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Influence of SARS-CoV-2 variants on COVID-19 epidemiological and clinical profiles: a comparative analysis of two waves of cases

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Abstract

Background The COVID-19 pandemic has been the most significant health challenge of the last century. Multiple and successive waves of COVID-19 cases, driven particularly by the emergence of new SARS-CoV-2 variants, have kept the world in a constant state of alert.

Methods We present an observational, descriptive, cross-sectional study aimed at identifying SARS-CoV-2 variants circulating during two local waves of COVID-19 cases in southern Bahia, Brazil (late 2021 and late 2022), and analyzing the association between the detected variants and the epidemiological and clinical characteristics of the disease. For this purpose, data and nasopharyngeal samples from individuals in southern Bahia, Brazil, with suspected COVID-19 were included. Viral detection was performed by RT-qPCR, and SARS-CoV-2 variants were identified by next-generation viral sequencing.

Results A total of 368 nasopharyngeal samples were tested. Approximately 23% of the samples from late 2021 tested positive for SARS-CoV-2, while in 2022, the positivity rate was about 56%. All sequenced samples from 2021 were identified as the Delta variant, while in 2022, all samples were classified as the Omicron variant. Overall, individuals who tested positive for SARS-CoV-2 in 2022 were younger than those who tested positive in 2021. Moreover, we observed significant differences in the clinical spectrum of SARS-CoV-2 infection when comparing the two periods. Individuals who presented with anosmia/ageusia were more likely to test positive for SARS-CoV-2 infection in 2021 but not in 2022. Additionally, fever, dry cough, pharyngalgia, headache, and rhinorrhea were more frequent among individuals infected with the Omicron variant than among those infected with the Delta variant.

Conclusions The profile of COVID-19 in southern Bahia differed when analyzing two distinct waves of the pandemic in the region. These differences are likely related to the variants, which may differ in transmissibility and virulence, thereby altering the dynamics of the pandemic. This underscores the importance of genomic surveillance in better understanding the behavior of viral infections.

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Keywords COVID-19, RT-qPCR, Genomic surveillance, SARS-CoV-2 variants

Introduction

The Coronavirus Disease (COVID-19) pandemic, caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), triggered a series of global challenges, significantly impacting public health [1, 2]. Among the measures adopted to combat this global crisis, the rapid development of vaccines to control the high rate of viral transmission stands out [3]. In Brazil, by the end of 2021, approximately 77% of the population had received at least one dose of the COVID-19 vaccine [4]. Indeed, the vaccines demonstrated great efficacy in reducing the severity of cases, hospitalizations and deaths. However, they were not able to prevent infections or reinfections [5, 6]. Even with the increase in vaccination coverage, the virus continued to be a concern worldwide, as many countries, including Brazil and others in South America, facing multiple waves of COVID-19 cases over time [7, 8].

One of the main factors contributing to the incidence of different waves of infections appears to be the emergence of new SARS-CoV-2 variants [9, 10]. During these waves, changes in the virus were observed, altering the transmissibility, pathogenicity, and symptoms of COVID-19 [11–14]. In this context, some variants of concern (VOCs) were detected and classified as Alpha, Beta, Gamma, Delta, and Omicron [8, 12], with the latter becoming dominant worldwide since February 2022 [15].

Considering the outcome of SARS-CoV-2 infection, although most of them can be asymptomatic, many individuals experience mild to moderate symptoms, such as fever, cough, and fatigue, and some develop severe conditions, such as pneumonia and acute respiratory distress syndrome (ARDS) [16, 17]. Pre-existing conditions, advanced age and comorbidities are risk factors that can lead to a poor prognosis [18, 19]. Additionally, a higher mortality among males has been described, and must be related to biological and behavioral factors [20]. Furthermore, some variants have been associated with a specific set of symptoms or can result in more severe or milder clinical outcomes [5, 6]. The Delta variant, for example, was associated with an increase in hospitalization and more severe symptoms, while Omicron has shown milder symptoms, but with a higher rate of viral transmission [21–23].

Beyond the impact of new variants and pre-existing conditions on the epidemiological and clinical profile of Covid-19, geographic, demographic, and sociodemographic factors also played a significant role in the epidemiology of COVID-19 [18, 19, 24–27]. In this context, it has been discussed that, in addition to age and the presence of chronic diseases, socioeconomic inequalities affected the initial course of COVID-19 epidemic and related deaths [28]. Our group previously demonstrated that community variables impacted COVID-19 dynamics in the State of Bahia, Brazil, and different clinical profiles were observed among various cities within the same state [26].

Taking all this data into account, we aimed to identify the circulation of SARS-CoV-2 variants during two local waves of COVID-19 cases in southern Bahia, Brazil, and to analyze the association between these variants and the epidemiological and clinical profile to understand how viral variants can alter the dynamics of COVID-19.

Materials and methods

Ethical consideration

The study was conducted in line with the principles of the Declaration of Helsinki and the National Health Council (Resolution no. 466/2012), and was approved by Research Ethics Committee of Universidade Estadual de Santa Cruz (Comitê de Ética em Pesquisa — CEP/UESC), under protocol number CAAE: 39142720.5.0000.5526.

Study design

An observational, descriptive, and cross-sectional study was carried out, using clinical and epidemiological data from individuals who underwent molecular testing for SARS-CoV-2 at the Laboratório de Farmacogenômica e Epidemiologia Molecular (LAFEM), using nasopharyngeal swab samples. LAFEM is located at the Universidade Estadual de Santa Cruz (UESC) in Ilhéus, Bahia, Brazil, and worked in partnership with the Laboratório Central de Saúde Pública Professor Gonçalo Moniz (LACEN/BA), supporting the routine diagnostics for SARS-CoV-2 detection in the southern region of Bahia, Brazil. This region was one of the main epicenters of COVID-19 in the state, and has the cities of Ilhéus (14°49′33.7″ S, 39°02′03.7″ W) and Itabuna (14°47′08″ S, 39°16′49″ W) as reference centers for healthcare for a large surrounding population, as well as for leisure and commerce (Fig. 1).

