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Original Article

Physical Medicine and Rehabilitation Section

# Prevalence of Fatigue and its Association with Pain Intensity, Psychological Status and Sleep Quality in Patients with Neck Pain

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## ABSTRACT

**Introduction:** Neck Pain (NP) is a major public health problem. Social and economic participation of many individuals gets negatively impacted due to NP. Fatigue and pain are common complaints in patients with this condition. Both can interfere with the daily life of patients by affecting the quality of sleep which can lead to psychological issues. But, the prevalence of fatigue and its association with pain, sleep quality and psychological factors have not been examined properly in patients complaining of NP.

**Aim:** To examine the prevalence of fatigue and its association with pain intensity, depression, anxiety, and sleep disturbance in patients with NP.

**Materials and Methods:** A cross-sectional study on 296 NP patients with a mean age of 30±7.2 years (181 males and 115 females) was conducted between March 2019 till November 2019. It was conducted at the Physiotherapy Department of the University and Amarjyoti College of Physiotherapy. The Multidimensional Fatigue Inventory (MFI), Hospital Anxiety and Depression, Pittsburgh Sleep Quality Index (PSQI) and Numeric Pain Rating Scale were used to evaluate fatigue, depression and anxiety, sleep quality and pain intensity, respectively. Spearman's rank correlation coefficient and Mann-Whitney U test were used for analysis.

**Results:** The point prevalence rate of severe fatigue in participants was 39.86%. Fatigue was significantly related with pain intensity, psychological factors, and sleep quality ($p<0.05$). We also observed a significant association between sleep quality and psychological factors in this sample ($p<0.05$).

**Conclusion:** Fatigue was a prominent factor in patients with NP and it was associated with pain intensity, depression, anxiety, and sleep disturbance. Prevalence of fatigue was higher in chronic stage of NP than in the acute sage. Identifying these factors may help in prevention and management of NP and its co-morbidities.


**Keywords:** Acute neck pain, Anxiety, Chronic neck pain, Depression, Fatigue symptoms, Sleep disturbances

## INTRODUCTION

Neck pain is a disabling musculoskeletal condition which frequently hinders the daily activities of patients [1]. One-year prevalence rate for NP ranges between 4.8% to 79.5% [2]. It causes significant financial burden for the individual as well as the community [3]. There are different physiological and psychosocial factors involved in NP [4]. Fatigue is one of these factors that could be involved in NP [5]. Fatigue is a complicated phenomenon and there is hardly an exact definition [6]. However, it has been defined as a subjective and internal feeling of tiredness that could or could not be related to physical activity. It can become chronic, thereby hampering daily routine activities [7].

Fatigue has as a deleterious impact on mental and physical health; it may impair or delay the recovery process and cause psychological impairments [8] as well as sleep disturbances [9]. It has also been found to be closely associated with pain intensity, and that association could be aetiological in nature for chronic pain participants [10].

A few studies have demonstrated a correlation between fatigue and depression as well as sleep disturbances in Chronic Low Back Pain patients (CLBP) and fibromyalgia [11-13]. For example, high prevalence of fatigue was observed in CLBP [11]. Poor sleepers have reported higher fatigue and pain level in comparison to good sleepers which depict an association between fatigue and sleep disturbance in CLBP [14]. A strong association between fatigue and depression has been also reported in CLBP [12]. However, such associations are poorly documented in NP. There is a dearth of studies for fatigue and its association with depression, anxiety, and sleep disturbance in NP patients. A more thorough research of the complexities of fatigue, psychological factors, and sleep disturbances is essential for the development of targeted interventions for treatment of NP.

As far as we know, no previous research has appropriately investigated the prevalence of subjective fatigue in acute and chronic stage of NP which is also an important concern in patient management. A thorough knowledge of the associations between all these factors would be useful in understanding and explaining how these factors interrelate and lead to high costs and sufferings.

Therefore, the objectives of the present study was two-fold: To study the prevalence of fatigue in acute and chronic stage of NP and secondly, to understand the relationship between fatigue, pain intensity, psychological factors, and sleep disturbances in NP patients. In this study, It has been hypothesised that NP participants will have a high prevalence of fatigue and that the fatigue would have a significant association with pain intensity, quality of sleep and psychological factors.

