

## Vulvovaginitis and diabetes

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### Abstract

Vulvovaginitis is a commonly encountered comorbid condition of diabetes, and is linked to poor glycaemic control. Proper, timely diagnosis and management is necessary to ensure optimal perineal/genital and metabolic health. Knowledge of current guidelines and recommendations helps in achieving this goal. This review describes the etiology, pathogenesis, clinical features, differential diagnosis, management and prevention of VV in diabetes.

**Keywords:** Bacterial vaginosis, candidiasis, SGLT2 inhibitors, Trichomonas.

### Introduction

Vulvovaginitis (VV) is a commonly encountered symptom in the diabetes clinic.<sup>1</sup> Many patients are diagnosed to have diabetes when they present with symptoms suggestive of VV. Others experience episode of uncontrolled or refractory hyperglycaemia which can be attributed to untreated VV. Yet others may develop VV as an adverse effect of glucose-lowering medication, or as a sexually transmitted disease (STD).<sup>2,3</sup> This review describes the etiology, pathogenesis, clinical features, differential diagnosis, management and prevention of VV in diabetes.

### Aetiology

The presenting symptom of VV is usually vaginal discharge, itching and/or odour. The common etiologies are bacterial vaginosis (BV), Trichomonas vaginalis (TV), and candidiasis (CVV). BV is due to replacement of normal vaginal flora by anaerobic bacterial overgrowth, including Prevotella sp, Mobiluncus sp, G. vaginalis, Mycoplasma and Ureaplasma. BV and TV can be STD, while CVV is rarely transmitted through sex.<sup>4</sup>

### Diagnosis

The diagnosis of VV is made through history, physical examination, and simple laboratory tests. It is extremely important, especially in the South Asian context, to take a

detailed history, in an empathic and non-judgmental manner, while providing privacy.<sup>5</sup> However, it must be remembered that history alone may miss the diagnosis in a significant number of cases.

Simple and economical tests, carried out in the clinic, help in correct diagnosis. Vaginal pH can be checked using pH strips. An elevated pH (>4.5) suggests BV or TV. Microscopic examination of a saline-solution specimen of vaginal discharge may reveal motile trichomonads or "clue cells" in BV. A KOH (potassium hydroxide) preparation will demonstrate hyphae or blastopores in CCV.<sup>4,6</sup> Culture may be required for confirmation, and urine microscopy may provide helpful clues to diagnosis as well.

### Bacterial Vaginosis (BV)

BV is usually associated with history of multiple sexual partners, change of partner, douching, lack of barrier contraception, lack of vaginal lactobacilli, and other comorbid STDs.

BV is diagnosed if any 3 of the following criteria are present<sup>7</sup>:

1. Homogenous, thin, white discharge that smoothly coats vaginal walls
2. "Clue cells" (vaginal epithelial cells studded with adherent coccobacilli) on microscopy.
3. Vaginal fluid pH. 4.5
4. Positive whiff test: fishy odour of vaginal discharge before or after addition of 10% KOH.

Treatment is done using either metronidazole 500mg per os, twice daily for 7 days, or metronidazole gel 0.75%, 5g once daily for 5 days, or intravaginally clindamycin cream 2%, 5g at night intravaginally for 7 days. Alternative regimes include tinidazole 2g orally once daily for 2 days, or 1g orally once daily for 5 days, or clindamycin 300mg orally, twice daily for 7 days, or clindamycin ovules 100mg intravaginally at night for 3 days.<sup>4</sup>

Follow up is not necessary if symptoms resolve. Recurrence can be treated with a repetition of the initial regime. Intravaginal boric acid 600mg o.d x 21 days and suppressive therapy with 0.75% metronidazole gel twice

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a week for 4-6 months can be used to prevent frequent recurrence. Oral therapy with metronidazole 2g and fluconazole 150 mg, administered once monthly, can also be tried.

### Trichomoniasis (TV)

TV is usually asymptomatic, but may present with a diffuse, malodorous, yellow-green vaginal discharge, with or without vulvar irritation. The commonest method of TV diagnosis is microscopic evaluation of wet preparations of genital secretions. Serological tests and culture may be ordered if available. Pap smear is not considered a diagnostic test for TV, though TV may be an incidental finding in the smear.

Treatment for TV is by nitroimidazole therapy. Any of oral metronidazole 2 g orally stat, oral tinidazole 2 g orally stat, or metronidazole 500mg orally twice a day for 7 days, can be prescribed. Metronidazole gel is not recommended for TV therapy. As reinfection is common, sexually active women should be retested for TV infection within 3 months of therapy. Reinfection must be differentiated from antimicrobial resistance (persistence of infection or recurrence of infection). Metronidazole stat therapy failure should be managed with a longer course (metronidazole 500mg orally twice daily for 7 days, OR tinidazole 2 g orally for 7 days). Intravenous tinidazole, &/ or intravaginal paromomycin, intazoxanide can be tried in refractory cases. Intravaginal betadine, clotrimazole, gentian violet, nonoxynol-9 and potassium permanganate are not effective in clearing TV.<sup>4</sup>

### Vulvovaginal Candidiasis (VVC)

VVC is most often caused by *Candida albicans*, through other species may also be involved. Pruritis, vaginal soreness, dyspareunia, dysuria and thick white curd-like vaginal discharge are frequent symptoms. All women with diabetes should be treated as having complicated VVC. Women with recurrent VVC, severe VVC, or non-*albicans* candidiasis are clubbed in the same category.

