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Comprehensive assessment of vaginal infections using a single swab

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ABSTRACT

Background The decision to use a particular test to diagnose patients presenting with symptoms of vaginitis and/or STI is based primarily on the prevailing standards of care in the clinic at which the patient evaluation takes place. As a result, laboratory testing of vaginal samples for these patients often involves either an STI or a vaginitis test, but rarely both options simultaneously, which complicates the diagnosis and management of concurrent infections.

Methods Using de-identified remnant vaginal specimens from symptomatic patients previously tested for STI (*Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (GC) and *Trichomonas vaginalis* (TV)) with the Becton Dickinson (BD) CTGCTV2 assay for BD MAX System, positivity for bacterial vaginosis (BV) and *Candida* spp (associated with vulvovaginal candidiasis (VVC)) were evaluated using the molecular-based BD MAX Vaginal Panel.

Findings The rate of STI/BV co-infection was 79.4% (227/286) in this symptomatic population, while that of STI/VVC was 27.0% (77/285). Women diagnosed with any one of the three STIs tested had an OR 2.86 (95% CI, 1.99, 4.11; p<0.0001) for a concurrent BV infection and OR 0.96 (95% CI, 0.67, 1.37; p=0.8085) for infection with *Candida* species.

Conclusion Our results suggest that women being tested for STI have a high prevalence of co-infection with BV and a lower, although appreciable, prevalence of co-infection with VVC. The detection of co-occurring vaginal infections can be facilitated by molecular testing using a single sample.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Despite the similarity of symptoms between STI and vaginitis, the selection by clinicians of a specific diagnostic test is mainly dictated by the prevailing standards of care at the facility where the patient is seen; consequently, in many cases, either STI or vaginitis testing is performed rather than both tests simultaneously.

WHAT THIS STUDY ADDS

⇒ This study confirms the high rate of concurrent STI/vaginitis (bacterial vaginosis) infections among symptomatic patients and discusses the benefits of using a comprehensive testing panel to ensure timely detection and management of co-occurring infections.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings of this study support the adoption of simultaneous STI and vaginitis testing in clinical practice.

INTRODUCTION

Vaginal symptoms account for more than 10 million physician visits in the USA annually, making them a leading cause of medical consultations among women.[1] Since vaginal symptoms such as vaginal discharge, odour, itching and burning can be indicative of a variety of bacterial or fungal infections for which pharmacological treatment is pathogen-specific, accurately identifying the cause of presenting symptoms is crucial in the clinical assessment process. The clinical and laboratory methods commonly used to detect pathogens responsible for vaginal symptoms in women include a visual assessment of vaginal discharge by the treating physician, wet prep microscopy, urine culture or the collection of vaginal swabs for subsequent molecular testing; each method has its own benefits and drawbacks in terms of results turnaround time, accuracy, costs, and availability.[2]

Determining symptom aetiology based on a clinical workup is notoriously inaccurate given the difficulty with microscopy (which is no longer available in many settings), the lack of specificity of the appearance of discharge and the high frequency of co-infections.[3 4] Clinical diagnosis has also been hampered by SARS-CoV-2 during the pandemic as many patients, even those with symptoms, were not undergoing full pelvic examinations with visualisation of the cervix.[5–7] This rendered the already difficult task of separating vaginitis from cervicitis as a cause of discharge nearly impossible. Given these challenges, laboratory diagnostics are needed to fully understand the pathogens that may be present in these patients.

Laboratory test orders for symptomatic women are often based on the standard of care at the clinic, the patient's medical history and the availability of diagnostic methods.[8] Moreover, the decision to order a specific laboratory test, or the breadth of pathogens to be tested, may also be swayed by external factors such as funding/reimbursement and stigma related to STI testing.[9] Therefore, laboratory workups may vary significantly among women seeking care for similar vaginal symptoms, depending on clinics' routine practices.