## MATERIALS AND METHODS

A cross-sectional survey of NP patients was conducted at the Centre for Physiotherapy and Rehabilitation Science, Jamia Millia Islamia and Amarjyoti College of Physiotherapy in New Delhi, India over a period of 10 months (March to December 2019) in New Delhi, India. The study received ethical approval from the Ethics Committee of the University (19/2/210/JMI/IEC/2019) prior to its commencement and was performed in accordance with the Helsinki Declaration (1964). The study was also registered under the clinical trials registry (CTRI/2019/09/021028).

**Sample size calculation:** A sample of 296 participants (181 males and 115 females) with NP was arrived at using free open-source

epidemiological statistics toolset (OpenEPI) by using the data of prevalence of fatigue in low back pain patients [11]. The number of participants were determined within a design effect of 1.0, and a confidence interval limit of 95%, and an anticipated frequency of 26%.

A total of 402 participants with NP were screened and finally 296 were recruited after applying inclusion and exclusion criteria.

**Inclusion criteria:** Participants in acute (<3 months) and chronic (>3 months) stage of pain [15]; participants aged 18 years and older; no spine surgery in the preceding year; preserved communication; and working knowledge of English, were included in this study.

**Exclusion criteria:** Cancer; acute or chronic medical conditions; and any medication or disease that precluded informed consent, were excluded from the study.

### Study Procedure

The principal investigators diligently screened and assessed the participants for eligibility. All the patients were explained about the procedure in detail and they were informed about their right to withdraw at any time during the study. They gave their written informed consent before enrollment for the study. Socio-demographic data was collected from NP participants which included questions about age, height, weight, body mass index, gender, marital status, level of education, income, and employment status (retired, employed, applicant). Questions related to lifestyle (physical activity status, smoking, alcohol consumption, coffee, and tea) were also asked. Each participant was required to complete MFI, Hospital Anxiety and Depression Scale (HADS), PSQI, and Numeric Pain Rating Scale.

### Outcome Measures

**Fatigue:** Fatigue was assessed by MFI. It is a self-reporting tool aimed to ascertain subjective fatigue [16]. It contains 20 items, purporting to assess five fatigue subscales: general fatigue, physical fatigue, mental fatigue, reduced activity, and reduced motivation. Each subscale contains five points. Each subscale has a score range between 4 and 20 and the total score range is between 20 and 100. A higher score indicates a higher level of fatigue. A score of ≥13 in general fatigue domain or ≥10 in reduced activity domain have been identified as an indicator of severe fatigue [17]. In the present research, the score of general fatigue subscale was preferred and used to indicate severe fatigue as previously recommended [16]. The MFI is a psychometrically suitable questionnaire to assess fatigue, with high internal consistency and validity [16].

**Psychological factors:** Depression and anxiety were examined by HADS. It is a valid self-rating scale that rates the level of depression and anxiety [18]. HADS consists of 14 items, seven of which refer to anxiety and the other seven to depression. Each question has four possible answers, corresponding to scores between 0 and 3. Therefore, the score for classification of depression and anxiety ranges from zero to 21 points: 0-7 indicating no depression and anxiety symptoms, 8-10 indicating mild symptoms, score range between 11-14 indicating moderate depression and anxiety, and finally, a score of ≥15 reflecting severe depression and anxiety symptoms [19]. HADS has performed consistently well in evaluating the severity of depression and anxiety symptoms in psychiatric and somatic primary care patients and the general population [20].

**Sleep quality:** The PSQI was administered to assess quality of sleep in NP patients. It is a self-reporting questionnaire that asks participants to describe their sleep quality in the one-month [21]. The PSQI has been widely and extensively used among different populations for clinical and research purposes. The PSQI contains 19 questions, distributed into seven components that accumulatively form a global score of PSQI. These seven components relate to: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medications and daytime dysfunction. Each component has a score range from 0-3. And the total score is made up from the sum of the scores obtained from the seven components giving a cumulated score range between 0-21; the higher the score, greater is the sleep disturbance. A score of more than five depicts a poor quality of sleep [21].

**Pain intensity:** Pain intensity was evaluated by using 11-point Numerical Pain Rating Scale (NPRS). The NPRS asks participants to rate their pain from 0-10, wherein 0 means "no pain" and 10 means the "worst possible pain". The NPRS is easy to administer and has been widely used in research and in different musculoskeletal conditions. It has a good validity, and previous research demonstrates a positive and significant association of NPRS with other measures of pain intensity [22].

