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Gardnerella Vaginalis Associated Bacterial Vaginosis: A Review Article

Nanda Rachmad Putra Gofur*[1], Aisyah Rachmadani Putri Gofur[2], Soesilaningtyas[3], Rizki Nur Rachman Putra Gofur[4], Mega Kahdina[4], Hernalia Martadila Putri[4],

[1]Department of Health, Faculty of Vocational Studies, Universitas Airlangga, Surabaya, Indonesia
[2]Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia
[3]Department of Dental Nursing, Poltekkes Kemenkes, Surabaya, Indonesia
[4]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

***Corresponding Author**: Nanda Rachmad Putra Gofur, Department of Health, Faculty of Vocational Studies, Universitas Airlangga, Surabaya, Indonesia.

Abstract

Introduction: Gardnerella vaginalis is associated with bacterial vaginosis. Bacterial vaginosis (bacterial vaginosis = BV) is a clinical syndrome due to replacement of Lactobacillus spp. producing hydrogen peroxidase (H2O2) in normal vagina with high concentrations of anaerobic bacteria (eg Bacteroides spp., Mobiluncus spp.), this clinical syndrome also has other names, namely Haemophilus vaginalis vaginitis, nonspecific vaginitis or Gardnerella vaginalis vaginitis. Because the cause of BV is bacteria which are normal vaginal flora, BV is referred to as an endogenous infection in the female reproductive tract. Previous published research on BV has shown disagreements about transmission through sexual contact. Post-puberty women without sexual experience experience BV less frequently than those who have sexual experience. However, longitudinal cohort studies provide evidence that women who have new sexual partners or have multiple sexual partners have an increased incidence of BV.The likelihood that a woman has BV has a 20-fold increase in risk if her partner has BV. This raises the suggestion that it is possible that BV can be transmitted through sexual contact. However, there was no association between the incidence of BV with smoking habits, a history of abnormal Pap smears, menstruation, and menarche. Aim of this article is to review gardnerella vaginalis infection in bacterial vaginosis.

Discussion: The presence of sexually transmitted diseases can also increase the risk of bacterial vaginosis. The normal vaginal ecosystem is a complex aspect. Lactobacillius is the dominant bacterial species (normal flora) in the vagina of women of childbearing age, but there are also other bacteria, namely aerobic and anaerobic bacteria. At the time BV appears, there is an overgrowth of some bacterial species which are normally present in low concentrations. Therefore, BV is categorized as an endogenous infection of the female reproductive tract.. Women with positive G. vaginalis cultures do not need routine therapy, unless they have BV symptomatically. All women with symptomatic BV require treatment, including pregnant women. Treatment of BV in pregnant women is to relieve signs and symptoms of vaginal infection, reduce the risk of infectious complications that accompany BV during pregnancy, and decrease other risk factors. Several studies using placebo have shown that treatment of sexual partners of women with BV does not improve clinical outcome of BV or decrease recurrence.
Conclusion: BV has a favorable prognosis, and spontaneous improvement is reported in over one-third of cases. With the treatment of metronidazole and clindamycin gave a high cure rate (84 - 96%).Prevention needs to be done to minimize the actions that can be taken to prevent bacterial vaginosis.

Keywords: BV, Gardnella vaginalis, management

Introduction

Gardnerella vaginalis is the normal vaginal flora and accounts for about 30%. These microorganisms are gram-negative rod bacteria which are usually found together with anaerobic bacteria (eg Bacteroides spp., Mobiluncus spp.). The use of more sensitive culture media G. vaginalis can be isolated in women without signs of vaginal infection. With selective media, it appears that G. vaginalis 40-50% in all fertile women. G. vaginalis was isolated in> 90% of women with BV (bacterial vaginosis). It is currently believed that G. vaginalis can interact with anaerobic bacteria and M. hominis to cause BV. Brewer and Heltai's study confirmed the relationship between nonspecific vaginitis, Gardner and Duke also isolated other organisms that could lead to the conclusion that H. vaginalis is not the only cause of non-specific vaginitis[1].

