



Perspective

Abnormal vaginal discharge among women of reproductive age in sub-Saharan Africa: the need for a paradigm shift from a syndromic approach to specific pathogen identification and directed treatment

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ABSTRACT

Background: An abnormal vaginal discharge is a frequent manifestation of reproductive tract infections, including sexually transmitted infections (STIs) and vulvovaginal candidiasis. It is also a manifestation of bacterial vaginosis, which has a prevalence of up to 50% among women of reproductive age. Reproductive tract infections are associated with a range of reproductive health challenges and increase the risk of HIV acquisition.

Methods: This study was performed to critically review and discuss the current diagnostic and treatment approaches to abnormal vaginal discharge among women of reproductive age in sub-Saharan Africa, and to call for a paradigm shift from the syndromic approach to specific pathogen identification and directed antimicrobial therapy.

Discussion: Young women have the highest incidence of HIV infection in sub-Saharan Africa. Countries in sub-Saharan Africa where the prevalence of both STIs and bacterial vaginosis is very high have been employing a syndromic approach for the treatment of abnormal vaginal discharge since around 1984. However, the syndromic approach has several limitations, with the potential to miss infections, over-diagnose and over-treat STIs, and propagate antimicrobial resistance, which is one of the greatest global health challenges of the 21st century.

Conclusions: The low to middle-income countries of sub-Saharan Africa must innovate and leverage improved diagnostics to capacitate primary health care and other levels for point-of-care diagnostic testing, in order to provide an immediate diagnosis and treatment for women with an abnormal vaginal discharge.

1. Introduction

An abnormal vaginal discharge is a frequent symptom of reproductive tract infection in women of reproductive age. Reproductive tract infections encompass sexually transmitted infections (STIs), vulvovaginal candidiasis, and bacterial vaginosis (BV). STIs remain a significant global health challenge; they are more prevalent in developing countries, and even more so in sub-Saharan Africa (SSA) (Torrone et al., 2018). The World Health Organization (WHO) estimates a daily incidence of one million STIs, with the majority in SSA (WHO, 2022). In 2020, there were an estimated 374 million new infections with one of four STIs, namely *Chlamydia trachomatis* (129 million), *Neisseria gonorrhoeae* (82 million), *Treponema pallidum* subspecies *pallidum* (syphilis; 7.1 million), and *Trichomonas vaginalis* (TV) (156 million) (WHO, 2022). *N. gonorrhoeae*, *C. trachomatis*, and *T. vaginalis* cause an abnormal vaginal discharge. Vulvovaginal candidiasis is caused by *Candida* species, mainly *Candida albicans*. Bacterial vaginosis (BV) is the most prevalent microbiological cause of abnormal vaginal discharge (Majigo et al., 2021; Cleveland Clinic, 2022). It is a microbial dysbiosis of the female genital tract with a prevalence of 30–50% among women of reproductive age (Abdullateef et al., 2017; Bayigga et al., 2019). Various intravaginal practices by women of reproductive age in SSA explain the high prevalence of BV in this population (Majigo et al., 2021).

STIs have short- and long-term adverse reproductive health sequelae, can be transmitted vertically to the foetus, and can spread to uninfected partners, propagating long chains of transmission where multiple sexual partners are involved. Ulcerative and non-ulcerative STIs are significant risk factors for HIV infection, with a relative risk (RR) of 2.0–23.5 (Fleming & Wasserheit, 1999). BV is linked to miscarriage, preterm labour, preterm prelabour rupture of the membranes, and postpartum endometritis (Bayigga et al., 2019), and is a risk factor for HIV

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acquisition (Bayigga et al., 2019). In a meta-analysis, BV was significantly associated with an increased risk of HIV acquisition (RR 1.6, 95% confidence interval 1.2–2.1) (Atashili et al., 2008). Correct identification and treatment of the aetiology of a vaginal discharge is critical for HIV prevention, vaginal health, and short- and long-term reproductive health. Physiological vaginal discharges do not require antimicrobial chemotherapy. Cervical and endometrial malignancies can cause an abnormal vaginal discharge and infectious aetiology may be suspected, leading to irrational antibiotic prescription.

