



## Research Article

### **Pain, Daytime Sleepiness, Anxiety and Depression Levels of Patients with Chronic Neuropathic Pain Syndromes**

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## Summary

**Objective:** The current study aims to determine pain, daytime sleepiness, anxiety and depression levels of patients with chronic neuropathic pain and compare different clinical conditions causing neuropathic pain in terms of these variables.

**Method:** 241 patients (105 patients with diabetic neuropathy, 39 patients with fibromyalgia, 27 patients with carpal tunnel syndrome, 27 patients with radiculopathy, 22 patients with trigeminal neuralgia and 21 patients with postherpetic neuralgia) were included in the study. The assessments were performed using socio-demographic data form, Visual Analog Scale (VAS), Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), Epworth Sleepiness Scale (ESS) and Hospital Anxiety and Depression Scale (HAD).

**Results:** Evaluation of pain with VAS and LANSS showed no statistical difference among subgroups. Scores of LANSS and VAS were positively correlated with each other. ESS scores were found to be above the cut-off point (>10) in all subgroups. LANSS, but not VAS scores were positively correlated with ESS scores. Depression scores were above the cut-off point (>7) in diabetic neuropathy, fibromyalgia and trigeminal neuralgia groups and anxiety scores were above the cut-off point (>10) in diabetic neuropathy, fibromyalgia, trigeminal neuralgia and carpal tunnel syndrome groups. No correlation was found between scores of both VAS and LANSS and scores of HADS. Depression scores correlated positively with ESS scores ( $r=0.153$ ,  $p<0.05$ ).

**Conclusions:** Daytime sleepiness, depression and anxiety are associated comorbidities with different neuropathic pain syndromes. Neuropathic character, but not the intensity of pain is associated with daytime sleepiness. Pain intensity does not predict anxiety and depression levels. Depression, but not anxiety shows a positive correlation with daytime sleepiness. These results might have implications for the better understanding of comorbidities in different neuropathic pain syndromes.

**Key words:** Pain, daytime sleepiness, anxiety, depression, chronic neuropathic pain syndromes

### **Kronik Nöropatik Ağrılı Hastalarda Ağrı, Gün içi uyukluluk, Anksiyete ve Depresyon Düzeyleri**

## Özet

**Amaç:** Mevcut çalışmanın amacı farklı klinik durumlarda nöropatik ağrılı hastalarda ağrı, gündüz uyukları, kaygı ve depresyon düzeylerini belirlemek.

**Yöntem:** 241 hasta (105 hastalarda diyabetik nöropati, 39 hastalarda fibromiyalji, 27 hastalarda karpal tünel sendromu, 27 hastalarda radikülopati, 22 hasta trigeminal nevralsi ve 21 hastalarda postherpetik neuralji) çalışmaya alındı.

**Sonuçlar:** Gruplar arasında Vizuel Analog Skor (VAS) ve LANSS değerlendirmesinde hiçbir fark istatistiksel fark yoktu. Epworth Sleep Skorları tüm alt gruplarda kesme noktası üzerinde ( $>10$ ) bulundu. Depresyon puanları 7 kesme noktası üzerinde ( $>7$ ) diyabetik nöropati, fibromiyalji ve trigeminal nevralsi gruplarında ve anksiyete 10 kesme noktası üzerinde ( $>10$ ) diyabetik nöropati, fibromiyalji, trigeminal nevralsi ve karpal tünel sendromu gruplarında yüksek bulundu. ESS ile depresyon puanları istatistiksel olarak olumlu ilişkili bulundu ( $p < 0,05$ ).

**Sonuçlar:** Farklı nöropatik ağrılı sendromlara gündüz uyku bozukluğu, depresyon ve anksiyete eşlik edebilir. Depresyon, gün içi uyku bozukluğu ile pozitif yönde birliktelik gösterirken anksiyete ile ilişkisi gösterilememiştir. Bu sonuçlarla farklı nöropatik ağrı sendromlarında eşlik eden durumların daha iyi anlaşılması için etkisi olabilir.

**Anahtar Kelimeler:** Ağrı, Gün içi uyku bozukluğu, anksiyete, depresyon, kronik nöropatik ağrı

## INTRODUCTION

The standard definition of chronic pain suggested by the International Association for the Study of Pain states that it is pain that persists after the healing phase following an injury<sup>(35)</sup>. Chronic pain, a costly and debilitating medical condition in industrialized countries, is now viewed as a biopsychosocial phenomenon, in which biological, psychological, and social factors dynamically interact with each other<sup>(49)</sup>. There is a significant association between chronic pain and anxiety, depression and changes in sleep quality. These symptoms can precede and predispose individuals to suffer from chronic pain or chronic painful pathologies can stimulate the emergence of these symptoms<sup>(13)</sup>.

The term chronic pain includes a large variety of clinical conditions. Neuropathic pain (NP) is one of the most prevalent chronic pain syndromes. Neuropathic pain has most recently been redefined by the International Association for the Study of Pain as "pain caused by a lesion or disease of the somatosensory system"<sup>(29)</sup>. Patients with various conditions like diabetic polyneuropathy, poststroke syndromes, postherpetik neuralji, trigeminal neuralji, multiple sclerosis, fibromyalgi,

carpal tunnel syndrome, radiculopathy and human immunodeficiency virus (HIV) sensory neuropathy frequently experience daily pain that impairs their quality of life<sup>(18)</sup>. As in other types of chronic pain, individuals with NP commonly have comorbidities, including mood disorders and sleep disturbances which lead to a poorer quality of life. Patients with NP suffer from a variety of Axis I (eg, affective disorders, generalized anxiety disorder, substance-use related disorders, and somatoform disorders) or Axis II personality disorders<sup>(5)</sup>. The prevalence of depression is higher among chronic pain patients and depressed patients complain of more pain symptoms than people who are not depressed. The percentage of chronic pain patients with depression ranges from 22% to 78%<sup>(19)</sup>. Annagür et al. stated that the most common psychiatric disorder was major depression in subjects with chronic pain<sup>(4)</sup>. Patients with chronic pain also have a higher prevalence of anxiety disorders and anxiety disorders have been related with somatic complaints such as pain<sup>(32)</sup>. More than 70% of patients with the complaint of chronic pain have sleep disturbances such as increased sleep latency, increased wakefulness after sleep onset, increased arousal and reduced slow wave sleep. These sleep problems usually result from pain<sup>(5)</sup>.

