**Original article**

# Age related comorbidities in chronic urogenital pain

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*Abstract:* Chronic urogenital pain affects women of all ages. Its prevalence peaks at age 25, however the incidence of comorbidities varies significantly between women of reproductive age and post-reproductive age. Gynecological, urological, gastroenterological and neuromuscular comorbidities increase significantly in the post-reproductive age group. Understanding the increased prevalence of comorbidities with increased age will enhance the management of CUP in post-reproductive age women.

*Keywords:* Chronic urogenital pain (CUP); Vulvodynia, Bladder Pain Syndrome (BPS); Comorbidities; Post-reproductive age (PRA).

## INTRODUCTION

Chronic urogenital pain (CUP) is associated with a number of comorbidities, including irritable bowel syndrome (IBS), pelvic floor dysfunction (PFD), headaches, fibromyalgia, allergies and musculoskeletal changes all of which have been well documented in literature[1-3]. Reports indicate that prevalence of CUP is comparable to lower back pain, asthma and migraines[4].

The two most common CUP conditions in women are vulvodynia and bladder pain syndrome (BPS). According to current estimates, vulvodynia affects up to 8.3% of women[5] and BPS up to 6.5% of women[6], though lifetime prevalence of these conditions may be much higher[7]. It is estimated that 10%-28% of women report experiencing chronic vulvar pain symptoms consistent with the diagnostic criteria for vulvodynia[8-11] and a similar pattern appears to exist in BPS[12-15]. CUP conditions expose the sufferers and health care systems to significant costs of management[16]. In the United States it is estimated that the economic impact of vulvodynia alone may be in the range of $31-72 billion dollars in direct and indirect costs[17]. The actual cost to the health care system would be even greater if all women were to disclose their symptoms, however most suffer in silence[18].

Reliable profile data on women with CUP is essential for improved understanding of CUP disorders and for the development of management guidelines. To date, there have been no studies specifically comparing age related profiles of women with CUP. This study, based on a large sample of women, examines the differences between women of reproductive age (RA) and those of post reproductive age (PRA). Women with CUP who are of PRA are understudied, and only recently are researchers paying more attention to the relationship between CUP and menopause[19].

Ageing in women is linked with anatomic and physiological changes that affect the urogenital, digestive, and musculoskeletal systems[20]. This is exemplified by reduction in muscle strength and fascial support[21], accelerated bone turnover, decreased gastric function, diminished colonic motility[22], reduced vaginal secretions and urethral closing pressure[20]. Postural changes such as kyphosis place a greater load on the pelvic structures that may predispose menopausal women to dyspareunia[21]. Vulvovaginal atrophy and genitourinary syndrome of menopause, IBS symptoms, back pain, urinary incontinence and a host of other neuromuscular changes create challenges for the management of CUP in PRA women[23,24].

## MATERIALS AND METHODS

This is a retrospective study based on data derived from questionnaires completed by women diagnosed with vulvodynia and BPS. The questionnaires were completed post diagnosis and prior to the commencement of therapy. The sample originated from an existing database consisting of 1143 de-identified questionnaire responses by women attending a network of private CUP clinics in Australia between the years of 2006-2016. The questionnaire contained 83 questions focusing on demographic information, birthing and health history, pain symptoms and sexual function. The response rate to specific questions varied between subjects depending on their personal relevance. All women over the age of 18 who suffered from CUP and provided written assent for their data to be used were entered into the database. The database was used in its entirety with no exclusions, thereby minimizing potential bias.

The clinics guidelines required all women to undergo screening by the referring doctor prior to the commencement of physical therapy. The specialists consisted of gynecologists, urologists, dermatologists, sexual health physicians and GP's who had a special interest in the management of CUP and women's health issues. All of the women attended the clinics for the purpose of conservative therapy that consisted of education, counseling, biofeedback and myofascial therapy. Subjects were divided into two groups for statistical analysis; those of RA and PRA. In Australia, women's reproductive years are considered to begin at age 15 and end at age 50[25] and this formed the basis for defining the RA group as age 18-49 and PRA group as 50 and above[24].

