

**Short Communication****Open Access****Aerobic vaginitis in women seen at the laboratory of the university hospital of Befelatanana, Antananarivo, Madagascar**

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**Abstract:**

**Background:** Vaginitis is common in women. The present study aims to identify the factors associated with aerobic vaginitis (AV) in women and evaluate the antibiotic resistance of bacteria responsible for this vaginitis.

**Methodology:** This was a retrospective cross-sectional study of 840 patients and analysis of the results of their cytobacteriological examinations of cervicovaginal samples from January 01, 2020 to December 31, 2022 at the Centre Hospitalier Universitaire Joseph Raseta Befelatanana (CHUJRB) laboratory, Antananarivo, Madagascar.

**Results:** Among the 840 patients, 35 had aerobic vaginitis, giving the prevalence of AV of 4.2%. Enterococcal vaginitis was the most common, representing 48.6% (n=17) cases of AV. Regarding associated factors, there was no significant difference in the prevalence of AV between women under age of 40 (4.4%, 29/653) and women over age of 40 years (3.2%, 6/187) ( $p=0.539$ ); hospitalized (6.6%, 10/152) and non-hospitalized outpatients (3.6%, 25/688) ( $p=0.115$ ); and pregnant (4.2%, 8/192) and non-pregnant women (4.2%, 27/648) ( $p=1.000$ ). The antibiotic resistance varies from 0% (vancomycin) to 90.0% (penicillin G) for the Gram-positive bacteria and 0% (imipenem and amikacin) to 100% (cotrimoxazole, ciprofloxacin, cefixime) for Gram-negative bacteria (*Pseudomonas* spp)

**Conclusion:** Cytobacteriological examination of cervicovaginal specimens in cases of genital disorders is necessary to improve the management of patients with AV in Madagascar. Similarly, empirical treatment should be properly guided and self-medication avoided, in order to limit the emergence of multidrug-resistant bacteria.

**Keywords:** Antibiotic resistance; bacteria; aerobic vaginitis; women; Madagascar

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**Vaginite aérobie chez la femme vue au laboratoire de l'hôpital universitaire de Befelatanana, Antananarivo, Madagascar**

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**Résumé:**

**Contexte:** La vaginite est fréquente chez les femmes. La présente étude vise à identifier les facteurs associés à la vaginite aérobie (AV) chez la femme et à évaluer la résistance aux antibiotiques des bactéries responsables de cette vaginite.

**Méthodologie:** Il s'agit d'une étude transversale rétrospective portant sur 840 patientes et analyse des résultats de leurs examens cytobactériologiques de prélèvements cervico-vaginaux du 01 janvier 2020 au 31 décembre 2022 au laboratoire du Centre Hospitalier Universitaire Joseph Raseta Befelatanana (CHUJRB), Antananarivo, Madagascar.

**Résultats:** Parmi les 840 patientes, 35 avaient une vaginite aérobie, soit une prévalence d'AV de 4,2%. La vaginite à entérocoques était la plus courante, représentant 48,6% (n=17) des cas d'AV. Concernant les

facteurs associés, il n'y avait pas de différence significative dans la prévalence de l'AV entre les femmes de moins de 40 ans (4,4%, 29/653) et les femmes de plus de 40 ans (3,2%, 6/187) ( $p=0,539$ ); patients hospitalisés (6,6%, 10/152) et non hospitalisés (3,6%, 25/688) ( $p=0,115$ ); et les femmes enceintes (4,2%, 8/192) et non enceintes (4,2%, 27/648) ( $p=1,000$ ). La résistance aux antibiotiques varie de 0% (vancomycine) à 90,0% (pénicilline G) pour les bactéries à Gram positif et de 0% (imipénème et amikacine) à 100% (cotrimoxazole, ciprofloxacine, céfixime) pour les bactéries à Gram négatif (*Pseudomonas* spp).

**Conclusion:** L'examen cytotabériologique des prélèvements cervico-vaginaux en cas de troubles génitaux est nécessaire pour améliorer la prise en charge des patients atteints d'AV à Madagascar. De même, le traitement empirique doit être correctement guidé et l'automédication évitée, afin de limiter l'émergence de bactéries multirésistantes.