Attal et al. reported that subjects with chronic pain of neuropathic in origin displayed greater impairment of quality of life and sleep, and more symptoms of anxiety and depression than those with chronic pain of other origins and the general population. The poor life quality of these patients is not only due to the severity or duration of the pain, but is also affected by the neuropathic nature of pain itself. These data strongly suggest that NP is a specific health condition not only in terms of the nature of pain, but also in terms of disability and functioning<sup>(6)</sup>.

As far as we know, there is no study in literature comparing levels of anxiety and depression and sleep disturbances between different clinical conditions with NP. In this study we aim to determine pain, daytime sleepiness, anxiety and depression levels of patients with chronic NP and compare different clinical conditions causing NP in terms of these variables.

## MATERIAL AND METHODS

### Sampling

This study was conducted at Department of Neurology of a 2. level State Hospital Samsun in Turkey between January 2010 and July 2010. This study was conducted at Neurology Department of Vezirköprü State Hospital, Samsun in Turkey between January 2010 and July 2010. (measurement periods yazılındiyebirrevizyonvar, bundanbaşkayazabileceğimizbir period varmı?) 458 patients who applied to neurology out-patient clinic were recruited. The exclusion criteria for the patients were as follows: having a chronic physical disease other than diabetes mellitus, taking regular medication for pain including psychotropic drugs, alcohol or substance abusers, patients with clinical conditions with probable impairment in cognition such as post-stroke syndromes, HIV sensory neuropathy and multiple sclerosis, diabetic patients with serious diabetic complications such as renal failure, retinopathy or foot ulcers. After applying the exclusion criteria, 241 patients (105

patients with diabetic neuropathy, 39 patients with fibromyalgia, 27 patients with carpal tunnel syndrome, 27 patients with radiculopathy, 22 patients with trigeminal neuralgia and 21 patients with postherpetic neuralgia) were included in the study.

Physical and neurological examinations were done by a neurologist and routine blood tests were applied to all subjects. The Ethical Committee of the institution approved the study. All subjects gave written informed consent to participate in this study. The assessments were performed using the scales below: Socio-demographic data form, Visual Analog Scale (VAS), Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), Epworth Sleepiness Scale (ESS) and Hospital Anxiety and Depression Scale (HAD).

### Measures

Socio-demographic data form: A form prepared by the researchers in order to obtain socio-demographic data (age, gender) and to assess clinical features (HbA1c levels and questions regarding the pain such in keeping with the objectives of the study).

Visual Analog Scale (VAS) For Pain: Visual Analog scale (VAS) for pain is a self-completed unidimensional measure of pain intensity<sup>(27)</sup>. It is widely used because of its simplicity and adaptability to a broad range of populations and settings. For pain intensity, the scale is most commonly anchored by “no pain” (0-1), mild pain (2-3), moderate pain (4-5), intense or severe pain (6-7), unbearable pain (8-11).

Leeds Assessment of Neuropathic Symptoms and Signs Scale (LANSS): The Leeds Assessment of Neuropathic Symptoms and Signs Scale (LANSS) is a standardized test to identify patients with predominant neuropathic pain mechanisms. This tool has two parts—a patient-completed section and a brief physical assessment. The LANSS

identifies patients with neuropathic pain by combining the scores of a patient's verbal description of pain and the results of neurological examination. A cut-off score of 12 points or more (out of a total of 24), when compared with expert opinion, had a sensitivity of 83% and a specificity of 87%<sup>(10)</sup>. The validity and reliability study for the Turkish population has been performed by Yücel et al<sup>(55)</sup>.

**The Epworth Sleepiness Scale (ESS):** The Epworth Sleepiness Scale (ESS) is an effective instrument used to measure average daytime sleepiness. The ESS differentiates between average sleepiness and excessive daytime sleepiness that needs intervention. The client self rates on how likely it is that he/she would doze in eight different situations. Scoring of the answers is 0-3, with 0 being "would never doze" and 3 being "high chance of dozing". A sum of 10 or more from the eight individual scores reflects above normal daytime sleepiness and require for further evaluation<sup>(36)</sup>. The validity and reliability study for the Turkish population has been performed by Ağargün et al<sup>(1)</sup>.

**Hospital Anxiety and Depression Scale (HADS):** The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression. The HADS is a 14-item scale that provides a brief state measure of anxiety and depression. Subjects respond to statements on a four-point Likert scale, with different response items for each question. Total scores range from 0 to 21. Higher score shows higher level of anxiety or depression. Turkish version of HADS is valid and reliable in medically ill patients and 7 was found to be the cut-off score for depression subscale and 10 for anxiety subscale<sup>(17)</sup>.

### Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) v.17.0 software program was used to construct the databases and perform the statistical analysis. The results of the continuous variables were presented in the form of mean±standard deviation.

The categorical variables were expressed as relative frequencies. Continuous variables were compared using KruskalWallis test and Mann-Whitney U test. Categorical variables were compared using Pearson's chi-squared test and Fisher's exact test. Correlations between variables were tested using Pearson and Spearman correlation coefficients. All the tests were two-tailed and were applied following verification of the prerequisites for their use. P-values < 0.05 were considered statistically significant.

