

# Chronic neuropathic pain: quality of life, depressive symptoms and distinction between genders

*Dor crônica neuropática: qualidade de vida, sintomas depressivos e distinção entre os sexos*

Laura Figueiredo Villa<sup>1</sup>, Ana Marcia Rodrigues Cunha<sup>2</sup>, Lilian Andreia Chessa Dias<sup>3</sup>, Marcos Henrique Dall'aglio Foss<sup>4</sup>, Marielza Regina Ismael Martins<sup>5</sup>

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## ABSTRACT

**BACKGROUND AND OBJECTIVES:** Neuropathic pain is a chronic pain which can be accompanied by comorbidities, such as sleep interferences and anxiety. The present study aimed to evaluate the neuropathic chronic pain impact and its comorbidities in life quality and depression symptoms, comparing this impact between genders.

**METHODS:** Thirty female and 30 male patients were evaluated. The research was based on the following instruments: half structured interview with sociodemographic questions, World Health Organization Quality of Life-BREF questionnaire, Beck Depression Inventory, pain signs and symptoms by Leeds Assessment of Neuropathic Symptoms and Signs, visual analog scale and drugs adherence by Morisky-Green test.

**RESULTS:** As for quality of life, the physical domain was the most affected and only the psychological domain showed statistical differences between genders ( $p=0.031$ ). The depression symptoms were observed in 56.7% of all patients, without important statistical difference between the genders ( $p=0,830$ ). The median of pain intensity was 8.0 points, indicating severe pain intensity among these patients. The medical adherence happened among

women and men, respectively in 7 (23.3%) and 11 (36.7%) of the patients ( $p=0.260$ ).

**CONCLUSION:** The presence of neuropathic pain and its comorbidities strongly and negatively affects quality of life and is related to depressive symptoms, with similar prevalence in both genders, although women have a greater impact on their quality of life.

**Keywords:** Chronic pain, Depression, Gender distribution, Quality of life.

## RESUMO

**JUSTIFICATIVA E OBJETIVOS:** A dor neuropática é uma dor crônica que pode se apresentar junto com comorbidades, como interferências no sono e ansiedade. O presente estudo teve como objetivo avaliar o impacto da dor crônica neuropática e suas comorbidades na qualidade de vida e sintomas depressivos, comparando esse impacto entre os sexos.

**MÉTODOS:** Foram incluídos 30 pacientes do sexo feminino e 30 do sexo masculino. Os instrumentos utilizados foram: entrevista semiestruturada com questões sociodemográficas, questionário de qualidade de vida *World Health Organization Quality of Life-BREF*, Inventário Beck de Depressão, sinais e sintomas da dor através do questionário *Leeds Assessment of Neuropathic Symptoms and Signs*, escala analógica visual e adesão farmacológica pelo teste de Morisky-Green.

**RESULTADOS:** Em relação a qualidade de vida, o domínio físico foi o mais acometido e apenas o domínio psicológico apresentou diferença estatística entre os sexos ( $p=0,031$ ). Os sintomas depressivos foram observados em 56,7% dos pacientes, sem diferença significativa entre os sexos ( $p=0,830$ ). A mediana de intensidade dolorosa foi 8,0 pontos, indicando dor intensa nesses pacientes. A adesão farmacológica foi menor nas mulheres que nos homens, respectivamente, em 7 (23,3%) e 11 (36,7%) pacientes ( $p=0,260$ ).

**CONCLUSÃO:** A presença de dor neuropática e suas comorbidades impacta negativamente a qualidade de vida e está relacionada com sintomas depressivos, com prevalência semelhante nos dois sexos, apesar de as mulheres apresentarem maior impacto na qualidade de vida.

**Descritores:** Depressão, Distribuição por sexo, Dor crônica, Qualidade de vida.

Laura Figueiredo Villa – <https://orcid.org/0000-0001-9506-6608>;  
Ana Marcia Rodrigues Cunha – <https://orcid.org/0000-0001-9503-6337>;  
Lilian Andreia Chessa Dias – <https://orcid.org/0000-0003-0250-9647>;  
Marcos Henrique Dall'aglio Foss – <https://orcid.org/0000-0002-9821-8029>;  
Marielza Regina Ismael Martins – <https://orcid.org/0000-0002-1140-7581>.

