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Original Research Paper

Gynaecology

AN OVERVIEW OF CANDIDA VAGINITIS

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ABSTRACT Candida vaginitis is a common cause of infective vaginal discharge experienced by women. Approximately 75% of all women experience at least one episode of vulvovaginal candidiasis (VVC) during their life time. Each year an estimated of 10 million health care office visits to gynaecologists are due to vulvovaginitis. Among the many causes of vaginitis, Candida vaginitis is the second most common cause after bacterial vaginosis and is diagnosed in up to 40% of women with vaginal complaints. It represents 20-25% of the vaginal discharge of infectious nature characterized by curdy vaginal discharge, itching and is associated with considerable health and economic cost. Candida vaginitis is classified by WHO as a sexually transmitted disease of frequent sexual transmission. It is a caused by abnormal growth of yeast-like fungi in the mucosa of female genital tract, and a significant problem for women of child bearing age.

KEYWORDS : Candida Vaginitis, Vulvovaginal Candidiasis, Vulval Pruritus, Vaginal Discharge

INTRODUCTION:

Candida vaginitis is one of the most common infection seen in general practice.[1] It is a fungal infection caused by overgrowth of Candida species affecting the genital tract as opportunistic pathogen.[2,3] Candida is harmless initially, but may become pathogenic when conditions in the vagina alter, particularly when there is a rise in vaginal pH or an excess of glycogen that has not been converted to lactic acid by lactobacilli.[4] Vulvovaginal candidiasis (VVC) is almost exclusively found between menarche and menopause.[5,6,7,8] It is uncommon in post menopausal women, unless they are on hormone replacement therapy or receiving tamoxifen for breast cancer.[8,9] It is a common type of vaginitis, a gynaecological disorder with white discharge, soreness, dyspareunia, irritation, itching, and can be a possible risk for other diseases e.g. HIV/AIDS.[3,10,11]

Reports show that 75% of all women experience at least one episode of vulvovaginal candidiasis in their lifetime.[12] Vaginal candidiasis is a frequent companion of pregnancy. Its frequency increases at the time when most women begin regular sexual activity.[10,13] It can be sexually transmitted[10] and several studies have reported an association between candidiasis and orogenital sex.[14] The VVC has a negative effect on women's personal confidence and self esteem. It may contribute or cause psychosexual problems namely introital dyspareunia, with progressive loss of genital arousal, loss of desire, and avoidance of sexual intimacy for fear of experiencing pain and recurrence of Candida vulvov aginitis.[12]

SYNONYMS:

Vaginal thrush,[4,15] Vaginal yeast infection,[15] Moniliasis,[15] Monilial vaginitis[6,16]

DEFINITION:

Vulvovaginal candidiasis is defined as signs and symptoms of inflammation in the presence of Candida *spp.* and in the absence of other infectious aetiology.[7]

CLASSIFICATION:

On the basis of clinical presentation, microbiology, host factors and response to therapy, CDC (centers for disease control and prevention) classified VVC into two groups.

Table.1: CDC (2015) classification of Candida vaginitis[17]

Uncomplicated VVC
Sporadic or infrequent vulvovaginal candidiasis or
Mild to moderate vulvovaginal candidiasis or
Likely to be C. albicans or
Non-immunocompromised women
Complicated VVC
Recurrent vulvovaginal candidiasis or
Severe vulvovaginal candidiasis or
Non-albicans candidiasis or
Women with uncontrolled diabetes, debilitation, or immunosuppression

RECURRENT VULVOVAGINAL CANDIDIASIS (RVCC):

RVCC is usually defined as four or more episodes of symptomatic VVC in 1 year.[17,18,19,20]

ETIOLOGY

Vulvovaginitis due to Candida is commonly caused by the species Candida albicans,[21] a small gram positive[15] dimorphic fungus that forms yeast-like buds, pseudohyphae and hyphae.[3] It may occasionally caused by C. glabrata, C. parapsilosis, C. krusei, C. pseudotropicalis, C. tropicalis and C. dubliniensis.[3]

RISK FACTORS / PREDISPOSING CONDITIONS

Several behavioural and host related risk factors have been associated with VVC. These are Pregnancy,[5,8,10,11,20], metabolic disorders e.g. uncontrolled diabetes mellitus,[5,8,11,20] hypoth yroidism and hyperth yroidism[11,22], immuno-compromised states such as AIDS and chronic systemic steroid use,[11,20,21], antibiotics use[5,7,8,11,20,21], oral contraceptive with high oestrogen levels,[5,7,8,10,11,20,21] IUD,[21,22] hormone replacement therapy,[5,8,10,20] luteal phase of menstrual cycle,[8,10] frequency of visits to STD clinic,[23] wearing of tight clothes,[7,11,16,21,22] poor personal hygiene and obesity,[14] genetic predisposition,[7] spermicidal creams and some sexual practices e.g. woman having oral sex[20,21]

