Aerobic Vaginitis

Aerobic vaginitis (AV) is a state of abnormal vaginal flora that is distinct from the more common bacterial vaginosis (BV) (Table 1). AV is caused by a displacement of the healthy vaginal Lactobacillus species with aerobic pathogens such as Escherichia coli. Group B Streptococcus (GBS), Staphylococcus aureus, and Enterococcus faecalis that trigger a localized vaginal inflammatory immune response. Clinical signs and symptoms include vaginal inflammation, an itching or burning sensation, dyspareunia, yellowish discharge, and an increase in vaginal pH > 4.5, and inflammation with leukocyte infiltration. (1) Severe, persistent, or chronic forms of AV can also be referred to as daquamificant inflammatory vaginitis (DIV). (2, 3)

BV is a common vaginal disorder associated with the overgrowth of anaerobic bacteria, a distinct vaginal malodorant discharge, but is not usually associated with a strong vaginal inflammatory immune response. Like AV, BV also includes an elevation of the vaginal pH > 4.5 and a depletion of healthy Lactobacillus vagins species. BV is treated with traditional metronidazole therapy that targets anaerobic bacteria. However, approximately 10% to 20% of women diagnosed with BV and treated with metronidazole will fail to respond to therapy at one week and will experience persistent symptoms. (4, 5)

It is believed that a subset of these patients may have been misdiagnosed and actually suffer from AV, which requires an antibiotic therapy with intrinsic activity against specific aerobic bacteria. AV has been implicated in complications of pregnancy such as ascending chorioamnionitis, premature rupture of the membranes, and preterm delivery.

Epidemiology

In a study of 631 patients attending routine prenatal care from a vaginitis clinic, 7.9% had moderate to severe AV signs and symptoms and 8% had ‘un-met’ BV (1).

In a study of 3,000 women, 4.3% were found to have severe AV, also called DIV. Furthermore, 49.5% of the women with DIV were peri- or postmenopausal. A reported hypothesis is that a drop in estrogen may trigger the development of AV in the aforementioned menopausal women, as well as postpartum nursing women. (3)

In a more recent study of 215 women, 19.1% were found to have a misdiagnosis caused by BV, of which 12.6% were found to have ‘inflammatory vaginitis’ (IV). (6) Of the IV group, 77.8% were characterized as having DIV. (11) In fact, 42.9% of the women with DIV were found to be GBS positive, a 5-fold increase over the healthy patients (17.7% positive). (11) This study was similar to an earlier study that found 43% of DIV patients were GBS positive. (4)

Pathogenesis

AV is associated with an increase in vaginal pH (> 4.5), depletion of vaginal healthy Lactobacilli, and an overgrowth of aerobic or facultative anaerobic bacteria, usually the Gram-negative bacilli E. coli or Gram-positive cocci GBS, and occasionally S. aureus and E. faecalis. The high concentration of these aerobic bacteria and the absence of healthy vaginal Lactobacilli results in triggering the immune system as evidenced by vaginal inflammation, high levels of proinflammatory cytokine production, recruitment of leukocytes, and the generation of toxic leukocytes and parabasal cells.

Table 1. A Comparison of Bacterial Vaginosis and Aerobic Vaginitis.

<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Bacterial Vaginosis</th>
<th>Aerobic Vaginitis (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogen</td>
<td>G. vaginalis, Atopobacter vaginae, Prevotella buetongii, Bacteroides vulgatus</td>
<td>G. vaginalis, Group B Streptococcus, Staphylococcus aureus, Enterococcus faecalis</td>
</tr>
<tr>
<td>Vaginal epithelial inflammation</td>
<td>None</td>
<td>Present</td>
</tr>
<tr>
<td>Elevation of pro-inflammatory cytokines (IL-1, IL-6, IL-8)</td>
<td>Moderate elevation</td>
<td>High elevation</td>
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<tr>
<td>Immune reaction (cytokines leukocyte)</td>
<td>Non-reactive</td>
<td>Reactive</td>
</tr>
<tr>
<td>pH (Normal = 3.8 – 4.2)</td>
<td>T = 4.2-4.5</td>
<td>BV = 4.5</td>
</tr>
<tr>
<td>Vaginal discharge characteristics</td>
<td>White, homogenous</td>
<td>Yellowish</td>
</tr>
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References are provided for treatment information; Fluoroquinolones, such as ciprofloxacin, ofloxacin, and levofloxacin, are contraindicated in pregnant women. Levofloxacin has improved efficacy against Streptococcus compared to ciprofloxacin. T = Translational.
Aerobic Vaginitis

The patient may present with all or some of these signs and symptoms of AV: yellowish discharge, itching or burning sensation, dyspareunia, odor, and pain during bimanual exam. These signs and symptoms are typically associated with BV, inflammation (Figure 1), toxic leukocyte infiltration, and the presence of parabasal cells and naked rounded vaginal epithelial cells (Figure 2).