1. Medical School of São José do Rio Preto, Medical Course, São José do Rio Preto, SP, Brazil.
2. Regional Medical Foundation of São José do Rio Preto, Base Hospital, Department of Anesthesiology, São José do Rio Preto, SP, Brazil.
3. Regional Medical Foundation of São José do Rio Preto, Base Hospital, Social Services, São José do Rio Preto, SP, Brazil.
4. Medical School of São José do Rio Preto, Department of Physical Therapy, São José do Rio Preto, SP, Brazil.
5. Medical School of São José do Rio Preto, Base Hospital, Pain Clinic, Department of Neurological Sciences, São José do Rio Preto, SP, Brazil.

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## Correspondence to:

Av. Brigadeiro Faria Lima, 5416 – Vila São Pedro  
15090-000 São José do Rio Preto, SP, Brasil.  
E-mail: marielzamartins@famcrp.br

## INTRODUCTION

Neuropathic pain (NP) is a type of chronic pain (CP) that affects 7 to 10% of the population. Patients with NP usually pre-

sent intense pain that is difficult to manage, affecting quality of life (QoL) due to the intense use of drugs and constant visits to health professionals<sup>1</sup>.

NP comprises several heterogeneous conditions, involving the somatosensory system, at a peripheral or central level, which can be caused by diseases such as diabetes mellitus, herpes-zoster, leprosy, trigeminal neuralgia and human immunodeficiency virus infection, medical interventions, surgery, chemotherapy, and injuries, such as brachial plexus injury<sup>2</sup>. These conditions cause structural and/or functional changes in the nervous system that manifest clinically as hyperalgesia and allodynia, hypoalgesia and hypoaesthesia.

Clinical manifestations are heterogeneous, especially between the genders. What contributes to this difference is the distinction in the initiation and maintenance of neuroinflammation, with less participation of the pro-inflammatory immune system and greater activation of the Diffuse Noxious Inhibitory Control (DNIC) in pain in men, contributing to a better response to analgesia<sup>3,4</sup>, and hormonal factors involved in the alteration of the pain threshold, since estrogen can be a triggering factor for greater pain intensity<sup>5</sup>. However, the symptoms and pathophysiology involved in CP are related to issues beyond gender, and it's necessary to analyze environmental, social, and psychological factors in order to understand the mechanism of pain in women and men<sup>6</sup>.

Despite the increase of studies on drugs for NP, many patients still suffer from insufficient pain relief<sup>7</sup>. The difficulty of treatment is due to the presence of comorbidities, such as sleep interference, depression, and anxiety, which make it necessary to provide individualized multidisciplinary care to the patient with CP<sup>8</sup>.

Although the studies on NP-related depression are increasing, few discuss its interference in QoL. The prevalence of CP in women increases twice the chance of developing depression<sup>9</sup>, and whether there is a distinction between genders on how this comorbidity behaves and its impact on QoL is still an issue to be more explored, besides being essential to pre-diagnose and direct more appropriate treatments to manage depression.

The present study is justified by the importance of elucidating the impact of neuropathic CP and its comorbidities on QoL in different genders. The study sought to refine the healthcare team's approach to patient characteristics to improve QoL.

## METHODS

A descriptive, exploratory cross-sectional study, carried out at the Pain Clinic Service of São José do Rio Preto's Base Hospital. Sixty patients, 30 female and 30 male, with neuropathic CP were included, estimated by sample calculation of 5% (error=0.05) and with a reliability degree of 95% ( $\alpha=0.05$  which provided  $z_{0.05/2}=1.96$ ), considering the true proportion of 50% ( $p=0.50$ ), a calculation based on the total number of patients who attended the follow-ups for NP in the Pain Clinic.

