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## A COMPREHENSIVE MOLECULAR EPIDEMIOLOGY STUDY OF SARS-COV-2 VIRUS REVEALS AN INITIAL LOCAL TRANSMISSION OF THE DELTA VARIANT IN PORTO ALEGRE, SOUTHERN BRAZIL.

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The SARS-CoV-2 virus has rapidly evolved into variants of concern (VOCs) exhibiting increased transmissibility and immune evasion properties that contributed to outbreaks uncontrolled worldwide. In Brazil, the Gamma and Delta VOCs have established sustained local transmission throughout 2021. However, there are still significant gaps in our understanding of the transition of dominance from Gamma to Delta at the municipality level. Considering this situation, we conducted a comprehensive molecular epidemiology study, including genotyping, genomics, and phylogenetics, to identify and estimate the introduction and local transmission of Delta in Porto Alegre, southern Brazil. A total of 808 nasopharyngeal swab samples with previous molecular diagnosis of COVID-19 were randomly selected from June to November 2021, representing a median of 30% (IQR 9.8–44.2%) of positive samples analyzed in this study. and a median of 5.2% (IQR 1.4-13.0%) of positive cases reported in Porto Alegre. Genotyping of S:T20N and S:P681R, lineage-defining mutations respectively from Gamma and Delta, was performed with Tagman assays. The presence of Delta was identified in 619 samples; of these, 30 genomes were sequenced with the Ion AmpliSea SARS-CoV-2 research panel. Temporal phylogenetic reconstructions were carried out in the Nextstrain pipeline with our samples and global sequences of AY.99.2 and AY.101 sublineages from the GISAID database (n=1,096). Results showed that Gamma was predominant in Porto Alegre in June (95.3%). when the first occurrence of Delta was identified. The prevalence of Delta increased progressively from July (31.7%) to October (97.6%), and in November, all samples were identified as Delta. Genomic sequences were classified as AY.99.2 (n=26), AY.98 (n=1), and AY.101 (n=3). The time-scaled phylogenetic tree showed a larger monophyletic subcluster associated with samples from the Porto Alegre metropolitan region (n=64), pointing to the first Delta sequence identified in this study (AY.99.2) as the likely common ancestral. This phenomenon of rapid replacement of variants by Delta is in accordance with reports from the different Brazilian States. Moreover, Delta sub-lineages described here were the most common circulating in Brazil during the analyzed timeframe. Finally, our data suggest that the AY.99.2 genotype was the first Delta strain introduced and later transmitted locally.

**Keywords:** SARS-CoV-2, variant of concern, Delta, epidemiology.