Prevalence and impact of comorbidities in women with chronic pelvic pain

Prevalência e impacto de comorbidades em mulheres com dor pélvica crônica

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ABSTRACT

BACKGROUND AND OBJECTIVES: Chronic pelvic pain (CPP) is a common condition in women and there are often associated comorbidities. The objective of this study was to evaluate the prevalence of comorbidities in patients with CPP and to seek associations between comorbidities and the manifestations of chronic pain.

METHODS: Observational case-control study with sociodemographic, behavioral and clinical information, including comorbidities, in 246 women, 123 with CPP and 123 without CPP (control group).

RESULTS: Anxiety, depression, migraine and endometriosis were the most frequent comorbidities in women with CPP. The comorbidities assessed in the CPP group were not associated with pain intensity score, history of abortion, physical violence or sexual violence (p>0.05). In the group of women with CPP and endometriosis, the median anxiety and depression score was significantly lower than in the group without endometriosis (14.5; 95% CI: 11.0-14.9) versus (17.0; 95% CI: 14.6-16.7), p=0.012 and (13.0; 95%CI: 11.1-15.9) versus (16.5; 95% CI: 14.5-17.6), p= 0.045, respectively. In patients with migraine, the median depression score was higher in the group of women with CPP compared to the group without CPP (15.0; 95% CI: 14.1-17.8) versus (10.0; 95% CI: 8.5-12.4), p=0.048.

CONCLUSION: The most prevalent comorbidities in women with CPP were mental disorders, migraine and endometriosis. Comorbidities were not related to pain intensity, physical violence or sexual violence. Having a diagnosis of endometriosis is associated with lower anxiety and depression scores in patients with CPP. Overlapping migraine and CPP were associated with a worse depression score.

Keywords: Chronic pain, Comorbidity, Endometriosis, Pelvic pain.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A dor pélvica crônica (DPC) é uma condição comum em mulheres e frequentemente há comorbidades associadas. O objetivo deste estudo foi avaliar a prevalência de comorbidades em pacientes de DPC e buscar associações entre comorbidades e as manifestações da dor crônica.

MÉTODOS: Estudo observacional de caso-controle com informações sociodemográficas, comportamentais e clínicas, incluindo comorbidades, em 246 mulheres, sendo 123 com DPC e 123 sem DPC (grupo controle).

RESULTADOS: Ansiedade, depressão, enxaqueca e endometriose foram as comorbidades mais frequentes em mulheres com DPC. As comorbidades avaliadas no grupo com DPC não se associaram com o escore de intensidade da dor, com história de aborto, de violência física nem de violência sexual (p>0,05). No grupo de mulheres com DPC e endometriose, a mediana do escore de ansiedade e de depressão foi significativamente menor do que no grupo sem endometriose (14,5; IC 95%: 11,0-14,9) *versus* (17,0; IC 95%: 14,6-16,7), p=0,012 e (13,0; IC 95%: 11,1-15,9) *versus* (16,5; IC 95%: 14,5-17,6), p=0,045, respectivamente. Em pacientes com enxaqueca, a mediana do escore de depressão foi maior no grupo de mulheres com DPC em relação ao grupo sem DPC (15,0; IC 95%: 14,1-17,8) *versus* (10,0; IC 95%: 8,5-12,4), p=0,048.

CONCLUSÃO: As comorbidades mais prevalentes em mulheres com DPC foram transtornos mentais, enxaqueca e endometriose. As comorbidades não se associaram à intensidade da dor, violência física ou sexual. O diagnóstico de endometriose associou-se a menores escores de ansiedade e de depressão em mulheres com DPC. A sobreposição de enxaqueca e DPC associou-se a um pior escore de depressão.

Descritores: Comorbidades, Dor crônica, Dor pélvica, Endometriose.

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HIGHLIGHTS

- Mental disorders, migraine and endometriosis are the most frequent comorbidities in women with chronic pelvic pain (CPP);
- Women with CPP and endometriosis had lower scores for mental disorders;
- Women with CPP and migraine had higher depression scores.

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INTRODUCTION

Chronic pelvic pain (CPP) is most often defined as a health condition characterized by non-cyclical pelvic pain which lasts for more than six months. CPP can be associated with cognitive, behavioral, sexual and emotional consequences[1]. Between 5.7% and 26.6% of women of reproductive age are affected by the disease worldwide[2]. Brazilian epidemiological data is similar to that from around the world, with a prevalence of CPP in 19% of Brazilian women aged between 14 and 60 years old[3].