We collected data and nasopharyngeal samples from 368 individuals in two periods: from September to November 2021 and from November to December 2022. These periods, here called local waves, were characterized by an increase in testing and registered cases, when compared to previous months. Data from city location, gender, age, symptoms, comorbidities and COVID-19 status vaccination were obtained from notification forms used by the Ministry of Health (Brazil) and from a structured questionnaire. Data and samples from individuals over 18 years old, suspected of having COVID-19 during the periods evaluated, were included. Individuals residing outside the southern region of Bahia or those with

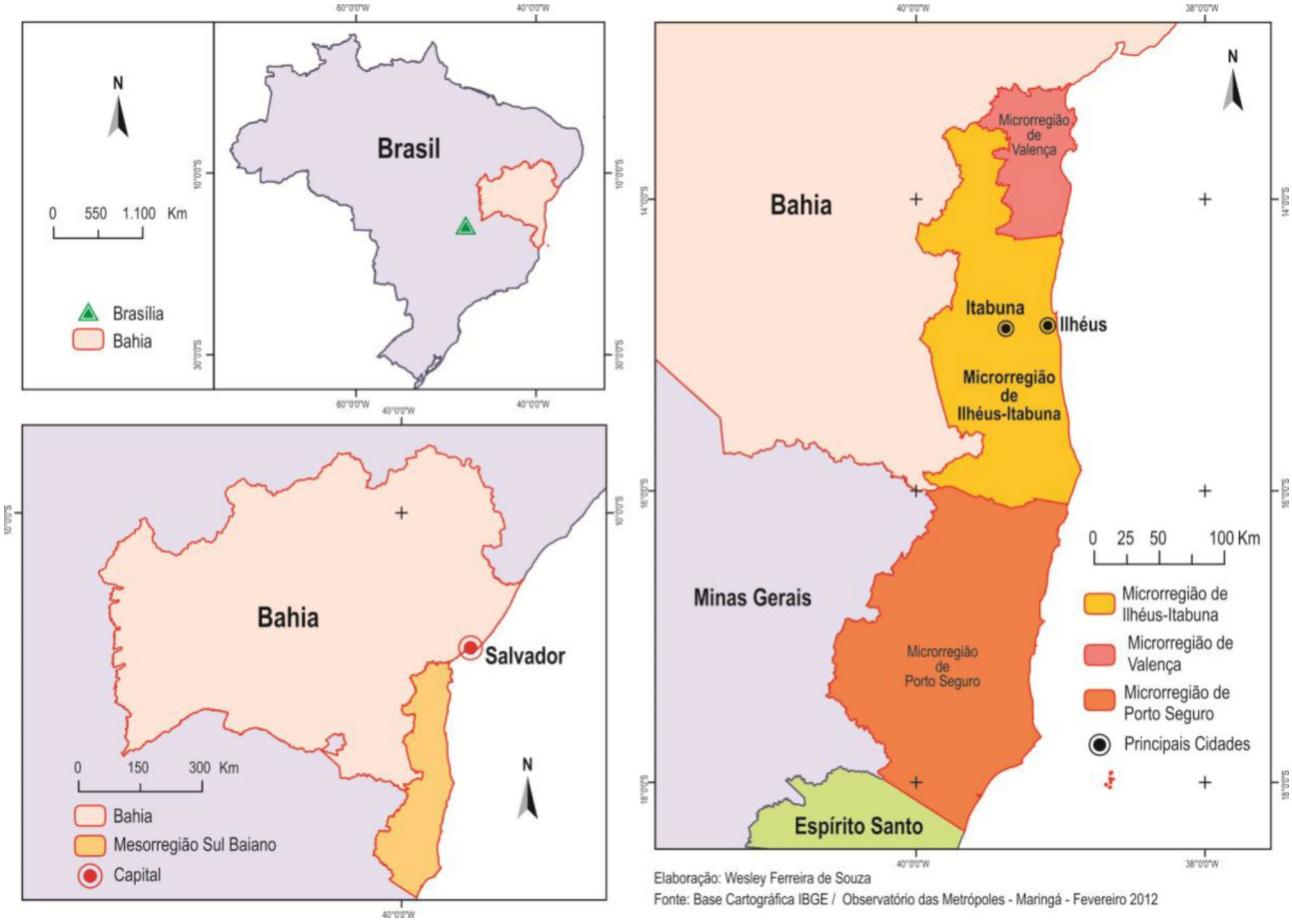

Fig. 1 Location of the Ilhéus-Itabuna microregion in the southern region of Bahia, Brazil. Source: Rangel, 2013 [29].

incomplete clinical and/or epidemiological data were excluded.

Laboratory diagnosis of SARS-CoV-2

Nasopharyngeal swab samples collected from all individuals were tested for the presence of viral RNA by RT-qPCR. Viral RNA extraction was performed using the automated extractor EXTRACTA 32 (Loccus, Cotia, São Paulo, Brazil) and the extraction kits MVXA-P016 (Loccus, Cotia, São Paulo, Brazil). The SARS-CoV-2 RNA detection was carried out using the 7500 Fast Real-Time PCR System thermal cycler (Applied Biosystems™, Life Technologies, Carlsbad, USA) and the SARS-CoV-2 EDx molecular kit (Bio-Manguinhos/Fiocruz, Rio de Janeiro, Brazil), following the manufacturer's protocol.

Genomic sequencing

For the identification of SARS-CoV-2 variants, positive SARS-CoV-2 samples with cycle threshold (CT) values ≤ 25 in the RT-qPCR were selected for genomic sequencing. This sequencing was performed on Illumina Sequencing Platform using the COVIDSeq kit (Illumina, San Diego, USA), and following the manufacturer's specifications. The results were described according to the Pango lineage classification system [30].

