Vaginitis in a Gynecologic Practice in Israel: Causes and Risk Factors

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Key words: vaginitis, candida, trichomonas, bacterial vaginosis

Abstract

Background: Vaginal symptoms are a leading reason for a patient to visit her gynecologist. Little is known about the prevalence of the different causes of vaginitis and the risk factors for this entity in Israel.

Objective: To determine the prevalence of the main forms of vaginitis: vulvovaginal candidiasis, bacterial vaginosis, and trichomoniasis, in a gynecologic practice in Israel.

Methods: We evaluated 208 patients presenting with vaginal symptoms to a gynecologic clinic 100 asymptomatic women who attended the clinic for routine check-up served as controls. Demographic, medical and gynecologic histories were obtained, and a pelvic examination was performed in all patients. Vaginal specimens were tested for pH and amine reaction, smeared for Gram-staining and cultured for yeasts and Trichomonas vaginalis. Bacterial vaginitis was diagnosed using the Nugent scoring system. Candida infection was diagnosed by microscopic examination and culture.

Results: Candida spp. was the most common pathogen, documented by microscopy and culture in 35.5% of symptomatic women and 15% of asymptomatic controls (P < 0.001). Detection by culture only (negative microscopy) was documented in 18.7% of symptomatic patients and 15% of controls (P = 0.5). Bacterial vaginosis (Nugent score ≥ 7) was diagnosed in 23.5% of patients and 13% of controls (P = 0.04). Trichomoniasis was present in 8.1% of symptomatic women and 4% of controls (P = 0.1). The main risk factors were antibiotic use for candidiasis and lack of use of oral contraception and condom use for trichomoniasis.

Conclusion: Candida was by far the most common pathogen detected in our population. A statistically significant difference between patients and controls was noted for the prevalence of microscopically diagnosed candidiasis and bacterial vaginosis.

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The purpose of the present investigation was to study the etiology of vaginal symptoms in patients of reproductive age visiting a gynecologic clinic in Israel and to compare the findings with those of asymptomatic women.

Patients and Methods

Patients

Patients were recruited at a gynecologic clinic located in Bat Yam, a town with a population of 150,000 that neighbors Tel Aviv, Israel. Consecutive patients of reproductive age consulting for vulvovaginal complaints (discharge, burning, itching, malodor) were included. Patients with clinical findings suggestive of pelvic inflammatory disease, pregnant patients and those older than 50 years of age were excluded. The control group consisted of asymptomatic women who presented at the same clinic for periodic Papanicolou test or for contraception. Women who had vulvovaginal symptoms in the preceding year or received antibiotics in the preceding month were excluded. A questionnaire covering demographic data, contraceptive use, recent antibiotic use, sexual history, medical history and history of vaginitis was completed for each of the participants, and the symptoms that precipitated the patient’s visit were recorded.

Physical examination and collection of samples

A complete pelvic examination was performed and the findings were recorded. A sample obtained from the outer third of the vaginal wall with a dry cotton wool-tipped swab was tested for pH. Additional specimens of vaginal discharge were obtained from the posterior fornix for amine test, Gram stain and cultures for yeasts and trichomonas. Cervical specimens were obtained for Neisseria gonorrhoeae and Chlamydia trachomatis cultures.

Laboratory procedures

The pH was determined using a pH indicator paper (Macherey-Nagel, Germany) with a pH range of 3.8–5.8. For the amine test (‘whiff’ test) a drop of potassium hydroxide 10% was added to a sample of vaginal discharge. The test was considered positive if the typical fishy odor was produced. A Gram-stained smear was examined by microscopy for the composition of bacterial morphotypes and presence of yeasts and leukocytes. For the diagnosis of bacterial vaginosis the Nugent scoring system was used [6]. This method is based on the quantity of three different bacterial morphotypes: large gram-positive rods, which represent lactobacilli, small gram-variable rods, which represent Gardnerella and...
Bacteroides/Prevotella species; and curved rods, which represent Mobiluncus species. On the basis of these results, the specimen is assigned a score from 0 to 10, with 0–3 as normal, 4–6 as intermediate, and 7–10 as bacterial vaginosis. Specimens for yeast culture were transported to the laboratory in modified Stuart’s medium and plated on Sabouraud dextrose agar, for trichomonas cultures the modified Diamond’s broth was used. Cervical specimens were transported to the laboratory in charcoal transport medium within a few hours and were plated on New York City medium (Hy Laboratories, Rehovot, Israel) for the detection of Neisseria gonorrhoeae. For Chlamydia trachomatis isolation, cervical specimens were initially inoculated into a transport medium (Chlamydia Transwab: Medical Wire & Equipment Co., Corsham, UK) and kept at -70°C until cultured. Cycloheximide-treated McCoy Cells were used for culture.

