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#### **ORIGINAL ARTICLE /** ARTIGO ORIGINAL

# Reference values for blood count laboratory tests in the Brazilian adult population, National Health Survey

Valores de referência para exames laboratoriais de hemograma da população adulta brasileira: Pesquisa Nacional de Saúde

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**ABSTRACT:** *Objective:* To describe reference values for blood counts obtained from laboratory tests in the Brazilian adult population according to laboratory results from the National Health Survey (*Pesquisa Nacional de Saúde* — PNS), by gender, age group and skin color. *Methods:* The initial sample consisted of 8,952 adults. To determine the reference values, individuals with prior diseases and outliers were excluded. Mean values, standard deviation and limits were stratified by gender, age group and skin color. *Results:* For red blood cells, men presented a mean value of 5.0 million per mm<sup>3</sup> (limits: 4.3–5.8) and women, 4.5 million per mm<sup>3</sup> (limits: 3.9–5.1). Hemoglobin levels were higher among men with a mean of 14.9 g/dL (13.0–16.9), and in women, 13.2 g/dL (11.5–14.9). The mean number of white blood cells among men was 6.142/mm<sup>3</sup> (2.843–9.440) and 6.426/mm<sup>3</sup> (2.883–9.969) for women. Other parameters showed close values between the genders. Regarding age groups and skin color, mean values, standard deviation and limits of the exams presented small variations. *Conclusion:* Hematological reference values based on the national survey allow for the establishment of specific reference limits for gender, age and skin color. The results presented here may contribute to the establishment of better evidence and criteria for the care, diagnosis and treatment of diseases.

Keywords: Blood cell count. Leukocytes. Hematologic tests. Hemoglobin. Health surveys.

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**RESUMO:** *Objetivo:* Descrever valores de referência para exames laboratoriais de hemograma da população adulta brasileira segundo os resultados laboratoriais da Pesquisa Nacional de Saúde (PNS) estratificados por sexo, faixa etária e cor da pele. *Métodos:* A amostra foi constituída inicialmente de 8.952 adultos. Para determinar os valores de referência, excluíram-se indivíduos com doenças prévias e os *outliers*. Valores médios, desvio padrão e limites foram estratificados por sexo, faixa etária e cor da pele. *Resultados:* Para glóbulos vermelhos, os homens apresentaram valor médio de 5,0 milhões por mm<sup>3</sup> (limites: 4,3–5,8) e as mulheres 4,5 milhões por mm<sup>3</sup> (limites: 3,9–5,1). Valores de hemoglobina entre homens exibiram média de 14,9 g/dL (13,0–16,9) e entre mulheres de 13,2 g/dL (11,5–14,9). A média dos glóbulos brancos entre os homens foi de 6.142/mm<sup>3</sup> (2.843–9.440) e entre as mulheres de 6.426/mm<sup>3</sup> (2.883–9.969). Outros parâmetros mostraram valores próximos entre os sexos. Com relação a faixas etárias e cor da pele, valores médios, desvio padrão e limites dos exames apontaram pequenas variações. *Conclusão:* Os valores de referência hematológicos com base em inquérito nacional permitem a definição de limites de referência específicos por sexo, idade e cor da pele. Os resultados aqui expostos podem contribuir para o estabelecimento de melhores evidências e critérios para o cuidado, diagnóstico e tratamento de doenças.

Palavras-chave: Contagem de células sanguíneas. Leucócitos. Testes hematológicos. Hemoglobinas. Inquéritos epidemiológicos.

#### INTRODUCTION

Health care should be based on scientific evidence, including appropriate parameters for biochemical testing<sup>1</sup>. Reference values are one of the most important elements of a laboratory examination, as they assist health professionals in interpreting results, care, diagnosis and treatment of diseases<sup>2</sup>. However, the origin of these values is rarely specified by laboratories, and these values are often used without observing if they apply to the specific population<sup>3-6</sup>. Reference values may be influenced by individual, populational and ecological factors such as age, gender, race, socioeconomic status, the presence of risk factors, physiological state, geography, and exposure to chemical, physical and biological agents. Therefore, they must be different between populations<sup>7-9</sup>.

