Psychological distress and quality of life in leprosy patients with neuropathic pain

FELIPE J.J. REIS, DAIANE LOPES, JÉSSICA RODRIGUES, ARTUR PADÃO GOSLING & MARIA KATIA GOMES
Faculdade de Medicina da Universidade Federal do Rio de Janeiro – Programa de Pós-Graduação em Clínica Médica UFRJ, Brasil

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Summary Leprosy is widely known because of progressive damage to the peripheral nerves. In spite of multidrug therapy, some patients develop chronic neuropathic pain after bacteriological cure. Chronic pain is associated with psychological distress and is also an important predictor of poor quality of life. The aim of this study is to assess psychological distress in leprosy patients with chronic neuropathic pain, and its repercussions on their quality of life. The sample of this cross-sectional study comprised patients with chronic neuropathic pain after multidrug therapy. Neuropathic pain was confirmed by clinical examination and by the Douleur neuropathique en 4 questions questionnaire. Pain intensity was assessed using a visual analogic scale (VAS) ruler. The psychological health of the participants was measured using the 12-item General Health Questionnaire, and the WHOQOL-bref was used to assess quality of life. The mean pain intensity reported by participants on the VAS was 7·1 cm (SD = 2·9). No differences in pain intensity with respect to gender were observed. Psychological distress was present in 76·2% of participants, being higher in those with Grade 2 of disability. Patients with psychological distress had the lowest mean scores in all domains of the WHOQOL-bref. The lowest mean scores according to domain were physical (9·9; SD = 3·3), followed by environment (11·9; SD = 3·0), psychological (13·5; SD = 2·6) and social relations (14·0; SD = 3·7). In conclusion, our study identified the presence of psychological distress in most of the participants. Patients with chronic neuropathic pain who were also found to have high psychological distress levels had higher pain intensity and a poorer quality of life.

Introduction

Leprosy is a chronic granulomatous infection caused by Mycobacterium leprae principally affecting the skin and peripheral nerves.1,2 Historically, leprosy has been associated with...
Neuropathic pain in leprosy

Neuropathy is the hallmark of leprosy, affecting peripheral nerves and leading to motor, sensory and autonomic alterations. Nerve damage in leprosy is well documented in the literature because of the potentially severe deformities and disfigurement it causes, which are associated with fear, stigma, and social exclusion.\textsuperscript{1,4–6}

As well as visible impairments caused by nerve involvement in leprosy, chronic neuropathic pain arises as a disabling condition after completion of multidrug therapy (MDT).\textsuperscript{7–12} Neuropathic pain has been defined as “...pain arising as a direct consequence of a lesion or disease affecting the somatosensory system.”\textsuperscript{12} The precise mechanism of chronic pain in leprosy is not yet fully understood and some different pathogenic mechanisms behind neuropathic pain have been suggested such as entrapment of the nerve, firing of the \textit{nervi nervorum}, axonal damage and regeneration, functional changes such as spontaneous discharges, lowered activation thresholds, and exaggerated responses of the nociceptors.\textsuperscript{1,2,7}

Psychological distress is widely used as an indicator of the mental health of the population in public health, in population surveys and in epidemiological studies. It can be considered as a construct defined as a multifactorial, unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with the disease, its physical symptoms and its treatment.\textsuperscript{13} It is well established that people who suffer from chronic conditions have an increased risk of developing mental distress. It is also well known that leprosy patients frequently have secondary psychosocial disabilities because of the chronic nature of the disease and the unsightly disfigurement, which results in prejudice, and stigmatization and social exclusion of those affected.

It is noteworthy that psychological aspects play an important role in the setting and perpetuation of pain. In leprosy patients, stigmatization, depression, anxiety and social exclusion might contribute to the increased or sustained chronic pain condition.\textsuperscript{14} This study was conducted to assess psychological distress in leprosy patients with chronic neuropathic pain and its repercussions on their quality of life.

\textbf{Methods}

A cross-sectional study was conducted in July–December 2012 at a referral hospital of the Federal University of Rio de Janeiro (HUCFF/UFRJ). All subjects included in the study received full information on the nature of the study and gave their written consent. The full protocol received approval from the Hospital Research Ethics Committee prior to commencement of the study. No financial incentives were given.

The sample consisted of patients who had completed a full course of MDT, were over 18 years of age, and had pain at the time of the interview that had persisted for at least 6 months. After examination, patients with cognitive deficit, doubtful diagnosis, current leprosy reactions, diabetic or other neuropathies, traumatic nerve injury, renal or cardiac insufficiency, planter ulcer or drop foot were not considered for the study.