Statistics
Categorical variables were compared using either Fisher’s exact test or the chi-square test. Student’s t-test was used to compare means between the groups.

Results
A total of 308 women, 208 symptomatic patients and 100 asymptomatic controls, were studied. The two groups were comparable in all parameters tested (Table 1). Vulvovaginal candidiasis defined as positive culture and positive smear was the most common diagnosis, being present in about one-third of symptomatic patients, followed by bacterial vaginosis diagnosed in 25% of patients. Trichomoniasis was diagnosed in 8.1% of patients. All three entities were significantly more common among symptomatic patients than asymptomatic controls (Table 2). Chlamydia trachomatis was isolated in 4 patients (1.9%) and 2 controls (2%). In none of the cases was N. gonorrhoeae cultured. Cases with low concentration of candida in the vagina (detected only by culture but not on microscopy) and cases with intermediate bacterial flora (score 4–6) were equally represented in the two groups (Table 2).

The comparison of the three clinical entities and a group of asymptomatic women with normal findings for various parameters is shown in Table 3. Statistically significant differences were observed in mean age, use of contraceptives and use of antibiotics in the preceding month. The normal controls had the lowest mean age (27.0 ± 8.3 years), while the patients with trichomoniasis were the oldest (34.4 ± 7.2 years). Trichomoniasis was associated with the lowest rate of barrier contraception and oral contraception and the highest rate of no contraception. Use of antibiotics in the preceding month was five times more common in patients with vulvovaginal candidiasis than in those with other

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**Table 1. Demography, method of contraception and sexual activity in patients and controls**

<table>
<thead>
<tr>
<th>Group (No. of cases)</th>
<th>Mean age (yrs) (± SD)</th>
<th>Married (%)</th>
<th>Education (yrs)</th>
<th>Vaginal douching (%)</th>
<th>Contraception IUD/oral/barrier (%)</th>
<th>&gt; 1 partner in preceding year (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n=208)</td>
<td>30.1 (± 8.2)</td>
<td>51</td>
<td>12.5</td>
<td>15</td>
<td>26/34/13.5</td>
<td>13</td>
</tr>
<tr>
<td>Controls (n=100)</td>
<td>30.1 (± 8.2)</td>
<td>59</td>
<td>12.7</td>
<td>10</td>
<td>24/34/9</td>
<td>9</td>
</tr>
<tr>
<td>P value</td>
<td>0.1</td>
<td>0.2</td>
<td>0.4</td>
<td>0.3</td>
<td>0.3</td>
<td>0.4</td>
</tr>
</tbody>
</table>

**Table 2. Etiology of vaginitis in patients and controls**

<table>
<thead>
<tr>
<th></th>
<th>Candida (%) (Pos. culture &amp; smear)</th>
<th>Candida (%) (Pos. culture only)</th>
<th>Bacterial vaginosis (%)*</th>
<th>Altered flora (%)**</th>
<th>Trichomoniasis (%)</th>
<th>Mixed infection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n=208)</td>
<td>74 (35.5)</td>
<td>39 (18.7)</td>
<td>49 (23.5)</td>
<td>29 (13.9)</td>
<td>17 (8.1)</td>
<td>18 (8.6)</td>
</tr>
<tr>
<td>Controls (n=100)</td>
<td>15 (15)</td>
<td>15 (15)</td>
<td>13 (11)</td>
<td>4 (4)</td>
<td>4 (4)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>P value</td>
<td>&lt; 0.001</td>
<td>0.5</td>
<td>0.04</td>
<td>0.5</td>
<td>0.1</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* Nugent score 7–10
** Nugent score 4–6