Gardnerella vaginalis is associated with bacterial vaginosis. Bacterial vaginosis (bacterial vaginosis = BV) is a clinical syndrome due to replacement of Lactobacillus spp. producing hydrogen peroxidase (H2O2) in normal vagina with high concentrations of anaerobic bacteria (eg Bacteroides spp., Mobiluncus spp.), Gardnerella vaginalis (G. vaginalis) and Mycoplasma hominis (M. hominis). This clinical syndrome also has other names, namely Haemophilus vaginalis vaginitis, nonspecific vaginitis or Gardnerella vaginalis vaginitis. Because the cause of BV is bacteria which are normal vaginal flora, BV is referred to as an endogenous infection in the female reproductive tract[2].

Previous published research on BV has shown disagreements about transmission through sexual contact. Post-puberty women without sexual experience experience BV less frequently than those who have sexual experience. There is a study that found none of the 18 girls who had BV were examined, while the women who had sexual experiences found that 69 (24%) had BV. However, longitudinal cohort studies provide evidence that women who have new sexual partners or have multiple sexual partners have an increased incidence of BV. Studies in lesbians provide further evidence of the role of sexual intercourse in BV transmission. About 101 lesbians who visited the gynecology clinic, 29% had BV as well as their partners. The likelihood that a woman has BV has a 20-fold increase in risk if her partner has BV. This raises the suggestion that it is possible that BV can be transmitted through sexual contact[3].

Another factor that also plays a role as a predisposing factor for BV is the use of douching. A cohort study of 182 women showed that the occurrence of BV was not only associated with a new sexual partner, and a decrease in H202-producing Lactobacillus, but was also associated with the use of vaginal douching. Research has found that BV is more common in women who frequently use intrauterine ingredients. In a prospective study, it was reported that BV was also increased among IUD users compared to oral contraceptives. Another retrospective study of female sex workers in Peru also revealed the same. However, there was no association between the incidence of BV with smoking habits, a history of abnormal Pap smears, menstruation, and menarche. Aim of this article is to review gardnerella vaginalis infection in bacterial vaginosis[4].

Discussion

Pathogenesis

The presence of sexually transmitted diseases can also increase the risk of bacterial vaginosis. The normal vaginal ecosystem is a complex aspect. Lactobacillius is the dominant bacterial species (normal flora) in the vagina of women of childbearing age, but there are also other bacteria, namely aerobic and anaerobic bacteria. At the time BV appears, there is an overgrowth of some bacterial species which are normally present in low concentrations. Therefore, BV is categorized as an endogenous infection of the female reproductive tract. It is known that there are 4 categories of vaginal bacteria that are associated with BV[5].

BV is initiated by changes in the normal vaginal flora microbiota of Lactobacillus with a mixed flora consisting of Gardnerella vaginalis, anaerobic bacteria, and Mycoplasma hominis. Previous studies studying the pathogenesis of BV have demonstrated changes that occur in the vaginal microbial ecosystem. A previous

study inoculated 29 normal women with 2 ml of a suspension containing 2-101U G. vaginalis. There were 7 (24%) in 29 women developing clinically to be infected after 3 weeks postinoculation. However, no research was carried out on the presence of anaerobic bacteria or genital mycoplasma which also appeared in the clinical symptoms that occurred[6].

In vivo studies on monkey, Gardnella vaginalis or Mobiluncus spp. those administered intravaginally did not show any symptoms of vaginitis separately. However, Gardnella vaginalis and Mobiluncus spp. given concomitantly produces vaginal discharge after 5 days of inoculation. Furthermore, it is confirmed by epidemiological data showing that the entry of organisms through sexual intercourse can change the normal vaginal flora and cause BV. The presence of Lactobacillus spp. can help normal women to avoid infections of the vagina and cervix. Vaginal lactobacillus inhibits G. vaginalis, Mobiluncus, and Bacteroides spp. in vitro trials. Several Lactobacillus strains produced H202, in one case control study and four cross-sectional studies showing that the H202-producing lactobacilli strain was more dominant in normal women than in women with BV. In addition, there is a prospective study of women with H202-producing Lactobacillus colonization less frequently with BV than women with negative H202-producing Lactobacillus colonization. The H202 produced by Lactobacillus inhibits the growth of anaerobic stem germs, Gardnerella, Mobiluncus, and Mycoplasma in the vagina either through the toxic effects of H202 or through the reaction of halide ion with peroxidase in the cervix which is part of the H202-halide-peroxidase antibacterial system[5].

