DOI: 10.1590/1980-549720190002.supl.2

ORIGINAL ARTICLE / *ARTIGO ORIGINAL*

Reference values for laboratory tests of cholesterol, glycosylated hemoglobin and creatinine of the Brazilian adult population

Valores de referência para exames laboratoriais de colesterol, hemoglobina glicosilada e creatinina da população adulta brasileira

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ABSTRACT: ***Introduction:*** This article aims to estimate reference values for laboratory tests of cholesterol, glycosylated hemoglobin and creatinine for the Brazilian adult population. ***Methods:*** A descriptive study carried out with laboratory data from the National Health Survey (*Pesquisa Nacional de Saúde* – PNS). Samples of blood and urine were collected in a PNS subsample of 8,952 individuals aged 18 years old or older. To determine the reference values, exclusion criteria were applied: presence of previous diseases and outliers, defined by values outside the range estimated by the mean ± 1.96 × standard deviation. Subsequently, reference values were calculated according to gender, age group and race/skin color. ***Results:*** Differences in reference values according to gender were observed. Women had higher values of total cholesterol, LDL-c and HDL-c. Glycosylated hemoglobin showed similar values in relation to gender, and creatinine was higher among men. The mean reference values were higher in the elderly population, aged 60 years old or older. The mean, lower and upper limits of total cholesterol and fractions of non-white people were slightly lower. There was no difference according to race/skin color for glycosylated hemoglobin and creatinine. ***Conclusion:*** The establishment of national reference parameters for laboratory tests, adapted to the sociodemographic and geographic characteristics, provides relevant information for evaluation of diagnosis and treatment of chronic diseases in Brazil.

Keywords: Reference values. Cholesterol. Glycated hemoglobin A. Creatinine. Health surveys.

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Conflict of interests: nothing to declare - **Financial support**: Health Surveillance Secretariat, Ministry of Health (TED 147).

RESUMO: ***Introdução:*** Este artigo teve o objetivo de estimar valores de referência de exames laboratoriais de colesterol, hemoglobina glicosilada e creatinina para a população adulta brasileira. ***Métodos:*** Estudo descritivo realizado com os dados laboratoriais da Pesquisa Nacional de Saúde (PNS). Foram coletadas amostras de sangue e urina em subamostra da PNS constituída de 8.952 indivíduos de 18 anos ou mais. Para determinar os valores de referência, aplicaram-se critérios de exclusão, como a presença de doenças prévias e dos *outliers*, definidos pelos valores fora do intervalo estimado pela média ± 1,96 × desvio padrão. Posteriormente, foram calculados os valores de referência segundo sexo, faixa etária e raça/cor. ***Resultados:*** Observaram-se diferenças nos valores de referência de acordo com o sexo. O colesterol total, a lipoproteína de baixa densidade colesterol (LDL-c) e a lipoproteína de alta densidade colesterol (HDL-c) apresentaram valores mais elevados entre as mulheres. A hemoglobina glicosilada alcançou valores semelhantes segundo sexo, e a creatinina foi mais elevada entre os homens. Os valores médios de referência foram mais altos na população idosa, de 60 anos ou mais. A média e os limites inferiores e superiores do colesterol total e frações dos indivíduos não brancos foram ligeiramente mais baixos. Não houve diferença segundo raça/cor para hemoglobina glicosilada nem para creatinina. ***Conclusão:*** O estabelecimento de parâmetros nacionais de referência de exames laboratoriais, adaptados às características sociodemográficas e geográficas, fornece subsídios relevantes para a avaliação do diagnóstico e tratamento de doenças crônicas no Brasil.

Palavras-chave: Valores de referência. Colesterol. Hemoglobina glicada. Creatinina. Inquéritos epidemiológicos.

INTRODUCTION

Laboratory tests are important in clinical practice and promote better evidence and criteria for disease prevention, diagnosis and treatment[1,2].

One of the most important elements of a laboratory examination is the reference value, as it helps health professionals to interpret the results[3], however research based on reference values is rarely specified by the laboratories[4-7]. In addition, they typically adopt the values provided by the exam manufacturers and do not verify applicability to their customers[3].

When establishing reference ranges for any parameter, some characteristics must be considered: age, gender, race, environmental factors, nutritional status, degree of physical activity, menstrual cycle period, medication use and existence of chronic disease[8], and on the other hand, taking into account variations in sample collection, handling and laboratory measurement error[9].

