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Review on Infectious Vaginitis

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ABSTRACT

Human vagina has various defence mechanisms to prevent infections. Any disturbance in the defence mechanisms can cause vaginitis. Vaginitis can be due to infectious or non infectious cause. Infectious vaginitis can be due to bacteria, fungi or trichomonas species. The infectious cause must be treated appropriately to prevent recurrence and emergence of any multidrug organisms. Hence, knowledge about the various causes of infectious vaginitis, their diagnostic and treatment modalities is very essential for the practitioners for effective management of various vaginal infections.

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INTRODUCTION

There is usually a well maintained balance existing in the women between her vagina and its normal flora. Any disturbance or variation in this balance can lead to vaginitis. There are various etiological factors causing vaginitis, which can be broadly classified as infectious or non-infectious. The infectious cause is mostly attributed to bacterial, fungal and trichomonial vaginitis.

Epidemiology:

Vaginitis affects around 5 – 10 million people every year [1]. Bacterial vaginitis occurs in any age group and bacterial vaginosis (BV) is found to be more common among the women of reproductive age group. Candidiasis is found to be more common in women around menopause. *Candida albicans* is found to be the causative agent for 80 to 92 percent cases of vulvovaginal candidiasis [2]. Nowadays non-albicans strains are also found to be highly prevalent in the community. Recurrence is very common in vaginal yeast infections. Trichomonial vaginitis occurs in 15-20% cases of infective vaginitis. Garbar [3] in his article mentioned that around 170 million cases are infected with trichomonas per year. Vanderpol *et al* [4] in their study concluded that *Trichomonas vaginalis* infection increases the risk of HIV infection.

Vaginal Flora of Women:

Studies [5] showed that Lactobacillus species (*L. crispatus*, *L. gasseri*, *L. jensenii, Lactobacillus iners*), are the most common organisms found in the cervix and vagina of healthy women. The vagina of women is rich in glycogen which makes it best suitable for glucose fermenting organisms like lactobacilli. The other normal vaginal flora includes *Staphylococcus epidermidis* (CONS – Coagulase negative Staphylococcus), *Micrococcus* and *Diphtheroids*. Other microorganisms in the vagina which may become pathogenic include *Staphylococcus aureus,* Group D *Streptococcus* (Enterococcus), Beta haemolytic *Streptococcus*, *Neisseria* sp., *Escherichia coli*, *Klebsiella sp., Proteus sp.* and *Candida* sp.

Role of Lactobacilli in Defence Mechanisms:

More than 50 species of microorganisms have been isolated from the vagina of women [6]. Lactobacilli play an important role in the prevention of vaginal infections. They adhere to the mucosal membrane of vagina and create a barrier which prevents the pathogens from attaching to vaginal epithelial cells. Studies have also found that *Lactobacillus* strains can displace *Gardnerella vaginalis* and *Candida albicans* from vaginal epithelial cells [7].The Lactobacilli also produce several antimicrobial products which prevents vaginal colonization by the pathogens. They also produce hydrogen peroxide (H2O2) which is found to inhibit the growth of some pathogens. Studies have shown that vaginal acidification by lactobacilli can prevent the growth by pathogens *G.vaginalis* and Mobiluncus [8]. But, Burton and Reid [9] found that *G.vaginalis* was detected along with Lactobacillus in a high vaginal sample and

concluded that pathogens still have a chance to coexist along with the commensals. However, another study showed *G.vaginalis* getting displaced when a single intravaginal instillation of probiotic lactobacilli was administered [10]. Also when *L.rhamnosus* GR-1 was instilled as probiotic into the vagina, it caused 3536 gene expression changes with antimicrobial defence [11].

