

ORIGINAL RESEARCH ARTICLE

Strategies for diagnosis of bacterial vaginosis in a resource-poor setting

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Summary: This study evaluated Amsel's criteria, the FemExam[®] card and pH plus amine methods for the diagnosis of bacterial vaginosis (BV) in a resource-poor setting. Two hundred Azerbaijani women participated in a study about reproductive health that included a gynaecological examination and an interviewer-administered survey. Using the WHO syndromic diagnosis algorithm, nearly all women (99%) had abnormal vaginal discharge. The prevalence of BV by Gram stain was 35%; using pH plus amine, the FemExam[®] card and Amsel's criteria, prevalence ranged from 29% to 49%. No behavioural or demographic characteristics were associated with BV as diagnosed by Gram stain. The sensitivity ranged from 0.59 to 0.74 and specificity from 0.65 to 0.92 using the three methods. The pH plus amine test is better than syndromic management protocols, and although it is not the most sensitive or specific of the three methods it will be easiest to implement in resource-poor settings.

Keywords: bacterial vaginosis, diagnostic methods, resource-poor settings, sensitivity, specificity

Introduction

Bacterial vaginosis (BV) is one of the most common causes of abnormal vaginal discharge among women of reproductive age.¹⁻⁵ The prevalence ranges from 17% among women seeking services at family planning clinics to 40% or more among those attending sexually transmitted disease (STD) clinics. BV is associated with a number of adverse pregnancy-related outcomes, including preterm labour, postabortal infection, premature rupture of membranes, amnionitis, chorioamnionitis and postpartum endometritis.^{1,6,7} BV has also been reported to be associated with conditions such as pelvic inflammatory disease, posthysterectomy vaginal cuff cellulitis and acquisition of HIV. Given the high prevalence and gravity of associated morbidity, it is critical to diagnose and treat women appropriately. To do this effectively, however, a sensitive and specific method is needed for diagnosis in settings with different diagnostic capabilities.

Syndromes such as BV, which have heterogeneous aetiologies, are difficult to diagnose. Not all diagnostic strategies can be implemented in all settings. The Gram stain method is not used in

clinical settings because of the time, resources and expertise required. Other strategies, such as syndromic management algorithms, the FemExam[®] (Litmus Concepts Inc., Santa Clara, CA, USA) test and clinical criteria (Amsel's criteria), have been shown to have variable, and sometimes poor, sensitivity and specificity in different settings compared with the Gram stain method.

In resource-poor settings, the World Health Organization (WHO) syndromic management protocol for vaginal discharge is most commonly used to diagnose BV.⁸ Unfortunately, as numerous studies⁹ have documented, this protocol has poor sensitivity and specificity for cervical and vaginal infections. In some settings, the addition of behavioural risk assessment has improved the sensitivity and specificity; however, the syndromic approach is often suboptimal.^{2,9} Behavioural and demographic factors commonly associated with BV include multiple sex partners, earlier sexual debut, douching and prior BV. Other risk factors are often context specific; behavioural assessment schemes are not necessarily useful in settings other than those in which they were developed.

Amsel's criteria for diagnosis based on clinical signs are reported to have better sensitivity and specificity; however, the strategy may require more

resources than are usually available in resource-poor settings.¹⁰ This strategy may under-diagnose BV because not all women present with signs or symptoms. The FemExam[®] card, a rapid test developed for BV diagnosis, assesses the pH and the presence of amines. Previous evaluation of this test compared it with Gram stain and found that it had acceptable sensitivity and specificity.¹¹ This test has not been evaluated in resource-poor settings where it has the potential to improve BV diagnosis.

The objectives of this analysis were to (1) identify behavioural and demographic correlates of BV, and (2) evaluate the sensitivity and specificity of different strategies for diagnosing BV using Gram stain as the gold standard.

Methods

A series of reproductive health fairs in rural Azerbaijan were conducted by a local non-governmental organization (International Association for Family and Society) based in Baku Azerbaijan during the spring and summer of 2001. These events included health education materials and basic clinical services for women in the community. All services were provided free of charge. Women attending the fair were asked if they would be interested in participating in a study about reproductive health. Of the 247 were approached to participate, 200 were eligible and provided informed consent. The majority of those who did not participate were ineligible because they were in menopause. The convenience sample of women between the ages of 18 and 48 who agreed to participate had a gynaecological exam and completed an interviewer-administered survey. As part of the gynaecological examination, reproductive tract infections were identified and treated using WHO syndromic management algorithms.⁸ Vaginal swabs were taken for the FemExam[®] and Gram stain tests for BV.¹²

The survey included basic demographic information and measures of potential risk behaviours associated with reproductive tract infections. The survey was developed in English, translated into Azeri and backtranslated to English to ensure linguistic equivalency. Most survey items used were from a similar study conducted among internally displaced Azeri women in 1999.^{13,14} The study protocol was reviewed and approved by human subjects review boards at the Centers for Disease Control and Prevention and the International Association for Family and Society.

