated factors in different Brazilian ethnic groups, especially among Afrodescendants, is not yet well established. To determine the prevalence and factors associated with coronary atherosclerosis among hypertensive Afrodescendants of Quilombola communities.The study evaluated 138 hypertensive individuals from the PREVRENAL study, a population-based cohort that evaluated Afrodescendants from 32 remaining Quilombola communities in the State of Maranhão. The coronary calcification score was obtained by non-contrast computed tomography. Clinical and laboratory data were collected from the PREVRENAL database. To evaluate the factors associated with the occurrence of atherosclerosis, the Poisson model with robust variance was adjusted. The data were processed in Stata 12.0 software. Among the individuals, 64.49% were female; the mean age was 60.93 (±12.25) years; 15.22% diabetics, 21.74% smokers and 21.74% reported alcohol consumption; 7.97% had GFR <60mL/min/1.73m², 22.46% albuminuria, 8.70% ultrasensitive C-reactive protein >1mg/dL, 20.29% mixed hyperlipidemia and 44.93% low HDL. There were 39.13% of patients with CCS>0. In the multivariate model, CCS was associated with: age > 60 years (PR 3.25, p-value=0.001), uric acid (PR=1.98, p-value=0.001). The prevalence of coronary calcification was significant in the group evaluated and was associated with age and uric acid.

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INTRODUCTION

Based on estimates from the Global Burden of Diseases, Injuries, and Risk Factors Study 2016 (GBD), the global prevalence of Coronary Artery Disease (CAD) worldwide was 154 million in 2016, representing 32.7% of the global burden of cardiovascular disease and 2.2% of the global burden of diseases (GBD, 2016). Among the risk factors for CAD, systemic arterial hypertension (SAH) stands out as one of the uncontrolled chronic diseases promoting the atherosclerotic process (Mozaffarian. *et al*., 2016). CAD is common, early, severe and, in hypertensive patients, being four times more common in hypertensive patients than in individuals with normal BP (Kazum *et al*., 2016). The black race is a strong predisposing factor for systemic arterial hypertension (SAH), exposing African descendants to the development of more severe forms of the disease, as well as a higher risk of angina, infarction and sudden death (Brazilian Hypertension Guidelines, 2016). Epidemiological studies show that mortality due to coronary artery disease (CAD) is higher in Afro descendants than in Caucasians (Williams *et al*., 1999; Benjamin *et al*., 2018; Friedman *et al*., 1988). The higher prevalence of hypertension, left ventricular hypertrophy, diabetes mellitus and chronic kidney disease, as well as reduced access to medical care (Go *et al*., 2014), are likely

contributing to the higher mortality rate from CAD in blacks. In Brazil, there is little information on coronary atherosclerotic disease in minority ethnic groups. Knowledge about the factors related to the prevalence of coronary atherosclerosis may allow the adoption of therapeutic and preventive measures that allow reducing the incidence of fatal and non-fatal cardiac events. Invasive coronary angiography (ICA) is the reference standard for the diagnosis of CAD, being indicated when coronary stenosis is suspected in patients with a high probability of CAD.Coronary angiography with multidetector computed tomography (MDCT) has been the modality of choice for the evaluation of coronary calcium score, which plays a relevant role in cardiovascular risk stratification, with a significant association with the occurrence of major cardiovascular events in medium and long-term follow-up (Neves & Andrade & Monção, 2017). Thus, the present study aimed to evaluate coronary atherosclerosis using coronary calcium score in hypertensive Afrodescendants from remaining Quilombola communities in Maranhão, with the objective of providing information on the occurrence of the disease and associated factors, filling important gaps in relation to the theme.

MATERIAL AND METHODS

This is a cross-sectional analysis with hypertensive Afrodescendants who participated in the PREVRENAL study: *"Prevalence of Chronic Kidney Disease in the municipality of São Luís and in Quilombola communities of Alcântara, State of Maranhão"*, which evaluated 1,539 Afrodescendants from 32 remaining Quilombola communities in northeastern Brazil (municipality of Alcântara, State of Maranhão), between August 2012 and April 2013. For this study, the sample calculation was estimated considering the population of hypertensive Afrodescendants previously diagnosed in the PREVRENAL study (n=439), using two-tailed hypothesis test, test power of 80%, confidence level of 95%, prevalence of coronary atherosclerosis in the exposed of 91% (Wagenknecht *et al*., 2007) and prevalence ratio of 1.25. Thus, the sample size was estimated at 138 individuals. The hypertensive individuals included in this study were randomly selected through a list obtained from the PREVRENAL database. A random draw of the first participant was held, who was considered the starting point and then the other participants, until completing the number established to make up the sample. For data collection, a pre-coded questionnaire was used at PREVRENAL, which sought information regarding demographic, socioeconomic, behavioral and clinical information of hypertensive patients included in the study. All researchers were previously trained to apply the questionnaires, and the interviews were conducted in the homes of the selected individuals.

