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Immunohaematological profile and ancestry informative markers in individuals with COVID-19

Perfil imunohematológico e marcadores informativos de ancestralidade em indivíduos com COVID-19

Perfil inmunohematológico y marcadores informativos de ascendencia en individuos con COVID-19

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ABSTRACT

Objective: To evaluate the hematological and lymphocyte profiles of individuals with COVID-19, as well as to identify the ancestral profile through Ancestry Informative Markers from two cities in the Northeast region of Brazil. **Methods:** Data from 58 individuals with COVID-19 who presented mild (39) and severe (19) clinical conditions were analyzed. The lymphocyte profile was identified by immunophenotyping and genotyping via PCR and qPCR analysis. Data were analyzed by descriptive statistics using IBM SPSS Statistics software. The study was approved by the Research Ethics Committee (ICS-UFBA). **Results:** Individuals in the severe group showed an increase in total leukocytes and neutrophils, and a decrease in erythrocytes, hemoglobin, hematocrit, and lymphocytes compared to individuals in the mild group. Likewise, the severe group showed a decrease in the cellular profiles of CD4+ T cells, CD8+ T cells, and B lymphocytes. Regarding the ancestral profile, both groups had a greater European ancestral genomic profile. However, the severe group had a higher percentage of African ancestry compared to the mild group. **Conclusion:** Ancestry was not associated with severity, but the results match findings that individuals' immune responses play a crucial role in COVID-19.

Keywords: COVID-19, Immunohaematological profile, Ancestry Informative markers, Mixed population.

RESUMO

Objetivo: Avaliar os perfis hematológicos e linfocitários de indivíduos com COVID-19, bem como, identificar o perfil ancestral por meio de Marcadores Informativos de Ancestralidade de duas cidades da região Nordeste do Brasil. **Métodos:** Foram analisados os dados de 58 indivíduos com COVID-19 que apresentavam condições clínicas leves (39) e graves (19). O perfil linfocitário foi identificado por imunofenotipagem e genotipagem via análise de PCR e qPCR. Os dados foram analisados por estatística descritiva usando o software IBM SPSS Statistics. O estudo foi aprovado pelo Comitê de Ética em Pesquisa (ICS-UFBA). **Resultados:** Os indivíduos do grupo grave apresentaram aumento de leucócitos totais e neutrófilos, diminuição de eritrócitos, hemoglobina, hematócrito e de linfócitos em comparação aos indivíduos do grupo leve. Assim como, o grupo grave apresentou diminuição nos perfis celulares de células TCD4+, TCD8+ e linfócitos B. Em relação ao perfil ancestral, ambos os grupos apresentaram maior perfil genômico ancestral europeu. No entanto, o grupo grave apresentou maior percentual de ancestralidade africana em comparação ao grupo leve. **Conclusão:** A ancestralidade não foi associada à gravidade, mas os resultados correspondem às descobertas de que as respostas imunes dos indivíduos desempenha um papel crucial na COVID-19.

Palavras-chave: COVID-19, Perfil imunohematológico, Marcadores informativos de ancestralidade, População miscigenada.

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RESUMEN

Objetivo: Evaluar los perfiles hematológicos y linfocitarios de individuos con COVID-19, así como identificar el perfil ancestral a través de Marcadores Informativos de Ascendencia de dos ciudades de la región Nordeste de Brasil. **Métodos:** Se analizaron datos de 58 personas con COVID-19 que presentaban condiciones clínicas leves (39) y graves (19). El perfil de linfocitos se identificó mediante inmunofenotipado y genotipado mediante análisis de PCR y qPCR. Los datos fueron analizados mediante estadística descriptiva utilizando el software IBM SPSS Statistics. El estudio fue aprobado por el Comité de Ética en Investigación (ICS-UFBA). **Resultados:** Los individuos del grupo grave mostraron un aumento de leucocitos y neutrófilos totales, una disminución de eritrocitos, hemoglobina, hematocrito y linfocitos en comparación con los individuos del grupo leve. Asimismo, el grupo severo mostró una disminución en los perfiles celulares de células TCD4+, TCD8+ y linfocitos B. En relación al perfil ancestral, ambos grupos presentaron un mayor perfil genómico ancestral europeo. Sin embargo, el grupo grave tenía un mayor porcentaje de ascendencia africana en comparación con el grupo leve. **Conclusión:** La ascendencia no se asoció con la gravedad, pero los resultados se corresponden con los hallazgos de que las respuestas inmunitarias de los individuos desempeñan un papel crucial en la COVID-19.

Palabras clave: COVID-19, Perfil inmunohematológico, Marcadores informativos de ascendencia, Población mixta.

INTRODUCTION

Coronavirus Disease-19 (COVID-19), caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), is a highly contagious disease that was declared a pandemic in March 2020. It is still a serious health problem. In Brazil, from the beginning of the pandemic till July 2024, more than 700,000 deaths were reported. Most individuals with COVID-19 have mild or moderate conditions; others may develop serious conditions characterized by Severe Acute Respiratory Syndrome (SARS) (HU B, et al., 2020). Immune responses greatly influence the pathogenesis of COVID-19.

