

Etiological Surveillance of Vaginal Discharge Syndrome in South Africa: 2019 to 2020

Ranmini Kularatne, MBChB, FCPATH(SA), *† Etienne Muller, PhD, * Venessa Maseko, BTech, * Bianca Da Costa Dias, PhD, * and Tendesayi Kufa, MBChB, PhD*‡

Background: The syndromic management of vaginal discharge syndrome (VDS) is challenging because of the prevalence of mixed infection with sexually transmitted infection (STI) pathogens and non-STI causes, such as bacterial vaginosis and candidiasis (CA). We aimed to determine the relative prevalence of VDS etiologies in women presenting to sentinel primary health care clinics in South Africa. Secondary objectives were to ascertain the predictive value of speculum findings for the presence of STI pathogens and the proportion of women presenting with clinical features of CA who had identifiable yeast on vaginal smear microscopy.

Methods: Consecutive, consenting women with complaints of abnormal vaginal discharge were enrolled between January 1, 2019, and December 31, 2020. Genital discharge swab and blood specimens were collected and transported to a central STI reference laboratory in Johannesburg.

Results: A total of 364 women were enrolled at 3 sentinel sites. Bacterial vaginosis was the most common cause of VDS (163 of 361 [45.2%]; 95% confidence interval [CI], 40.1%–50.3%); however, a significant proportion had STI coinfection (71 of 163 [43.6%]; 95% CI, 35.8%–51.5%). The predominant STI etiology was *Chlamydia trachomatis* (73 [20.2%]; 95% CI, 16.4%–24.7%). An abnormal speculum finding had poor predictive value for STIs, and Gram stain microscopy showed yeast in only 37.2% of vaginal smears from women with CA symptoms.

Conclusions: Bacterial vaginosis is the predominant cause of VDS in South Africa; however, STI coinfection is common. Clinical findings are poorly predictive of STI etiologies or candidiasis; therefore, a rapid and accurate STI point-of-care test would be useful in optimizing VDS management.

An abnormal vaginal discharge is attributable to a variety of sexually transmitted infections (STIs), as well as to conditions that are not considered STIs but may be sexually transmissible such as bacterial vaginosis (BV) and candidiasis (CA).¹ The syndromic management of vaginal discharge syndrome (VDS) is complex because of the relatively high proportion of mixed infections. In

South Africa, the commonest causes of VDS are BV and vulvovaginal CA; however, a significant proportion of patients with either condition are coinfecting with STI pathogens.² Syndromic management of VDS therefore tends to overtreat patients, as it is difficult to accurately stratify infections into STIs and non-STIs.¹

Before 2018, the South African national VDS treatment algorithm segregated patients for treatment on the basis of age.³ Those patients who were 35 years or older received treatment primarily for BV and/or *Candida*, whereas those who were younger were administered treatment for common STI pathogens such as *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), and *Trichomonas vaginalis* (TV). However, stratification by age revealed that there was no age cutoff that could accurately identify women with and without STIs, and that the proportion of those 35 years or older infected with STI pathogens was not insignificant.⁴ The latest 2018 South African STI syndromic management guidelines have been amended to include treatment for STI pathogens with single doses of ceftriaxone and azithromycin (for NG and CT) and metronidazole (for TV) based on a history of sexual activity within the preceding 3-month period.⁵ The national VDS treatment algorithm also recommends that clotrimazole treatment should be added for vulvovaginal CA based on common clinical manifestations (vulvar redness, itching, curd-like discharge), regardless of history of sexual activity. If women report that they have not been sexually active in the past 3 months, they are treated for CA (based on the presence of suggestive clinical findings) or BV.⁵ In addition, speculum examination is recommended for signs of cervicitis (cervical inflammation, mucopurulent discharge, erosion, friability, edema), especially in sexually nonactive women who have not responded to treatment for BV/CA, and routinely in all sexually active women presenting with VDS.⁵ However, findings on clinical examination have variable performance characteristics in predicting the presence of VDS etiologies.^{6,7} There are no local data on how useful these parameters are in clinical practice for optimal patient management.