The variables related to socioeconomic characteristics were: income (in minimum wages) and schooling (in years). The other variables studied were: age (in years), gender, smoking, alcohol intake, body mass index. Smoking was defined as current consumption of ≥ 1 cigarette/day and alcohol consumption as alcohol consumption ≥ 1 time/week. Weight (kg) and height (m) were measured to calculate body mass index (BMI, calculated as kg/m²).Individuals with BMI >30 kg/m^2 were classified as obese (WHO, 1998). Diabetes mellitus (DM), history of cerebrovascular accident, acute myocardial infarction (AMI)/angina and medication use were reported by study participants based on the history of previous medical diagnosis. The BP was evaluated using the oscillometric method using the Omron 705-IT device (HEM-759-E, Omron Corporation, Kyoto, Japan). For blood pressure measurement, as well as for the classification, the recommendations proposed by the International Society of Hypertension were used (Unger *et al*., 2020). Venous samples were collected after a 12-hour fast and included the following biochemical dosages: creatinine, cystatin C, blood count, glucose, uric acid, lipid profile, high-sensitive c-reactive protein (hs-CRP). Uric acid was considered high, when above 7mg/dL for men and above 6mg/dL for women. The glomerular filtration rate (GFR) was estimated from the formula derived from the CKD-EPI study, using the creatinine value (Levey *et al*., 2009) as a reference for the calculation. For the composition of the groups, the research subjects were characterized as having normal or reduced GFR, with reduced GFR defined when < 60mL/min/1.73m².

The value of urinary albumin was obtained from the relationship between albuminuria and creatininuria, in a sample isolated in the second urine of the day. The patient with laboratory value > 30mg/g of urinary creatinine was defined as having albuminuria. Dyslipidemia was categorized into (1) isolated hypercholesterolemia: isolated elevation of LDL (≥ 160 mg/dl); (2) isolated hypertriglyceridemia: isolated elevation of triglycerides (≥ 150 mg/dl); (3) mixed hyperlipidemia: LDL ≥ 160 mg/dL and triglycerides ≥ 150 mg/dL; and (4) low HDL: < 40 mg/dL in men and < 50 mg/dL in women (Faludi *et al*., 2017). The images were obtained through a 64-detector CT scanner (computed tomography) (Aquilion 64, Toshiba Medical Systems, Tochigi, Japan) without the use of contrast. Each patient was positioned in supine position in the device, and images were obtained with 3.0 mm thickness, on average, without intervals between them. The duration of the examination was around 10 minutes. The presence of calcium was considered when its density was above 130 Housfield units (HU) in at least three continuous pixels (>1mm²) in the same artery. The coronary calcium score (CCS) constituted the sum of the individual scores of the right and left coronary arteries. The result was given as positive in the presence of calcium score greater than zero (Agatston *et al*., 1990). CCS was also analyzed by categories: zero (no evidence of atheroma), 1-10 (minimal evidence of atheroma), 11-100 (mild evidence of atheroma), 101-400 (moderate evidence of atheroma) and ≥ 400 (extensive evidence of atheroma) (McClelland *et al*., 2006). The numerical variables were presented as mean and standard deviation (mean±SD) and categorical variables, as frequencies and percentages. The association between the several variables analyzed and the presence of coronary atherosclerosis was evaluated by chi-square with a significance level of 5%. To evaluate the association between the occurrence of coronary atherosclerosis and different variables under study, the Poisson regression model with robust variance was used, with the results expressed in prevalence ratios (PR) and their respective confidence interval (95% CI). The variables that presented $p<0.20$ in the unadjusted analysis were included in the multivariate model, remaining in the final model only those with $p<0.05$. The data were analyzed with the help of Stata 12.0 software. The study was approved by the Research Ethics Committee at the University Hospital of the Federal University of Maranhão (Opinion n. 41492/2012), in compliance with the requirements required by the National Health Council, Resolution n. 466/12 and its supplements for researches involving human beings.

RESULTS

The study sample consisted of 138 hypertensive Afrodescendant patients, with a mean age of 60.93 (± 12.25) years, of whom 89 (64.49%) were women, 35 (25.36%) smokers, 30 (21.74%) alcohol consumers and 33 (23.91%) with BMI ≥30Kg/m².