Cell dysregulation and exacerbation of pro-inflammatory cytokines are determinants of tissue damage during infection. Some studies have shown that an increase in neutrophils and a decrease in T and B lymphocytes can worsen the severity of the disease (AZKUR AK, et al., 2021; SONG JW, et al., 2020; MERAD M, et al., 2022). The mechanism by which SARS-COV-2 infection affects different ethnic groups is not known. However, some researchers found that minority ethnic populations are more susceptible to the severity of COVID-19, either due to biological or sociodemographic factors (MACKEY K, et al., 2020; NORIN AJ, et al., 2021; BORGES GM e CRESPO, 2020).

Among the factors that might be associated with worse outcomes of COVID-19, the following are significant: prevalence of Human Leukocyte Antigen (HLA) B 53 alleles in Afro-descendant patients with severe COVID-19 and hospitalization (NORIN AJ, et al, 2021). Glucose-6-phosphate dehydrogenase (G6PD) deficiency in severe cases of COVID-19 among individuals of African and Asian descent (JAIN SK, et al., 2020; AL-ABDI S e AL-AAMRI M, 2020). Low vitamin D levels in African Americans (COZIER, et al., 2021). Besides these factors, comorbidities such as cardiovascular diseases, arterial hypertension, and diabetes mellitus are common among ethnic minorities (FERDINAND K, et al., 2020; FERREIRA RBS e CAMARGO CL, 2021).

Information on the contribution of ancestry based on Ancestry Informative Markers (AIMs) and clinical manifestations of COVID-19 is limited. AIMs are molecular tools that can infer the genomic ancestry of mixed populations, as they present frequency differentials (δ) >30% between geographically distinct populations (SHRIVER MD, et al., 1997; PENA SDJ, 2005). Based on its historical characteristics, the current Brazilian population is considered tri-hybrid, resulting from the miscegenation of three main parental groups (Sub-Saharan Africans, Europeans, and Amerindians) (CAVALCANTE LN, et al., 2015). However, this ethnic contribution is not homogeneous.

In Salvador, the state capital of Bahia, about 80% of the population comprises people of African descent, represented by the sum of blacks and browns, classified according to the self-denomination of color or race (IBGE, 2010; ABE-SANDES K, et al., 2010).

As COVID-19 is multifactorial and ethnic disparities are prominent in the Brazilian population, identifying the ancestral genetic profile in a mixed-race population can greatly help in understanding how the disease can affect ethnic minorities, besides providing valuable information for making public service policies to serve these groups better. In this study, was evaluated the haematological parameters and lymphocytic profiles of individuals suffering from severe and mild clinical conditions due to COVID-19 and evaluated the genotypic profile of AIMs.

METHODS

Ethical Considerations

This study was coordinated by the State University of Feira de Santana (UEFS) in partnership with the Federal University of Bahia (UFBA). The samples were analysed at the Laboratory of Immunology and Molecular Biology, Institute of Health Sciences, UFBA. A structured questionnaire was used to collect data related to demographic conditions. All participants signed the Free and Informed Consent Form (TCLE) following the Guidelines and Regulatory Norms of the National Health Council (Resolution n° 466/12 and Operational Norm 001/13).

Ethical approval for this study was provided by the review board of the National Research Ethics Commission under approval nº 4,014,165 and CAAE 30764720.1.0000.0053. This study complied with the ethical principles of the revised Declaration of Helsinki. All participants provided informed consent.

Study population

For the sample calculation, an exposure of 75% was considered among the controls, with a confidence level (bichaldal) of 95% and power of 80%, in a proportion of 1:1. Blood samples were collected from 58 individuals between June 2020 and December 2020. The inclusion criteria were as follows: i) individuals who were at least 18 years old; ii) individuals who were diagnosed with SARS-CoV-2 via molecular (PCR) or serological (IgM) examinations. The exclusion criteria were as follows: i) pregnant women; ii) those with active autoimmune disease; iii) individuals with active malignant neoplasm.

The selected individuals were divided into two groups based on whether they had a mild disease (n = 39) or severe disease (n = 19), according to their clinical manifestations. The classification of clinical presentation followed parameters recommended by the Ministry of Health.

The condition was considered to be mild when the patient had a fever, myalgia, los of smell and taste, headache, runny nose, and general malaise. The condition of individuals was considered to be severe when they were diagnosed with Severe Acute Respiratory Syndrome (SARS). All individuals in the severe group were admitted to the ICU and recruited at Hospital Couto Maia (HCM), Salvador-BA or Hospital EmpreendimentoMédicoCirúrgico (EMEC), Feira de Santana-BA. The participants in the mild group were recruited at the Collection Service - LABIMUNO (ICS-UFBA) or through the home collection.

Clinical, laboratory, and Demographic data

Demographic data on individuals with a mild condition were obtained using a structured questionnaire, whereas laboratory data on patients with a severe condition were collected from tests performed at the hospital.

Biological samples and cell separation

Peripheral blood (4 mL) was collected in a tube containing ethylenediaminetetraacetic acid (EDTA) anticoagulant Vacuette® and processed to separate plasma and peripheral blood mononuclear cells (PBMCs). Cell separation was performed using the density gradient technique using Histopaque ® –1077 (SIGMA, UK). The extracted cells were stored at –70° C.

