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Vaginal Infection: Review Article

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***Abstract*—Vaginitis is a disorder characterized regarding to abnormal bad odor vaginal discharge, discomfort , itching, and burning. Bacterial vaginosis, particularly *Gardnerella vaginalis*, vulvovaginal candidiasis, particularly *Candida albicans*, and trichomoniasis are the most common causes of vaginitis. When a cause is established, bacterial vaginosis is implicated in 40% to 50% of cases, with vulvovaginal candidiasis accounting for 20% to 25% of cases and trichomoniasis accounting for 15% to 20% of cases. Physical examination , symptoms, , and laboratory testing are used for final identification. *Gardnerella vaginalis* DNA or vaginal fluid sialidase activity, as well as Gram stain, are now available in newer laboratory assays. A mixture of clinical manifestations, as well as potassium hydroxide microscopy, are used to diagnose vulvovaginal candidiasis. Culture and DNA probe testing are also available. For such diagnosis of trichomoniasis in asymptomatic or high-risk women, molecular approaches (nucleic acid amplification) are indicated. This study aimed to review the most recent knowledge on vaginal infection, with the most common causal agents being bacteria, yeast, and parasites Keywords—component, formatting, style, styling, insert**

key words: Vaginitis, bacteria, parasite

I. INTRODUCTION

A. Vaginal infection

Inflammation of the vaginal canal is also known as vaginitis. It's caused by an imbalance of yeast and bacteria in the vaginal microflora. Vaginal yeast infections, bacterial vaginosis, and other sexually transmitted illnesses can all produce variations in vaginal discharge (1).

Vaginitis is well-defined as an infection caused by a microorganisms, also an unusual sign of a bacteria, parasite, or fungal that occurs in small amounts. Gardnerella, Neisseria gonorrhoeae, Trichomonas vaginalis, and Candida albicanus infections are the most common (2-4).

A diverse diversity of anaerobic and aerobic microorganisms makes up the vaginal flora of healthy women. The species Lactobacillus (Döderlein Bacillus) is the most common (5). Because of vaginal disorders, lactobacilli serve a vital role in maintaining the natural flora of the vagina, especially during pregnancy (6). Lactobacillus species boost the body's defenses against infections and keep opportunistic microorganisms at bay. Estrogen promotes the maturation, proliferation, and storage of glycogen in vaginal epithelial cells at higher levels (VEC). Lactobacilli thrive in an acidic environment provided by glycogen metabolism (7).

B. Sign and symptoms of vaginitis

Discharge with a change in color and a foul odor, burning, itching, pain in the pelvic or during sexual intercourse are the most common symptoms (8). Infections, vaginal flora imbalances, and pH abnormalities are all possible causes of abnormal discharge. Occasionally, there is no established cause for atypical vaginal discharge. In one study, about 34 percent of women who came to the clinic with vaginal discharge or a foul odor in their vagina had bacterial vaginosis, whereas 23 percent had vaginal candidiasis (9). A potassium hydroxide (KOH) test or a vaginal pH study may be done to help in the diagnosis of abnormal vaginal discharge. Vaginitis is a condition in which abnormal discharge is gone with burning, irritation, or itching on the vulva. Bacteria, Candida spp., and Trichomonas sp. are the most relevant reasons for vaginitis (10,11). Each causative agent of vaginitis has signs and symptoms (12), as illustrated in table (1).