Data curation

Nasopharyngeal samples tested were classified as positive, negative or inconclusive for SARS-CoV-2. Inconclusive results were excluded from the analyses. Ages were standardized to years and grouped by decades. Individuals were classified based on their COVID-19 vaccination status at the time of sample collection. An individual was considered "fully vaccinated" if they had received at least 2 doses of the vaccine in 2021 or at least 3 doses in 2022; "partially vaccinated" if they had received fewer doses than expected for the period; and "unvaccinated" if they had not received any vaccine doses.

Statistical analysis

All statistical analyses were performed using GraphPad Prism version 9.0.0 (San Diego, CA, USA) for Windows. For continuous variable analyses, data were checked for normal distribution using the Kolmogorov-Smirnov test with the corrected *P* value (Dallal-Wilkinson-Lilliefors). Two-tailed Student's t-test and two-tailed

Mann-Whitney test were used for parametric and non-parametric data, respectively. Data were represented as median and interquartile range (IQR). For age frequency analyses, the individuals were grouped (age: <20, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79) according to sex. Age pyramids and age curve overlays were created in GraphPad Prism version 9.0.0 (San Diego, CA, USA). The association between categorical variables was analyzed using the Chi-square test and the two-tailed Fisher's Exact test. Data were presented as frequency (n), percentage (%), odds ratio (OR), and 95% confidence interval (95% CI). An alpha of 5% was established for all analyses, and p values < 0.05 were considered statistically significant.

Results

General characteristics of the study population

Clinical, epidemiological, and laboratory data from 368 individuals with suspected COVID-19 were included (Fig. 2). 155 were from the late 2021 (September to November) and 213 from the late 2022 (November to December). Our sample showed a higher frequency of females in both periods, 2021 (58.7%) and 2022 (67.1%), aged between 20 and 29 years old (29.7% in 2021; 46.5% in 2022) (Table 1), and residents of Itabuna city (59.5%). Another 36.4% of individuals resided in Ilhéus city, and the remaining 4.1% were from surrounding municipalities, such as Uruçuca, Una, Canavieiras, Buerarema, Camamu, Floresta Azul, and Ibicaraí.

We observed an important difference in the positive rate for SARS-CoV-2, being much higher in 2022 (56%) than in 2021 (23%). Besides, a low frequency of individuals with comorbidities were observed (5.8% and 15.8%

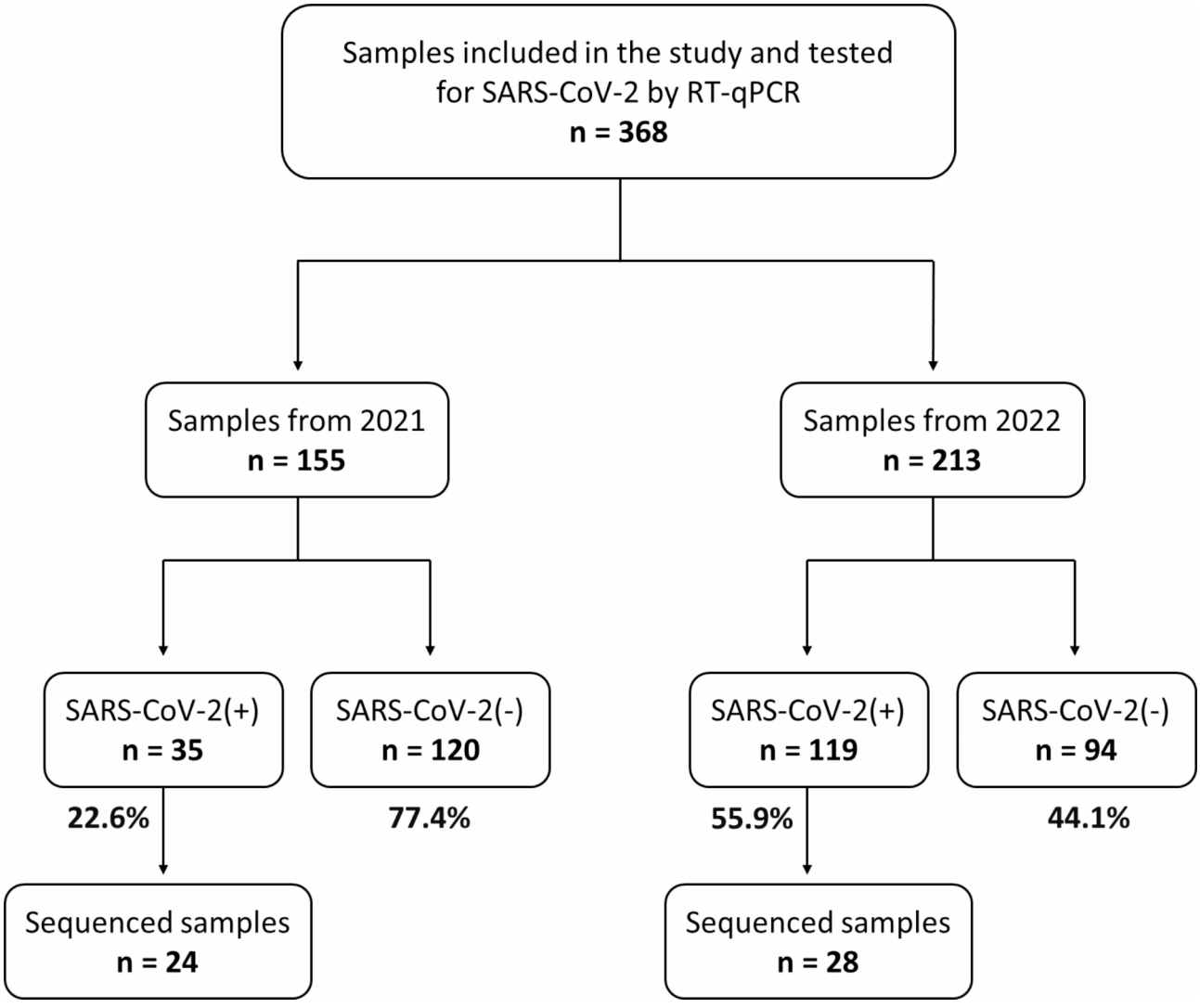

Fig. 2 Diagram showing the study development flow

Table 1 Characteristics of the study population ($n=368$), according to the year of sample collection