### RESULTS

Two hundred forty-one patients, with a mean age of  $53.1 \pm 8.2$  years (31-65) were evaluated. Among 241 patients, 49.8% (n=120) were men and 50.2% (n=121) were women. Table 1 shows the diagnostic subgroups of the patients. One hundred and five patients had diabetic neuropathy (DN), 39 patients had fibromyalgia (FM), 27 patients had carpal tunnel syndrome (CTS), 27 patients had radiculopathy (RP), 22 patients had trigeminal neuralgia (TN) and 21 patients had postherpetic neuralgia (PHN).

Evaluation of pain with VAS and LANSS showed no statistical difference among these subgroups. When all the patients were considered, mean VAS score was  $71.1 \pm 15.1$  which points to intense or severe pain and mean LANSS score was  $15.7 \pm 3.7$ . Scores of LANSS and VAS were positively correlated with each other ( $r=0.447$ ,  $p<0.01$ ).

ESS scores were found to be above the cut-off point ( $>10$ ) in all subgroups (Figure 1). DN and FM groups had the highest ( $13.2 \pm 1.8$  and  $13.4 \pm 2.2$ , respectively) ESS scores. Mean ESS score of DN group was significantly higher than mean ESS scores of both CTS and TN groups ( $p<0.001$  for both). Mean ESS score of FM group was also significantly higher than mean ESS scores of CTS and TN groups ( $p<0.001$  and  $p<0.05$ , respectively).

ESS scores were positively correlated with LANSS scores ( $r=0.151$ ,  $p<0.05$ ), but not with VAS scores.

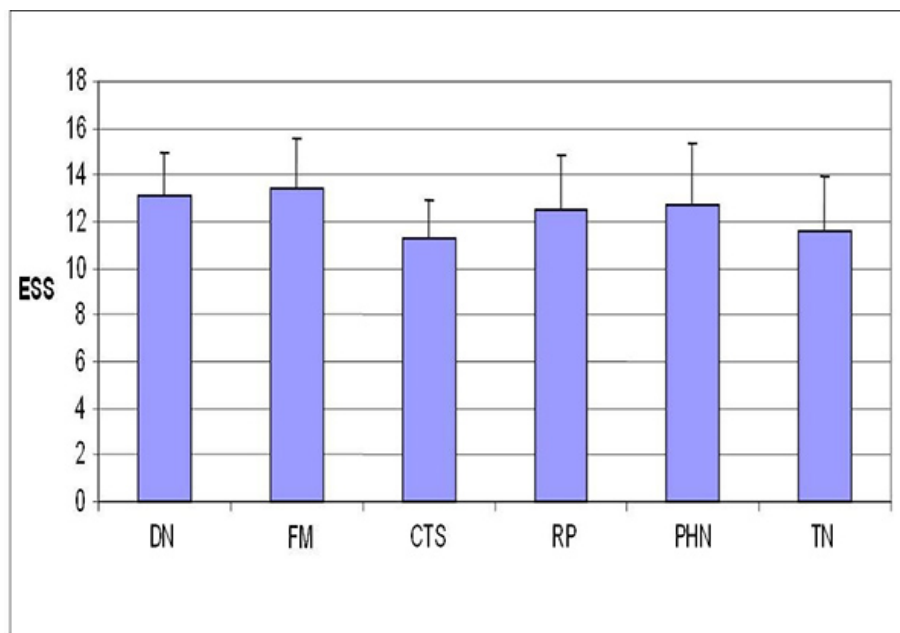
Assessment of patients with HADS revealed that depression scores of DN, FM, TN groups were above the cut-off point ( $>7$ ) and anxiety scores of DN, FM, TN, CTS groups were above the cut-off point ( $>10$ ) (Figure 2 and 3). FM group had the highest depression ( $10.1 \pm 3.4$ ) and anxiety

( $12.8 \pm 2.9$ ) scores. No correlation was found between HADS scores and scores of both VAS and LANSS. Depression scores, but not anxiety scores, were positively correlated with ESS scores ( $r=0.153$ ,  $p<0.05$ ).

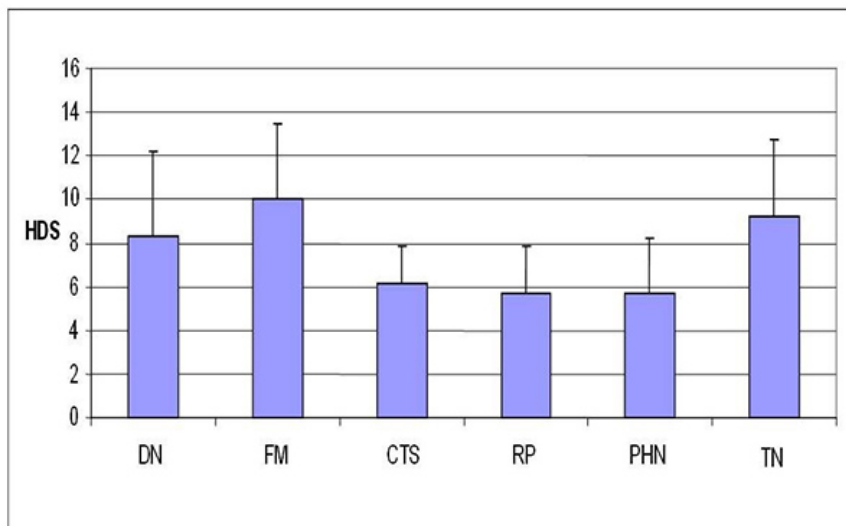
HbA1c levels of DN patients were positively correlated with anxiety scores ( $r=0.246$ ,  $p<0.05$ ), but not with depression scores.