Sensitivity and specificity analysis of the FemExam[®] card and Amsel's criteria (clinical diagnosis) was conducted using Nugent's score as the gold standard. In order to be diagnosed with BV according to Amsel's criteria, women had to have at least three of the criteria (pH>4.5, presence of clue cells, abnormal vaginal discharge and positive amine). Microscopy was performed by a study

physician who had extensive clinical and laboratory experience. Furthermore, the study physician was trained and supervised by two of the principal investigators (JK, FA) as well as a laboratory specialist. The Gram stains were read by an independent lab that was blinded to the clinical presentation of the study participants. To eliminate ambiguity in the data, the denominator for the sensitivity analysis was the number of women whose Nugent's score was ≥ 7 . The denominator for the specificity analysis was the number of women with a Nugent's score between 0 and 3. The sensitivities of the FemExam[®], amine plus pH and Amsel's criteria were compared using relative sensitivity (ratio of two sensitivity estimates) among those with a Nugent's score of 7 or greater.¹⁵ Similarly, the specificities of the three tests were compared among those with a Nugent's score between 0 and 3.

Results

Two hundred women attending reproductive health fairs participated in this study (Table 1).

Table 1 Demographic characteristics

| Variable | No. | Percent |
|--|------|--------------------|
| Currently married | 188 | 94.0 |
| One lifetime sex partner | 194 | 97.0 |
| 11 or more years of education | 56 | 28.0 |
| Ever heard of HIV | 74 | 41.8 |
| Currently employed | 18 | 9.0 |
| Partner currently employed | 55 | 29.3 |
| Relocated because of the conflict with Armenia | 198 | 99.0 |
| Have running water at home | 23 | 12.0 |
| Not enough money for basics in the last 3 months | 115 | 57.5 |
| Homeless in the last 3 months | 9 | 4.5 |
| Physically attacked in the past 3 months | 5 | 2.5 |
| Ever forced to have sex | 29 | 14.5 |
| Forced sex after relocation | 27 | 90.0 |
| Contraceptive use | | |
| Condoms | 13 | 6.5 |
| Oral contraceptives | 8 | 4 |
| IUD | 3 | 1.5 |
| Pregnant at least once | 177 | 88.5 |
| Ever had an abortion | 144 | 78.7 |
| Sought abortion to terminate last pregnancy | 121 | 66.1 |
| Douching behaviour (all women douche) | | |
| Washing inside | 111 | 56.1 |
| Sharing equipment | 154 | 77 |
| | Mean | Standard deviation |
| Income (USD) | 44.4 | 19.9 |
| Current age | 33.9 | 6.6 |
| Time since last forced to have sex (years) | 3.2 | 6.1 |
| Number of live births | 2.94 | 1.33 |
| Number of miscarriages/still births | 0.80 | 1.11 |
| Number of children living | 2.54 | 1.07 |

Table 2 Prevalence of bacterial vaginosis using different diagnostic techniques

| | No. | Percent | Sensitivity | Specificity |
|---|-----|---------|---------------------|---------------------|
| FemExam [®] card | | | | |
| FemExam amine | 70 | 42 | 0.64 (0.52–0.76) | 0.73 (0.64–0.82) |
| FemExam pH | 107 | 64 | 0.94 (0.89–1.00) | 0.57 (0.47–0.67) |
| FemExam card (positive pH and amine) | 49 | 30 | 0.59 (0.47–0.71) | 0.92 (0.86–0.98) |
| Amine (whiff test) | 74 | 45 | 0.67 (0.55–0.79) | 0.71 (0.61–0.81) |
| pH paper | 117 | 70 | 0.97 (0.92–1.00) | 0.48 (0.38–0.58) |
| Both (positive pH and amine) | 66 | 40 | 0.65 (0.53–0.77) | 0.78 (0.69–0.87) |
| Amsel's criteria | 85 | 51 | 0.74 (0.63–0.85) | 0.65 (0.55–0.75) |
| Nugent's Score | | | | |
| 0–3 | 97 | 49 | | 1(ref) [*] |
| 4–6 | 34 | 17 | | |
| 7–10 | 69 | 35 | 1(ref) [*] | |
| Positive on number of diagnostic strategies | | | | |
| 0 | 81 | 41 | | |
| 1 | 53 | 26 | | |
| 2 | 28 | 14 | | |
| 3 | 38 | 19 | | |

*Nugent scores of 4–6 were excluded for analysis of sensitivity and specificity.

