

TITLE: INFLAMMATORY RESPONSE IN A DIABETIC AND NON-DIABETIC HOST IN EXPERIMENTAL VULVOVAGINAL CANDIDIASIS BY *Candida tropicalis*

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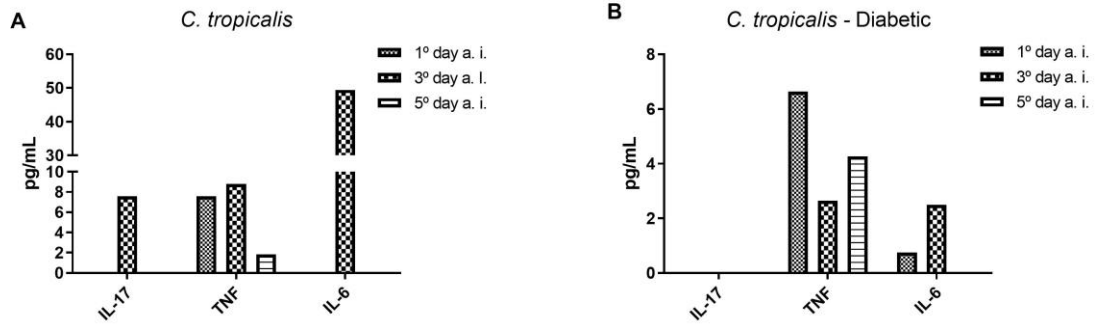
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ABSTRACT:

Vulvovaginal candidiasis (VVC) is considered an important public health problem, affecting women especially in the reproductive age. *Candida albicans* is the most frequent species, however, the frequency of *Candida* non-*C. albicans* is increasing, and *C. tropicalis* stands out as important species due to its high virulence capacity. Diabetes mellitus is an important risk factor for the development of this infection, as it promotes an increase in glycogen levels in the vaginal tissue and causes an insufficient immune response against fungal infections. The objective of this study was to evaluate possible changes in the systemic inflammatory response mediated by cytokines in diabetic and non-diabetic Balb/c mice, infected with *C. tropicalis*. Diabetes mellitus were induced with Alloxan[®] (Sigma-aldrich) (80mg / kg). After confirmation of the diabetogenic state (glycemia > 120mg/dL), the diabetic and non-diabetic groups were estrogenized weekly with subcutaneous injections of β -estradiol 17-valerate (Sigma[®], USA), (0.3mg / kg). The groups were inoculated intravaginally with *C. tropicalis* (2×10^7 CFU/mL) and evaluated 1, 5 and 10 days after infection. Serum from each animal was collected and stored at -80°C. Th1 (TNF- α), Th2 (IL-6) and Th17 (IL-17) cytokines were dosed through a kit (BD Cytometric Bead Array (CBA) and performed according to the manufacturer's instructions. All animal experiment was approved by (CEUA n^o 3624120717). We detected a stable release of TNF- α at all times analyzed (7.59, 8.78 and 1.83 pg/mL, respectively) in the non-diabetic group, and 6.64, 2.65 and 4.27 pg/mL, respectively, in the diabetic group. IL-6 showed high release fifth days post infection in the non-diabetic group (49.43 pg/mL). On the other hand, diabetic group presented low release in the first and fifth time evaluated (0.75 and 2.49 pg/mL, respectively). IL-17 was only released in the non-diabetic group at the second time point (7.58 pg/mL). It is known that IL-6 has the ability to induce the release of IL-17, whose function is to improve antifungal defenses. This response is impaired in the diabetic host and it is possible that the decrease of this inflammatory response results in the persistence of fungal infections. TNF- α is one of the main cytokines in the acute inflammatory process, released in both groups. Therefore, release of cytokines may have influenced the persistence VVC by *C. tropicalis* in a diabetic model.

Keywords: vulvovaginal candidiasis, *C. tropicalis*, diabetes mellitus, inflammatory marker

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Pro-inflammatory cytokines IL-17, TNF- α and IL-6 in non-diabetic (A) and diabetic (B) mice infected with *C. tropicalis*. Cytokines were evaluated in at least three animals per group at key times during the experiment. The absence of bars represents undetected (non-detectable - ND) levels of the respective cytokine at the time evaluated. Dosages were performed in duplicate. a.i.: after infection.