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Study on the prevalence and factors associated to vulvodynia in Spain

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ABSTRACT

Objective: To study the prevalence and epidemiological characteristics of women with vulvodynia. To assess the risk factors associated to the disease.
Study design: A cross-sectional study was made in which questionnaires were anonymously and confidentially distributed to Spanish women over 18 years of age between April 2016 and September 2017. The questionnaires were distributed by e-mail and through social networks, women's associations and specific websites. This type of questionnaire has been validated and used in many studies of this kind. The women answered questions referred to epidemiological aspects, demographic parameters, medical history, the presence of vulvodynia, associated factors, and comorbidities.
Results: A total of 684 questionnaires were completed. The prevalence of vulvodynia was 6.6% (45 women). Thirteen percent (95 women) had experienced vulvodynia at some point in life. The factors associated to vulvodynia were prior vaginal deliveries ($p = 0.001$), vulvovaginal candidiasis ($p < 0.001$) and urinary tract infections ($p < 0.001$). Other pain syndromes such as fibromyalgia ($p = 0.012$), painful bladder syndrome/ interstitial syndrome ($p < 0.001$), temporomandibular joint pain ($p = 0.021$), coxofemoral pain ($p = 0.001$) or headache ($p = 0.001$) have also been associated to vulvodynia.
Conclusions: The prevalence of vulvodynia in Spain is similar to that found in other countries. Many factors are involved in its development and persistence, particularly the presence of other pain syndromes and recurrent infections that could trigger complex inflammatory reactions.

Introduction

In 2015, the International Society for the Study of Vulvovaginal Disease defined vulvodynia as vulvar pain lasting at least three months, with no clearly identifiable cause, but with potentially associated elements including psychological, genetic, inflammatory or neuroproliferative factors [1]. This definition modifies the terminology and classification of 2003, which defined vulvodynia as vulvar pain lasting at least three months and mainly described as burning pain occurring in the absence of relevant clinical findings or neurological disorders [2]. The new definition assigns a multidimensional character to vulvodynia, in which different potential factors have been studied as being strongly or weakly associated to the disease. This situation would therefore change the management of vulvodynia, with the possibility of acting upon these factors on a multidisciplinary basis.

The estimated prevalence of vulvodynia in the United States is 7–8%. Up to 13 million women may have experienced the disorder at some point in life [3–5]. In European countries such as Portugal, the estimated prevalence is 6.5% [6]. There are currently no studies on the prevalence of the disease in Spain.

Vulvodynia is associated to numerous disorders, including physical disability, limitation of daily activities, sexual dysfunction and decreased quality of life [23,24], as well as to other psychological alterations such as anxiety and depression [7,8]. The estimated annual cost of vulvodynia management in the United States is approximately 31–72 billion USD, without considering the costs of the psychological burden involved [5].

Vulvodynia has been recognized as a major health problem, and given the lack of data in Spain, we carried out a study whose primary objective was investigate the prevalence and epidemiological characteristics associated to vulvodynia in this country and as secondary objective assess the potential factors associated to this disease.

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Materials and methods

A cross-sectional study was made between April 2016 and September 2017 using standardized and validated vulvodynia questionnaires. These questionnaires have been previously validated by Reed et al. [9] for the diagnosis of vulvodynia, and have been used in prevalence of vulvodynia studies in the US and Portugal [3,4,6]. The questionnaires were distributed anonymously and confidentially to women over 18 years of age and living in Spain by e-mail among the contacts of the authors, through women's associations, midwives, social networks and websites.

Women who agreed to participate in the study were included after giving informed consent at the start of the online form. We excluded those women who did not agree to participate, that were receiving cancer treatment, and those with degenerative neurological diseases that could interfere with the vulvodynia symptoms. The participating women answered questions about epidemiological aspects, demographic characteristics, obstetric and gynecological history, the presence of current or past vulvodynia, associated disorders, duration of vulvodynia symptoms, and comorbidities.

Current vulvodynia was considered when vulvar pain, burning sensation and/or discomfort was reported currently and for more than three months. Past vulvodynia was considered when the woman had experienced such vulvodynia symptoms for more than three months previously but not currently.

The study was approved by the Ethics Committee of Hospital Clínico San Carlos (Madrid, Spain), and complied with the national and European regulations on clinical studies, and with the international ethical recommendations on research.