The current treatment approaches for an abnormal vaginal discharge in SSA, based on syndromic approaches, are insufficient and no longer suitable. This study was performed to critically review the different approaches to diagnosis and propose a paradigm shift towards pathogen detection and directed therapy. It is argued that this will lead to effective treatment, reduce antimicrobial resistance (AMR), and raise early suspicion of malignancies.

2. The syndromic approach to the treatment of abnormal vaginal discharge

Syndromic or laboratory-based approaches are utilized in diagnosing STIs (Wi et al., 2019). The laboratory-based method is the best; however, it is not always feasible in the low to middle-income countries (LMICs) of SSA (Garrett et al., 2018). Using this strategy can lead to treatment delays due to limited access to laboratory tests. Some women may be lost to follow-up before receiving care. As testing is expensive, women in SSA may not be able to afford to pay (Mayaud & Mabey, 2004). In 1984, the WHO established a syndromic approach to STIs for high-prevalence areas lacking diagnostic facilities, skilled healthcare personnel, and transport facilities, in order to address the challenges of the laboratory-based method. Many countries in SSA still utilize this strategy as standard of care (WHO, 2015).

The syndromic approach is premised upon the identification of recurrent clusters of clinical symptoms and easily recognizable signs. According to the signs and symptoms, the infections are categorized into syndromes such as ‘vaginal discharge syndrome’ and ‘genital ulcer syndrome’ (WHO, 2005). Flowcharts are employed for the diagnosis and to select the best intervention to address all significant causes of the syndrome (WHO/UNAIDS, 1999). This is fairly accurate when identifying STIs in symptomatic patients. It caters for mixed infections, common in SSA. The approach is economical, can be used at the primary healthcare level, requires fewer referrals to specialized facilities, and eliminates laboratory fees. It standardizes diagnosis, treatment, referral, and reporting, allowing for better programming and surveillance (Bosu, 1999). Treatment begins at first contact, preventing delays and losses to follow-up. In addition to breaking chains of transmission and reducing complications from untreated infections, this improves patient satisfaction. When the effectiveness of the drugs chosen is sufficient and properly monitored, this approach is linked to high cure rates (Altini & Coetzee, 2005).

However, there are several drawbacks. Significant proportions of the population have asymptomatic infections, hence the approach cannot be utilized in these (Yin et al., 2008). A syndromic diagnosis cannot reliably predict *N. gonorrhoeae* and *C. trachomatis* infections. Most women with a vaginal discharge lack these pathogens (Wi et al., 2019). Many STI diagnoses are missed when using a syndromic approach, hence the need for laboratory tests (Otieno et al., 2014). Syndromic approaches may lead to over-diagnosis and over-treatment, possibly increasing the burden of AMR, vaginal dysbiosis, and drug costs (Moges et al., 2013). Furthermore, treatment must be based on an accurate aetiological diagnosis due to the rising incidence of AMR in *N. gonorrhoeae* and the limited number of available treatment options (Garrett et al., 2018). Over-treatment of the women’s partners, some of them without STIs, can have social and physical repercussions for the woman (Altini & Coetzee, 2005).

3. Current laboratory techniques for investigating abnormal vaginal discharge

Laboratory tests can identify the causative organisms of a discharge (Otieno et al., 2014). The Amsel criteria are used to diagnose BV clinically, while the Nugent score reads vaginal smears. The Nugent score has been used in research settings for reproducibility. BV is diagnosed on a Gram-stained smear by scoring the vaginal bacteria morphotypes (Ison & Hay, 2002). After interpreting the smear, the bacteria counts are summed, and the score is used to diagnose BV in a range of 0 to 10. There is a good correlation between the rapid clinical Amsel criteria and the laboratory Nugent score, as shown in Table 1.

Urogenital specimens are used to detect *N. gonorrhoeae* using culture and nucleic acid amplification tests (NAATs) (Papp et al., 2014). *N. gonorrhoeae* infections can also be diagnosed using stained urogenital tissues. Antigen tests and serology to detect antibodies have limited sensitivity and specificity (Meyer & Buder, 2020). Gram-stained smears can be used for point-of-care (POC) diagnostics in low-resource situations. Antimicrobial susceptibility testing is only possible through culture. *N. gonorrhoeae* is fastidious and cannot survive dehydration, hence must be inoculated immediately after collection. It needs selective and non-selective media, high humidity, a pH of 6.75 to 7.5, and a 4–6% carbon dioxide environment (Visser et al., 2020).