We describe results of STI surveillance in adult females presenting with vaginal discharge to sentinel primary health care centers (PHCs) in Gauteng (GP), KwaZulu Natal (KZN), and the Western Cape (WC) provinces in 2019 to 2020. The primary objectives of surveillance were to determine the etiologies of VDS and proportions of coinfections (i.e., HIV, syphilis) among participants presenting with VDS. Secondary objectives were to determine the association between specific findings on vaginal or speculum examination and VDS etiologies.

METHODS

Design

We conducted an observational cross-sectional study of the prevalence of VDS etiologies in symptomatic participants.

Setting

Three primary care facilities that are high-volume STI sentinel sites were as follows: Alexandra Community Health Centre

From the *Centre for HIV & STI, National Institute for Communicable Diseases; and †Department of Clinical Microbiology & Infectious Diseases, School of Pathology and ‡School of Public Health, University of the Witwatersrand, Johannesburg, South Africa

Acknowledgments: The authors thank Ms Valentia Kekana and Mr Alex Zezi (Gauteng), Ms Nokuthula Nzuza (KwaZulu Natal), and Ms Zukiswa Mithani (Western Cape) for participant enrollment, questionnaire administration, and specimen collection at sentinel surveillance sites. In addition, the authors wish to acknowledge Mr Frans Radebe for supervision of clinical surveillance at sentinel sites.

Conflict of Interest and Source of Funding: All authors have no conflicts of interest to declare. Funding for this work was obtained from the operational cost center of the Centre for HIV & STI at the National Institute for Communicable Diseases, South Africa.

Correspondence: Ranmini Kularatne, MBChB, FCPATH(SA), Centre for HIV & STI, National Institute for Communicable Diseases, Johannesburg, South Africa. E-mail: ranminik11@gmail.com.

Received for publication January 25, 2022, and accepted May 6, 2022.

DOI: 10.1097/OLQ.0000000000001646

Copyright © 2022 American Sexually Transmitted Diseases Association. All rights reserved.

(GP), Spencer Road Clinic (WC), and Prince Cyril Zulu Communicable Disease Centre (KZN). Surveillance has been conducted annually at Alexandra CHC since 2008. Surveillance was commenced at Spencer Road Clinic in May 2019 and at Prince Cyril Zulu CDC in April 2020.

Participants

Consecutive consenting females presenting with VDS to the selected PHCs between January 1, 2019, and December 31, 2020, were enrolled in the surveillance. Inclusion criteria included participants 18 years and older with a new episode of clinically confirmed VDS. The target sample size per site per 12-month period was 100 cases of VDS, to measure NG positivity of $15\% \pm 5\%$ among females with VDS. Following eligibility ascertainment and informed consent procedures, a nurse-administered questionnaire (paper-based or electronic) was used to document demographic, behavioral, and clinical information. Each participant was assigned a unique survey ID number that was not linked to any personal identifiers.

Specimen Collection

Professional surveillance nurses collected cotton swab specimens of discharge from lateral and posterior vaginal fornices. Vaginal discharge specimens were smeared on glass slides, which were placed in slide boxes for transport to the STI reference laboratory in Johannesburg, GP. Speculum insertion was done to visualize the cervix and collect endocervical Dacron swab specimens. In addition, a 10-mL venous blood specimen was collected from each participant for serological testing. Swab and blood specimens were transported on ice to the STI reference laboratory and arrived, on average, within 24 to 48 hours of collection.

Laboratory Testing

Microscopy

At the STI reference laboratory, Gram stain microscopy of vaginal discharge smears was performed to observe for yeast (*Candida* species) and to diagnose BV using the Nugent scoring method.

Molecular Testing

Total nucleic acid was extracted from swab specimens using the QIAcube HT instrument (Qiagen, Hilden, Germany). DNA extracts were tested using validated in-house real-time multiplex polymerase chain reaction (PCR) assays for discharge-causing STI pathogens: NG, CT, TV, and *Mycoplasma genitalium* (MG). All real-time PCR assays were performed on the RotorGene real-time PCR system (Qiagen).