**Mots-clés:** Résistance aux antibiotiques; bactéries; vaginite aérobie; femmes; Madagascar

## Introduction:

The female reproductive tract is composed of the vagina, cervix, uterus, fallopian tubes, and ovaries, with the cervix connecting the upper reproductive tract to the vagina (1). The existence and invasion of microbes in the female reproductive tract have long been known to impact genital and reproductive health. Species of *Lactobacillus*, generally the most abundant taxa in the vaginal microbiome (VMB), produce lactic acid and probably bacteriocins that inhibit dysbiosis-associated microbes and work to maintain homeostasis and reduce risks of disease. A *Lactobacillus*-dominated VMB has been the hallmark of female reproductive health (2).

Vaginitis is a term to describe various conditions of infection or inflammation of the vagina. The most common kinds of vaginitis are bacterial vaginosis, vulvovaginal candidiasis or yeast vaginitis, trichomonas vaginitis and aerobic vaginitis (2). Aerobic vaginitis (AV) is an imbalance of the vaginal flora and was first mentioned in 2002 by Donders and others (3). The main characteristic is an abnormal vaginal flora that contains aerobic and intestinal pathogens and different degrees of vaginal inflammation (4). The frequency of AV varies from 12% to 23.7% in symptomatic women who are not pregnant and 4% to 8% during pregnancy (5), and is an increased risk for sexually transmitted diseases (5).

The causative agents of AV include *Enterococcus faecalis*, *Escherichia coli*, group B streptococcus and *Staphylococcus aureus*. The most frequently isolated AV pathogen is *Enterococcus faecalis* in about 31% of cases (6). These AV cause discomfort in women and can have serious repercussions, particularly in pregnant women. Thus, in order to improve the care of women suffering from AV, the present study was carried out with the aim of identify the factors associated with AV in women and evaluate the antibiotic resistance of bacteria responsible for this type of vaginitis.

## Materials and method:

### Study setting:

This study was carried out at the laboratory of the University Hospital of Befelatanana, Antananarivo, the capital city of Madagascar. This laboratory is versatile and performs haematological, immunological, biochemical and microbiological analyses on clinical samples.

### Study design:

This was a descriptive cross-sectional study of 840 patients and analysis of the results of their cytotabériological examinations of cervicovaginal samples from Jan 01, 2020 to December 31, 2022 at the Centre Hospitalier Universitaire Joseph Raseta Befelatanana (CHUJRB) laboratory.

### Study participants:

All women with results of cytotabériological examinations of cervicovaginal samples during the study period were included in the study. The participants were out-patients or hospitalized patients with various genitourinary symptoms such as leukorrhoea, dyspareunia, lower back pain or patients who came for routine health checks. Women with polymicrobial infections were excluded from the study.

### Ethical consideration:

The study was smoothly incorporated into the standard care delivery framework and did not interfere with patient treatment. Given its alignment with routine healthcare procedures and the absence of any negative impact on patient management, no evaluation by the Research Ethics Committee was required in accordance with national regulations of Madagascar. However, patient anonymity and confidentiality were maintained.

### Specimen collection and laboratory analysis:

Two sterile swabs were routinely used to collect specimens from the endocervix and ectocervix/vagina of each woman participant.

A disposable speculum was used for the cervicovaginal smear collection except for participants who were virgin, in whom simple only vulvar swabs were collected. The specimens were collected by a doctor, midwife or laboratory technician.

In the laboratory, microbiological culture was done on 2 types of agar plates. The endocervical swab was plated on heated blood agar and incubated at 37°C for 48 hours in an atmosphere rich in CO<sub>2</sub> for isolation of *Neisseria gonorrhoeae*. The ectocervical swab was plated on an ordinary chromogenic agar (Uriselect®) and incubated at 37°C for 24 hours for the detection of vaginal candidiasis and other uropathogens.

Smears of colonies from the culture plates were made on the slide with physiological serum and covered with cover slide for microscopic examination, and also for Gram staining microscopic examination, which allowed for visualization and counting of the vaginal flora and establishment of the Nugent score to classify the vaginal flora of each participant

After 48 hours of incubation, the colonies which appeared on the culture media were identified using identification tests including catalase test (Gilbert®), oxidase test (Oxoid®), API®20 Strep (BioMérieux®) and API® 20 NE (BioMérieux®). Antibiotic susceptibility test was carried out on the isolates by the disc diffusion method on Mueller-Hinton agar and interpreted according to the recommendations of the "Comité de l'Antibiogramme de la Société Française de Microbiologie" (7). The antibiotics (Oxoid®, UK) tested include penicillin G (1U), ampicillin (2µg), cefixime (5µg), cefepime (30µg), ceftazidime (30µg), imipenem (10µg), gentamicin (10µg), tobramycin (10µg), amikacin (30µg), ciprofloxacin (5µg), levofloxacin (5µg), norfloxacin (10µg),

cotrimoxazole (1.25/23.75µg), erythromycin (15µg), clindamycin (2µg), tetracycline (30 µg) and vancomycin (30µg).