**Physical activity:** The level of physical activity was screened by asking "In the past week, on how many days have you done a total of 30 minutes or more of physical activity, which was enough to raise your breathing rate. This may include activities such as brisk walking or cycling for recreation but should not include activities that could be part of your job". The question has a valid open-response ranging from zero to seven days in the past week [23]. This question has shown moderately validity and demonstrated strong repeatability, suggesting that this single item has the potential for screening participants for a range of physical activity interventions [23].

## STATISTICAL ANALYSIS

Initially, the distribution of data was checked by Kolmogorov-Smirnov test as the data was not normally distributed. The data was entered into a database and analysed using the SPSS-version 21. The associations between fatigue, pain, sleep, and psychological factors were measured using Spearman's correlation coefficient, at an alpha level of less than 0.05. Mann-whitney U test was used for comparisons of fatigue prevalence, depression, anxiety, and sleep disturbance between (acute-chronic) NP participants, and between male and female participants.

## RESULTS

### Prevalence of fatigue in NP Patients

Among the recruited participants, 167 patients had chronic (duration >3 months) and 129 had acute (duration <3 months) pain. A 41.7% of the participants were married, 94% had completed at least graduation level, and 43.7% were employed. The average age of participants was 29.85±11.1 years and the average present pain intensity was 4.84±1.7. Demographic and clinical characteristics of NP patients are represented in [Table/Fig-1].

Overall, 118 participants (39.86%) presented MFI general fatigue of >13 and therefore, 115 (38.85%) participants were classified as severely fatigued [Table/Fig-2]. When the data was divided into two groups (acute stage and chronic stage), we observed that participants in acute and chronic stage of NP differ considerably in regard to the level of fatigue. A higher prevalence of fatigue (49.1%) was documented among chronic NP patients as compared to 27.1% prevalence point of fatigue in acute NP patients ($p<0.05$). No significant gender difference was noted in fatigue severity $p>0.05$ [Table/Fig-2].

### Psychological factors, sleep disturbance and physical activity status in NP patients

More than half of the participants reported sleep disturbances, and anxiety symptoms, and almost half of the participants reported depressive symptoms. The results did not reveal a gender difference in depression, anxiety and sleep disturbance $p>0.05$, but significant differences were observed between chronic and acute stage of NP in which chronic NP patients reported more depressive and anxiety symptoms as well as sleep disturbances $p<0.05$ [Table/Fig-3,4]. An

| Variables | Minimum | Maximum | Mean±SD† |
|---|---|---|---|
| Age (in years) | 21 | 57 | 30.3±7.2 |
| Body mass index (kg/m$^2$) | 15.6 | 33.8 | 23.6±3.0 |
| Present pain intensity | 1 | 9 | 4.85±1.7 |
| Average pain intensity | 0 | 9 | 4.6±4.6 |
| **MFI‡** | | | |
| Global score | 4 | 80 | 53.4±12.4 |
| General fatigue | 1 | 19 | 11.5±3.2 |
| Physical fatigue | 4 | 20 | 11.3±3.0 |
| Mental fatigue | 1 | 20 | 10.4±3.2 |
| Reduced activity | 4 | 19 | 10.5±3.0 |
| Reduced motivation | 3 | 19 | 10.0±3.0 |
| **PSQI§** | | | |
| Global score | 0 | 13 | 6.3±3.0 |
| Sleep quality | 0 | 3 | 1.3±0.7 |
| Sleep latency | 0 | 4 | 1.4±0.9 |
| Sleep duration | 0 | 3 | 1.0±0.7 |
| Sleep efficiency | 0 | 3 | 0.6±0.8 |
| Sleep disturbance | 0 | 3 | 0.9±0.5 |
| Sleep medication | 0 | 3 | 0.1±0.4 |
| Daytime dysfunction | 0 | 3 | 1.0±0.8 |
| **HADS‖** | | | |
| Anxiety score | 0 | 20 | 8.6±3.8 |
| Depression score | 0 | 18 | 7.2±3.3 |