Predisposing Factors for Infectious Vaginitis:

There are many predisposing factors which can alter the growth of microorganisms in the vagina. Factors such as menstrual status, hormonal changes (mainly estrogen), vaginal pH, and glycogen content can affect the ability of lactobacilli to adhere to epithelial cells [12]. Witkin *et al* [13] mentioned that host's innate immunity plays a very important role in changing from a healthy state to Bacterial vaginosis (BV) state. An altered pH favours vaginal infections. Diabetes can result in several changes in the host defence system. Lakshmi *et al* [14] have shown that diabetic women are at a higher risk of vaginal infections when compared to nondiabetic women. The menstrual cycle can also cause changes in the vaginal microbiota. Estrogen levels regulate the thickness of the vaginal epithelial lining. With the decrease in estrogen levels after menopause, there is also a decrease in lactobacilli present in the vagina of postmenopausal women [10]. Lack of estrogen makes the vagina thinner and weaker causing it more vulnerable to injuries along with invasion of microorganisms. Hormone replacement therapy (HRT) has been found to alter the vaginal bacterial growth of postmenopausal women restoring lactobacilli and also decreases the incidence of urinary tract infections (UTI) [15]. Studies have shown that postmenopausal women are at a higher risk of acquiring bacterial vaginal infections [16]. Heinemann *et al* have shown that the postmenopausal women not receiving HRT are at a risk of acquiring pathogens [17]. The risk of BV is more with multiple sexual partners and condoms were found to be protective against BV [18]. Previous literature also reported that BV is found to be absent in women with no history of sexual activity [19]. *Candida* vaginitis can occur in pregnancy [20] and there is a risk of vertical transmission. The risk of Candida vaginitis is more in HIV-infected women [21], during or after treatment with antibiotics [22] and due to some genetic factors [23].

Etiology of Infective Vaginitis:

The three most common causes of infectious vaginitis are Bacteria, Candida sp. and Trichomonas sp.

Bacterial vaginitis is usually an aerobic vaginitis caused by bacteria like *Staphylococcus aureus*, *Escherichia coli*, Group B Streptococci (GBS), *Listeria, Mycoplasma* and *Ureaplasma* species [24]. Bacterial vaginosis is caused by *Gardnerella vaginalis, Prevotella, Bacteroides* and *Mobiluncus* species (spp), and *Ureaplasma* species [25].The other organisms like *Atopobium vaginae*, Megasphera spp, Eggerthella spp, and Leptotrichia spp are also associated with BV [26].

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Candida vaginitis is a vaginal yeast infection which is one of the most common causes of infectious vaginitis. *C.albicans* is the common cause of symptomatic episodes of vaginal candidiasis [27]. Of the non-albicans yeast species, *C.glabrata* is considered the most common [28]. Other species of the *Candida* genus include *C.tropicalis, C.parapsilosis, C.krusei* and *Saccharomyces cerevisiae*1-2% [29].

Trichomonial vaginitis is caused by *Trichomonas vaginalis*. It is found to be associated with sexually transmitted diseases. However, it is also found in sexually inactive asymptomatic postmenopausal women.

Other Causes of Vaginitis:

Chlamydia which is one of the most common infections in young women with multiple sex partners can cause vaginitis. Viral vaginitis can be caused by herpes simplex virus which is sexually transmitted. Non-infectious vaginitis is usually caused by allergy or irritation due to sprays, douches, sanitary pads, soaps, detergents, fabric softeners or spermicidal products.

Table No.1: Symptoms and Signs of Infectious Vaginitis

	BV	Candida	Trichomonas
Symptoms	Vaginal discharge and itching sensation in the vagina	Thick vaginal discharge and itching sensation in the vagina	Usually asymptomatic, few cases have itching, pain during micturition, pain during sexual intercourse
Vaginal Discharge	Thin, white, foul smelling homogenous	Thick, white	Grey or greenish, frothy discharge, foul smelling
Vaginal pH	>4.5	Usually ≤4.5	>4.5
KOH "whiff test"	Positive	Negative	Often Positive
Saline Wet Mount	Clue cells can be seen	Few WBCs	Motile flagellated Protozoa can be seen with many WBCs
KOH Wet Mount		Pseudohyphae may be seen	

DIAGNOSIS

Various diagnostic methods are available for detection of infectious vaginitis.