Clinical Significance

Patients with AV present with distinct clinical signs and symptoms of abnormal vaginal flora that can be confused with common vaginal etiologies such as BV, TVC, and TV (Table 1). In a study of patients presenting with AV, we detected the presence of aerobic bacteria, which correlated with the AV flora discussed in the clinical AV scoring characterization. The presence of aerobic bacteria is important for the diagnosis of AV. (1, 14)

Treatment for Aerobic Vaginitis

The therapy for aerobic vaginitis should include an antibiotic with an intrinsic activity against the majority of bacteria of fecal origin.

Effect on the normal flora

A study measuring the minimum inhibitory concentrations (MICs) of the four most common vaginal species (E. coli, GBS, S. aureus, and E. faecalis) in a study that measured the minimum inhibitory concentrations (MICs) of pefloxacin, ciprofloxacin, ofloxacin, erythromycin, doxycycline, clindamycin, ampicillin, kanamycin, and vancomycin antibiotics for 73 vaginal swabs revealed that the CT infection rate of 23.9% found in this high-risk population was higher than in other Brazilian studies with pregnant women from 6 other cities. The high rate of C. trachomatis in this study can be explained by the design of the study. In this study comprising a high risk population for STI, aerobic vaginitis was found to be associated with CT detection.


The aim of this work was to study the vaginal flora of female sex workers from Comodoro Rivadavia, Chubut. A total of 229 female sex workers attended public health centers. Vaginal secretions were analyzed by Gram and Giemsa stains.

The following results were obtained: normal microbiota 35.37 %, intermediate microbiota 15.72 %, bacterial vaginosis 23.14 %, microbial non-specific vaginitis 10.48 %, yeast vulvovaginitis 8.30 %, and trichomoniasis 6.99 %.

The intermediate microbiota was characterized by a decrease in the number of lactobacilli and the presence of diphtheroid bacilli cell types. The population studied shared increased values of vaginal dysfunctions. These results are considered risk factors for obstetric and gynecologic diseases.
Aerobic Vaginitis

have demonstrated clindamycin treatment failures due to clindamycin resistant isolates. (16) Approximately 21% (17) to 38% (18) of GBS clinical isolates were reported to be clindamycin resistant; furthermore, clindamycin is not effective against E. coli.

Group B Streptococci are uniformly susceptible to penicillin, ampicillin, amoxicillin, amoxicillin-clavulanic acid, and ceftazolin, and aztreonam are not currently recommended for empirical therapy in pregant women. Women who are cured with clindamycin must be treated with additional therapy for a minimum of 3 days. (20)


Medical Diagnostic Laboratories, L.L.C.
New Tests Announcement

A. Bacterial Vaginosis (BV) C. Trichomoniasis vaginitis (TV)

B. 10% to 20% D. 35% to 40%

pathogen was detected? ‘Mixed Flora, not indicative of a UTI’. How can it not be indicative of a UTI if the urinary pathogen was mixed flora.

not properly collect the specimen utilizing a “clean catch technique”, contamination from their everyday flora may be introduced into the specimen. This type of contamination will present during the antibiotic resistance portion of testing as the presence of several different organisms as mixed flora.

To facilitate proper specimen collection, we can provide your office with Clean Catch instructions to better assist your patients with this process.

For results to the electronic epidemiology Quiz, please visit www.mdlab.com and click on the e-Quiz link.
Polymerase Chain Reaction (PCR) testing is a DNA-based detection method with very high sensitivity. Therefore minute amounts of the organism can be detected. If the patient does not properly collect the specimen utilizing a “clean catch technique”, contamination from their normal flora may be introduced into the specimen. This type of contamination will present during the antibiotic resistance portion of testing as the presence of several different organisms as mixed flora.

To facilitate proper specimen collection, we can provide your office with Clean Catch instructions to better assist your patients with this process. Please contact your MDL sales representative or our Client Services Department toll free at 877.269.0090 to request a copy. If you have a question you would like addressed in future issues, please email your question(s) to Q&A@mdlab.com.