**[Table/Fig-1]:** Demographic and clinical characteristics of neck pain patients.
†Standard deviation; ‡Multidimensional fatigue inventory; §Pittsburgh sleep quality index; ‖Hospital anxiety and depression scale

| Fatigue domains | Group | Mean rank | Significant level (Z) |
|---|---|---|---|
| Global MFI* score | Acute | 125.69 | <0.001 (-3.93) |
| | Chronic | 165.10 | |
| General fatigue | Acute | 126.64 | <0.001 (-3.78) |
| | Chronic | 164.37 | |
| Physical fatigue | Acute | 121.61 | <0.001 (-4.68) |
| | Chronic | 168.23 | |
| Mental fatigue | Acute | 134.11 | 0.014 (-2.46) |
| | Chronic | 158.65 | |
| Reduced activity | Acute | 134.97 | 0.021 (-2.3) |
| | Chronic | 157.99 | |
| Reduced motivation | Acute | 137.11 | 0.054 (-1.9) |
| | Chronic | 156.35 | |
| Global MFI score | Male | 142.36 | 0.122 (-1.54) |
| | Female | 158.16 | |
| General fatigue | Male | 140.85 | 0.052 (-1.94) |
| | Female | 160.55 | |
| Physical fatigue | Male | 141.46 | 0.074 (-1.78) |
| | Female | 159.58 | |
| Mental fatigue | Male | 142.85 | 0.152 (-1.433) |
| | Female | 157.85 | |
| Reduced activity | Male | 145.61 | 0.464 (-0.732) |
| | Female | 153.04 | |
| Reduced motivation | Male | 145.27 | 0.413 (-0.819) |
| | Female | 153.59 | |

**[Table/Fig-2]:** Items of multidimensional fatigue inventory (Results of Mann-whitney test).
*Multidimensional Fatigue Inventory

analysis of the association between psychological factors and sleep quality shows a significant association between these factors. Only 14% of the sample were physically active, and 86% did not meet the minimum recommended level of physical activity that is 150 minutes of moderate-intensity aerobic physical activity throughout the week [24].

| Anxiety symptoms | Participants N (%) |
|---|---|
| Normal (0-7) | 105 (35.6%) |
| Borderline case (8-10) | 95 (32.1%) |
| Case (11-21) | 96 (32.3%) |
| **Depression symptoms** | **Participants (N=296)** |
| Normal (0-7) | 155 (52.4%) |
| Borderline case (8-10) | 94 (31.7%) |
| Case (11-21) | 47 (15.7%) |

**[Table/Fig-3]:** Hospital Anxiety and Depression Scale.

| Pittsburgh sleep quality index | Participants (N=296) |
|---|---|
| Normal sleep quality (0-5) | 117 (31.1%) |
| Mild disturbance (6-8) | 113 (38.2%) |
| Moderate disturbance (9-12) | 62 (20.9%) |
| Severe disturbance (>12) | 4 (1.4%) |

**[Table/Fig-4]:** Sleep quality in neck pain patients

### Correlations of Pain Intensity, Anxiety and Depression and Sleep with Fatigue

The Global score and all MFI domains except mental fatigue are significantly correlated with pain intensity ($p<0.005$). A significant correlation was also found between the Global fatigue score and its domains with psychological factors ($p<0.005$). Also, all fatigue domains and Global MFI score were significantly associated with quality of sleep ($p<0.005$). In addition, a significant association of psychological factors with sleep quality was observed ($p<0.005$) [Table/Fig-5].

## DISCUSSION

The study was designed to examine the prevalence of fatigue in acute and chronic stage of NP and to assess if there exists any correlation of fatigue with depression, anxiety, and sleep disturbances. Up to the best of our knowledge, no prior studies have examined the prevalence of subjective fatigue among acute and chronic NP patients. The current study reveals that fatigue is a notable problem in NP. The fatigue prevalence in this sample was high (39.86%), which is higher than chronic fatigue syndrome observed in the general population which is 9.9% and 0.9% [25]. A previous study with a smaller sample of chronic NP patients (N=33) documented that, fatigue is a significant complaint in chronic NP patients [5]. The study was the first study that used fatigue inventory to clearly document fatigue in chronic NP and CLBP patients. The results and discussion of this study mainly relied upon the data gathered from CLBP patients (N=175) rather than the chronic NP patients (N=33). Moreover, the said study recruited only chronic pain participants [5]. A high prevalence rate of fatigue has also been observed among CLBP patients which were 26% and 70% [11,12], respectively.