Regarding comorbidities, 21 (15.22%) had diabetes mellitus. Ten individuals (7.25%) reported a history of CVA. Moreover, 104 (75.36%) presented SBP >140mmHg and 62 (44.93%) DBP>90mmHg (Table 1). Coronary artery calcification (CAC) was identified in 54 patients (39.13%). CAC was more present in females (42.70%), aged from 60 to 79 years (57.75%) and high uric acid (68.42%), according to Tables 1 and 2.

Table 1. Distribution of clinical and epidemiological characteristics according to the presence of coronary calcification assessed by computed tomography. São Luís-MA, 2013.

		No calcification	Calcification	
Variable	n (%)	n (%)	n (%)	p-value
Gender				0.247
Male	49 (35.51)	33 (67.35)	16 (32.65)	
Female	89 (64.49)	51 (57.30)	38 (42.70)	
Age				<0.001
< 60 years	62 (44.93)	51 (82.26)	11 (17.74)	
60-79 years	71 (51.45)	30 (42.25)	41 (57.75)	
≥ 80 years	5 (3.62)	3 (60.00)	2 (40.00)	
Schooling				0.064
0-4 years	95 (68.84)	64 (67.36)	31 (32.63)	
5-8 years	27 (19.57)	13 (48.15)	14 (51.85)	
>8 years	16 (11.59)	7 (43.75)	9 (56.25)	
Income				0.916
Up to 1/2 m.w.	52 (37.68)	32 (61.54)	20 (38.46)	
>1/2 - 1 m.w.	56 (40.58)	33 (58.93)	23 (41.07)	
>1 m.w.	30 (21.74)	19 (63.33)	11 (36.67)	
DM history				0.177
No	117 (84.78)	74 (63.25)	43 (36.75)	
Yes	21 (15.22)	10 (47.62)	11 (52.38)	
Use of ACEI/ARB				0.963
No	77 (55.80)	47 (61.04)	30 (38.96)	
Yes	61 (44.20)	37 (60.66)	24 (39.34)	
Statin use				0.136
No	134 (97.10)	83 (61.94)	51 (38.06)	
Yes	4 (2.90)	1 (25.00)	3 (75.00)	
Use of AAS				0.942
No	123 (89.13)	75 (60.98)	48 (39.02)	
Yes	15 (10.87)	9 (60.00)	6 (40.00)	
Smoking				0.601
No	103 (74.64)	64 (62.14)	39 (37.86)	
Yes	35 (25.36)	20 (57.14)	15 (42.86)	
BMI (Kg/m²)				0.234
< 30	105 (76.09)	61 (58.10)	44 (41.90)	
≥ 30	33 (23.91)	23 (69.70)	10 (30.30)	
Alcohol consumption				0.755
No	108 (78.26)	65 (60.19)	19 (63.33)	
Yes	30 (21.74)	43 (39.81)	11 (36.67)	
SBP (mmHg)				0.598
< 140	34 (24.64)	22 (64.71)	12 (35.29)	
≥ 140	104 (75.36)	62 (59.62)	42 (40.38)	
DBP (mmHg)				0.428
< 90	76 (55.07)	44 (57.89)	32 (42.11)	
≥ 90	62 (44.93)	40 (64.52)	22 (35.48)	

m.w.- minimum wage; DM - diabetes mellitus; ACEI/ARB - angiotensin converting enzyme inhibitor/angiotensin II AT1 receptor blocker; AAS - acetylsalicylic acid; BMI - body mass index; SBP - systolic blood pressure; DBP - diastolic blood pressure

Table 2. Distribution of laboratory characteristics according to the presence of coronary calcification assessed by computed tomography. São Luís-MA, 2013