The normal vaginal flora which is dominated by Lactobacillus has a low pH <4.5 due to the presence of lactate production. The pH level in the BV condition usually increases> 4.7 as a result of the predominance of G. vaginalis and anaerobic bacteria. G. vaginalis and anaerobic bacteria can occur in symbiosis, where G. vaginalis produces amino acids, while anaerobic bacteria convert these amino acids into amine compounds so as to increase the pH where G. vaginalis grows. The metabolism of these organisms causes the production of amines, which cause a fishy smell (fish odor) in vaginal fluid. This flora also causes a low oxygen oxidation-reduction potential (Eh). Eh levels below 100 Mv are common in BV. At this level, O2 is available for aerobic metabolism[7].

So far, no host factor increases susceptibility to BV. Previous studies have shown an association with IUD use, however, the mechanism by which IUD use increases the incidence of BV is not known. The redox potential (Eh) of vaginal epithelial surfaces in BV is lower than in normal women. After metronidazole therapy in patients with BV, the redox potential of the vaginal epithelium returns to normal ranges. This suggests that a low vaginal Eh is not a persistent host factor in the development of BV[8].

It is estimated that the amount of amen production by the microbial flora, due to the presence of mycrobial decarboxylase, results in fishy odor when vaginal fluid is mixed with 10% KOH. This situation is called the "whiff test" which is thought to be due to reduced volatility of aromatic amines, including putrescine, cadaverine, and trimethylalamine at alkaline pHs. Mobiluncus can produce trimethylalamine, it is unknown what other microbes are capable of producing amines. Recent data show that trimethylalamine can be detected at relatively high concentrations in the vaginal fluid of BV patients, with an average concentration of 5 mM. The presence of trimethylalamine in vaginal fluids is thought to be the cause of the characteristic odor of vaginal discharge with BV[5].

The effect of changing the form of organic acids is still doubtful, although it has been shown that the succinic acid produced by anaerobes inhibits the chemotactic response of white blood cells. The vaginal fluid of women with BV has elevated levels of endotoxin, siliadase, and mucinase. The increased response of the host to BV is the occurrence of increased levels of interleukin-1α and prostaglandins in cervical mucus in women with BV. The effect of BV on vaginal epithelium and epithelial cell turnover is not known. However, increasing the concentration of anaerobic pathogens in the vaginal fluid of BV patients can increase the risk of

ascending upper reproductive tract infection. In BV, recurrences often occur, due to the inability to prevent BV recurrence, due to a lack of knowledge about the causes of recurrence or the etiology of the disease. The mechanism of BV recurrence is not fully understood, but there are 4 possible explanations, namely as follows[6].

1. Recurrent infection of a partner with the microorganism that causes BV. Men whose female sexual partner is infected with G. vaginalis, contains G. vaginalis with the same biotype in the urethra but does not cause urethritis or is asymptomatic in men, so women who have undergone BV treatment are less likely to relapse as a result of non-use sexual contact. protector.

2. Recurrence is often caused by the microorganisms from BV which are only inhibited during treatment but not killed.

3. Failure during treatment to restore Lactobacillus as normal flora which functions as a protector in the vagina.

4. The persistence of other microorganisms whose host factors have not been identified in sufferers, makes them susceptible to recurrence.

Clinical Manifestations and Diagnosis

A cross-sectional study of BV patients using Gram staining was significantly associated with symptoms of malodor vaginitis (49% of BV patients versus 20% of non-BV patients) and vaginal secretions (50% of BV patients versus 37% of non-patients), and with signs of a homogeneous, white, non-viscous vaginal discharge sign that is flat against the vaginal wall, often seen on the labia and fourchette before the speculum is inserted. Although one-third of women with BV complain of yellow vaginal discharge, most studies have found insignificant increases in PMN (polymorphonuclear) leukocytes that occur with BV[7].