To estimate reference values, it is important to conduct studies based on representative population surveys for the correct interpretation of results<sup>1</sup>. These values can be obtained through cross-sectional or longitudinal studies, in which individuals are followed over time<sup>10</sup>.

Determining laboratory test benchmarks is a major challenge because it requires proper methodology, which includes representative population sampling and methodological care in the collection, processing, and transport, and in the biochemical and statistical analyses<sup>10</sup>. As such, estimating specific parameters for each population is not yet a reality for some countries, being restricted to developed countries that conduct population surveys. These surveys are therefore, used as global parameters<sup>9,11</sup>.

To obtain estimates that are appropriate for their population, some countries adopt specific surveys, such as the Canadian Laboratory Initiative on Pediatric Reference Intervals (CALIPER)<sup>12-14</sup> or the Canadian Health Measures Survey (CHMS)<sup>14,15</sup>. In Australia, laboratories enrolled in the Royal College of Pathologists of Australasia Quality Assurance Program set parameters on hematology reference ranges<sup>16</sup>.

In Brazil, the reference values of other countries are still used, however the National Health Survey (*Pesquisa Nacional de Saúde* — PNS) included the collection of biochemical blood and urine tests in its scope<sup>17</sup> and thus, among other objectives obtained the first reference values for the Brazilian adult population. The establishment of specific reference values for the Brazilian population can provide important information that allows for a more reliable and adequate interpretation of laboratory test results. In addition, it avoids the use of reference values from other countries, mainly because the Brazilian population is characterized by the miscegenation of a diversity of races, ethnicities, peoples, in addition to social and economic segments.

Due to the importance of standardizing reference values, this study aimed to describe reference values for the laboratory tests showing blood counts from the Brazilian adult population according to the laboratory results from the PNS.

#### METHODS

The study was a descriptive, epidemiological survey, and used data from PNS laboratory exams from 2014 to 2015.

The PNS is a nationwide household-based, cross-sectional survey that uses three-stage probabilistic samples. The primary sampling units (UPAs) were the census tracts or set of tracts, the secondary units, the households, and the tertiary units, the adult residents aged 18 years or older. Details on the sampling and weighting processes are provided in the PNS publications on the results<sup>17,18</sup>.

The PNS was performed in 69,954 households and 60,202 adult individuals were interviewed. The adult individuals were selected in each household. The selection of the subsample for the laboratory was defined in 25% of the census tracts, obeying the stratification of the PNS sample. However, several factors caused a larger loss in the subsample of individuals indicated for the laboratory exams. Among these factors, the hired laboratory's difficulty in locating the address and the selected resident's refusal to participate in the collection of biological material stand out. Thus, the sample consisted of 8,952 people, and post-stratification weights were adopted according to gender, age, education and region. Despite the losses, the subsample allowed us to find, for the first time in Brazil, reference values for laboratory tests, including blood counts.

The research participants signed the informed consent form and were instructed on how to receive the report containing the test results. Subsequently, peripheral blood collections occurred.

Samples were collected at any time of the day, using ethylenediamine tetraacetic acid (EDTA). Samples were examined using an automated cell analyzer. Complete details regarding the exam collection procedure are available in the Sample Collection and Submission Procedures Manual<sup>19</sup>.

The collection and analysis of the biological material were carried out through a consortium with private laboratories. The laboratories were chosen based on the fact that they met the quality control criteria of the Ministry of Health and they complied with current rules for collection, transport and processing of biological material<sup>12</sup>.

For the calculation of the reference values, women who reported being pregnant at the time of the survey, those with a diagnosis of severe medical disease or chronic diseases such as cardio-vascular disease (CVD) – infarction, angina, stroke – , cancer, arthritis, and chronic kidney disease (glomerular filtration rate < 60) were excluded from the database. In the case of the reference values calculation for red cells, we also exclude people with any hemoglobinopathy.

After excluding the cases, the population base without a previous diagnosis of certain diseases was stratified according to gender (male and female), age group (18 to 59 years and 60 years or older) and race/skin color (dark-skinned black, light-skinned black, and white). For each stratum, the mean, standard deviation (SD), and minimum and maximum values were calculated. The data from each stratum then underwent the process of removing outliers, defined as values above or below the range (mean  $\pm$  1.96 SD).