Immunophenotyping and cytometry

To determine the cellular immune response, cells were washed with phosphate-buffered saline and conjugated with monoclonal antibodies against the membrane receptors of the target cells. Then, the cells

were resuspended in a 0.9% saline solution and analysed using a BD FACS Calibur™ cytometer (USA). For identification, antibodies labelled with fluorescein isothiocyanate, fluorophore (FITC), phycoerythrinfluorophore (PE), and chlorophyll peridinin protein (PerCP) from BD Biosciences™ (USA) were used. Were identified in T helper cells: CD3+ (FITC), CD4+ (PE), and CD45+ (PerCP); Cytotoxic T-cells: CD3+ (FITC), CD8+ (PE), and CD45+ (PerCP); B cells: CD5+ (FITC), CD19+ (PE), and CD45+ (PerCP).

Genomic DNA extraction

Genomic DNA was extracted from PBMCs using the PureLink™ Genomic DNA Mini Kit (Invitrogen ®; CA, USA), following the manufacturer's recommendations and protocol.

Genotyping of Ancestry Informative Markers

We analysed 10 ancestry markers, (Table 1) three with Alu insertions and one INDEL. AT3 I/D primer sequences (F = 5'-CCACAGGTGTAACATTGTGT-3'R = 5'-GAGATAGTGTGATCTGAGGC-3) produced an insertion of 572 base pairs (bp); APO (F = 5'-AAGTGCTGTAGGCCATTTAGATTAG-3'R = 5'-AGTCTTCGATGACAGCGTATACAGA-3') produced an insertion of 409 bp; PV92 (F = 5'-AACTGGGAAAATTTGAAGAGAAAGT-3' R = 5'-TGAGTTCTCAACTCCTGTGTGTTAG-3) produced an insertion of 400 bp, and Sb19 (F = 5'-TCTAGCCCCAGATTTATGGTAACTG-3' and R = 5'-AAGCACAATTGGTTATTTTCTGAC-3') produced an insertion of 457 bp. The PCR conditions used in the reaction were similar to those used in other studies. Six SNP markers, including FYnull, CKMM, LPL, GC-1F, GC-1S, and CYP3A4, were used.

SNPs were identified using Taq-Man® Assays – SNP genotyping probes (ThermoFisher, USA), following the manufacturer's protocol and recommendations. PCR was performed using the QuantStudio 3™ Software v1.5.2 (ThermoFisher Scientific, USA). The alleles were designated as allele1* and allele2*. In INDEL and Alu, the insertion of allele 1* was marked by the presence of the insertion. In SNPs, the nucleotide abolishes the restriction site in the 1* allele.

Table 1- Loci, SNP-ID, chromosomal location, polymorphism type, alleles and population frequency for allele 1 of the AIMs used in the study.

Loci	dbSNP (rs) / Chromosomal location	Polymorphism	Allele 1* / Allele 2	Population allele frequency 1*
AT3-I/D	3138521 - 1q25.1	INDEL	572pb* / 496pb	African
LPL	285 - 8p21.3	SNP	T* / C	African
GC-1F	7041 - 4q13.3	SNP	T* / G	African
PV92	3138523 - 16q23.3	Aluinsertion	400pb* / 100pb	Amerindian
CKMM	4884 - 19q13.32	SNP	T* / C	Amerindian
CYP3A4	2740574 - 7q22.1	SNP	A* / G	Amerindian
APO	3138522 - 11q23.3	Aluinsertion	409pb* / 110pb	European
Sb19.3	3138524 - 19p12	Aluinsertion	457pb* / 150pb	European
FYnull	2814778 - 1q23.2	SNP	A* / G	European
GC-1S	4588 - 4q13.3	SNP	C * / A	European

Source: Almeida GB, et al., 2025.

Parental population

The ancestral genetic reference population consisted of 399 individuals, divided into Africans (134 Nigerians), Europeans (23 Germans), and Amerindians (242 Native Americans). The samples used as parents were analyzed at the University of Pennsylvania (USA) and the genotypes obtained were kindly provided by Dr Mark Dr. Shriver to the Laboratory of Immunology and Molecular Biology (UFBA) - personal communication.

Statistical analysis

Laboratory data were analysed using the IBM SPSS Software to calculate variable frequencies. Blood count indices and cytometric data were evaluated using IBM SPSS and GraphPad Prism 8. To confirm that the variables followed a normal distribution, the Kolmogorov–Smirnov Test (KS) was performed. For parameters

that followed a normal distribution, the Student's t-test was performed, and for variables that did not follow a normal distribution, the Shapiro-Wilk test was performed. All results were considered to be statistically significant at $p < 0.05$. For genetic data, allele frequencies and the Hardy-Weinberg balance were determined using GENEPOP v. 4.7 (RAYMOND; ROUSSET, 1995; https://genepop.curtin.edu.au/). Structure 2.2 was used to evaluate the ancestral contribution of each individual (study population) based on the genotypes of the Amerindian, European, and African ancestral populations.

The software was also used to estimate the admixture assuming a tri-hybrid model (available at https://web.stanford.edu/group/pritchardlab/home.html). To precisely determinethe groupings that presented individuals belonging to the populations considered parental, the Use pop info selection FLAG option was enabled. In the Ancestry Model option, Use Population Information was selected. Analyzes were performed with K = 3 as the predefined parameter for the number of populations assumed to be parental with 30,000 interactions for burn-in period and 100,000 additional interactions to obtain parameter estimates.