TABLE I. SIGN AND SYMPTOMS OF VAGINITIS

TABLE 1

Signs and Symptoms of Vaginitis

Diagnosis	Etiology	Symptoms	Signs	Other risks
Bacterial vaginosis	Anaerobic bacteria (*Prevotella, Mobiluncus, Gardnerella vaginalis, Ureaplasma, Mycoplasma*)	Fishy odor; thin, homogenous discharge that may worsen after intercourse; pelvic discomfort may be present	No inflammation	Increased risk of HIV, gonorrhea, chlamydia, and herpes infections
Vulvovaginal candidiasis	*Candida albicans*, can have other *Candida* species	White, thick, cheesy, or curdy discharge; vulvar itching or burning; no odor	Vulvar erythema and edema	–
Trichomoniasis	*Trichomonas vaginalis*	Green or yellow, frothy discharge; foul odor; vaginal pain or soreness	Inflammation; strawberry cervix	Increased risk of HIV infection Increased risk of preterm labor Should be screened for other sexually transmitted infections
Atrophic vaginitis	Estrogen deficiency	Thin, clear discharge; vaginal dryness; dyspareunia; itching	Inflammation; thin, friable vaginal mucosa	–
Irritant/allergic vaginitis	Contact irritation or allergic reaction	Burning, soreness	Vulvar erythema	–
Inflammatory vaginitis	Possibly autoimmune	Purulent vaginal discharge, burning, dyspareunia	Vaginal atrophy and inflammation	Associated with low estrogen levels

HIV = human immunodeficiency virus.
Information from references 10, 14, and 15.

1-Bacterial vaginitis (BV)

Bacteria such as Staphylococcus aureus, Escherichia coli, Group B Streptococci (GBS), Listeria, Mycoplasma, and Ureaplasma species can cause aerobic vaginitis (13).

Gardnerella vaginalis, Prevotella, Bacteroides, and Mobiluncus species can also cause bacterial vaginosis (14). Other organisms associated with Bacterial vaginitis (BV) include Atopobium vaginae, Megasphera spp, Eggerthella spp, and Leptotrichia spp (15). Bacterial vaginosis occurs in 40 percent to 50 percent of vaginal infection cases (16).

The vagina suffers from a decrease in lactobacilli and an increase in a variety of anaerobic bacteria, the most prevalent of which is Gardnerella vaginalis (17). A gram stain demonstrating of lactobacilli and a polymicrobial gram negative variable rods, and cocci is the gold standard for diagnosis. Oral or intravaginal antibiotics, as well as lactobacillus, can be used to treat BV (18). According to Swidsinski et al. (2014), BV- could be borne by polymicrobial biofilm "clue cells" which are epithelial cells of vagina covered with coccobacillary bacteria (19). Virulent factors of Gardnerella spp. like cytotoxicity, adhesion, and biofilm formation are not like other types of BV bacteria .

To make the diagnosis, thin, homogeneous discharge, a positive whiff test, the presence of clue cells on microscopy, Gram stain, and vaginal pH greater than 4.5 are all necessary. When compared to Gram stain and molecular test with Gardnerella vaginalis DNA probes or detection of vaginal fluid sialidase activity showed higher sensitivity ranged 92-100% and specificity ranged 92- 98 % (20,21).

C. Pathogensis

A biofilm generated by Gardnerella vaginalis and other species like Mobiluncus mulieris, A. vaginae, and Prevotella bivia are related to bacterial vaginosis (22,23). A polymicrobial biofilm cause the high recurrence rate of BV, as it protects bacteria from lactic acid, H2O2, bacteriocins, and antibiotics that used as treatment (such as flagyl and tinidazole), as well as provides resistance against immunity, for example preventing macrophage phagocytosis or chemo-taxis (24-26,22). Gene expression of antimicrobial resistance proteins by G. vaginalis consider special relevance. Figures 1 A&B depicted clue cells under a microscope, while Figure 1C depicted vaginal and cervix discharge (22).

Despite the fact that Lactobacillus iners and Lactobacillus crispatus have the same inhibitory effects on BV-associated bacteria adherence (27), G. vaginalis adherence was increased in the presence of Lactobacillus iners, which could be because of L. ners's limited protective activity.