Bacterial vaginitis:

The aerobic organisms causing bacterial vaginitis can be diagnosed by culture of the high vaginal swab samples in basal media like nutrient agar, Mac Conkey agar and blood agar. The isolates can be diagnosed using standard biochemical methods. The anaerobic organisms can be diagnosed by culture in anaerobic environment. *Gardnerella vaginalis* can be identified by beta-haemolytic colonies on human blood agar plate but not on sheep blood agar, growth in

Columbia agar, Gram-variable pleomorphic coccobacilli in Gram stain and negative catalase and oxidase reactions. Mobiluncus spp., Bacteroides spp.and other anaerobic organisms can be grown in blood agar, chocolate agar under anaerobic conditions. The *Bacteroides* spp grow on bile medium and hydrolyse aesculin, but *Prevotella* spp fails to grow on bile or hydrolyse aesculin. Culture is often difficult in routine clinical work. Spiegel *et al* [30] analysed the pattern of non-volatile fatty acids in vaginal discharge by gas liquid chromatography. The gram stain appears to be better than gas-liquid chromatography, the proline aminopeptidase test, or vaginal cultures in predicting infection [31,32].

Diagnostic Criteria for Bacterial Vaginosis:

Since there is no clear symptom of bacterial vaginosis, various scoring systems [33,34,35] are available to diagnose the BV.

Amsel clinical criteria**:** It includes four criteria. Among them, three must be present for diagnosis of bacterial vaginosis[33].

1) Thin, homogenous white discharge
2) Vaginal fluid pH > 4.5
3) A whiff test which yields an amine odor with the addition of 10% potassium hydroxide to vaginal discharge and
4) The presence of clue cells on a microscopic examination of vaginal smear.

The presence of clue cells is the most important criteria for diagnosis of bacterial vaginosis [36].

Spiegel Criteria: Gram-stained vaginal smears are used for evaluating BV in Spiegel criteria [34]. Bacteria are grouped into different categories based on their morphology, with Lactobacillus as elongated bacteria and Gardnerella as short bacteria. BV is diagnosed by the comparing the number of Lactobacilli to the numbers of other morphotypes.

Hay/Ison criteria [37] has a grading system which is defined as follows

- Grade 1 (Normal): Lactobacillus morphotypes predominate.
- Grade 2 (Intermediate): Mixed flora with some Lactobacilli present, but Gardnerella or Mobiluncus morphotypes also present.
- Grade 3 (Bacterial Vaginosis): Predominantly Gardnerella and/or Mobiluncus morphotypes. Few or absent Lactobacilli.

Nugent Criteria [35]: Nugent score is often used in research and is based on analysis of Gram stained vaginal smear. Gram stains are used to score the amount of three morphotypes: *Lactobacillus* (large uniform gram-positive rods), *G. vaginalis* (small pleomorphic Gram-variable rods) or *Prevotella/Bacteroides* (small Gram-negative rods), and *Mobiluncus* (curved Gram-variable rods).

The scores are as follows:

- 0–3 is considered negative for BV
- 4–6 is considered intermediate
- 7+ is considered indicative of BV.

Nugent criteria showed a sensitivity of 89% and a specificity of 83%, while Spiegel criteria have sensitivity and specificity of 62% and of 95%, respectively compared to Amsel criteria [38,39].

Candidal Vaginitis:

Culture is considered as the “gold standard” in diagnosing *Candida* vaginitis [40]. Candida vaginitis is also diagnosed by microscopic detection of yeast cells on a vaginal smear along with the presence of a white, mucous-like vaginal discharge on physical examination. Saline or 10% KOH wet mount may show yeast cells and pseudohyphae. Candida culture is usually done on Sabouraud’s dextrose agar and Gram stain of the colony shows gram positive yeast cells. Germ tube test can be used for differentiation of Candida albicans species from non-albicans species. *Candida spp.* can also be identified serologically, using specific antisera. DNA probes are also available for Candida spp detection.

Trichomonas Vaginitis:

Trichomonas vaginitis is more often difficult to diagnose because of its heterogeneous presentation. Vaginal pH is often more than 4.5. Many cases give a positive amine (KOH) test ("whiff" test). *T. vaginalis* was traditionally diagnosed via a wet mount, in which polymorphonuclear response and a "corkscrew" motility can be observed. The most common method of diagnosis is by culture. Despite the low cost, culture of trichomonas is not routinely practised in many laboratories. Culture requires Diamond's medium. The In Pouch TV culture system is now found to be a good alternative to traditional culture techniques [41]. Other methods like rapid antigen testing and transcription-mediated amplification are not in widespread use [42]. The presence of *T. vaginalis* can also be diagnosed by direct fluorescent antibody test, enzyme immune assay and PCR [43].

