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Genetic Ancestry Is Associated With Systolic Blood Pressure and Glucose in Brazilian Children and Adolescents

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Abstract

Background: Studies in admixed populations show that the prevalence of obesity and related diseases, such as type 2 diabetes and hypertension, may vary by ethnic group. The aim of this study was to investigate the relationship of genetic ancestry with phenotypes associated with obesity in a sample of school children and adolescents from Ouro Preto, Minas Gerais.

Methods: We used data from genetic ancestry of 189 individuals previously determined by 15 ancestry informative markers (AIMs), and segregated individuals into three ancestral groups (predominantly African (PAFR), predominantly mixed (PMIX), and predominantly European (PEUR)) using the proportion of ancestry. The ancestral groups were compared with mean values of anthropometric, clinical, biochemical, and demographic variables. The simple linear regression analysis was used to test whether differences in mean values of the dependent variables (blood pressure and glucose) between the ancestral groups were dependent on the other variables.

Results: Our results show that the proportions of African ($F = 144.2$, $P < 0.001$), Amerindian ($F = 15.5$, $P < 0.001$) and European ($F = 184.9$, $P < 0.001$) ancestry differed significantly ($P < 0.001$) among the three ancestral groups. PAFR individuals had higher mean blood pressure ($P \leq 0.029$) and glucose ($P = 0.025$) as compared to PEUR. In the linear regression model, the difference in systolic blood pressure (SBP) values remained significant in all models tested and independent of confounding variables ($P \leq 0.041$). The difference in diastolic blood pressure values observed in PAFR and PEUR groups did not remain significant when the metabolic profile was included in the tested model ($P = 0.097$). The difference in glucose values was significant only between PMIX and PEUR groups and independent of the settings ($P \leq 0.037$).

Conclusion: The positive correlation between genetic ancestry and SBP and glucose in Brazilian children and adolescents suggests the need for special care in the subgroups of this population.

Keywords: Genetic ancestry; Obesity-related risk phenotypes; Brazilian population

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Introduction

Admixed populations formed by mixing European (EUR), African (AFR), and Amerindians (AMR), such as the United States, Argentina, Puerto Rico, Mexico, and Brazil [1-5], have been studied to know the history of their ethnic background using ancestry-indicative markers (AIMs). AIMs are genetic markers that differ in allele frequencies between ancestral populations and have been used to infer the ethnic origin of populations [6]. In addition to being important in anthropological studies, knowing the ancestry of the population allows a better understanding of some diseases whose prevalence varies by ethnicity, for example, obesity, hypertension, and type 2 diabetes [7-12]. Studies in the US population, one of the most well-studied admixed populations, show a positive correlation between African ancestry and higher values of body mass index (BMI), weight, leg length, lean mass, bone mineral density and lower values of fat mass, and total, intra- and subcutaneous abdominal fat [9, 13, 14]. Conversely, European ancestry has been inversely correlated with lean body mass, BMI, weight, hip circumference, and skinfold thickness subscapularis, and positively correlated with waist circumference adjusted for BMI [14-16].

The population of Ouro Preto, State of Minas Gerais, southeastern Brazil, presents significant African influence as well as other admixed populations [1, 4]. Data from the census conducted by the Brazilian Institute of Geography and Sta-

Table 1. Anthropometric, Biochemical, Clinical, and Demographic Characteristics of the Ancestral Groups, Predominantly African (PAFR), Predominantly European (PEUR) and Predominantly Mixed (PMIX)