#### Data collection and statistical analysis:

Data were collected from microbiological analysis request form, laboratory register notebooks and antibiogram result sheets. Data entry and analysis were done using EPI INFO 3.5.2 software. Association of dependent variables (results of vaginitis) with independent variables (age, hospitalization, pregnancy and antibiogram results) was determined using Pearson Chi square test. The threshold of statistical significance of the results chosen was  $p < 0.05$ .

### Results:

Among the 840 patients who participated in the study, 35 had aerobic vaginitis, giving the prevalence of AV of 4.2% (Fig 1). Enterococcal vaginitis was the most common, representing 48.6% of all AV cases (n=17) (Fig 2). Regarding associated factors, there was no significant difference in the prevalence of AV between women under age of 40 (4.4%, 29/653) and women over age of 40 years (3.2%, 6/187) ( $p=0.539$ ); hospitalized (6.6%, 10/152) and non-hospitalized women (3.6%, 25/688) ( $p=0.115$ ); and pregnant (4.2%, 8/192) and non-pregnant women (4.2%, 27/648) ( $p=1.000$ ) (Table 1).

The antibiotic resistance varies from 0% (vancomycin) to 90% (penicillin G) for the Gram-positive bacteria (Fig 3). The 2 isolates of *Pseudomonas* spp., were sensitive to imipenem and amikacin, but resistant to co-trimoxazole, ciprofloxacin and cefixime. One of the 2 *Pseudomonas* isolates was resistant to tobramycin, gentamicin, levofloxacin and cefepime.

Table 1: Factors associated with aerobic vaginitis in women seen at the laboratory of the university hospital of Befelatanana, Antananarivo, Madagascar

Associated factors	Parameters	Aerobic vaginitis (n=35)		Non-aerobic vaginitis & others (n=805)		Total (n=840)	OR (95% CI)	p value
		n	%	n	%			
Age (years)	<40	29	4.4	624	95.6	653	1.40 (0.57-3.43)	0.539
	≥40	6	3.2	181	96.8	187		
Status of women	Non-pregnant	27	4.2	621	95.8	648	1.00 (0.45-2.24)	1.000
	Pregnant	8	4.2	184	95.8	192		
Department	Out-patient	25	3.6	663	96.4	688	0.54 (0.25-1.14)	0.115
	In-patient	10	6.6	142	93.4	152		