In recent years, comprehension on the etiology of CPP has advanced considerably, with increasing awareness of its complex and multifactorial nature, involving predisposing factors such as the catastrophization of pain, the occurrence of adverse events in childhood and the association with anxiety and depression[4]. Current literature indicates that CPP is a chronic pain syndrome that combines pelvic floor muscle malfunction and a pain perception disorder linked to psychological and cognitive factors involved, for example, in processing of pain[5].

The relationship between certain comorbidities and CPP usually influences its diagnosis and treatment. Therefore, the etiology and perpetuation of CPP are closely related to chronic pain comorbidities. Visceral structures such as the uterus, intestine and bladder, and somatic structures such as the skin, muscles, fascia and bones, share neural pathways, which make similar symptoms difficult to differentiate (viscero-visceral and viscero--somatic convergence). The role of the central nervous system in modulating pain makes the coexistence of pelvic and non--pelvic conditions even more challenging in the clinical context[6]. Comorbidities such as endometriosis, irritable bowel syndrome (IBS), interstitial cystitis (IC), among others, are associated with one third of cases of CPP[7-9].

It is important to highlight a lack of randomized, controlled studies on the treatment of CPP. Observational studies and expert reports describe that treatment is primarily aimed at pain control and encourage investigation of the cause of pain in order to better target treatment. In this way, investigating the frequency of comorbidities in women with CPP, their association with pain intensity, physical or sexual violence and mental health, constitutes information that can help in the gap of understanding and integrality of the treatment of this health condition.

METHODS

An observational case-control study was conducted between May 2018 and August 2021 at the CPP and family planning outpatient clinics of the University Hospital of the *Federal University of Goiás*, Goiânia, Goiás, Brazil. This study is derived from a larger study which assessed parenting style, mental health and pain catastrophizing in women with CPP[10].

All the procedures carried out met the requirements set out in the Declaration of Helsinki. The Internal Ethics Committee of the University Hospital of the Federal University of Goiás reviewed and approved the study protocol under reference number 2631464 and CAAE 66461217.5.0000.5078. All the participants signed a Free and Informed Consent Term (FICT).

Sample size

The sample size calculation was carried out for the study involving the assessment of parental attachment, catastrophizing and mental health in women with CPP[10]. It was based on the following parameters: significance level of 0.05 (α=0.05), statistical power of 0.80 (β=0.20), ratio of cases to controls of 1 (k=1), odds ratio of 2.5 (OR = 2.5), and an expected proportion of dysfunctional parenting style of 54.4% in women with CPP. The minimum number of women required for the total sample was estimated at 202, of which 101 had CPP and 101 were pain-free (control group).

Procedures

Individual interviews were conducted in order to obtain sociodemographic, behavioral and clinical information. Specific instruments were used to assess anxiety and depression. The interviews were conducted in private rooms to guarantee the participants' privacy. In addition to the participants' spontaneous information about having endometriosis, the medical records of the 246 study participants were checked for signs of endometriosis on physical examination and imaging tests (transvaginal/wall or/and abdominal ultrasound or/and pelvic MRI or/and surgical procedures).

Sociodemographic, behavioral and clinical data

The following sociodemographic, behavioral, and clinical characteristics were investigated in both groups: age, years of education (<12 years/≥12 years), smoking (yes/no), alcohol consumption in the last three months (yes/no). Women who currently smoke or who stopped smoking in the previous year were considered smokers, while those who had never smoked or who had stopped smoking more than a year ago were considered non-smokers. Physical violence was investigated using the question: "Have you ever suffered physical violence?" (yes/no). Sexual violence was investigated by asking: "Have you ever suffered sexual violence?" (yes/no).

Difficulty relating to others was assessed based on the answers to the question: "Are you having difficulties relating to someone or are you in conflict with someone?" (yes/no). A history of abdominal and/or pelvic surgery was investigated with yes/no answers. Pain intensity was assessed using a numerical pain scale (0-10), where zero meant no pain and 10 meant the worst pain ever experienced. The history of chronic diseases was investigated based on the answers to the following question: "Do you have any of the chronic diseases listed here? Hypertension (high blood pressure), diabetes, hypothyroidism, migraine, fibromyalgia, irritable bowel syndrome, interstitial cystitis (yes/no) or any other chronic illness?" (yes/no), and if so, which illness?".