RESULTS

Demographic data

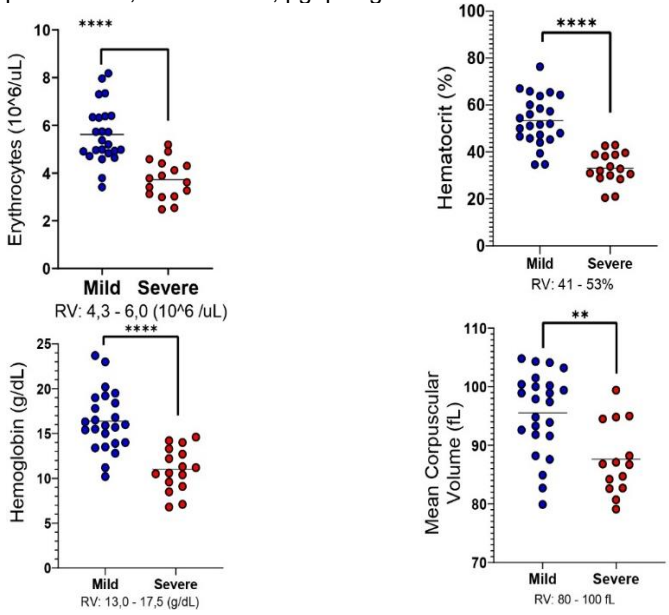
The mild group was composed mainly of individuals between 18-39 years of age (n=22 / 56.4%), while the severe group was >62 years of age (n=11 / 57.8%). Female individuals were more frequent in both groups. Mild: females (n=20 / 51.2) and males (n=17 / 43.5%). Severe: females (n=11 / 57.8%) and males (n=8 / 42.1%). Regarding self-reported ethnicity, the mild group had whites (n=13 / 33.3%), browns (n=15 /38.4%) and blacks (n=8 / 20.5%). Severe: browns (n=8 / 42.1%), in this group some individuals did not respond or did not want to declare ethnicity.

Haematological Indices

Blood count data were collected from individuals with mild and severe conditions. For the erythrogram data, the severe group had significantly lower erythrocyte, haemoglobin, and haematocrit compared to the mild group. Although the difference in Mean Blood Volume (MBV) between the groups was significant, the average values were within the normal reference values. The Mean Globular Haemoglobin (MGH), Mean Globular Haemoglobin Concentration (MGHC), Red Cell Distribution Width (RDW), and Platelets were not within normal values, and differences between the groups were not significant (**Figure 1 A and B**).

Figure 1 - Mean for erythrogram and platelet parameters of individuals with COVID-19 divided into mild and severe. R.V: reference value; g⁄dL: grams per deciliter; fl: fentoliters; pg: picograms.

A



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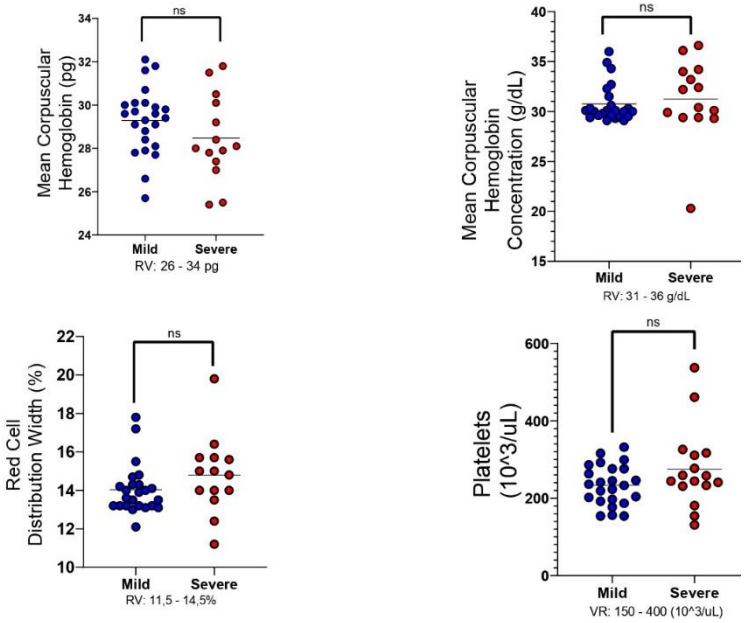
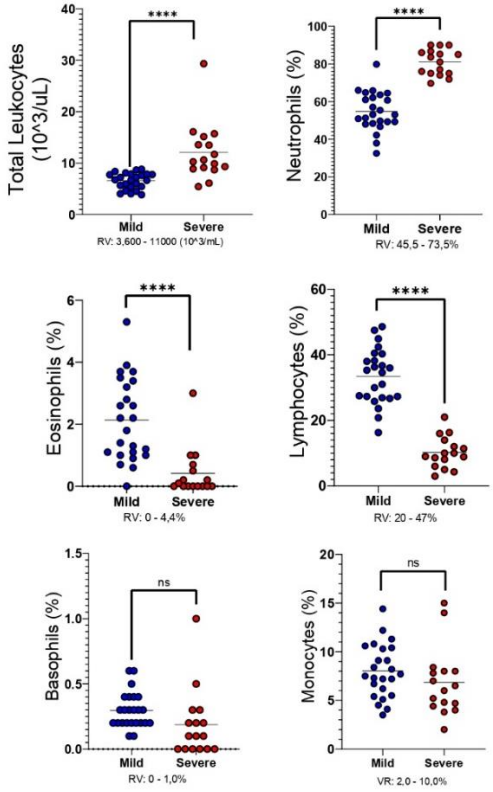


Source: Almeida GB, et al., 2025.

