



Diabetes and Vulvovaginal Conditions

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Eighteen million American women are living with diabetes, and 43.7 million women have prediabetes (1–3). Diabetes is well known to increase the risks of multiple acute and chronic medical conditions, including cardiovascular disease, kidney disease, autonomic and peripheral neuropathy, and retinopathy. However, diabetes is also associated with increased risk of a wide range of vulvovaginal concerns. Acute, chronic, and recurrent vulvovaginal conditions—both infectious and noninfectious—can occur, especially when blood glucose is inadequately controlled (4,5). The risk of some vulvovaginal conditions is higher in women with type 1 diabetes than in those with type 2 diabetes, whereas other conditions are associated with obesity and occur more frequently in the setting of type 2 diabetes (6,7).

The development of vaginal noninfectious conditions and infections is a complex process regardless of diabetes status and is affected by sex hormones, homeostasis of the vaginal flora, and mechanisms of immunity (8). One of the strongest risk factors for vulvovaginal infection is the age-associated increase in vaginal pH. Among premenopausal women, the predominant components of vaginal flora include *Lactobacillus* spp., which produce hydrogen peroxide to regulate bacterial homeostasis and lower vaginal pH, thereby preventing infection (9,10). However, with menopause, the proportion of *Lactobacillus* spp. decreases, and these flora are replaced by other bacteria. This change causes the vaginal pH to rise and increases the risk of vaginal infection (9).

Penetrative sexual activity and a higher number of lifetime sexual partners also increase women's risk of vaginal infection. These risk factors are also associated with susceptibility to different infectious vulvovaginal conditions compared with women who are less sexually

active and have fewer lifetime partners. Menses, use of contraceptives, contact irritants, excessive cleansing, and vaginal douching can also disrupt the vaginal flora, raising the risk of infection (10).

These risk factors for infection are exacerbated and compounded in the setting of diabetes. The immune system undergoes several changes that are caused or exacerbated by diabetes, including decreases in leukocyte chemotaxis and phagocytosis. Additionally, impairment in vascular reaction weakens immune function and increases susceptibility to infection (11).

Women with diabetes are also affected by highly prevalent noninfectious vulvovaginal conditions, including skin disorders (e.g., acanthosis nigricans, skin tags, and vitiligo), pelvic organ prolapse, and pelvic pain (e.g., vulvodynia). Some of these conditions are specific to diabetes (e.g., pelvic neuropathic pain), others are driven by metabolic derangements associated with diabetes (e.g., acanthosis nigricans, skin tags, and pelvic organ prolapse), and few are associated with autoimmune disorders that are more prevalent in people with diabetes (e.g., vitiligo), especially type 1 diabetes (12).

Person-centered care is predicated on holistic identification and management of all comorbid conditions of people living with diabetes. Although substantial attention has been paid to diagnosing and treating cardiovascular, kidney, neurologic, ophthalmologic, oral, and mental health conditions associated with diabetes, the gynecological health of women with diabetes has been largely overlooked (13). Because one in seven U.S. women have diabetes, understanding the effect of diabetes on vulvovaginal health is vitally important for all health care providers, particularly those who deliver primary and gynecological care. In this article, we explore the role of diabetes in vulvovaginal health and discuss the most common infectious and noninfectious vulvovaginal conditions affecting women living with diabetes.

Fungal Infections

Vulvovaginal Candidiasis

Increased rates of vaginal candidiasis, including initial and recurrent infections, have been extensively documented for women with diabetes (14,15). Women may

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be asymptomatic or may have pruritis, vulvar erythema, vaginal soreness, dyspareunia, dysuria, and white vaginal discharge. The reported prevalence of vaginal *Candida* colonization in women overall ranges from 12 to 67.5%, with higher prevalence rates observed for women with diabetes (14,16). Higher A1C levels and glucosuria are associated with increased risk of vaginal candidiasis (6,14,17). Other risk factors include increased age (perimenopause and menopause), pregnancy, immunosuppression, genetics, antibiotic use, glucocorticoid treatment, oral contraceptives, intrauterine contraceptives, hormone replacement therapy, obesity, sexual activity, HIV, and substance use disorder (14,16,18,19).

