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Self-taken vaginal swabs versus clinician-taken for detection of candida and bacterial vaginosis: a case-control study in primary care.

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Are self-taken vaginal swabs equivalent to clinician-taken for the detection of candida and bacterial vaginosis?

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Abstract

Background: Vaginal discharge and vulvitis are common presenting symptoms in general practice. Few studies have specifically looked at the validity of self-taken low vulvovaginal swabs (LVS) for the diagnosis of vulvovaginal candidiasis (VVC) and bacterial vaginosis (BV).

Aim: To assess if patient self-taken LVS is a valid alternative to clinician-taken high vaginal swabs (HVS) for the detection of VVC and BV.

Design and Setting: Case controlled study with the patient acting as their own control in an urban sexual health centre.

Method: Women aged 16-65 years attending with symptomatic vaginal discharge, vulval irritation, genital pain and an offensive genital smell were recruited into the study. Participants took a self-taken LVS prior to vaginal examination, during which a clinician took a HVS (reference standard). Main outcome measures were the diagnosis of BV or VVC infection.

Results: A total of 104 women were enrolled. Of those 45 were diagnosed with VVC and 26 with BV. The sensitivities of self-taken LVS for VVC and BV were 95.5% and 88.5% respectively. Cohen Kappa's coefficient showed "strong agreement" for the detection of both VVC and BV. Vulval itching was the most common symptom associated with VVC (49%), while 65% of women diagnosed with BV presented an offensive discharge. Both symptoms had poor positive predictive values (0.63 and 0.5, respectively).

Conclusion: Self-taken LVS appears to be a valid alternative to clinician-taken HVS for detecting VVC and BV infections. Symptoms were found to be a poor indicator of underlying infection.

Keywords: vaginal examination, vulvovaginal candidiasis, bacterial vaginosis, general practice.

How this fits in:

For a woman presenting for the first time with a change in vaginal discharge, current guidelines for management in General Practice do not generally advocate HVS as a diagnostic tool (1). However a number of clinical scenarios do require microbiological confirmation for the diagnosis of abnormal discharge (2). We present our finding for the validity of a self-taken vaginal swab in these circumstances.

Introduction

Bacterial Vaginosis (BV) is the commonest cause of infective vaginal discharge in women of reproductive age (3). Vulvovaginal candidiasis (VVC) is the second most common and particularly affects women aged 20 to 30 years (3, 4). Symptomatic vulvovaginal discharge and vulval irritation are frequent and often distressing presenting symptoms in women attending both general practice surgeries (5) and sexual health services (4, 6). Classical symptoms of VVC are vulval itching associated with a thick, white, curdy discharge whilst BV typically presents as a non-irritant, thin, grey, offensive discharge (4, 6). However, vaginal symptoms and signs are not a reliable indicator of underlying aetiology. BV may cause vulval irritation (7) while VVC may present solely with a change in discharge (8). Even women with previously confirmed episodes of VVC are poor at self-diagnosis (9) and as few as 16% of women with recurrent symptoms typical of candida have VVC confirmed on culture (10). Other infective causes of a discharge should always be considered and screening is offered for chlamydia, gonorrhoea and trichomonas, particularly in women less than 25 years of age (2). Non-infective causes for vulval irritation/itching are common (up to half the women in one study presenting with symptoms suggestive of VVC were shown to have another condition) (4). These include atopy, eczema, lichen sclerosis and vulval carcinoma. In order to make a definitive diagnosis, clinicians should ideally perform a genital examination which includes the

insertion of a speculum and the collection of bacteriological samples for microscopy, culture and sensitivity.

In primary care various constraints such as time pressure and lack of a chaperone combined with a patient's reluctance to be examined, can conspire to make a genital inspection with speculum examination difficult if not impossible. Clinicians may therefore opt to treat vaginal discharge and vulval irritation syndromically without microbiological evidence of infection (5). In cases where vulval itching is not in fact due to candidiasis but is triggered by other pathology such as atopy, atrophic vaginitis or lichen sclerosis, women may experience symptomatic relief from the moisturising action of anti-fungal creams particularly if combined with the anti-inflammatory action of hydrocortisone, further muddying the water with regards to diagnosis.

If a high vaginal swab (HVS) is required there is a general consensus in current guidelines that a blind swab is acceptable (1, 2). Two large well conducted studies in Leeds in 2014 showed that a self-taken low vaginal swab (LVS) is in fact superior to a clinician-taken endocervical swab for the detection of chlamydia and gonorrhoea (11,12) and current guidelines have changed to reflect this with regards to STI screening (13). There is a reasonable body of research to support the use of a self-taken LVS for detection of abnormal vaginal bacteria but very little on the validity of this method for the detection of Candida (14, 15). This study was therefore designed to see if a patient self-taken LVS is as reliable as clinician-taken HVS in the diagnosis of both VVC and BV.