OR=Odds Ratio; CI=Confidence Interval; n=number

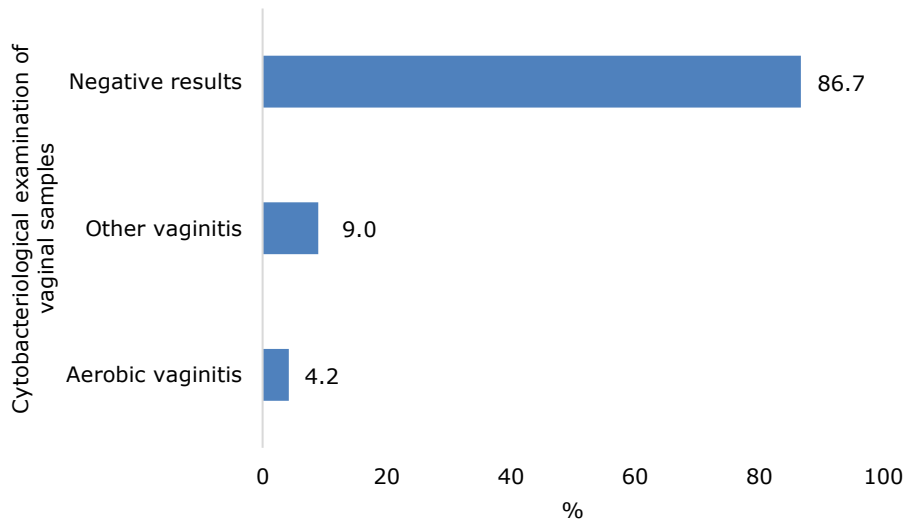


Fig 1: Prevalence of aerobic vaginitis among the study participants

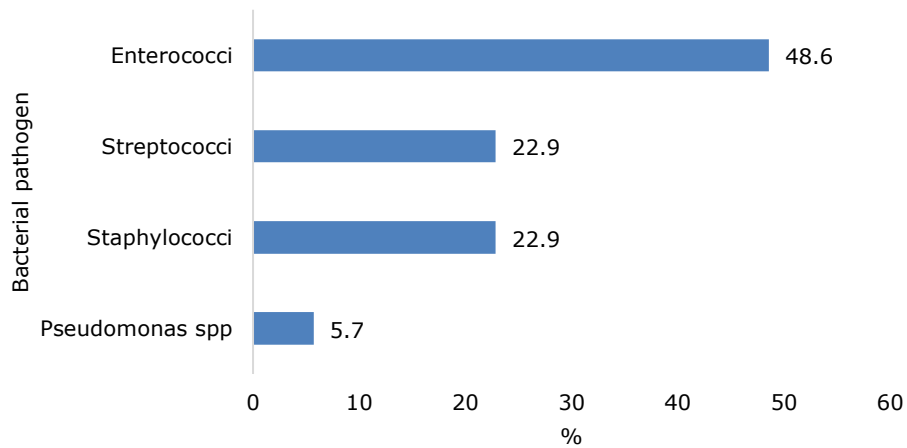


Fig 2: Bacteria responsible for aerobic vaginitis among the study participants

## Discussion:

In the present study, the prevalence of AV was 4.2%. Other studies also found low prevalence of <10.0% (8,9). In the literature, bacterial vaginosis (BV) and vaginal candidiasis (VC) are the most predominant among vaginitis. Bacterial vaginosis is considered the most common form of vaginitis and affects approximately 30.0% of women (10). Because most women who have AV exhibit no or minor symptoms, there is a tendency to overlook this condition. Similarly, women who harbor *Candida* organisms in their vaginas have a spectrum of manifestations ranging from asymptomatic colonization to severe acute symptomatic infection. Yeast colonization occurs relatively frequently, with up to 30.0% of healthy asymptomatic women having a positive culture for yeast at any single point of time and up to 70.0% if followed longitudinally over a 1-year period (10).

Although rare, AV should not be underestimated because they can cause serious complications if not treated quickly.

In the present study, enterococcal vaginitis was the most common, representing 48.6% of cases AV. Other studies have also reported the similar results (6). The pathogenic effect of *Enterococcus faecalis* shows that it is the cause of spontaneous abortion, premature birth, puerperal sepsis, abscess and infection of the urinary system (11). New reports indicate the presence of HPV 16 gene and genome in *E. faecalis* in biopsied materials from cervical cancer, as well as the ability that HPV 16 genes can be translated and transcribed in these bacteria. The fact that HPV gene can form viral particles in these bacteria leads to certain connection that can be a risk factor in the progression of cervical lesions to cancer (12). *Enterococcus faecalis* as a cause of AV is very often unrecognized or ignored and may be the reason for neglected