Statistical analysis

Qualitative variables were expressed as frequencies and percentages. Continuous variables were expressed as the mean ± standard deviation. Normal data distribution was assessed using the Kolmogorov-Smirnov test. Associations between qualitative variables were analyzed with the chi-squared test or with the Fisher exact test when the former could not be applied. Associations between quantitative variables with two categories were explored using the Student *t*-test for independent samples in the case of normal data distribution, and using the Mann-Whitney *U* test if otherwise. Lastly, the independent variables associated with the presence of vulvodynia were studied using a multivariate logistic regression model, calculating the odds ratio (OR) and 95% confidence interval (95%CI). In all cases, statistical significance was considered with $p < 0.05$. The SPSS version 22.0 statistical package was used throughout.

Results

A total of 692 questionnaires were received, of which 8 were excluded from the analysis: two because of inconsistencies in answering, and 6 due to missing data. A total of 684 questionnaires were thus included and analyzed.

The baseline characteristics of the participants, as well as the comparative characteristics of the women with current or past vulvodynia versus those without vulvodynia are shown in Table 1.

The mean age was 39.1 ± 10.4 years (range 18–71), and the vast majority of the women were Caucasian (n = 681; 99.6%).

Overall, 140 women with vulvodynia (current or past) were identified. The prevalence of current vulvodynia in the total population was 6.6% (45 women). Ninety-five women (13.9%) claimed to have experienced past vulvodynia. The mean age of the 140 women with current or past vulvodynia in our study was 40.5 ± 11.7 years. Of these women, 98 (67.9%) consulted a physician and 21 (15%) consulted three or more professionals.

A higher prevalence of vulvodynia was associated in women with previous vaginal deliveries ($p = 0.011$), lower educational level ($p = 0.005$), chronic urinary tract infections ($p < 0,001$), repeated candidiasis ($p < 0.001$) and history of vulvar condyloma ($p = 0.007$).

Urinary incontinence was also associated to vulvodynia ($p = 0.002$), which developed in three of the four women subjected to surgery for incontinence ($p = 0.029$).

Other diseases and painful syndromes were associated with vulvodynia, such as fibromyalgia ($p = 0.006$), coxofemoral joint pain ($p = 0.013$), temporomandibular joint pain ($p = 0.021$), painful bladder syndrome/ interstitial cystitis ($p < 0.001$), headache ($p = 0.001$) and scoliosis ($p = 0.008$)

In the multivariate analysis, the variables independently associated to vulvodynia were seen to be age > 47 years (OR = 2.1, 95%CI [1.3–3.4]), four or more episodes of candidiasis (OR = 2.2, 95%CI [1.5–3.4]), four or more urinary tract infections (OR = 1.7, 95% CI [1.1–2.6]), coxofemoral joint pain (OR = 1.8, 95%CI [1.1–3.2]) and a history of headache (OR = 1.8, 95%CI [1.2–2.3]) (Table 2).

Discussion

The prevalence of current vulvodynia in our study was similar to other countries [3,4,6]. However, the prevalence of past vulvodynia was slightly greater than in other studies, which estimated a 9,5% of prevalence [6]. These differences are because that studies defined vulvodynia as vulvar discomfort lasting more than 6 months instead of three months as has been defined in our study. Harlow and Stewart [5], in a sample of 4915 women found up to 16% of past vulvodynia [5].

Latin american women have been found to suffer more vulvodynia than the rest of ethnic groups [10], with an estimated relative risk of developing vulvodynia of 1.4 when compared with Caucasian or black women [4]. Our data were unable to confirm this observation, since we only enrolled a single latin American woman who reported past, but no current vulvodynia.

Our study showed a clear association between recurrent Candida infection and vulvodynia. Some studies have related urogenital infections to vulvodynia [6,12]. It is known that the inflammatory response that such infections produce could be the first triggering factor leading to pain. However, antifungal therapy has not been found to improve vulvodynia, which would imply that Candida infection, by itself, is not present in the following stages of vulvodynia.

In this context, candida infection could induce changes in the vaginal microbiota, with an abnormal production of cytokines - thereby implicating an altered immune response and microbiota in the etiopathogenesis of vulvodynia [11,13].

The role of human papilloma virus (HPV) and condylomas in vulvodynia is not clear. Sonnendecker et al. [14] found HPV infection in almost 80% of the vulvar biopsies in women with vulvodynia but no condylomas. Subsequent studies have associated the history of vulvar condylomas with an increased vulvodynia [12,27]. However, other studies have found no relationship between condylomas and vulvodynia [6]. Some authors have suggested that the relationship is not explained by the presence of condylomas but by the treatment applied to them [15]. We did observe a relationship between the presence of condylomas and vulvodynia ($p = 0.007$). This association could be due to changes in the vaginal microbiota influencing HPV contagion and persistence [26].