		No calcification	Calcification	
Variable	n (%)	n (%)	n (%)	p-value
ACR (mg/g)				0.230
< 30	107 (77.54)	68 (63.55)	39 (36.45)	
≥ 30	31 (22.46)	16 (51.61)	15 (48.39)	
hs-CRP (mg/dL)				0.421
< 1	126 (91.30)	75 (59.52)	51 (40.48)	
1-3	10 (7.25)	8 (80.00)	2 (20.00)	
> 3	2 (1.45)	1 (50.00)	1 (50.00)	
eGFR/CKD-EPIcr (mL/min/1,73m²)				0.083
≥ 60	127 (92.03)	80 (62.99)	47 (37.01)	
< 60	11 (7.97)	4 (36.36)	7 (63.64)	
Isolated hypercholesterolemia				0.561
No	118 (85.51)	73 (61.86)	45 (38.14)	
Yes	20 (14.49)	11 (55.00)	9 (45.00)	
Isolated hypertriglyceridemia				0.843
No	106 (76.81)	65 (62.32)	41 (38.68)	
Yes	32 (23.19)	19 (59.38)	13 (40.63)	
Mixed hyperlipidemia				0.200
No	110 (79.71)	64 (58.18)	46 (41.82)	
Yes	28 (20.29)	20 (71.43)	8 (28.57)	
Low HDL				0.253
No	76 (55.07)	43 (56.58)	33 (43.42)	
Yes	62 (44.93)	41 (66.13)	21 (33.87)	
Fasting blood glucose (mg/dL)				0.853
< 100	55 (39.86)	34 (61.82)	21 (38.18)	
≥ 100	83 (60.14)	50 (60.24)	33 (39.76)	
Uric acid				0.005
Normal	119 (86.23)	78 (65.55)	41 (34.45)	
High	19 (13.77)	6 (31.58)	13 (68.42)	

ACR - albuminuria: creatininuria ratio; hs-CRP - high sensitive C-reactive protein; eGFR - estimated glomerular filtration rate; CKD-EPIcr - Chronic Kidney Disease Epidemiology Collaboration (use of creatinine); CKD-EPIcy - Chronic Kidney Disease Epidemiology Collaboration (utilização da cistatina C); HDL - high density lipoprotein

Table 3. Distribution of coronary calcification scores. São Luís-MA, 2013

CCS	n	%
ZERO	84	60.87
1-10	15	10.87
11-100	12	8.70
101-400	14	10.14
>400	13	9.42
	138	100.00

CCS - coronary calcification score

Table 4. Unadjusted analysis to assess the association of coronary calcification with clinical variables. São Luís-MA, 2013

Variable	PR	CI (95%)	p-value
Gender			
Female	1		
Male	1.30	0.81-2.09	0.264
Age			
< 60 years	1		
60-79 years	3.25	1.83-5.77	<0.001
≥ 80 years	2.25	0.67-7.51	0.186
DM history			
No	1		
Yes	1.42	0.88-2.28	0.143
Smoking			
No	1		
Yes	1.13	0.71-1.78	0.595
Alcohol consumption			
No	1		
Yes	0.92	0.54-1.55	0.759
BMI (Kg/m²)			
< 30	1		
≥ 30	0.72	0.41-1.27	0.262
SBP (mmHg)			
< 140	1		
≥ 140	1.14	0.68-1.91	0.607
DBP (mmHg)			
< 90	1		
≥ 90	0.84	0.54-1.29	0.433

PR - prevalence ratio; CI - confidence interval; DM - diabetes mellitus; BMI - body mass index; SBP - systolic blood pressure; DBP - diastolic blood pressure

Table 5. Unadjusted analysis to assess the association of coronary calcification with laboratory variables. São Luís-MA, 2013

Variable	PR	CI (95%)	p-value
ACR (mg/g)			
< 30	1		
≥ 30	1.32	0.85-2.06	0.210
hs-CRP (mg/dL)			
< 1	1		
1-3	0.49	0.13-1.74	0.274
> 3	1.23	0.30-5.04	0.769
eGFR/CKD-EPIcr (mL/min/1,73m²)			
≥ 60	1		
< 60	1.71	1.03-2.84	0.035
Isolated hypercholesterolemia			
No	1		
Yes	1.18	0.68-2.02	0.547
Isolated hypertriglyceridemia			
No	1		
Yes	1.05	0.64-1.70	0.843
Mixed hyperlipidemia			
No	1		
Yes	0.68	0.36-1.28	0.235
Low HDL			
No	1		
Yes	0.78	0.50-1.20	0.262
Fasting blood glucose (mg/dL)			
< 100	1		
≥ 100	1.04	0.67-1.60	0.853
Uric acid			
Normal	1		
High	1.98	1.33-2.94	0.001

PR - prevalence ratio; CI - confidence interval; ARC - albuminuria: creatininuria ratio; hs-CRP - high sensitive C-reactive protein; eGFR - estimated glomerular filtration rate;CKD-EPIcr - Chronic Kidney Disease Epidemiology Collaboration (use of creatinine); CKD-EPIcy - Chronic Kidney Disease Epidemiology Collaboration (use of creatinine); HDL - high density lipoprotein

Table 6. Adjusted analysis to assess the association of coronary calcification with the variables studied. São Luís-MA, 2013

Variable	PR	CI (95%)	p-value
Age 60-79 years	1.29	1.12-1.49	<0.001
DM history	1.10	0.88-1.37	0.374
eGFR/CKD-EPIcr (mL/min/1,73m²)	1.08	0.80-1.44	0.603
ACR (mg/g)	1.12	0.93-1.34	0.220
Uric acid	1.30	1.04-1.63	0.021

PR - prevalence ratio; CI - confidence interval; DM - diabetes mellitus; ARC - albuminuria: creatininuria ratio; hs-CRP - high sensitive C-reactive protein; eGFR - estimated glomerular filtration rate; CKD-EPIcr - Chronic Kidney Disease Epidemiology Collaboration (use of creatinine).

