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Research Letter

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SARS-CoV-2 genomic surveillance in Northeast Brazil: timing of emergence of the Brazilian variant of concern P1

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel enveloped, single-stranded RNA betacoronavirus associated to the coronavirus disease 2019 (COVID-19). The viral genome is ∼30 kb and consists of 10 open reading frames that encode structural, non-structural and accessory proteins. The structural proteins include nucleocapsid (N), spike (S), membrane (M) and envelope (E) proteins that play a critical role in the life cycle of the viral particles. There is evidence that the critical determinant of the SARS-CoV-2 genome is the S protein that mediates the virus entry into human host cells through interactions with the angiotensin-converting enzyme 2 receptor.[1]

RNA viruses have distinct characteristics including high spontaneous mutation rates and short replication times. It has been found that the relatively large SARS-CoV-2 genome and low-fidelity polymerase are the contributing factors for the higher rate of adaptive mutations, leading to the viral evolution, genome variability and coexistence of pathogenic viral strains worldwide.[2] Despite most viral mutations have little to no effect on viral replication and transmission, accumulated mutations may become molecular markers of virus spread geographically. Recently, emergent SARS-CoV-2 lineages with multiple S protein mutations identified in the UK (B.1.1.7 lineage), South Africa (B.1.351 lineage) and Brazil (P.1 and P.2, both derived from the B.1.1.28 lineage) have been associated with increased transmissibility and changes in antigenic profile.

In this report, we presented the results of genomic surveillance for patients with SARS-CoV-2 infection and described the prevalence of SARS-CoV-2 lineages from March 2020 to February 2021 in Sergipe state, Northeast Brazil. Sergipe is the smallest state in Brazil and is located in the poorest region of the country. The state has an estimated population of ∼2.3 million people and Human Development Index of 0.665. The first case of COVID-19 in Sergipe was confirmed on 14 March 2020 in a female patient with recent travel to Spain, infected with SARS-CoV-2 lineage B.1, and by 25 February 2021, 169 458 cases and 3368 deaths had been registered.

A total of 147 patients with a median age of 40 years (minimum 6 and maximum 99 years) were enrolled in this study: 41 diagnosed with COVID-19 in the first 6 months of the outbreak in Sergipe (14 March 2020–31 August 2020) and 106 between 1 September 2020 and 25 February 2021. All patients had a laboratory confirmation for SARS-CoV-2 infection, defined as a positive result on real-time reverse transcription polymerase chain reaction assay of respiratory tract samples based on the World Health Organization's interim guidelines. The whole-genome sequences of SARS-CoV-2 for these samples were recovered using nanopore sequencing protocol previously established and used by Genomic Coronavirus Fiocruz Network to recover high-quality genomes.[3] The lineage was determined using the Pangolin tool (https://pangolin.cog-uk.io/).

Since March 2020, 11 lineages of SARS-CoV-2 have been identified in Sergipe: B1, B.1.1, B.1.80, B.1.1.7, B.1.1.28, B.1.1.33, B.1.1.119, B.1.212, B.1.1.251, P1 and P2. During the first 6 months (March–August 2020) of COVID-19 outbreak,

