

ORIGINAL ARTICLE

Co-Morbid Depression in Neuropathic Pain Sufferers: Prevalence and Effect on Quality of LifeNAVEED AHMED DURRANI¹, SUMARA TABASSAM², SAQIB BAJWA³, MUHAMMAD HASAN WASIM⁴, ABDUL WASAY TOOR⁵, MUFASSAR NISHAT⁶¹FCPS, M. Sc. Pain Medicine Consultant Anesthesia and Pain Management Kulsoom International Hospital Islamabad²Associate prof Anaesthesia MBBS, FCPS (Anaesthesia) Aziz Fatima Medical & Dental College Faisalabad³Assistant prof. and head of psychiatry department Gujranwala medical college⁴Fellow Pain Medicine Shifa International Hospital Islamabad⁵Assistant Professor Anesthesiology CMH Lahore Medical College and institute of Dentistry Lahore cantt⁶MBBS,FCPS(Plastic surgery) Associate professor plastic surgery University medical & dental college. Faisalabad

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INTRODUCTION

The treatment of neuropathic pain is notoriously challenging, and this is often attributed to the psychiatric comorbidity that is commonly misunderstood as being the primary cause of the patient's suffering. Our study aimed to determine the relationship between depressive symptoms and the characteristics of neuropathic pain (NP), on the one hand, and quality of life (QoL), on the other hand, in a group of individuals who sought treatment for neuropathic pain (NP) regardless of the etiology of their condition. NP is a type of pain that is caused by damage to the nerves in the body.

Study Pace: Kulsoom International Hospital Islamabad**Study Duration:** 6months (Feb 2021 to July 2021)

Methods: We conducted a study with 60 individuals who came in seeking advice for neuropathic pain. The study was a cross-sectional design. We evaluated these participants based on their levels of five different parameters: their levels of neuropathic pain, as measured by DN4, their levels of pain intensity, as measured by EVA, their levels of anxiety and depression, as measured by the HADS, and their levels of quality of life.

Results: The participants' average age was 55.23 ± 20.67 years, the ratio of males to females was 0.54. The mean age of the people who took part in the study was 55.23 years. The three conditions that were seen most commonly as causes of neuropathic pain were postherpetic pain, carpal tunnel syndrome, and diabetic neuropathy. Depression affected the mental health of 64.9% of persons, while anxiety was a problem for 70.5% of individuals. The quality of life was significantly lower than expected given the average scores of 34.82 on the SF-12 physical subscale and 38.26 on the SF-12 mental subscale. On the BPI, the total mean score was 5.60, and the standard deviation was 1.77. Patients with high DN4 scores showed a significantly increased risk of becoming depressed ($p = 0.024$), compared to patients with lower DN4 values. This was demonstrated to be the case by the fact that there was a statistically significant positive association between the depression score and the level of pain ($p = 0.001$, $r = 0.41$). Patients who were diagnosed with depression were found to have a poor quality of life using both the SF-12 and the BPI.

Conclusion: Given the impact that depression has on the components of neuropathic pain as well as quality of life, screening for this comorbidity ought to be a part of the baseline assessment for ND.

INTRODUCTION

Patients seek medical assistance for a variety of reasons, but one of the most common of them is pain. Pain is described as "an unpleasant sensory and emotional experience, connected with existing or probable tissue injury or characterized in words suggestive of such harm," as stated by the International Association for the Study of Pain (IASP), which was established in 1979. This definition comes from the organization's definition of pain. One of the basic types of pain is referred to be "excess of nociception," while the other type is referred to as "neuropathic pain." Pain may be split down into these two primary categories. These classifications are determined by whether or not there has been injury to a nerve (NP).