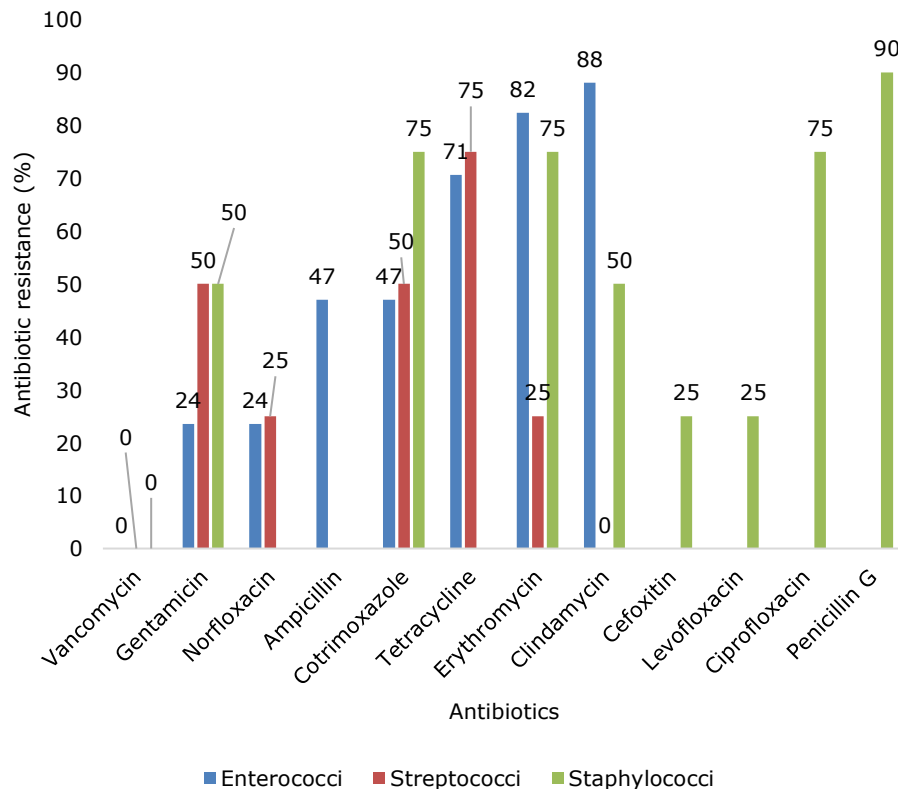


Fig 3: Antibiotic resistance of Gram-positive bacteria responsible for aerobic vaginitis

diagnosis. If this AV is not diagnosed or neglected in HPV-positive women, there is a justified possibility of long-term infection due to the presence of HPV in *E. faecalis*. The presence of HPV in this bacterium can lead to persistent HPV infection and the occurrence of high-grade cervical intraepithelial neoplasia (CIN) as well as progression to cervical cancer (12,13). Thus, in the event of genitourinary disorders, cytobacteriological examination of the cervicovaginal smear is required in order to quickly diagnose possible vaginitis and treat the patient in time to avoid complications.

With respect to the associated factors analysed, there was no significant association between participants age groups, origin or patient status with prevalence of AV in our study. We can say that aerobic bacteria are present in the community and in hospital environment and can affect all patients regardless of their age. Thus, intimate hygiene is very important and the young individuals should be educated about this. However, according to a study carried out in pregnant women, cervical shortening is a risk factor for AV (14). Similarly, the literature confirms that the nosocomial pathogens present in hospitals can contaminate women during invasive healthcare procedures, which may explain the high frequency of AV among hospitalized women (15). The small number of AV cases in our study may be responsible

for not obtaining factors significantly associated with AV. A larger sample size or multi-center study will be required to determine the factors significantly associated with AV in women

Regarding antibiotic resistance, Gram positive cocci (GPC) were highly resistant to penicillin and clindamycin and Gram-negative bacilli (GNB) to cotrimoxazole, ciprofloxacin and cefixime. This result is not at all surprising because these antibiotics are easily purchased in pharmacies without the need for a medical prescription in Madagascar. These antibiotics are also sold in small grocery stores, thus, these antibiotics are consumed indiscriminately by the populace because of easy access and poor regulations. Studies in the literature have reported that self-medication by the populace is one of the major factors for the emergence of antibiotic resistance (16). Fortunately, no resistance of GPC to vancomycin was detected in our study. Indeed, vancomycin is a reserved antibiotic for the treatment for multidrug-resistant GPC (17). Furthermore, none of the *Pseudomonas* spp was resistant to amikacin and imipenem. It has been reported in the literature that imipenem represents the 'reserved' drug for treatment of infections caused by multidrug-resistant *Pseudomonas* spp (18). Similarly, amikacin is a broad-spectrum antibiotic that is effective against MDR GNB such as *Pseudomonas* spp and *Acinetobacter* spp (19).

## Conclusion:

The present study showed that AV is frequently caused by enterococci and affects young individuals and hospitalized patients in the majority of cases. Enterococci infections in pregnancy may be associated with complications and the pathogen may also promote the development of cervical cancer along with high-risk HPV. Therefore, cytobacteriological examination of cervicovaginal smears must be systematic in cases of genital disorders to improve the management of patients with AV. Similarly, empirical treatments should be well guided and self-medication avoided in order to limit the emergence of MDR bacteria.

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## Contributions of authors:

RZD is involved in the study design, data collection, and writing of the manuscript; RII was involved in methodological designs, statistical analysis and presentation of results; RSS was involved in bibliographic search and writing the discussions; RAL was involved in writing the discussions; and RA was involved in correcting and editing the manuscript. All authors approved the final manuscript.

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## Conflict of interest:

No conflict of interest is declared

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