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Depression and Posttraumatic Stress Disorder Among Women with Vulvodynia: Evidence from the Population-Based Woman to Woman Health Study

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Background: Psychological disorders may affect the pain experience of women with vulvodynia, but evidence remains limited. The present study aimed to describe the magnitude of the association of depression and posttraumautic stress disorder (PTSD) with the presence of vulvodynia in a nonclinical population from southeastern Michigan.
Methods: Baseline data from 1,795 women participating in the Woman to Woman Health Study, a multiethnic population-based study, was used for this analysis. Validated screening questionnaires were conducted to assess vulvodynia, depression, and PTSD. Modified Poisson regression models with a robust variance estimation were used to estimate prevalence ratios (PR) and their 95% confidence intervals (CI) for the association between vulvodynia status and two mental health conditions, depression and PTSD.
Results: In the adjusted models, women who screened positive for depression had a 53% higher prevalence of having vulvodynia (PR = 1.53; 95% CI: 1.12, 2.10) compared with women who screened negative for depression. Women who screened positive for PTSD had more than a two-fold increase in the prevalence of having vulvodynia (PR = 2.37; 95% CI: 1.07, 5.25) compared with women who screened negative for PTSD.
Conclusions: The increased prevalence of vulvodynia among those screening positive for depression or PTSD suggests that these disorders may contribute to the likelihood of reporting vulvodynia. Alternatively, vulvodynia, depression, and PTSD may have a common pathophysiological and risk profile. Prospective studies are needed to improve our understanding of the temporal relation between mental health conditions and vulvar pain.

Introduction

Vulvodynia, a chronic pain syndrome associated with burning, stinging, irritation, or sharp vulvar pain, has a prevalence in the United States of 7%–10%.[1,2] Pain presentation varies and may be described as spontaneous, provoked by stimulation (i.e., intercourse or tampon use), or both.[1,3] While some studies have documented that women with vulvodynia report a poor quality of life[4,5] and suffer from psychological distress manifested as anxiety and depression,[6–10] evidence of an association between vulvodynia and mental health outcomes remains limited.

Pain is a complex perceptual phenomenon that is modulated by sensory, psychological, and social influences.[11] Data suggest symptoms of physiological arousal (e.g., racing heart, sweating palms, dizziness) and experiencing negative thoughts and emotions—common symptoms in anxiety and depression disorders—may be associated with the maintenance or exacerbation of symptoms of vulvar pain.[7,12–14] Likewise, one or more aspects of the pain experience (e.g., physiological arousal, pain-related catastrophizing, avoidance of physical exertion) may exacerbate clinically significant symptoms of anxiety and depression.[15] As such, it is plausible that the pathway between vulvodynia and psychological disorders such as anxiety, posttraumatic stress disorder (PTSD), and depression is bidirectional. A cycle of symptoms associated with anxiety, depression, PTSD, and pain may perpetuate distress and functional disability.[11,15] Alternatively, pain and psychological disorders may share an etiologic pathway or common susceptibility.[15]

Women with vulvodynia may have greater brain activation in regions of the central nervous system that are associated with pain and sensory processing.[16] In particular, activation in the insula, a sensory integration region involved in pain and sensory processing, has been found to be associated with anxiety disorders such as PTSD,[17] as well as vulvar pain.[16–18]

Serotonin and norepinephrine are neurotransmitters that have been implicated in the underlying pathophysiology of

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chronic pain and are known to be associated with anxiety and depressive disorders.[19–21] Recognizing that anxiety and depression cause a significant burden of morbidity and disability[22,23] and that the nature of the interrelationship between vulvar pain and mental health remains unclear, the aim of this paper was to describe the magnitude of the association between PTSD and/or depression and the presence of vulvodynia among a racially/ethnically diverse population-based sample of women.

Materials and Methods

Data source and participants

This cross-sectional study was conducted using data from the Woman to Woman Health Study, which was approved by the University of Michigan Medical Institutional Review Board. As previously described,[24] the Woman to Woman Health Study (2008–2013) was designed to determine the prevalence of vulvodynia among a multiethnic population-based sample of women from four counties in southeastern Michigan. Women aged 18 and older were recruited using random digit dialing by the Survey Research Center in the Institute of Social Research at the University of Michigan. Participants were asked to complete an online or written survey within 2 weeks of enrollment, and follow-up surveys repeated every 6 months for 3 years. Informed consent was obtained at the time of the telephone recruitment call and again with each subsequent survey.