In order to estimate the reference values, studies are performed based on a random sample of individuals from a given population through statistical modeling[4], and cross-sectional or longitudinal studies are often used. Such studies are predominantly performed in developed countries and their values are used as a global reference standard[1,10-12]. For example, The Canadian Health Measures Survey[2], collected more than 40 biomarkers in children, adults and the elderly in Canada and has become a benchmark for biochemical tests for Canadian and global populations, however these studies may not correspond to other countries, due to the different population characteristics.

Determining laboratory test reference values is a major challenge because it requires adequate methodology, which includes a representative sample of the population and care in the collection, processing, transport, and biochemical and statistical analyzes[1]. Therefore, the estimation of specific parameters for each population is not yet performed in most countries[13,14].

In Brazil, the reference values of other countries are still employed, which may cause interpretations that are not always reliable, since the Brazilian population is characterized by the miscegenation of a diversity of races, ethnicities, people, social and economic segments. It is therefore very important to obtain their own reference values. By conducting research on laboratory tests in a subsample of previously interviewed adult individuals in the National Health Survey (PNS) in 2014 and 2015, it was possible to obtain the first national reference values of the Brazilian adult population.

The aim of this study was to describe reference values for laboratory tests of cholesterol, glycosylated hemoglobin and creatinine in the Brazilian adult population based on the results of the PNS.

METHODS

This was a descriptive study using data from the PNS laboratory tests between 2014 and 2015. The PNS is a nationwide home-based study that uses three-stage probabilistic samples. Primary sampling units (PSUs) were the census tracts (or set of sectors). In each PSU, 10 to 14 households were randomly selected, and in each household, a resident aged 18 years or older was chosen. The PNS was performed in 69,954 households and 60,202 adult individuals, selected in each household with equal probability, were interviewed[15].

The selection of the subsample for the collection of biological material occurred in 25% of the census tracts, chosen with probability proportional to the size, which was measured by the inverse of the minimum distance between a small municipality and a large population municipality, obeying the stratification of the PNS sample. Assuming the non-response rate of 20%, the expected number of individuals with laboratory data was approximately 12,000, however laboratory tests were performed in a sample of 8,952 individuals, with a greater than expected loss. Among the limitations, the following stand out: the difficulty of locating the address by the hired laboratory; the refusal of the selected resident to collect biological material; the long time between the application of the questionnaire and the visit of the laboratory agent; the operational difficulties of transporting biological material, in addition to the nature of this study, which requires more from the participant and, admittedly, has a high refusal rate[16].

Given that the non-response rates were different according to the PNS strata, it was necessary to use a post-stratification procedure based on the total PND sample. Post-stratification weights were estimated according to gender, age, education level, race / skin color and geographic macroregion, based on the data of the residents selected for the individual interviews in the initial phase of the PNS. Despite the losses, the subsample of more than eight thousand people made it possible to find reference values for several biological markers for the first time in Brazil.

The research participants signed the informed consent form, received explanations about the collection of peripheral blood and urine and were instructed on how to receive the report containing the test results. Samples were collected at any time of the day, using ethylenediamine tetra acetic acid (EDTA) tubes and serum gel tubes. Samples were evaluated by automated cell analyzer. Full details of the exam collection procedure are available in the sample collection and submission procedures manual[17].

Total cholesterol, low density lipoprotein (LDL) and high density lipoprotein (HDL) were collected in a gel tube. Waiting 30 minutes for the clot to retract and then centrifuging was performed. The sample was sent refrigerated between 2 and 8°C, with temperature control in the various stages. These parameters were measured by automated enzymatic/colorimetric method. Glycosylated hemoglobin was collected in an EDTA tube and dosed by high performance liquid ion exchange chromatography (HPLC). Then, creatinine was collected in a gel tube and was dosed by the Jaffé method without deproteinization.