In diabetes, acute and chronic hyperglycemia impairs neutrophil function, which limits the ability to phagocytose and clear *Candida* organisms (6). Hyperglycemia also enhances the virulence of *Candida* pathogens because increased urinary secretion of glucose provides nutrients for *Candida* organisms and thus aids in colonization (6,10,18).

Vulvovaginitis may also develop as an adverse effect of treatment with sodium–glucose cotransporter 2 (SGLT2) inhibitors (4,5,17). SGLT2 inhibitor therapy has multiple benefits for patients with diabetes, including cardiorenal protection, antihypertensive and diuretic properties that are helpful for heart failure, a positive impact on weight, and a low risk of hypoglycemia (13). However, SGLT2 inhibitors work by promoting urinary glucose excretion, which can increase the risk of vulvovaginitis (9,17). In a study by Yokoyama et al. (14), 114 women with type 2 diabetes received a vaginal candidiasis test before and after starting treatment with an SGLT2 inhibitor. After 6 months of SGLT2 inhibitor therapy, 36.9% of the women were newly positive for *Candida* colonization, and 15.8% had symptomatic vaginitis. *C. albicans* was the most common species identified in symptomatic patients, whereas the nonalbicans species *C. glabrata*, which is not easily recognized by microscopy and is resistant to azoles, was most common in asymptomatic colonization (1–3,14,18).

Vaginal candidiasis affects female children and adolescents with diabetes as well. Atabek et al. (6) reported that, among girls aged 8–16 years with type 1 diabetes, 39% had colonization with *Candida*. Again, *C. albicans* and *C. glabrata* species were the most prevalent, accounting for 50% and 37% of cases, respectively (6).

Women with symptomatic vaginal candidiasis should receive treatment with topical or oral antifungal agents. Women with diabetes should be presumed to have complicated vulvovaginal candidiasis and should complete a prolonged (7- to 14-day) course of conventional treatment (Table 1) (4,5). Asymptomatic *Candida* colonization does not require treatment, but women with colonization have a higher risk of symptomatic vaginitis that does require pharmacologic treatment (18).

Superficial Dermatophyte Infection

Other superficial mycoses also occur more frequently in women with diabetes compared with women without diabetes. Tinea corporis, which can occur anywhere on the body (including the vulva), is associated with microangiopathy and poor glycemic control (11). It can present with pruritus, pain, and a circular, scaly, erythematous rash with central clearing.

Superficial mycoses can be treated successfully with topical or oral antifungal agents, but prolonged treatment regimens often are required, with rare cases extending for months to years (20). Treatment commonly lasts for 1–3 weeks, and we recommend treating until symptoms resolve. Topical antifungals include azoles, allylamines, butenafine, and ciclopirox. Oral antifungals such as terbinafine and itraconazole are indicated for extensive involvement or when topical antifungals alone are insufficient.

Ultimately, treatment may not be successful if glycemic control is not attained. Thus, special attention must be given to optimizing medical nutrition and glucose-lowering therapies (4,5). SGLT2 inhibitors can be used by women with diabetes but should not be started in those with active vulvovaginal candidiasis. Among women experiencing recurrent vulvovaginal candidiasis (defined as four or more episodes within 1 year), discontinuation of the SGLT2 inhibitor should be considered (4,5).

Nonpharmacologic practices to reduce the risk of fungal infection follow general recommendations for vulvar and vaginal care. Recommendations are geared to maintaining homeostasis by avoiding irritants and include washing the vulvar area with warm water only, applying petroleum jelly if the area is itchy, and wearing white cotton briefs. Women should avoid wearing thong underwear and should avoid shaving and douching. If symptoms of infection are present, women can sleep with loose-fitting underwear or without underwear, and they should avoid intercourse for ≥ 1 week.