Nearly all women with BV have a vaginal discharge pH ≥ 4.5 when measured on pH indicator paper. Although this pH probe helps in clinical examination it is not specific for BV. Fishy odor occurs when a 10% KOH drop in vaginal fluid (whiff test) occurs. Microscopic examination of vaginal fluid with high strength (400X) showed clue cells in 81% of BV patients compared to 6% of non-patients with BV. Clue cells are epithelial cells that are attached by bacteria so that the edges are uneven. The bacteria that cover the clue cells are Gardnerella vaginalis and Mobiluncus[8].

Patients with BV usually do not find vulvar or vaginal inflammation. BV can occur with trichomoniasis or cervicitis, so in addition to BV features can also be found a picture of the infection. Recurrent BV symptoms are basically the same as when you first had BV. Recurrent BV patients may also be asymptomatic or have a vaginal odor such as a distinctive fish odor and the smell increases during sexual intercourse. The basis for a clinical diagnosis of BV is based on at least three of the following signs[9]:

1. Homogeneous white vaginal discharge

2. pH of vaginal fluid> 4.5

3. The presence of fishy odor from the vaginal fluid dripped with 10% KOH (whiff test)

4. On the microscope examination found the presence of Clue cells.

- Vaginal discharge[5]

Douching, recent sexual intercourse, menstruation, and any accompanying infections can alter the picture of vaginal discharge in BV. Usually, the vaginal secretions in BV are white, adhering to the vaginal wall, the amount is only slightly to moderate increase compared to normal women.

- Vaginal fluid pH[8]

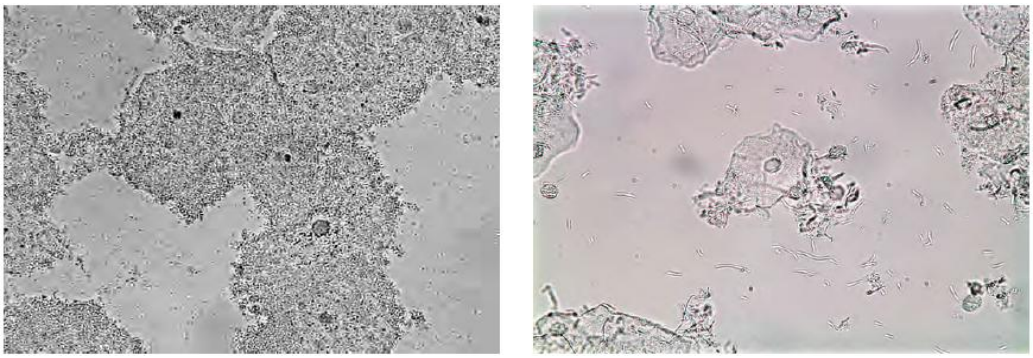
Vaginal pH testing requires pH indicator paper with an appropriate range between 4.0 and 6.0. It is best to collect specimens for examination of vaginal pH on the lateral or posterior vaginal fornix and tap directly onto the pH paper. Alternatively, pH paper can be placed on the vaginal fluid collection after the speculum has been removed from the vagina. Cervical mucus should be avoided because it has a higher pH than the vaginal pH (pH 7.0). A study on 178 women with a pH <4.4, no clue cells were found. Meanwhile, from 257 women who had a pH> 4.7, the clue cells were 20%. Of the 257 women, 89% had homogeneous secretions, fishy odor, or both. Vaginal pH has the highest sensitivity to BV but has the lowest specificity.

- Vaginal Malodor (Whiff Test)[9]

Vaginal malodor is the most common symptom of women with BV, and the appearance of fishy odor after 10% KOH drop helps the clinician detect malodor. A drop of vaginal fluid is placed on a glass object and a drop of 10% KOH will immediately produce an amine odor. This smell quickly disappeared. Although this test is very helpful in diagnosis, the sensitivity is also low. Research shows that this predictive value is 76% compared to Gram stain.