The frequent occurrence of vaginal and/or cervical co-infections adds to the complexity of

Table 1 Summary of demographic information

Characteristics	Total (N=606)	Any STI (n=287)	No STI (n=319)	P value
Mean age	28.7	27.9	29.5	0.038
Median age (range)	26 (18–64)	25 (18–55)	26.0 (18–64)	0.218
Clinic type, % (n)				
STD/HIV	27.9% (169)	35.2% (101)	21.3% (68)	<0.001
Family planning	29.2% (177)	27.5% (79)	30.7% (98)	0.421
OB/GYN	36.1% (219)	29.3% (84)	42.3% (135)	0.001
Other	6.8% (41)	8.0% (23)	5.6% (18)	0.261
Symptoms, % (n)				
Pelvic/uterine/adnexal pain	17.5% (106)	15.7% (45)	19.1% (61)	0.285
Abnormal vaginal discharge	71.9% (436)	73.2% (210)	70.8% (226)	0.528
Odour	42.9% (260)	48.4% (139)	37.9% (121)	0.011*
Itching	34.3% (208)	34.8% (100)	33.9% (108)	0.864
Dysuria	8.6% (52)	8.7% (25)	8.5% (27)	1.000
Coital discomfort, pain or bleeding	10.4% (63)	9.8% (28)	11.0% (35)	0.690

*p<0.05
OB/GYN, obstetrics/gynaecology.

selecting the most appropriate diagnostic test and suggests that a siloed approach to testing (ie, testing for STI or vaginitis) may not be sufficient to detect co-occurring infections.[8] The prevalence of concurrent vaginal infections and patients' susceptibility to such infections are often mentioned in the literature, especially for bacterial vaginosis (BV) or *Candida* spp (associated with vulvovaginal candidiasis (VVC)) concurrently with gonorrhoea or chlamydia.[10–12] As such, assessing the presence of multiple pathogens through laboratory testing may increase the ability of providers to comprehensively address patients' needs in terms of both accurate diagnosis and treatment.[13]

When comprehensive testing is warranted, minimising sample collection reduces the burden on the patient and clinic flow and may increase clinical efficiency, making molecular-based testing using a single vaginal swab a preferred option. This study sought to assess the occurrence of BV and VVC with CT, GC and TV in vaginal swabs previously tested for STI to determine the utility of single vaginal swab collection in supporting multiple pathogen testing.

MATERIALS AND METHODS

Population and samples

This study used a subset of de-linked and de-identified self-collected remnant vaginal specimens from a previously conducted CTGCTV2 clinical performance study evaluating the performance of the BD CTGCTV2 assay for the BD MAX System using samples from male and female participants with symptoms of STI.[14] More specifically, this subset of data acquired from the parent study included all 287 STI-positive vaginal specimens collected from symptomatic female patients, as well as a random selection of 319 STI-negative specimens from the 1281 STI-negative vaginal specimens in the parent study population. Participants were classified as symptomatic if they reported symptoms such as dysuria, abnormal vaginal discharge, itching and/or odour, coital pain/discomfort, bleeding, or pelvic, uterine, or adnexal pain. All specimens included in the study were stored at ≤70°C until testing and had enough volume (500 µL) to perform at least one MAX Vaginal Panel test, and all individuals had consented to future use of their samples through the informed consent process in the parent study.

Testing of the remnant specimens was performed at the University of Alabama at Birmingham site by vortexing the thawed BD Molecular Swab Sample Buffer Tubes (SBT) briefly before placing them in the BD MAX system and testing according to the package insert instructions.[15] To ensure unbiased estimates of positivity, verification bias adjustments were performed that gave greater weight to symptomatic participants negative for CTGCTV2 pathogens since only a fraction of all symptomatic BD MAX negative participants from the parent study were included in the investigation.

As part of the parent study consent process, permission for future use of residual samples was obtained from the participants. The Guidelines on Good Publication Practice (GPP3)[16] were followed in the writing of this manuscript.

Table 2 Positivity rates of BD MAX Vaginal Panel across STI-positive and STI-negative participants

Condition	Positivity rates		
	Any STI % (n)	No STI % (n)	Total % (n)
Any vaginitis	93.4% (268/287)	71.5% (228/319)	81.8% (496/606) Adjusted: 75.6%
BV	79.4% (227/286*)	57.4% (183/319)	67.8% (410/605‡) Adjusted: 61.4%
VVC	27.0% (77/285†)	27.9% (89/319)	27.5% (166/604§) Adjusted: 27.8%

VVC, *Candida* spp.
*One unreportable BV result was excluded from the total 287 STI-positive specimens.
†Two VVC unreportable results were excluded from the total 287 STI-positive specimens.
‡One unreportable BV result was excluded from total 606 tested specimens.
§Two unreportable VVC result were excluded from the total 606 tested specimens.
BV, bacterial vaginosis; VVC, vulvovaginal candidiasis.