Diagnosis is confirmed by a wet preparation (saline, 10% KOH) or gram stain of vaginal discharge showing budding yeasts, hyphen or pseudo hyphae, and a positive culture, in a setting of normal vaginal pH (<4.5). *Candida glabrata* does not form pseudo hyphae or hyphae, and is difficult to diagnose on microscopy.<sup>4</sup>

While short term therapy is recommended for most women with VVC, those with diabetes need prolonged courses (7-14 days) of conventional treatment. Examples include oral fluconazole at day 1, 4 and 7, in a dose of 100mg, 150mg or 200 mg. Topical therapy with clotrimazole 1% cream 5 mg once daily for 7-14 days, or

**Table:** Pharmacology of anti-mycotic agents.

Class	Example	Route
Polyenes	Nystatin	PV
	Amphotericin B	PV,IV
Imidazoles	Clotrimazole	PV
	Miconazole	PV
	Econazole	PV
	Fenticonazole	PV
Oral imidazoles	Ketoconazole	P.O.
Triazoles	Fluconazole	P.O, IV
	Itraconazole	P.O
Ciclopirox	Ciclopirox olamine	PV
Echinocandin	Micafungin	IV

Key: IV= intravenous; PO= per oral; PV= per vaginum.

miconazole 2% cream 5 mg once daily for 7 days can also be used. Miconazole vaginal suppositories can be used in a dose of 100mg once daily for 7 days, 200mg once daily for 3 days, or 1200mg stat.

Non *albicans* VVC is more common in women with RVVC and in women with type 2 diabetes. While the optimal course of treatment for non-*albicans* VVC is not clear, non-fluconazoleazole regimens, using either oral or topical therapy, are preferred. These include terbinafine or itraconazole. Recurrence can be managed by intravaginal administration of 600mg boric acid once daily for 14 days. Various anti-mycotic drugs are listed in Table.

German guidelines on the management of VV candidiasis (spelt as candidosis) are more exhaustive (7). They report using amphotericin B suppositories, or vaginal 17% flucytosine, or 800mg oral fluconazole, daily for 2-3 weeks, or oral posaconazole in combination with local nystatin &/or ciclopirox olamine, or micafungin, to treat *C. glabrata* infections. *C. krusei* must be treated with local imidazoles such as clotrimazole or ciclopirox olamine, or boric acid, as it is resistant to fluconazole and itraconazole.

Some patients of RVVC may benefit from once weekly fluconazole (200mg) for 8 weeks, followed by fortnightly administration for 4 months, and monthly dosage for the next 6 months ( Donders' regime).<sup>8</sup>

### General Considerations

Simultaneous treatment of both the partners is necessary for bacterial/ parasitic eradication of BV and TV. Such therapy is not required in CVV. Perineal hygiene and safe sex practices must be explained to patients.<sup>9</sup> Intrauterine contraceptive devices should be removed if recurrent VV occurs.

Treatment of VV cannot be successful unless diabetes is

well controlled. Recurrent VV is a red flag for poorly controlled diabetes, and should prompt careful reconsideration of the anti-diabetic prescription. Insulin may be indicated in women with recurrent VV who are already on "adequate" doses of oral glucose-lowering drugs.

SGLT2i (sodium glucose transporter 2 inhibitors) should not be prescribed to a person with active VV. Once the infection has been cured, SGLT2i may be used for diabetes management if otherwise deemed appropriate. A single episode of VV should not be taken as a reason to discontinue SGLT2i therapy. If however, recurrent episode of VV occur, discontinuation of SGLT2i may be considered. While there is no recommendation regarding when to do so, we may seek guidance from the 2015 Sexually Transmitted Diseases Treatment guidelines of the Centers for Disease Control and Prevention (CDC), which define recurrent VVC (RVVC) as 4 or more episodes of symptomatic VVC within 1 year.<sup>4</sup>

Guidelines discourage self-administration of antimycotic therapy, but this is frequently practiced in many centres.

### Summary

VV is a frequently encountered acute and recurrent complication of diabetes mellitus, which contributes to, and is worsened by poor glycaemic control. Proper, timely

diagnosis and management is necessary to ensure optimal perineal/genital and metabolic health. Knowledge of current guidelines and recommendations helps in achieving this goal.

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