Nearly all women had relocated because of the conflict with Armenia (99%). The average age of the women was 34 (range 20–48). Nearly all were married (94%), and reported having one lifetime sex partner (97%). Very few women (9%) or their husbands (29%) were employed. Very few had running water at home (12%). The average household income was equal to US\$44 per month. Approximately 15% of the women reported being forced to have sex at some point in their life; of these nearly all (90%) reported that they had been forced to have sex since relocating because of the conflict with Armenia. None of the demographic or behavioural variables was found to be associated with a Nugent's score of 7 or greater (compared with a normal [0–3] score), Amsel's criteria or the FemExam[®] card.

The prevalence of BV as diagnosed with the FemExam[®] card was approximately 30%, while analysis of the Gram stain data indicated that approximately 35% had BV (Nugent's score of 7 or greater) (Table 2). Using Amsel's criteria, 49% of the women had BV. Approximately one in five women tested positive for BV using all the three diagnostic methods (Nugent's score, FemExam[®] card and Amsel's criteria). Another 14% of the women tested positive for BV using two of the three strategies and 27% were BV positive using only one strategy. Just over 40% of the women were not diagnosed with BV using any of the strategies.

Because all the women (99%) had abnormal vaginal discharge as identified using the syndromic management protocols, this method was not included in the sensitivity analysis. The sensitivity and specificity of the FemExam[®] amine were 0.64 (95% confidence intervals [CI] 0.52–0.76) and 0.73

(95% CI 0.64–0.82), and for the pH tests were 0.94 (95% CI 0.89–1.00) and 0.57 (95% CI 0.47–0.67). The sensitivity for the combined FemExam[®] pH and amine scores was 0.59 (95% CI 0.47–0.71) and the specificity was 0.92 (95% CI 0.86–0.98). The results for the potassium hydroxide amine (whiff) test were similar to those for the FemExam[®] amine test sensitivity (0.67, 95% CI 0.55–0.79) and specificity (0.71, 95% CI 0.61–0.81). Similarly, the results of the pH test (sensitivity 0.97 [95% CI 0.92–1.00], specificity 0.48 [95% CI 0.38–0.58]) were similar to those for the FemExam[®] pH. The sensitivity of the pH plus amine tests was 0.65 (95% CI 0.53–0.77) and the specificity was 0.78 (95% CI 0.69–0.87). Finally, Amsel's criteria had a sensitivity of 0.74 (95% CI 0.63–0.85) and a specificity of 0.65 (95% CI 0.55–0.75).

There was no significant difference in sensitivities of the FemExam[®] and pH plus amine test; however, Amsel's criteria were significantly more sensitive than either FemExam[®] (RSN = 1.24, 95% CI 1.07–1.42) or pH plus amine (RSN = 1.13, 95% CI 1.03–1.23). The FemExam[®] test was significantly more specific than the pH plus amine test (RFP = 2.65, 95% CI 2.04–3.21) or Amsel's criteria (RFP = 4.25, 95% CI 3.68–4.89). The pH plus amine test was significantly more specific than Amsel's criteria (RFP = 1.62, 95% CI 1.35–1.88).

Discussion

The estimated prevalence of vaginitis ranged from approximately 28% to nearly 100% depending on the diagnostic strategy. Based on Gram stain, the gold standard, the prevalence of BV was 35%. The

syndromic management algorithm clearly over-diagnosed using this setting. No behavioural factors were found to be associated with BV as determined by Gram stain, Amsel's criteria or the FemExam[®] card. Nearly all the women reported having one sexual partner (lifetime and last 30 days), being married and having no new partners – and therefore denied behavioural risk factors that have been used in other settings to improve the sensitivity and specificity of the syndromic diagnosis algorithms. Almost all women with positive amine and elevated pH met Amsel's criteria for BV, because most of them also had abnormal vaginal discharge. None of the strategies had both high sensitivity and specificity compared with the Gram stain.

We continue to need a sensitive and specific diagnostic strategy for BV in resource-poor settings. The FemExam[®] card, Amsel's criteria and the combination of amine test plus pH all have benefits over syndromic diagnosis, especially where behavioural risk assessment methods are not informative as was observed in this study. The combination of the amine and pH tests has sensitivity similar to that of the FemExam[®] card, but significantly lower sensitivity than Amsel's criteria. Specificity was significantly greater when pH plus amine was compared with Amsel's criteria; however, it was significantly lower than that of the FemExam[®] card. A diagnostic strategy that uses the pH and amine tests is most likely the best solution in resource-poor settings because, although it is not the most sensitive or specific test, it offers a middle ground on sensitivity and specificity compared with the more expensive (FemExam[®]) and more technologically demanding (Amsel's criteria) techniques. Moreover, this pH and amine diagnostic technique performs better than the syndromic diagnostic algorithm.

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(Accepted 3 September 2003)