**Table 3. Demography, sexual activity, contraceptives and antibiotic use according to etiology of vaginitis**

<table>
<thead>
<tr>
<th></th>
<th>Mean age (yrs) (± SD)</th>
<th>Married (%)</th>
<th>Education (yrs)</th>
<th>Vaginal douching (%)</th>
<th>&gt; 1 partner in preceding year (%)</th>
<th>Contraception IUD/oral/barrier (%)</th>
<th>Antibiotic use in preceding month (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vulvovaginal candidiasis (n=68)</td>
<td>29.1 (± 7.9)</td>
<td>52.9</td>
<td>12.2</td>
<td>20.6</td>
<td>11.8</td>
<td>27/9/32/4/14.7</td>
<td>23.5</td>
</tr>
<tr>
<td>Bacterial vaginosis (n=63)</td>
<td>31.9 (± 8.7)</td>
<td>65.1</td>
<td>12.5</td>
<td>14.0</td>
<td>7.0</td>
<td>30.2/20/9/18.6</td>
<td>4.7</td>
</tr>
<tr>
<td>Trichomoniasis (n=20)</td>
<td>34.4 (± 8.7)</td>
<td>65.0</td>
<td>12.3</td>
<td>15.0</td>
<td>5.0</td>
<td>35.2/5.0/5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Normal (n=65)</td>
<td>27.0 (± 8.7)</td>
<td>51.1</td>
<td>13</td>
<td>8.9</td>
<td>9.1</td>
<td>8.9/8.7/8/11.1</td>
<td>0.02</td>
</tr>
<tr>
<td>P value</td>
<td>0.002</td>
<td>0.2</td>
<td>0.2</td>
<td>0.3</td>
<td>0.7</td>
<td>0.03</td>
<td>0.002</td>
</tr>
</tbody>
</table>
diagnoses. The groups did not differ significantly regarding marital status, years of education, vaginal douching, and having more than one sexual partner in the preceding year.

Discussion
In the present study Candida spp. was by no means the dominating organism, isolated in more than a half of the symptomatic patients and detected on Gram-stained smear in about a third of these women. Bacterial vaginosis was diagnosed in approximately a quarter of the symptomatic cases, while T. vaginalis was responsible for the symptoms in less than 10% of the cases. The clinical relevance of these organisms was demonstrated by their higher prevalence in symptomatic patients than in asymptomatic controls.

Although a common condition, identifying the cause of vaginitis remains a challenging task. The clinical presentations of various vaginal conditions are not specific enough to permit establishing the etiologic diagnosis. Even with the optimal diagnostic means (office microscopy, culture) the relationship between symptoms and laboratory findings is not always clear. This is best exemplified by the presence of Candida spp. in the vagina. High concentrations of candida in the vaginal fluid are usually associated with symptomatic infection, whereas vaginal colonization is characterized by low concentrations of the yeast [7]. However, high concentrations (10^5 colony forming units/ml) can be isolated from 10-15% of asymptomatic women [7–8]. On the other hand, about 25% of women with vulvovaginal symptoms will harbor low concentrations of candida [7]. This overlap was observed also in the present study. Although high concentrations of candida, evidenced by positive cultures and smears, were significantly more common in symptomatic patients, they were still present in 15% of asymptomatic women. Low concentrations of candida, which could be demonstrated on culture only, were present in similar proportions in the two groups and were the only finding in 18.7% of the symptomatic patients.

Gram-stained vaginal smear graded ≥ 7 according to the Nugent's scoring system were significantly more common in symptomatic women, confirming the clinical relevance of bacterial vaginosis. The 13% prevalence of the entity in the control group correlates with the results of other studies in symptom-free populations [9,10] and attests to the common occurrence of bacterial vaginosis as an asymptomatic condition.