Variables	2021	2022
	$n=155$	$n=213$
Sex	**n (%)**	**n (%)**
Female	91 (58.7)	143 (67.1)
Male	64 (41.3)	70 (32.9)
Age range[a]		
< 20	5 (3.4)	14 (6.6)
20 — 29	44 (29.7)	99 (46.5)
30 — 39	34 (23.0)	40 (18.8)
40 — 49	34 (23.0)	36 (16.9)
50 — 59	15 (10.1)	19 (8.9)
60 — 69	11 (7.4)	5 (2.3)
70 — 79	5 (3.4)	0
Not reported	7	0
Comorbidities		
Yes	7 (5.8)	33 (15.8)
No	114 (94.2)	176 (84.2)
Not reported	34	4
COVID-19 vaccination status[b]		
Fully vaccinated	101 (67.3)	196 (92.9)
Partially vaccinated	39 (26.0)	15 (7.1)
Not vaccinated	10 (6.7)	0
Not reported	5	2

[a]All individuals were over 18 years old. [b]An individual was considered "fully vaccinated" if they had received at least 2 doses of the vaccine in 2021 or at least 3 doses in 2022; "partially vaccinated" if they had received fewer doses than expected for the period; and "unvaccinated" if they had not received any vaccine doses

in 2021 and 2022, respectively) (Table 1). As expected, a higher coverage of SARS-CoV-2 vaccination was observed in 2022 with 92.9% of the individuals fully vaccinated and none unvaccinated, whereas, in 2021, 67% were fully vaccinated and around 7% were not vaccinated.

Differences of age and sex distribution between the two periods (late 2021 and late 2022)

Initially, we assessed age variations among the two periods studied. In general, individuals from 2022 were younger (median 28 years, IQR 22–41) than those from 2021 (37 years, IQR 27–48; $p<0.0001$; Fig. 3A). However, when we stratified the groups as SARS-CoV-2 positive and negative separately for each year, we did not observe any difference (Fig. 3B and C). As an intra-group difference could exist, we then compared SARS-CoV-2 infection status from 2021 to 2022. We observed that SARS-CoV-2 positive individuals from 2022 were younger (28 years, IQR 22–41) than those from 2021 (39 years, IQR 28–48; $p=0.0015$), and SARS-CoV-2 negative individuals from 2022 were also younger (29 years, IQR 22–43) than those from 2021 (35 years, IQR 26–47; $p=0.0085$; Fig. 3D).

As gender may be a risk factor for a wide range of infectious diseases, we try to identify the impact of gender in our study. We observed that the majority of positive cases for SARS-CoV-2 occurred in females in 2021 and 2022 (Fig. 4A-C). Interestingly, a variation in age distribution was observed between this period. During 2021 mainly females were in the age group of 40 to 49 years (Fig. 4A), while during 2022 the higher percentage was in the age group of 20 to 29 years (Fig. 4B).

As mentioned above, individuals who tested positive for SARS-CoV-2 in 2021 were significantly older than those infected by SARS-CoV-2 in 2022 ($p=0.0015$; Fig. 3D), and this is clearly seen when separated by sex. When the frequencies of positive cases in both years are overlaid, separated by sex, a clearly different curve pattern is observed for females, with 2021 showing a higher frequency of positivity in older ages compared to 2022 (Fig. 4D-E).

Differences in the clinical spectrum of SARS-CoV-2 infection

The association between clinical symptoms and SARS-CoV-2 infection in 2021 and 2022 are presented in Tables 2 and 3. A clear difference was observed between the symptoms profile of individuals between 2021 and 2022.

The most frequent symptoms during 2021 period were: cough (37.9%, $n=36$) and headache (33.7%, $n=32$), pharyngalgia (26.3%, $n=25$), and rhinorrhea (25.3%, $n=24$) (Table 2). In contrast, during 2022 were: pharyngalgia (52.1%, $n=111$), headache (51.2%, $n=109$), cough (47.9%, $n=102$) and rhinorrhea (47.3, $n=97$; Table 3).

Furthermore, we observed no difference in the symptom profile among SARS-CoV-2 positive and negative individuals in 2021, except for anosmia/ageusia. Individuals who presented anosmia/ageusia were more likely to test positive for SARS-CoV-2 infection in 2021 (Odds Ratio [OR] 5.583; CI 95% 1.525–18.61; $p=0.0151$; Table 2).

On the other hand, a large number of symptoms were associated with SARS-CoV-2 positivity during 2022 (Table 3). Individuals who presented symptoms such as pharyngalgia (OR 4.169; CI 95% 2.332–7.498; $p<0.0001$), fever (OR 3.117; CI 95% 1.604–6.189; $p=0.0008$), rhinorrhea (OR 3.09; CI 95% 1.733–5.567; $p<0.0001$), cough (OR 3.006; CI 95% 1.712–5.267; $p=0.0001$), headache (OR 2.557; CI 95% 1.475–4.375; $p=0.0008$), and myalgia (OR 2.269; CI 95% 1.247–4.228; $p=0.0077$) presented high odds ratio and were more likely to test positive for SARS-CoV-2 (Table 3). Additionally, anosmia/ageusia were not associated with SARS-CoV-2 positivity in 2022 as observed in 2021.