TREATMENT

Bacterial Vaginal Infections:

Antibiotics usually recommended for bacterial vaginosis are metronidazole, clindamycin, tinidazole. Therapy may not be necessary for asymptomatic women with BV and for male partners of women with BV. But, asymptomatic patients with BV who are to undergo surgical abortion should be treated. Pregnant women with symptomatic disease should also be treated. There is no evidence of teratogenicity from metronidazole, even when used in first trimester. Intravaginal clindamycin cream is not recommended in pregnant women due to increased risk

of premature delivery. Experts recommend screening and treatment of asymptomatic pregnant women at high risk for pre-term delivery (i.e., those who have previously delivered a premature infant) at the first prenatal visit.

Candida Vaginitis:

Vaginitis due to *Candida albicans* usually responds well to antifungal therapies. But vaginitis caused by non-albicans species of Candida are often nonresponsive to conventional antifungal therapies. Uncomplicated VVC responds well to short course of oral antifungal therapy. In contrast, complicated VVC or recurrent VVC occurring in uncontrolled diabetes and other immunocompromised states may require longer duration of topical imidazoles. In pregnant patients, only topical imidazoles are recommended. Fluconazole should not be used. In cases associated with severe vulvitis and intensepruritis, topical use of low potency corticosteroid cream or nystatin cream may be helpful.

For recurrent vulvovaginal candidiasis (RVVC), an initial intensive regimen of 7-14 days of topical treatment or sequential oral doses of fluconazole followed by a maintenance regimen for at least six months is recommended. Weekly fluconazole (150 mg single oral dose) reduces the frequency of episodes of RVVC.

Trichomonial Vaginitis:

All patients with trichomoniasis need to be treated (whether symptomatic or asymptomatic). Metronidazole is recommended for trichomoniasis. Paramomycin is an alternative for metronidazole allergy. In pregnancy also metronidazole is recommended. Tinidazole is not recommended. Recommendations for treatment in pregnancy are often changing, but with evident safety of metronidazole in pregnancy [44]. A regimen of 2 g of metronidazole in a single dose is the treatment of choice for trichomonas infection in women in all trimesters of pregnancy. If invasive technologies such as chorionic villous sampling or cerclage placement are necessary in pregnancy, pre- procedure prophylaxis in infected patients is indicated to avoid procedure-related infection and complication.

A combination of vaginal metronidazole by suppository concurrently with oral metronidazole therapy or intravenous metronidazole has been effective in resistant trichomonas cases [45].

PREVENTION

Bacterial Vaginal Infections:

Douching which can remove the protective lactobacilli should be avoided. If BV is recurrent, then the male partners can be suggested to use condoms.

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Candida Vaginitis:

Some male partners who acquire balanitis may benefit from topical antifungal agents. Control of the predisposing factors like diabetes may be beneficial.

Trichomonas Vaginitis:

The individuals who are positive for HIV along with Trichomonas infection are found to have multiple partners. These patients are to be identified early and should be educated on the protection and prevention of spread of infection by following safe practices. Prevention strategies (abstinence, monogamy, condoms, limit number of sex partners, etc.) may be helpful. Latex condoms, when used consistently and correctly, can reduce the risk of transmission of Trichomonas.

CONCLUSION

Infectious Vaginitis is one of the common conditions in women of all ages. Knowledge about the causative agents, diagnostic methodologies and treatment modalities of infectious vaginitis is needed for all practitioners in order to start an appropriate treatment. Most of the practitioners start on empirical therapy with antifungal drugs for any type of vaginitis. Many resistant organisms also have been evolved in the recent decades because of irrational use of antibiotics and other drugs. Hence proper diagnosis of the cause and efficient management of vaginitis after performing the patient's antimicrobial susceptibility pattern to various drugs is recommended.

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