In order to determine the reference values, individuals who did not have test result information, those with a reported diagnosis of certain diseases and pregnant women were initially excluded, since the results of laboratory tests of these persons could affect national reference values. Considering the questions of the PNS regarding pregnancy status and concerning the diagnosis of chronic noncommunicable diseases, cited in parentheses, the exclusion criteria applied were:

- Total cholesterol, LDL-c and HDL-c: exclusion of pregnancy (P005), heart disease (Q063), diabetes (Q030), stroke (Q068), and estimated glomerular filtration rate (GFR) <60 mL / min / 1.73 m2 (1,521 cases for total cholesterol, 1,538 cases for HDL-c and 1,520 cases for LDL-c);
- Glycosylated hemoglobin: exclusion of those indicating diabetes (Q030), stroke (Q068) and estimated GFR <60 mL / min / 1.73 m2 (1,191 cases);
- Creatinine: exclusion of those who report renal failure (Q124) and estimated GFR <60 mL / min / 1.73 m2 (665 cases).

After excluding the cases, the population sample without previous diagnosis of specific diseases was stratified according to gender (male and female), age group (18 to 59 years and 60 years or older) and race/skin color (black, brown and white). Mean, standard deviation (SD), minimum and maximum values and distribution curve were calculated for each stratum. Data from each stratum then underwent the process of removing outliers, defined as values above or below the range [mean + 1.96 SD].

After removing the outliers, a database of the population without previous diagnosis of specific diseases, stratified by sex, age group and race/skin color were obtained, allowing to estimate the reference values (mean value of the stratified distribution) and the lower limits. (average - 1.96 SD) and higher (average + 1.96SD) according to gender, age range and race / color. The analyzes were performed using the Statistical Analysis System (SAS) software.

RESULTS

Reference values were calculated for the following biochemical tests: total cholesterol, HDL-c, LDL-c, glycosylated hemoglobin and creatinine. In the example in Figure 1, the behavior of total cholesterol distribution with the normalization of values according to sex can be observed. After excluding pregnant women, individuals with heart disease, diabetes, or stroke and those with estimated GFR less than 60 mL/min/1.73 m^2, the mean total cholesterol for males was 181.6. mg/dL (Figure 1A), and for females, 187.0 mg/dL (Figure 1C). By removing the outliers, the curve is flattened and the values changed: averages 178.8 mg/dL for males (Figure 1B) and 184.2 mg/dL for females (Figure 1D).

Table 1 shows the reference values of biochemical markers for the population according to gender. Women had higher mean values than men regarding total cholesterol, HDL-c and LDL-c. The values obtained for glycosylated hemoglobin were similar, however for creatinine the values were higher for males, with a lower limit (LL) of 0.7 mg/dL and an upper limit (UL) of 1.2 mg/dL (1.0 mg/dL) than for females, who showed an LL of 0.5 mg/dL and UL of 1.0 mg/dL (average 0.8 mg/dL).

Table 2 shows the reference values for males according to age group. Regarding total cholesterol, the LL and UL for the 18 to 59 age group were 112.5 and 241.4 mg/dL, respectively (mean 176.9 mg/dL), and for those 60 years or older, the values increased to 131.2 and 246.8 mg/dL (mean 189.0 mg/dL). As for HDL-c, the limits and mean values for the age groups were similar. Regarding LDL-c, the elderly had higher values, with LDL-c limits of 62.1 mg/dL and 156.0 mg/dL (mean 109.1 mg/dL). For glycosylated hemoglobin, LL and UL and mean values presented values close to the age groups, but slightly higher among the elderly (average of 5.3% for individuals from 18 to 59 years and 5.5% for individuals of 60 years or older). The values for creatinine were similar; the mean value was 1.0 mg/dL for both age groups analyzed, with limits of 0.7 and 1.2 mg/dL for individuals aged 18 to 59 years, and among the elderly, limits of 0.7 and 1.3 mg/dL.

Table 3 shows the reference values of biochemical markers for females according to age group. Practically all exams showed higher average limits and values for the age group 60 years and older. For total cholesterol, the female population aged 18 to 59 years reached an average of 180.3 and 202.4 mg/dL among the elderly. HDL-c showed similar values, regardless of age group. LDL-c had an average of 100.7 mg/dL (LL = 53.3 mg/dL and UL = 148.1 mg/dL) among women aged 18 to 59 years, and in the group 60 years or older, the mean was 114.9 mg/dL (LL = 66.4 mg/dL and UL = 163.3 mg/dL). Glycosylated hemoglobin exhibited values similar to those found in the male population. Creatinine was lower among women, with an average of 0.7 mg/dL for the 18 to 59 year old group and 0.8 mg/dL for the 60 or older age group.