Inclusion criteria were patients with NP lasting at least 6 months and who agreed to participate in the study after signing the Free and Informed Consent Term (FICT). Patients who did not agree to participate in the study and those with sensory and limiting deficits screened by the Mini-Mental State Exam<sup>10</sup> were excluded.

The following instruments were used: a semi-structured interview containing sociodemographic questions, as well as the World Health Organization Quality of Life - Bref (WHOQOL-bref)<sup>11</sup> questionnaire, with 26 questions divided into the physical, psychological, social relations and environmental domains; higher scores in each domain indicate higher QoL. The depressive signs that could develop due to pain and its interference in QoL were analyzed by the Beck Depression Inventory (BDI)<sup>12</sup>, composed of 21 questions with scores from zero to 3 on how the patient felt in the previous week; according to the score acquired, depression could be considered as absent/minimal, mild, moderate, and severe.

The signs and symptoms of NP were assessed by the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)<sup>13</sup> scale and its intensity by the visual analogue scale (VAS). Drug adherence was assessed by the Morisky-Green test (MGT)<sup>14</sup>, composed of four questions about irregularity in daily intake and at pre-established times, with a positive answer to any of them classifying the patient as non-adherent.

The present study was approved by the FAMERP Human Research Ethics Committee, under protocol code CAAE 62298816.0.0000.5415. Participants were informed of their rights according to Resolution 466/2012 of the Brazilian Health Council.

## Statistical analysis

Analysis was performed using the Statistical Package for the Social Sciences software (SPSS - Windows 11.5). The comparison between two independent groups to verify the distinctions between genders was performed using the Student's *t* test or the Mann-Whitney test for numerical variables and using the Pearson's Chi-square test or Fisher's Exact test for categorical variables<sup>15,16</sup>. Correlation between numeric or ordinal variables was performed by Spearman's correlation coefficient<sup>15</sup>. Values of  $p<0.05$  were considered significant.

## RESULTS

Sixty patients were evaluated, with a mean age of  $55.6\pm 10.5$  years and median of 53.5 years, 30 women with a mean age of  $55.3\pm 11.78$  years and median of 51.5 years, and 30 men with a mean age of  $55.8\pm 9.2$  years and median of 55 years. As for schooling, 38.3% of patients had incomplete elementary school education and 13.3% had complete college education.

Table 1 presents data regarding the clinical characteristics of pain, such as its etiology and its relationship with the development of changes in these patients' daily actions and emotions. Regarding the signs and symptoms of NP, 83% presented shock pain with no motivating event, 82% unpleasant sensations on the skin, such as tingling, and 75% presented sensitivity alteration, in addition to 67% presenting allodynia, with alteration of the threshold by needle stimulus present in 90%. The mean pain intensity assessed by the VAS was 8.23, higher in women (8.5) than in men (7.9) ( $p=0.279$ ). Pharmacological adherence in 30% of patients, lower in females (23.3%) than in males (36.7%), although there was no statistical difference ( $p=0.260$ ).

**Table 1.** Clinical pain characteristics of the study's patients

Characteristics	n and %	Male n (%)	Female n (%)
What do you think caused the pain?			
Disease	25 (41.7)	13 (43.3)	12 (40.0)
Trauma (accidents, surgeries)	15 (25.0)	8 (26.7)	7 (23.3)
Work	14 (23.3)	6 (20.0)	8 (26.7)
Others	6 (10.0)	3 (10.0)	3 (10.0)
How was your life when you started having pain?			
Good quality of life	41 (68.3)	19 (63.3)	22 (73.3)
Regular quality of life	9 (15.0)	7 (23.3)	2 (6.7)
Low quality of life	7 (11.7)	2 (6.7)	5 (16.7)
Doesn't remember	3 (5.0)	2 (6.7)	1 (3.3)
Did the pain generate changes in your life?			
Yes, disabling changes	41 (68.3)	21 (70.0)	20 (66.7)
Yes, not disabling	16 (26.7)	7 (23.3)	9 (30.0)
Didn't generate any changes	3 (5.0)	2 (6.7)	1 (3.3)
Comparing the time when you began feeling pain and today, has the way you face problems changed? From the time you started feeling pain until now, do you feel the same way or has anything changed over time?			
Worsening	27 (45.0)	12 (40.0)	15 (50.0)
Improvement	25 (41.7)	13 (43.3)	12 (40.0)
Remains the same	8 (13.3)	5 (16.7)	3 (10.0)
Has pain generated any emotional effects on you?			
Yes, diagnosed emotional effects	28 (46.7)	11 (36.7)	17 (56.7)
Yes, undiagnosed emotional effects	21 (35.0)	13 (43.3)	8 (26.6)
No	11 (18.3)	6 (20.0)	5 (16.7)
How do you imagine will be your life from now on?			
Expectation of improvements	42 (70.0)	19 (63.3)	23 (76.7)
No expectation	16 (26.7)	10 (33.4)	6 (20.0)
Expectation of worsening	2 (3.3)	1 (3.3)	1 (3.3)