Serology

Serum specimens were screened for HIV using the Architect HIV Ag/Ab Combo assay (Abbott Diagnostics, Wiesbaden, Germany). Syphilis coinfection was detected by screening with an automated specific treponemal assay (Architect Syphilis TP; Abbott Diagnostics) and reflexed, if positive, to a manual Immuprep rapid plasma reagin (RPR) assay (Omega Diagnostics Ltd, Alva, United Kingdom). Syphilis was diagnosed based on RPR assay reactivity.

Data Analysis

Data from clinical questionnaires and Excel spreadsheets of laboratory data were exported into Stata 16 (Stata Corporation, College Station, Texas, TX) for analysis. Participant characteristics were described using frequencies and proportions for categorical

data, and medians and interquartile ranges (IQRs) for continuous variables. The relative prevalence of the different STI pathogens and seroprevalence of HIV, and RPR positivity were determined as proportions with binomial exact 95% confidence intervals (CIs) around them. Descriptive statistics were used to calculate the sensitivity, specificity, and positive and negative predictive values (PPV and NPV) of speculum findings for the presence of cervical STI pathogens (NG/CT/TV). Sensitivity represented the proportion of women positive for NG/CT/TV by laboratory testing who had clinical findings consistent with these infections (i.e., any abnormal speculum finding, cervical inflammation, cervical discharge, cervical erosion, and cervical friability/edema). Specificity represented the proportion of women testing negative for NG/CT/TV who did not have clinical findings consistent with these infections. The PPV of clinical findings was represented by the proportion of participants with clinical findings consistent with infection who had laboratory-confirmed results of NG/CT/TV. The NPV of clinical findings was correlated with the proportion of participants without clinical findings who had negative laboratory results for these infections. In addition, we investigated the proportion of women with symptoms/signs of CA who had evidence of vulvovaginal CA on microscopy.

RESULTS

Patient Demographic and Clinical Characteristics

A total of 364 participants were enrolled during the surveillance period, the majority (61%) from GP (Table 1). The median age of participants was 28 years (IQR, 24–34 years). Overall, less than 20% self-reported condom use at last sexual encounter. Condom use was significantly lower in KZN and WC compared with GP. The median number of sexual partners in the past 3 months was 1, and 90% of women reported being monogamous. There was 1 outlier who reported 20 sex partners in the previous 3-month period. Only 3 women reported having no recent sex partners; their ages ranged from 23 to 26 years. Approximately one-fifth of participants overall had been diagnosed with an STI syndrome within the preceding 12-month period. A greater proportion of participants in GP reported recent sex with a partner in another province (24%) or country (31%). In total, 333 (91.5%) participants self-reported knowledge of their HIV status; of these 62 (18.6%) stated they were HIV positive, and 53 of 62 HIV-infected participants (85%) had taken antiretroviral therapy in the past 3 days.

Laboratory Results

STI Syndrome Etiologies

Among 361 women with VDS and valid genital specimen results (Fig. 1), 41.0% had a detectable STI pathogen in single or mixed infections (148; 95% CI, 35.9%–46.2%). The commonest STI etiology was CT (73 [20.2%]; 95% CI, 16.2%–24.7%), followed by NG (54 [15.0%]; 95% CI, 11.4%–19.1%). *Trichomonas vaginalis* was detected in 11.6% (42; 95% CI, 8.5%–15.4%) of VDS cases, and MG in 6.9% (25; 95% CI, 4.5%–10.1%). Of 326 women who reported having only 1 partner in the previous 3-month period, 132 (40.5%) were infected with an STI pathogen. Sexually transmitted infection pathogens were also detected in 2 of the 3 women who reported having no sex partners in the previous 3 months; both women were infected with CT. There was no difference in the proportion of STI pathogens among women who reported having 1 partner in the preceding 3-month period compared with those who had multiple (≥ 2) partners (40.5% [132 of 326] vs. 43.8% [14 of 32]; $P = 0.720$).