The severe group showed an increase in total leukocytes and neutrophilia compared to the mild group ($p<0.005$). Lymphopeniawas also observed in the severe group and was statistically significant. The values for eosinophils and basophils were statistically significant between the groups but were within the reference values. The monocyte differences between the groups were insignificant, but the monocyte numbers were within the normal range (**Figure 2**).

Figure 2- Leukocyte value (blood count) and immunophenotype of individuals divided into mild and severe groups. **2.A** Blood cell profile (%); VR: reference value. **2.B** Median and standard deviation for leukocyte profiles (TCD4+, TCD8+ and lymphocyte B) of individuals with COVID-19.

A



Source: Almeida GB, et al., 2025.

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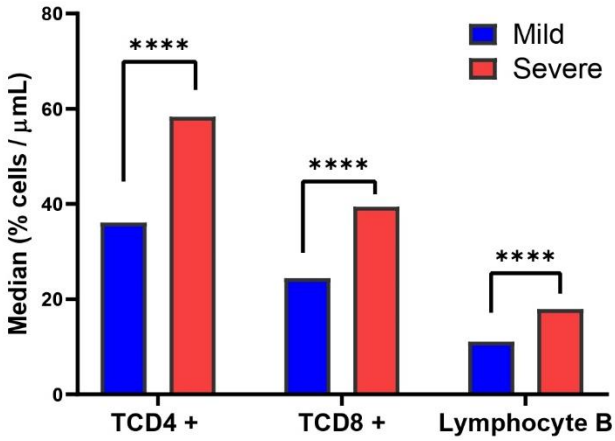


Source: Almeida GB, et al., 2025.

For immunophenotyping, the lymphocyte profiles of 36 (mild) and 18 (severe) individuals were analyzed. The severe group had lower frequencies of T lymphocyte profiles (CD3+, CD4+, and CD8+) and B lymphocytes (CD5+, CD19+ and CD45+) compared to the mild group (p<0,005) (**Figure 2.B**).

Genetic ancestry analysis

Allele frequencies based on the parental genotype of Africans, Europeans, and Amerindians compared to the COVID-19 study population are presented in (**Tables 2 and 3**). Among the allele frequencies in the studied population, the markers Sb19.3, APO, FyNull, LPL, and CYP3A4 presented frequencies above 50%. In the Hardy-Weinberg equilibrium analysis, the CYP3A4 and GC markers did not adhere to the equilibrium ($p < 0.05$), showing an excess of homozygotes and heterozygotes, respectively.

For this finding, the reduced sample size, the non-randomization of individuals recruited in the research and the fact that they were convenience samples admitted to few reference centers may have contributed to the aggregation of individuals who shared the same genotypes and not contribute to the expected outcome.

Table 2- Percentage of genotypes for each ancestral marker and allele frequency.

AIM	Genotype	Mild N (%)	Allele Frequency 1*	Severe N (%)	Allele Frequency 1*
AT3 I/D Indel	A/A	13 (33,3)	**0.397**	7 (36,8)	**0.344**
	P/A	21 (53,8)		7 (36,8)	
	P/P	5 (12,8)		2 (10,5)	
	N.G	-		3 (15,7)	
Sb19.3 Alu	A/A	2 (5,1)	**0.778**	3 (15,7)	**0.694**
	P/A	12 (30,7)		5 (26,3)	
	P/P	22 (56,4)		10 (52,6)	
	N.G	3 (7,6)		1 (5,2)	
APO Alu	A/A	1 (2,5)	**0.889**	-	**0.972**
	P/A	6 (15,3)		1 (5,2)	
	P/P	29 (74,3)		17 (89,4)	
	N.G	3 (7,6)		1 (5,2)	
PV92 Alu	A/A	18 (46,1)	**0.284**	9 (47,3)	**0.324**
	P/A	17 (43,5)		5 (26,3)	
	P/P	2 (5,1)		3 (15,7)	
	N.G	2 (5,1)		2 (10,5)	
FyNull SNP	A/A	26 (66,6)	Alele A **0.816**	8 (42,1)	Alele A **0.676**
	A/G	10 (25,6)		7 (36,8)	
	G/G	2 (5,1)		2 (10,5)	
	N.G	1 (2,5)		2 (10,5)	
CKMM SNP	C/C	21 (53,8)	Alele T **0.289**	10 (52,6)	Alele T **0.263**
	C/T	12 (30,7)		9 (47,3)	
	T/T	5 (12,8)		1 (5,2)	
	N.G	1 (2,5)		-	