Aerobic Vaginitis

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References

Aerobic Vaginitis

Now Available on the OneSwab®:

1. True of False

Medical Diagnostic Laboratories, L.L.C.

Now Available on the OneSwab®:

182 Aerobic Vaginitis (AV) Panel by Real-Time PCR (GBS, S. aureus, E. coli, E. faecalis)
127 Group B Streptococci (GBS) by Real-Time PCR
153 Enterococci faecalis by Real-Time PCR
141 Escherichia coli by Real-Time PCR
184 Staphylococcus aureus by Real-Time PCR

Now Available on the OneSwab®:

Automatic colony counts at no additional charge for:

176 Urinary Pathogens Antibiotic Resistance Testing

(E. coli, Enterococcus faecalis, Enterococcus faecium, Klebsiella species, Proteus mirabilis)

Medical Diagnostic Laboratories, L.L.C.

New Tests Announcement

é-Quiz

1. True of False. Both Aerobic Vaginitis and Bacterial Vaginosis are caused by aerobic bacteria.
2. Which of the following pathogens are NOT associated with Aerobic Vaginitis?
   a. A. e. coli
   b. Gardnerella vaginalis
   c. Group B Strp (GBS)
   d. None of the above
3. True of False. The optimal treatment for AV includes antibiotics that have little effect on the normal flora, commonly Lactobacillus species, while effectively eradicating the Gram-negative enteric pathogens.
4. Approximately 5% of women diagnosed with BV and treated with metronidazole will fail to respond to therapy at one week and will experience persistent symptoms
   a. 5% to 10%
   b. 10% to 20%
   c. 25% to 30%
   d. 35% to 40%
5. Aerobic Vaginitis (AV) can often be confused with which of the following common vaginitis etiologies?
   a. Bacterial Vaginosis (BV)
   b. Trichomoniasis vaginitis (TV)
   c. Gardnerella vaginalis
   d. VulvoVaginal Candidiasis (VVC)
   d. All of the above

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Aerobic Vaginitis

The patient may present with all or some of these signs and symptoms of AV: yellowish discharge, itching or burning sensation, dyspareunia, and local pain. These symptoms are typically associated with BV, inflammation (Figure 1), toxic leukocyte infiltration, and the presence of parabasal cells and naked rounded vaginal epithelial cells (Figure 2).

In 2002, Donders Laboratory Diagnosis of GBS in pregnant women found a new mediator that triggers the inflammatory response, are proposed to be the peptidoglycan and hemolysin and associated with triggering labor. Cellular components of GBS such as E. coli, GBS, S. aureus, and E. faecalis. Along with the clinical signs, the Aerobic Vaginitis (AV) Panel by PCR developed and validated by Medical Diagnostic Laboratories, L.L.C. utilizes four qPCR reactions to detect the most common AV-associated bacteria (E. coli, GBS, S. aureus, and E. faecalis). The Aerobic Vaginitis (AV) Panel by PCR developed and validated by Medical Diagnostic Laboratories, L.L.C. utilizes four qPCR reactions to detect the most common AV-associated bacteria (E. coli, GBS, S. aureus, and E. faecalis).

Continued from... pg 7

Figure 1. Aerobic vaginitis inflammation. Clinical pictures adopted from Donders et al., 2002, demonstrates patients with controls to severe AV. Discrete Patients A & B, moderate (Patients C & D), and severe ulcerations (Patients E & F) are observed along with yellowish discharge and inflammation of the vagina. (1)

Figure 2: Aerobic Vaginitis microscopy. Images of phase-contrast microscopy (a,b) adopted from Donders et al., 2002, of vaginal fluid from patients with AV: Discrete (Patients A & B), moderate (Patients C & D), and severe ulcerations (Patients E & F) are present in high numbers (c). Parabasal cells or rounded-up vaginal epithelia, typical for GBS (b). Leukocytes and 'toxic' leukocytes (full of lysozymic granules) (x400) adopted from Donders et al., 2002, demonstrates patients with moderate to severe AV. Discrete (Patients A & B), moderate (Patients C & D), and severe ulcerations (Patients E & F) are observed along with yellowish discharge and inflammation of the vagina. (1)

Clinical Significance

Patients with AV present with distinct clinical signs and symptoms of abnormal vaginal flora that can be confused with common vaginal etiologies such as BV, TV, and VC (Table 1).