Overall, single STI pathogens were detected in 108 VDS cases (29.9%; 95% CI, 25.2%–34.9%), and mixed infections with

TABLE 1. Demographic and Behavioral Characteristics of Participants With VDS (N = 364)

Variable	All (N = 364), n (%)	GP Site, n (%)	KZN Site, n (%)	WC Site, n (%)	P
Current age (n = 363), median (IQR), y	28 (24–34)	28 (24–34)	29 (23–36)	28 (24–33)	0.918
Black Africans	353 (97.0)	222 (100.0)	73 (100.0)	58 (84.1)	<0.001
Age at first sex, median (IQR), y	18 (16–19)	18 (17–19)	18 (17–19)	17 (16–18)	0.058
Heterosexual orientation	361 (99.2)	221 (99.6)	73 (100)	67 (97.1)	0.099
Condom use at most recent sexual encounter*	63 (17.3)	58 (26.1)	3 (4.1)	2 (2.9)	<0.001
Sex outside province (past 3 mo)*	55 (15.1)	53 (23.9)	1 (1.4)	1 (1.5)	<0.001
Sex outside country (past 3 mo)*	71 (19.5)	69 (31.1)	0 (0.0)	2 (2.9)	<0.001
Sexual encounter with a nonregular sexual partner (past 3 mo)*	36 (9.9)	20 (9.0)	4 (5.5)	12 (17.4)	0.060
STI syndrome diagnosed in the past 12 mo	82 (22.5)	40 (18.0)	18 (24.7)	24 (34.8)	0.013
Treated for an STI syndrome with no success (past 3 mo)	9 (2.5)	2 (0.9)	5 (6.9)	2 (2.9)	0.017
Know their HIV status	333 (91.5)	193 (86.9)	71 (97.3)	69 (100.0)	<0.001
Self-reported being HIV positive†	62 (18.6)	20 (10.4)	27 (38.0)	15 (21.7)	<0.001
Taken ARVs in the past 3 d‡	53 (85.5)	16 (80.0)	26 (96.3)	11 (73.3)	0.075

*Fisher exact χ^2 P value.

†Among those who reported knowing HIV status (n = 333).

‡Among those who self-reported being HIV positive.

ARVs indicates antiretroviral therapy.

multiple (≥ 2) STI pathogens were detected in 40 (11.1%; 95% CI, 8.0%–14.8%). Most VDS cases were attributed to conditions that are not traditionally considered to be STIs: BV was identified in 163 of 361 (45.2%; 95% CI, 40.1%–50.4%). Vulvovaginal CA accounted for 103 of 361 (28.5%; 95% CI, 23.9%–33.5%). An identifiable pathogen or cause was not found for 76 VDS cases (20.1%; 95% CI, 17.0%–25.6%).

A significant proportion of participants with VDS were coinfecting with STI and non-STI etiologies. Only 14.4% (52; 95% CI, 10.9%–18.5%) of VDS cases tested for all causes could be attributed solely to infection with 1 or more STI pathogens, whereas 26.6% (96; 95% CI, 22.1%–31.5%) had an STI plus BV and/or CA.

Overall, 71 VDS cases (19.7%) had BV-STI coinfections, and 34 VDS cases (9.4%) had CA-STI coinfections. Therefore, 71 of 163 patients with BV (43.6%; 95% CI, 35.8%–51.5%) and 34 of 103 patients with CA (33.0%; 95% CI, 24.1%–43.0%) had STI coinfections. The most common STI pathogen implicated in both BV and CA coinfection was CT (Table 2). There were no significant differences in VDS etiology by site.

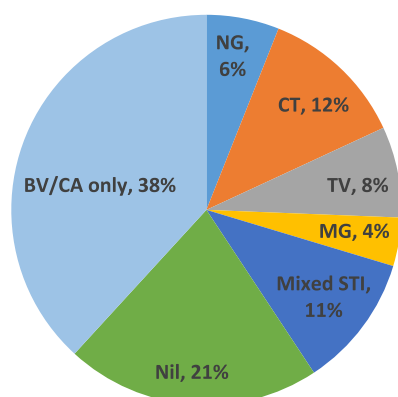
Based on the current VDS algorithm, of 358 women who reported recent sexual activity, 212 (59.2%) would have received unnecessary treatment for an STI. In addition, 120 of 358 (33.5%) who were not infected with TV and also did not have BV coinfection would have received unnecessary metronidazole treatment.