Neuropathic pain was confirmed by neuroanatomical pain distribution and neurological examination demonstrating positive or negative sensory or motor loss in the innervated areas of the affected peripheral nerves. After clinical examination, patients completed the \textit{Douleur...}
neuropathique en 4 questions (DN4) questionnaire. The DN4 consists of seven items related to symptoms and three related to clinical examination. A total score of 4 out of 10 or higher suggests neuropathic pain. After completing the DN4, clinical assessment of the area was undertaken, evaluating ‘hypoesthesia to touch’ by applying a light touch with a finger on the painful area and a non-painful area simultaneously, and ‘hypoesthesia to pinprick’ using 300 g Semmes-Weinstein monofilaments. Mechanical allodynia was evaluated using a brush on the painful area.15

Pain intensity was assessed using a visual analogic scale (VAS) ruler. Subjects were asked to indicate their average pain intensity during the previous two weeks by marking a 10·0 cm-long horizontal line labeled ‘no pain’ at one end and ‘worst pain possible’ at the other.16

The psychological health of the participants was measured using the 12-item General Health Questionnaire (GHQ-12). The GHQ is a screening tool used to identify the severity of psychological distress experienced by an individual within the past few weeks. For the purpose of this study, a four-point scale of less than usual, no more than usual, rather more than usual, and much more than usual was used to evaluate each item; the scoring system in the current study was the GHQ score (0-0-1-1) method. By this method each person could score from 0 to 12 points. A score of 4 or higher was categorised as indicating a high psychological distress level. On the basis of the existing evidence this questionnaire is consistent and reliable (Cronbach’s alpha coefficient = 0·87) in general population screening.17,18

In addition, the World Health Organization Quality of Life Assessment BREF (WHOQOL-bref) was used. The WHOQOL-bref was developed to assess quality of life (QoL) and contains 26 items divided into four domains: physical, psychological, social relationships, and environmental. Each item uses a five-point response scale, with higher scores indicating a better QoL. The final scores of overall QoL and of each domain are calculated by a syntax that considers the answers for each question that composes the domain, resulting in final scores on a scale from 4 to 20.19,20

A descriptive analysis was performed to determine the distributional characteristics of socio-demographic variables, the subjects’ levels of psychological health and their quality of life. The totals, means and standard deviations, along with the minimum and maximum scores on the GHQ and WHOQOL-bref, were calculated. A t-test analysis was performed to determine if the GHQ and WHQOQOL-bref domains scores would vary between low and high psychological distress groups. Data analyses were performed using the Statistical Package for Social Science (SPSS) version 13·0, with significance levels set at $P \leq 0.05$.

Results

SAMPLE PROFILE

During the period of the study, 33 leprosy patients with chronic pain complaints in the upper or lower extremity were evaluated. The final sample consisted of 21 (66·3%) patients that met the criteria for neuropathic pain diagnosis. Twelve patients were excluded because the diagnosis of neuropathic pain could not be confirmed by physical examination and the DN4 questionnaire.

The sample consisted of 13 men and eight women, with a mean age of 47·7 years (SD = 9·4). Seventeen (81%) patients had multibacillary leprosy, and four (19%) had paucibacillary leprosy. The mean period since MDT discharge was 7·6 years (SD = 5·6).
Regarding the WHO disability criteria for leprosy, eight (38·1%) patients had sensory loss (Grade 1), and 13 (61·9%) had deformities (Grade 2) in their eyes, hands or feet.

**PAIN AND PSYCHOLOGICAL DISTRESS**

The pain intensity reported by participants on the VAS ranged from 40 mm to 100 mm with a mean of 7·1 cm (SD = 2·9). Differences in pain intensity with respect to gender were minimal: 6·9 cm (SD = 3·2) in male patients versus 7·0 cm (SD = 2·6) in females. Multibacillary patients had a lower mean pain intensity of 68 mm (SD = 3·2) when compared with paucibacillary patients (8·2 cm, SD = 1·3). Patients with both Grade 1 and 2 disability had a mean pain intensity of 7·1 mm.

The descriptive analysis showed that the mean GHQ score for the sample was 6·80 (SD = 3·26). Using the cut-off point of 4, the study revealed that five (23·8%) of the respondents scored below 4 on the GHQ-12, while 16 (76·2%) obtained scores of 4 and higher. Considering the leprosy classification, all four paucibacillary patients were classified as having high levels of psychological distress against 12 (57·1%) of the multibacillary patients. The GHQ-12 mean score was also higher in paucibacillary patients, being 8·75 (SD = 3·5), compared with 6·3 (SD = 3·1) in multibacillary patients. Concerning the presence of physical disability, patients with grade disability had a GHQ-12 mean score of 3·4 (SD = 1·2) and those with Grade 2 had a mean of 3·2 (SD = 0·9). Seven (33·3%) Grade 1 and nine (42·9%) Grade 2 patients were considered to have high psychological distress levels.