Anxiety assessment

Anxiety symptoms were investigated using the Generalized Anxiety Disorder-7 (GAD-7) scale, translated and validated for Brazilian Portuguese[11]. It is a self-report questionnaire with seven items, referring to the last two weeks, with questions such as: "Do you worry a lot about different things?" or "Do you get easily upset or irritated?". The scores range from 0 to 3 for each item (0 = none; 1 = several days; 2 = more than half the days; and

3 = almost every day). The total score ranges from 0 to 21, with ≥10/21 being the cut-off score for anxiety[12].

Depression assessment

The 9-item Patient Health Questionnaire (PHQ-9), translated and validated for Brazilian Portuguese, was used to identify symptoms of depression in the last two weeks[13]. This self-administered questionnaire is based on the diagnostic criteria for major depression described in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) and includes the question: "During the past two weeks, how often have you been bothered by any of the following problems?", such as: "feeling tired or low on energy". Scores range from 0 to 3 for each item, with 0 meaning "not at all"; 1 "several days; 2 "more than half the days" and 3 "almost every day". A score ≥10/27 is considered an indicative of depression[12].

Statistical analysis

In the descriptive analysis, absolute and relative frequencies were calculated for qualitative or categorical variables, and means and standard deviations (SD) were calculated for continuous quantitative variables. Fisher's exact test was used to compare absolute and relative frequencies. The Mann-Whitney test was used to compare age between the groups with and without CPP, as well as to check for possible associations between median anxiety and depression scores in women with CPP with and without chronic non-mental comorbidities. Logistic regression analysis (unadjusted and adjusted) was used to compare anxiety and depression scores in women with migraine in the groups with and without CPP. The SPSS software, version 20, was used for all statistical analysis. The significance level was set at 0.05.

Table 1. Characteristics of the study participants, n (%).

	With CPP (n=123)		Without CPP (n=123)		p-value*
Schooling					0.347
< 12 years	46	37.4	38	30.9	
≥ 12 years	77	62.6	85	69.1	
Smoking					0.055
Yes	10	8.1	21	17.1	
No	113	91.9	102	82.9	
Alcohol consumption					0.002
Yes	48	39.0	73	59.3	
No	75	61.0	50	40.7	
Physical violence					0.003
Yes	39	31.7	18	14.6	
No	84	68.3	105	85.4	
Sexual violence					0.062
Yes	27	22.0	15	12.2	
No	96	78.0	108	87.8	
Relationship difficulties					0.001
Yes	49	39.8	24	19.5	
No	74	60.2	99	80.5	
Abdominal/pelvic surgery					0.017
Yes	96	78.0	78	63.4	
No	27	22.0	45	36.6	

CPP = chronic pelvic pain; *Chi-square test.

RESULTS

246 women were included, 123 with CPP and 123 without CPP. The mean age of the participants was 37.0±6.9 years in the CPP group and 31.9±7.2 in the non- CPP group (p<0.001). Table 1 shows other features of the participants.

Table 2 shows the prevalence of chronic comorbidities in both groups with and without CPP. Anxiety, depression and migraine were the most frequent comorbidities in both groups. Endometriosis, IC and IBS only appeared in the group with CPP. Other less frequent comorbidities not listed in table 2, such as low back pain, rheumatological diseases, respiratory allergies and epilepsy, among others, were similarly distributed in the two groups (p=0.226).

The presence of the comorbidities assessed in the 123 women with CPP was not significantly associated with pain intensity, physical violence or sexual violence (data not shown).

Table 3 shows that the median anxiety score in women with endometriosis (median: 14.5; 95% CI: 11.0-14.9) was significantly

Table 2. Evaluation of the frequency of chronic comorbidities in 246 women *n (%)*.