In the present study, the data was divided based on gender (male or female), and the stage of NP (acute or chronic). It was found out that there were no differences in fatigue based on gender; however, there was a significant difference in fatigue between acute and chronic stage of NP. Fatigue is a prominent complaint among both acute and chronic stage of NP, but participants in the chronic stage reported significantly higher fatigue level compared to those in the acute stage of NP. There is a broad body of literature (17 high quality articles) evaluated by Fishbain DA et al., 2003, which points to a significant relationship of fatigue level with pain intensity across various clinical conditions [10]. A previous study conducted on rheumatic arthritis patients also reported a significant association between fatigue and pain [26]. A recent study similarly reported strong and significant association of pain severity with fatigue level amongst CLBP patients [27]. The present results, therefore, support previous studies on the association of pain with fatigue.

| Parameters | Present pain | Average pain | MFI* global | GF† | PF‡ | MF§ | RA‖ | RM** | PSQI†† global | Anxiety score | Depression score |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Present pain | - | - | 0.331** | 0.352** | 0.261** | 0.125* | 0.213** | 0.322** | 0.434** | 0.340** | 0.283** |
| Average pain | - | - | 0.308** | 0.303* | 0.214** | 0.163** | 0.174** | 0.298** | 0.405** | 0.379** | 0.302** |
| MFI global | 0.331** | 0.308** | - | - | - | - | - | - | 0.473** | 0.429** | 0.456** |
| GF | 0.352** | 0.303** | - | - | - | - | - | - | 0.407** | 0.410** | 0.296** |
| PF | 0.261** | 0.214** | - | - | - | - | - | - | 0.299** | 0.322** | 0.348** |
| MF | 0.125* | 0.163** | - | - | - | - | - | - | 0.425** | 0.300** | 0.296** |
| RA | 0.213** | 0.174** | - | - | - | - | - | - | 0.309** | 0.277** | 0.271** |
| RM | 0.322** | 0.298** | - | - | - | - | - | - | 0.378** | 0.310** | 0.390** |
| PSQI global | 0.434** | 0.405** | 0.473** | 0.407* | 0.299** | 0.425** | 0.309** | 0.378** | - | 0.409** | 0.429** |
| Anxiety score | 0.340** | 0.379** | 0.429** | 0.410* | 0.322** | 0.300** | 0.277** | 0.310** | 0.409** | - | 0.613** |
| Depression score | 0.283** | 0.302** | 0.456** | 0.296* | 0.348** | 0.296** | 0.271** | 0.390** | 0.429** | 0.613** | - |

**[Table/Fig-5]:** Spearman rank correlation coefficient.
*Multidimensional fatigue inventory; †General fatigue; ‡Physical fatigue; §Mental fatigue; ††Pittsburgh sleep quality index; ‖Reduced activity; **Reduced motivation; *Correlation is significant at the 0.05 level (2-tailed); **Correlation is significant at the 0.01 level (2-tailed)

The aetiopathogenesis of fatigue symptoms is not well-known. However, the structures that are related to pain physiology can explain the fatigue-pain association. Involvement of structural lesions that impair the normal process of activations in pathways linked the higher cortical centre and basal ganglia, thalamus, limbic system [28]. These similarities may explain the close association between fatigue and pain found in the relevant literature. Previous findings have shown that improvement in fatigue level could be secondary to reduction in pain intensity [29]. And this association could be aetiological in nature, as previous literature suggests that fatigue reduction is mediated by pain reduction, night pain, and sleep interference [9,10].

One of the most remarkable findings to emerge from the present results is the significant association of fatigue domains with depression, anxiety, and sleep disturbance in this population. The association between fatigue with depression and anxiety seems to be important, as both symptoms perpetuate fatigue [30]. It has been demonstrated that higher depression scores are linked with an aggravation of fatigue [31]. It is also essential to consider that fatigue is one of the diagnostic criteria for depression [32]. Fewer studies in the literature have examined the relationship between fatigue symptoms and anxiety. The evidence could appear to indicate that anxiety is linked with poor fatigue prognosis [33], so delineating the exact nature of the association may be complicated and requires further research.

Proposing the association between fatigue and sleep disturbance would appear intuitive, as it is logical that fatigue leads to sleep disturbance or vice versa. However, the nature of their relationship is not well-documented. However, previous studies have noticed that there is a relationship between the magnitude of fatigue observed and corresponding disturbances [34]. The most persuasive evidence concerning the association between fatigue and sleep disturbance emerges from the experimental study, which demonstrated an increased level of fatigue with experimentally created sleep deprivation [35,36]. It is essential to consider that there seems to be a complex interrelationship association between fatigue and sleep [35]. It's also important to consider that none of the studies in the literature were found to exactly determine whether sleep disturbance has a direct impact on fatigue, or this association could be mediated through the increased level of pain that was found after poor sleep [37].