After excluding the outliers, a database of the population without a previous diagnosis of certain diseases stratified by gender, age range and race/skin color was obtained, allowing for the estimation of reference values (mean value of the stratified distribution) and the lower (mean - 1.96 SD) and upper (mean + 1.96 SD) limits according to gender, age range and race/color. Analyses were performed using the Statistical Analysis System (SAS) software.

The following items were evaluated in the exams: red blood cells, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red blood cell distribution width (RDW), white blood cells, absolute neutrophils, neutrophils, absolute eosinophils, eosinophils, absolute basophils, basophils, absolute lymphocytes, lymphocytes, absolute monocytes, monocytes, platelets and platelet volume.

The PNS was approved by the National Research Ethics Commission (*Comissão Nacional de Ética em Pesquisa* – CONEP) of the Ministry of Health. Adult participation in the research was voluntary and confidentiality of their information was guaranteed. Subjects selected for the research provided informed consent for all of the research procedures, including interviewing and blood and urine collection.

#### RESULTS

The red blood cells in men averaged 5.0 million/mm<sup>3</sup> (limits: 4.3–5.8). These values were lower for women, with an average of 4.5 million/mm<sup>3</sup> (limits: 3.9–5.1). Hemoglobin values among men averaged 14.9 g/dL (limits: 13.0–16.9) and among women, 13.2 g/dL (limits: 11.5–14.9). Hematocrit was higher among men, with an average of 45.8% (limits: 39.7–52.0), than in women, with an average of 40.7% (limits: 35.3–46.1). The MCV in men averaged 91.2 fL (limits: 81.8–100.6) and in women, 90.6 fl (limits: 81.0–100.2). The mean MCH value in men was 29.8 pg (limits: 26.9–32.6) and in women 29.4 pg (limits: 26.3–32.4). The MCHC in men was 32.6 g/dL (limits: 30.6–34.6) and among women, 32.4 g/dL (limits:

30.5–34.3). The average RDW among men was 13.6% (limits: 12.0–15.3) and among women, 13.7% (limits: 11.9–15.5) (Table 1).

For the white blood series, the average white blood cell count among men was 6,142 per mm<sup>3</sup> (limits: 2,843–9,440) and for women, 6,426 per mm<sup>3</sup> (limits: 2,883–9,969). Absolute neutrophil values among men averaged 3,273 per mm<sup>3</sup> (limits: 576–5,971); and for eosinophils, the average was 258 per mm<sup>3</sup> (limits: 0–660). For basophils, the average was 29 per mm<sup>3</sup> (limits: 0-62); and lymphocytes showed an average of 2,045 average per mm<sup>3</sup> (limits: 720-3,370). For monocytes, an average of 412 per mm<sup>3</sup> was found (limits: 11–812). Absolute values among women were: for neutrophils, an average of 3,543 per mm<sup>3</sup> (limits: 612–6,474); for eosinophils, an average of 210 per mm<sup>3</sup> (limits: 0–550); for basophils, an average of 31 per mm<sup>3</sup> (limits: 0–72); for lymphocytes, an average of 2,105 per mm<sup>3</sup> (limits: 796–3,414); and for monocytes, an average of 357 per mm<sup>3</sup> (limits: 22–692). For platelets, the average among men was 213,975 per mm<sup>3</sup> (limits: 128,177–299,774), and for women, 239,325 platelets per mm<sup>3</sup> (limits: 135,606–343,044). The platelet volume for men was 10.2 fL (limits: 8.–12.4), and for women, 10.3 fL (limits: 8.0–12.5) (Table 2).