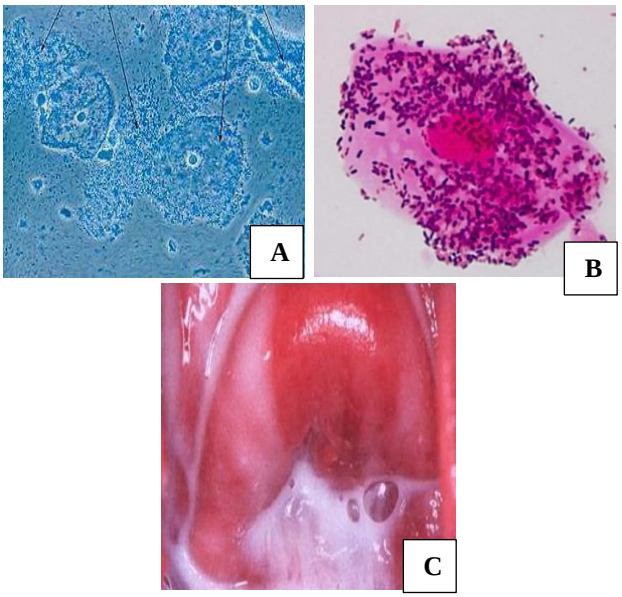


Fig. 1. A, B: vaginal epithelial cell infected with Gv- and Gv+ bacterial species including G. vaginalis, revealing of Clue cells. C: Abnormal vaginal & cervix discharge

D. Diagnosis

1-Despite numerous molecular and genomic investigations undertaken at the species or micro biome level, no consensus has been reached on the group of bacteria which may cause actual BV (28,29). High numbers of L. iners in BV could be due to its genetic makeup altering vaginal habitats (30). For example, BV demonstrated the expression of genes involved in glycogen, mannose, and maltose breakdown (31).

2-Clinically , BV is identified by the Nugent score (32). Microscopic examination and vaginal swab culture are used to detect changes in the vaginal environment (33).

3-Quantification of Gram-stained bacteria, distinct vaginal morphotypes, and the detection of clue cells are used to diagnose BV (34).

4-Finally, Amsel's criteria for a positive BV diagnosis involves saline microscopy and have been improved via the existence of a thin watery homogenous discharge, high vaginal pH (>4.5), around 20 percent of clue cells , and a fishy amine odor after adding 10% of KOH to vaginal discharges (whiff test) (35).

E. Treatment

BV has Increased antibiotic resistance and different sensitivity patterns in vitro to flagyl and secnidazole (36).

2-Candida vaginitis

Vulvovaginal candidiasis (VVC) is caused by an excess of yeasts, primarily Candida albicans that are part of the vaginal flora (37). One of the most prevalent causes of infectious vaginitis is a vaginal yeast infection, which can be caused by both C. albicans and non-albicans yeast (38,39). Further Candida species for example C.tropicalis, C.parapsilosis, C.krusei, and Saccharomyces cerevisiae account for 1-2 percent of the total (40). Seventy percent of women will contract candida at some point in their lives (41). In yeast infections, vaginal discharge is often white, thick, odorless, and clumpy (Cottage cheese-like) (42,43), accompanying vaginal itching, irritation, burning, soreness,

and pain during urination or intercourse (41). Taking antibiotics, diabetes, pregnancy, and HIV/AIDS are all risk factors, although kind of underwear, tight clothing, and personal cleanliness are not (44, 45).

F. Pathogensis

During Candida vulvovaginitis, Candida species penetrate the vagina's mucosal lining. This causes Candida species to be drawn to the vagina's mucosal surface as an inflammatory response (46).

Many factors cause Candida spp. infection are include : multiple transcriptional trails, morphological and phenotypic switching, biofilm formation, evasion of phagocytosis, adhesion and invasions, extracellular hydrolytic enzymes, metabolic flexibility, genome plasticity, and the ability to adapt to changes in the environment. The fact that there are many connections, and relations between altogether of these factors, are unique features that show significant roles in the development of Candida infections (47).

G. Diagnosis

Vaginal candidosis can be diagnosed by looking at a person's medical history, looking at their symptoms, and looking at the yeast in their blood or urine. (48)

1- A wet amount of yeast (hyphae) can be seen with a microscope, and it can also be grown in a lab. Antigen tests can also be done to see if the yeast is preset (49-50).

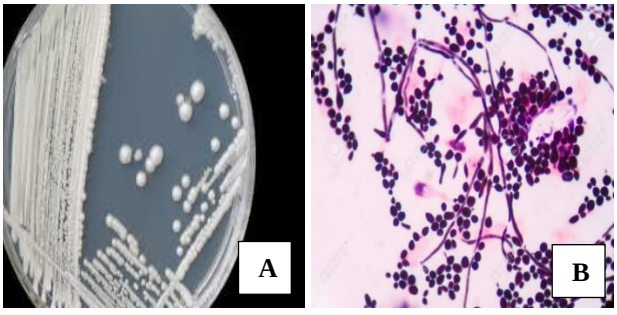
2- Sabouraud glucose agar is the most common medium for cultures. Chrome agar, on the other hand, is thought to be sensitive and reliable (49).