Variable	PAFR (n = 16), mean (SD)	PMIX (n = 122), mean (SD)	PEUR (n = 51), mean (SD)	P
Proportion of African markers	0.705 (0.1)	0.374 (0.2)	0.119 (0.1)	< 0.001
Proportion of Amerindian markers	0.113 (0.1)	0.202 (0.2)	0.090 (0.1)	< 0.001
Proportion of European markers	0.182 (0.1)	0.424 (0.2)	0.791 (0.1)	< 0.001
Age (years)	11.6 (2.0)	10.6 (1.9)	10.2 (2.2)	0.043
Weight (kg)	46.5 (15.6)	41.8 (14.7)	39.9 (15.5)	0.306
Height (cm)	147.7 (11.7)	143.9 (12.2)	141.8 (13.8)	0.246
Body mass index (kg/m^2)	20.7 (4.6)	19.6 (4.5)	19.2 (4.1)	0.484
Percentage of body fat (%)	32.3 (3.8)	31.1 (7.8)	29.5 (8.2)	0.338
Waist circumference (cm)	70.9 (12.0)	66.5 (11.3)	65.0 (13.0)	0.228
Birth weight (kg)	3.0 (817.3)	3.0 (662.1)	3.1 (564.2)	0.843
Diastolic blood pressure (mm Hg)	67.4 (10.1)	63.2 (9.3)	60.4 (9.3)	0.029
Systolic blood pressure (mm Hg)	107.6 (12.8)	102.1 (12.7)	97.1 (13.1)	0.011
Total cholesterol (mg/dL)	161.9 (29.1)	165.3 (27.4)	168.4 (31.4)	0.685
HDL-C (mg/dL)	50.7 (10.1)	54.8 (12.5)	55.2 (14.7)	0.455
LDL-C (mg/dL)	98.4 (27.6)	94.1 (25.8)	95.3 (32.6)	0.832
Triglycerides (mg/dL)	63.6 (36.9)	82.0 (37.5)	89.6 (68.8)	0.167
Glucose (mg/dL)	84.0 (8.9)	85.9 (8.1)	82.2 (7.7)	0.025
Insulin (μU/mL)	8.2 (4.8)	8.8 (8.3)	6.9 (3.8)	0.415
HOMA-IR	1.8 (1.2)	1.9 (2.0)	1.4 (0.8)	0.329

Data are reported as means ± SD. P value for ANOVA for continuous variables tested for comparison of frequency between ancestral groups. LDL-C: low-density lipoprotein-cholesterol; HDL-C: high-density lipoprotein-cholesterol; HOMA-IR: homeostasis model assessment of insulin resistance.

tistics (IBGE) conducted in 2010 show that the city's population is composed of 14.4% black, according to the classification of self-reported skin color [17]. Previous studies of genetic ancestry revealed that the African genetic contribution is even greater in this population, accounting for 33.3% [18]. Additionally, the population is marked by a high prevalence of excess weight and obesity in adults (30% overweight and 11.9% obese), in children and adolescents (8.7% overweight and 6.2% obese) [19, 20], and high morbidity (27.5%) due to diseases related to the circulatory system [17]. Among children and adolescents of this city, a prevalence has been observed for hypertension (5%), high prevalence of physical inactivity (73.9%), and high concentrations of total cholesterol (36.9%) and low-density lipoprotein-cholesterol (LDL-C) (5.8%), and low concentrations of high-density lipoprotein-cholesterol (HDL-C) (18.6%). In addition, 44.4% of children participants had 2 - 3 risk factors and 8.2% had 4 - 6 risk factors for cardiovascular diseases [20]. These data indicate that the population of Ouro Preto requires care. Although it is known that the prevalence of obesity and diseases related to cardiovascular morbidity, e.g., type 2 diabetes, hypertension, and dyslipidemia [8], may differ between ethnic groups, no epidemiological study has been carried out using genetic ancestry to segregate ethnic groups in the population.

In this study, we segregate a sample of Ouro Preto's population into groups according to the predominance of AIMs and evaluate the distribution of risk factors for cardiovascular diseases.

Materials and Methods

Study design

The study sample was composed of 189 individuals (10.6 ± 2.04 years) randomly selected from the cross-sectional study performed in 2006 in Ouro Preto, in southeastern Brazil [20]. The volunteers' legal guardians signed a consent form. This project was approved by the Research Ethics Committee of the Federal University of Ouro Preto.