			Masculi	ne		Feminine					
Tests	Average	Lower limit	Upper limit	Standard deviation		Average	Lower limit	Upper limit	Standard deviation	Sample	
Red blood cells (millions/mm³)	5.0	4.3	5.8	0.4	3,232	4.5	3.9	5.1	0.3	3,303	
Hemoglobin (g/dL)	14.9	13.0	16.9	1.0	3,251	13.2	11.5	14.9	0.9	3,289	
Hematocrit (%)	45.8	39.7	52.0	3.2	3,262	40.7	35.3	46.1	2.8	3,278	
Average corpuscular volume (fL)	91.2	81.8	100.6	4.8	3,239	90.6	81.0	100.2	4.9	3,264	
Average corpuscular hemoglobin (pg)	29.8	26.9	32.6	1.5	3,251	29.4	26.3	32.4	1.5	3,280	
Average corpuscular hemoglobin concentration (g/dL)	32.6	30.6	34.6	1.0	3,218	32.4	30.5	34.3	1.0	3,278	
Red cell distribution range (RDW) (%)	13.6	12.0	15.3	0.8	3,324	13.7	11.9	15.5	0.9	3,337	

Table 1. Reference values of the hematological markers of the red blood series according to gender. National Health Survey, Brazil, 2014–2015.

Concerning the red blood series and age group, the red blood cells of men in the 18-59 age group had an average value of 5.1 million (limits: 4.4–5.8 million per mm<sup>3</sup>), and in the group 60 years and older, the average was 4.8 million (limits: 4.0–5.6 million per mm<sup>3</sup>), while for women, the average was 4.5 million for both age groups (limits: 3.9–5.1 million per mm<sup>3</sup> for younger women and 3.8–5.1 million per mm<sup>3</sup> for older women). The other values by age are described in Table 3.

Regarding the white series according to age group, the mean absolute values of white blood cells in men were higher among the elderly group (average: 6,246; limits: 2,818–9,675) when compared to that of the younger group (average: 6,124; limits: 2,844–9,403). For women, the average was higher for the 18-59 age group (mean: 6,478; limits: 2,908–10,047), compared with the group aged 60 or older (average: 6,197; limits: 2,971–9,424). The average absolute platelet values for younger males was 215,301 (limits: 128,418–302,183) and for the elderly, 206,421 (limits: 128,926–283,915). For younger women, the average was 241,312 (limits: 137,881–344,744), and for women 60 years and older, 229,056 (limits: 126,639–331,474). The other results are shown in Table 4.

Regarding race, the average red blood cell count in the male white, light-skinned black, and dark-skinned black population was 5.0 million, with slight variations in the reference

			Masculine	e		Feminine						
Tests	Average	Lower limit	Upper limit	Standard deviation	Sample	Average	Lower limit	Upper limit	Standard deviation	Sample		
White blood cells (mm³)	6,142	2,843	9,440	1,683	3,160	6,426	2,883	9,969	1,808	3,223		
Absolute neutrophils (mm³)	3,273	576	5,971	1,376	3,136	3,543	612	6,474	1,495	3,208		
Absolute eosinophils (mm³)	258	0	660	205	3,109	210	0	550	174	3,140		
Absolute basophils (mm³)	29	0	62	17	2,928	31	0	72	21	3,059		
Absolute lymphocytes (mm³)	2,045	720	3,370	676	3,124	2,105	796	3,414	668	3,151		
Absolute monocytes (mm³)	412	11	812	204	3,157	357	22	692	171	3,221		
Platelets (mm³)	213,975	128,177	299,774	43,775	3,126	239,325	135,606	343,044	52,918	3,279		
Platelet volume (fL)	10	8	12	1	2,560	10	8	13	1	2,761		

Table 2. Reference values of hematological markers of the white blood series according to gender. National Health Survey, Brazil, 2014–2015.

values (limits <sub>white</sub>: 4.3–5.7 million red cells per mm<sup>3</sup>; limits <sub>dark-skinned black</sub>: 4.1–5.8 million per mm<sup>3</sup>; limits <sub>light-skinned black</sub>: 4.3–5.7 million per mm<sup>3</sup>). White, dark-skinned black and light-skinned black women averaged 4.5 million red blood cells per mm<sup>3</sup>. (limits <sub>white</sub>: 3.9–5.1; dark-skinned limits <sub>dark-skinned black</sub>: 3.9–5.2; limits <sub>light-skinned black</sub>: 3.9–5.1). For white blood cells, the average absolute blood cell count in white men was 6,221 per mm<sup>3</sup> (limits: 2,960–9,483), in dark-skinned black men, 6,016 per mm<sup>3</sup> (limits: 3,181– 8,850) and