This subgrouping of women forms the basis of subsequent statistical comparison. A range of statistical analyses were used, including Pearson correlation coefficient, analysis of variance, t-test for comparison of two means, chi-square test for independence between categorical variables. Institutional review board approval was obtained from the University of South Australia's Human Research Ethics Committee.

## RESULTS

### *Age*

The age of all subjects in the study ranged from 18-70, with a mean age of 30.6 years (±10.3). The 1143 subjects were subdivided into two groups consisting of 1048 (92%) subjects in the RA group and 95 (8%) subjects in the PRA group.

Due to the policy of the private clinics from which the database was obtained, the analysis focused only on wom-

en over the age of 18, thus the age range of this study was 18-70 years. An analysis of the age distribution of the sample showed that prevalence of CUP peaks at age 25, with women in the 21-30 age bracket constituting over half of the sample (56.8%). Three-quarters of the group (76.6%) were under the age of 35 years. By age 36, prevalence decreased noticeably and plateaued from age 37 onwards, dropping to less than 1% per each age group from 60 years onwards.

*Associated factors & comorbidities*

Candidiasis in CUP women was reported by 76.6% (*n*=914) and 90.3% in RA and PRA women respectively. A total of 68.1% of these women's symptoms were confirmed via swab test.

| Candidiasis Symptoms | RA (*n*=914) | PRA (*n*=72) | Significance |
|---|---|---|---|
| Candidiasis Dx | 76.6% | 90.3% | p = 0.006 |
| Frequency of Symptoms | Total Group (RA + PRA) | | |
| Occasional | 54.3% | | |
| Frequent | 25.3% | | |
| Chronic | 20.4% | | |

Figure 1. – Frequency of candidiasis reported by RA and PRA women

Thrush diagnoses showed a statistically significant increase with age (p=0.006), however there was no statistically significant difference between the RA and PRA groups in relation to frequency or treatment methods (p = 0.656).

| Treatment of Candidiasis | RA (*n*=519) + PRA (*n*= 52) |
|---|---|
| Topical meds | 38.7% |
| Oral meds | 10.3% |
| Both | 51% |

Figure 2. – Frequency of candidiasis treatments reported by total sample of women (RA + PRA)

Prevalence of the PRA group's gynecological symptoms was double that of the RA group. Ovarian cysts and adhesions were reported by 26.2% and 57.5% of RA (*n*=915) and PRA (*n*=73) subjects respectively. The frequency with which subjects reported such diagnoses is summarized in Figure 3. Cysts were present in 17.7% of RA women, increasing to 48% in PRA women (p<0.001). Adhesions increased from 3.7% in RA women to 21.9% of PRA women (p<0.001). Significant differences between RA and PRA groups were established using the chai-squared test.

| Gynecological Symptom | RA (n=913) | PRA (n=73) | p |
|---|---|---|---|
| Adhesions | 3.7% | 21.9% | <0.001 |
| Cysts | 17.7% | 48% | <0.001 |

Figure 3.- Frequency of gynecological symptoms reported by RA and PRA women

## Urological history

Women answered questions regarding urological diagnoses and symptoms of dysuria, urge, frequency, incontinence and BPS. In the RA group 33.8% reported at least one of these symptoms compared with 69.3% in the PRA women. The results are statistically significant for all variables as the frequency with which the PRA group reported symptoms was more than double that of the RA women. Incontinence was an exception as it was five times higher in the PRA than RA women. The results are summarized in Figure 4.

| Urological Symptom | RA (n=913) | PRA (n=73) | p |
|---|---|---|---|
| Dysuria | 6.6% | 14.7% | 0.009 |
| Urinary Urge | 4.9% | 14.7% | <0.001 |
| BPS | 24.1% | 52.0% | <0.001 |
| Urinary Frequency | 9.9% | 24.0% | <0.001 |
| Incontinence | 4.8% | 26.7% | <0.001 |