The levels of lipids and glucose were performed by enzymatic colorimetric assay using a commercial kit (In Vitro Diagnostics, Itabira, MG, Brazil) and the Airone 200 (Crony Instruments, Rome, Italy). Insulin was determined by test access ultrasensitive insulin (Access Immunoassay System®) and homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the formula: (fasting plasma glucose (mmol/L) × fasting plasma insulin (mU/L))/22.5. Weight was measured using a Tanita BF542® (Tanita Corporation of America, Arlington Heights, IL, USA), and height and waist circumference (WC) were measured using a stadiometer (WCS Cardiomed, Curitiba, Brazil). BMI was calculated by dividing the weight (kg) and height squared (m^2). The tetrapolar bioelectrical impedance method was used to

Table 2. Simple Linear Regression Analysis for Distribution of Blood Pressure and Glucose Among Different Ancestral Groups Adjusted for Covariates

Dependent variable	Independent variables	PAFR, mean (SD)	PMIX, mean (SD)	PEUR, mean (SD)	P
Diastolic blood pressure (mm Hg)	Gender, age	65.9 (2.3)	63.1 (0.8)	61.0 (1.3)	0.155
	Gender, age, BMI, WC	65.7 (2.1)	63.2 (0.8)	61.1 (1.2)	0.143
	Gender, age, BMI, WC, glucose, LDL-C, HDL-C, TG	66.1 (2.1)[a]	63.3 (0.8)	60.9 (1.3)[a]	0.097
Systolic blood pressure (mm Hg)	Gender, age	106.4 (3.1)a	102.0 (1.1)	97.8 (1.8)a	0.041
	Gender, age, BMI, WC	106.3 (3.0)[a]	102.0 (1.1)[b]	98.0 (1.8)[a, b]	0.040
	Gender, age, BMI, WC, glucose, LDL-C, HDL-C, TG	106.8 (3.1)[a]	102.2 (1.1)[b]	97.3 (1.8)[a, b]	0.015
Glucose (mg/dL)	Gender, age	83.1 (2.0)	85.9 (0.7)[a]	82.6 (1.1)[a]	0.037
	Gender, age, BMI, WC	83.5 (1.9)	85.9 (0.7)[a]	82.1 (1.1)[a]	0.013
	Gender, age, BMI, WC, DBP, SBP, LDL-C, HDL-C, TG	84.7 (2.0)	85.9 (0.7)[a]	81.6 (1.2)[a]	0.009

Data are reported as mean ± SD. PAFR: predominantly African; PEUR: predominantly European; PMIX: predominantly mixed; BMI: body mass index; WC: waist circumference; DBP: diastolic blood pressure; SBP: systolic blood pressure; LDL-C: low-density lipoprotein-cholesterol; HDL-C: high-density lipoprotein- cholesterol; TG: triglycerides. *P value for simple linear regression analysis for distribution of blood pressure and glucose among different ancestral groups adjusted for covariates. [a, b]Significant differences between pairs of ancestral groups (PAFR, PMIX, and PEUR).

assess body fat percent by Deurenberg et al (1990) [21]. Blood pressure was measured three times at intervals of 10 min using pressure monitor Onrom® 705CP (Onrom Healthcare, Kyoto, Japan) with the volunteer being seated and his/her left arm held at heart level, and repeated by auscultation when the average exceeded the 90th percentile. The mean of three blood pressure measurements was considered.

Using the data of predetermined genetic ancestry for this same population sample [18], we subdivided the sample of individuals into two groups: 1) predominantly African (PAFR) and 2) predominantly European (PEUR), according to the predominance in proportion of AIMs (≥ 65%) of each African or European parental population, respectively. The third group (predominantly mixed (PMIX)) was composed by a single individual who presented ≥ 65% of Amerindian AIMs and by all individuals who showed no predominance of any of the markers (< 65% of the all ancestral AIMs).

To test for differences between ancestries groups, we used one-way analysis of variance (ANOVA) for continuous variables. The simple linear regression analysis was used to test whether differences in mean values of the dependents variables (blood pressure and glucose) between the ancestral groups (PAFR, PEUR and PMIX) were independent of the other variables: gender, age, BMI, WC, glucose, LDL-C, HDL-C, triglycerides (TG), systolic blood pressure (SBP), and diastolic blood pressure (DBP). Statistical analyses were performed using SPSS 18.0 (Chicago, IL, USA). P values equal to or less than 0.05 were considered statistically significant.

Results

This study involved a sample of 189 subjects, 101 (53.4%) girls and 88 (46.6%) boys, with a mean age of 10.6 ± 2.04 years.