For both sexes, the mean values of most tests increased in the age group of 60 years or older. The mean values and estimated limits for total cholesterol, HDL-c and LDL-c in the female population were higher than those found for the male population.

Regarding race/skin color, it was observed that the mean values and LL of total cholesterol, LDL-c and HDL-c are higher among women. Brown individuals of both sexes had the lowest reference values for most of the exams performed. The mean total cholesterol of white male subjects was 180.3 mg/dL (LL = 114.2 mg/dL and UL = 246.4 mg/dL), while the average black individuals was 179.3 mg/dL (LL = 120.3 mg / dL and UL= 238.2 mg / dL)

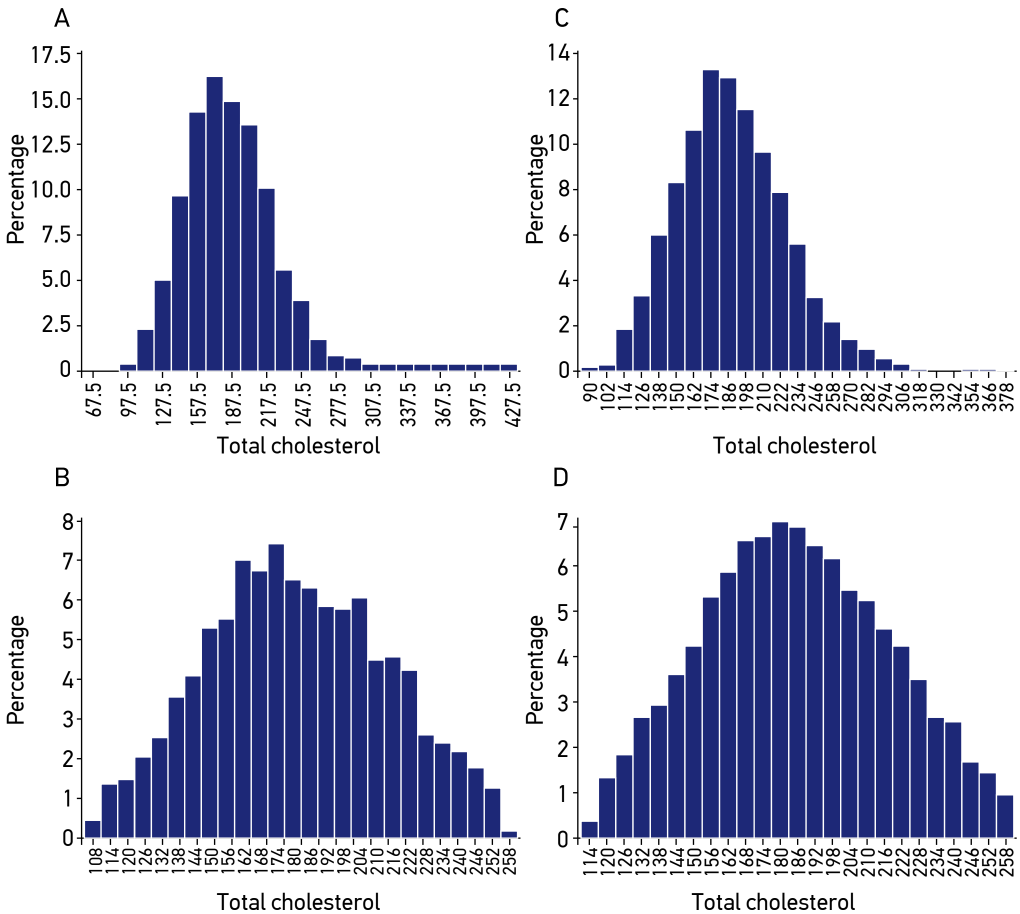

Figure 1. Exemplification of the methodology for calculating the reference values for total cholesterol: (A) after exclusion of heart disease, diabetes and stroke (stroke) and people with glomerular filtration rate (GFR) <60 / Male: mean = 181.6 mg/dL, standard deviation (SD) = 38.5 mg/dL; minimum = 68 mg/dL; maximum = 433 mg/dL; total observations = 3,607; (B) after exclusion of outliers (mean ± 1.96 SD) / Male: mean = 178.8 mg/dL, standard deviation (SD) = 32.8 mg/dL; minimum = 107 mg/dL; maximum = 257 mg/dL; total observations = 3,468; (C) after exclusion of pregnancy, heart disease, diabetes and stroke and people with GFR <60 / Female: mean = 187.0 mg/dL, standard deviation (SD) = 37.1 mg/dL; minimum = 84 mg/dL; maximum = 379 mg/dL; total observations = 3,825; (D) after first exclusion of outliers (mean ± 1.96 SD) / Female: mean = 184.2 mg/dL, standard deviation (SD) = 32.3 mg/dL; minimum = 115 mg/dL; maximum = 259 mg/dL; total observations = 3,658.