The NAAT is the most sensitive *N. gonorrhoeae* laboratory test and is superior to culture (Papp et al., 2014; Bromhead et al., 2013; Cook et al., 2005). NAATs are more sensitive in testing *N. gonorrhoeae* because live bacteria are independent (Papp et al., 2014). The NAAT is preferable to cultures because it can employ any sample type without live microorganisms. It requires fewer hands than culture and may be automated, thereby increasing the throughput (Cheng & Kirby, 2014). The *N. gonorrhoeae* NAAT can be performed together with *C. trachomatis* (Papp et al., 2014). Despite being sensitive, the NAAT has reduced accuracy due to genetic variation, the genomic plasticity of *N. gonorrhoeae* species, and the loss or modification of target regions (Ison & Hay, 2002). Specificity may be reduced by cross-reactive non-pathogenic *Neisseria* species, as well as the horizontal transfer of *N. gonorrhoeae* gene sequence to commensal *Neisseria* (Frosch & Meyer, 1992).

Table 2 shows various statistics of the methods used in the laboratory diagnosis of *N. gonorrhoeae*.

C. trachomatis is labile and hence caution is required when transferring and storing samples (Chernesky, 2005). The laboratory detection of *C. trachomatis* employs the use of NAATs, culture, and antibody and antigen tests.

C. albicans spores are present as normal flora in over 20% of women of reproductive age. Wet mount microscopic examination is costly and time-consuming. Yeast microscopy has a 50–60% sensitivity. Chromogenic media recognize *C. albicans* following incubation (Eckert et al., 1998).

T. vaginalis is identified by microscopy of vaginal secretions mixed with saline. Pear-shaped, tumbling trichomonads are 100% specific for *T. vaginalis*. Even with an experienced microscopist and quick specimen evaluation, direct microscopy is less sensitive than molecular assays. Liquid-based Pap tests are more accurate for microscopic examination, with sensitivity of 60–90% and specificity of 98–100%. Liquid culture *T. vaginalis* amplification improves sensitivity over direct microscopy. The most common culture is modified Diamond medium. Compared to molecular tests, culture sensitivity ranges from 44% to 75% for *T. vaginalis* detection. Based on the visualization of viable trichomonads, culture is 100% specific for detecting *T. vaginalis* (Patil et al., 2012). As with other STIs, the NAAT provides more sensitive and specific new methods for diagnosing *T. vaginalis*. The NAAT is more sensitive than non-amplified tests and preserves nucleic acid material but not live organisms. The sensitivity of the NAAT ranges from 76% to 100%, making it acceptable for screening asymptomatic patients (Andrea & Chapin, 2011). More details are presented in Supplementary Material File S1.

Table 1
Comparison between the rapid clinical Amsel criteria and the laboratory Nugent score.

	Sensitivity	Specificity	PPV	NPV	Reference
Amsel criteria	50%	98.2%	87.5%	88.8%	(Bhujel et al., 2021)
Nugent score	65.6%	97.3%	80.8%	94.2%	(Chajareenont et al., 2004)

PPV, positive predictive value; NPV, negative predictive value.

Table 2
Sensitivity, specificity, and positive predictive value of laboratory methods for the diagnosis of *Neisseria gonorrhoeae*.

	Sensitivity	Specificity	PPV	Reference
Gram stain direct microscopy	95%	97%	-	(Menforth et al., 2018)
Gram stain of endocervical swabs	40–60%	-	-	(Thorley & Radcliffe, 2015)
<i>Neisseria gonorrhoeae</i> culture	85–95%	100%	(Meyer & Buder, 2020)	
MALDI-TOF	-	-	99.3%	(Carannante et al., 2015; Buchanan et al., 2016)
NAAT	95–98%	95–98%	-	(Papp et al., 2014)

PPV, positive predictive value; MALDI-TOF, matrix-assisted laser desorption/ionization time-of-flight; NAAT, nucleic acid amplification test.