Serological Results

Overall, 102 of 350 participants (29.1%; 95% CI, 24.6%–34.1%) were HIV coinfecting, and HIV prevalence ranged from 23.4% (95% CI, 13.8%–35.7%) in the WC to 47.2% (95% CI, 35.3%–59.3%) in KZN. Syphilis serology (RPR) was positive in 11 of 351 (3.1%; 95% CI, 1.6%–5.5%).

Performance Characteristics of Clinical Findings in Predicting VDS Etiologies

Table 3 depicts the performance characteristics of speculum findings in predicting STI causes of cervicitis. An abnormal speculum finding (210 of 342 [61.4%]) had moderate sensitivity (76.0%; 95% CI, 71.5%–80.5%) and NPV (81.8%; 95% CI, 77.7%–85.9%),



Any STI pathogen (single/ mixed infections): 41.0% (148/361)
Overall prevalence (single + mixed infections)

- NG : 15%
- CT : 20%
- TV : 12%
- MG : 7%

STI only: 14% (52/361)

BV: 45.2% (163/361)

- Overall BV with STI: 19.7% (71/361)
- Of those with BV: 43.6% had STI (71/163)

CA: 28.5% (103/361)

- Overall CA with STI: 9.4% (34/361)
- Of those with CA: 33.0% had STI (34/103)

Figure 1. Relative prevalence of VDS etiologies (N = 364). Figure 1 can be viewed online in color at www.stdjournal.com.

TABLE 2. Prevalence of STI Coinfections in BV and CA

	NG	CT	TV	MG
BV (163)	28 (17.2; 11.7–23.8)*	40 (24.5; 18.1–31.9)*	13 (8.0; 4.3–13.3)*	14 (8.6; 4.8–14.0)*
CA (103)	10 (9.7; 4.8–17.1)*	17 (16.5; 9.9–25.1)*	6 (5.8; 2.2–12.2)*	9 (8.7; 4.1–15.9)*

*Values in n (%; 95% CI).

but a low PPV (36.2%; 95% CI, 31.1%–41.3%) for NG or CT. Much of this was attributable to the presence of a mucopurulent discharge on speculum examination, which was the commonest finding (185 [54.1%]). Cervical inflammation had moderate specificity and NPV for NG and CT, but low PPV. The presence of erosion or cervical friability/edema had relatively high specificity for gonorrhea and chlamydial infection, but the numbers in each category were small. The addition of TV did not improve the predictive value of speculum findings.

In total, 156 of 361 (43.2%) had clinical features of CA. Of these, more than one-third (58 of 155 [37.2%]) had microscopic evidence of yeasts on vaginal smear.

DISCUSSION

Our findings reveal that in South Africa, non-STI causes (BV and CA) account for the majority of VDS cases. Bacterial vaginosis was the leading cause of VDS and prevalent in 45% of females. This finding has been consistently observed in sentinel and national etiological surveillance studies conducted in previous years.^{2,8} A considerable proportion of women with BV were coinfecting with 1 or more STI pathogens. This suggests that BV is associated with risk factors for traditional STI infections, and also provides further evidence for the incorporation of etiological testing into VDS management algorithms. *Chlamydia trachomatis* was the commonest STI pathogen identified, which is in keeping with sentinel surveillance findings from other regions of the country in previous years.⁸ *Chlamydia trachomatis* also causes a relatively high proportion of asymptomatic infections in adolescent girls and young women aged 15 to 24 years in South Africa, with prevalence of up to 40% in Cape Town.⁹ The overall HIV prevalence among patients presenting with VDS is higher than the UNAIDS 2021 estimated prevalence of 24.7% for women aged 15 to 49 years in the general South African population.¹⁰ This underscores the

importance of linkage to universal HIV testing and treatment for STI patients and supports the national policy of universal testing and treatment (early antiretroviral therapy initiation) in those who are HIV infected.