The data relating genital herpes to vulvodynia are contradictory. We found no association between vulvodynia and a history of genital herpes. This is consistent with some studies [12], but contrasts with others that report a strong association [6]. In our

Table 1
Baseline characteristics of the women with and without vulvodynia (current or past). Data reported as frequencies and percentages (%) or mean ± standard deviation.

Variable		Global N = 684	No vulvodynia	Presence of vulvodynia	P-value
N = 684			N = 544	N = 140	
Age (years) *mean*		39.1(±10.4)	38.7(±9.9)	40.5(±11.7)	0.066
>47 years		127(18.6%)	90(16.5%)	37(26.4%)	0.007
Body mass index >25 kg/m2		194(28.4%)	146(26.8%)	48(34.3%)	0.081
Ethnicity	Caucasian	681(99.6%)	543(99.8%)	138(98.6%)	0.083
	Asian	1(0.1%)	0(0%)	1(0.7%)	
	Afro-American	2(0.3%)	1(0.2%)	1(0.7%)	
Marital status	Married/partner	409(59.8%)	323(59.4%)	86(61.4%)	0.531
	Single	218(31.9%)	178(32.7%)	40(28.6%)	
	Separated/divorced/widowed	57(8.3%)	43(7.9%)	14(10.0%)	
Educational level	Primary education	31(4.5%)	22(4.0%)	9(6.4%)	0.005
	Secondary education	132(19.3%)	93(17.1%)	39(27.9%)	
	Higher education	521(76.2%)	429(78.9%)	92(65.7%)	
Menopause		99(14.5%)	72(13.3%)	27(19.3%)	0.074
Smokers		148(21.6%)	123(22.6%)	25(17.9%)	0.223
Alcohol (≥2 drinks/day)		26(3.8%)	16(2.9%)	10(7.1%)	0.020
Sexual intercourse in last 6 months		613(89.6%)	485(89.2%)	128(91.4%)	0.431
Premenstrual syndrome		326(47.7%)	255(48.2%)	71(53.8%)	0.251
Menstrual irregularities		261(38.2%)	199(37.3%)	62(45.3%)	0.090
Dysmenorrhea		437(63.9%)	343(64.5%)	94(68.6%)	0.364
Vaginal deliveries		333(48.7%)	251(46.9%)	82(59.0%)	0.011
Current oral contraceptive use		85(12.4%)	71(13.1%)	14(10.1%)	0.342
Past oral contraceptive use		504(73.7%)	399(73.9%)	105(75.0%)	0.789
Current IUD use		63(9.2%)	51(9.4%)	12(8.6%)	0.778
Past IUD use		112(16.4%)	86(15.9%)	26(18.6%)	0.447
Current ring use		25(3.7%)	20(3.7%)	5(3.6%)	0.950
Past ring use		148(21.6%)	117(21.6%)	31(22.1%)	0.895
Candidiasis (≥4 episodes)		186(27.2%)	126(23.3%)	60(43.2%)	<0.001
Urinary tract infections (≥4 episodes)		200(29.2%)	139(25.8%)	61(43.6%)	<0.001
History of condylomas		29(4.2%)	17(3.2%)	12(8.8%)	0.007
History of genital herpes		21(3.1%)	16(3.0%)	5(3.6%)	0.697
Fibromyalgia		17(2.5%)	9(1.7%)	8(5.8%)	0.006
Coxofemoral joint pain		70(10.2%)	48(8.8%)	22(16.1%)	0.013
Temporomandibular joint pain		125(18.3%)	90(16.7%)	35(25.2%)	0.021
Painful bladder syndrome/ Interstitial cystitis		79(11.5%)	48(8.9%)	31(22.8%)	<0.001
Headache		284(41.5%)	208(38.4%)	76(54.7%)	0.001
Scoliosis		152(22.2%)	109(20.2%)	43(30.7%)	0.008
Irritable bowel syndrome		59(8.6%)	43(8.0%)	16(11.5%)	0.190
Depression		82(12.0%)	59(11.0%)	23(16.8%)	0.066
Urinary infection		92(13.5%)	62(11.4%)	30(21.6%)	0.002
Urinary incontinence surgery		4(0.6%)	1(0.8%)	3(2.2%)	0.029

series, the lack of an association could be due to the small number of women with a history of genital herpes.

