Urogenital Symptoms and Pain History as Precursors of Vulvodynia: A Longitudinal Study

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Abstract

Background: We sought to assess vulvodynia incidence and risk factors among those with and without premorbid urogenital symptoms.

Methods: Women’s Health Registry members who completed a baseline assessment in 2004 were sent a 2-year and 4-year follow-up survey containing a validated screen for vulvodynia. Subgroup analysis of vulvodynia incidence rates was performed, and risk factors associated with incidence were assessed.

Results: Of 1037 original enrollees, 723 (69.7%) completed consecutive surveys (initial and 2-year or initial, 2-year, and 4-year), 660 of whom did not have current or past vulvodynia at baseline. Of these 660, 71 (10.8%) first met criteria for vulvodynia within the 4-year period, for an annual incidence rate of 3.1% (95% confidence interval [CI] 2.5-4.0). Baseline strict controls were less likely to develop criteria for vulvodynia diagnosis (annual incidence rate of 1.4%) compared to those with an intermediate phenotype (presence of dyspareunia or history of short-term vulvar pain), for whom the incidence rate was 5.6% (p < 0.001). Risk factors for incident vulvodynia differed between these two groups. Among the strict controls, an increased risk was noted among younger women (incidence rate ratio [IRR] 3.6). For those with an intermediate phenotype, risk was increased among nonwhite women and those reporting pain with or after intercourse (IRR 2.2, 3.4, and 3.1, respectively). In both control groups, incident vulvodynia risk increased among those reporting urinary burning at enrollment (IRR 4.2 and 2.8 for strict and intermediate phenotype controls, respectively).

Conclusions: The annual incidence of vulvodynia is substantial (3.1%) and is greater among women reporting a history of dyspareunia or vulvar pain that did not meet criteria for vulvodynia compared to those without this history, suggesting that generalized urogenital sensitivity may be a common underlying mechanism predating the clinical presentation of vulvodynia.

Introduction

VULVODYNIA IS A DISORDER characterized by hypersensitivity at the vulva or vaginal introitus (vestibule) that typically causes sexual intercourse to be painful or intolerable.1 Its prevalence has been reported to be between 3.1% and 15%.2-5 Limited data are available on the incidence of vulvodynia in the general population5,7 and on the relationship between prior experiences with vulvar symptoms and onset of vulvodynia.

Cross-sectional studies have suggested that vulvodynia is associated with other pain symptoms and with comorbid medical conditions, such as fibromyalgia, chronic fatigue syndrome, recurrent vulvovaginal infections, and yeast infections.6,8-11 However, the cross-sectional study design does not allow differentiation between those symptoms that are precursors to vs. comorbid with vulvodynia. Few prospective data are available.6,7 A prior analysis from this current prospective study after 2 years of follow-up estimated the annual incidence of vulvodynia to be 1.8% among strict controls (defined as those without dyspareunia or a history of vulvar pain)6 and found younger age and a history of pain after intercourse to be associated with the new onset of vulvodynia.6 After 4 years of follow-up, the current analysis reassessed vulvodynia incidence rates among women who did not meet criteria for current or past vulvodynia at enrollment but who might not have been totally asymptomatic (a definition of greater relevance to the general population) and

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evaluated the relationship between the presence of premorbid urogenital symptoms and the onset of vulvodynia during the study period.

Institutional review board approval for this study was obtained from the University of Michigan Medical Human Subjects Committee.

Materials and Methods

In 2004, 1037 members of the University of Michigan’s Women’s Health Registry completed either an online or a written survey regarding the presence of symptoms suggestive of vulvodynia. Further clinical investigation of a subset of those women demonstrated excellent reliability and validity of survey responses for predicting vulvodynia, and no further validation was performed in this study. In 2006 and 2008, follow-up surveys were sent to all women who had participated in the baseline assessment. Women with e-mail addresses were sent links to an online survey (SurveyMonkey.com, Portland, OR), and a written survey was mailed to all women who had no valid e-mail address and to those from whom no completed online surveys were received. A total of 723 (69.7%) women completed the 2-year survey, 660 (63.6%) completed the 4-year follow-up survey, and 573 (55.3%) completed all three surveys.

Participants were assigned to one of four clinical statuses, based on previously validated survey responses. Cases were defined as women having current vulvar pain (at the vaginal opening) that occurred over ≥3 months. Past cases were defined as women who reported previous symptoms of vulvodynia but did not have them at present. Strict control status was assigned based on reporting no current pain with intercourse and no history of vulvar pain lasting ≥3 months. The intermediate phenotype control category was composed of two subgroups: those women who reported pain with intercourse within the past 6 months but no vulvar pain and those who reported having had vulvar pain at some point but did not meet criteria for current or past vulvodynia (typically denying pain occurred for ≥3 months). Those with data at consecutive rounds (initial and 2-year but not 4-year follow-up or initial, 2-year, and 4-year follow-up rounds) were included in the analysis (n = 723, or 69.7% of the initial cohort). Of these, 660 (91.3%) did not screen positive for vulvodynia at the initial round and could be evaluated for new onset vulvodynia over the course of the study.