TABLE 1 Treatment of Vulvovaginal Conditions Associated With Diabetes

Condition	Suggested Treatment for Patients With Diabetes
<i>Fungal infections</i>	
Vulvovaginal candidiasis	Prolonged (7- to 14-day) course of conventional treatment <ul style="list-style-type: none"> ● Topical antifungal <ul style="list-style-type: none"> ○ Clotrimazole 1% cream once daily ○ Miconazole 2% cream once daily ● Oral antifungal <ul style="list-style-type: none"> ○ Fluconazole 100, 150, or 200 mg on days 1, 4, and 7 ● Vaginal suppository <ul style="list-style-type: none"> ○ Miconazole 100 mg once daily
Superficial dermatophyte infection	Prolonged treatment regimen with topical or oral antifungal in addition to glucose-lowering therapies <ul style="list-style-type: none"> ● Topical antifungal <ul style="list-style-type: none"> ○ Clotrimazole 1% cream twice daily ○ Terbinafine 1% cream once to twice daily ○ Butenafine 1% cream once daily ○ Ciclopirox 0.77% cream twice daily ● Oral antifungal <ul style="list-style-type: none"> ○ Terbinafine 250 mg/day for 1-3 weeks ○ Itraconazole 200 mg/day for 1 week
<i>Bacterial infections</i>	
Cutaneous infection	Prolonged antibiotics and close follow-up
Urinary tract infection	Requires 7 days of antibiotics; specific treatment is determined by bacterial susceptibility profile <ul style="list-style-type: none"> ● Amoxicillin ● Pivmecillinam ● Nitrofurantoin ● Amoxicillin-clavulanate ● Cefixime ● Fluoroquinolone
Vaginal infection	Prolonged, ≥7-day course of antibiotics (compared with 3- or 5-day courses for patients without diabetes)
<i>Noninfectious vulvovaginal conditions</i>	
<i>Skin disorders</i>	
Acanthosis nigricans	Weight loss Physical therapy Medication <ul style="list-style-type: none"> ● Metformin ● Retinoid (topical or systemic) ● Keratolytic agent (salicylic acid, lactic acid, and urea)
Skin tags	Do not require treatment; optional therapies include: <ul style="list-style-type: none"> ● Weight loss ● Excision ● Cryotherapy
Vitiligo	No treatment is curative; treatments are slow to show improvement, and results can fade over time <ul style="list-style-type: none"> ● Cosmetics ● Topical corticosteroid ● Topical calcineurin inhibitor ● Ultraviolet light ● Laser ● Depigmentation ● Skin grafting
Pelvic organ prolapse	Pessary Pelvic floor training or Kegel exercises Weight loss (if obese) Surgery

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TABLE 1 Treatment of Vulvovaginal Conditions Associated With Diabetes (Continued)

Condition	Suggested Treatment for Patients With Diabetes
Urinary incontinence	Lifestyle modification <ul style="list-style-type: none"> ● Fluid management ● Voiding frequently ● Double voiding ● Avoiding bladder irritants ● Managing constipation Pelvic floor training Treatment of comorbid conditions (including overweight and diabetes) Medication <ul style="list-style-type: none"> ● Anticholinergic agent ● β_3 Agonist
Neuropathic pain	Glycemic control Medication <ul style="list-style-type: none"> ● Tricyclic antidepressant ● Gabapentin ● Pregabalin ● Phenytoin ● Lamotrigine ● Dextromethorphan

Bacterial Infections

Cutaneous Infection

Although the association between diabetes and candidiasis is well established, less is known about diabetes and bacterial infections (10). Skin pH is higher for patients with diabetes, which increases their risk of bacterial infections (21). Infections with *Staphylococcus* and *Pseudomonas* are most common, and they can cause boils, abscesses, and carbuncles that affect the vulva (11,12). When these lesions occur on the vulva, patients may present with erythema, swelling, warmth to the touch, fluctuance, pain, and fever. Depending on the severity of the infection, patients may require prolonged oral or systemic antibiotics, close follow-up, and management of complicated wounds. Frequent or persistent infections may require referral to an infectious disease specialist or endocrinologist.

Urinary Tract Infection

The most common presenting characteristics of urinary tract infection include dysuria, increased urinary frequency and urgency, hematuria, and change in urine odor. Presentations are similar for women with or without diabetes, but urinary tract infections are more prevalent for women with diabetes (4,5). For women with diabetes, urinary tract infections should be managed as complicated infections, requiring treatment with antibiotics for 7 days (22). Options for

treatment include amoxicillin, pivmecillinam, nitrofurantoin, amoxicillin-clavulanate, cefixime, or fluoroquinolones, depending on local bacterial susceptibility profiles (22).