AJHSC, and funisitis. However, systematic evaluation of AV has yet to be elucidated. Nevertheless, evidence is accumulating that this condition may, like BV, have a negative effect on the course of pregnancy, resulting in an increased risk of preterm birth, chorioamnionitis and funisitis. However, systematic evaluation of AVF on the incidence of preterm birth, preterm rupture of the membranes, fetal infection and neurologic injury is needed.

The Aerobic Vaginitis (AV) Panel by PCR developed and validated by Medical Diagnostic Laboratories, L.L.C. utilizes four qPCR reactions to detect the most common AV-associated bacteria (E. coli, GBS, S. aureus, and E. faecalis). Along with the clinical signs, the Aerobic Vaginitis (AV) Panel by PCR developed and validated by Medical Diagnostic Laboratories, L.L.C. utilizes four qPCR reactions to detect the most common AV-associated bacteria (E. coli, GBS, S. aureus, and E. faecalis).

Treatment for Aerobic Vaginitis

The therapy for aerobic vaginitis should include an antibiotic with an intrinsic activity against the majority of bacteria of fecal origin.

To increase the safety and compliance, it is best to use a topical formulation which has slow or little absorbency, but is able to maintain the correct pharmaceutical concentration in situ. (8)

The optimal treatment includes antibiotics that have little effect on the normal flora, commonly Lactobacillus species, while effectively eradicating others, especially Gram-negative enterics such as E. coli, and Gram-positive GBS, S. aureus, and E. faecalis. In a study that measured the minimum inhibitory concentrations (MIC) of pefloxacin, ciprofloxacin, ofloxacin, enoxacin, doxycycline, clindamycin, ampicillin, kanamycin, and vancomycin antibiotics for 73 vaginal Lactobacillus species, the MICs for kanamycin, ciprofloxacin, and ampicillin were reported to be the greatest and in a concentration range categorized as intermediate or resistant for AV pathogens.

In a study by Tema et al., topical kanamycin ointment (100 mg, corresponding to 83 mg of active compound; one ointment per day for 6 days) was shown to have clinical success for the treatment of AV. (7, 8)

Fluoroquinolones, such as ciprofloxacin, have also been reported to have clinical success. These fluoroquinolones were reported to have little effect on the normal flora allowing for a rapid recovery. (8) A study measuring MICs of the four most common vaginal Lactobacillus species found that the three healthy Lactobacillus species, L. crispatus, L. gasseri, and L. jensenii, were resistant to ciprofloxacin, while 4% of patients relapsed after 2 weeks and 43.4% of patients relapsed after 23 weeks. (5) However, GBS vaginitis case reports scoring method used for bacterial vaginosis determination, which is based on a Gram-stained microscopic evaluation that enumerates specific bacterial morphotypes. The signs and symptoms of aerobic vaginitis, such as E. coli, Gram-positive Lactobacillus and anaerobic BV associated Gram-negative, positive and Gram-negative bacilli, contribute to the overall Nugent Score. A Nugent score of 0 to 3 indicates normal flora, 4 to 6 intermediate flora, and 7 to 10 bacterial vaginosis.

The determination of AV is also established by an ’AV’ score. The score is calculated with the use of high-power field microscopy to evaluate the presence or absence of healthy Lactobacilli, number of leukocytes, number of toxic leukocytes, type of vaginal flora, and parabasal epithelial cells (Table 2). Here, the presence of the healthy Gram-positive Lactobacilli is compared to the presence of aerobic Gram-negative bacilli (E. coli and Klebsiella species).

Table 2. Criteria for the microscopic diagnosis of Aerobic Vaginitis (AV) (40X0 magnification, phase contrast microscopy). (1, 14)


Aerobic vaginitis (AV) is an alteration in vaginal bacterial flora that differs from bacterial vaginosis (BV). AV is characterized by an abnormal vaginal microflora accompanied by an increased localized inflammatory reaction and immune response, as opposed to the suppressed immune response that is characteristic of BV. Given the increased local production of interleukin (IL)-1, IL-6 and IL-8 associated with AV during pregnancy, not surprisingly AV is associated with an increased risk of preterm delivery, chorioamnionitis and funisitis of the fetus. There is no consensus on the optimal treatment for AV in pregnant or non-pregnant women, but a broader spectrum drug such as clindamycin is preferred above metronidazole to prevent infection-related preterm birth. The exact role of AV in pregnancy, the potential benefit of screening, and the use of newer local antibiotics, disinfectants, probiotics and immune modulators need further study.

