

# Bacterial vaginosis

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## ABSTRACT

Bacterial vaginosis is an important public health issue, affecting women worldwide. Despite its increased incidence, the etiology is yet unclear. In all symptomatic cases, treatment must be started immediately to cure this condition that favors the acquirement of sexually transmitted diseases. Symptomatic pregnant women should always be treated, and treatment regimens are the same for pregnant and non-pregnant women. Possible complications of this disease include infertility, sexually transmitted diseases, HIV, premature rupture of membranes, premature birth, intra-amniotic infections and postpartum endometritis.

**Keywords:** bacterial vaginosis, *Gardnerella vaginalis*, dysbiosis, sexually transmitted diseases

## INTRODUCTION

The vaginal microbiota varies in composition and density and it's very important for reproductive cyclicity and healthy pregnancies or births. The presence in the vagina of numerous lactic acid producing bacteria (*Lactobacillus* spp.) and a thick vaginal stratified squamous epithelium covered by a protective mucus layer, usually corresponds to a healthy condition, whereas the absence (or even a reduced population) of these bacteria corresponds to an abnormal condition. The microbiota is very important in preventing colonization of the vagina with anaerobic and micro aerophilic pathogens, and whenever a marked unbalance of the vaginal microbiome occurs, we talk about bacterial vaginosis (BV) [1].

BV is the most common vaginal disorder among sexually active women worldwide and is associated with significant public health problems such as preterm birth, acquisition and transmission of sexually transmitted diseases and other complications that will be described below [2,3].

Although so common the disorder, its etiology remains unclear. It is however clear that it repre-

sents a dysbiosis characterized by the decline of healthy *Lactobacilli* spp. (that produce hydrogen peroxide and lactic acid) and the increase in concentrations of other bacterial species, including Gram-negative bacilli, Gram-positive cocci and facultative anaerobes [3-6].

Unlike the case of vaginitis, clinical inflammation is not present in BV, but a proinflammatory response is described at the molecular level [7,8].

Numerous complications affecting both pregnant and non-pregnant women are associated with BV. In non-pregnant women, the vaginal changes related to BV correspond to an increased risk of contracting sexually transmitted infections (*Chlamydia*, human papilloma virus, *Gonorrhoeae*) that usually involve the upper genital tract as well and many times result in infertility. Also, this disorder favors HIV infection [1,9,10].

In pregnant women, BV increases the risk of miscarriage (early / late), recurrent abortion, postabortion sepsis, histological chorioamnionitis, preterm labor, preterm rupture of membranes, preterm labor, preterm birth, low birth weight and postpartum endometritis [1,3,9].

Bacteria commonly associated with BV include *Gardnerella vaginalis*, *Ureaplasma spp.*, *Mycoplasma spp.*, *Megasphaera spp.*, *Prevotella spp.*, *Dialister spp.*, *Atopobium vaginae*, *Mobiluncus spp.*, *Sneathia amnii*, *Sneathia sanguinegens* and *Porphyromonas spp* [9,11-13].

Although BV is usually asymptomatic (80% in general population in USA), some women may experience itching, burn-sensation, unpleasant vaginal odor and vaginal discharge [3,9,14].

## METHODS

A PubMed, Web of Science electronic search was undertaken using keywords like “bacterial vaginosis”, “Gardnerella”, “vaginal odor”, “dysbiosis”, “sexually transmitted diseases”. The search results included systematic reviews, randomized controlled trials, review articles, meta-analyses and international guidelines and resulted in more than 150 articles, from which only 30 papers were further included in the final review.

## EPIDEMIOLOGY AND RISK FACTORS

BV is the most common cause of vaginal discharge and malodor among women, being estimated that 29% of women worldwide are affected. In the sub-Saharan Africa region studies have reported prevalence values of up to 50%. Among pregnant women, a Canadian study shows an incidence of 14% [10,15,16].

The human vaginal microbiome is constantly changing and is significantly influenced by aging and various behavioural / lifestyle factors including nutrition, alcohol intake, smoking, sexual activity and the use of contraception devices. Menstruation also has been related to alterations of the vaginal microbiota. Confirmed risk factors for BV include smoking, douching, race, sexual activity, multiple sexual partners, not using condoms, sex with women.[1,13,15,17].

It appears that women who use oral contraceptives have a lower risk of BV, probably due to the estrogens supplementation that may have a nurturing effect on the lactobacilli in the vagina or it may also be the fact that they are usually monogamic and more conservative in their sexual behavior [18].

## DIAGNOSIS

The management of BV requires a specific diagnosis, which can be made by combining the naked eye examination and the laboratory workup of the vaginal discharge [19].

Women with BV usually present vaginal discharge, vaginal malodor and sometimes vulvar irri-

tation. Examination of the vagina often shows off-white, thin, homogenous vaginal discharge with an unpleasant, fishy odor that it's more pronounced especially after intercourse and around menstruation [6,14].

Paraclinical assessment requires the collection of vaginal discharge with a cotton tipped swab from the lateral and posterior vaginal walls for pH measurement and wet mount microscopy [20].

The vaginal pH value plays an important role in assessing vaginal health. The neutral pH is equal to 7, while the vaginal pH normally ranges between 3.8 and 5.0, which is moderately acidic. A more acidic vaginal pH (lower value) comparing to the blood / interstitial fluids pH can protect vaginal mucosa from pathogenic organisms [21].