Table 1 summarizes the distribution of the mean values of anthropometric, biochemical, clinical, and demographic characteristics evaluated for the individuals of the PAFR, PEUR, and PMIX groups. The PAFR group had on average 70.5% of African ancestry markers. The PEUR group had on average 79.1% of European ancestry markers. The PMIX group had on average 42.4%, 37.4%, and 20.2% of the European, African, and Amerindian markers, respectively. The ANOVA by a factor revealed that the average proportions of African ($F = 144.2$, $P < 0.001$), Amerindian ($F = 15.5$, $P < 0.001$), and European ($F = 184.9$, $P < 0.001$) ancestry differed significantly ($P < 0.001$) among the three ancestral groups. According to the distribution of average values of the variables, the PAFR group showed higher values by age ($P = 0.043$), DBP ($P = 0.029$), SBP ($P = 0.011$), and glucose ($P = 0.025$) as compared to the PEUR group. The PMIX group had higher glucose and intermediate values of blood pressure values as compared to the other two groups (PAFR and PEUR). There was no significant difference between the ancestral groups regarding the average values of other tested continuous variables (Table 1).

Table 2 shows analysis results using the simple linear regression model. According to the DBP values, although the PAFR group had DBP values higher than the other groups, this difference was significant only among the PAFR and PEUR groups for the third model tested. Moreover, this difference did not remain significant after adjustment for glucose, LDL-C, HDL-C, and TG ($P = 0.097$). The PAFR group had significantly higher SBP than did the PEUR, as well as the PMIX and PEUR groups in almost all models. This observed difference in SBP values between the ancestral groups was independent of sex, age, BMI, WC, glucose, LDL-C, HDL-C, and TG ($P \leq 0.041$). The PAFR group showed higher but not significant glucose values than that observed for PEUR. Significant differences in glucose values were observed between the PMIX and PEUR groups in all models. These differences were independent of gender, age, BMI, WC, SBP, DBP, LDL-C, HDL-C, and TG ($P \leq 0.037$).

Discussion

In this study, we investigated whether there is relationship between genetic ancestry and obesity-related risk phenotypes in a sample of children and adolescents (n = 189) from Ouro Preto, Minas Gerais, Brazil. To conduct this study, we used the highest cutoff point value of the AIMs (65%), which provided a reasonable number of individuals per ancestries groups. We believe that this cutoff value is appropriate because it is greater than the average value of the European AIMs described for Ouro Preto's population (50.3-53.9%) [18], and is the average of which is observed to southeastern Brazilian population (55.2-79.9%) [5, 22-24].

Although the prevalence of obesity, type 2 diabetes, and hypertension differs between ethnic groups, there are few correlation studies between genetic ancestry and risk phenotypes for these diseases. The association of higher SBP values with a higher proportion of African AIMs observed in our study corroborates with the results obtained for other admixed populations [25-28]. However, different results have also been observed [1, 29]. According Rizos and Elisaf (2014) [30], hypertension is an important risk factor in the development and progression of cardiovascular disease. Furthermore, hypertension manifests differently according to the patient's ancestral origin. Patients with African ancestry, for example, have a higher prevalence, higher severity, and early onset of hypertension, and a distinct response to treatment by antihypertensive medication as compared to the general population. Thus, it is important to consider all factors that could affect the choice, conduct, and response to treatment of arterial hypertension.

The association of higher glucose values with a higher proportion of African AIMs as compared to Europeans AIMs observed in our study corroborates with the results obtained by Reiner et al (2005) [1]. Additionally, the positive association between a higher proportion of African markers and insulin resistance has been reported in the US population [29], and different results have been described for the association between African markers and type 2 diabetes [25, 31].

The small number of subjects per ancestral group and the small number of the AIMs used were limitations to this study. However, this is an original study of an understudied population, and our results reinforce the idea that the prevalence of hypertension and diabetes may vary according to the proportion of AIMs in a population. Therefore, the search for risk factors, clinical manifestations, and treatment for these diseases should consider their genetic differences.

In conclusion, our results revealed associations between genetic ancestry and SBP and glucose values in Brazilian children and adolescents, which could suggest increased risk for cardiovascular diseases or type 2 diabetes for individuals with a prevalence of African AIMs.

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Conflicts of Interest

The authors declare no conflicts of interest.

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