This analysis included data from the baseline survey ($n = 2,277$). The questionnaire included previously validated screening questionnaires to assess vulvodynia,[25] depression,[26,27] and PTSD,[28] as well as information on sociodemographic characteristics and reproductive health history.[25] A total of 123 respondents were excluded due to missing screening data for vulvodynia status ($n = 84$) or depression ($n = 39$). We restricted the analysis to women aged 18–65 years old, as data in women older than 65 years was sparse, yielding a final sample of 1,795 participants.

Measures

We used a previously validated screening instrument of self-reported genital symptoms of vulvodynia with a sensitivity of 81.8% and specificity of 96.6% when compared with clinical examination.[25] Women were classified into one of three vulvodynia status categories: vulvodynia case, short-term or past vulvar symptoms not meeting criteria for current vulvodynia, and women without vulvar symptoms. A woman screened positive for vulvodynia if she reported pain at the introitus (opening of the vagina), had vulvar symptoms that were provoked (e.g., sexual intercourse or tampon use) or unprovoked, and whose symptoms had lasted a minimum of 3 months. Women with similar vulvar pain symptoms or dyspareunia that were not current or had not been present for at least 3 months were classified as having short-term or past vulvar symptoms. The no vulvar symptom group was defined as women with no history of vulvar pain lasting 3 months or longer, and no current vulvar pain or pain with intercourse.

The Patient Health Questionnaire depression scale (PHQ-8), a standardized and validated instrument, was used to screen for current depression.[26,27] This screening scale asks about eight of the nine criteria on which the Diagnostic and Statistical Manual, Fourth Edition, (DSM-IV) diagnosis of depressive disorders is based.[29] Each item asks patients to indicate the frequency with which they experienced the symptom during the 2 weeks before the interview, scored on a four-point Likert scale from ''not at all'' to ''every day or nearly every day.'' A PHQ-8 score of ≥ 10 has 88% sensitivity and 88% specificity for major depression[30] and typically represents clinically significant depression.[31,32]

PTSD was defined as positive, suggestive, or negative as assessed by the primary care PTSD screen.[28] This instrument consists of four items that assess the presence of the main PTSD symptom clusters (intrusive experiencing, avoidance behaviors, hypervigilance, and emotional numbing). Participants receive one point for each item endorsed. A score of three or more has demonstrated sensitivity and specificity for identifying individuals diagnosed with positive PTSD in primary care (78% and 87%, respectively) or having clinically significant PTSD symptoms,[28,33] A score of two is considered suggestive of PTSD.

The following covariates included in this analysis were theory driven.[7,12,34–36] and based on our prior analyses of the prevalence and incidence of vulvodynia:[1,24] age in years, self-reported race/ethnicity (white, African American, Hispanic, and other), marital status or living with a partner (yes/no), sexual intercourse within the past 6 months (yes/no), and education (high school or less, some college, and graduated college).

Statistical analysis

We calculated frequencies and conducted bivariate analyses with cross tabulations using chi-squares and *t*-tests to assess associations between depression, PTSD, and covariates with vulvodynia status. Unadjusted and adjusted modified Poisson regression models with a robust variance estimation were used to estimate prevalence ratios (PRs) and their 95% confidence intervals (CI)[37] for the association between vulvodynia status and the two mental health conditions (depression and PTSD). This statistical approach was chosen because it is considered to be a direct and less biased approach to estimating the PRs. We fit separate binary modified Poisson regression models,[38,39] one model for women with vulvodynia and another one for women with short-term or past vulvar symptoms defining women without vulvodynia as the referent group. Adjusted models included both depression and PTSD as well as the covariates specified above. We also evaluated the potential interaction between depression and PTSD. All analyses were performed using SAS version 9.2 (SAS Institute, Inc., Cary, NC) with PROC GENMOD and the robust variance estimator provided by the REPEATED statement that uses the method of generalized estimating equations to estimate the model and give a proper estimate of the standard error of the PRs.