**Table 1.** Diagnostic subgroups of patients with neuropathic pain

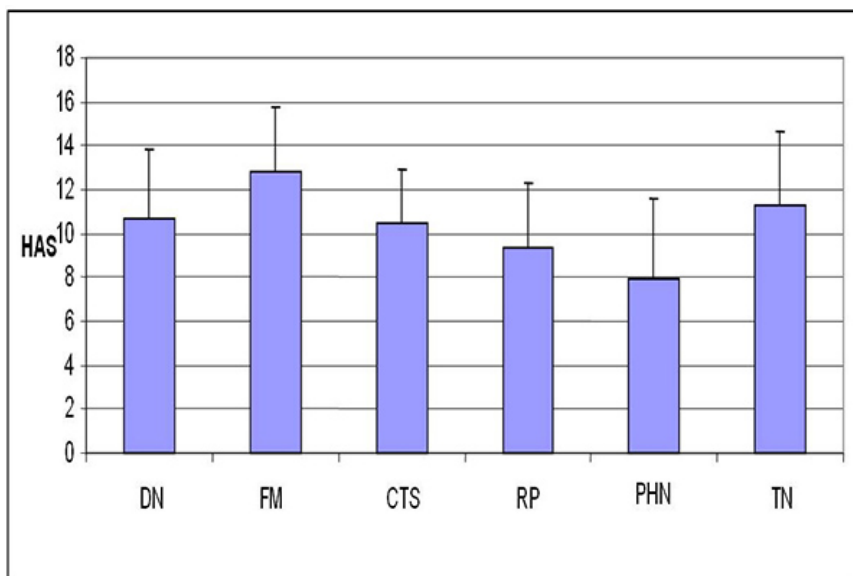
Type of neuropathic pain	n	%
Diabetic polyneuropathy	105	43.6
Fibromyalgia	39	16.2
Carpal tunnel syndrome	27	11.2
Radiculopathy	27	11.2
Postherpetic neuralgia	21	8.7
Trigeminal neuralgia	22	9.1



**Figure 1:** ESS scores of the six neuropathic pain syndromes



**Figure 2:** HDS scores of the six neuropathic pain syndromes



**Figure 3:** HAS scores of the six neuropathic pain syndromes

## DISCUSSION

In the present study, we found that there was a positive correlation between LANSS and VAS scores. ESS scores were found to be above the cut-off point in all subgroups. DN and FM groups had the highest ESS scores. ESS scores were positively correlated with LANSS scores. Depression

scores of DN, FM, TN groups and anxiety scores of DN, FM, TN, CTS groups were above the cut-off point. There was no correlation between HADS scores and scores of both VAS and LANSS.

In the literature, both the female gender and older age are listed as risk factors for chronic pain<sup>(25)</sup>. In our study, a mean age

of  $53.1 \pm 8.2$  years is congruent with literature data, but the number of females and males did not differ significantly.

The LANSS scale was developed as a clinic based instrument for identifying patients whose pain is predominantly neuropathic in origin. Bennett reported a sensitivity and specificity of 83% and 87% respectively for the scale<sup>(10)</sup>. In our study we found a mean LANSS score of  $15.7 \pm 3.7$  pointing to the predominant neuropathic origin of pain. No statistically significant difference was observed among subgroups in terms of LANSS and VAS scores. Patients complained of severe pain as indicated by a mean VAS score of  $71.1 \pm 15.1$ . LANSS and VAS scores were found to be positively correlated.

Sleep is an important element of normal functioning and well-being. Sleep problems are associated with anxiety, depression, impaired social functioning, chronic medical illnesses and mortality. Sleep disturbance is common in chronic pain. Radat et al. stated in their study that two-thirds of the subjects with neuropathic pain experienced interference with their sleep<sup>(41)</sup>. There are studies confirming the association of painful diabetic neuropathy (DN), a common complication of diabetes in which nerves are damaged as a result of hyperglycemia, with sleep impairment<sup>(16,24,51,56)</sup>. Polyneuropathy contributes to impaired sleep via several potential mechanisms. First, neuropathic pain itself may lead to disturbed sleep<sup>(56)</sup>. Second, polyneuropathy can impair thermoregulation. It has been proposed that autonomic changes in skin temperature modulate the neuronal activity of the thermo sensitive neurons in the pre-optic area/anterior hypothalamus which regulates vigilance and sleepiness<sup>(42)</sup>. There are few studies reporting excessive daytime sleepiness in diabetic patients<sup>(23,47)</sup>. Van Dijk et al. found no significant differences in reported daytime sleepiness between Type 1 diabetic patients and controls<sup>(50)</sup>. In another study

impaired sleep quality and daytime sleepiness were associated with decreased diabetes self-management in Type 2 diabetic adults<sup>(14)</sup>. We also found increased daytime sleepiness in patients with DN with a mean ESS score of  $13.2 \pm 1.8$  suggesting impaired sleep due to polyneuropathy.