- Clue Cells Check[5]

Clue cells are squamous vaginal epithelial cells covered with a lot of bacteria so that they give an uneven edge. These uneven edges are a result of adhering to bacteria including Gardnerella and Mobiluncus. Lactobacillus can also adhere to the vaginal wall, the concentration is less to resemble clue cells. This cell examination used a sample of vagma fluid taken with a swab and placed on a glass object then dripped with 1 or 2 drops of physiological salt, then covered with a cover glass. The preparation is examined under a microscope with high magnification (400X). This examination has a sensitivity of 60% and a specificity of 98%. Clue cells are the best criteria for BV diagnosis.



(A) **(B)**

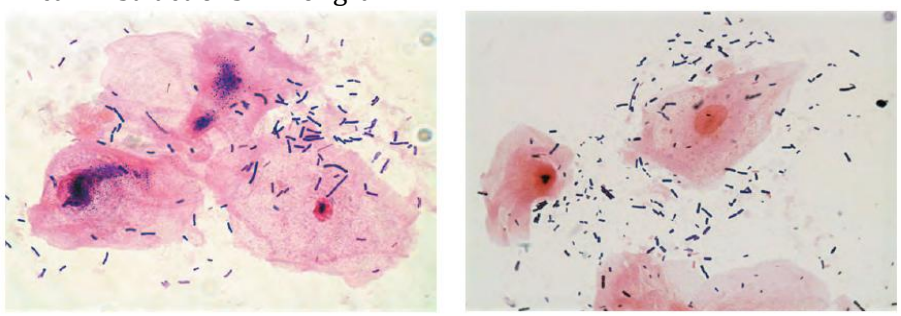
Image 7. (A) Wet smear of vaginal fluid showing clue cells typical of a woman with bacterial vaginosis. (B) Base preparation of vaginal fluid in the absence of clue cells and presence of long lactobacillus morphotype (X400 magnification)[8]

- Culture

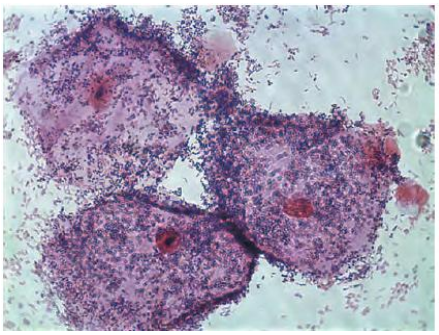
Gardnerella vaginalis culture examination will only provide a slight advantage in diagnosing BV, because this bacteria is also a normal vaginal flora so it is also found in normal female vaginal fluids even in low concentrations.[10]

- Gram stain

Investigators suggest examining vaginal smears using a gram stain for the diagnosis of BV. Spiegel and colleagues then published clinical instructions. The gram stain scoring system is used as the standard method for BV diagnosis based on three morphotypes, namely: large gram-positive rods (Lactobacillus), small or variable gram-negative rods (Gardnerella and anaerobic stem bacteria), and Mobiluncus. This method is based on the shift in morphotype from the dominant Lactobacillus to Gardnerella and anaerobic bacteria including Mobiluncus. The gram test has a sensitivity of 89% and a specificity of 83%.[11]



A **B**



C

Image 8. (A) Gram stain of normal vaginal fluid, showing gram-positive rods, with blunt tip showing lactobacillus (X1000 enlargement); (B) Gram stain of vaginal fluid with intermediate vaginal flora (Nugent score 5) (X1000 magnification); (C) Gram stain of the vaginal fluid of women with bacterial vaginosis, showing the absence of lactobacilli and a large number of gram-negative or variable coccobacilli. (X1000 magnification).[8]

Management and Prevention

The course of BV has not been widely studied, but spontaneous improvement has been reported in over a third of cases. Women with positive G. vaginalis cultures do not need routine therapy, unless they have BV symptomatically. All women with symptomatic BV require treatment, including pregnant women. The goals of BV treatment in nonpregnant women are to eliminate signs and symptoms of vaginal infection, and reduce the risk of developing infectious complications. Treatment of BV in pregnant women is to relieve signs and symptoms of vaginal infection, reduce the risk of infectious complications that accompany BV during pregnancy, and decrease other risk factors[11].