Aerobic vaginitis (AV) is an entity that differs in many aspects from BV, although both conditions are linked to a disturbed lactobacillary flora. AV is still under-recognized, as wet-mount microscopy is needed for diagnosis and is not commonly performed by doctors worldwide. Therefore, many details about the prevalence, epidemiology and pathogenesis of AV have yet to be elucidated. Nevertheless, evidence is accumulating that this condition may, like BV, have a negative effect on the course of pregnancy, resulting in an increased risk of preterm birth, chorioamnionitis and funisitis. However, systematic evaluation of AV on the incidence of preterm birth, preterm rupture of the membranes, fetal infection and neurologic injury is needed.


This was a cross-sectional study, performed in an outpatient clinic of Bauru State Hospital, São Paulo, Brazil. A total of 142 women were included from 2006 to 2008. Inclusion criteria were dyspareunia, pain during bimanual exam, presence of excessive cervical mucus, cervical ectopy, or three or more episodes of abnormal vaginal flora (AVF) in the previous year before enrollment. Endocervical CT testing was performed by PCR. Vaginal swabs were collected for microscopic assessment of the microbial flora pattern. Gram-stained smears were classified in normal, intermediate or bacterial vaginosis (BV), and recognition of Candida sp. morphotypes. Wet mount smears were used for detection of Trichomonas vaginalis and aerobic vaginitis (AV).

Thirty-four of 142 women (23.9%) tested positive for CT. AVF was found in 50 (35.2%) cases. The most frequent type of AVF was BV (17.6%). CT was strongly associated with the presence of AV (P = 0.018), but not BV (n = 25, 17.6%, P = 0.80) or intermediate flora (n = 18, 12.7%, P = 0.28). This study was conducted in a high risk population for STDs. The CT infection rate of 23.9% found in this high-risk population was higher than in other Brazilian studies with pregnant women from 6 other cities. The high rate of C. trachomatis in this study can be explained by the design of this study. In this study comprising a high risk population for STI, Aerobic vaginitis was found to be associated with CT detection. Bologno R, Diaz YN, Giraldo MC, et al. 2011. Importance of studying the balance of vaginal content (BAVACO) in the preventive care of sex workers. Rev argent microbial 43(4): 246-250.

The aim of this work was to study the vaginal flora of women attending a male sex work health facility from Comportamento, Rivadavia, Chubut. A total of 229 female sex workers attended public health centers. Vaginal secretions were analyzed by Gram and Giemsa stains.

The following results were obtained: normal microbiota 35.37 %, intermediate microbiota 15.72 %, bacterial vaginosis 23.14 %, microbial non-specific vaginitis 10.48 %, yeast vulvovaginitis 8.3 %, and trichomoniasis 6.9 %. The intermediate microbiota was characterized by a decrease in the number of lactobacilli and the presence of diphtheroid bacilli cell types. The population studied shared increased values of vaginal dysfunctions. These results are considered risk factors for obstetric and gynecologic diseases.
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In a more recent study of 215 women, 19.1% were found to have vaginitis caused by BV, GBS, and multiple aerobic pathogens. The results of this study indicate that a significant increase in aerobic pathogens is associated with a higher risk of developing a vaginal inflammatory response. (3) Additionally, 5.9% of the women in the AV group were found to be GBS positive, a 5-fold increase over the women with DIV. (11) In fact, 42.9% of the women with DIV were found to be GBS positive, a 5.9% increase over the healthy patients (17.7% positive). (11) This study was comparable to an earlier study that found 43% of BV patients were GBS positive. (4)

Pathogenesis

AV is associated with an increase in vaginal pH (> 4.5), depletion of vaginal healthy Lactobacilli, and an overgrowth of aerobic or facultative anaerobic bacteria, usually the Gram-negative bacilli E. coli or Gram-positive cocci GBS, and occasionally S. aureus and E. faecalis. The high concentration of these aerobic bacteria and the absence of healthy vaginal Lactobacilli results in triggering the immune system as evidenced by vaginal inflammation, high levels of proinflammatory cytokine production, recruitment of leukocytes, and the generation of toxic leukocytes and parasial cells.

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<td>Reactive</td>
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<td>Epithelial atrophy (percentage)</td>
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<td>Gram staining</td>
<td>Positive</td>
<td>Negative</td>
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<td>Treatment</td>
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<td>Metronidazole + Clindamycin</td>
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<td>E. faecalis is traditionally treated with ampicillin. (6)</td>
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