	Ago		ne		Feminine						
Tests	Age group	Average	Lower limit	Upper limit	Standard deviation	Sample	Average	Lower limit	Upper limit	Standard deviation	Sample
Red blood cells (millions/ mm³)	18 to 59 years	5.1	4.4	5.8	0.4	2.723	4.5	3.9	5.1	0.3	2,747
	60 years or older	4.8	4.0	5.6	0.4	510	4.5	3.8	5.1	0.3	539
Hemoglobin	18 to 59 years	15.0	13.1	16.9	1.0	2.738	13.2	11.5	14.8	0.9	2,749
(g/dL)	60 years or older	14.5	12.3	16.8	1.1	519	13.2	11.3	15.1	1.0	545
Hematocrit	18 to 59 years	46.0	39.9	52.1	3.1	2.747	40.7	35.4	45.9	2.7	2,722
(%)	60 years or older	44.7	38.0	51.4	3.4	517	40.9	35.1	46.7	3.0	539
Mean	18 to 59 years	90.9	81.5	100.2	4.8	2.726	90.5	81.0	100.1	4.9	2,730
corpuscular volume (fL)	60 years or older	92.7	83.6	101.8	4.6	509	91.0	81.2	100.7	5.0	537
Mean corpuscular	18 to 59 years	29.7	26.9	32.5	1.4	2.734	29.3	26.3	32.3	1.5	2,735
hemoglobin (pg)	60 years or older	30.3	27.6	33.1	1.4	515	29.5	26.3	32.6	1.6	547
Mean corpuscular	18 to 59 years	32.6	30.6	34.6	1.0	2.702	32.4	30.5	34.3	1.0	2,742
hemoglobin concentration (g/dL)	60 years or older	32.5	30.6	34.5	1.0	510	32.4	30.5	34.3	1.0	537
Red cell distribution	18 to 59 years	13.6	12.0	15.2	0.8	2.804	13.7	11.9	15.4	0.9	2,775
range (RDW) (%)	60 years or older	14.1	12.1	16.0	1.0	536	13.9	12.2	15.7	0.9	556

Table 3. Reference values of hematological markers of the red blood series according to gender and age group. National Health Survey, Brazil, 2014–2015.

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in light-skinned black men, 6,093 per mm<sup>3</sup> (limits: 2,681–9,506). In white women, the average was 6,608 per mm<sup>3</sup> (limits: 3,143–10,074), dark-skinned black women, 6,165 per mm<sup>3</sup> (limits: 2,430–9,900) and light-skinned black women 6,288 per mm<sup>3</sup> (limits: 2,772–9,803) (Table 5).

				Masculin	e		Feminine					
Tests	Age group	Mean	Lower limit	Upper limit	Standard deviation	Sample	Mean	Lower limit	Upper limit	Standard deviation	Sample	
White blood	18 to 59 years	6,124	2,844	9,403	1,673	2,651	6,478	2,908	10,047	1,821	2,682	
cells (mm³)	60 years or older	6,246	2,818	9,675	1,749	512	6,197	2,971	9,424	1,646	529	
Absolute neutrophils	18 to 59 years	3,230	552	5,909	1,367	2,633	3,577	597	6,557	1,520	2,671	
(mm <sup>3</sup> )	60 years or older	3,528	724	6,332	1,431	508	3,366	728	6,005	1,346	536	
Absolute eosinophils	18 to 59 years	255	0	649	201	2,610	208	0	546	172	2,618	
(mm <sup>3</sup> )	60 years or older	272	0	718	228	499	217	0	574	182	522	
Absolute basophils	18 to 59 years	29	0	62	17	2,459	31	0	73	22	2,546	
(mm <sup>3</sup> )	60 years or older	29	0	60	16	464	29	0	62	17	496	
Absolute lymphocytes	18 to 59 years	2,086	767	3,405	673	2,610	2,122	825	3,419	662	2,623	
(mm <sup>3</sup> )	60 years or older	1,835	582	3,088	639	508	2,039	716	3,362	675	520	
Absolute	18 to 59 years	410	13	807	203	2,648	353	19	688	171	2,688	
monocytes (mm³)	60 years or older	423	2	845	215	509	375	43	707	170	532	
Platelets	18 to 59 years	215,301	128,418	302,183	44,328	2,628	241,312	137,881	344,744	52,771	2,742	
(mm <sup>3</sup> )	60 years or older	206,421	128,926	283,915	39,538	495	229,057	126,639	331,474	52,254	536	
Platelet	18 to 59 years	10	8	13	1	2,145	10	8	13	1	2,300	
volume (fL)	60 years or older	10	8	12	1	412	10	8	12	1	460	

Table 4. Reference values of hematological markers of the white blood series according to gender and age group. National Health Survey, Brazil, 2014–2015.