We analysed the GHQ-12 in a factor model. Table 1 shows the frequencies for depression (questions 1, 4, 7, 8, 12; $\alpha = 0·72$); anxiety (questions 2, 5, 9; $\alpha = 0·76$) and self-efficacy (3, 4, 6, 10, 11; $\alpha = 0·76$), as defined by Gouveia et al.\textsuperscript{17}

Pain intensity differed between groups, and the patients classified as having low psychological distress levels had a mean pain intensity of 6·7 cm (SD = 4·4), whereas those with high psychological distress levels had a mean pain intensity of 7·2 cm (SD = 2·5) ($P = 0·01$).

**Table 1.** Frequencies distribution considering GHQ correlated factors (depression, anxiety and self-efficacy)

<table>
<thead>
<tr>
<th>GHQ-12</th>
<th>Yes N (%)</th>
<th>No N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Depression</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Been able to concentrate on whatever you are doing</td>
<td>8 (38·1)</td>
<td>13 (61·9)</td>
</tr>
<tr>
<td>Been able to enjoy your normal day-to-day activities</td>
<td>4 (19·0)</td>
<td>17 (81·0)</td>
</tr>
<tr>
<td>Lost much sleep over worry</td>
<td>6 (28·6)</td>
<td>15 (71·4)</td>
</tr>
<tr>
<td>Felt constantly under strain</td>
<td>7 (33·3)</td>
<td>14 (66·7)</td>
</tr>
<tr>
<td>Been thinking of yourself as a worthless person</td>
<td>17 (81·0)</td>
<td>4 (19·0)</td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Felt that you are playing a useful part in things</td>
<td>12 (57·1)</td>
<td>9 (42·9)</td>
</tr>
<tr>
<td>Been able to face up to your problems</td>
<td>11 (52·4)</td>
<td>10 (47·6)</td>
</tr>
<tr>
<td>Felt you couldn’t overcome your difficulties</td>
<td>8 (38·1)</td>
<td>13 (61·9)</td>
</tr>
<tr>
<td><strong>Social dysfunction</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Been losing confidence in yourself</td>
<td>13 (61·9)</td>
<td>8 (38·1)</td>
</tr>
<tr>
<td>Been feeling unhappy and depressed</td>
<td>7 (33·3)</td>
<td>14 (66·7)</td>
</tr>
<tr>
<td>Felt capable of making decisions about things</td>
<td>10 (47·6)</td>
<td>11 (52·4)</td>
</tr>
<tr>
<td>Been feeling reasonably happy</td>
<td>8 (38·1)</td>
<td>13 (61·9)</td>
</tr>
</tbody>
</table>
QUALITY OF LIFE AND PSYCHOLOGICAL DISTRESS

Regarding QoL, patients with high levels of psychological distress had the lowest mean scores in all domains of the WHOQOL-bref. The lowest mean scores were physical domain, with a mean of 9·9 (SD = 3·3), followed by environment (11·9; SD = 3·0), psychological (13·5; SD = 2·6) and social relations (14·0; SD = 3·7) (Table 2).

Discussion

The prevalence of psychiatric comorbidity in leprosy patients differs widely across the range of existing studies. Kumar and Verghese\textsuperscript{21} found that 10\% of leprosy patients suffered some psychiatric disorder, with depression being the most common. Olivier\textsuperscript{22} noted that 46\% suffered from an affective disorder. Soykan, Kundakc and Erdem\textsuperscript{23} found that 65\% of hospitalised patients with leprosy were clinically depressed. A study by Leekassa, Stewart and Sagduyu\textsuperscript{24} with a sample size of 786, found that the prevalence of mental distress in leprosy patients was 52·4\%, compared with 7·9\% in those with other skin conditions. In another study by Lasry-Levy \textit{et al.}\textsuperscript{15} 14·9\% of patients had psychological morbidity, and Sanyal \textit{et al.}\textsuperscript{25} reported that 53·8\% of 93 leprosy patients had psychiatric diseases. More recently, Rocha-Leite \textit{et al.}\textsuperscript{26} noted that 30·8\% of their sample were diagnosed with current depression and 32·5\% had had depression in the past. According to these authors, 15·8\% met the diagnostic criteria for panic disorder; 11·7\% for agoraphobia; and 15\% for obsessive-compulsive disorder. In addition, 11·7\% had body dysmorphic disorder; 9·2\% generalised anxiety disorder; 9·2\% social phobia; and 5·8\% somatoform pain disorder. The risk of suicide was low in 16·7\%, moderate in 54·2\% and high in 7·5\%. In the general population, the prevalence of psychological distress ranges from 5\% to 27\%.\textsuperscript{27}