Comorbidities	With CPP (*n*=123)		Without CPP (*n*=123)		p-value*
Anxiety	98	79.7	70	56.9	<0.001
Depression	90	73.2	69	56.1	0.002
Migraine	58	47.2	41	33.3	0.027
Endometriosis	39	31.7	0	0.0	<0.001
SAH	13	10.6	13	10.6	1.000
Fibromyalgia	10	8.1	9	7.3	1.000
IC	7	5.7	0	0.0	0.014
Diabetes	6	4.9	9	7.3	0.596
IBS	5	4.1	0	0.0	0.060
Hypothyroidism	4	3.2	5	4.1	1.000
Others	37	30.1	47	38.2	0.226

SAH = systemic arterial hypertension; CPP = chronic pelvic pain; IC = interstitial cystitis; IBS = irritable bowel syndrome. *Teste de Mann- Whitney.

Table 3. Anxiety score and chronic non-mental comorbidities in 123 women with chronic pelvic pain.

Comorbidities	Yes	No	p-value*
	Median (CI 95%)	Median (CI 95%)	
SAH	15.0 (9.9-17.5)	16.0 (13.9-15.9)	0.520
Diabetes	13.0 (6.7-18.3)	16.0 (13.9-15.9)	0.258
Hypothyroidism	14.0 (4.1-22.9)	16.0 (13.9-15.9)	0.622
Migraine	16.0 (13.6-16.5)	16.0 (13.2-15.9)	0.514
Fibromyalgia	13.5 (9.5-17.9)	16.5 (13.9-15.9)	0.636
IC	17.0 (8.9-20.7)	16.0 (13.8-15.8)	0.831
IBS	19.0 (9.9-23.6)	16.0 (13.7-15.7)	0.295
Endometriosis	14.5 (11.0-14.9)	17.0 (14.6-16.7)	0.012
Others	15.0 (11.8-16.1)	16.0 (14.1-16.2)	0.521

SAH = systemic arterial hypertension; CI = confidence interval; IC = interstitial cystitis; IBS = irritable bowel syndrome. *Mann-Whitney's test.

Table 4. Depression score and chronic non-mental comorbidities in 123 women with chronic pelvic pain.

Comorbidities	Yes	No	p-value*
	Median (CI 95%)	Median (CI 95%)	
SAH	16.0 (11.2-20.8)	15.0 (13.8-16.6)	0.648
Diabetes	17.0 (8.9-23.7)	15.0 (13.9-16.6)	0.711
Hypothyroidism	21.5 (12.2-27.2)	15.0 (13.8-16.5)	0.217
Migraine	15.0 (14.1-17.8)	15.0 (12.8-16.5)	0.345
Fibromyalgia	14.0 (9.8-20.3)	15.0 (13.9-16.7)	0.930
IC	20.0 (11.3-22.9)	15.0 (13.8-16.5)	0.498
IBS	15.0 (4.2-28.6)	15.0 (13.9-16.5)	0.700
Endometriosis	13.0 (11.1-15.9)	16.5 (14.5-17.6)	0.045
Others	13.0 (11.4-16.8)	16.0 (14.3-17.3)	0.308

SAH = systemic arterial hypertension; CI = confidence interval; IC = interstitial cystitis; IBS = irritable bowel syndrome. *Mann-Whitney's test.

Table 5. Anxiety and depression scores in women who reported migraine, 58 women with CPP and 41 women without CPP.

Variables	With CPP Median (95% CI)	Without CPP Median (95% CI)	p-value*	p-value**
Anxiety	16.0 (13.7-16.5)	11.0 (9.6-12.9)	< 0.001	0.263
Depression	15.0 (14.1-17.8)	10.0 (8.5-12.4)	< 0.001	0.048

CPP = chronic pelvic pain. *Logistic regression analysis. **Logistic regression analysis adjusted for age, alcohol consumption, physical violence, relationship difficulties, abdominal/pelvic surgery, anxiety and depression.

lower than in women without endometriosis (median: 17.0; 95% CI: 14.6-16.7), p=0.012.

Table 4 shows that in women with CPP the median depression score was significantly lower in women with endometriosis (median: 13.0; 95% CI: 11.1-15.9) than in women without endometriosis (median: 16.5; 95% CI: 14.5-17.6), p= 0.045.

The study on patients who reported migraine shows a depression score was higher and statistically significant in the group of women with CPP when compared to the group of women without CPP, as shown in table 5.

DISCUSSION

The most prevalent comorbidities in women with CPP were anxiety, depression, migraine, endometriosis, hypertension and fibromyalgia. The present analysis showed a significantly higher frequency of anxiety, depression, migraine, endometriosis and interstitial cystitis in the group of women with CPP compared to those in the control group.