According to the scarce existing literature, a relationship among vaginal deliveries, perineal traumatisms and vulvodynia is unlikely. However, we found women with vaginal deliveries to have more vulvodynia, and this could be explained by disorders of the pelvic floor muscles or chronic pain after delivery. Barret et al. found dyspareunia in the 62% of the women after delivery, 31% at 6 months and 12% at one year [16].

We found no association between the use of hormonal contraceptives or intrauterine devices and the presence of vulvodynia. Harlow et al. [17], in a study of 177 cases, found association between the use of oral contraceptives and the presence of vulvodynia, but only in women who had started before 18 years of age. These results agree with previous studies, although they are limited by a small sample and the fact that they analysing women with vestibulodynia, which is a localized form of vulvodynia [8]. The association of hormonal contraceptives and vulvodynia could be explained by an increased use of healthcare services among women who use contraceptives, resulting in an increase in the diagnosis. However, although this association is controversial, recent studies have found no relationship between the use of oral contraceptives or intrauterine devices and vulvodynia [19].

Table 2
Multivariate analysis.

	β	Exp(β)	95%CI for Exp(β)		P-value
			Lower	Upper	
Age >47 years	0.8	2.1	1.3	3.4	0.002
Urinary tract infections	0.5	1.7	1.1	2.6	0.011
Candidiasis	0.8	2.2	1.5	3.4	<0.001
Headache	0.6	1.8	1.2	2.3	0.005
Coxofemoral joint pain	0.6	1.8	1.1	3.2	0.046

A high educational level was associated to lower prevalence of vulvodynia. That could be explained by self-control mechanisms and better coping with the disease. These results have been confirmed by other studies [25]. The literature describes a clear association between vulvodynia and depression or irritable bowel syndrome [6,8,13,20,21]. However, although we found such disorders to be more frequent in women with vulvodynia, statistical significance was not reached. This may be due to the high prevalence of women who report having these diseases though without diagnostic confirmation, i.e., false-positive cases.

The association between vulvodynia and other pain syndromes such as fibromyalgia or painful bladder syndrome/ interstitial cystitis has been widely evidenced [6,8,13,20,21], and has been confirmed by our own findings. The high prevalence of painful bladder syndrome/Interstitial Cystitis in our sample could be due to the women having confused their diagnosis with other conditions like urgency or overactive bladder, without ruling out

that it is a more common condition in women and that there are studies to suggest that it is infradiagnosed in the general population [28], which would reinforce the correlation between vulvodynia and this painful syndrome. The high prevalence in our sample of women with temporomandibular joint pain may be due to the fact that, since it is a clinical diagnosis, women have confused it with orofacial pain, whose prevalence is estimated at 26% [29] with temporomandibular pain.

Our findings reinforce the idea that vulvodynia is a neuropathic disease that originates in the nervous system. A study on the relationship between altered central sensitivity and a subgroup of patients with vulvodynia has suggested that there is a possible correlation between the two conditions [22].

Our study has some limitations. The questionnaires may have been answered more frequently by women with vulvodynia seeking a solution to their problem and by younger women with a higher cultural level, familiarized with the new technologies and with greater awareness of their health. On the other hand, we made no distinction between generalized or localized vulvodynia, and each of them may have different physiopathological mechanisms. Finally, despite the use of questionnaires validated for the diagnosis of vulvodynia, there was no clinical confirmation of the disorder.

The strength of our study is that it is a pioneering initiative in Spain. In effect, no previous study on the prevalence of vulvodynia and its associated factors has been carried out in this country. In other hand, this is representative of the Spanish population, because almost all Spanish regions has been represented. Furthermore, since this was an anonymous study, the women were likely freer to answer questions about their private life than they would have been in a consulting room.

In conclusion, the estimated prevalence of vulvodynia at the time of the survey (current vulvodynia) in our population was 6.6%, and 13% of the women had experienced the disorder at some point during their lifetime (past vulvodynia). Many risk factors are implicated in the development and persistence of vulvodynia, particularly vulvovaginitis by Candida and recurrent urinary tract infections, as well as the presence of other pain syndromes such as headache and coxofemoral joint pain. Vulvodynia is a serious health problem with an ambiguous etiology that remains a challenge for investigators. Further studies on this disorder are therefore needed, addressing its impact upon patient quality of life and effective treatment.

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