- Metronidazole oral 2 grams in a single dose. Less effective than the 7 day regimen; 84% cure. Has moderate activity against Gardnerella vaginalis, but very active against anaerobic bacteria, its effectiveness is related to anaerobic inhibition.

- Metronidazole gel 0.75% intravaginally, full applicator (5 grams), twice daily.

-Intravaginal 2% clindamycin cream, full applicator (5 grams), used at bedtime for 7 days or twice a day for 5 days.

- Clindamycin 300 mg 2 times a day for 7 days.

- Oral augmentin (500 mg amoxicillin +125 mg clavulanic acid) 3 times a day for 7 days.

- Cephalexin 500 mg 4 times a day for 7 days.

The Ministry of Health of the Republic of Indonesia in 2015 made the following guidelines for bacterial vaginosis therapy:[12,13]

- Metronidazole 2 grams orally as a single dose OR

- Metronidazole 2 x 500 mg / day orally for 7 days OR

- Clindamycin 3 x 300 mg / day orally for 7 days

Topical Therapy[12,13]

1. Metronidazole gel intravagina (0.75%) 5 grams, twice daily for 5 days

2. Clindamycin cream (2%) 5 grams, once a day for 7 days.

3. Intravaginal tetracyclines 100 mg once daily. Very effective at treating BV, but induces vaginal candidiasis and ulcerative vaginal lesions.

4. Triple sulfonamide cream or tablets (Sulfacetamid 2.86%, Sulfabenzamide 3.7% and Sulfathiazole 3.42%) 1 tablet or 1 applicator full of cream into the vagina 2x a day for 10 days. But recently the reported cure rate is only 15 - 45%.

Sexual Partner Treatment and during Pregnancy

Several studies using placebo have shown that treatment of sexual partners of women with BV does not improve clinical outcome of BV or decrease recurrence. On the other hand, a recent study reported no significant difference in BV response to treatment or recurrence within 4 to 12 weeks of therapy in women with BV whose sexual partners were not treated. Another study revealed that there was no significant effect of treatment on sexual partners in

terms of complaints, clinical symptoms, or isolation of G. vaginalis from women 1 to 5 weeks after BV therapy. Because some studies have shown that treatment of the sexual partners of women with BV is not beneficial, the U.S. The Centers for Diseases Control Guideline for STD Treatment does not recommend therapy for sexual partners with BV[14,15].

Routine therapy during pregnancy is not recommended, as problems can arise. Metronidazole although small but has potential teratogenic, mutagenic, and carcinogenic, which is limited use during pregnancy, at least during the first trimester. Lower doses are recommended during pregnancy to reduce side effects. Penicillin is safe to use during pregnancy but ampicillin and amoxicillin are clearly not as effective as metronidazole in nonpregnant women where both antibiotics give a low cure rate. In the first trimester, vaginal clindamycin cream is given because clindamycin has no side effects on the fetus. In the II and III trimesters oral metronidazole may be used although metronidazole vaginal gel or clindamycin cream may be preferred[16,17].

The incidence of BV is high in women with pelvic inflammatory disease. Although there are no studies showing that BV treatment reduces the risk of pelvic inflammatory disease later in life. The other complications of BV are as follows[18,19]:

- BV is accompanied by endometritis and pelvic inflammatory disease after termination of pregnancy.

- BV during pregnancy is accompanied by pregnancy complications including preterm delivery, premature rupture of membranes and post-partum endometritis.

- BV is accompanied by an increased risk of urinary tract infection.

- There is an increase in upper genital tract infection associated with BV. High concentrations of microorganisms at one site tend to increase the frequency of infection in adjacent sites.

Conclusion

BV has a favorable prognosis, and spontaneous improvement is reported in over one-third of cases. With the treatment of metronidazole and clindamycin gave a high cure rate (84 - 96%).Prevention needs to be done to minimize the actions that can be taken to prevent bacterial vaginosis, for example, avoid using vaginal douching or other women's hygiene products, such as disinfectants, vaginal givers, vaginal tighteners and dryers, and clean the outside of the vagina with soapy water, using a condom during sexual intercourse. clean contraceptives properly after use (such as diaphragms, cervical caps, and spermicide).

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