LPL SNP	T/T	14 (35,8)	Alele T **0.595**	4 (21)	Alele T **0.643**
	T/C	16 (41)		10 (52,6)	
	C/C	7 (17,9)		-	
	N.G	2 (5,1)		5 (26,3)	
CYP3A4 SNP	A/A	4 (10,2)	Alele A **0.757**	4 (21)	Alele A **0.567**
	A/G	9 (23)		5 (26,3)	
	G/G	22 (56,4)		6 (31,5)	
	N.G	4 (10,2)		4 (21)	
GC SNP	F/F	3 (7,6)	*1F	5 (26,3)	*1F **0.444** *1S **0.306** 2 0.250
	F/S	17 (43,5)	**0.333**	5 (26,3)	
	F/2	1 (2,5)	*1S	1 (2,5)	
	S/S	5 (12,8)	-	1 (2,5)	
	S/2	9 (23,0)	**0.500**	4 (21,0)	
	2/2	1 (2,5)	2	2 (10,5)	
	N.G	3 (7,6)	0.167	1 (2,5)	

Note: *Frequent allele in the population. A/A = homozygous for absence of insertion; P/P = homozygous for the presence of the insert; P/A = heterozygous. The genotype for GC is based on the combination of alleles at positions 34 and 45 of the gene, respectively. F/F = T/T and C/C; F/S = T/G and C/C; F/2 = T/T and C/A; S/S = G/G and C/C; S/2 = T/G and C/A; 2/2 = T/T and A/A. N.G = no genotype. **Source:** Almeida GB, et al., 2025.

Table 3 - Specific allele frequencies for parental populations and in individuals with COVID-19. Ancestral population data according to Shriver.

Variable	African	European	Amerindian	COVID-19 (Mild)	COVID-19 (Severe)
AT3					
Presence*	0.881	0.261	0.156	**0.397**	**0.344**
Absence	0.119	0.739	0.844	0.603	0.656
APO					
Presence*	0.459	0.913	0.945	**0.889**	**0.972**
Absence	0.541	0.087	0.055	0.111	0.028
Sb19.3					
Presence*	0.455	0.826	0.675	**0.778**	**0.694**
Absence	0.545	0.174	0.325	0.222	0.306
PV92					
Presence*	0.198	0.109	0.764	**0.284**	**0.324**
Absence	0.802	0.891	0.236	0.716	0.676
FY-Null					
A *	0.000	1.000	0.996	**0.816**	**0.676**
G	1.000	0.000	0.004	0.184	0.324
CKMM					
C	0.847	0.630	0.116	0.711	0.737
T *	0.153	0.370	0.884	**0.289**	**0.263**
LPL					
T *	0.974	0.565	0.444	**0.595**	**0.643**
C	0.026	0.435	0.556	0.405	0.357
CYP3A4					
G	0.744	0.043	0.081	0.243	0.433
A *	0.256	0.957	0.919	**0.757**	**0.567**
GC					
1-F *	0.851	0.152	0.340	**0.333**	**0.444**
1-S *	0.080	0.587	0.532	**0.500**	**0.306**
2	0.069	0.261	0.128	0.167	0.250

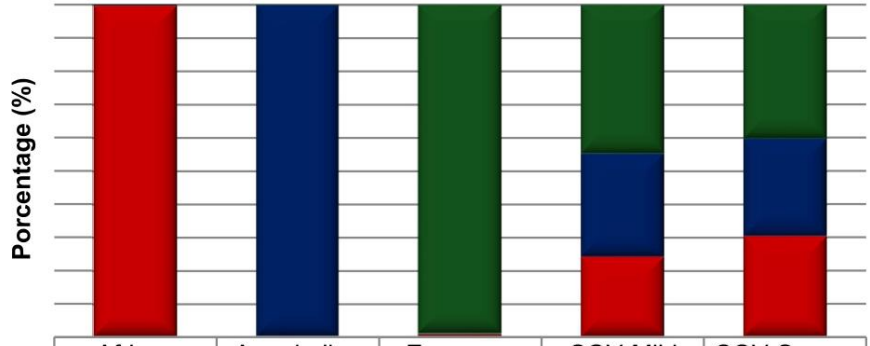
Source: Almeida GB, et al., 2025.

The results of the comparative analysis of the allele frequencies (Structure) in comparison withof the parental population and the COVID-19 study population, it was reported indicated that the markers used were able tocould be used to discriminate differentiate between the ancestral populations.

Regarding the proportion ratio between the groups, as well as and the estimate of the population mix for individuals with COVID-19, was heterogeneous, with higher percentages of European genomic ancestry (**Figure 3**).

Figure 3- 3.A Percentage of the ancestral profile of individuals with COVID-19 (mild and severe) and grouping by parental population. **3.B** COVID-19 population grouping (yellow) compared to parent African (red), Amerindian (blue) and European (green) parent population - mild group; **3.C** severe group. **3.D** Bar Plot parental population and mild group individuals. **3.E** Bar Plot parental population and severe group individuals.