Pain intensity was  $8.4 \pm 1.3$  among adherents and  $8.2 \pm 2.0$  among non-adherents ( $p=0.987$ ), with no significant difference. Among the total, 56.7% of patients showed some sign of depression, with no difference between genders ( $p=0.830$ ) (Table 2).

**Table 2.** Descriptive and comparative analysis of depression, according to gender

	Genders		p-value
	Male n=30	Female n=30	
Depression, n (%)			
Absent or Minimal	14 (46.7)	12 (40.0)	
Mild	14 (46.7)	14 (46.7)	
Moderate	2 (6.7)	3 (10.0)	
Severe	0 (0.0)	1 (3.3)	
BDI, score	12.0 (0 – 23)	13.5 (4 – 37)	0.830

Numeric variables described in median (variation); BDI = Beck Depression Inventory

Regarding QoL, the physical domain had the lowest score, meaning lower QoL. In the psychological domain there was a statistically significant difference between genders ( $p=0.031$ ) (Tables 3 and 4). The score of the QoL domains lowered as depression worsened (Table 5), with a statistical difference between pain intensity and the domains, i.e., the more intense the pain, the lower the patient's QoL (Table 6).

**Table 3.** Quality of life of patients included in the study, according to the WHOQOL-Bref domains

QoL Domains	Mean	Median	SD	Minimum	Maximum
Physical	42.0	39.3	12.5	21.4	75.0
Psychological	55.8	58.3	17.3	4.2	87.5
Social relationships	52.1	58.3	22.9	0.0	91.7
Environmental	65.7	65.6	11.9	43.8	90.6

QoL = quality of life; SD = standard deviation.

**Table 4.** Comparative analysis of quality of life, according to the WHOQOL-Bref domains and gender

Domains	Genders		p-value
	Male n = 30	Female n = 30	
Physical	40.7 ± 14.1	43.3 ± 10.8	0.223
Psychological	60.8 ± 15.4	50.8 ± 17.9	0.031
Social relationships	52.8 ± 24.3	51.4 ± 22.0	0.852
Environment	65.1 ± 10.2	66.3 ± 13.5	0.727

**Table 5.** Descriptive analysis of quality of life, according to the domains of the WHOQOL-Bref, according to the categories of depression, according to the BDI

Domains	Depression			
	Minimal n=26	Mild n=28	Moderate n=5	Severe* n=1
Physical	51.2 ± 11.9	35.2 ± 6.5	35.0 ± 11.9	28.6
Psychological	67.6 ± 11.5	50.0 ± 14.1	37.5 ± 5.6	4.2
Social relationships	66.7 ± 15.6	45.8 ± 19.0	18.3 ± 20.7	16.7
Environmental	73.1 ± 8.8	61.2 ± 10.6	56.3 ± 11.7	46.9

Numeric variables described as mean ± standard deviation.

\*Only one patient fell into this category, thus standard deviation is not presented.