The term "pain originated or caused by primary injury or malfunction of the nerve system" has been used to characterize NP by the International Association for the Study of Pain (IASP) ever since the year 1994. The term "pain coupled with an injury or disease damaging the somatosensory system" (NP) has been proposed as a definition for NP in more recent times. [NP] It is estimated that around one-third of people who are living with chronic pain are also impacted by this ailment. It is considered that this condition affects 8% of the general population. Despite the advancements that have been achieved in pharmaceutical research and our knowledge of the neurophysiological processes that underlie NP, this entity is still difficult to manage effectively. In point of fact, one of the key causes that helps to explain the complexity of NP management is psychiatric co-morbidity. According to the findings of study that was carried out by Averill and colleagues depression is one of the most common psychological illnesses that might be related with having to endure pain. On the other hand, this sickness is still misdiagnosed the

large majority of the time, which slows down the therapeutic management of chronic issues.

In addition, people who have NP are more likely to have discomfort, which can impair their quality of life (QoL) and cause limits, both of which can increase the likelihood that they will be excluded from society and marginalized. According to the World Health Organization (WHO), quality of life is directly proportional to an individual's perception of his place in life, in the context of the cultural and value system in which he lives, in relation to his goals, his expectations, his standards, and his worries. All of these factors are taken into consideration when determining an individual's quality of life. All of these aspects are evaluated in light of their connections to one another. This concept incorporates a variety of aspects, some of which are objective while others are subjective. Some of these aspects are objective, while others are subjective. These aspects include the person's physical condition of health, his functional abilities, his physical sensations, the status of his psychological health, his social position, and the environment in which he maintains his relationships with other people. As a result, one of the fundamental objectives of any form of therapeutic care is to enhance the overall quality of life of patients (QoL). Therefore, screening individuals with NP for depression and treating it if it is found to be a comorbid disease could have the effect of reducing the detrimental impact that NP has on quality of life.

In Pakistan, the sensation of pain is still not taken into account in the same way that it should be in the many care settings that we have available. In point of fact, the vast majority of our medical staff do not have appropriate knowledge of, or sensitivity to, concerns relevant to the treatment of pain. This is a problem because pain therapy is one of the most important

aspects of our work. In point of fact, there is just one pain treatment center (PTC) in the entire nation, and it can be found in the Kulsoom International Hospital, which can be found in the city of Pakistan, which serves as the country's capital. First, we want to determine the prevalence of depression in a sample of subjects who are being followed up for NP. Next, we want to investigate the link between this psychiatric comorbidity and NP characteristics as well as the quality of life in this population. These are the objectives that we have set for ourselves. This is due to the fact that there is a lack of consistency among the research that have been conducted on the quality of life and depressive disorders in NP patients, and data are restricted in our environment.

METHODS

Feb 2021 to July 2021, a multicenter cross-sectional study was conducted at the Kulsoom International Hospital Islamabad. Both of these institutions are located in Pakistan. The duration of the study was a complete quarter of a year.

The Group That Is Being Investigated: Patients receiving therapy for NP ranged in age from 20 to 85 years old. Patients were diagnosed with NP. On the Neuropathic Pain (NP4) questionnaire, each and every one of them has a score that is either equal to the number four or higher than the number four.

Patients who were pregnant, patients who had a personal record of mental treatment, and patients who had undergone traumatic events within the previous three months were not permitted to participate in the study. The death of an ascendant or descendant parent, the disclosure of a serious illness or prognosis reserved for a parent or in the patient, a conflict within the family or marriage (such as a divorce, separation, or violence), a conflict within the workplace (such as harassment or conflict), rape, a serious automobile accident, or a significant financial loss are all examples of traumatic events.

Patients who did not grant their consent for the study or who suffered from some form of cognitive impairment were also not allowed to participate.

Measuring Devices and Their Applications: We created a questionnaire with a format that is both semistructured and unstructured so that we could collect the sociodemographic data and records from the participants.

We adopted a four-question Neuropathic Pain (NP4) questionnaire for the diagnosis. This cutting-edge instrument is simple to operate and could provide a definitive diagnostic in a relatively short period of time. In addition to the three queries that pertain to the physical examination, there are a total of seven questions that pertain to the clinical description of the discomfort. A threshold value of an overall score that is larger than or equal to 4/10 is required in order to establish a diagnosis of NP. This score must be greater than or equal to the value. In the course of this particular inquiry, we made use of the Urdu version that had been double-checked and validated.