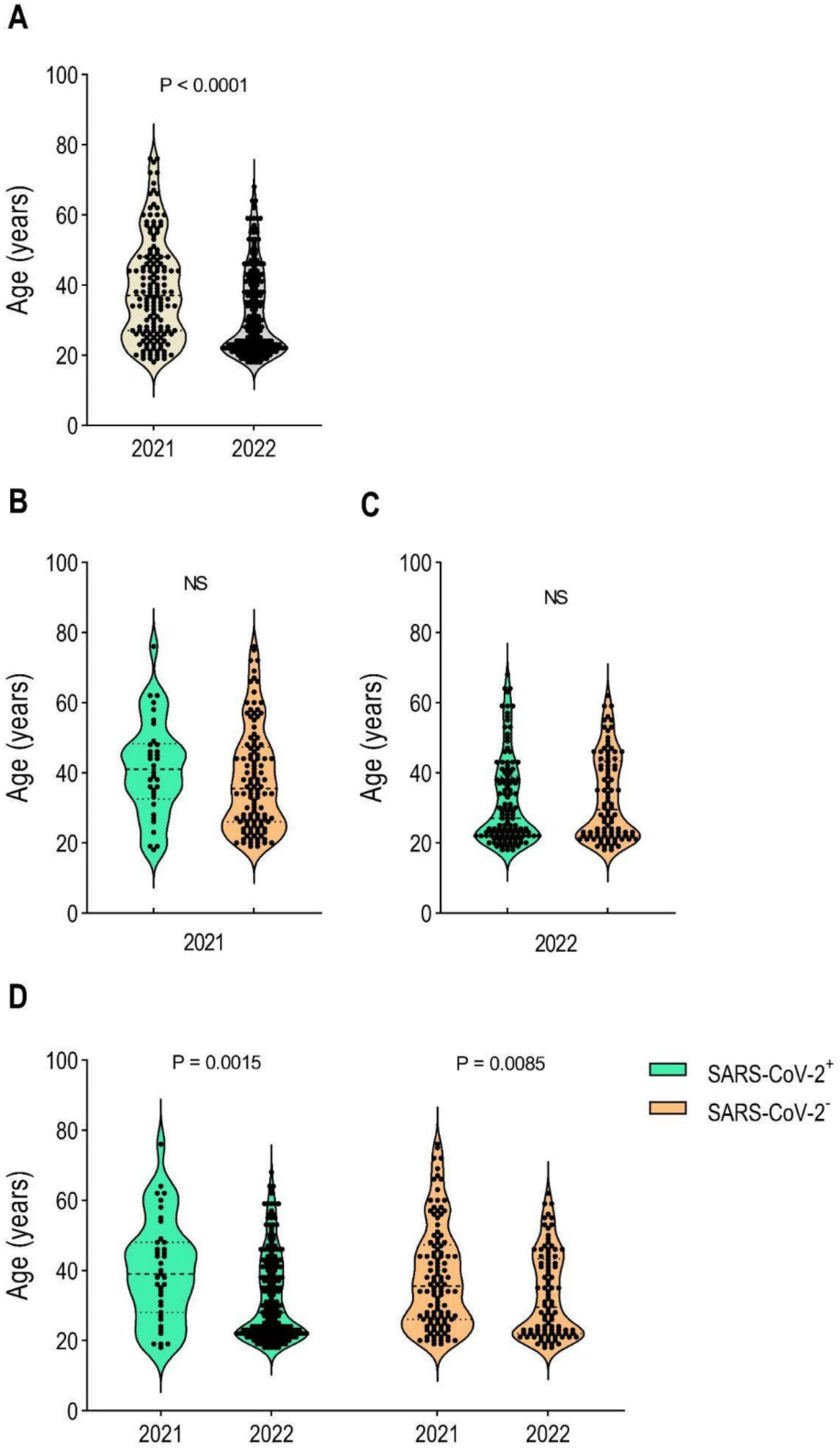

Fig. 3 Changes in age of individuals who tested for SARS-CoV-2. (**A**) Overall age of individuals tested for SARS-CoV-2 by year, and by SARS-CoV-2 detection (**B**) in 2021 and (**C**) 2022. (**D**) Comparison between age of individuals who tested positive (left) and negative (right) for SARS-CoV-2