Methods

Study population

From May to August 2015, women between 16-65 years of age who presented to The New Croft Centre for Sexual Health in Newcastle-upon-Tyne, UK, with symptoms of vaginal discharge, genital irritation or offensive genital smell were recruited into the study, after providing informed consent.

Women already diagnosed with VVC or BV and those with established immunodeficiency, were excluded from the trial. No patient was entered more than once. The study was approved by the NHS Research Ethics Committee (REC).

Data collection

Those enrolled in the trial were seen by either a doctor or a nurse trained in genito-urinary medicine (GUM) and were given both verbal and written instructions on how to perform a LVS. They were advised to insert the cotton end of the swab stick 6 cm into the vagina, rotate it for 10 seconds and then place the swab into Aimes transport medium. The women then underwent a speculum examination and a HVS was collected from the posterior fornix by the examining clinician. This was also placed into a different Aimes transport medium. Symptom data was collated by summarizing the presenting complaints into 4 categories: vulval irritation/itching, offensive discharge, genital pain with abnormal discharge and any other changes to the woman's normal discharge

Laboratory assessment

Both self-taken and physician collected swabs were then sent to the microbiology laboratory for microscopy and culture for candida species and organisms causing BV. For the diagnosis of candida, the HVS specimen was cultured on Sabourauds culture medium incubated in air at 35-38 degrees centigrade for 48hrs and any growing colonies analysed for candida (16). The diagnosis of BV was made by gram staining the swab specimens and then using the Hay-Ison scoring methodology (17). In addition to swabs being sent for laboratory diagnosis all patients had in-house wet mount phase microscopy for trichomoniasis and gram staining of specimens looking for evidence of candida plus Hay-Ison scoring for BV. Patients with candidiasis were treated with a single dose of oral Fluconazole 150mg those with BV were given oral Metronidazole 400mg twice daily for 7 days .

Data analysis

Data was analysed using VassarStats on line statistical computation. Descriptive analyses were conducted for all relevant variables and outcomes, using appropriate measures of location (mean or median) and dispersion (standard deviation or range) for continuous variables. Categorical variables were summarised using absolute frequencies and proportions. The patient self-taken swab diagnostic test performance was assessed using the sensitivity, specificity and positive and negative predictive values. The Cohen's Kappa statistic (18) was used to investigate the level of agreement between the two test methods.

We followed the interpretation of Cohen's Kappa suggested by Cohen: values ≤ 0 as indicating no agreement, 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement. When applicable, 95% CI were reported.

Results

Figure 1 summarises the enrolment figures of the patients included in the study, while the resulting outcomes of both diagnostic tests for VVC and BV are summarized in Table 1.

The median age of the participants was 26 years old (range 17 – 49). Out of the 104 women that were enrolled during the study period, 97 had complete laboratory data for BV and 99 for VVC. (Data was incomplete for 7 patients due to loss of one or both swabs in transit between our community based site and the main hospital laboratory.)

Using the clinician HVS as the reference standard, the prevalence of VVC was 45.5% (n=45) while the prevalence of BV was 26.8% (n=26). Five women had both VVC and BV and 31 women had neither BV nor candida. In addition, eight patients (8.7%) were diagnosed with chlamydia, two (2.2%) with chlamydia and gonorrhea and two (2.2%) with herpes.

Fig. 1. CONSORT chart outlining the study plan and enrolment figures.