Table 1. Reference values of biochemical markers by sex, Brazil, National Health Survey (PNS), 2014–2015.

Exams	Sex	Average	LL	UL	Min.	Max.	SD	Sample
Total Cholesterol total (mg/dL)	Male	178.8	114.5	243.0	107.0	257.0	32.8	3,468
	Female	184.2	121.0	247.5	1150	259.0	32.3	3,658
HDL cholesterol (mg/dL)	Male	42.0	23.0	61.0	20.0	66.0	9.7	3,430
	Female	48.8	27.4	70.3	24.0	76.0	10.9	3,659
LDL cholesterol (mg/dL)	Male	100.8	51.0	150.5	46.0	159.0	25.4	3,460
	Female	103.3	54.7	151.8	49.0	163.0	24.8	3,639
Glycosylated Hemoglobin (%)	Male	5.3	4.5	6.1	4.1	6.7	0.4	3,667
	Female	5.3	4.4	6.2	4.1	6.7	0.4	3,922
Creatinine (mg/dL)	Male	1.0	0.7	1.2	0.7	1.3	0.1	3,805
	Female	0.8	0.5	1.0	0.5	1.0	0.1	4,146

LL: lower limit (2.5% confidence interval - unilateral left 2.5%CI); UL: upper limit (right unilateral 2.5% CI); Min .: minimum value; Max .: maximum value; SD: standard deviation; HDL: high density lipoprotein; LDL: low density lipoprotein.

Table 2. Reference values of biochemical markers by age group and male gender, Brazil, National Health Survey (PNS), 2014–2015.

Exams	Male							
	Age group	Average	LL	UL	Min.	Max.	SD	Sample
Total cholesterol (mg/dL)	18 to 59 years	176.9	112.5	241.4	104.0	256.0	32.9	2,887
	60 years or older	189.0	131.2	246.8	123.0	254.0	29.5	572
HDL cholesterol (mg/dL)	18 to 59 years	42.1	23.1	61.0	20.0	66.0	9.7	2,851
	60 years or older	41.4	22.7	60.1	20.0	65.0	9.6	575
LDL cholesterol (mg/dL)	18 to 59 years	99.2	49.7	148.8	45.0	158.0	25.3	2,879
	60 years or older	109.1	62.1	156.0	55.0	165.0	23.9	575
Glycosylated Hemoglobin (%)	18 to 59 years	5.3	4.5	6.1	4.2	6.5	0.4	3,011
	60 years or older	5.5	4.6	6.5	4.0	7.2	0.5	657
Creatinine (mg/dL)	18 to 59 years	1.0	0.7	1.2	0.7	1.2	0.1	3,001
	60 years or older	1.0	0.7	1.3	0.6	1.4	0.2	752

LL: lower limit (2.5% confidence interval - unilateral left 2.5% CI); UL: upper limit (right unilateral 2.5% CI); Min .: minimum value; Max .: maximum value; SD: standard deviation; HDL: high density lipoprotein; LDL: low density lipoprotein.

and the brown 177.5 mg/dL (LL = 113.2 mg / dL and UL = 241.8 mg / dL). Total cholesterol also differed by race / color for females. HDL-c among the black race/black individuals averaged 42.7 mg/dL for the male population, while black and brown individuals showed lower values. In relation to males and LDL-c, there was a decreasing gradient between whites (102.4 mg/dL), blacks (102.0 mg/dL) and browns (99.3 mg/dL), respectively, with limits varying. from 49.8 to 153.0 mg/dL. However, for females, the black race/skin color showed the lowest mean value for LDL-c (white: 104.3 mg/dL; black: 100.7 mg/dL; brown: 102.6 mg/dL), with limits ranging from 53.3 to 153.0 mg/dL. For glycosylated hemoglobin, the reference intervals indicated no differences according to gender and race/skin color. Although lower among women, there was also no differences in creatinine regarding race/skin color (Table 4).