4. Leveraging on improved diagnostics to shift from a syndromic approach to specific pathogen-directed treatment

The increasing availability of POC tests and widespread availability of cartridge-based PCR assays imply that even the most remote settings can have improved access to diagnostics with a fairly rapid turnover of results. In some countries, the COVID-19 pandemic saw the decentralization of laboratory testing with real-time PCR and GeneXpert to lower levels of care. A study conducted in several countries in SSA, including South Africa, Rwanda, Zimbabwe, Nigeria, and Ethiopia, revealed laboratory capacity enhancement during the COVID-19 pandemic. The existing laboratories were expanded, while new ones were also created. There was an expanded decentralization of laboratory capacity, and new capacities in existing laboratories, such as molecular biology, were added. Additional laboratory staff were also trained during the pandemic (Binder et al., 2021). As an example, Zimbabwe, which has one National Microbiology Reference Laboratory, decentralized diagnostic testing for COVID-19 from this single laboratory to provincial and district laboratories, leveraging on existing human resources and platforms. This became a game-changer in active COVID-19 surveillance, significantly improving the country's testing capacity. POC testing can result in task-shifting of testing for STIs from laboratory scientists to nurses. A systematic review conducted in three continents revealed that if nurses are trained with the support of laboratory professionals, they can perform good-quality POC testing (Liikanen & Lehto, 2013). During the COVID-19 pandemic, the Ministry of Health and Child Care of Zimbabwe adopted task-shifting, based on WHO guidance, and capacitated nurses, microscopists, and laboratory personnel at all levels to perform POC COVID-19 testing. Nurses in Zimbabwe have traditionally been capacitated to perform simple POC tests for malaria, syphilis, and HIV among other examples, and in a country that has been hit by a massive brain drain, this has allowed efficient use of the scarce human resources. SSA must leverage improved diagnostics arising from the COVID-19 pandemic to increase access to STI testing for the population and fight against irrational prescribing of antibiotics and widespread AMR.

A community-based strategy will increase diagnostic sensitivity and specificity in LMICs, since most services are self-funded. Clinicians can perform POC pH tests, employ potassium hydroxide (KOH), and microscopically check the vaginal fluid for clue cells, motile trichomonads, yeast buds, and pseudohyphae (Hillier et al., 2021). A study conducted among healthcare workers in SSA who had been trained in POC testing revealed that it was feasible to perform POC testing for STIs. However, some specimens may need to be sent to laboratories for confirmation of the diagnoses as a quality control measure (Parkes-Ratanshi et al.,

2019). Regarding *Candida* infections, a pH >4.5 suggests BV or trichomoniasis. BV is diagnosed when there is a grey–white discharge, vaginal fluid pH >4.5, a positive whiff test, and clue cells on wet mount microscopy with >20% of total epithelial cells. Side room microscopic screening for motile *T. vaginalis* using a self-collected swab within 10 minutes offers a sensitivity of 45–60%, depending on experience. Confirmation is by using a fast antibody test, which boosts sensitivity to 94% and specificity to 95% (Sherrard et al., 2018). Candidiasis appears as budding yeast and pseudohyphae. Rapid immunochromatography strips can be used to detect *N. gonorrhoeae*, *T. vaginalis*, and *C. trachomatis* antibodies if resources permit. Undiagnosed cases should be referred for NAAT or examined for non-infectious reasons.

In a 2016 meta-analysis, microscopy screening for *T. vaginalis* and BV improved diagnostic accuracy, leading to better treatment, fewer misdiagnoses, and less overtreatment and missed treatment (Zemouri et al., 2016). Due to limited sensitivity and specificity and the impact of misinterpretation on relationship dynamics, it is necessary to apply risk assessment to combined syndromic and POC microscopy methods. Specific pathogen identification is ideal and can be facilitated by these POC microscopy methods; however, this will not always be possible in all settings. In low STI prevalence settings, the present authors strongly recommend leveraging the already available PCR platforms to perform laboratory-based NAATs.

5. Conclusions

The treatment of abnormal vaginal discharge in the LMICs of SSA has been based mainly on a syndromic approach; however, recent changes in the aetiology, antimicrobial susceptibility, and discoveries such as the association of STIs and BV with HIV acquisition among women of reproductive age, make correct pathogen identification and treatment critical. This would also be associated with a decreased incidence of AMR. The countries of SSA must work towards a shift from a syndromic approach to specific pathogen identification and directed treatment in order to effectively treat STIs and reduce the significant morbidity that results from them.

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Ethical approval

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Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

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