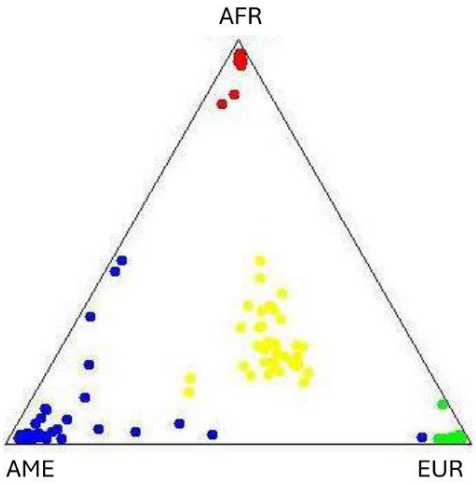
A



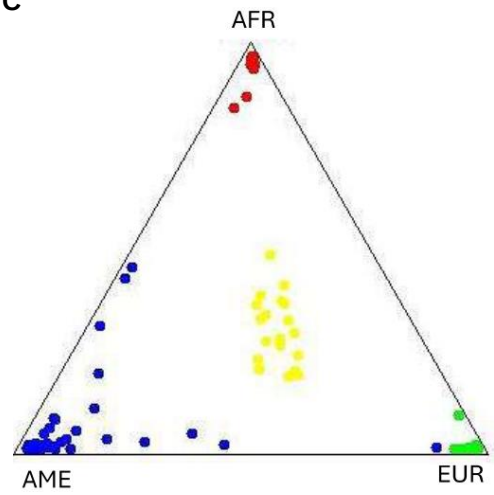
	African	Amerindian	European	COV-Mild	COV-Severe
European	0,03%	0,17%	98,10%	44,80%	40,20%
Amerindian	0,20%	97,40%	0,11%	30,90%	29,40%
African	99,50%	0,10%	0,80%	24,30%	30,40%

Source: Almeida GB, et al., 2025.

B

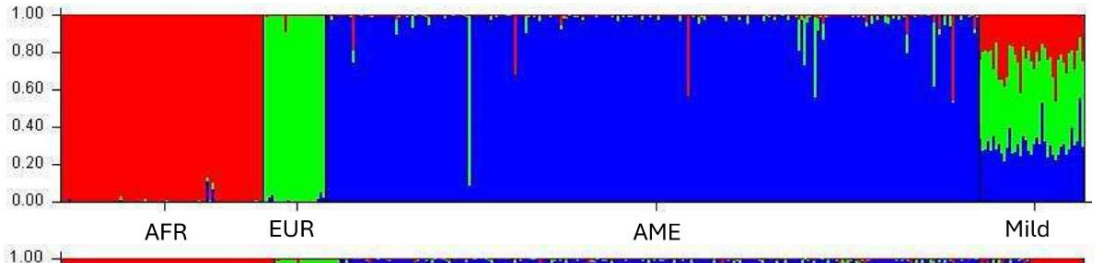


C

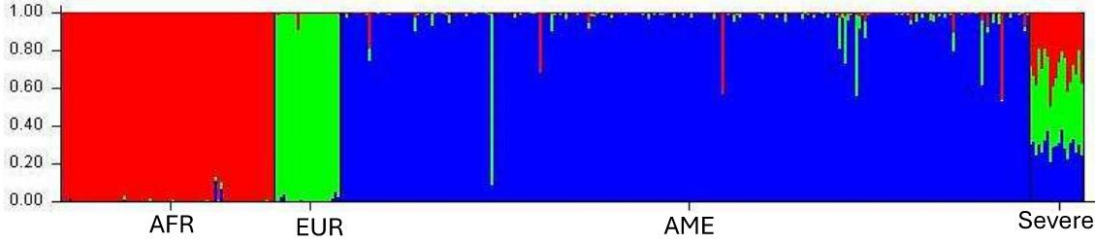


Source: Almeida GB, et al., 2025.

D



E



Source: Almeida GB, et al., 2025.

DISCUSSION

Some studies have shown that older individuals and males are more prone to severe effects of COVID-19 (AZKUR AK, et al.,2020). Our results agreed with the age-related findings, considering that a large proportion of individuals ≥ 62 years old were found in the severe group. In relation to sex, the mild and severe groups had higher percentages of female individuals. Laboratory findings can be used to assess the clinical course of SARS-CoV-2 infection (TAO Z, et al., 2020). However, Laboratory and immunohaematological profile may differ between elderly and non-elderly individuals (FARSHBAFNADI M, et al., 2021).

Physiological and immunological conditions may increase with age, in addition, common comorbidities in the elderly are influential factors that may favor the exacerbation of COVID-19 (GHOBADI H, et al., 2022). Haematological changes in erythrocytes, haemoglobin, and haematocrit parameters were associated with the severity of COVID-19, which might explain the decrease in these parameters in individuals in the severe group (KARIMI SHAHRI M, et al., 2020). ao Z (2020) stated that anaemia is an independent factor for worse clinical outcomes. However, these findings must be interpreted cautiously, as they may be associated with other pathological conditions or underlying comorbidities.

Low haemoglobin levels may be correlated with severity, as individuals suffer from a decrease in the ability of haemoglobin to satisfy tissue demands for oxygen supply due to hypermetabolic states during viral infection (SU S, et al., 2020). The number of platelets was not significantly different between the groups in our study. Some studies have shown significant changes related to thrombocytopenia in severe cases of COVID-19 (WOOL GD, et al., 2020). The increase in the total number of leukocytes, neutrophilia, and lymphocytosis described can be used as predictors of severity during the course of an infection (AZKUR AK, et al., 2020; SONG JW, et al., 2020; MERAD M, et al., 2022). Our results corroborate the data, as a significant difference in these parameters was found between the groups.