Management of VDS is challenging in the clinical setting; there are no clear demographic or risk variables criteria for identifying women infected with STI pathogens.¹ The vast majority of women in our study reported recent sexual activity, and absence of recent sex partners in a few women did not correlate with a lack of detectable STI pathogens. From the demographic variables examined, we could not identify any that correlated with the presence or absence of an STI pathogen (data not shown). A significant proportion of women who reported being in a monogamous relationship were infected with an STI pathogen(s). This could be due to reporting (social desirability) bias with respect to number of sexual partners, or due to partner concurrency among their male partners. Male partner concurrency is well described in South Africa, particularly among women in age-disparate intergenerational relationships.¹¹ A study evaluating syndromic management guidelines showed that only 56% of women presenting with VDS to PHCs in rural Limpopo province, South Africa, would have received adequate treatment for STI based on the national VDS treatment algorithm in use at the time.¹² Similarly, in a high-risk female sex worker population in India, the national treatment guidelines for VDS were poorly predictive of STI pathogen etiologies, with moderate sensitivity but low specificity and PPVs for cervicitis caused by NG and CT.¹³ Our etiological findings indicate that nearly 60% of women would have been treated unnecessarily for STIs based on a history of recent sexual activity, as per the current VDS treatment algorithm. In Papua New Guinea, where there was a high burden of VDS (73%) among women attending sexual health clinics and a relatively high pathogen prevalence similar to ours, the VDS algorithm had low predictive value for STI pathogens.¹⁴ This meant unnecessary treatment for 60% to 70% of symptomatic

TABLE 3. Performance of Speculum Examination Findings in the Prediction of STI Etiology (N = 342)*

Speculum Findings	Presence of Cervical Pathogens on Laboratory Testing							
	Sensitivity, % (95% CI)		Specificity, % (95% CI)		PPV, % (95% CI)		NPV, % (95% CI)	
	NG/CT†	NG/CT/TV‡	NG/CT	NG/CT/TV	NG/CT	NG/CT/TV	NG/CT	NG/CT/TV
Any abnormal speculum finding (n = 210)	76.0 (71.5–80.5)	70.4 (65.6–75.2)	44.6 (39.4–49.9)	43.8 (38.5–49.0)	36.2 (31.1–41.3)	41.9 (36.7–47.1)	81.8 (77.7–85.9)	72.0 (67.2–76.7)
Inflammation (n = 86)	32.0 (27.1–36.9)	29.6 (24.8–34.4)	78.1 (73.7–82.5)	77.9 (73.5–82.3)	37.6 (32.5–42.8)	43.5 (38.3–48.8)	73.5 (68.9–78.2)	65.7 (60.7–70.8)
Discharge (n = 185)	70.0 (65.1–74.9)	64.8 (59.7–69.9)	52.5 (47.2–57.8)	52.1 (46.8–57.4)	37.8 (32.7–43.0)	43.8 (38.5–49.0)	80.9 (76.7–85.1)	72.0 (67.2–76.3)
Erosion (n = 48)	20.0 (15.8–24.2)	18.4 (14.3–22.5)	88.4 (85.0–91.8)	88.5 (85.1–91.9)	41.7 (36.4–46.9)	47.9 (42.6–53.2)	72.8 (68.1–77.5)	65.3 (60.3–70.4)
Friability/Odema (n = 25)	10.0 (6.8–13.2)	9.6 (6.5–12.7)	93.8 (91.2–96.4)	94.0 (91.5–96.5)	40.0 (34.8–45.2)	48.0 (42.7–53.3)	71.6 (66.8–76.4)	64.3 (59.3–69.4)

*Women with speculum examination and valid laboratory results.

†NG/CT positive: 100 of 342.

‡NG/CT/TV positive: 125 of 342.

women. Speculum findings in our study revealed that, individually, the parameters examined for were poorly predictive of infection with STI pathogens. These findings are corroborated by a meta-analysis reviewing published studies (2001–2018), which concluded that the pooled diagnostic accuracy was low for VDS algorithms using risk assessment and speculum examination for STIs.⁷ In a population with an NG or a CT prevalence of 15%, the low-moderate specificity would result in high numbers of false positives leading to overtreatment, and the low sensitivity would result in high numbers of false negatives leading to missed treatment.⁷ Speculum examination for this study was done by trained surveillance nurses; therefore, its predictive value for STIs in VDS may be even lower with less experienced personnel.

