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LITERATURE REVIEW: CANDIDA GLABRATA

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Abstract: Introduction: Candida Glabrata, species of the Candida group, called non-albicans, is responsible for several infections that are difficult to treat. It is opportunistic and targets immunocompromised individuals. The diagnosis is made through the analysis of vaginal discharge, followed by a treatment that guarantees the improvement of symptoms. **Goals:** This review aims to expose conclusions about the pathogen Candida Glabrata and elucidate the management of cases. **Methods:** This is an integrative literature review. It included selected research between 1991 and 2020, a total of 17 studies. Inclusion and exclusion criteria were selected and the search was carried out through databases of renowned platforms. **Results:** The various types of Candida are commensal beings and are part of the vaginal microbiota, however, when there is an imbalance in immunity, they proliferate, causing symptoms. Glabrata became known for its aggressiveness and resistance to treatment with Fluconazole. Its diagnosis is made through clinical examination and laboratory tests of vaginal discharge that confirm the type of Candida that the individual has, helping in the correct treatment. **Conclusion:** Candida Glabrata is still a diagnostic hypothesis not explored by health professionals, due to the lack of information on the subject. It is considered a saprophyte of the vagina and presents a clinical picture when there is an immunological imbalance in the patient. Furthermore, it is resistant to treatment with Fluconazole and responds well to the use of Flucytosine. It is necessary to demystify the subject so that patients receive adequate care. **Keywords:** Candida Glabrata; Vulvovaginal Candidiasis; Vaginitis; Health; Women's Health.

INTRODUCTION

Vaginitis is considered a common complaint of the female public in modern times, therefore, it is considered one of the most frequent reasons for seeking care in gynecology offices (KENT,1991). The gender: *Candida* is an important cause of fungal infections affecting about 75% of women at some stage of life. Fungi of this genus are considered the most frequent pathogens that cause infections and include a total of more than 150 heterogeneous species.

Fungi of the genus *Candida* are naturally found in the microbial flora of humans and live commensally on the skin, gastrointestinal, urogenital and even respiratory tracts, however, in specific cases these can become infectious pathogens.

Candida glabrata is a species of the *Candida* group called no *albicans* and in recent decades it has been responsible for a significant increase in the incidence of new cases of candidiasis. (RAMOS, 2014). However, despite the estimated incidence, little is said about this pathogen and minimal information is found in medical records. It is known that this species was for a long time considered a non-pathogenic fungus, but it has emerged in recent decades as the second opportunistic pathogen that causes complicated and difficult-to-treat candidiasis, only surpassed by *C. albicans*. (BADER *et al*, 2004).

This genus of the *Candida* group has as one of its characteristics the opportunism of installation in immunocompromised individuals, patients with long hospital stays and who have made previous use of antibiotics and fluconazole (an antifungal drug often used in the treatment of *C. albicans*). (ALVES, 2011).

Thus, the virulence and the lack of concrete information about the species are evident: *Candida glabrata* and their respective importance of study. The objective of this

review is to expose about this pathogen and elucidate about the management of cases.

METHODOLOGY

This article is an integrative literature review. Initially, selected surveys from 1991 to 2020 were included, which reported on the management and the main characteristics known about the *Candida glabrata*. In addition, with the intention of providing more precise knowledge, articles were added on the definitions of vulvovaginal candidiasis, for the comparison of types in a scientifically based way.

Exclusion criteria were articles that did not analyze characteristics about the *Candida glabrata*, those that did not contemplate the established time limit and those that did not allow full access to the material.

The selected keywords were: *Candida Glabrata*; Vulvovaginal Candidiasis; Vaginitis; Health; Women's Health. All descriptors used for this research are registered in the DeCS (Portal of Health Sciences Descriptors).

The bibliographical research of the references used took place through databases with different literatures, such as scientific articles published on recognized platforms, such as documents made available by the Virtual Health Library (VHL), PubMed, Scientific Electronic Library Online (SciELO), National Center for Biotechnology Information (NCBI) and journals from colleges located in Brazil.

Thus, among the materials found, 17 articles were selected that contemplated the objectives proposed by the article, these bibliographic Sources were the ones that made the development of this document possible, with the intention of making it critical and having an effective scientific foundation.