Fig.1: The Candida growth cycle

PATHOGENESIS AND PATHOLOGY:

The pathogenesis of VVC is multifactorial and the causes may be idiopathic or secondary to a variety of host or microbial factors.[20]The mechanism by which Candida produces disease is not well defined. When the normal ecosystem of the vagina is disturbed by any one of the predisposing factor, rapid fungal overgrowth may take place, reaching levels of $10^3$to 10^4 organisms per millilitre.[6] Germination of Candida *spp.* enhances colonization and facilitates tissue invasion. By direct hyphal invasion of epithelial tissue Candida *spp.* may cause cell damage resulting in inflammation. It is possible that proteases and other hydrolytic enzymes facilitate cell penetration with resultant inflammation; mucosal swelling, erythema and exfoliation of vaginal epithelial cells.[23] Filamentous forms (hyphae and pseudohyphae) are associated with active disease. Pseudohyphae have been observed to penetrate vaginal epithelial cells and they are more adherent to cells than are budding yeasts. Adherence appears to be an important pathogenic feature of Candida species. Sub lethal concentrations of antifungal agents may ameliorate disease by reducing adherence.[13] The characteristic non-homogenous vaginal discharge consists of a conglomerate of hyphal elements and exfoliated nonviable epithelial cells with few polymorphonuclear leucocytes (PMNs).[23] The extensive areas of pruritus and inflammation often associated with minimal invasion of the lower genital tract epithelial cells suggest that an extracellular toxin or enzyme may play a role in the pathogenesis of the disease.[24] Candida *spp.* may also induce symptoms by hypersensitivity or allergic reactions, particularly in women with idiopathic RVCC.[23,24] This is further supported by the clinical response of 30% of women with RVCC to an anti-allergic treatment with the leukotriene receptor antagonist like zafirlukast.[25] The new hypothesis is that VVC is associated with signals following Candida-vaginal epithelial cells interactions that promote a non protective inflammatory PMN response and concomitant clinical symptoms.[26]

HOST FACTORS

Symptomatic VVC is frequently observed during or after courses of systemic antibiotics, which are thought to act by eliminating the normal protective vaginal bacterial flora. The natural flora provides a colonization-resistance mechanism and prevents germination of Candida *spp*. The provider of this protective function has been singled out to be Lactobacillus *spp*.[23,24] Lactobacillus-Candida interaction includes competition for nutrients, steric interference with adherence of Candida *spp*. and elaboration of bacteriocins inhibiting yeast proliferation and germination. During pregnancy the vagina is more susceptible to infections resulting in higher incidence of vaginal colonization, vaginitis and lower cure rate.[23] The high levels of reproductive hormones and increased glycogen content of vagina favours candidiasis in pregnancy.[2] A cyto solic receptor for oestrogen has been identified in Candida *spp*. and oestrogen has been shown to promote the germi nati on of yeast in vitro.[27]

PATHOGENESIS OF RECURRENT AND CHRONIC CANDIDA VAGINITIS

Three theories have been proposed to explain the RVCC.[21,23] **Intestinal reservoir theory** suggests that the recurrences are a result of persistence of the organism in the gastrointestinal tract and later re-infection of the vagina.[12] **Sexual trans mission theory** views the partners as a source of re-infection. Indeed, at least 20% of the partners of women with RVCC harbour the same yeast species in their mouth, fingers or genital area. **Vaginal relapse theory** maintains that even after treatment some women remain colonized with small number of yeasts. These yeasts increase in number and cause a new clinical episode of vulvovaginal candidiasis as soon as they get favourable conditions.

Current theories about the pathogenesis of RVCC include qualitative and quantitative deficiency in the normal protective vaginal bacterial flora and an acquired often transient-antigen specific deficiency in T-lymphocyte function that similarly permits unchecked yeast proliferation. Another theory is that of an acquired acute hypersensitivity reaction to Candida antigen which is accompanied by elevated vaginal titres of Candida antigen-specific IgE. This theory has a clinical basis in those patients with RVCC who often present with severe vulval manifestations with minimal exudative vaginal changes and lower number of organisms.[23]

CLINICAL PRESENTATION

Intense itching is the cardinal sign of fungal vulvovaginitis.[6] The pruritus is out of proportion to the discharge.[15] Hypersensitivity to the organism may contribute to severity of symptoms found in even mild infections.[6]

SYMPTOMS :