DISCUSSION

In the present study, national reference values for biochemical tests were calculated according to sex, age and race/skin color for total cholesterol and fractions, glycosylated hemoglobin and creatinine. Guidelines used include reference ranges that cover 95% of the population with no previous diagnosis of certain diseases, such as diabetes, stroke or kidney failure.

Table 3. Reference values of biochemical markers by age group and female gender, Brazil, National Health Survey (PNS), 2014–2015.

Exams	Female							
	Age group	Average	LL	UL	Min	Max	SD	Sample
Total cholesterol (mg/dL)	18 to 59 years	180.3	119.2	241.5	113.0	254.0	31.2	3,005
	60 years or older	202.4	142.5	262.3	133.0	274.0	30.6	638
HDL cholesterol (mg/dL)	18 to 59 years	48.8	27.3	70.4	24.0	76.0	11.0	3,025
	60 years or older	49.1	27.6	70.6	24.0	78.0	11.0	640
LDL cholesterol (mg/dL)	18 to 59 years	100.7	53.3	148.1	47.0	159.0	24.2	3,002
	60 years or older	114.9	66.4	163.3	58.0	174.0	24.7	638
Glycosylated Hemoglobin (%)	18 to 59 years	5.2	4.4	6.1	4.0	6.6	0.4	3,219
	60 years or older	5.6	4.7	6.5	4.3	6.9	0.4	703
Creatinine (mg/dL)	18 to 59 years	0.7	0.5	1.0	0.5	1.0	0.1	3,294
	60 years or older	0.8	0.5	1.1	0.5	1.2	0.1	907

LL: lower limit (2.5% confidence interval - unilateral left CI2.5%); UL: upper limit (right unilateral 2.5% CI); Min .: minimum value; Max .: maximum value; SD: standard deviation; HDL: high density lipoprotein; LDL: low density lipoprotein.

The results showed differences by gender, with women showing higher values than men regarding total cholesterol and HDL-c, probably related to hormonal factors and menopause due to estrogen reduction[18,19]. The mean values for LDL-c were similar. This result is noteworthy, since LDL-c has been considered the main marker and predictor of cardiac risk and should be monitored[20].

In 2015, The Canadian Health Measures Survey[2], found HDL-c reference values of 31 to 70 mg/dL, a median of 46 mg/dL among men aged 15 to 79 years, and in women, values from 35 to 89 mg/dL (median 58 mg/dL).

Regarding LDL-c, a study conducted in Canada[2] showed reference limits for the 25 to 49 year age group of 62 and 189 mg/dL (median 124 mg/dL) for men and 50 to 178 mg/dL (median 104 mg/dL) for women. For the age group between 50 and 79 years, LDL-c values were the same for men and women, 73 to 189 mg/dL (median of 127 mg dL). In Brazil, although the reference values for LDL-c were estimated for different age groups from those used in the study in Canada[2], the reference values for the total population were lower and followed the same upward trend in the older age groups.

Table 4. Reference values of biochemical markers, according to race / color and sex, Brazil, PNS, 2014-2015.

Exams	Race / color	Male					Female				
		Average	LL	UL	SD	Sample	Average	LL	UL	SD	Sample
Total cholesterol (mg/dL)	White	180.3	114.2	246.4	33.7	1,615	186.2	121.3	251.1	33.1	1,738
	Black	179.3	120.3	238.2	30.1	325	185.4	130.9	239.9	27.8	329
	Brown	177.5	113.2	241.8	32.8	1,506	182.6	119.6	245.6	32.2	1,544
HDL cholesterol (mg/dL)	White	41.8	23.0	60.6	9.6	1,583	49.9	27.7	72.1	11.3	1,719
	Black	42.7	21.8	63.7	10.7	327	49.5	28.8	70.1	10.5	337
	Brown	41.8	23.4	60.2	9.4	1,480	47.5	27.2	67.9	10.4	1,551
LDL cholesterol (mg/dL)	White	102.4	51.7	153.0	25.9	1,595	104.3	55.6	153.0	24.8	1,713
	Black	102.0	54.8	149.2	24.1	326	100.7	55.9	145.4	22.8	332
	Brown	99.3	49.8	148.7	25.2	1,510	102.6	53.3	151.9	25.2	1,551
Glycosilated Hemoglobin (%)	White	5.3	4.5	6.1	0.4	1,707	5.3	4.5	6.1	0.4	1,837
	Black	5.4	4.7	6.2	0.4	332	5.4	4.4	6.5	0.5	355
	Brown	5.3	4.5	6.1	0.4	1,577	5.3	4.4	6.2	0.5	1,667
Creatinine (mg/dL)	White	1.0	0.7	1.2	0.1	1,759	0.8	0.5	1.0	0.1	1,993
	Black	1.0	0.7	1.3	0.2	357	0.8	0.5	1.1	0.1	406
	Brown	1.0	0.7	1.2	0.1	1,619	0.8	0.5	1.0	0.1	1,727