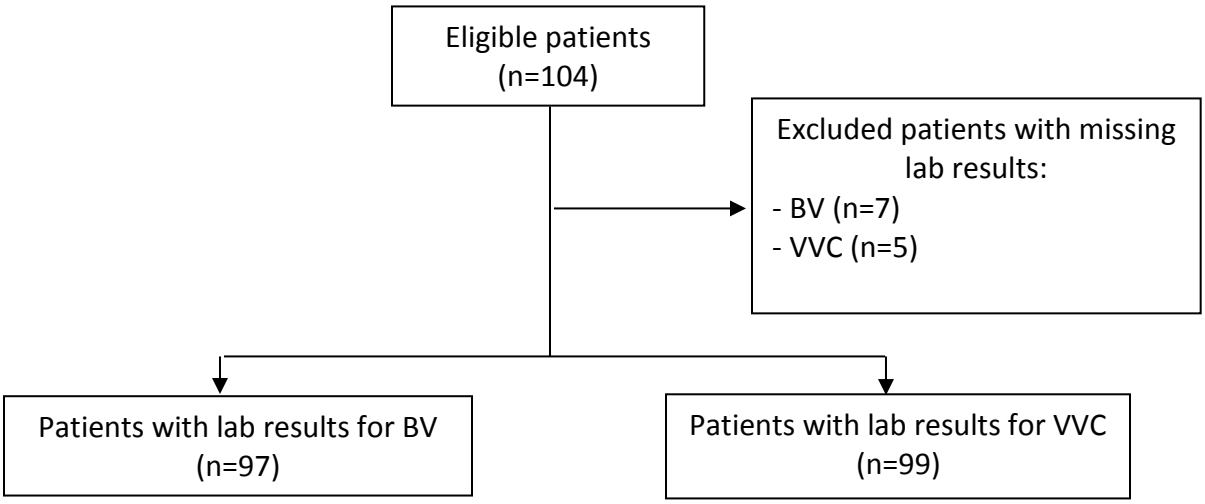

Table 1. Summary of the outcome of self-taken LVS and clinician-taken HVS

		Clinician-taken HVS Not detected	Clinician-taken HVS Detected	Total
VVC	Self-taken LVS Not detected	50	2	52
	Self-taken LVS Detected	4	43	47
	Total	54	45	99
BV	Self-taken LVS Not detected	68	3	71
	Self-taken LVS Detected	3	23	26
	Total	71	26	97

Performance of patient self-taken LVS

For VVC, four patients had a false positive result and two were false negatives, while for BV, three resulted in false positives and three in false negatives (Table 1). Using the clinician-taken HVS as the reference standard, the sensitivities of self-taken vulvovaginal swabs for BV and VVC were 88.5% (95% CI 68.7-97.0) and 95.6% (95% CI 83.6-99.2) respectively, as reported in Table 2. Specificity of self-taken swab for BV and VVC were 95.8% (CI 87.3-99.0) and 92.6% (CI 81.3-97.6) respectively, giving a PPV of 88.5% for BV and 91.5% for VVC.

Table 2. Performance measures for the patient self-taken LVS (clinician-taken HVS as the reference standard)

Infection	**Sensitivity % (95%CI)**	**Specificity % (95%CI)**	**PPV %**	**NPV %**	**Cohen's Kappa (κ)**
BV	88.5 (68.7-97.0)	95.8 (87.3,99.0)	88.5	95.8	0.84 (0.72,0.96)
VVC	95.5 (83.6-99.2)	92.6 (81.3,97.6)	91.5	96.2	0.88 (0.78,0.97)

With regards to assessing the level of agreement of the two diagnostic tests for BV, the number of observed agreements between clinician-taken HVS and patient taken LVS were 91 (93.81% of the observations) and the number of agreements expected by chance were 58.9 (60.76% of the observations). Therefore **κ** = 0.84 for BV which indicates "almost perfect agreement".

For VVC the number of observed agreements were 93 (93.9%) while the number of agreements expected by chance were 49.7 (50.2%), which resulted in **κ** = 0.88 which again indicates "almost perfect agreement".

Symptom data

Data relating the symptoms presented by the patients are summarized in Table 3. The commonest presenting symptom was offensive discharge (n=38; 39%) followed by vulvo-vaginal itching (n=35; 36%). A change in normal discharge was present in 21% (n=21) of patients and 3% (n=3) presented with genital pain.

	BV (N=21)	VVC (N=40)	BV and VVC (N=5)	Negative (N=31)	Total (N=97)
Vulval irritation/itching, n (%)	3 (9%)	22 (65%)	2 (6%)	8 (20%)	35 (36%)
Offensive discharge, n (%)	17 (45%)	6 (16%)	2 (5%)	13 (34%)	38 (39%)
Genital pain (w/ abnormal discharge), n (%)	0 (0%)	2 (67%)	0 (0%)	1 (33%)	3 (3%)
Any other changes to normal discharge, n (%)	1 (4%)	10 (48%)	1 (4%)	9 (44%)	21 (21%)

Looking at the relation between the symptoms and laboratory diagnosis, using the 97 patients for whom we had complete laboratory data for both VVC and BV, of the 35 women who presented with vulval itching/irritation 71% were diagnosed with VVC. Of the 38 women who presented with an offensive discharge 50% were diagnosed with BV.

With regards to the accuracy of symptoms in the syndromic management of symptomatic vaginal discharge, the sensitivity of vulval itching as an indicator of VVC was 0.533 (CI 0.380-0.680), specificity was 0.745 (CI 0.607-0.849) giving a positive predictive value (PPV) of 0.631. The sensitivity of an offensive discharge as an indicator of BV was 0.73 (CI 0.519-0.876) Specificity was 0.733 (CI 0.612-0.827) giving a PPV of 0.5.

Discussion

Summary:

We found an excellent level of agreement between self-taken and physician collected vaginal swabs for the diagnosis of VVC and BV in the study population of women attending our clinic. PPV for VVC was 0.915 and 0.885 for BV, showing promising evidence supporting the use of a self-taken specimen for the diagnosis of VVC and BV.