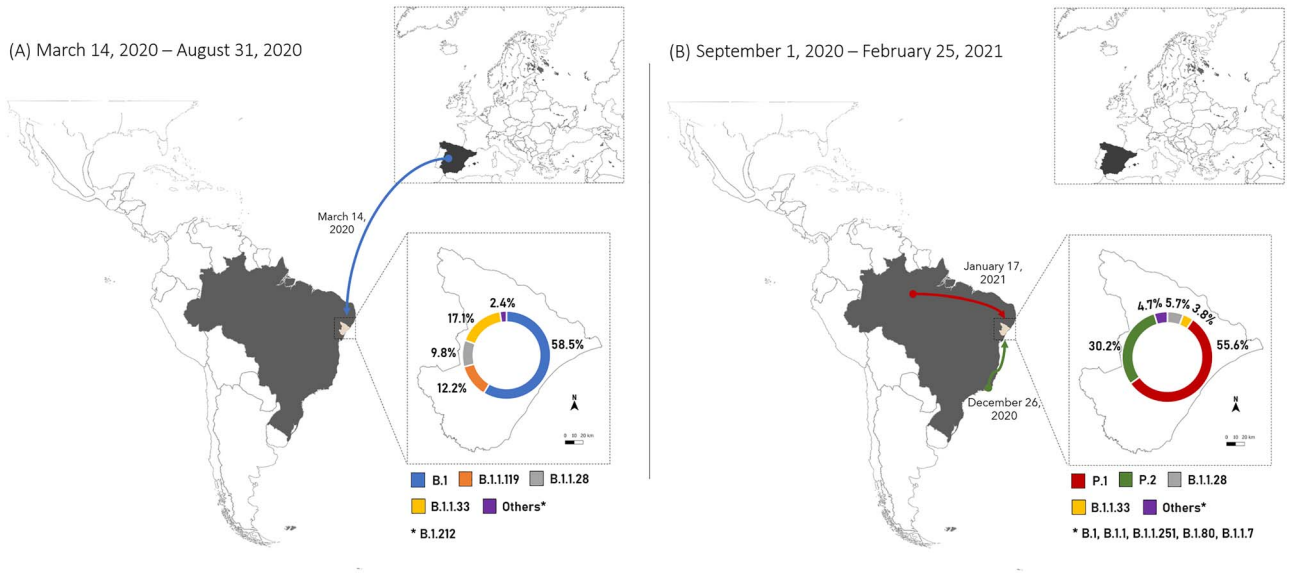

Figure 1. Dynamics of SARS-CoV-2 lineages in Sergipe state, Northeast Brazil, from (A) March to August 2020 and from (B) September 2020 to February 2021.

there was a higher frequency of B.1 (58.5%), followed by B.1.1.33 (17.1%), B.1.1.119 (12.2%) and B.1.1.28 (9.8%) lineages. From September 2020 to February 2021, there was an increased frequency of P.1 (55.6%) and P.2 (30.2%) lineages, and significant reduction in circulation of B.1.1.28 (5.7%) and B.1.1.33 (3.8%) lineages. We identified the first case of P.1 lineage in the city of Aracaju (Sergipe) in a sample collected on 17 January 2021, from a patient residing in the city of Manaus (Amazonas) who travelled to Sergipe to visit his family. By tracking close contacts, other four members of this family were diagnosed with SARS-CoV-2 infection with P.1 lineage. On 24 January 2021, another case of SARS-CoV-2 P.1 lineage was identified in a resident of Aracaju city who travelled to Manaus on business. On 29 January 2021, we identified the first reported case of an individual infected with the B.1.1.251 lineage in Brazil,[4] and, recently, a case of B.1.1.7 lineage has been investigated (Figure 1).

The genomic surveillance is essential for better understanding the dispersal and evolutionary patterns of SARS-CoV-2 during the ongoing pandemic. Moreover, the early detection of SARS-CoV-2 lineages in each country is necessary to evaluate whether virus mutations might impact viral fitness and transmissibility. The genomic surveillance of SARS-CoV-2 lineages largely focuses on mutations in the S glycoprotein, which has a pivotal role for host cell entry and is the primary target of neutralizing antibodies.

In this study, we observed a higher prevalence of B.1 and B.1.1.33 in the first 6 months of COVID-19 outbreak in Sergipe. The B.1 lineage was initially identified as the most common lineage in the world with a cosmopolitan distribution and strongly associated with prior travels to high-risk areas. In the beginning of COVID-19 pandemic (February–April 2020), it was shown that B.1.1.33 had a prevalence of 33% in Brazil, 5–18% in other South American countries, and a very low prevalence in Canada, USA, England, Portugal, Scotland and Australia (1%). After the end of the first wave of COVID-19 in Brazil, there were changes in the circulation of SARS-CoV-2 lineages, with a high detection of B.1.1.28 and its descendent P.2. The P.2 lineage was first described in October 2020 in the state of Rio de Janeiro and has become the most prevalent lineage in several Brazilian states in the late 2020 and early 2021. On the other hand, the B.1.1.28 was more prevalent in Brazil until late 2020 (http://www.genomahcov.fiocruz.br/).

At the time of writing this manuscript, two variants of concern were identified in our state: the P.1 lineage with several mutations of known biological importance in the S protein (K417T, E484K and N501Y) and the B.1.1.7 that also presents mutations (N501Y, P681H, H69-V70 and Y144/145) associated with increased transmissibility. In addition, there is evidence that E484K mutation may alters the S protein conformation and may affect the neutralizing antibody response. Recently, studies have described cases of reinfection associated to the presence of E484K mutation in the B.1.1.248,[5] B.1.1.28[6] and P.1[7] lineages in Brazil.

Since the SARS-CoV-2 genetic diversity in Brazil seems to be associated to the long delay in imposing air travel restrictions[8,9] and the poor control of domestic travels,[10] genomic surveillance is critical to understand the dynamics of the pandemic in every state. In Brazil, the relaxing distancing control, the increasing intercity population mobility and the slow pace of vaccination have contributed to the emergence and spread of lineages across different regions of the country. In conclusion, this study contributes to the identification and circulation pattern of SARS-CoV-2 lineages during the COVID-19 pandemic in our state. Further studies are needed to evaluate the virulence of these variants and the future impact in COVID-19 vaccination campaign.

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Authors' Contributions

All authors contributed equally to the manuscript.

Conflict of Interest: None declared.

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