Fibromyalgia (FM) syndrome is a chronic musculoskeletal pain disorder of unknown etiology, characterized by chronic widespread pain and muscle tenderness and the presence of tender points on examination. Evidence was shown for central pain processing abnormalities in almost all FM patients. These anomalies including hyperalgesia, allodynia, abnormal activation of pain-related brain regions and abnormal temporal summation of pain which strongly indicate a neuropathic pain syndrome. This new information led to the proposal that FM may be a neuropathic pain syndrome maintained by central nervous system sensitization and sympathetic hyperactivity<sup>(20)</sup>. Other common accompanying features are fatigue, sleep disturbances, stiffness, paraesthesias, headaches, Raynaud's like symptoms, depression and anxiety<sup>(15)</sup>. Sleep disturbances are generally regarded as a major comorbidity associated with FM<sup>(9)</sup>. Polysomnographic findings in FM patients include an alpha frequency rhythm, termed alpha-delta sleep anomaly. Sleep pattern is altered in these patients and there is evidence of an increase in stage 1 sleep, a reduction in delta sleep, and an increased number of arousals<sup>(26)</sup>. Patients with FM have been found to be significantly more likely to experience difficulties initiating or maintaining sleep than controls<sup>(46)</sup>. In particular, previous studies have identified difficulty falling asleep, staying asleep and waking up too early in the morning as the most common sleep associated symptoms among the FM population<sup>(52)</sup>. In a study, the occurrence of daytimehypersomnolancein FM patients was found to be related to a greater

severity of fibromyalgia symptoms and to more severe polysomnographic alterations<sup>(43)</sup>. FM group had the highest ESS score ( $13.4 \pm 2.2$ ) in our study.

Pain associated with chronic radiculopathy is caused by compression or lesion of a dorsal root or its ganglion. As the pain involves pathology of a peripheral nerve trunk, it is thought to be mainly of neuropathic origin. In a recent study, it is reported that the frequency and severity of depression, sleep disturbance and anxiety were similar in RP, DN and PHN. Somnolence occurred a little less frequently in patients with RP than in patients with DN<sup>(34)</sup>. We found increased daytime sleepiness in RP patients with a slightly but not significantly decreased ESS score compared with DN, FM and PHN patients. Sleep disturbances are commonly reported in low back pain<sup>(3,8)</sup> but to our knowledge, there is no study investigating daytime sleepiness in RP in the literature.

Postherpetic neuralgia is the most common complication associated with Herpes Zoster, particularly in the elderly. Patients with PHN can experience a variety of constitutional symptoms, including chronic fatigue, anorexia, weight loss, physical inactivity, and insomnia, as well as psychological problems like depression and difficulty in concentration<sup>(44)</sup>. Weinke et al. Stated that patients with Herpes zoster and postherpetic neuralgia expressed feelings of helplessness and frustration mixed with depression, sadness, orrage<sup>(53)</sup>. As far as we know there is no data in literature about daytime sleepiness in PHN patients. We found that ESS scores of patients with PHN were above cut-off indicating increased daytime sleepiness.

Trigeminal neuralgia is a disorder of the fifth cranial nerve that causes episodes of intense, stabbing and electric-shock-like pain in the facial distribution of the nerve<sup>(6)</sup>. As during the day, pain paroxysms during sleep are typically induced by natural stimuli at TN trigger points and cause disturbance of sleep<sup>(17)</sup>.

According to our findings, patients with TN also had increased daytime sleepiness.

Carpal tunnel syndrome (CTS) is the most common form of peripheral nerve compression. Classic symptoms of CTS include night waking with pain, tingling, and numbness. Patients with CTS have significant problems with a wide variety of sleep disturbances<sup>(40)</sup>. Patel et al. reported decreased sleep duration and quality in patients with CTS<sup>(39)</sup>. In our study, we showed that there was increased daytime sleepiness in patients with CTS.

In our study LANSS scores were positively correlated with ESS scores. But we could not find a significant positive correlation between VAS scores and ESS scores. This finding may indicate that daytime sleepiness is associated with the nature of pain rather than the intensity of pain. Results of a French nationwide survey also confirms that the neuropathic nature of the pain resulted in poorer quality of life, regardless of pain severity<sup>(27)</sup>.

Neuropathic pain is a complex condition caused by a variety of conditions forming a very heterogeneous group of affected individuals. It is one of the pain syndromes that is most difficult to treat. It strongly affects daily functioning interfering with psychological and social well-being. Depression and anxiety are frequently associated with neuropathic pain syndromes and reinforce the adverse effects of pain<sup>(54)</sup>.

High degree of comorbidity between depression and chronic pain disorders is documented and evidence show that the incidence of depression among persons with chronic pain is higher than for other chronic medical illnesses<sup>(6)</sup>. Anxiety is commonly associated with chronic medical illnesses and develops more quickly than any other association between a psychiatric disorder and a chronic medical condition. Chronic pain patients have a high prevalence of anxiety disorders<sup>(22)</sup>. In a large scale study, Berger et al. reported that prevalences of depression (4.3% vs. 2.6%),



and anxiety (2.8% vs. 1.7%) were higher in patients with painful neuropathic disorders compared with control group<sup>(11)</sup>. In a multicentre study, Radat et al. reported that the prevalence of current mood disorders in patients suffering from neuropathic pain was 29.7% (47% for lifetime) and that of current anxiety disorders was 20.3% (39% for lifetime)<sup>(41)</sup>. Our study results revealed that depression scores were above the cut-off point (>7) in FM, DN and TN groups. The mean depression score of FM group was  $10.1 \pm 3.4$  and was significantly higher ( $p < 0.05$ ) than all groups except TN. In the present study anxiety scores were above the cut-off point (>10) in DN, FM, TN and CTS groups. FM patients had the highest anxiety score ( $12.8 \pm 2.9$ ) again significantly higher ( $p < 0.01$ ) than all groups except TN.

Depression and anxiety are among the most common comorbidities of FM, with prevalence rates ranging in studies from 20–80% and 13–63.8%, respectively. Increased frequencies have been observed not only in clinical studies, but also in community and population studies<sup>(21)</sup>. It has long been known that major depression is highly prevalent in patients with FM, with the rates of current depressive disorders ranging from 28.6% to 70%, and the life time rates ranging from 62% to 86%. Besides, FM is the second most frequent general medical condition associated with major depressive disorder<sup>(2)</sup>. Regarding these data, increased depression and anxiety scores in FM in our study is congruent with literature.

