

TITLE: GENETIC PROFILE OF CHRONIC PULMONARY BURKHOLDERIA CEPACIA COMPLEX INFECTIONS FROM CF PATIENTS IN TWO REFERENCE CENTRES IN RIO DE JANEIRO, BRAZIL

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ABSTRACT:

Burkholderia cepacia complex (Bcc) constitutes an important group of pathogens in cystic fibrosis (CF) lung disease. Currently, 21 genetically distinct species are recognised as Bcc. Chronic respiratory Bcc colonization is associated with a significantly poor prognosis, high morbimortality and patient-to-patient transmissibility. Profiling of lineages and dissemination of these microorganisms have played major role in public health and epidemiology in CF. The aim of this study was to investigate the species and genetic diversity of isolates from CF patients chronically colonized with Bcc from two reference centres in Rio de Janeiro, Brazil. A total of 111 Bcc isolates from 28 patients were obtained between 2010 and 2018. Bacterial identification was performed both by phenotypic methods (matrix-assisted laser desorption/ionization-time of flight mass spectrometry - MALDI-TOF MS) and *recA* gene sequencing. All isolates were genetically profiles by pulsed-field gel electrophoresis (PFGE) in order to check the clonal relatedness among them. *B. vietnamiensis* was the most frequent species (n=41; 41.4%), followed by *B. cenocepacia* IIIA (n=25; 22.5%), *B. multivorans* (n=21;18.9%), *B. cenocepacia* IIIB (n=15;13.5%), *B. stabilis* (n=2;1.8%), *B. contaminans* and *B. cepacia* (n=1; 0.9%). The longitudinal analysis showed that all patients harboured different species, although in some cases one species persisted over years. The genetic diversity of the Bcc by PFGE showed 78 pulsotypes. Ten patients with at least five isolates collected at different periods were evaluated longitudinally. Despite the chronic infection by Bcc, most patients was colonized by intermittent pulsotypes. Only one patient maintained the same specie (*B. vietnamiensis*) showing pulsotypes with similarity $\geq 85\%$ during the two last years of the study. Results suggest that genetic diversity of isolates diverge longitudinally during infection process in CF, proposing that early colonization can be originated by individual strains commuting multiple genotypic variations. The possibility of following substitutions of Bcc strains during chronic infection should be considered while adopting effective practices, such as infection prevention and control measures.

Keywords: Cystic Fibrosis, Burkholderia cepacia complex, Pulsed-field Gel Electrophoresis.

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