

## Vulvovaginal candidiasis (VVC): A review of the literature



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### ABSTRACT

Vulvovaginal candidiasis (VVC) is the second most common cause of vaginitis after bacterial vaginosis. VVC often occurs in women of reproductive age (20-40 years). Risk factors for VVC can be divided into two, such as host factors (pregnancy, hormone replacement, uncontrolled diabetes mellitus, immunosuppression, antibiotics, use of glucocorticoids, genetic influences) and behavioral factors (oral contraceptives, sexual habits, hygiene, and clothes that are used). To diagnose VVC in a person, evaluation from anamnesis and clinical manifestation can be conducted. It can also be confirmed by laboratory examination. The management is based on the

classification. Uncomplicated VVC is most effectively treated with topical azoles, but a single dose of fluconazole can also be given orally. Treatment of VVC with complications can be given fluconazole 150 mg for 3 days or topical azole for 7 days. However, when the VVC case that caused by non-*albicans Candida* not responding to conventional treatment such as antimycotics, the amphotericin B can be given to cure the disease. VVC caused by *Candida glabrata* can be given topical boric acid or flucytosine. This article consists of several theoretical references that have been viewed to have a better understanding of candidiasis vulvovaginitis.

**Keywords:** vulvovaginal candidiasis (VVC), vaginitis, itching, *Candida* spp., antifungal

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### INTRODUCTION

Vulvovaginal candidiasis (VVC) is an infection of the vaginal mucosa and/or vulva caused by *Candida* species. *Candida albicans* is the species that most commonly found (80-95%), and the non-*albicans Candida* species that can cause VVC are *Candida glabrata* (10-20%). VVC can be symptomatic and asymptomatic. The yeast blastospores (blastoconidia) of *Candida* spp. usually tend to be asymptomatic but the germinating yeasts that produce mycelia (hyphae) are often found to cause symptomatic vaginitis.<sup>1</sup>

The first infection that occurs in the vagina is called vaginitis, and it can be extended to the vulva (vulvitis). Around 70-75% of women are being infected with VVC at least once during their lifetime, mostly in their reproductive years (20-40 years) and about 50% tend to experience a recurrence or second attack of infection. Around 5-10% of adult women experience recurrent VVC which is defined as four or more episodes of symptomatic VVC each year known as recurrent vulvovaginal candidiasis (RVVC).<sup>2</sup>

Symptoms of VVC that are commonly found are a pain in the vaginal area, irritation, burning sensation, dyspareunia, and dysuria, which is preceded by acute pruritus and vaginal discharge

(fluor albus).<sup>1,2</sup>

The impact of *Candida* infection on health should be a concern because it is very detrimental to women. For example, many women experience itching in the vaginal area that causes blisters and uncomfortable sex. Furthermore, candidiasis can also facilitate infection of the human immunodeficiency virus (HIV).<sup>1,2</sup>

Preventive efforts such as providing accurate information to women are needed and necessary, in view of the fact that until now, women still consider vaginal discharge as a normal thing which is in fact it could be a symptom of vulvovaginal candidiasis. The incorrect understanding of the situation is worsening by improper treatment that makes candidiasis a problem, not only for patients themselves but also for their sexual partners. This review provide information regarding theoretical references to increase the knowledge and practice regarding vulvovaginal candidiasis.

### Epidemiology

VVC is one of the infections that most women complain about. After bacterial vaginosis, VVC is considered to be the second most common cause of vaginitis. Around 70-75% of women are being infected with VVC at least once during their lifetime, mostly in their reproductive years (20-40 years).

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And about 50% tend to experience a recurrence or second attack of infection. Around 5–10% of adult women experience recurrent VVC, which is defined as four or more episodes of symptomatic VVC each year known as recurrent vulvovaginal candidiasis (RVVC).<sup>2</sup>

According to epidemiological studies, the highest incidence was reported by epidemiological studies conducted in African countries, such as Nigeria (57.3%) and Tunisia (48.0%), followed by Brazil (47.9%) and Australia (30.5%). The lowest incidence was reported in European countries, such as Greece (12.1%) and Italy (19.5%).<sup>2</sup>

According to research that is conducted in the Sexual Transmitted Division of Outpatient Clinic of Dermatology and Venereology Department at General Hospital Doctor Soetomo, Surabaya, East Java, Indonesia from 2011 to 2013, from 869 cases of vaginal discharge, 213 cases were obtained. The cases continued to increase every year. In 2011, 69 cases (22.77%) out of 303 patients with vaginal discharge. In 2012, VVC was found in 69 cases (22.69%) out of 304 patients who experienced vaginal discharge. In 2013, the total number of VVC cases was increased to 75 (28.63%) out of 262 patients who had a vaginal discharge.<sup>1</sup>

### Etiology

There are several *Candida* species that can cause VVC, such as *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, *Candida parapsilosis*, and *Candida krusei*.<sup>2</sup> The most common species identified in women with VVC were *Candida albicans*, followed by *Candida glabrata*. During the examination, one or more of *Candida* species can be found. Where mixed infection is usually obtained between *Candida albicans* with *Candida glabrata*.<sup>2,3</sup> Risk factors for VVC can be divided into two, such as host factors and behavioral factors. Host-related risk factors include pregnancy, hormone replacement, uncontrolled diabetes mellitus, immunosuppression, antibiotics and glucocorticoid use and genetic influences. Meanwhile, behavioral risk factors for VVC include the usage of contraceptives, personal hygiene, sexual behaviour, and also clothes that are used.<sup>3,4</sup>