Descriptive statistics were calculated for all variables. Characteristics (at enrollment) of the 660 women who completed consecutive surveys, compared to those who also did not screen positive for vulvodynia at the baseline but who did not complete consecutive surveys (n = 267), were assessed using chi-square analysis. The annual incidence rate and risk factors for vulvodynia overall and for various diagnostic subgroups were estimated using a negative binomial regression model (generalized linear model), with demographic and premorbid conditions included as independent variables, the logarithm of time (minimum of incidence-free observation time or time until incidence) used as the offset, and the annual incidence rate as the outcome.

Results

Characteristics of the potential participants for this analysis, stratified by whether they completed consecutive surveys, were compared (Table 1). This consisted of the 660 women included in the analysis who filled out consecutive surveys (including the initial and 2-year only [n = 165] or the initial, 2-year, and 4-year surveys [n = 495]) and those who did not (n = 267) (Table 1). Compared to those lost to follow-up, those with consecutive data were more likely to be older and nonwhite and to report higher education and household income. They were also slightly more likely to have an intermediate symptom phenotype, compared to being a strict control, than were those who did not complete consecutive surveys.

Prevalence of vulvodynia

The proportion of participants completing consecutive surveys who met criteria for vulvodynia at the 2-year and the 4-year follow-up were 9.4% and 10.8%, respectively. However, the specific individuals constituting the case or noncase subgroups differed between rounds. For example, of the 573 women completing both the 2-year and the 4-year follow-up rounds, 25 (44.6%) of the 56 cases at the 2-year round were still cases at the 4-year follow-up, with the rest no longer reporting ongoing symptoms.

Incidence of vulvodynia

The incidence rates of vulvodynia, categorized by enrollment case-control classification, are shown in Table 2. Over the 4-year follow-up period, of 660 participants who did not report current or past vulvodynia at the initial survey (ranging in age from 19 to 83 years), a total of 71 (10.8%) developed symptoms of vulvodynia, for an estimated annual incidence rate of 3.1% (95% confidence interval [CI] 2.5, 4.0). The annual incidence rate of vulvodynia among those defined as strict controls at enrollment was 1.4%, similar to that reported previously using a similar definition of “strict control.” We further evaluated the incidence rates over the 4-year period among each of the diagnostic groups, including those with
intermediate symptoms at enrollment who did not meet criteria for vulvodynia (Table 2). The annual incidence rate among those with an intermediate phenotype at enrollment was substantially higher (annual incidence of 5.6%) than that for the strict control group (annual incidence of 1.4/100 women), as shown ($p<0.001$).

**Risk factors for incident vulvodynia**

Table 3 compares the baseline characteristics of those who became incident vulvodynia cases by the time of the 4-year follow-up in contrast to those who remained noncases, for all controls, and also stratified by whether they were strict controls or had an intermediate phenotype at the time of the initial survey. Shown are the results for the multivariable analyses, controlling for age, ethnicity, and income. Among the women in general, new onset vulvodynia was associated with a number of premorbid characteristics at baseline (including younger age [<50], history of a yeast infection in the previous 2 years, pain reported with first tampon use or first intercourse, a history of pain with intercourse or pain after intercourse), with vulvar or urinary burning, with having an intermediate phenotype (as compared to being a strict control), and with a trend noted with genital itching. Among strict controls at enrollment, new onset vulvodynia was less likely in older women ($\geq50$ years) and more likely in those reporting urinary burning at enrollment. Among those with an intermediate phenotype, incident vulvodynia cases were more likely to occur among nonwhite women and among those reporting pain after intercourse or urinary burning or both on their enrollment survey.

**Discussion**

The incidence of vulvodynia, as diagnosed using validated survey-based criteria, is substantial, and occurs over a wide range of ages (23–78 years). However, this incidence rate varies considerably among women who fall into different noncase subgroups. Those categorized as strict controls at enrollment (no dyspareunia or past vulvar pain lasting $\geq3$ months) were less likely to develop vulvodynia (incidence rate 1.4%) compared to those reporting dyspareunia without ongoing vulvar pain or those with a history of vulvar pain not meeting criteria for current or past vulvodynia (incidence rate 5.6%). Given this increased risk, healthcare providers may wish to educate women with these symptoms about the characteristics of vulvodynia, thereby increasing the possibility of earlier identification and treatment should the symptoms progress to those consistent with this disorder.

Data on whether oral contraceptive (OC) use is associated with the presence of vulvodynia are conflicting, with some reports suggesting an association and others, including this study, suggesting none. Few account for whether the OCs were started before or after the development of the vulvar symptoms. We found no association between current use of OCs as was reported at enrollment with new onset of vulvodynia over the 4-year follow-up period.