In order to gauge the level of discomfort that the patient was experiencing, we made use of a tool known as the Visual Analogic Scale (VAS). The visual analog scale (VAS) is comprised of a ruler that is one hundred millimeters in length and has a movable cursor attached to the side that is facing the patient. The cursor moves along a line that is straight, with one end of the line corresponding to the phrase "absence of pain" and the other end of the line corresponding to the phrase "maximum imaginable misery." Neither end of the line is curved.

The patient has to slide the cursor along this line so that he can provide a more accurate assessment of the level of discomfort he is experiencing. The doctor may view the other side, which consists of graduations just like the first. By moving the pointer so that it is positioned near to the patient, the physician is able to gain an idea of the level of discomfort that the patient is experiencing.

Reading the VAS makes it possible to categorize the level of intensity in line with the following interpretation: a value of 0 shows that there is no pain. 1–4: aches and pains that are on the

moderate end of the spectrum 5–7: annoyance at a moderately intense level >7: excruciating pain at a very high level

In order to conduct the depression screening, we utilized the Urdu translation of the Hospital Anxiety and Depression Scale (HADS). The ratings on this scale run from 0 to 3, and there are a total of 14 separate items. There are seven questions that relate to the anxious dimension, and there are also seven questions that relate to the depressive dimension. Consequently, it is possible to gain two scores by making use of this scale, with the greatest possible score on each being equal to 21. If you have a score that is lower than 10, it means that the symptomatology cannot be challenged.

The patients' quality of life was rated using two different scales: the Short Form 12-item survey (SF-12) and the Brief Pain Inventory (BPI), both of which were given out in their Urdu translations. Both of these surveys were given in both English and Urdu.

The SF-12 is a shorter and more concise version of the SF-36 questionnaire that only includes the most significant items from that instrument. Because of this, the overall evaluation may now be completed in half the time as a result of the reduction in the amount of questions. It determines two scores, one for the individual's physical quality of life and another for their mental quality of life. Both of these scores are summed together to form the total score. While the physical field investigates the functional capacity associated with pain, the psychological field investigates the influence that NP has on a patient's morale, mood, and overall sense of well-being. In other words, the physical field looks at how pain affects a patient's ability to function.

We considered employing a cutoff that was established by determining the average of the general population's physical and mental scores in Pakistan. This was an option that we considered. The Brief Pain Inventory (BPI) is a condensed pain self-assessment questionnaire that was initially devised to evaluate the pain related with cancer. The BPI was named after its acronym, which stands for "Brief Pain Inventory." Nonetheless, it can also be utilized for the purpose of assessing the pain that is connected with a variety of diseases. We determined the degree to which the pain interfered with seven distinct functions by using an evaluation scale that ranged from 0 (no interference) to 10 (complete interference). These functions included normal activity, mood, walking ability, normal work, relationship with other people, sleep, and the joy of life. On a scale that ranged from 0 (no interference) to 10, each of these functions was rated on how much interference there was. The possible range for the overall score is from 10 points to zero points (adding the scores of the seven items and then dividing by seven).

The participants in the study were briefed on the purpose of the investigation, and their verbal consent was solicited before moving forward with the investigation. It was suggested that all of the participants who had been diagnosed with psychiatric diseases should have a conversation with a specialist in the relevant sector.

Statistical Analysis: After collecting the necessary information, it was entered into a computer program known as Statistical Package for the Social Sciences (SPSS), which was subsequently used to do an analysis on the data (23rd version). In order to perform a comparison between the distribution of continuous variables and a normal distribution,

We came up with both the absolute and relative frequencies for the qualitative variables (in terms of percentages). In addition to this, we determined the maximum and minimum values that were possible, as well as the means, medians, and standard deviations of the quantitative variables.