Other Vaginal Infections

In a study by Kusunoki et al. (9), 10 gram-negative bacteria were identified by culture in women with diabetes; cultured species included *Escherichia coli*, *Klebsiella pneumoniae*, *Morganella morganii*, *Citrobacter farmeri*, *Gardnerella vaginalis*, *Enterobacter cloacae*, *K. aerogenes*, *C. freundii*, *Acinetobacter baumannii*, and *Proteus vulgaris*. Risk of vaginal infection, most likely with *Enterococcus faecalis*, is increased for women treated with an SGLT2 inhibitor and for those who are postmenopausal. In contrast, premenopausal women more often have *E. coli* infection.

The likelihood of bacterial infection and of an inadequate response to treatment increases in the setting of inadequate glycemic control. Diabetes, particularly when not controlled, also hinders wound healing. As a result, complicated skin and soft tissue infections (e.g., boils, abscesses, and carbuncles) must be monitored closely and treated as complicated infections. A prolonged ≥ 7 -day course of antibiotics is recommended for women with diabetes, whereas, in the absence of diabetes, a 3- or 5-day antibiotic course is typically adequate.

Noninfectious Vulvovaginal Conditions

Skin Disorders

One of the most common skin findings associated with insulin resistance and type 2 diabetes is acanthosis nigricans, which presents as thickened, velvety discoloration of the skin and is caused by hyperinsulinemia via the accumulation of type 1 insulin growth factor (11). Acanthosis nigricans typically appears in skinfolds and can affect the inguinal folds and the perineum (12). Although the impact of acanthosis nigricans is mostly cosmetic, its presence can cause psychological distress and, in rare circumstances, can be associated with intra-abdominal cancer. No effective treatment exists for acanthosis nigricans itself (12), but weight loss and physical activity can help resolve or improve this condition by reversing the associated metabolic disturbances (11). Metformin, topical emollients, retinoids (topical or systemic), and keratolytic agents (salicylic acid, lactic acid, and urea) may improve physical appearance but require a long duration of use (11,12). Age-appropriate cancer screenings should be encouraged because of the rare associated malignancy.

Skin tags (also called “acrochordons”) are benign, flesh-colored or hyperpigmented, pedunculated lesions that also are associated with diabetes and obesity (11,12). Skin tags can develop anywhere on the body but are commonly found in areas of friction, including the groin, vulva, and perineum (23). They can be asymptomatic or can be associated with irritation, itching, bleeding, and cosmetic or psychological concerns. Treatment is not required, but excision or cryotherapy may be options if skin tags are irritating or cosmetically concerning. Weight loss reduces the risk of new skin tags forming (23).

Vitiligo is an autoimmune disorder that causes hypopigmentation or white patches of skin. It is estimated to affect 1–7% of people with diabetes (especially type 1 diabetes) compared with 0.2–1% of people without diabetes (11). Vitiligo often occurs near openings of the skin, including the perineum and rectum (11). Although vitiligo is mostly asymptomatic and a cosmetic concern, it can cause considerable psychological distress (11). The pathogenesis is largely unknown, but suggested mechanisms include autoimmune, genetic, infectious, and mechanical (i.e., the Koebner phenomenon) causes (11). Importantly, because of its frequent comorbidity with other autoimmune disorders, it is reasonable to screen patients presenting with vitiligo for conditions such as type 1 diabetes, autoimmune thyroid disease, and pernicious anemia (11). Other potentially comorbid autoimmune

conditions include alopecia areata, psoriasis, inflammatory bowel disease, linear morphea, myasthenia gravis, lupus, and Sjögren syndrome; screening for these disorders should be considered for select patients with additional signs and symptoms (24,25). Treatment options for vitiligo include cosmetics, topical corticosteroids, topical calcineurin inhibitors, ultraviolet light, laser, depigmentation, and skin grafting (26). However, treatments are not curative, they can be slow to show improvement, and their results can fade with time (27).