Because of the duality of expression of the two main causes of vaginitis, the causality between the laboratory diagnosis and the patient's complaints can sometimes be assessed only after a therapeutic trial. Consequently, one should be very cautious when declaring treatment failure solely on the basis of clinical response. It is not uncommon to observe persistence of symptoms despite eradication of the infection, in which case one can conclude that there was no association between the two.

Risk factors significantly associated with vaginal infection were antibiotic use in the preceding month for candidiasis, and lack of oral contraception and barrier method use for trichomoniasis. The association between yeast infection and antibiotic consumption has been demonstrated in several studies [11,12]. The mechanism whereby antibacterial drugs predispose to yeast vaginitis is not as clear as it may seem. Lactobacillus elimination or reduction is not a prerequisite for vaginal yeast proliferation [13]. Actually, both yeast and lactobacillus colonization are estrogen-dependent [14,15], suggesting that the lactobacillus and candida populations should not exhibit an antagonistic relationship. Hence, the interaction between antibiotic use and candida colonization involves other mechanisms rather than bacterial suppression. Although the protective role of consistent condom use with regard to sexually transmitted diseases has been well documented, the inverse relationship between hormonal contraception and trichomoniasis may appear less obvious. It has been suggested that exogenous hormones may inhibit estrogen and androgen receptors in T. vaginalis [16]. We did not observe an association between trichomoniasis and increased number of partners or being single. The mean age of our patients with trichomonal infection (34.3 years) was higher than that observed in American studies (24 years) [5] and similar to European reports [5,17]. One may assume that the majority of the infected women in our study acquired the parasite from their unfaithful husbands. No relationship was noted between vaginitis and vaginal douching or use of an intrauterine device. It is possible that there was an over-reporting of vaginal douching among our study population. We assume that some of the participating women did not distinguish between external genital hygiene and vaginal douching, which is in fact a rare practice in Israel. On the other hand, vaginal douching is a common behavior among American, particularly black, women. Douching may alter the number and the type of microorganisms inhabiting the vagina [18] and has been associated with bacterial vaginosis and pelvic inflammatory disease [19].

Conclusion
Candida spp. appears to be the predominant cause of vaginitis among Israeli women, although the occurrence of the less familiar entity of bacterial vaginosis was not negligible. Trichomoniasis was the most common non-viral sexually transmitted infection. The prevalence of candida colonization and bacterial vaginosis was relatively high among asymptomatic women.

References
People everywhere confuse
What they read in newspapers with news.

A.J. Lisbling, 20th-century journalist for, among others, the New Yorker, who wrote about politics, the media, food, and sports.

Research Projects

The cell adhesion molecules N-cadherin and N-CAM regulate human growth hormone: a novel mechanism for regulating pituitary hormone secretion

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Pituitary growth hormone (GH) secretion is regulated by hypothalamic hormones and by peripheral factors. Cell-cell contact may also have an important role in regulating pituitary hormone expression and secretion. The role of pituitary cell-cell contact-mediated by N-cadherin and N-CAM cell adhesion molecules (CAMs) was studied in regulation of GH secretion. Reverse transcription-polymerase chain reaction (RT-PCR) showed N-cadherin mRNA expression in 8/12 of GH-secreting adenomas compared to 1/7 of PRL-cell adenomas. N-cadherin and N-CAM were similarly expressed in adenomas, and in adult and fetal normal pituitary tissues. The effects of CAM homophilic binding on GH secretion from dispersed human fetal pituitary cultures were studied by manipulating CAM-mediated cell-cell contact using either soluble N-cadherin-Fc or pituitary cells co-cultured with NIH-3T3 cells stably expressing CAMs. CAM stimulation increased GH secretion from pituitary fetal cultures by 40–60% (P<0.05), and also from cultured GH-adenoma cells, by 40–75% (P<0.05). Disrupting N-cadherin homophilic binding by anti-N-cadherin antibody decreased fetal but not tumorous GH secretion by 40% (P<0.05). This study indicates that pituitary cell-cell contact mediated by homophilic interactions between adhesion molecules regulates human GH secretion.

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