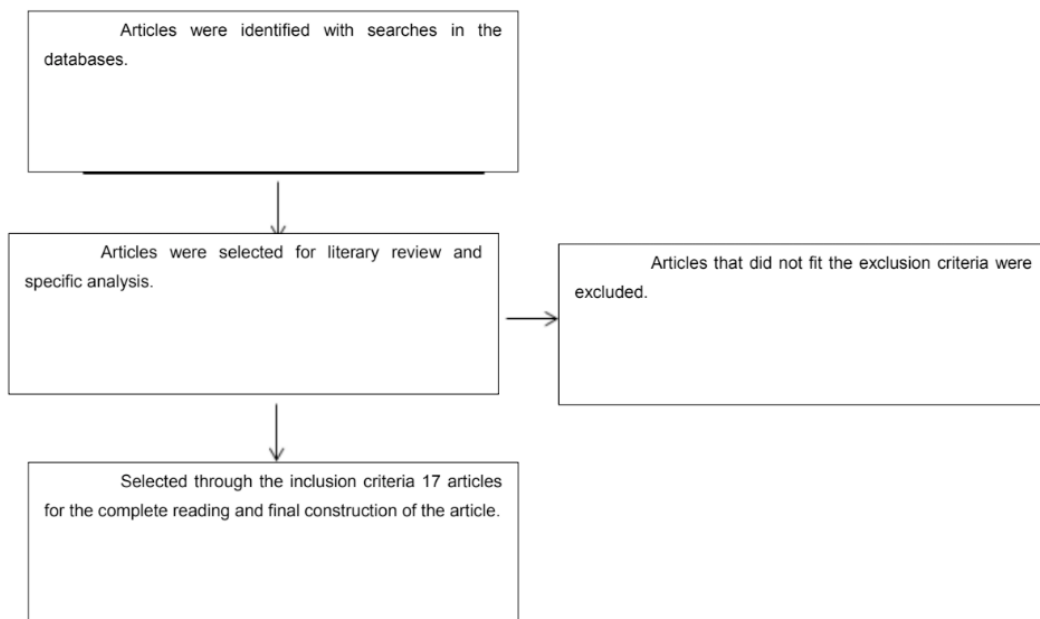


Figure 1: Representation of the selection of articles

Source: Elaborated by the authors, 2022.

RESULTS AND DISCUSSION

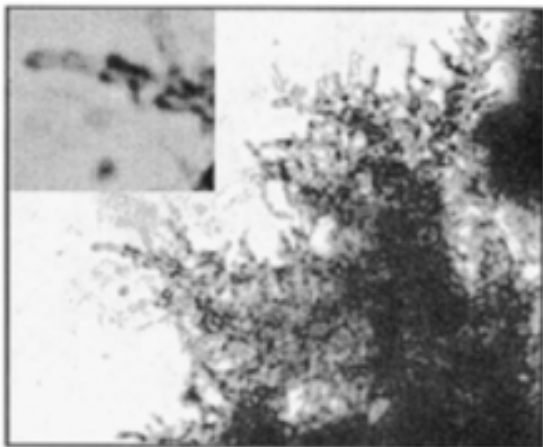
PATHOPHYSIOLOGY

According to several studies, it has been proven that *Candida* species reside as commensals, forming part of the normal microbiota of healthy individuals. However, when there is a disruption in the normal balance of the microbiota or the host's immune system is compromised, species of the genus *Candida* tend to aggressive manifestations, becoming pathogenic. As for the origin, it can be endogenous, when it comes from the microbiota; or exogenous, such as an STI (PEIXOTO et al., 2014).

There are at least 15 distinct *Candida* species that cause human disease, but >90% of invasive disease is caused by the 5 most common pathogens, *C. albicans*, *C. glabrata*, *C. tropicalis*, *C. parapsilosis* and *C. krusei*. Each of these organisms has unique potential for virulence, antifungal susceptibility, and epidemiology, but as a whole, significant infections caused by these organisms are

commonly referred to as invasive candidiasis. (PAPPAS et al, 2016);

Currently, the most commonly isolated microorganism in invasive candidiasis is *Candida albicans*. However, disease caused by other species of *Candida* spp. has increased significantly, with rates of up to 73% according to studies conducted in Turkey (SÜTÇÜ et al., 2017, GÜLTEKIN et al., 2011). Studies reveal that candidiasis caused by the fungus of the *glabrata* species became known due to the fact that the microorganism acquired resistance to fluconazole – a drug widely used in the treatment of candidiasis caused by *Candida albicans* – and other azoles - antifungal chemotherapy drugs consisting of a pentagonal ring, which contains three nitrogen atoms (triazoles) and two carbon atoms, or two nitrogen atoms (imidazoles) and three carbon atoms.



Picture 1 - *C. glabrata* exhibits pseudohyphal growth in response to nitrogen deprivation.

Source: Csank (2000)¹.

DIAGNOSIS

In order to achieve isolation and identification of the pathogen, it is important that the type and quality of the biological sample submitted to the mycology laboratory is of good quality. Asepsis before collection and sample quantity are key factors for the success of fungal diagnosis by yeasts of the genus *Candida*. Procedures for collecting samples are established according to the clinical manifestation, for example, nails, scrapings from the oral, vaginal or anal mucosa, respiratory tract secretions, blood, cerebrospinal fluid, urine, feces, among others (PEIXOTO et al., 2014).