Several reports in the literature have documented the high prevalence of mental health disorders in women with CPP, especially anxiety[12,13], which corroborates the findings of this study. Anxiety is a very important comorbidity in women with CPP and should be diagnosed and treated, as also recommended in other studies of women with CPP[1,6,14]. Depression has been found to be highly prevalent in women with CPP and coexisted with anxiety in 54% of these women in a previous study[15]. In the current study, anxiety and depression affected around three out of four patients, which suggests the importance of diagnosis at the initial consultation in order to offer more appropriate treatment to these women.

Other comorbidities in this population have been little studied. In this study, the presence of endometriosis in 31.7% of women with CPP is very close to the findings of a study[7], which found 33% endometriosis in 1524 women with CPP who underwent laparoscopy[7]. Endometriosis is undoubtedly the most important comorbidity associated with CPP, after anxiety and depression. Endometriosis has been considered the cause of pain when present in women with CPP[16,17], but the fact that many women with endometriosis feel no pain and the severity of endometriosis has no correlation with the intensity of pain is still intriguing. The catamenial worsening of pain in women with CPP is indicative of the need to induce amenorrhea, regardless of the presence of endometriosis[17,18].

Nevertheless, this diagnosis seems to have a positive influence on the degree of both anxiety and depression, since the presence of the disease was associated with low scores for these comorbidities. The assumption is that the absence of a diagnosis is a stress factor for patients with CPP. Despite this, laparoscopy has not been effective in resolving the long-term pain experienced by these patients and, for this reason, it has been less and less indicated[18,19]. On the other hand, the diagnosis of endometriosis through physical examination and non-invasive tests such as transvaginal ultrasound and/or magnetic resonance imaging of the pelvis can help with diagnosis and treatment, either by helping to reduce anxiety and depression scores or by directing better therapy.

CPP and migraine are chronic pains that are considered somatofunctional syndromes[20]. Therefore, the coexistence of these two morbidities observed in most of the women in this study is not surprising. The current study found an even higher prevalence of migraine in women with CPP previously[3], but both report a significantly higher frequency of migraine in the CPP group when compared to the control group. In addition, the comorbidity of migraine with CPP was associated with worse depression scores. This corroborates the description of the existence of neuronal circuits and neurotransmitters that promote a bidirectional association between depression and chronic pain[10]. Therefore, the presence of migraine comorbidity makes it even more relevant to look closely at the mental health of women with CPP.

IBS and IC have often been related to CPP[8,9]. In this study, the frequency found was lower than expected. The lack of a specific diagnostic tool to characterize them probably contributed to the lower frequency observed, since the participants were asked if they had these diagnoses. However, even though endometriosis was not directly asked about, as was the case with IC and IBS, it presented a high frequency, which was very similar to that found in a relevant publication in the literature[7]. IBS and IC are probably even less frequent in this sample and in the study region. Even so, there was a significant difference for IC compared to the control group, which was not the case for IBS, which would probably have occurred if the sample of participants in the study had been larger.

When analyzing this study, it is necessary to bear in mind certain limitations. Consideration should be given to the differences between the study and the general population due to the research being carried out with patients from a tertiary hospital. Even the women who made up the group without CPP, because they are followed up in a highly specialized referral service, are probably not free of comorbidities, making it a relatively less representative group of the general population. There were also limitations inherent to the very methodology of observational case-control studies, since it is not possible to establish a cause and effect relationship between CPP and comorbidities.

The highlights of this study are the considerable sample size of a population of women with CPP undergoing clinical follow-up, in addition to the control group being followed up at a family planning outpatient clinic, a group considered to be more "normal" in a tertiary hospital. As far as it is known, this is the largest observational study investigating the frequency of comorbidities in women with CPP compared to a control group without CPP.

CONCLUSION

Anxiety, depression, migraine and endometriosis were the most prevalent comorbidities in women with CPP. Comorbidities were not associated with pain intensity, physical or sexual violence. The diagnosis of endometriosis was associated with lower anxiety and depression scores in women with CPP. The overlap of migraine and CPP was associated with a worse depression score.

AUTHORS' CONTRIBUTIONS

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Data Collection, Conceptualization, Project Management, Research, Writing - Preparation of the original, Visualization

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