Figure 4.- Frequency of urological symptoms reported by RA and PRA women

## Gastroenterological history

A total of 31.3% of RA (n=281) women reported at least one GI symptom, with incidence rising to 52.8% in PRA women (n=38) (p<0.001). Results were statistically significant for differences in the frequency of reported abdominal pain, distension and bloating between RA and PRA groups. There was no statistically significant difference between the groups in relation to constipation and diarrhea. Prevalence of specific GI symptoms in RA and PRA groups is summarized in Figure 5.

| Gastroenterological Symptom | RA (n=897) | PRA (n=72) | p |
|---|---|---|---|
| Abdominal pain | 13.7% | 29.2% | <0.001 |
| Distension and bloating | 14.6% | 38.7% | <0.001 |
| Constipation and/or diarrhoea | 21.8% | 27.8% | 0.238 |
| Passage of mucus | 4.0% | 4.2% | 0.951 |

Figure 5.- Frequency of gastroenterological symptoms reported by RA and PRA women

A summary of the frequency of gynecological, urological, and gastroenterological symptoms is provided in table 6. Prevalence for most of the conditions listed doubled for the PRA group.

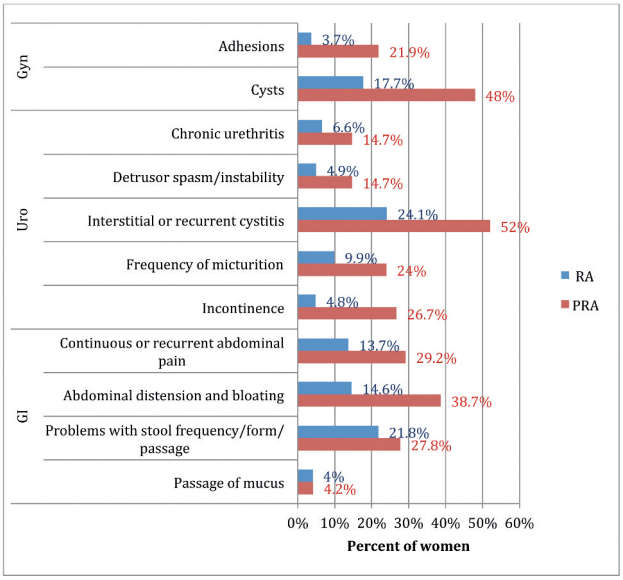


Figure 6.- Frequency of all symptoms reported by RA and PRA women

## Neuromuscular changes

Muscle, joint and bone conditions are three times more prevalent in the PRA group (59%, n=70) when compared with the RA group (17%, n=865). There was no significant difference between the RA and PRA groups in prevalence of headaches (35%, n=329), anxiety (32.4%, n=305) and depression (26.5%, n=250).

## Sexual activity and pain

Due to a lack of statistically significant differences between the two groups, the combined sexual difficulties re-

ported included pain (87.1%), muscle spasm/tension (56.9%) and lack of lubrication (39.6%). A higher percentage of RA women responded affirmatively to the question, "Is sex still enjoyable?' than PRA women (p= 0.008) as summarized in Figure 7.

| Is Sex Still Enjoyable? | RA (*n*=796) | PRA (*n*=64) |
|---|---|---|
| No | 41.3% | 56.3% |
| Yes | 24.4% | 28.1% |
| Sometimes | 34.3% | 15.6% |

Figure 7. – Enjoyment of sexual activity reported by women of RA and PRA

## DISCUSSION

Chronic urogenital pain disorders such as vulvodynia and BPS are common among women. Recent publications have focused on the prevalence of these disorders and the potential influence of genetics, physiological and sensory characteristics as well as immunological factors[26-28]. Nonetheless, there has been a lack of studies examining the role of aging in relation to symptoms and comorbidities in CUP. This study contributes unique insights into age related changes in a population of women diagnosed with CUP. The outcomes of this study may assist with the development of age appropriate management strategies.