Prior studies have estimated that 28% of DN patients have depression and 35% have moderate to severe anxiety. In the present study, depression and anxiety scores of above cut-off levels in DN, is in line with literature. The presence of anxiety and/or depression leads to poorer outcomes for micro and macrovascular complications of diabetes. Patients with diabetes and anxiety

were found to have poorer glycemic control and less frequent blood glucose monitoring<sup>(45)</sup>. Congruent with these literature data, HbA1c levels and anxiety scores were positively correlated in DN group ( $r = 0.246$ ,  $p < 0.05$ ) in our study.

Trigeminal neuralgia (TN) is an excruciating neuropathic pain which is considered as one of the worst causes of suffering associated to pain<sup>(12)</sup>. There are some studies indicating that patients with trigeminal neuralgia and chronic facial pain have high levels of anxiety and depression<sup>(33)</sup>. Our study results of TN group with anxiety and depression scores close to FM group also support literature data.

Studies investigating association of CTS with anxiety and depression are scarce in literature. Hobby et al. found a strong association between psychological disturbance and increased self-reported symptoms and disability in patients with carpal tunnel syndrome<sup>(28)</sup>. In the present study, anxiety but not depression scores of CTS group were above the cut-off level.

The literature indicates a clear link between psychological variables and back pain. The prevalence of major depression in patients with chronic low back pain is approximately three to four times greater than reported in the general population<sup>(48)</sup>. Mahn et al. made a direct comparison of psychological variables in painful RP, DN and PHN and found that the incidence of depression and anxiety associated with RP did not differ from that in other neuropathic pain disorders<sup>(34)</sup>. In our study, depression and anxiety scores of both RP and PHN were found to be below cut-off levels.

The relation of pain intensity to mood is uncertain: some work finds no correlation, but other evidence suggests a relation between intensity of pain and severity of mood disturbance<sup>(31)</sup>. Anxiety can modulate pain threshold, decrease tolerance to pain and increase patient self-reported pain ratings<sup>(5)</sup>. However, our

results do not support the literature data that pain intensity is associated with depression and anxiety severity. We found no correlation between HADS scores and VAS and LANSS scores. Contradicting with this result, Nakamura et al. reported that HADS score was significantly correlated with the VAS score and the duration of pain<sup>(38)</sup>. However, Keltner et al. reported that greater severity of depression symptoms is more highly correlated with worse well-being than is pain intensity in HIV related neuropathic pain. Pain intensity was more strongly correlated with physical health scores than was severity of depressed mood<sup>(31)</sup>. Myburgh et al. stated that chronic, intense pain and anxiety do not always appear to be related as the patients suffering from neck pain in their study had experienced a relatively high intensity of pain but appeared not to be anxious<sup>(37)</sup>. Radat et al. found that the only pain characteristic associated with mood disorders was moderate to severe minimal pain intensity suggesting that high minimal pain intensity causes more emotional distress than severe maximal pain in neuropathic pain patients<sup>(41)</sup>. In our study although the patients had severe intensity of pain, their mean depression and anxiety scores were mild. This fact may indicate that pain intensity does not determine depression and anxiety levels.

In the present study, there was a positive correlation with depression scores and ESS scores ( $r=0.153$ ,  $p<0.05$ ). Psychological distress is generally more severe among chronic pain patients with poor sleep than in those without sleep disturbance. Poor sleep in chronic pain has been associated with emotional distress in the form of depression, anger/hostility, fatigue, and confusion. Furthermore, depressed mood, but not anxiety, is likely to predict poor sleep in chronic pain patients. Morin et al. found no correlation of sleep disturbances with depression and anxiety in chronic pain patients<sup>(36)</sup>. Our results suggest that daytime sleepiness is associated with depression but not with anxiety.

There are some limitations of the present study. First of all, the sample size is small hindering the generalis ability of our results. Secondly, the distribution of gender was a result of the patient population that was willing to participate in the study and therefore may not represent the actual gender distribution in neuropathic pain syndromes. Thirdly, cross-sectional design does not allow to infer causality but only to show associations. Fourth limitation is the lack of a psychiatric structured interview which could have resulted in the under diagnosis of depression and anxiety. Nevertheless, we believe that our study could make a significant contribution to literature as it compares patients suffering from six different origins of neuropathic pain and focuses on daytime sleepiness which has not been a commonly studied parameter in neuropathic pain patients.

In conclusion, we have shown that daytime sleepiness, depression and anxiety are associated comorbidities with different neuropathic pain syndromes. Neuropathic character, but not the intensity of pain is associated with daytime sleepiness. Pain intensity does not predict anxiety and depression levels. Depression, but not anxiety shows a positive correlation with daytime sleepiness. These results might have implications for the better understanding of comorbidities in different neuropathic pain syndromes, future research strategies and the design of controlled clinical trials with larger sample sizes.

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**Received by:** 20 May 2015

**Revised by:** 12 October 2015

**Accepted:** 08 December 2015

### **The Online Journal of Neurological Sciences (Turkish) 1984-2016**

This e-journal is run by Ege University  
Faculty of Medicine,  
Dept. of Neurological Surgery, Bornova,  
Izmir-35100TR  
as part of the Ege Neurological Surgery  
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URL: <http://www.jns.dergisi.org>

Journal of Neurological Sciences (Turkish)

Abbr: J. Neurol. Sci.[Turk]