**Table 6.** Correlation analysis between the Visual Analog Scale and quality of life, according to the WHOQOL-Bref domains

Domains	Visual Analog Scale	
	Coefficient $r_s$	p-value
Physical	-0.389	0.002
Psychological	-0.422	0.001
Social relationships	-0.246	0.058
Environmental	-0.382	0.003

$r_s$  = Spearman correlation.

## DISCUSSION

The mean age was 55.6 years, which is in agreement with literature data pointing to a higher prevalence of NP over 50 years

old<sup>1</sup>. Schooling is in agreement with data from the Brazilian public health system (SUS – *Serviço Único de Saúde*), with a reduction in the use of its services as education increases<sup>17</sup>.

The signs and symptoms: 83% electrical sensations, 82% tingling, 75% loss of sensitivity and 67% allodynia, is in agreement with the literature on NP<sup>18,19</sup>. The main causes of pain were the presence of previous comorbidities (41.7%) and trauma (25%), such as post-herpetic neuralgia, trigeminal neuralgia, neoplasms, stroke, surgeries, which is also in agreement with the literature<sup>20</sup>. The mean pain intensity 8.23 confirms intense pain in patients, in accordance with the literature<sup>21</sup>, with no statistical difference between genders.

There are several pharmacological treatment options that aim to control pain intensity and improve patients' QoL. Choosing a pharmacological treatment varies according to the patient's comorbidities and adaptation. Currently, tricyclic antidepressants and selective serotonin and norepinephrine reuptake inhibitors are the most used<sup>22</sup>. Although most patients were prescribed pain control drugs, only 30% were adherent to treatment, which is not in agreement with the study<sup>23</sup>, in which more than 50% of the patients were not adherent. However, there was no statistically significant difference in pain intensity between non-adherent and adherent patients, i.e., pain intensity remained high regardless of the drug administered. According to the literature, although tricyclic antidepressants and selective serotonin and norepinephrine reuptake inhibitors are therapeutic options, they are not effective in all cases because NP is multifactorial, requiring a careful approach with different forms of treatment<sup>24</sup>.

NP has a significant negative impact on QoL of patients, with increased pain scores and greater changes in the patients' routine, data present in the literature<sup>25</sup>. Among the justifications pointed out for the decrease in QoL is the association of CP with the interruption of daily activities<sup>26</sup>, which was evidenced in this study, since the physical domain had the lowest score and was the most affected by CP (42.0±12.5). Only in the psychological domain there was a significant difference between genders ( $p=0.031$ ), which shows that negative feelings such as bad mood, anxiety, and sadness interfere more in the QoL of females than males. Some studies report that women have undertreatment of their pain complaints, while men are more quickly sent to specialists and have better treatment<sup>27</sup>, which could contribute to the better response of males in this aspect.

Both men and women exhibited depression scores, with 56.7% having some level of depression, with no significant difference between genders ( $p=0.830$ ). The lower the patient's QoL score, the higher the rate of depression, which is in agreement with a study on NP and depression, in which patients with a higher degree of depression presented more affected QoL scores<sup>21</sup>. Some studies also point out the relationship between CP and depression, which is accentuated by the lack of empathy from health professionals towards the patient, who feels even more frustrated and neglected, which can contribute to worsen their clinical condition<sup>28</sup>.

## CONCLUSION

The data obtained show the negative influence of NP and its comorbidities on QoL, besides contributing to the development

of depressive symptoms. The prevalence of depression associated with NP is similar in both genders, although women present a greater impact on their QoL. The results reveal the need for multidimensional and empathetic care, with careful and individualized evaluation for each patient.

## AUTHORS' CONTRIBUTIONS

### Laura Figueiredo Villa

Statistical Analysis, Funding acquisition, Data collection, Conceptualization, Research, Methodology, Writing - Preparation of the original, Writing - Review and Editing

### Ana Marcia Rodrigues Cunha

Visualization

### Lilian Andreia Chessa Dias

Visualization

### Marcos Henrique Dall'aglio Foss

Visualization

### Marielza Regina Ismael Martins

Conceptualization, Resource Management, Project Management, Methodology, Writing - Preparation of the original, Writing - Review and Editing, Supervision

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