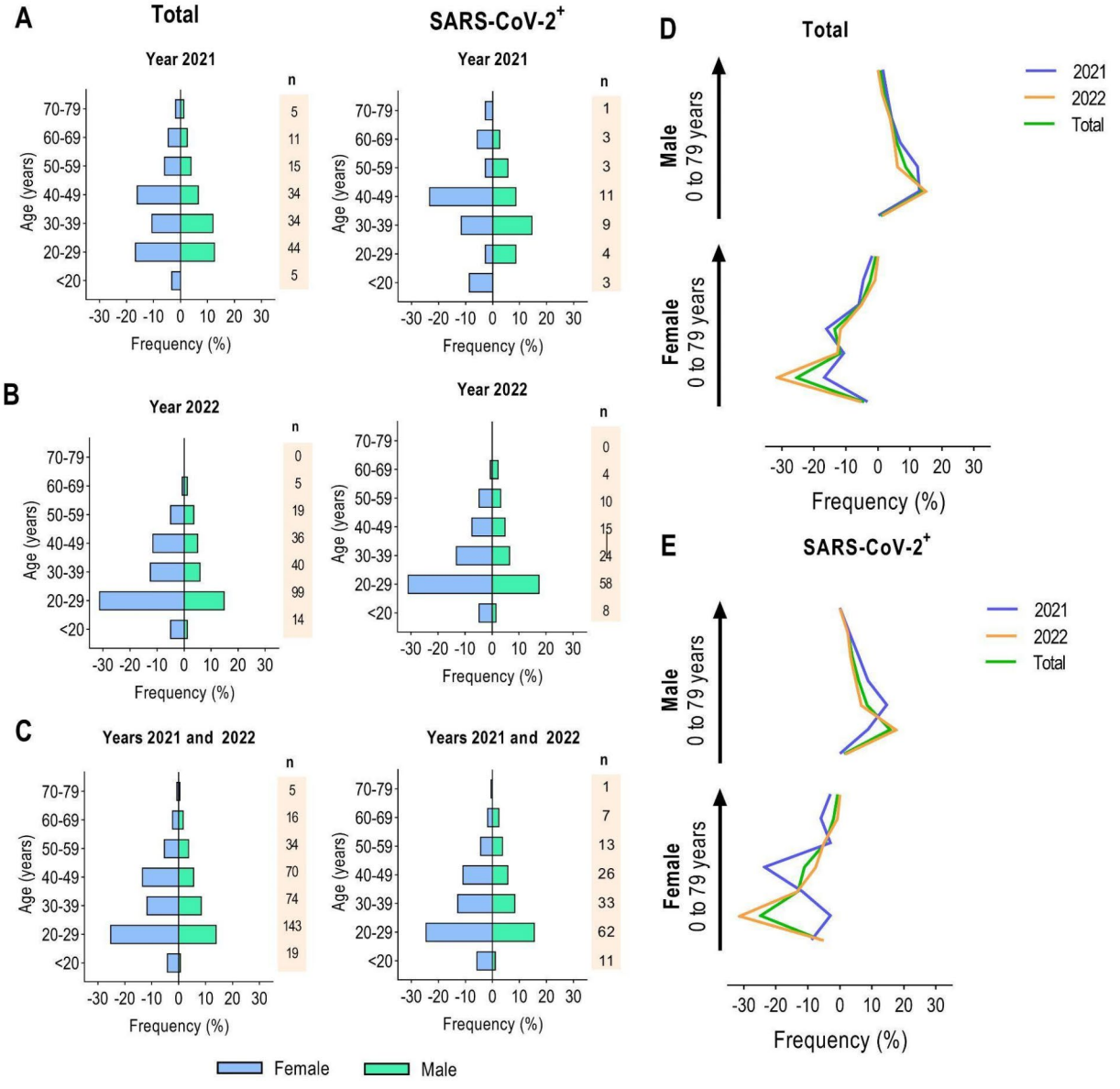

Fig. 4 Age pyramid of individuals tested for SARS-CoV-2. Age distribution of total study population (left) and SARS-CoV-2 positive individuals (right) by sex. (**A**) 2021, (**B**) 2022, (**C**) 2021 and 2022. Frequency of individuals in overlaid curves for (**D**) total population and (**E**) SARS-CoV-2 positive individuals

SARS-CoV-2 variants identification and their association with clinical symptoms

To confirm the impact of SARS-CoV-2 variants in our two local waves of Covid-19 cases (20201 and 2022), we sequenced a total of 62 samples (Fig. 2). From 2021, all samples were identified as Delta variants, especially AY.124 lineage (62.5%, $n=15$). Other lineages were less frequent, as follows: AY.99.2 (20.8%, $n=5$), AY.43.2 (12.5%, $n=3$), and AY.34.1.1 (4.2%, $n=1$) (Table 4). From 2022, all samples were identified as Omicron variants, especially BQ.1.1 lineage (78.6%, $n=22$). Other lineages found were: BE.10 (10.7%, $n=3$), BQ.1 (7.1%, $n=2$), and BA.5.3.1 (3.6%, $n=1$) (Table 5).

Finally, we compared the frequency of clinical symptoms between the variants identified (Fig. 5). Omicron variants were associated with a higher frequency of symptoms. Fever (OR 0.2308; CI 95% 0.073–0.884; $p=0.0371$), dry cough (OR 0.1667; CI 95% 0.0515–0.557; $p=0.0026$), pharyngalgia (OR 0.1247; CI 95% 0.0370–0.4471; $p=0.0007$), headache (OR 0.195; CI 95% 0.0566–0.6315; $p=0.0054$), and rhinorrhea (OR 0.0947; CI 95% 0.0299–0.3709; $p=0.0003$) were less frequent among individuals infected with Delta than among those

Table 2 Symptom profile of individuals tested for SARS-CoV-2 during 2021

Symptoms (*n* = 95)	Total individuals (%)	RT-qPCR for SARS-CoV-2		OR	CI 95%	*p*-Value*
		Positive (%)	Negative (%)			
Fever						
Yes	21 (22.1)	6 (28.6)	15 (71.4)	1.244	0.405–3.839	0.6926
No	74 (77.9)	18 (24.3)	56 (75.7)			
Fatigue						
Yes	1 (1.1)	0 (0)	1 (100)	0	0.000-26.630	> 0.9999
No	94 (98.9)	24 (25.5)	70 (74.5)			
Cough						
Yes	36 (37.9)	11 (30.6)	25 (69.4)	1.557	0.593–3.926	0.3538
No	59 (62.1)	13 (22.0)	46 (78.0)			
Myalgia						
Yes	18 (18.9)	5 (27.8)	13 (72.2)	1.174	0.417–3.496	0.7581
No	77 (81.1)	19 (24.7)	58 (75.3)			
Dyspnea						
Yes	6 (6.3)	2 (33.3)	4 (66.7)	1.523	0.274–6.883	0.6405
No	89 (93.7)	22 (24.7)	67 (75.3)			
Pharyngalgia						
Yes	25 (26.3)	7 (48.6)	18 (51.4)	1.212	0.466–3.399	0.7137
No	70 (73.7)	17 (58.6)	53 (41.4)			
Diarrhea						
Yes	6 (6.3)	0	6 (100.0)	0	0.000-2.164	0.3319
No	89 (93.7)	24 (27.0)	65 (73.0)			
Headache						
Yes	32 (33.7)	10 (31.3)	22 (68.8)	1.529	0.628–4.070	0.3385
No	63 (66.3)	14 (22.2)	49 (77.8)			
Vomiting						
Yes	2 (2.1)	0	2 (100.0)	0	0.000-6.429	> 0.9999
No	93 (97.9)	24 (25.8)	69 (74.2)			
Rhinorrhea						
Yes	24 (25.3)	4 (16.7)	20 (83.3)	0.51	0.172–1.698	0.415
No	71 (74.7)	20 (28.2)	51 (71.8)			
Anosmia/Ageusia						
Yes	10 (10.5)	6 (60.0)	4 (40.0)	**5.583**	**1.525–18.61**	**0.0151**
No	85 (89.5)	18 (21.2)	67 (78.8)			

*Chi-square test and the two-tailed Fisher's Exact test. OR, odds ratio. 95% CI, confidence interval. Values of $p < 0.05$ were considered statistically significant. Bold values indicate statistical significance

infected with Omicron. Other symptoms, like myalgia, dyspnea, and anosmia were not affected with the presence of Omicron variants.