Analyses

The positivity rate of BV and VVC with and without CT, GC or TV infections was estimated with 95% CIs using the Wilson score method.[17] In addition, positivity ORs between CTGCTV2 positive and negative populations were estimated with a 95% CI. The Fisher exact test[18] was used to determine the p values, with $p \leq 0.05$ considered statistically significant. Population positivity rates were adjusted using weighted values which were calculated for negative samples by dividing the number of STI-negative samples in the original study by the number of STI-negative samples in the present one. A similar calculation was performed to adjust the weight of the positive samples. Bootstrapping was used to calculate CI for adjusted rates, using the

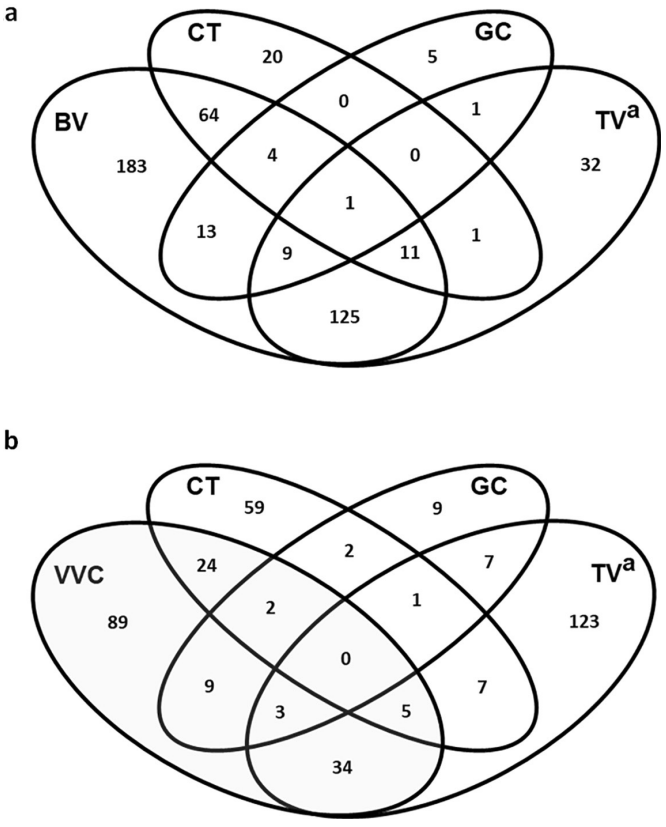

Figure 1 Venn diagrams depicting the co-occurrence of BV (diagram 1A) and *Candida* spp (diagram 1B) with CT and *Neisseria gonorrhoeae*. The specimens were initially tested for STI (CT, GC and TV) with the BD MAX CTGCTV2 assay and subsequently tested using the BD MAX Vaginal Panel to determine the concurrent positivity of those specimens for BV and Candida spp. TV[a] represents CTGCTV2 results. BV, bacterial vaginosis; CT, *Chlamydia trachomatis*; GC, *Neisseria gonorrhoeae*; TV, *Trichomonas vaginalis*; VVC, vulvovaginal candidiasis.

entire CTGCTV2 population prior to weight recalculation. Data analysis was performed with R V.4.3 software.[19]

RESULTS

A total of 606 female participants who had STI swabs collected as part of the CTGCTV2 study were included in this investigation. The mean age of the women in the current sample was 28.7 years and the median age was 26 (range 18–64) years. Samples collected in obstetrics/gynaecology (OB/GYN) clinics accounted for 36.1% of all collected swabs, whereas swabs collected in family planning clinics, STD/HIV clinics and other facilities accounted for 29.2%, 27.9% and 6.8% of all swabs tested, respectively (table 1). Except for the 'odour' category, no significant differences were observed in the frequency of reported vaginal symptoms in the STI versus no-STI group (table 1).

Among women previously diagnosed with any one of the three STIs, 93.4% (268/287) had a concurrent infection with at least one pathogen tested with the BD MAX Vaginal Panel assay (table 2).

When no STI was present, the positivity rate for any vaginal cause of infection in the study sample was 71.5% (228/319). Regardless of STI status, BV occurred more frequently than VVC in our sample. Hence, when assessed in conjunction with any STI, the rate of BV was 79.4% (227/286), whereas the VVC rate was 27.0% (77/285); one BV specimen and two VVC specimens were excluded from the analysis due to unreportable results (incomplete, unresolved or indeterminate). Without any STI, BV and VVC positivity rates were 57.4% (183/319) and 27.9% (89/319), respectively (table 2). Venn diagrams depicting the distribution of positive BV and VVC specimens in relation to concurrent STI are presented in figure 1. Diagnosis with any one of the three STIs had an OR of 2.86 (95% CI, 1.99, 4.11, p<0.0001) for a concurrent BV infection and OR 0.96 (95% CI, 0.67, 1.37, p=0.8085) for a VVC infection (table 3).