Risk factors identified included not only those previously suggested, such as pain after intercourse, but also a newly identified risk factor of urogenital symptoms, such as vulvar burning and urinary burning, reported before the onset of vulvar pain meeting criteria for vulvodynia. A history of yeast infections has long been reported to be associated with vulvodynia. History of yeast infections was associated with risk of new onset vulvodynia only among those in the strict control group but not when controlled for age, ethnicity, and income. Because the diagnosis of yeast infections is often made based on symptoms alone or in-office microscopic assessment without culture, the validity of this reported history remains uncertain and needs laboratory confirmation in a longitudinal study.

A history of pain after intercourse and the reported presence of genital symptoms, such as burning with urination, were associated with subsequent onset of vulvodynia among both strict controls and those with an intermediate phenotype. The presence of these symptoms before the diagnosis of vulvodynia suggests that a premorbid state of neuronal hypersensitivity in the introital area may exist that only later meets criteria for clinical vulvodynia.

There are limitations to this study. Validation of case status in the office was conducted previously on a subset of participants at the time of the baseline survey, but no further in-office validation was performed for the 2-year and 4-year follow-up rounds. Based on previous validation studies, the probability of misclassification among a small proportion of participants based on concurrent infection or dermatologic disorders is thought to be small. In addition, although the cohort of women assessed in this series of surveys was not selected from a clinic-based population or from those with genitourinary symptoms, participation in the Women’s Health Registry, from which the women in this study were enrolled, is voluntary and may not represent the population at large.
### Table 3. Assessment of Potential Risk Factors for Subsequent Incident Vulvodynia Among Those Who Were Not Cases or Past Cases at Baseline: Overall and Stratified by Baseline Status (Strict Controls or Having Intermediate Phenotype at Baseline)

<table>
<thead>
<tr>
<th>Demographic data at enrollment</th>
<th>All (n=660)</th>
<th>Strict controls (n=320)</th>
<th>Intermediate phenotype controls (n=288)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 50</td>
<td>41.6</td>
<td>42.8</td>
<td>39.9</td>
</tr>
<tr>
<td>Caucasian</td>
<td>87.8</td>
<td>88.5</td>
<td>86.6</td>
</tr>
<tr>
<td>Married or living as married</td>
<td>59.4</td>
<td>57.5</td>
<td>61.9</td>
</tr>
<tr>
<td>Education level 16 years or more</td>
<td>71.3</td>
<td>70.3</td>
<td>72.6</td>
</tr>
<tr>
<td>Household income ≥ $60,000 or more</td>
<td>54.4</td>
<td>53.7</td>
<td>55.2</td>
</tr>
<tr>
<td>Historical data at enrollment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Using OCs at enrollment</td>
<td>17.5</td>
<td>14.8</td>
<td>21.1</td>
</tr>
<tr>
<td>History of yeast infections</td>
<td>27.4</td>
<td>22.0</td>
<td>34.5</td>
</tr>
<tr>
<td>in previous 2 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain reported at enrollment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain with first tampon</td>
<td>30.5</td>
<td>24.8</td>
<td>37.5</td>
</tr>
<tr>
<td>Pain with first intercourse</td>
<td>26.4</td>
<td>13.5</td>
<td>43.7</td>
</tr>
<tr>
<td>History of pain with intercourse</td>
<td>58.5</td>
<td>36.7</td>
<td>87.8</td>
</tr>
<tr>
<td>Pain after intercourse</td>
<td>28.5</td>
<td>11.3</td>
<td>51.4</td>
</tr>
<tr>
<td>Genital itching</td>
<td>27.1</td>
<td>19.6</td>
<td>37.1</td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>26.6</td>
<td>15.8</td>
<td>29.3</td>
</tr>
<tr>
<td>Vulvar burning</td>
<td>7.6</td>
<td>4.7</td>
<td>14.3</td>
</tr>
<tr>
<td>Urinary burning</td>
<td>8.8</td>
<td>4.2</td>
<td>2.35</td>
</tr>
<tr>
<td>Case status at enrollment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate phenotype (vs. strict control)</td>
<td>43.5</td>
<td>4.7</td>
<td>14.3</td>
</tr>
</tbody>
</table>

*a* Incidence rate ratio (IRR). Multivariable analysis using a negative binomial regression model, controlling for age (≥50 vs. younger), ethnicity (white vs. other), and income level (household income ≥ $60,000).

*b* Did not converge.

OC, oral contraceptive.
Conclusions

This 4-year follow-up study of women volunteers in a Women’s Health Registry indicates that the annual incidence of vulvodynia over time is approximately 3% and that a new onset of symptoms of vulvodynia is more likely to develop in women with intermediate symptoms of dyspareunia or with a history of short-term vulvar pain than in those denying this history. Further, women with new onset vulvodynia frequently have a premorbid history of nonspecific urogenital symptoms that may suggest neuronal hypersensitivity, which may allow detection of those at increased risk for subsequent vulvodynia.

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Disclosure Statement

No competing financial interests exist.

References


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