Results

A total of 221 (12.5%) of the 1,795 women screened positive for vulvodynia, and an additional 609 (33.9%) reported short-term or past vulvar symptoms. Table 1 presents the characteristics of the study population stratified by vulvodynia status. The mean age of women in the study was 44.6 years (standard deviation, SD = 12.74), most were white (73.6%), married (68.0%), and had had sexual intercourse in the last 6 months (73.3%). Slightly more than half of the population had graduated from college (51.9%) and had household income

Table 1. Sociodemographic Characteristics of 1,795 Women Aged 18–65 Years by Vulvodynia Status: The Woman to Woman Health Study

Characteristics	*Total* n *(%)*	*Women with vulvodynia* n *(%)*	*Women with short-term or past vulvar symptoms* n *(%)*	*Women without vulvodynia* n *(%)*	p
Total	1,795	221 (12.5%)	609 (33.9%)	965 (53.8%)	
Race and Ethnicity					
White	1,321 (73.6)	179 (81.0)	464 (76.2)	678 (70.3)	0.0001
African-American	325 (18.1)	21 (9.5)	94 (15.4)	210 (21.8)	
Hispanic	50 (2.8)	8 (3.6)	22 (3.6)	20 (2.1)	
Other	99 (5.5)	13 (5.9)	29 (4.8)	57 (6.0)	
Education					
High school or less	426 (23.8)	45 (20.4)	132 (21.7)	249 (25.8)	0.05
Some college	437 (24.4)	50 (22.6)	141 (23.2)	246 (25.5)	
Graduated college	931 (51.9)	126 (57.0)	336 (55.2)	469 (48.7)	
Income[a]					
>60,000	892 (57.0)	118 (60.2)	336 (61.0)	438 (53.6)	0.02
≤60,000	672 (43.0)	78 (39.8)	215 (39.0)	379 (46.4)	
Married					
Yes	1211 (68.0)	174 (79.1)	426 (70.5)	611 (63.9)	<0.0001
No	570 (32.0)	46 (20.9)	178 (29.5)	346 (36.2)	
Had sexual intercourse in the past 6 months					
Yes	1287 (73.3)	173 (79.4)	494 (82.2)	620 (66.1)	<0.0001
No	470 (26.8)	45 (20.6)	107 (17.8)	318 (33.9)	
Screened positive for depression					
Yes	248 (13.8)	46 (20.8)	76 (12.5)	126 (13.1)	0.005
No	1,547 (86.2)	175 (79.2)	533 (87.5)	839 (86.9)	
Screened positive for PTSD					
Yes	229 (12.8)	44 (19.9)	93 (15.3)	92 (9.5)	<0.0001
Suggestive	156 (8.7)	25 (11.3)	64 (10.5)	67 (6.9)	
No	1,410 (78.6)	152 (68.8)	452 (74.2)	806 (83.5)	

[a]Income data missing in 231 cases.
PTSD, posttraumatic stress disorder.

greater than $60,000 per year (57.0%). The mean age was 45.0 (standard deviation [SD] = 12.37) for women with vulvodynia, 43.0 (SD = 12.53) for those with short-term or past vulvar symptoms, and 46.0 (SD = 12.8) for those without vulvodynia. Women without vulvodynia were more likely to be African American and less likely to graduate from college or to have incomes greater than $60,000 a year, to be married or report having had sexual intercourse in the past 6 months.

A total of 13.8% of the women screened positive for depression, and 13.0% screened positive for PTSD. Women with vulvodynia were more likely to screen positive for depression (20.8%) than women with short-term or past vulvar symptoms (12.5%) and women without vulvodynia (13.1%). Women with current vulvodynia were most likely to screen positive for PTSD (20.0%) than women with short-term or past vulvar symptoms (15.3%), and women without vulvodynia (9.5%). Among women with vulvodynia, 12.0% of women screened positive for both depression and PTSD (data not shown).