Discussion

In this study, we analyzed cases from different local waves of COVID-19 and observed that the positivity rate for SARS-CoV-2 was more than twice as high in 2022 compared to 2021 (56% vs. 23%, respectively). During these periods, there was a lower demand for hospital care in 2022, which coincided with increased vaccination coverage. However, 2022 also saw greater viral spread and transmission, as reported by Dutta [31]. This finding aligns with the higher positivity rate observed in our study for 2022. The increased transmissibility and positivity were attributed to the emergence of the Omicron variant [32], which corresponds with the variants detected in our study.

Furthermore, we identified epidemiological and clinical differences when comparing individuals tested during the two periods: late 2021 and late 2022. Individuals tested for SARS-CoV-2 in 2022 were significantly younger than those tested in 2021. As activities gradually returned to normal, younger adults faced higher exposure risks to respiratory infections due to social behaviors, such as leaving home for work, attending social gatherings, or visiting crowded places [33, 34]. These findings illustrate the evolving nature of the pandemic as new pharmacological and non-pharmacological measures were implemented or relaxed.

In terms of sex distribution, the majority of SARS-CoV-2 positive cases occurred in females. However, the

Table 3 Symptom profile of individuals tested for SARS-CoV-2 during 2022

Symptoms (*n* = 213)	Total individuals (%)	RT-qPCR for SARS-CoV-2		OR	CI 95%	*p*-Value*
		Positive (%)	Negative (%)			
Fever						
Yes	56 (26.3)	42 (75.0)	14 (25.0)	**3.117**	**1.604–6.189**	**0.0008**
No	157 (73.7)	77 (49.0)	80 (51.0)			
Fatigue						
Yes	12 (5.6)	6 (50.0)	6 (50.0)	0.779	0.235–2.584	0.6734
No	201 (94.4)	113 (56.2)	88 (43.8)			
Cough						
Yes	102 (47.9)	71 (69.6)	31 (30.4)	**3.006**	**1.712–5.267**	**0.0001**
No	111 (52.1)	48 (43.2)	63 (56.8)			
Myalgia						
Yes	68 (31.9)	47 (69.1)	21 (30.9)	**2.269**	**1.247–4.228**	**0.0077**
No	145 (68.1)	72 (49.7)	73 (50.3)			
Dyspnea						
Yes	4 (1.9)	4 (100)	0	Infinity	0.787-Infinity	0.1318
No	209 (98.1)	115 (55.0)	94 (45.0)			
Pharyngalgia						
Yes	111 (52.1)	80 (72.1)	31 (27.9)	**4.169**	**2.332–7.498**	**< 0.0001**
No	102 (47.9)	39 (38.2)	63 (61.8)			
Diarrhea						
Yes	12 (5.6)	8 (66.7)	4 (33.3)	1.622	0.511–4.965	0.5557
No	201 (94.4)	111 (55.2)	90 (44.8)			
Headache						
Yes	109 (51.2)	73 (67.0)	36 (33.0)	**2.557**	**1.475–4.375**	**0.0008**
No	104 (48.8)	46 (44.2)	58 (55.8)			
Vomiting						
Yes	2 (0.9)	2 (100)	0	Infinity	0.366-Infinity	0.5046
No	211 (99.1)	117 (55.5)	94 (44.5)			
Rhinorrhea						
Yes	93 (43.7)	66 (71.0)	27 (29.0)	**3.09**	**1.733–5.567**	**< 0.0001**
No	120 (56.3)	53 (44.2)	67 (55.8)			
Anosmia/Ageusia						
Yes	11 (5.2)	7 (63.6)	4 (36.4)	1.406	0.430–4.399	0.7585
No	202 (94.8)	112 (55.4)	90 (44.6)			

*Chi-square test and the two-tailed Fisher's Exact test. OR, odds ratio. 95% CI, confidence interval. Values of $p < 0.05$ were considered statistically significant. Bold values indicate statistical significance

Table 4 Frequency of SARS-CoV-2 lineages identified through viral genomic sequencing of samples from September to November 2021

SARS-CoV-2 Lineages	*n*	%
AY.124 (Delta)	15	62.5
AY.34.1.1 (Delta)	1	4.2
AY.43.2 (Delta)	3	12.5
AY.99.2 (Delta)	5	20.8
Total	24	100

Table 5 Frequency of SARS-CoV-2 lineages identified through viral genomic sequencing of samples from November to December 2022

SARS-CoV-2 Lineages	*n*	%
BA.5.3.1 (Omicron)	1	3.6
BE.10 (Omicron)	3	10.7
BQ.1 (Omicron)	2	7.1
BQ.1.1 (Omicron)	22	78.6
Total	28	100

tested population was predominantly female (58.7% in 2021 and 67.1% in 2022), reflecting the sociodemographic characteristics of the State of Bahia [35]. This higher testing rate among females may also be linked to the greater preventive healthcare-seeking behavior typically observed in women.

Regarding clinical symptoms, the most common in 2021 were cough, headache, pharyngalgia, and rhinorrhea. Although less frequent, individuals with anosmia/ageusia were five times more likely to test positive for SARS-CoV-2 infection, making these symptoms the most specific indicators of the infection during that period.