3-A woman with typical symptoms had positive yeast hyphae on a 10% KOH preparation (49) in the third step.

4-Antigen or DNA probe testing (51-53).

H. Treatment

Antifungal drugs that can be used inside the vaginal canal or a single dose of fluconazole taken orally are commonly used to treat vaginal candidiasis. For serious infections that do not improve, more treatments may be required. These therapies include taking higher doses of fluconazole or using other vaginal drugs including boric acid, nystatin, or flucytosine (54). Figures 2 A,B exhibit candida albicans cultivated on Sabouraud agar with gram staining showing budding and hyphae, while Figure 2C shows vulvovaginal candidiasis with cheesy discharge.



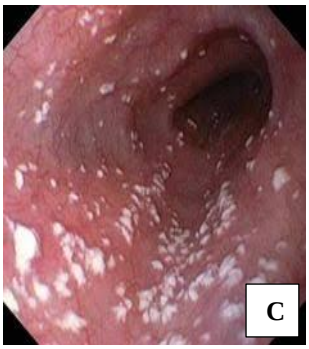


Fig. 2. A: culture of candida on Sabouraud glucose agar B: showed budding yeast cells with pseudohyphae. C: cheesy like discharge (Vulvovaginal candidiasis)

I. Trichomonial vaginitis

The most prevalent cause is Trichomonas vaginalis. It has been discovered to be linked to sexually transmitted diseases (STD). Trichomoniasis is also found in postmenopausal women, with trichomoniasis cases ranging from 15% to 20% (55). Trichomonas vaginalis is regarded as a primordial eukaryote due to it is anaerobic metabolism and lack of mitochondria. It is recently found to have hydrogenosomes (56). T. vaginalis, like other Trichomonas species, has a great number of transposable elements (TEs) in its huge haploid genome of 160 Mb (57). Trichomonas vaginalis has recently been discovered to have meiosis-specific genes, a cyst-like stage with a cell wall, despite the fact that T. vaginalis is thought to be asexual and only present as a trophozoite-stage. This could result in a reassessment of the treatment aspect (58,59). T.vaginalis is a flagellate protozoan parasite that causes vaginitis, and described clinically by severe signs and symptoms. Trichomonasis caused 140.8 million cases worldwide in 2015, a 15.4% increase from 2005 to 2015 (60). T.vaginalis is a sexually transmitted infection that has a significant recurrence rate, particularly if the male partner is not treated.

In terms of signs and symptoms, women with T. vaginalis may have a yellowish-green discharge with a frothy foul odor in nature.

In addition to soreness and vulvar itching accompanied by dysuria and dyspareunia, erythematous or "strawberry patches" in the vaginal and cervix have been reported (61). In rural South Africa, there was a significant prevalence of Vaginal trichomoniasis, which is mostly asymptomatic (62).

J. Pathogenesis

The vaginal flora can be divided into five community state types, with lactobacilli dominating the first four, and anaerobic bacteria (e.g. Gardnerella vaginalis) and mollicutes (e.g. Mycoplasma spp.) dominating the fifth (63). T. vaginalis is linked to CST-IV, which raises vaginal pH, and the presence of particular anaerobic bacteria is linked to T. vaginalis acquisition. Lactobacilli thrive in an acidic environment (pH 4.5). (64,65). The interesting fact is that CST-IV improved T. vaginalis adherence to epithelial cells by forming a biofilm (66), and both of them can integrate vaginal epithelium by disrupting intercellular connections, although lactobacilli cannot (67). Pinhenio et al. (2018) found that Lactobacillus gasseri strain ATCC 9857 inhibits T. vaginalis adherence to host cells in a contact-dependent

manner, and that this strain can even displace trichomonads away from vaginal epithelial cells (68). Aggregation-promoting factor 2 (APF-2) is responsible for this remarkable ability, which is encoded by lactobacilli. In addition, T. vaginalis have the ability to kill bacteria by expressing 9 peptidoglycan hydrolases of the NlpC/P60 family (69).