### Pathogenesis

The cell wall plays an important role in virulence because it is the part that interacts directly with host cells. *Candida* not only sticks to the mucosa, but it also penetrates. By means of immunomodulation and adhesion, *Candida* can invade host cells. Immunomodulation is the potential ability of *Candida* cells to modulate the host immunological system in the form of stimulation to increase or

decrease the host immune reaction. There are several ingredients that are contained in the cell walls that play a role in the immunomodulation process, such as chitin, glucans, and mannoproteins. The immunomodulating response causes the production of a number of proteins known as heat shock proteins (HSP) which play a role in the stimulation of the immune response and the growth process of *Candida*.<sup>2,5</sup> The initial step for colonization is adhesion, in which *Candida* attaches to the host cell through hydrophobic interactions. This reduces the level of clearing the fungus from the body through normal immune regulation. When *Candida albicans* penetrates the surface of the host mucosa, the fungal form changes from spores to pseudohyphae which will release several degradative enzymes such as various proteinases, aspartic proteinases, and phospholipases, which result in helping the fungus to invade the host tissue.<sup>2,5</sup>

### Clinical presentation

The most common symptoms for VVC are itching in the vulva area and fluor albus, cheese-like. In addition, in severe cases of VVC, other symptoms may also appear, such as burning sensation, edema, and erythema of the vulva and vaginal, dysuria, dyspareunia, and vaginal pain.<sup>3,5</sup> On physical examination, there is erythema and swelling of the labia and vulva, there may also be papulopustular lesions around it and yellowish-white patches with cheese-like appearance can be found.<sup>3,6</sup>

### Diagnosis

Diagnosis of vulvovaginal candidiasis can be confirmed based on anamnesis, clinical manifestation, and supported by other laboratory examinations such as direct microscopic examination, culture, biochemical tests, serology, and molecular biology to identify *Candida* spp.<sup>7,8</sup>

By using saline preparations on microscopic examination, the presence of yeast cells and mycelia are able to be detected, approximately around 30% - 50% of patients with VVC. However, the sensitivity of 10% potassium hydroxide was higher than the saline in identifying yeast cells and hyphae. On a 10% KOH examination, 50%-70% can recognize yeast and hyphae that are germinating, but they are less specific in detecting non-*albicans* *Candida* species. With giemsa stain, can also identify with or without pseudohyphae, and can identify a mixture of two organisms.<sup>6</sup>

Vaginal culture is the most accurate method of diagnosis for establishing a case of VVC. It is also indicating a suspected VVC case or high risk for non-*albicans* *Candida* species when a negative result appears on microscope.<sup>7</sup>

Biochemical tests to confirm *Candida* species can be carried out by carbohydrate assimilation. This examination requires an incubation time of 10 days at 37°C. The growth/change in pH that occurs in the tested media using sugar as the basic material indicates a positive result.<sup>7</sup>

The immunofluorescent/fluorescent antibody test method can be used in the serological examination of *Candida albicans*. Meanwhile, the molecular biology examinations for *Candida albicans* were carried out by polymerase chain reaction (PCR), restriction fragment length polymorphism (RFLP), peptide nucleic acid fluorescence in situ hybridization (PNA FISH), and sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). Molecular biology tests for *Candida albicans* are very useful because they can give faster results than tests with culture.<sup>7</sup>

### Treatment

The treatment of VVC is carried out based on the classification, such as VVC without complications and VVC with complications. For VVC without complications, topical treatment is chosen. Azole derivatives were found to be more effective than nystatin. In cases of uncomplicated VVC, short-term treatment with topical azole can be performed within 3 days, and it is said to be effective in 80–90% of cases. Several types of topical drugs available are clotrimazole, butoconazole, and miconazole.<sup>3,8,9</sup>

In a study conducted by Mendling et al., it obtained better results by combining 2% clotrimazole cream with clotrimazole vaginal suppositories compared with clotrimazole vaginal suppositories alone. In addition to topical treatment, in cases of VVC without complications, oral treatment can be chosen, such as with a single dose of 150 mg of fluconazole.<sup>7</sup>

In the treatment of VVC with complications, it will require a longer treatment than VVC without complications. Fluconazole 150 mg for 3 days or topical azole class for 7 days can be given to patients with complicated VVC.<sup>3,8,9</sup> Medicines that are used in continuous therapy to treat recurrent VVC are fluconazole 150 mg/week or ketoconazole 100 mg/day for 6 months. However, continuous therapy with ketoconazole has been avoided because of its hepatotoxicity. Amphotericin B 50 mg for 2 weeks can be given intravaginally when VVC is caused by non-*albicans Candida* not responding to treatment with conventional antimycotics. VVC caused by *Candida glabrata* can be administered topically with boric acid at a dose of 600 mg for 14 to 21 days intravaginally. Flucytosine may be an option if the patient does not respond to boric acid.<sup>3</sup>

### CONCLUSION

Vulvovaginal Candidiasis (VVC) is the second most common cause of vaginitis after bacterial vaginosis. *Candida albicans* is the species most frequently found. Risk factors for CVV can be divided into two, such as host factors and behavioral factors. Some of the common symptoms that can be found are itching and discharge. In severe cases, symptoms may include burning sensation, edema, and erythema of the vulva and vaginal, dysuria, dyspareunia, and vaginal pain. To diagnose VVC in a person, evaluation from anamnesis and clinical manifestation can be conducted. It can also be confirmed by laboratory examination. The treatment is based on the classification. In the treatment of CVV without complications will require a shorter treatment than CVV with complications.

### CONFLICT OF INTEREST

None.

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