A clinical diagnosis of BV has traditionally been made by investigating for the presence of at least 3 of 4 Amsel criteria.¹⁵ Amsel criteria had a moderate PPV of 63% among a population of women with a Nugent score–diagnosed BV prevalence of approximately 48% in the Gambia.¹⁶ However, 2 FemExam cards (Litmus Concepts, Santa Clara, CA) used to detect vaginal pH, presence of amines, and TV enzymatic activity had a high sensitivity and NPV for BV, although it was relatively more expensive than Gram-stain Nugent scoring.¹⁶ The sensitivity and specificity of microscopy for clue cells, yeast, and trichomonads in the diagnosis of vaginitis can vary and are often suboptimal.^{6,15} Within community-practice settings in the United States, the Centers for Disease Control Prevention–recommended point-of-care testing, which included parameters assessed in Amsel criteria and microscopic examination of discharge for *Candida* yeast cells and TV trophozoites, was performed infrequently.¹⁷ More than 40% of women with a reference laboratory–diagnosed cause of vaginitis had received inappropriate treatment at point of care.

The World Health Organization recently advocated a transition from syndromic to etiologic STI management as a strategy to mitigate the global public health threat of STIs by 2030.¹ For this to become practicable at resource-constrained primary health care level, accurate, affordable, technically simple rapid diagnostic tests (RDTs) would need to be incorporated into the VDS management algorithm. Sexually transmitted infection RDTs could improve the diagnostic accuracy of the VDS algorithm, promote antimicrobial stewardship by enabling specific pathogen-directed therapy, and facilitate expedited partner treatment.¹⁸ The Cepheid GeneXpert NG/CT and TV assays have shown excellent performance characteristics relative to reference laboratory assays, even with the use of patient-collected vaginal swab specimens.^{19,20} Although South Africa has a well-established GeneXpert platform for tuberculosis screening, instruments are mostly located in National Health Laboratory Service public-sector laboratories, and the costs of testing may be prohibitive in more resource-constrained regions. An accurate, rapid lateral flow immunochromatographic assay would be an ideal cost-effective point-of-care intervention; however, sensitivities of currently available lateral flow RDTs for NG and CT are 50% or lower, or have been evaluated in only few studies with small sample sizes.^{21,22} Mathematical modeling has shown that a moderately sensitive RDT with 70% to 80% sensitivity, 95% specificity, and a cost of 1 to 2 US dollars would be a cost-effective strategy to decreasing inappropriate and missed treatment for NG and CT in high-prevalence settings.²³ Limitations of our study include reporting and recall bias in the questionnaire responses of some participants. In addition, a majority of women (61.0%) were enrolled at 1 urban site (GP), thus limiting the generalizability of findings. We considered that in symptomatic women with VDS, gram-stained smear microscopy for yeast and pseudohyphae would be sufficient for establishing the diagnosis of vulvovaginal CA in surveillance specimens¹⁵; however, *Candida* culture is a more sensitive diagnostic method. This may explain

some of the discrepancy between suggestive clinical manifestations of CA and microscopy findings.

In conclusion, the syndromic management of VDS remains complex because behavioral and clinical findings do not seem to improve the predictive value of treatment algorithms for STI pathogens. A rapid, accurate, affordable, and technically simple point-of-care test for NG and CT would enable optimization of VDS management in primary health care settings.