Vaginal and vulval pruritus, vulval soreness,[5,11,20]non offensive vaginal discharge[5,11,20] and burning sensation of vestibule,[5,27] supe rficial dyspareunia[5,11,20] & external dysuria (splash dysuria).[11,20]

Table.2: Differential diagnosis[14]

Category	Physiologic (normal)	Bacterial vaginosis	Candidiasis	Trichomoniasis	Bacterial (Streptococcal, Staphylococcal,E coli)
Chief Complaint	None	Bad odor, increased after intercourse	Itching, burning, discharge	Frothy discharge, bad odor, dysuria, pruritis, spotting	Thin, watery discharge, pruritis
Discharge	White, clear	Thin, gray or white, adherent, often increased	White "cottage cheese" like discharge	Green-yellow, frothy, adherent, Increased	Purulent
KOH whiff test	Absent	Present (fishy)	Absent	May be present	Absent
Vaginal pH	3.8-4.2	>4.5	<4.5	>4.5	>4.5
Microscopic findings	N/A	'Clue cells', slight increase in WBCs, clumps of bacteria(saline wet mount)	Hyphae and buds in 10% KOH (wet mount)	Trichomonads (protozoa with 3-5 flagella) may be seen moving on saline wet mount	Many WBCs

CLINICAL SIGNS:

vulvar erythema,[5,20] vulvar fissu ring & excoriation,[20] non offensive curdy vaginal discharge (adherent, thick and plaque like)[11,20] also known as thrush patches,[16] vulval oedema.[18]

DIAGNOSIS[18]

MICROSCOPY:

Yeasts or pseudohyphae on wet preparation with either 10-20% KOH solution or saline (sensitivity 40 - 60%) of vaginal discharge. Pseudohyphae or Yeasts on Gram stain (sensitivity up to 65%) of vaginal discharge

CULTURE:

Vaginal culture positive for a Candida species.

PREVENTION

It is generally recommended to avoid excessive washing of the vulval area and to avoid potential irritants such as perfumed soaps, bubble baths, powder or vaginal sprays. Synthetic underwear and tight-fitting pants may lead to sweating and should be avoided.[21] In women with confirmed recurrent VVC linked to frequent courses of systemic antibiotics, prophylactic antimycotics are justified. A useful regimen is fluconazole 100mg weekly once for the duration of antibiotic therapy. In women prone to VVC, avoiding use of oral contraceptives, intrauterine devices and the contraceptive sponge is prudent.[23] Studies are also being conducted on the prospects for development of a vaccine to prevent and control vaginal candidiasis. To date several antigen formulation have been tested with modest results. The latest vaccine study reported in the literature is a B- glucan conjugate vaccine that induces anti B-glucan antibodies, administered with a human compatible adjuvant.[26]

MANAGEMENT:

Several topical, oral and intravaginal antimycotic agent are effective, but no one is found to be superior over another.

Table.3: Recommended regimens by CDC(2015) for treatment of Candida vaginitis[17]

OTC (over the counter) Intravaginal agents(any one): Clotrimazole 1% cream 5 g intravaginally to be used daily for 7–14 days 2% Clotrimazole cream 5 g intravaginally to be used daily for 3 days 2% Miconazole cream 5 g intravaginally to be used daily for 7 days 4% Miconazole cream 5 g intravaginally to be used daily for 3 days Miconazole 100 mg vaginal suppository, one suppository to be used daily for 7 days Miconazole 200 mg vaginal suppository, one suppository to be used for 3 days Miconazole 1,200 mg vaginal suppository, one suppository to be used for 1 day 6.5% Tioconazole ointment 5 g intravaginally to be used in a single application
Prescription Intravaginal Agents (any one): 2% Butoconazole cream (single dose bioadhesive product), 5 g to be used intravaginally in a single application 0.4% Terconazole cream 5 g to be used intravaginally daily for 7 days Terconazole cream 5 g to be used intravaginally daily for 3 days 8% Terconazole 80 mg vaginal suppository, one suppository to be used daily for 3 days
Drug for Oral use: 150 mg Fluconazole tablet to be taken orally in a single dose

CONCLUSION:

Although vaginal candidiasis is treatable, when left untreated is a possible risk for acquisition of HIV/AIDS as well as other complications such as PID, infertility, ectopic pregnancy, pelvic abscess, menstrual disorders, spontaneous abortion and premature delivery. Recurrent vulvovaginal candidiasis (RVCC) is a highly troublesome and emotionally traumatic condition for women. The VVC has a negative effect on women's personal confidence and self esteem. In most Candida species antifungal resistance has been reported. Therefore alternative or adjunct bio-antimycotic means of controlling pathogenic Candida species is needed.

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