This study is based on a retrospective review of data derived from a questionnaire specifically designed for pretherapy screening of women who had been diagnosed with vulvodynia and/or BPS. Given that a complete database of 1143 was used without exclusions, risk of bias was reduced however the results should not be generalized to other pain population groups. Numbers varied significantly between the two groups with 92% of the women forming the RA group and only 8% in the PRA group. However, the numbers of participants were sufficient to complete several statistically significant comparisons.

From the analysis of age distribution it is evident that women of all ages are affected by CUP. As has been highlighted in previous studies, the prevalence peaks among younger women of RA as reflected in the mean age of 30.6 years. This differs from earlier reports that suggested that prevalence of CUP increased with age[29-31].

The role of comorbidities in CUP is acknowledged in some classification systems and guidelines[3]. Conditions such asfibromyalgia, chronic fatigue syndrome, temporomandibular joint pain, headaches, anxiety, depression and IBS are frequently mentioned[3,32,33]. Some have suggested that these comorbidities are manifestations of different levels of centrally mediated sensitization[1,8,5]. However, it has been argued that most of the changes are mediated by peripheral mechanisms that in time give rise to centrally mediated sensitization[34].

This study, using a large sample of women, shows a significant connection between gynecological, urological and gastrointestinal symptoms in CUP patients. In the case of vulvodynia, the most common comorbidity was BPS and IBS. In the case of BPS the most common comorbidity was vulvodynia and IBS. The prevalence with which BPS and vulvodynia coexist may have significant implication for understanding the underlying mechanisms of these two CUP disorders[35]. The coexistence of these disorders may be linked on account of common embryological origins of the bladder and vulva, but in the case of the IBS, it may be due to the close proximity of the gastrointestinal tract to the reproductive and urinary systems and neural cross-talk[36].

Gastroenterological symptoms are also prevalent in women with CUP, with a third of women reporting IBS symptoms, including increased abdominal distension and bloating. The presence of gastroenterological symptoms more than doubled in the PRA group, a trend consistent with other research[37]. Urological indicators like dysuria, urge, frequency and BPS are common but show a significant rise in the PRA group and positively correlate with increased age. Functional changes are more prevalent in the PRA group, this may be due to morphological changes and to weakening structural supports for pelvic viscera, well illustrated by increased prevalence of stress incontinence.

Candidiasis is commonly reported as a chronic and recurrent problem for a large percentage of women[35,38].The incidence of candidiasis was significantly higher among women in the PRA group. However, the high number of associated gynecological variables reported raised some uncertainty as to whether they were confirmed by pathology tests or considered potential alternative causes of CUP. One of the shortcomings of this study was that there was no way of identifying whether the increase in reported candidiasis in the PRA group reflected a lifetime or point prevalence. Caution needs to be exercised in interpreting these findings.

CUP is also associated with a number of musculoskeletal comorbidities such as back pain and temporomandibular joint pain. PRA women report more than three times as many muscle, joint and bone conditions. The presence of headaches, anxiety and depression is common in the PRA group but not significantly different to the RA group. It is uncertain if neuromuscular disorders have a causal relationship or are secondary to CUP[39-42]. This study did not find the incidence of comorbid fibromyalgia and chronic fatigue to be as common as reported elsewhere[32,35,43].

Given the increased incidence of comorbidities in the PRA group, it is not surprising that older women reported sexual activity to be less enjoyable.

## CONCLUSION

This study provides insight into two age differentiated profiles of women with CUP. The variables identified between groups may assist health care providers to develop better management strategies for women with CUP with their age and common comorbidities in mind[40,44,45]. An individualised approach involving gerontologists and urogynecologists with a special interest in age related changes and chronic pain special is recommended for women of PRA.

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