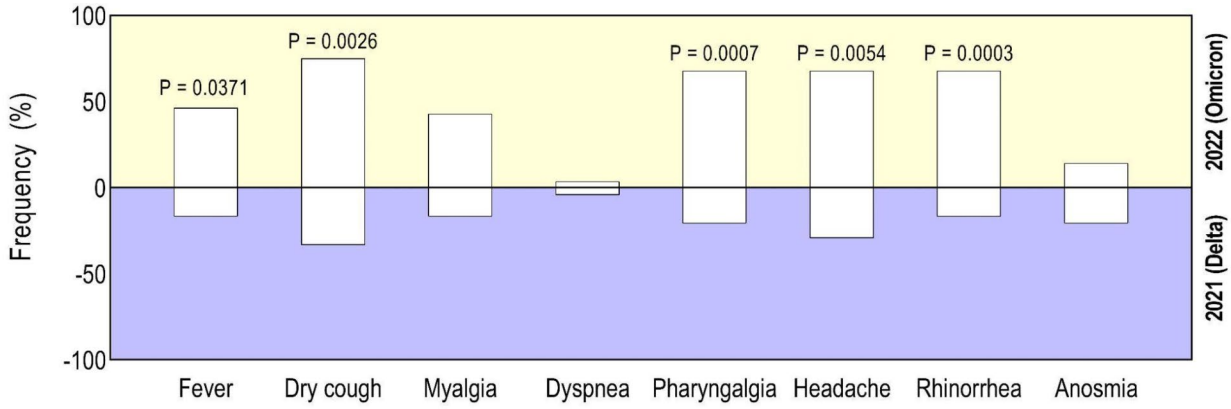

Fig. 5 Frequency of clinical symptoms reported, according to SARS-CoV-2 variants detected by viral sequencing. Chi-square test and the two-tailed Fisher's Exact test. Values of $p < 0.05$ were considered statistically significant

In contrast, in 2022, the most frequent symptoms were pharyngalgia, headache, cough, and rhinorrhea, with pharyngalgia being the symptom most associated with SARS-CoV-2 infection. Notable differences in symptom frequency and profiles were observed between the two periods. According to Fernandes et al. [6], these differences are likely related to the circulating viral variants, which may have contributed to changes in infection profiles and clinical presentations.

In terms of viral sequencing, all samples from September to November 2021 were identified as the Delta variant, with the majority (62.5%) belonging to the AY.124 lineage. This is consistent with data from that period, which indicated that the Delta variant was dominant in many countries, including Brazil, during the second half of 2021 [13, 36]. In the State of Bahia, a report released by LACEN/BA indicated that this variant became predominant in September 2021, accounting for over 95% of sequenced cases during that period [37].

Conversely, all sequenced samples from November to December 2022 were identified as the Omicron variant, with the majority (78.6%) classified as BQ.1.1. This aligns with the literature, which notes that Omicron, first identified in South Africa in November 2021, rapidly became the dominant variant worldwide, surpassing Delta lineages [38]. According to reports from LACEN/BA, the BQ.1 lineage and its sublineages were first observed in the State of Bahia in October 2022, becoming dominant by November, with a prevalence of 75% and reaching over 84% in December 2022 [39].

When correlating symptoms with variants, we observed that five of the eight evaluated symptoms were more frequent among individuals infected with the Omicron variant (fever, dry cough, pharyngalgia, headache, and rhinorrhea) compared to those infected with the Delta variant (Fig. 5). Studies have shown that Omicron has a higher affinity for cells in the upper respiratory tract [40, 41], leading to symptoms such as pharyngalgia and fever, which are characteristic of acute upper respiratory tract infections, but with minimal or no radiographic changes in the lungs [42, 43].

One limitation of this study is the reliance on notification forms, which were often not fully completed. This limitation may have hindered the analysis of some cases, complicating the development of a comprehensive clinical-epidemiological profile of the study population.

The differences observed in this study underscore the importance of genomic surveillance, as variants can alter the virus's transmissibility and symptomatology, as demonstrated by our results. Routine and continuous molecular analyses are crucial for ensure timely and appropriate public health responses. The data presented here contribute to a better understanding of the dynamics of COVID-19 and the clinical and epidemiological implications of different viral variants.

Conclusion

By analyzing two distinct local waves of COVID-19 cases in southern Bahia, Brazil, we identified significant differences in the epidemiological and clinical-laboratory profiles of the disease, particularly in the frequency of clinical symptoms and the distribution of viral variants. The higher detection rate observed in 2022, alongside an increase in reported respiratory symptoms, coincided with the widespread circulation of the more transmissible Omicron variant, despite the expansion of vaccine coverage. The prevalence of symptoms such as pharyngalgia and rhinorrhea in Omicron cases reflects its greater tropism for the upper respiratory tract. These findings highlight the critical role of genomic surveillance in the ongoing monitoring of viral variants. Such surveillance is essential for enhancing our understanding of the pandemic's evolution and for enabling the early implementation of targeted mitigation strategies to contain future outbreaks.

Abbreviations

CI	Confidence interval
COVID-19	Coronavirus disease 2019
CT	Cycle threshold
LACEN/BA	Laboratório Central de Saúde Pública Professor Gonçalo Moniz
LAFEM	Laboratório de Farmacogenômica e Epidemiologia Molecular
OR	Odds ratio
RT-qPCR	Reverse transcription quantitative polymerase chain reaction
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
UESC	Universidade Estadual de Santa Cruz

Supplementary Information

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Supplementary Material 1

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Author contributions

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Data availability

All relevant data are within the manuscript and its Supplementary Information files.

Declarations

Ethics approval and consent to participate

The study was conducted following the Declaration of Helsinki and National Health Council (Resolution n. 466/2012) and approved by the Research Ethics Committee of the Universidade Estadual de Santa Cruz under registration: CAAE 58404622.5.0000.5526. The individuals' data was completely de-identified, ensuring complete anonymity to protect privacy and confidentiality.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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