

TITLE: SURVEY OF FUNGAL COINFECTION IN LEPROSY PATIENTS AND CORRELATION WITH CARD9 SINGLE NUCLEOTIDE POLYMORPHISM IN THE SERGIPE STATE, BRAZIL.

AUTHORS: SANTOS-FILHO, M.A.¹; PINHEIRO, C.S.¹; SILVA, L.M.¹; CAZZANIGA, R.A.¹; SANTOS, C.N.O.¹; RODRIGUES, D.R.¹; ALMEIDA, R.P.¹; RIBEIRO DE JESUS, A.M.¹; PERES, N.T.A.^{1,2}.

INSTITUTION: ¹FEDERAL UNIVERSITY OF SERGIPE (UFS). ²FEDERAL UNIVERSITY OF MINAS GERAIS (UFMG).

Leprosy is a bacterial infectious disease caused by *Mycobacterium leprae*, which infects phagocytic cells of the skin and Schwann cells of peripheral nerves. The infection leads to a broad range of clinical manifestations, including skin lesions, decreased local sensitivity, and may also cause physical deformities. Although there was a significant reduction in its prevalence after the widespread use of multidrug therapy, leprosy remains endemic in some regions, such as India and Brazil. In 2018, the State of Sergipe reported 320 new cases of leprosy, and in 2019, so far, there was 79 new cases reported. The clinical forms of the disease are associated with the host immune response triggered by the bacteria. While a Th1 response is associated with the tuberculoid and paucibacilar (PB) form, the Th2 response leads to lepromatous leprosy (multibacilar form - MB). Moreover, recent studies have demonstrated the influence of the Th17 response in the control of *M. leprae* multiplication, and its association with the PB leprosy presentation. The Leprosy Outpatient clinic in the University Hospital of Sergipe (HU-UFS) have been extensively diagnosing, treating and following several patients with leprosy, which is contributing greatly to the control of the disease spread. Thus, in this study, we show the clinical observations and surveillance of fungal coinfection cases in leprosy patients with the lepromatous form attended by the Leprosy Outpatient clinic team of physicians, nurses, researchers, and students. In this case-control study with patients diagnosed with MB and PB leprosy, there was a significant statistical difference between the clinical groups with the presence of dermatophytosis, in which the majority of dermatophytosis cases occurs in MB. Furthermore, it has been showed that mutations in the Caspase-Associated Recruitment Domain 9 (card9) gene is associated with severe and invasive dermatophytosis, with a concomitant decrease in serum IL-17. Thus, in the attempt to understand this coinfection, and whether genetic factors are involved in the susceptibility to leprosy and/or to this fungal coinfection, the card9 single nucleotide polymorphism SNP rs_4077515 was evaluated in these patients. This analysis showed an association of this SNP with leprosy *per se*, suggesting that the gene card9 is associated with susceptibility not only to fungi but also to leprosy.

Keywords: leprosy, dermatophytosis, coinfection, card9, single nucleotide polymorphism.

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