The individuals in the study had median CCS equal to 126 (1-3,538). CCS equal to zero was observed in 84 (60.87%) patients, 15 (10.87%) presented CCS 1-10, 12 (8.70%) 11-100, 14 (10.14%) 101-400 and 13 (9.42%) values greater than 400 (Table 3). Tables 4 and 5 present the PR estimates in the unadjusted analysis. The occurrence of CAC was statistically associated with: age 60-79 years (PR=3.25, p-value<0.001), high uric acid (PR=1.98, p-value=0.001). In the adjusted analysis (Table 6), only the age between 60 and 79 years (PR=1.29, p-value<0.001) remained statistically associated.

DISCUSSION

The present study, with the objective of evaluating the score of coronary calcification by multislice computed tomography, and its associated factors, in hypertensive Afrodescendants living in remaining Quilombola communities, identified a prevalence of coronary calcification of 39.13%, presenting as a factor independently associated with age. A higher prevalence of coronary calcification was evidenced among hypertensive Afrodescendant women. The prevalence of CAD varies widely according to geographic location, ethnicity and gender (Go *et al*, 2014). CAD develops on average 7 to 10 years later in women than in men, being still the leading cause of death in women aged over 65 years (Appelros & Stegmayr & Terént, 2009). Tremollieres *et al*. (1999) found a 36% higher prevalence of CAD in postmenopausal women. After multivariate analysis, age and high uric acid levels showed a statistically significant association with the prevalence of coronary calcification among the evaluated Afrodescendants. Age is an important non-modifiable risk factor for atherosclerosis, and has been associated with increased prevalence of calcification among Afrodescendants evaluated here. Some authors consider atherosclerosis as part of the aging process (Clarke, 2014; Wang & Bennett, 2012).The isolated influence of age at the beginning of the atherosclerotic process remains uncertain. Age-accelerated vascular injury is commonly considered as a result of increased oxidative stress, leading to inflammation and endothelial dysfunction, but the definitive mechanisms of this process have not been identified yet (Madamanchi & Runge, 2007).

Uric acid is an independent predictor of mortality in patients with CAD. Bickel *et al.* (2002), upon evaluating 1,017 patients with CAD, followed for roughly 2.2 years, with death from all causes defined as a final point of the study, found mortality rates five times higher in patients with high uric acid levels.Hyperuricemia increases platelet aggregate stability, the initial event in thrombosis, and, therefore, increases the incidence of thrombosis and arterial disease in hyperuricemic individuals (Strazzullo & Puig, 2007; Lin *et al.*, 2013). Although previous studies point to smoking (Benchimol & Benchimol & Saad, 1987; Lubin *et al*., 2016), diabetes mellitus (Al Rifai *et al*., 2015), dyslipidemia (Penalva *et al.*,

2008), hs-CRP levels (Quaglia, Freitas & Soares *et al*., 2014) and glomerular filtration rate (Choi, 2015)as factors associated with atherosclerosis and cardiovascular risk, in our analysis, such variables were not associated with the occurrence of coronary calcification in the group of Afrodescendants after multivariate analysis. Finally, this study has some limitations. The first is related to its cross-sectional design, which prevents conclusions about the impact of the variables evaluated on the occurrence of future cardiovascular events. Secondly, as a highly specific group of patients was evaluated, the results cannot be automatically extrapolated to the entire Brazilian Afrodescendant population.On the other hand, our study presents as the main positive aspect the fact that it is the first study to quantify and seek factors associated with coronary calcification in black descendants of African slaves living in isolated communities in Brazil, filling an existing gap in relation to the theme. The prevalence of coronary calcification was significant in the evaluated group, but lower than that described in the international literature. The presence of coronary atherosclerosis was associated only with traditionally described factors such as age. There was no association with other variables studied, including markers of kidney injury, inflammation and dyslipidemia.These results represent the first step towards further researches investigating other associations and outcomes of coronary atherosclerotic disease in Brazilian population groups with similar epidemiological characteristics.

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