In this descriptive study we sought to investigate psychological distress in leprosy patients with chronic neuropathic pain. The majority of the participants had high psychological distress levels. In patients affected by leprosy, comorbid psychiatric disorders may be caused by visible dermatological lesions, deformities or even social exclusion and stigmatization. However, it is also possible that patients with chronic pain have an increased occurrence of co-existent psychological distress; most notably, depression and anxiety disorders.\textsuperscript{28}
Psychological distress may contribute to the maintenance of the pain state. In a Delphi study by Boogaard et al., psychological factors, mainly depression and pain catastrophizing, were recognised as important predictors of persistent neuropathic pain. In a study on HIV-associated neuropathy, 20% of patients had sensory neuropathy and 36% showed evidence of depression. The possibility of reverse causality cannot be fully discarded, since psychiatric patients have been shown to have a decreased threshold for pain. In our study, we could not differentiate between psychological comorbidity arising because of leprosy or chronic pain.

Lasry-Levy et al. found that 41% of 22 patients with neuropathic pain had psychological morbidity; however, the study did not exclude patients with potential pathologies such as diabetes or other painful neuropathies, nor was any information provided about pain intensity and QoL of patients with mental distress. These factors differentiate this study from the present one.

We found a higher prevalence of psychological distress in leprosy patients with higher disability levels (Grade 2). These findings are in accordance with those of Leekassa et al., who concluded that the presence of disability seems to increase the risk of mental distress, probably because of disfigurement.

The General Health Questionnaire (GHQ) was chosen for this study because it is the screening scale that is probably most used for common mental disorders; it has been found to have high sensitivity and specificity for current mental status including depression, dysthymia, panic disorder, generalised anxiety disorder, and somatisation disorder. We preferred to use the GHQ scoring method (0-0-1-1) rather than the simple Likert scale of 0-1-2-3, to help to eliminate any biases which might result from the respondents who tend to choose responses 1 and 4 or 2 and 3, respectively. Furthermore, it has been used in other studies of leprosy patients and has been validated for the Brazilian population.

Regarding QoL, patients with high levels of psychological distress had low scores in all domains of the WHOQOL-bref; they also had higher levels of pain intensity compared to those with low psychological distress levels. The most affected domain was the physical domain, probably because pain might affect specific items of this domain, such as dependence on medicinal substances and medical aids; pain and discomfort; sleep and rest; and work capacity. In a previous study on chronic neuropathic pain and QoL in leprosy patients, we found that these variables scored low and the patients were more satisfied with their mobility. Surprisingly, the psychological domain was not the most affected in patients with high psychological distress levels, but ranked third. We speculate that this might happen because the WHOQOL-bref is not an instrument designed to detect mental disorders, having no sensitivity or specificity in that domain.

This study has inherent limitations such as the sample size and the absence of a control group. However, the sample represents all patients with neuropathic pain caused by leprosy in our pain service during the period of the study. Considering these limitations, it was not possible to establish any cause-and-effect relationship between pain intensity and the GHQ-12 score, since it is difficult to distinguish if psychological distress is an antecedent or consequence of chronic neuropathic pain. Furthermore, we did not investigate the influence socio-cultural and socio-demographic risk factors have upon psychological distress. It should also be noted that the diagnosis of psychological morbidity was not based on clinical psychiatric evaluation but on GHQ-12 scores only. Since this was not a prospective study, the duration of leprosy, modification of pain characteristics (intensity, quality and localisation) and psychiatric illness, were not evaluated. Future studies are required with a larger sample.
size and that use psychological treatments as a means of improving management of leprosy and chronic pain.

Accepting these limitations, this study highlights the importance of psychological evaluation in leprosy patients with chronic neuropathic pain in order to reduce negative impacts on their QoL. We postulate that the presence of psychological morbidity in leprosy patients with chronic neuropathic pain might be a factor that contributes to their pain state. Some studies highlight the association of chronic pain with anxiety, depression, poor quality of sleep and a reduced capacity to perform daily and occupational activities, and suggest that it also impairs participation in social activities.33–38 These factors should be investigated in the future. Finally, it is important to continue research in this field in order to identify whether a reduction in perceived levels of pain leads over time to a decrease in psychological distress, and a better quality of life.

Conclusion

Our results suggest that most patients with leprosy have psychological morbidity. Patients with chronic neuropathic pain together with a high psychological distress level had a higher pain intensity and also a poorer quality of life in all domains. It is possible that leprosy and chronic neuropathic pain may have a separate, or perhaps a simultaneous, interaction that contributes to psychological morbidity or even to the maintenance of the pain state. Further studies with larger sample sizes are necessary to confirm our conclusions.

References