By scarifying the lesions and applying a potassium hydroxide (KOH) preparation or Gram stain, the diagnosis can be confirmed by identifying budding yeasts or pseudohyphae. If the pathology is recurrent or resistant to previous treatment, a culture must be requested to identify whether the agent is a more resistant species, such as *C. glabrata* or *C. krusei*. As for vulvovaginal candidiasis, the diagnosis is clinical, and the test is highly reliable for identifying the pathology, showing excellent correlation with the positive culture for *Candida*. However, only a positive culture

does not necessarily confirm vulvovaginal candidiasis (PEIXOTO et al., 2014).

Therefore, the diagnosis of vulvovaginal candidiasis can only be established with certainty through laboratory evaluation of the discharge. For this, the gynecologist needs to perform a gynecological examination in which he uses a kind of cotton swab to collect material from the vaginal wall. This material is sent to the laboratory, so that the germ causing vaginitis can be identified (PINHEIRO PEDRO, 2020).

If microscopic examination of vaginal secretions in a potassium hydroxide preparation is negative but clinical suspicion is high, fungal cultures must be obtained. After treatment of the acute episode, subsequent prophylaxis (maintenance therapy) is important.

TREATMENT

The treatment of vulvovaginal candidiasis (VVC) aims to ensure the improvement of symptoms, and can be performed orally or topically.

Epidemiologically, non-*albicans* species are gaining relevance as they become more and more frequent causative agents of candidiasis. The indiscriminate use of drugs to combat the different varieties of candidiasis has brought about a significant increase in the number of yeasts resistant to traditional antifungals. This way, products of plant origin can be used as an alternative to synthetic antifungals. (FILHO et al, 2019)

Due to the emergence of *Candida* spp. resistant to certain drugs, it is necessary to apply antifungal sensitivity tests so that physicians can use the correct drugs in the treatment of fungal diseases (VALLABHANENI et al., 2017, PAPPAS et al., 2016).

The *non-albicans* species, more commonly *C. glabrata*, are isolated in 5–10% of episodic VVCs but cannot be distinguished from

C. albicans on clinical criteria. They are inherently relatively azole resistant and may not respond well to conventional courses of antifungal treatment (VANTHUYNE et al, 2006).

Study results indicate a comparable 3-month mycological cure rate among patients treated with fluconazole and boric acid supporting the use of boric acid in the acute treatment of VVC in view of its superior short-term response in women with *Candida glabrata* infections. (RAY et al, 2007).

Considering this, boric acid is expected to be a safe, alternative and cost-effective option for women with recurrent and chronic symptoms of vaginitis when conventional treatment fails due to *Candida* spp involvement. Not *albicans*. or azole resistant strains (LAVAZZO et al, 2011).

Furthermore, studies have shown flucytosine to be well suited to the effective treatment of *glabrata* candidiasis, making it a useful addition to therapy for women with azole-refractory *C. glabrata* vaginitis.

- For *C. glabrata* vulvovaginitis unresponsive to oral azoles, topical intravaginal boric acid, given in a gelatin capsule, 600 mg daily, for 14 days is an alternative (strong recommendation; low-quality evidence) (PAPPAS et al, 2016);
- Another alternative agent for infection by *C. glabrata* are intravaginal nystatin suppositories, 100,000 units daily for 14 days (strong recommendation; low-quality evidence), (PAPPAS et al, 2016).
- A third option for infection by *C. glabrata* is topical flucytosine 17% cream alone or in combination with AmB 3% cream administered daily for 14 days (weak recommendation; low-quality evidence) (PAPPAS et al, 2016).
- Since many patients experience recurrences once prophylaxis is

discontinued, long-term therapy may be warranted. Patients are more likely to comply when antifungal therapy is administered orally, but oral treatment has a greater potential for systemic toxicity and drug interactions (Ringdahl, 2000).

FINAL CONSIDERATIONS

This article was made through a bibliographic review and aimed to elucidate information about the pathophysiology and case management related to the pathogen: *Candida glabrata*.

Thus, it is known that fungi of the genus *Candida* live in symbiosis with the human body, however when there is a deficit in the host's immunity, these fungi are aggressive.

Candida glabrata proved to be resistant to the drug Fluconazole, this fact became notorious due to the need for a new look at the clinical management of this disease.

Therefore, for clinical management to occur effectively and resolutely, it is necessary to use sensitivity tests, due to the resistance created by the indiscriminate use of drugs.

Thus, when analyzing several pre-existing studies, it is noted that the treatment whose result presents more positive results against *Candida glabrata* is the use of flucytosine.

However, there is a factor that impairs the effectiveness of the treatment and encourages the resistance of the fungus to the drug, this factor is the discontinuous prophylaxis. Thus, it is well known that the treatment carried out correctly is extremely important in the fight against acute cases of vulvovaginitis caused by *Candida glabrata*.

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