Pelvic Organ Prolapse

Pelvic organ prolapse, a subtype of pelvic floor dysfunction, may present as pelvic pressure, a sensation of incomplete emptying, difficulty evacuating stool, and passage of tissue beyond the vaginal opening. Pelvic organ prolapse occurs five times more often among women with diabetes than among those without diabetes (28). Pelvic organ prolapse further elevates the risk of other gynecological issues, including urinary incontinence, bowel dysfunction, and vaginitis symptoms, and it can impair a woman's social, physical, and psychological health (28,29). Risk factors for pelvic organ prolapse are multifactorial and include pregnancy, vaginal delivery, previous pelvic or pelvic floor surgery, being multigravida, age >40 years, and conditions associated with increased intra-abdominal pressure such as obesity, chronic cough, constipation, and repeated heavy lifting (28). Diabetes is an independent risk factor for pelvic organ prolapse (28).

The management of pelvic organ prolapse must be personalized to the patient. Symptomatic women may choose conservative options such as a pessary, pelvic floor muscle training, Kegel exercises, or weight loss for those with obesity, or they may undergo a more invasive option such as surgery (28). Asymptomatic or mildly symptomatic women may not want treatment and may focus instead on preventing the progression of symptoms, primarily through weight loss and avoiding heavy lifting.

Urinary Incontinence

The risk of urological complications is estimated to increase by 50–200% in women with diabetes compared with those with normal blood glucose levels (30). Neuropathic complications of diabetes include weakness of the pelvic floor muscles that control the flow of urine out of the bladder (31). Weakness of these muscles is a manifestation of neuropathy and can result in various types of urinary incontinence, including urge, stress,

functional, overflow, and mixed incontinence (31). Excess adiposity can further increase pressure on the pelvic floor and thus increase the risk of incontinence (31). Elevated A1C levels (particularly $\geq 9\%$) are associated with a greater likelihood of limitations in quality of life due to incontinence (32).

Multiple treatment options are available for urinary incontinence. Lifestyle modifications such as fluid management, voiding frequently, double voiding, avoiding bladder irritants, and managing constipation are important and foundational to other therapies (33). Further treatment options include pelvic floor training, treating comorbid conditions (including overweight and diabetes with the goal of maintaining A1C levels $< 9\%$), and prescribing medications such as anticholinergic agents or β_3 agonists (31).

Neuropathic Pain

Kalra et al. (4,5) suggest a possible association between vulvodynia and unrecognized diabetic neuropathic pain. Yet, despite the similarities in symptoms between the two conditions, including increased sensitivity to normal and abnormal stimuli, the association is not clearly understood, and little guidance exists regarding diabetes screening for patients with vulvodynia. Vulvodynia may be an isolated symptom or may present with other neuropathic abnormalities in women with diabetes (34) because hyperglycemia can damage nerves, weaken muscles, and cause neuropathic pain. Similar to other types of diabetes-related neuropathic pain, vulvodynia can be distressing and may diminish quality of life (34).

Treatment of vulvodynia resembles that of other peripheral neuropathies and includes glycemic control, tricyclic antidepressants, gabapentin, pregabalin, phenytoin, lamotrigine, and dextromethorphan (34). Despite treatment, pain is generally reduced by only 30–50%, and each of these medications has important adverse-effect profiles that need to be considered (34). We typically screen women for diabetes and other causes of neuropathic pain if they present with vulvodynia and are not known to have diabetes already.

Conclusion

Optimal management of infectious and noninfectious vulvovaginal conditions is predicated on improving glycemic control and weight management (4–6). Women with diabetes should be routinely screened for vulvovaginal symptoms at well-person or diabetes follow-up

appointments, and they should be educated about the increased risk of vulvovaginal and other medical conditions. To prevent or reduce the risk of acute and chronic vulvovaginal conditions, diabetes management should include individualized glycemic control, weight management, regular exercise, and healthy eating strategies.

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DUALITY OF INTEREST

No potential conflicts of interest relevant to this article were reported.

AUTHOR CONTRIBUTIONS

D.J.O. reviewed the literature, and, with R.G.M., wrote and revised the manuscript. D.J.O. is the guarantor of this work and, as such, takes responsibility for the integrity and accuracy of the contents.

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PRACTICAL POINTERS

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