LL: lower limit (2.5% confidence interval - unilateral left CI2.5%); UL: upper limit (right unilateral 2.5% CI); SD: standard deviation; HDL: high density lipoprotein; LDL: low density lipoprotein.

The values presented in this article reinforce the need for further studies on therapeutic targets, especially for individuals at cardiovascular risk. According to the Brazilian Guideline for Dyslipidemias and Prevention of Atherosclerosis[21], individuals must maintain LDL-c level <130 mg/dL to be considered low cardiovascular risk. According to the reference values found here, with critical upper limits of approximately 150 mg/dL, 13% of the population would be eligible for statin use as per current guidelines, although they are within the reference range.

The Guideline of the American College of Cardiology/American Heart Association (ACC/AHA) [22], in its update, does not adopt therapeutic targets, but rather risk calculators to estimate the risk of cardiovascular complications in 10 years. Therefore, it is suggested that these results be evaluated by the Brazilian Society of Cardiology for further discussion of risk and drug treatment protocols.

Glycosylated hemoglobin is an important marker of diabetes and prediabetes[23]. Based on the PNS data, no differences were found in gender or race/skin color for the Brazilian population.

In Canada[2], creatinine values for men aged 16 to 79 years were 0.7 to 1.2 mg/dL, with a median of 0.9 mg/dL, and for women, 0.6 to 1 0.0 mg/dL, with a median 0.7 mg/dL. In Brazil, the values were similar to those found in Canada, slightly higher for men than for women, which may be due to the greater muscle mass of men.

The current study also found that creatinine has similar baseline values according to race/skin color, differing from findings in US studies that proposed changes in the calculation formula for GFR estimation by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)[24,25] among people of African descent. As with other Brazilian studies[26] that conducted cross-sectional studies of serum creatinine levels, the findings of the present study show that it is not justified to use different formulas to estimate GFR according to race/skin color. Thus, further studies are needed, especially those which compare creatinine, considering the specificities between the different race/skin color categories and among people who already have renal function impairment.

The reference values for the elderly may differ from younger people due to the aging process, as well as subclinical diseases and common comorbidities among the elderly[18]. Lipid markers (total cholesterol, LDL-c and HDL-c) showed higher mean reference values among the elderly, and may reflect the adopted lifestyles, such as diet, physical inactivity and obesity[1]. Renal markers such as creatinine may increase with age due to physiological aging of the kidneys and may be due to diseases such as diabetes mellitus and hypertension[27].

Among the limitations of the present study, it is mentioned that, despite the exclusion of individuals previously diagnosed with certain diseases, the population eligible for the study cannot be considered as healthy, since sick people without previous diagnosis may have been included, besides obese or drug users, which may affect the reference values. However, this study, pioneering the initiative to calculate reference values through population health survey information, will contribute to a broader discussion of the use of nationally estimated biochemical markers to monitor certain health conditions.

CONCLUSION

The PNS made it possible to carry out the first national study that establishes the benchmarks of laboratory tests adapted to the ethnic, socio-cultural, environmental, genetic characteristics and, therefore, more appropriate to the population of Brazil. In this sense, adopting standards of reference for one's own country is an important measure in clinical practice.

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Received on: 01/08/2019
Final version presented on: 03/11/2019
Approved on: 03/19/2019

Author contributions: C. L. S. coordinated the statistical analysis of the data. A. W. F. and W. S. A. were responsible for preparing the results and tables. D. C. M. elaborated the discussion of the results. All authors participated in the elaboration of the text.