Results from the crude and adjusted modified Poisson regression models are presented in Table 2. After adjustment for race/ethnicity, marital status, and sexual intercourse in the past 6 months, prevalence ratios comparing women with current vulvodynia to women without vulvodynia remained significantly elevated for both PTSD and depression. In the adjusted models, women who screened positive for depression had a statistically significant higher prevalence of current vulvodynia (PR = 1.53; 95% CI: 1.12, 2.10) compared with women who screened negative for depression. Women who screened positive for PTSD had a statistically significant doubling in the prevalence of current vulvodynia (PR = 2.37; 95% CI: 1.07, 5.25) compared to women who screened negative for PTSD. The prevalence of current vulvodynia was also significantly higher (PR = 1.54; 95% CI: 1.04, 2.29) among women with suggestive PTSD than among women who screened negative for PTSD. The prevalence of having short-term or past vulvar symptoms were also significantly elevated among women who screened positive for PTSD (PR = 1.62; 95% CI: 1.07, 2.44) but not among women who screened positive for depression (PR = 0.85; 95% CI: 0.69, 1.06) compared to those who screened negative for these conditions respectively. When we included an interaction term for depression and PTSD in each model, the interaction was not statistically significant (data not shown).

Discussion

Our results indicate a strong association between screening positive for PTSD or depression and screening positive for vulvodynia in this multiethnic population-based study. While it is well documented that individuals with depression and/or PTSD have a significant increase in various pain conditions.[11,15,18,40,41] little research has addressed this question among women with vulvodynia.[7,12] We found that women who

Table 2. Unadjusted and Adjusted Estimates of Prevalence Ratios for Vulvodynia Status and Mental Health Conditions (Depression and PTSD) from the Woman to Woman Health Study

	Unadjusted models[a]				*Adjusted model*[b]			
	Vulvodynia		*Short-term or past vulvar symptoms*		*Vulvodynia*		*Short-term or past vulvar symptoms*	
Mental health condition	*Prevalence ratios*	*95% Confidence interval*	*Prevalence ratios*	*95% Confidence interval*	*Adjusted prevalence ratios*	*95% Confidence interval*	*Adjusted prevalence ratios*	*95% Confidence interval*
Screened positive for depression[c]	1.64***	1.22–2.20	0.89	0.73–1.09	1.53**	1.12–2.10	0.85	0.69–1.06
PTSD screening[d]:								
Suggestive positive for PTSD	1.49*	1.01–2.19	1.28*	1.04–1.57	1.54*	1.04–2.29	1.27*	1.03–1.56
Screen positive for PTSD	2.21*	1.01–4.81	1.64*	1.09–2.46	2.37*	1.07–5.25	1.62*	1.07–2.44

[a]Unadjusted models were analyzed as separate models for depression and PTSD. The models compared vulvodynia with women without vulvodynia (reference).
[b]Adjusted model includes depression, PTSD, and race/ethnicity, marital status, education, and sexual intercourse in the past 6 months. The model compared vulvodynia with women without vulvodynia (reference).
[c]Women who screened negative for depression are the referent.
[d]Women who screened negative for PTSD are the referent.
*$p \le 0.05$, **$p \le 0.01$, ***$p \le 0.001$.

screened positive for PTSD had more than a two-fold increase in the prevalence of screening positive for vulvodynia, while women who screened positive for depression or suggestive PTSD had a 50% increase in the prevalence of having this gynecological pain condition.

A previous community-based case-control study reported antecedent anxiety and depressive disorders were associated with vulvodynia using DSM-IV criteria and a structured clinical interview (SCID).[7] These authors also reported that vulvodynia was associated with subsequent risk of anxiety and depression, suggesting a possible bidirectional relationship and/or a common risk profile. However, establishing definitive dates of onset of vulvodynia is difficult and subject to recall bias, a limitation of the case-control approach. A clinical study of vulvodynia patients reported that anxiety and depression scores, based on the Symptom Checklist 90 Revised, were modestly correlated with pain severity.[34] Our findings are consistent with these previous findings.[7,12,34] Ours is the first paper to consider PTSD as a potential risk factor and suggests that depression and PTSD are independently associated with the prevalence of having vulvodynia. These findings would be consistent with the hypothesis that depression and/or PTSD may contribute to the risk of vulvodynia but would also be consistent with these disorders having a common pathophysiology and risk profile. Further research is needed to clarify the temporal relationship between these conditions.