This finding has been described as a risk factor for elderly patients (ZHOU F, et al., 2020). In another study, it was reported that the neutrophil/lymphocyte ratio was common in the elderly compared to young individuals and is indicative of the severity of the disease (GHOBADI H, et al., 2022).Codd AS (2021) reported that the increase in neutrophils was closely associated with lung injury. Another study indicated that SARS-associated diseases, such as influenza and SARS-CoV infections, play key roles in pathology. Neutrophils can participate in immune responses against viruses through interactions with other immune cells, the release of cytokines, and neutrophil extracellular traps (NETs) (CODD AS, et al., 2020; WANG J, et al., 2020).

Another well-known characteristic among these cells is the relationship between neutrophilia and lymphopenia, which can act as a biomarker of inflammation during the early stages of SARS-CoV-2 infection (FU J, et al., 2020; TERPOS E, et al., 2020; DU RH, et al., 2020). The reduction in the number of circulating lymphocytes can be justified by a cytopathic action of the viruses on these cells, dysregulation of apoptotic pathways, depletion of T cells, and the use of immunosuppressant drugs administered to individuals admitted to the U.T.I (CODD AS, et al., 2020; TERPOS E, et al., 2020). The severe COVID-19 group showed a decrease in the lymphocyte profile compared to the mild group; this finding was similar to those of studies in which it was reported that the decrease in TC4+ and TC8+ is correlated with the severity of COVID-19 (DU RH, et al., 2020; MOSS P, 2022).

In the elderly, the potential for differentiated cytotoxic T and memory was reduced, showing that these individuals have impaired cellular immunity against SARS-COV-2 (WESTMEIER J, et al, 2020). Furthermore, the lymphocyte profile may reflect the extent of the viral infection and be considered a poor prognosis in elderly individuals (WANG L, et al., 2020). The decrease in the number of these cells hinders immune responses, as TC4+ lymphocytes can differentiate into various helper cells, which facilitate the activation of other lymphocytes (TCD8+ and B cells), recruitment of innate cells, secretion of cytokines, and immunomodulatory activity.

CD8+ T lymphocytes participate in the antiviral response through cellular cytotoxicity, which is a crucial component of antiviral defence(JESENAK M, et al., 2020). Regarding B lymphocytes, the metabolic environment during SARS-CoV-2 infection affects the survival, activation, and activity of these cells, as they are essential for humoral response in the early stages of infection and also in the long term through the

formation of memory cells. The reduction in CD19+ expression decreases BCR receptor signaling, which is associated with the non-responsiveness of these lymphocytes (JING Y, et al., 2021).

The mechanism by which SARS-CoV-2 infection affects populations and the degree of vulnerability of individuals to the infection are not known. Assuming that the outcomes of COVID-19 are multifactorial, some studies have suggested that the genetic characteristics of the hosts strongly influence the course of the disease and the association between ethnic conditions and the prognosis of the disease (MACKEY K, et al., 2020; PENA SDJ, et al., 2020).

Some studies considered genomic ancestry and other factors such as sociodemographics may be associated a factor for vulnerability to diseases (ABE-SANDES K, et al., 2010; CAVALCANTE LN, et al., 2015). In this study, AIMs were used to determine the genomic ancestry in individuals with COVID-19 (divided into severe and mild groups) in Salvador and Feira de Santana (BA, Brazil). Both cities have large percentages of self-declared individuals of brown colour (IBGE, 2010). However, we could not associate the ancestral profile with the clinical outcomes of COVID-19. We found that the study population was a mix of different races, with a higher percentage of European genomic ancestry, corroborating data describing the high European ancestral genetic contribution in the Northeast region of Brazil (PENA SDJ, et al., 2020).

The severe group had a higher African ancestry profile (30.4%) than the mild group (24.3%). Although the groups (severe and mild) had higher percentages of self-declared “brown” individuals, the European contribution was higher in both. The correlation between skin color and genomic ancestry is imperfect; at an individual level, it is not possible to predict skin color based on their level of African, Amerindian, or European ancestry (PENA SDJ, et al., 2020). Although some studies have reported that severe conditions of COVID-19 are prevalent in minority groups (African Americans), social, demographic, and economic components can be used as determinants in the analyses (QUEIROZ EM, et al., 2013; PRICE-HAYWOOD EG, et al., 2020; SHELTON JF, et al., 2021).

Social status can be a confounding factor when associating race or ethnicity with the disease (ABE-SANDES K, et al., 2010). Minority groups are prone to diseases because of various factors, such as poor housing conditions, crowded environment, poor education level, low per capita income, lack of basic sanitation, lack of access to medical care and others. These factors can explain the differences in the incidence of diseases across various socioeconomic groups and affect the quality of life of these ethnic groups (SANTOS MPAD, et al., 2020; BORGES GM e CRESPO CD, 2020).

CONCLUSION

To summarise, we considered that the differences between the erythrogram indices (erythrocytes, haemoglobin, and haematocrit), leukogram (total leukocytes, neutrophils, and lymphocytes), and lymphocyte profile (TCD4+, TCD8+, and B lymphocytes) were identified with the severity of COVID-19. However, the ancestral genotypic profile did not correlate with the clinical outcomes of the disease. Although both groups have a higher percentage of individuals with European genomic ancestry. A greater proportion of individuals with African ancestry were found in the severe COVID-19 group than in the mild COVID-19 group. The allelic data presented in this study provided new information that can be used to evaluate the role of individual genomic ancestry and clinical conditions in COVID-19.

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