These finding highlights that, little is known about the existence of fatigue and its association with depression, anxiety, and sleep disturbance in patients with NP. These results have a significant value for understanding the determinants of NP and for improving and managing the signs and symptoms associated with it. Our results are in accordance with results reported by Fishbain DA et al., 2004 that observed an association between depression and fatigue in CLBP patients and chronic NP patients [5]. The study reported that depression is a significant predictor of fatigue in CLBP and chronic NP patients. Furthermore, depression was strongly associated with fatigue in CLBP patients [12].

There is scarcity of research on the association between fatigue and sleep in NP patients. The present findings demonstrate a significant association between fatigue and sleep. Interesting, results obtained by Moxham EG, 1999, have shown that sleep disturbance mediates the association between fatigue and pain in fibromyalgia patients [38]. Similar findings have also been observed in fibromyalgia patients in which fatigue was significantly associated with sleep disturbance [13]. A recent study conducted by Saravanan A et al., 2019, reported that CLBP co-exists with fatigue, sleep disturbance, and depression [27].

The present study findings regarding the psychological factors and sleep quality in NP patients are also important. The results show that symptoms of anxiety, depression and sleep disturbance are prominent and significantly correlated in NP patients. Presence of depression was reported as significant predictor for sleep disturbance in chronic pain participants [39]. Prior findings have revealed a significant association between depression and sleep disturbance in CLBP [40]. The present findings also show that symptoms of anxiety, depression and sleep disturbance, are more prominent in chronic stage of NP than acute stage.

The results of the index study may provide a crucial data on the pathogenesis of acute and chronic NP. Generally, it is believed that the exact cause of NP is not known, although there is consensus that the most likely causes of NP are multi-factorial in nature. Many patients with NP who suffer with chronic pain also state that in the early history of their illness, the symptoms were simply acute, and then later evolved into a long-term condition. In the last few decades, efforts have been made to identify patients with acute pain who are at high risk to develop chronic pain. This process of identification has significant theoretical and clinical importance. Previous research has recognised the role of psychosocial factors such as depression and anxiety in the pathophysiology of acute and chronic pain and in the transition from acute to chronic pain conditions [41]. The present results supplement the existing literature about the transition from acute to chronic stage of NP. The results show that fatigue, depression, anxiety, and sleep disturbances are more prominent in chronic stage of NP than acute stage, thus implying that the above-mentioned factors might have a role in the aetiology of acute NP as well as in the transition from acute to chronic stage of NP. Therefore,

management of these factors is probably essential in preventing or controlling the symptoms of NP. The present study results establish a link between fatigue, depression, anxiety, and sleep disturbance thus prompting us to suggest treating these symptoms as early as they are diagnosed.

This study highlights the role of fatigue, depression, anxiety, and sleep disturbance in NP. Appropriate intervention for these factors may help in decreasing pain associated co-morbidities in NP. Our findings suggest that fatigue management, reduction of depression and anxiety symptoms, and restoration of healthy sleep might be beneficial to NP patients to reduce their pain or to reduce his/her vulnerability to develop more severe stages of pain. The higher incidence of fatigue in chronic NP can also be used as a predictor for the development of chronicity. Consequently, improving these co-morbidities could reduce vulnerability to NP, and allow therapeutic interventions to be used more effectively.

### Limitation(s)

The present study did not include objective methods for assessing fatigue and other variables. Because of the large sample size, it was difficult to take care of all the confounders such as age, stress, fear, and pain catastrophising. Future research may address these limitations, using a different methodology that allows substantiating this association.

## CONCLUSION(S)

The current study found a relatively high prevalence of fatigue in NP patients. Pain intensity, anxiety, depression, and sleep were significantly associated with fatigue. Further research is required to determine the factors that might be associated with fatigue in NP patients. It seems that the relationships among these variables suggest that an indirect pathway exists between them, but further research is required to extensively investigate this issue. Fatigue, sleep disturbance, and psychological factors in NP are quite unexplored and poorly understood. Future research needs to further substantiate this association and to examine the prognostic capacities of these factors. Further interventional and cross-sectional studies are required to investigate when and how these factors develop and how they interrelate and impact the pain intensity. Moreover, further research explaining the effect of different treatment approaches on these factors are needed.

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