ISSNe 1302-1664

### **REFERENCES**

1. Ağargün MY, Çilli AS, Kara H, Bilici M, Telcioğlu M, Semiz ÜB et al. Validity and Reliability of the Epworth Sleepiness Scale. *Turkish Journal of Psychiatry* 1999; 10(4): 261 – 267.
2. Alciati A, Sgiarovello P, Atzeni F, Sarzi-Puttini P. Psychiatric problems in fibromyalgia: clinical and neurobiological links between mood disorders and fibromyalgia. *Reumatismo*. 2012;64(4):268-74.
3. Alsaadi SM, McAuley JH, Hush JM, Bartlett DJ, Henschke N, Grunstein RR et al. Detecting insomnia in patients with low back pain: accuracy of four self-report sleep measures. *BMC Musculo skelet Disord*. 2013 Jun 27;14(1):196.
4. Annagür BB, Uguz F, Apiliogullari S, Kara I, Gunduz S. Psychiatric disorders and association with quality of sleep and quality of life in patients with chronic pain: a SCID-based study. *Pain Med* 2014;15(5):772-81.
5. Argoff CE. The Coexistence of Neuropathic Pain, Sleep, and Psychiatric Disorders. *Clin J Pain* 2007; 23(1): 15 – 22.
6. Attal N, Lanteri-Minet M, Laurent B, Fermanian J, Bouhassira D. The specific disease burden of neuropathic pain: Results of a French nation wide survey. *Pain* 2011; 152: 2836 – 2843.
7. Aydemir Ö. Validity and Reliability of Turkish Version of Hospital Anxiety and Depression Scale. *Turkish Journal of Psychiatry* 1997; 8(4): 280 – 287.
8. Bahouq H, Allali F, Rkain H, Hmamouchi I, Hajjaj-Hassouni N. Prevalence and severity of insomnia in chronic low back pain patients. *RheumatolInt*. 2013 May;33(5):1277-81
9. Belt NK, Kronholm E, Kauppi MJ. Sleep problems in fibromyalgia and rheumatoid arthritis compared with the general population. *Clin Exp Rheumatol* 2009; 27(1): 35 – 41.
10. Bennett M. The LANSS Pain Scale: The Leeds assessment of neuropathic symptoms and signs. *Pain* 2001; 92:147-157.
11. Berger A, Sadosky A, Dukes E, Edelsberg J, Oster G. Clinical characteristics and patterns of health care utilization in patients with painful neuropathic disorders in UK general practice: a retrospective cohort. *BMC Neurol* 2012 Mar 6;12:8.
12. Castro AR, Siqueira SR, Perissinotti DM, Siqueira JT. Psychological evaluation and cope with trigeminal neuralgia and temporomandibular disorder. *Arq Neuropsiquiatr* 2008; 66: 716 – 719.
13. Castro MMC, Daltro C. Sleep Patterns and Symptoms of Anxiety and Depression in Patients with Chronic Pain. *Arq Neuropsiquiatr* 2009; 67(1): 25 – 28.
14. Chasens ER, Korytkowski M, Sereika SM, Burke LE. Effect of poor sleep quality and excessive daytime sleepiness on factors associated with diabetes self-management. *Diabetes Educ*. 2013; 39(1):74-82.
15. Chong YY, Ng BY. Clinical aspects and management of fibromyalgia syndrome. *Ann Acad Med Singapore*. 2009 Nov;38(11):967-73
16. Dermanovic Dobrota V, Hrabac P, Skegro D, Smiljanic R, Dobrota S, Prkacin I et al. The impact of neuropathic pain and other comorbidities on the quality of life in patients with diabetes. *Health Qual Life Outcomes* 2014 3;12:171
17. Devor M, Wood I, Sharav Y, Zakrzewska JM. Trigeminal neuralgia during sleep. *Pain Pract*. 2008 Jul-Aug;8(4):263-8.
18. Dworkin RH, Backonja M, Rowbotham MC et al. Advances in Neuropathic Pain. *Arch Neurol* 2003; 60: 1524 – 1534.
19. Eisendrath SJ. Psychiatric aspects of chronic pain. *Neurology* 1995; 45(suppl 9): 26 – 34.
20. Eyigör S, Kirazlı Y. Fibromyalgia syndrome from the perspective of neuropathic pain. *Agri*. 2008 Jan;20(1):8-12.
21. Fietta P, Fietta P, Manganelli P. Fibromyalgia and psychiatric disorders. *Acta Biomed*. 2007 Aug;78(2):88-95.
22. Fishbain DA. Approaches to Treatment Decisions for Psychiatric Comorbidity in the Management of the Chronic Pain Patient. *Med Clin North Am*. 1999 May;83(3):737-60.
23. Gislason T, Taube A. Prevalence of sleep apnea syndrome—estimation by two stage sampling. *Ups J Med Sci* 1987; 92(2):193–203
24. Gore M, Brandenburg NA, Dukes E, Hoffman DL, Tai KS, Stacey B. Pain severity in diabetic peripheral neuropathy is associated with patient functioning, symptom levels of anxiety and depression, and sleep. *J Pain Symptom Manage* 2005; 30: 374 – 385.