Trichomonas infection was classified as an STI since that is the primary mode of transmission of *T. vaginalis*. However, because it is a cause of vaginitis rather than cervicitis, it has long been included in tests designed for vaginitis. The BD MAX assays include detection of *T. vaginalis* in both the STI and the vaginitis assays so providers using only one of the two tests will receive a trichomonas result. In this study, where the trichomonas test was run with both assays, the overall percent agreement was 97.6% (95% CI, 96.1%, 98.6%) and Cohen's Kappa was 0.94 (95% CI, 0.91, 0.97).

Table 3 Likelihood of vaginitis among women with STI (CT, GC and/or TV)

BV	STI positive (n=286*)	STI negative (n=319)
Positive	79.4% (227)	57.4% (183)
Negative	20.6% (59)	42.6% (136)
OR (95% CI)	2.86 (1.99, 4.11)	
P value	<0.0001	
VVC	**STI positive (n=285†)**	**STI negative (n=319)**
Positive	27.0% (77)	27.9% (89)
Negative	73.0% (208)	72.1% (230)
OR (95% CI)	0.96 (0.67, 1.37)	
P value	p=0.8085	

VVC, *Candida* spp.
*One unreportable BV result was excluded from the total 287 STI-positive specimens.
†Two VVC unreportable results were excluded from the total 287 STI-positive specimens.
BV, bacterial vaginosis; CT, *Chlamydia trachomatis*; GC, *Neisseria gonorrhoeae*; TV, *Trichomonas vaginalis*; VVC, vulvovaginal candidiasis.

DISCUSSION

In the population of symptomatic women evaluated in this study, of which nearly two-thirds (65.3%) were recruited from OB/GYN or family planning clinics, positivity for causes of vaginitis was quite high (81.8% positive for BV or VVC) regardless of STI infection. While the rate of BV was significantly higher among women with a concurrent STI, the positivity of both BV and VVC was high enough to warrant testing for all pathogens. Regardless of STI positivity, BV positivity was high (>50%); however, significantly more cases of BV were found among women with an STI. This high frequency of co-infection and the lack of specific symptoms that could differentially identify the cause strongly support the use of tests that can identify both STI and vaginitis. Anecdotally, many clinicians believe that if a woman has VVC, she will not have an STI because the vulvar vestibulitis is likely the result of antibiotic use, which might have cleared the STI. Our findings suggest that this is not the case, as over one-quarter of women with an STI also had VVC.

Collectively, these data demonstrate the need for comprehensive testing for women presenting with vaginal symptoms including discharge, dysuria and other common complaints associated with either vaginitis or cervical infections. Adoption of such testing can be facilitated by using assays that allow the collection of a single vaginal sample as this reduces the burden on clinical staff related to sample collection and handling.

Moreover, because these samples can be self-collected, women reporting vaginal symptoms as the reason for an office visit can be provided with a collection device immediately following registration and before doctor consultation, as this process has been shown to be effective for STI testing.[20] The sample can then be used for comprehensive testing, avoiding the need for additional sample collection during the examination. This strategy can be adopted in settings where a full examination is being performed or where only limited examinations are offered (eg, emergency or urgent care settings).

Limitations

This study has limited ability to accurately predict the impact of STI and vaginitis causes on one another since only a subset of the population from the parent study was tested. However, applying statistical weight allowed us to determine the expected positivity for vaginitis causes based on the presence or absence of an STI. Further, the estimates for BV and VVC are likely conservative as this study was performed using stored, residual specimens.

CONCLUSION

A single vaginal sample is sufficient to support comprehensive diagnostics for women presenting with vaginal/cervical symptoms when using assays such as the BD MAX Vaginal Panel and the BD MAX CTGCTV2. Comprehensive testing is also warranted to treat women for all causes of vaginal symptoms as it can reduce follow-up visits, which can occur when only a single cause is treated in women with multiple infections. Given the similarity of symptoms across pathogens, it is clear that tests that can accurately detect multiple causes from a single vaginal sample can provide comprehensive and efficient care.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by University of Alabama at Birmingham (UAB) Institutional Review Board (IRB WCG 20161602). Participants gave informed consent to participate in the study before taking part.

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