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## DISCUSSION

The PNS made it possible to carry out the first national study that establishes the parameters for laboratory reference values, based on a representative sample of the Brazilian adult population and adapted to the ethnic, sociocultural, environmental and genetic characteristics of Brazil. It allowed for reference values to be estimated, and thus helped identify the current state of health of the country's population.

Table 5. Reference values of hematological markers of the red and white blood series according to gender and color/race. National Health Survey, Brazil, 2014–2015.

			١	9	Feminine						
Tests	Color or race	Mean	Lower limit	Upper limit	Standard deviation	Sample	Mean	Lower limit	Upper limit	Standard deviation	Sample
	Whites	5.0	4.3	5.7	0.4	1,488	4.5	3.9	5.1	0.3	1,543
Red blood cells (millions/	Dark-skinned blacks	5.0	4.1	5.8	0.4	318	4.5	3.9	5.2	0.4	319
mm³)	Light-skinned blacks	5.0	4.3	5.7	0.4	1,398	4.5	3.9	5.1	0.3	1,389
	Whites	15.1	13.2	16.9	1.0	1,490	13.3	11.7	14.9	0.8	1,549
Hemoglobin (g/dL)	Dark-skinned blacks	14.6	12.2	17.1	1.2	325	12.9	11.2	14.6	0.9	321
	Light-skinned blacks	14.8	13.0	16.7	1.0	1,409	13.1	11.3	14.8	0.9	1,382
	Whites	6,221	2,960	9,483	1,664	1,438	6,608	3,143	10,074	1,768	1,539
White blood cells (mm³)	Dark-skinned blacks	6,016	3,181	8,850	1,446	311	6,165	2,430	9,900	1,906	305
	Light-skinned blacks	6,093	2,681	9,506	1,741	1,377	6,288	2,772	9,803	1,793	1,333
	Whites	3,362	651	6,074	1,383	1,439	3,693	860	6,527	1,446	1,524
Absolute neutrophils	Dark-skinned blacks	3,112	693	5,530	1,234	310	3,221	534	5,908	1,371	300
(mm³)	Light-skinned blacks	3,224	475	5,974	1,403	1,363	3,441	389	6,493	1,557	1,342
	Whites	212,076	128,770	295,382	42,503	1,427	244,413	141,488	347,337	52,513	1,542
Platelets (mm³)	Dark-skinned blacks	227,742	135,387	320,096	47,119	307	240,890	138,140	343,640	52,423	313
	Light-skinned blacks	210,861	129,733	291,989	41,392	1,338	234,053	129,497	338,609	53,345	1,384

It is worth noting that, in order to reach these results, criteria were applied to exclude sick people or patients with conditions that could alter the results of the exams studied. The outliers were also removed. Therefore, reference intervals were calculated that allowed for the determination of specific limits according to gender, age, and skin color of the Brazilian population.

Knowledge of reference hematological parameters is fundamental for the evaluation of the health status and the disease pattern of populations. Concern around assessing the population's health level through hematimetric parameters and defining normality indices emerged in Brazil in the 1930s, but current studies are essential, since the population is living in environments that contain substances capable of modifying hematological patterns. From a public health point of view, recognizing the existence of these factors and their sanitary control should be emphasized<sup>20</sup>.

The objectives of the blood count are to evaluate general practice and diagnose anemia, polycythemia, spinal cord aplasia, infectious processes, leukemia/leukosis, thrombocytosis, and thrombocytopenia<sup>21</sup>. Blood counts are one of the most widely used analyses in medical practice because their general data allow for an extensive assessment of patients' clinical condition<sup>22</sup>.