25. Hans G, Masquelier E, De Cock P. The diagnosis and management of neuropathic pain in Daily practice in Belgium: an observational study. *BMC PublicHealth* 2007; 7:170
26. Harding SM. Sleep in fibromyalgia patients: subjective and objective findings. *Am J MedSci*. 1998;315:367–76.
27. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), Mc Gill Pain Questionnaire (MPQ), Short-Form Mc Gill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care and Research* 2011; 63(11): 240 – 252
28. Hobby JL, Venkatesh R, Motkur P. The effect of psychological disturbance on symptoms, self-reported disability and surgical outcome in carpal tunnel syndrome. *J Bone Joint Surg Br*. 2005 Feb;87(2):196-200.
29. Jensen TS, Baron R, Haanpää M, et al. A new definition of neuropathic pain. *Pain*. 2011;152(10):2204-2205.
30. Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. *Sleep* 1992; 15: 376-381.
31. Keltner JR, Vaida F, Ellis RJ, Moeller-Bertram T, Fitzsimmons C, Duarte NA et al.; CHARTER Group. Health-related quality of life 'well-being' in HIV distal neuropathic pain is more strongly associated with depression severity than with pain intensity. *Psychosomatics*. 2012 Jul-Aug;53(4):380-6.
32. Koenig TW, Clark MR: *Advances in comprehensive pain management*. *Psychiatric Clin North Am* 1996; 19: 589 – 611.
33. Mačianskytė D, Janužis G, Kubilius R, Adomaitienė V, Ščiupokas A. Associations between chronic pain and depressive symptoms in patients with trigeminal neuralgia. *Medicina (Kaunas)*. 2011;47(7):386-92.
34. Mahn F, Hüllemann P, Gockel U, Brosz M, Freynhagen R, Tölle TR et al. Sensor symptom profiles and co-morbidities in painful radiculopathy. *PLoS One*. 2011 May 9;6(5):e18018
35. Mersky H, Bogduk N. *Classification of chronic pain*. 2nd edn. Seattle: IASP Press, 1994:394.
36. Morin CM, Gibson D, Wade J. Self-reported sleep and mood disturbance in chronic pain patients. *Clin J Pain*. 1998 Dec;14(4):311-4.
37. Myburgh C, Roessler KK, Larsen AH, Hartvigsen J. Neck pain and anxiety do not always go together. *Chiropr Osteopat*. 2010 Mar 11;18:6.
38. Nakamura M, Nishiwaki Y, Sumitani M, Ushida T, Yamashita T, Konno S et al. Investigation of chronic musculoskeletal pain (third report): with special reference to the importance of neuropathic pain and psychogenic pain. *J Orthop Sci* 2014; 19:667–675.
39. Patel A, Culbertson MD, Patel A, Hashem J, Jacob J, Edelstein D et al. The negative effect of carpal tunnel syndrome on sleep quality. *Sleep Disord*. 2014;2014:962746.
40. Patel JN, McCabe SJ, Myers J. Characteristics of sleep disturbance in patients with carpal tunnel syndrome. *Hand (N Y)*. 2012 Mar;7(1):55-8.
41. Radat F, Margot-Duclot A, Attal N. Psychiatric morbidities in patients with chronic peripheral neuropathic pain: A multicentre cohort study. *Eur J Pain* 2013; 17(10):1547-57
42. Raymann RJ, Swaab DF, van Someren EJ. Skin deep: enhanced sleep depth by cutaneous temperature manipulation. *Brain* 2008; 131:500–513
43. Sarzi-Puttini P, Rizzi M, Andreoli A, Panni B, Pecis M, Colombo S et al. Hypersomnolence in fibromyalgia syndrome. *Clin Exp Rheumatol*. 2002 Jan-Feb;20(1):69-72.
44. Schmader KE. Epidemiology and impact on quality of life of postherpetic neuralgia and painful diabetic neuropathy. *Clin J Pain* 2002; 18: 350 – 354.
45. Selvarajah D, Cash T, Sankar A, Thomas L, Davies J, Cachia E et al. The contributors of emotional distress in painful diabetic neuropathy. *Diabetes & Vascular Disease Research* 2014; 11(4): 218–225.
46. Sivertsen B, Krokstad S, Øverland S, Mykletun A. The epidemiology of insomnia: associations with physical and mental health. The HUNT-2 study. *J Psychosom Res*. 2009;67:109–116.
47. Sridhar GR, Madhu K. Prevalence of sleep disturbances in diabetes mellitus. *Diabetes Res Clin Pract* 1994; 23(3):183–186.
48. Sullivan MJ, Reesor K, Mikail S, Fisher R. The treatment of depression in chronic low back pain: review and recommendations. *Pain* 1992; 50: 5 – 13.
49. Turk DC, Flor H. Chronic pain: a biobehavioral perspective. In: Gatchel RJ, Turk DC, editors. *Psychosocial factors in pain: critical perspectives*. New York: Guilford Publications; 1999: 8–34.
50. Van Dijk M, Donga E, van Dijk JG, Lammers GJ, van Kralingen KW, Dekkers OM et al. Disturbed subjective sleep characteristics in adult patients with long-standing type 1 diabetes mellitus. *Diabetologia* 2011; 54(8):1967-1976.
51. Viala-Danten M, Martin S, Guillemin I, Hays RD. Evaluation of the reliability and validity of the Medical Outcomes Study sleep scale in patients with painful diabetic peripheral neuropathy during an international clinical trial. *Health and Quality of Life Outcomes* 2008; 6:113.
52. Wagner JS, DiBonaventura MD, Chandran AB, Cappelleri JC. The association of sleep difficulties with health-related quality of life among patients with fibromyalgia. *BMC Musculoskelet Disord*. 2012 Oct 17;13:199.
53. Weinke T, Glogger A, Bertrand I, Lukas K. The societal impact of herpes zoster and postherpetic neuralgia on patients, life partners, and children of patients in

- Germany.Scientific World Journal*  
2014;2014:749698.
54. *Wetering EJ, Lemmens KM, Nieboer AP, Huijsman R. Cognitive and behavioral interventions for the management of chronic neuropathic pain in adults--a systematic review. Eur J Pain. 2010 Aug;14(7):670-81.*
  55. *Yücel Y, Senocak M, Kocasoy-Orhan E, Çimen A, Ertas M. Results of Leeds assessment of neuropathic symptoms and signs pain scale in Turkey: A validation study. The Journal of Pain 2004; 5:427-432.*
  56. *Zelman DC, Brandenburg NA, Gore M.Sleep impairment in patients with painful diabetic peripheral neuropathy. Clin J Pain 2006; 22:681-685.*

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