**TITLE:** SARS-COV-2 CIRCULATING LINEAGES AND P.1 MUTATIONS AMONG PATIENTS ATTENDING AT HOSPITAL DE CLÍNICAS DE PORTO ALEGRE

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**ABSTRACT:**

The *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) adapted and evolved quickly around the world and multiple variants have emerged since the beginning of the COVID-19 pandemic. In Brazil, a new variant of concern (VOC) P.1, also known as Gamma, emerged in December 2020, and was associated with the second wave of infection in some Brazilian states. The aim of this study was to describe the lineages of SARS-CoV-2 circulating in a COVID-19 reference center in Rio Grande do Sul (RS) from March 2020 to May 2021, and to analyze the mutations observed in specimens of VOC P.1. A total of 200 SARS-CoV-2 specimens obtained from oro/nasopharyngeal swabs were submitted to whole-genome sequencing. Among the 74 specimens from 2020, the lineages B.1.1.28 (n=25) and B.1.1.161 (n=25) were the most prevalent, followed by B.1.1 (n=6), B.1.1.33 (n=4), B.1.91 (n=4), P.2 (n=3), B.1.1.409 (n=2), B.1 (n=1), B.1.1.462 (n=1), B.1.1.370 (n=1), B.1.1.12 (n=1) and P.1 (n=1). Among the 126 specimens from 2021, most of them were identified as P.1 (n=97), followed by P.2 (n=12), P.1.2 (n=6), B.1.1.28 (n=6), P.1.1 (n=2), B.1.1.161 (n=1), B.1.575 (n=1) and C.37 (n=1). The identification of the lineage C.37 (Lambda), considered a variant of interest by the World Health Organization, is worrisome since it has been associated with high rates of transmission and its possible spread in Southern Brazil is of concern. From the 106 P.1 sequences (98 P.1, 6 P.1.2, 2 P.1.1), 99 (93.4%) carried the 22 lineage-defining mutations, including the three mutations in the receptor-binding domain in the Spike (S) protein (K417T, E484K and N501Y), associated with immune system escape and more transmissibility. All the P.1 sequences accumulated other important mutations as P314L in the ORF1ab and R203K/G204R in the Nucleocapsid gene (N) and 38.7% (n=41) accumulated one mutation in the S protein (D614G). Among the five specimens classified as P.1.2 lineages, four of them carried the three defining-mutations that results in amino acid substitutions: one in the ORF1ab (D762G), one in the ORF3a (T1820I), and one in the N (D155Y), and one specimen carried all of them except the T1820I mutation. Our data demonstrate that there was a replacement of circulating lineages in 2020 by the VOC P.1, which became the lineage currently more prevalent in RS state. Furthermore, there is a high genetic diversity among P.1 genome sequences, suggesting a continuous evolution and community spread of the virus.

**Keywords:** COVID-19, SARS-CoV-2, P.1 lineage, Gamma, C.37 lineage

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