The Nugent criteria to evaluate a Gram-stained vaginal discharge smear represents the gold standard in BV diagnosis, this method involving identification and enumeration of lactobacilli, *G. vaginalis*, *Mobiluncus spp* and *Bacteroides spp.* [21,22]. This test takes into consideration the shapes and the sizes of the bacteria and assigns a score from 0 to 10. A score of 0-3 considered normal is showing the predominance of lactobacilli, a score of 4-6 is intermediate indicating the presence of mixed Gram negative / variable flora, while a score of 7-10 indicates the presence of a small number (or the absence) of the lactobacilli and the predominance of Gram negative / variable bacteria. A score of 7 or greater indicates the diagnosis of BV. Even though the Nugent criteria method has a higher sensibility and it's easier reproducible, it is not routinely used as this method requires time and well-trained personnel [1,13].

In daily medical practice, physicians use Amsel criteria which are simple and easy to use in any laboratory equipped with a microscope [23,24]. For positive diagnosis of BV, at least three of the following four criteria must be met: thin homogenous white vaginal discharge, vaginal pH > 4.5, 20% or more clue cells on the vaginal smear, fishy odor after application of 10% potassium hidroxide solution on the slide (whiff test) [1,21,25].

Nowadays, with the development of culture-independent or metagenomics-based techniques, identifying markers such as DNA allows the identification of various microbial communities, these methods becoming preferrable whenever possible, when investigating the human vaginal microbiota [1].

There are alternative tests with acceptable performances that can be used for diagnosis of BV if microscopy is not available.[13] OSOM BV Blue (Sekisui Diagnostics, Framingham, MA) is a rapid test that detects vaginal fluid sialidase activity at levels greater than 7.8 U and uses color change technology

offering a result in a few minutes, but the test cannot rule out the presence of other microorganisms (eg. yeast, *Trichomonas vaginalis*) in cases with mixed vaginal infections [13,26,27]. Affirm VP III (Becton Dickinson, Sparks, MD; a DNA hybridization probe test for high concentrations of *G. vaginalis*) can also be mentioned here. PCR utility in the diagnosis of BV has been researched, some saying that molecular analysis is more sensitive than Amel's criteria in the diagnosis of BV, but additional validation is necessary. Identification of vaginal flora indicating BV on a Pap smear cytology has low specificity and sensibility making this test not useful in the case of the current discussed pathology [13,24].

Giving that BV is a common condition with and great a public health burden, the development of a test that is quick, low cost, accurate, temperature-stable and doesn't require microscopic capabilities is very useful in improving the diagnosis and treatment of BV [27].

## TREATMENT

BV treatment is recommended for symptomatic women. The CDC last treatment guideline recommends Metronidazole 500 mg orally 2 times / day for 7 days or Metronidazole gel 0.75 % one full applicator (5 g) intravaginally, once a day for 5 days or Clindamycin cream 2% one full applicator (5 g) intravaginally at bedtime for 7 days. It is recommended to avoid sexual contact during treatment in all treatment schemes, and 5 days after, if using Clindamycin cream which is oil based and might weaken latex condoms [13].

Alternative treatment regimens that should be taken into consideration are Clindamycin 300 mg orally 2 times / day for 7 days or Clindamycin ovules 100 mg intravaginally once at bedtime for 3 days or Secnidazole 2 g oral granules in a single dose or Tinidazole 2 g orally once daily for 2 days or Tinidazole 1 g orally once daily for 5 days. Regarding the treatment for sex partners, it may be recommended only in cases of recurrent BV [13].

Alcohol intake is prohibited during treatment with all nitroimidazoles and also 72 hours after tinidazole administration to minimize the chances of a disulfiram-like reaction [13].

Pregnant women with BV should be treated to avoid adverse unfavorable pregnancy outcomes such as premature rupture of membranes with preterm birth, intraamniotic infections or postpartum endometritis. Pregnant women can be treated with the same recommended regimens as non-pregnant women [28].

If symptoms resolve, follow-up visits are unnecessary. In case of recurrence, using a different recommended treatment regimen can be taken into consideration. However, the same treatment can be used for treating persistent or recurrent BV after the first occurrence [29].

In case of multiple recurrences, either 0.75% metronidazole gel or 750 mg metronidazole vaginal suppository twice weekly for > 3 months has been reported to reduce recurrences. Another option to be taken into consideration is an oral nitroimidazole followed by intravaginal boric acid 600 mg daily for 21 days and suppressive 0.75% metronidazole gel twice weekly for 4-6 months. Monthly oral metronidazole 2 g administered with fluconazole 150 mg reduces the BV incidence and promotes colonization with normal vaginal microbiota [30].

## CONCLUSIONS

BV is a very common health issue among women worldwide and it also represents an important public health issue, partly due to the high rates of recurrence that occurs in the case of up to half of the women treated with the recommended regimens.

BV recurrences can have a great impact on women's health and quality of life, so, the unacceptable high recurrences rates of BV highlight the need for new and more efficient treatment regimens.

Also, further research is warranted in order to understand the mechanisms of recurrences and to delineate adequate prophylaxis methods.

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