T. vaginalis kills epithelial cells in two different ways. Direct cell contact and the release of cytotoxic compounds are two ways that cytotoxic substances can be released. It also attaches to host plasma proteins, blocking the alternative complement pathway and host proteinases from recognizing the parasite. Both, the number of polymorphonuclear leukocytes and the vaginal pH will increase during infection. PMNs are the most common host immune respond against T vaginalis, and they react to trichomonad chemotactic chemicals (70). During infection, Both locally and in serum, an antibody response against T. vaginalis infection has been reported (71).

K. Diagnosis

1-Wet preparation: it revealed the presence of infection by showing motile trichomonads in the samples. However, women's sensitivity is 45–60 percent, while men's is even lower (72).

2-Pap smear or cervical smear with normal cervix squamous cells (pink/blue) and T. vaginalis appear as tiny blue patches (72).

3-Culture: Trichomonad culture has a greater sensitivity than microscopy, but it can take up to five days to provide a result. The 'gold standard culture' was modified Diamond media, however molecular testing has found to be more sensitive (73).

4- Nucleic Acid Amplification Techniques (NAATs) have highest sensitivity for detecting T. vaginalis. This technique identifies T.vaginalis DNA in vaginal or endocervical swabs, as well as urine samples from male and female, with high sensitivity and specificity (97% ,99% respectively) (74–77). T. vaginalis under a microscope and vaginal discharge illustrated in in Figure 3A, B, 3C.

5- Recently Trichomonas V® antigen-based rapid diagnostic strip test was introduced but with no data on its reliability and should not be considered as an alternative test (78).

L. Treatment

As an anti-trichomonadal chemotherapy, metronidazole is still the drug of choice (79). A seven-day regimen of 500 mg twice daily was prescribed. During the course of 5-nitroimidazoles, alternate treatments such as secnidazole or new compounds are recommended (80-82)

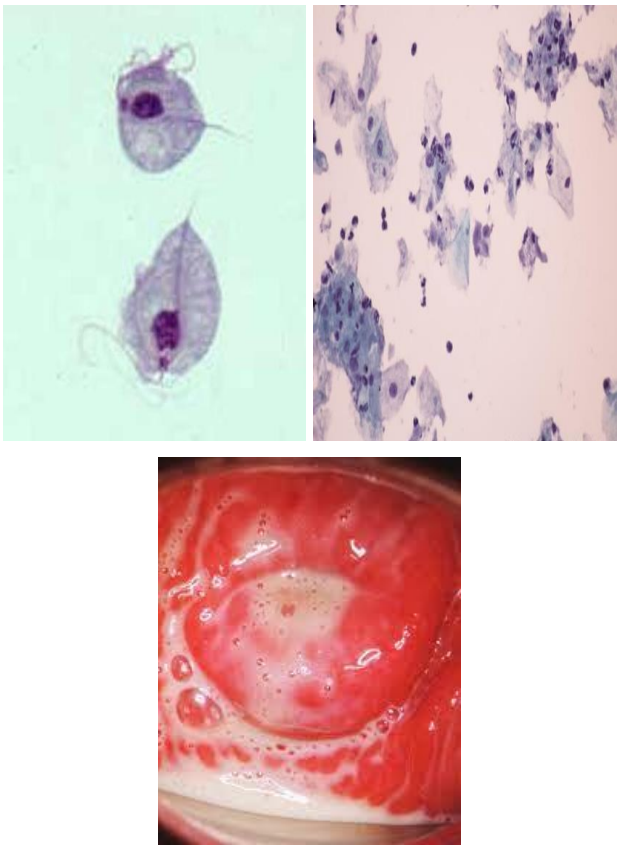


Fig. 3. A: showed Trichomonas vaginalis diagnosis under microscope by Giemsa stain. B: showed Trichomonas vaginalis diagnosis under microscope by pap smear C: Frothy vaginal discharge with Trichomonas vaginalis

II. Acknowledgment

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