Relatively little is known about the mechanisms underlying the relationship between anxiety disorders and pain conditions, but it is well recognized that PTSD and chronic pain share a number of symptoms (e.g., anxiety and hyperarousal, avoidance behavior, emotional lability, and somatic focus).[11] Similarly, both PTSD and chronic pain are multidimensional constructs comprising symptom clusters in the cognitive, behavioral, and physiological domains.[11]

Clinical and experimental evidence suggest that the experience of emotional trauma in and of itself may relate to significant differences in the functioning of emotional processing circuits. PTSD and depression can be triggered by stressful life events[42–44] that are characterized by activation in the physiological and neuroendocrine systems.[45–47] Increased anterior insula activation is commonly observed in anxiety and PTSD[18] and has also been reported in patients with vulvar pain.[16] Evidence suggests that stress can also trigger the neuroinflammatory system in the brain, and inflammatory mediators such as cytokines (potent modulators of behavior and affect) that can induce depressive symptoms are also involved in the process of pathological pain.[40,48–50]

Investigations into chronic musculoskeletal pain and the co-occurrence of PTSD suggest that physiological, affective, and behavioral components of PTSD may maintain or exacerbate symptoms of pain.[41] Likewise, cognitive, affective, and behavioral components of chronic pain may maintain or exacerbate symptoms of PTSD.[15]

An important limitation of this analysis is the cross-sectional design, and hence the temporal relationship between vulvar pain and the psychological conditions (depression and PTSD) cannot be established. While we used validated screening instruments with strong psychometric properties to assess depression and PTSD, these instruments only measure current mental health status. We also lacked information from clinical structured interviews—the gold standard—to assess these disorders. Furthermore, it is possible that women with vulvar pain may be more likely to report symptoms of depression and PTSD compared with women without vulvar pain. While we cannot precisely determine the extent to which differential reporting might bias our results, such misclassification may lead to an overestimation of the prevalence ratio estimates. However, the direction and magnitude of the associations we observed are consistent with previous studies.[5–7,12] Misclassification of vulvodynia status is also possible since cases of vulvodynia were not clinically confirmed. However, we used a validated screening questionnaire, with high sensitivity (81.8%) and specificity (96.6%) when compared with clinical examination.[25] We cannot rule out residual confounding related

to unmeasured factors such as inflammation, childhood victimization, and affect-based chronic stressors that may be associated with vulvodynia status and mental health outcomes (depression and PTSD).[36,40,51]

Despite these limitations, our study has important clinical and public health implications. The prevalence of vulvodynia was more than two-fold higher among women who screened positive for PTSD than among other women in this population-based study. Given the association between vulvar pain and these mental health disorders, a holistic approach to the treatment of women with vulvodynia may be advantageous. Beyond established pharmacological treatments, cognitive behavioral therapy (CBT) and the use of psychological techniques such as relaxation and stress management might be useful. An example of this approach is mindfulness-based cognitive therapy,[52] an evidence-based program on stress reduction for coping with stress, chronic illness, or pain that enables the patient to increase her awareness and facilitate early recognition of any recurring thought pattern that may be associated with depressive symptoms, anxiety, and/or pain.[52–54] Support for the efficacy of cognitive behavioral therapy for the treatment of women with vulvodynia has been investigated in two uncontrolled[55,56] and two randomized clinical trials.[57,58] In these studies, women with vulvodynia in the CBT condition had a 21%–42% decrease in pain severity.[57,58] CBT, relative to supportive psychotherapy, resulted in significantly greater improvement in pain severity during physician examination ($p=0.014$), and greater improvement in sexual function ($p=0.034$), from pretreatment to posttreatment.[58]

In summary, this paper documented a strong association between PTSD and the risk of having vulvodynia and a moderate association between depression and the risk of having vulvodynia. A better understanding of the temporal relationships between vulvar pain and these mental health conditions will help to advance research in this area. Improving our knowledge of how stressful life events influence risk of vulvar pain, depression, and PTSD may be a fruitful area for future research. Further research on the interconnection between the neurobiological pathways that involve vulvar pain, PTSD, and depression is warranted. Research on treatment approaches that address both the pain component as well as any associated psychological conditions may also improve the quality of life of women with vulvodynia and ameliorate the profound impact that PTSD, depression, and vulvar pain have on women's lives.

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Author Disclosure Statement

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