REFERENCES

- Guidelines for the Management of Symptomatic Sexually Transmitted Infections. Geneva, Switzerland: World Health Organization, 2021. Licence: CC BY-NC-SA 3.0 IGO.
- Kularatne R, Radebe F, Kufa-Chakezha T, et al. Sentinel Surveillance of Sexually Transmitted Infection Syndrome Aetiologies and HPV Genotypes Among Patients Attending Primary Healthcare Facilities in South Africa, April 2014–September 2015. Johannesburg, South Africa: National Institute for Communicable Diseases; Centre for HIV & STIs, 2017.
- Sexually Transmitted Infections Management Guidelines. Pretoria, South Africa: National Department of Health, 2015.
- Kufa T, Gumede L, Maseko DV, et al. The demographic and clinical profiles of women presenting with vaginal discharge syndrome at primary care facilities in South Africa: Associations with age and implications for management. *S Afr Med J* 2018; 108:876–880.
- Primary Healthcare Standard Treatment Guideline and Essential Medicine List. 6th ed. Pretoria, Republic of South Africa: National Department of Health, 2018.
- Hainer BL, Gibson MV. Vaginitis. *Am Fam Physician* 2011; 83:807–815.
- Wi TE, Ndowa FJ, Ferreyra C, et al. Diagnosing sexually transmitted infections in resource-constrained settings: Challenges and ways forward. *J Int AIDS Soc* 2019; 22(Suppl 6):e25343.
- Kularatne R. Aetiological Surveillance of Sexually Transmitted Infection Syndromes at Sentinel Sites: GERMS SA 2018. Johannesburg, South Africa: National Institute for Communicable Diseases, 2019. GERMS-SA Surveillance Review 2018.
- Barnabas SL, Dabee S, Passmore JS, et al. Converging epidemics of sexually transmitted infections and bacterial vaginosis in southern African female adolescents at risk of HIV. *Int J STD AIDS* 2018; 29:531–539.
- UNAIDS 2020, 2nd Edition. 2021. Available at: https://www.unaids.org/sites/default/files/media_asset/JC3032_AIDS_Data_book_2021_En.pdf.
- Street RA, Reddy T, Ramjee G. The generational effect on age disparate partnerships and the risk for human immunodeficiency virus and sexually transmitted infections acquisition. *Int J STD AIDS* 2016; 27:746–752.
- van der Eem L, Dubbink JH, Struthers HE, et al. Evaluation of syndromic management guidelines for treatment of sexually transmitted infections in South African women. *Trop Med Int Health* 2016; 21:1138–1146.
- Desai VK, Kosambiya JK, Thakor HG, et al. Prevalence of sexually transmitted infections and performance of STI syndromes against aetiological diagnosis, in female sex workers of red light area in Surat, India. *Sex Transm Infect* 2003; 79:111–115.
- Vallely LM, Toliman P, Ryan C, et al. Performance of syndromic management for the detection and treatment of genital *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis* among women attending antenatal, well woman and sexual health clinics in Papua New Guinea: A cross-sectional study. *BMJ Open* 2017; 7:e018630.
- Unemo M, Ballard R, Ison C, et al. Laboratory Diagnosis of Sexually Transmitted Infections, Including Human Immunodeficiency Virus. Geneva, Switzerland: World Health Organization, 2013. ISBN 978 92 4 150584 0.
- West B, Morison L, Schim van der Loeff M, et al. Evaluation of a new rapid diagnostic kit (FemExam) for bacterial vaginosis in patients with vaginal discharge syndrome in The Gambia. *Sex Transm Dis* 2003; 30: 483–489.
- Hillier SL, Austin M, Macio I, et al. Diagnosis and treatment of vaginal discharge syndromes in community practice settings. *Clin Infect Dis* 2021; 72:1538–1543.

18. Garrett NJ, Osman F, Maharaj B, et al. Beyond syndromic management: Opportunities for diagnosis-based treatment of sexually transmitted infections in low- and middle-income countries. *PLoS One* 2018; 13:e0196209.
19. Gaydos CA, Van Der Pol B, Jett-Goheen M, et al. Performance of the Cepheid CT/NG Xpert rapid PCR test for detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. *J Clin Microbiol* 2013; 51: 1666–1672.
20. Schwebke JR, Gaydos CA, Davis T, et al. Clinical evaluation of the Cepheid Xpert TV assay for detection of *Trichomonas vaginalis* with prospectively collected specimens from men and women. *J Clin Microbiol* 2018; 56:56(2).
21. Unemo M, Bradshaw CS, Hocking JS, et al. Sexually transmitted infections: Challenges ahead. *Lancet Infect Dis* 2017; 17:e235–e279.
22. Murtagh M. The Point-of-Care Diagnostic Landscape for Sexually Transmitted Infections (STIs). Geneva, Switzerland: World Health Organization, 2019.
23. Vickerman P, Watts C, Peeling RW, et al. Modelling the cost effectiveness of rapid point of care diagnostic tests for the control of HIV and other sexually transmitted infections among female sex workers. *Sex Transm Infect* 2006; 82:403–412.