Gender-specific reference ranges are essential, as the literature indicates that there are statistically significant differences between genders in hemoglobin, hematocrit, MCH, MCHC, platelets, platelet volume, and erythrocyte parameters<sup>23</sup>. Men are reported to have a higher level of red blood cells, hemoglobin, and hematocrit than women<sup>24,25</sup>. This difference can be influenced by factors such as androgenic hormone in erythropoiesis and blood loss during the menstrual period in women<sup>25,26</sup>. In contrast, women have higher platelet and white blood cell counts than men<sup>24</sup>. For the reference values described here, the differences were partly confirmed in relation to the averages, but without any differences in the limits.

In the scientific literature, evidence has been found that age may influence hemoglobin values, resulting in lower reference values in the elderly compared with adults, which may be explained by factors of senescence itself, such as: reduction of parent reserve hematopoietic factors, hematopoietic growth factors and erythropoietin production<sup>27</sup>. In the PNS, hemoglobin concentration was lower for older men and there were no differences between red blood cells according to age among women.

It is worth noting that RDW values also increased with age. The RDW is a laboratory parameter that measures the difference in size of circulating red blood cells. It is used in the differential diagnosis of hematological diseases and as an independent predictor of severity in CVD patients<sup>28</sup>, and mortality in the elderly<sup>29,30</sup>. The mechanism is not entirely clear, but this association depends on several factors, including inflammatory responses, anemia, nutritional status, and age-related diseases. The literature indicates that RDW values increase with age and strongly predict mortality, and it is conceivable that anisocytosis may reflect the impairment of multiple physiological systems related to the aging process and age-related diseases<sup>29,30</sup>. It is important to highlight that, among women, no differences were observed between adult and elderly women for RDW, with a small increase in men, as shown in the PNS.

It is worth pointing out that racial/ethnic differences in relation to the reference values of various laboratory tests have been recognized and documented, especially between dark-skinned black and white people. The literature describes that, in comparison with whites, dark-skinned black people present significantly higher platelet, hematocrit, MCH and hemoglobin values<sup>31</sup>, while total leukocytes and neutrophils counts are lower. The PNS did not find differences according to race/color for the red series and found a slight reduction in the mean values between dark-skinned blacks and light-skinned blacks in the white series. It is important to verify natural variations in the distribution of laboratory test results between racial/ethnic groups<sup>32</sup>.

Among the limits of the study, first, the sample losses stand out, however the post-stratification weights adopted allowed for estimations to be made with 95% certainty, reducing possible biases. Second, the methodology adopted in this paper is based on sample distributions, which is useful for the definition of reference values, however, in cases where it is necessary to identify people at higher risk of disease or requiring treatment, clinical practice should define the appropriate procedures. Exclusion criteria from the sample were self-reported, and therefore, people with diseases not known by the participants may have been included in the survey, which possibly affected the results, however the exclusion of outliers reduces this bias, removing the extreme values.

In the analysis, according to race/skin color, other racial groups (indigenous people, Asians) were excluded due to the small sample size. In addition, the sample for dark-skinned black people was about 600 participants. It is also noted that skin color was self-reported for all participants, and there may be differences between the stated and the observed skin color.

This is the first study on laboratory reference intervals of the PNS. Therefore, it is important to highlight that, in the literature, there are studies that applied other methodologies by calculating the median, not the average, in addition to other techniques to exclude outliers<sup>1</sup>.

Therefore, further studies are recommended in the future using the PNS laboratory database, applying different techniques and including the analysis of the difference in reference ranges according to gender, age group and race/color. It is also worth noting that the biochemical methods employed in the laboratory analysis may vary according to the manufacturer, and thus change the values found here.

### CONCLUSION

Specific hematological reference values for the Brazilian population were not available, which could result in unreliable clinical interpretations, mainly because Brazil is a developing country, with distinct population groups regarding genetics, dietary patterns and environmental factors. Determining gender-, age-, and skin-specific reference values is also essential, as there are differences between the parameters of these groups.

The PNS laboratory study provided specific reference values by gender, age and race, which are representative of the Brazilian adult population. They can be used to improve clinical practice, promote better evidence and criteria for care, diagnosis, treatment, and disease control.

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