Self-taken LVS are by no means a reliable substitute for a thorough genital examination but in a time constrained service, combined with patient reluctance to be examined, they appear to have similar detection rates to HVS. This swab could be taken in conjunction with self-taken NAATs for chlamydia, gonorrhoea and trichomonas thus allowing a number of infections to be investigated without the need for a genital examination. This is a particularly attractive screening method for adolescent women where up to 80% prefer self-testing to a pelvic examination (19). We therefore conclude from this study that self-taken LVS appears to be a valid alternative to clinician-taken HVS for detecting VVC and BV infections.

Apart from the very strong agreement between the two swab techniques, an incidental finding which is of interest was the apparent invalidity of typical symptoms with regard to directing the diagnosis. Vulval irritation as an indicator of VVC showed a poor PPV of 0.63. Equally, offensive discharge appeared unreliable for the empirical diagnosis of BV, having a very poor PPV of 0.50. This supports other research which has shown that patient perception of their discharge is not a reliable indicator of likely pathology (9).

Strengths and Weaknesses:

Although the sample size of our study is relatively small, the 95% CI for Cohen's kappa indicates that we are confident that the level of agreement between the two testing methods is at least

substantial (minimum **κ** =0.72 for BV and minimum **κ** = 0.78 for VVC).Therefore we surmise that a further extension of the study would show similar results.

A limitation of this study is that although we tested for trichomoniasis using in-house wet mount microscopy, (the laboratory also used a wet mount screening test) we did not use a nucleic acid amplification test (NAAT) which is more reliable (wet mount sensitivity 45-60% as opposed to NAAT sensitivity 98-99%) (20). We have a low incidence of trichomoniasis in our service of <1% but it is possible that undiagnosed trichomoniasis may have impacted on the figures for symptom correlation with microbiological findings

Another limitation of our study was that the laboratory staff who analysed the swabs were not blinded as to whether the swab was self-collected or physician collected. However we do not think this would have impacted significantly upon the data. All swabs were cultured using the same media and analysed in a way which was unlikely to have been biased.

Comparison with Existing Literature:

Self-taken LVS have been shown in numerous studies to be accurate for the detection of chlamydia, gonorrhoea, and trichomoniasis. Two notable studies conducted in Leeds General Infirmary, showed that self-taken LVS are superior to clinician-taken endocervical swabs for NAAT detection of chlamydia and gonorrhoea (11, 12). A number of studies have also shown self-taken LVS are highly acceptable to patients (21, 22) and are extremely cost effective (23). There are however only a few studies comparing the accuracy of self-taken LVS to clinician-taken HVS for the detection of BV (14,15) and a particular paucity of evidence supporting self-taken LVS for the diagnosis of VVC.

Implications for Research and/or Practice:

In general practice HVS has a place in the first line management of a number of specific clinical scenarios (see text box). In the management of an uncomplicated first presentation of abnormal vaginal discharge it is however of debatable use particularly in the diagnosis of BV (2, 3). The flora typical of BV can be found in up to 40% of asymptomatic women in the UK (6) while *Candida Albicans* is an asymptomatic commensal in 10-20% of women (4). Recommended guidelines for the initial management of abnormal vaginal discharge in primary care rely on a combination of detailed clinical story with an examination which includes the use of PH paper and not necessarily the collection of a HVS (21).

There are a number of clinical scenarios when an HVS is recommended (2). HVS should be part of the management plan in recurrent candidiasis, screening for group B strep infections, post-partum and post instrumentation infections, vaginitis without discharge, symptoms not characteristic of BV or VVC, previous treatment failure and recurrent vaginal discharge (>= 4 cases year). In these instances if vaginal examination for whatever reason is deferred our study suggests that self-taken LVS may be as useful in assisting the diagnosis as clinician-taken HVS.

In the light of the finding of this study we would also suggest that in first presentation of cases suggestive of VVC, a LVS, particularly if it were to be negative, would be helpful in directing the diagnosis.

With regards to trichomonas (TV), infection with this sexually transmitted and may present with symptoms suggestive of BV thereby creating the potential for misdiagnosis (24). Although the treatment for TV is the same as for BV (400mg metronidazole BD for 7 days) TV being an STI requires partner notification. Although our regional rate for TV is low, it is significantly higher in other areas such as London and the West Midlands (25). Interpretation of our study findings should therefore be made with consideration of local rates for TV. In women presenting with recurrent symptoms suggestive of BV trichomonas should be excluded.

Text box:

Instances in primary care where a HVS is recommended for the detection of vaginal flora in women of reproductive age with a vaginal discharge (2):

- Previous treatment failure
- Recurrent (≥ 4 cases/year)
- Pre or post Gynaecological surgery.
- Pre or post termination of pregnancy
- Postnatal or post miscarriage
- Symptoms not characteristic of BV or VVC
- Vaginitis without discharge

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Competing interests: None

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