The methods that were used in the research of the connections that exist between the qualitative variables were the chi-square test, which was established by Pearson, and the exact test, which was developed by Fisher. Both of these tests were applied. The Pearson correlation test, which is also known as "r," the Student t-test, and the coefficient of determination, which is also known as "R2," were the statistical tools that were used to

investigate the nature of the connection that exists between the quantitative variables. These tests and measurements are all known by their respective abbreviations. The "ANOVA" test was used to carry out the task of establishing how the various averages compare to one another so that the results might be interpreted. The value of p that must be lower than 0.05 was established as the cutoff for statistical significance.

RESULTS

The Group That Is Being Investigated: In total, there were 60 patients involved in our research; 38 of them were drawn from the Patient Treatment Center (PTC), while the other 22 were drawn from the Functional Exploration Service. In all, there were 36 females and 24 men in the population, 77.5 percent had attained some level of education beyond high school. In point of fact, 44% of the people in the instances had completed their secondary school, while just 20% had completed their primary education and only 15% had completed their further education. Twenty-four patients, or 40.1% of the total, were actively participating in the experiment when it was being conducted.

Determine the Average Level of Living Conditions of the Population: According to the findings of the Short Form 12-item Health Survey (SF-12), the mean scores for physical health were 33.76 and 8.03, respectively, while the mean scores for mental health were 37.78 and 11.52, respectively. On the Brief Pain Inventory (BPI), the average score was 5.53, and the standard deviation was 1.76. The results of the ratings that were collected across all of the primary dimensions are presented in figure 1.

The Connection Between the Symptomatology of Depression and the Clinical Characteristics of Neuropathic Pain: The findings of our study, which made use of a dimensional approach, showed that the presence of depressed symptoms is related to parameters such as the onset, severity, and NP history . In point of fact, it indicated a relationship between the degree of depression and that of NP as measured by the VAS (p=0), which suggests that this correlation does exist. This association is demonstrated by the fact that this association exists.

Table 1
NP characteristics of the study population.

NP4 score	5.45 ± 2.01	
Pain Etiology	Diabetic neuropathy	7
	Post herpetic pain	12
	Pain of rheumatic origin	50
	Others	11
	5.61 ± 1.23	
Pain intensity according to EVA	Moderate intensity	13
	Severe intensity	45
Pain history	2 years (min: 1 week, max: 30 years)	
Pain evolution	≥5 months	46
	<5 months	14
Treatment	Without treatment	18
	With treatment	42
Treatment duration	2 years (min: 0, max: 10 years)	
Number of treatments	Monotherapy	14
	Polytherapy (≥2 medicines)	26
Treatment nature	Morphine	4
	Tramadol	15
	Paracetamol	23
	NSAIDs	6
	Tricyclic antidepressants	15
	New antiepileptics	14
	Classical antiepileptics	2

The Relationship Between Depressive Symptoms and Signs and How They Affect One's Quality of Life: According to the results of the SF-12 questionnaire, the vast majority of depressive patients were found to have a quality of life that was considerably

affected both intellectually (r = 0.47, p=0) and physically (r = 0.42, p=0.001) by their condition. Additionally, it was shown that there is a substantial connection between the degree of depressive symptoms and the overall BPI, in addition to a few of the interference items . Patients who were suffering from severe depression had quality of life scores that were significantly impacted, with the highest negative impact being shown in patients with severe depression The Relationship Between Sociodemographic Factors and the Manifestations of Depression

According to the findings of our study, there is a correlation between depressed symptoms and both having a low socioeconomic level

DISCUSSION

The results of this particular research project indicate that the prevalence of depression is roughly 65.6% of the population. There was a correlation between the intensity and length of the NP therapy, as well as a more degraded quality of life, and depression. This correlation was also found to be positive. The link between NP and depression, as well as the impact of NP on one's quality of life, has been brought to light as a direct result of the findings that we have uncovered.

It is essential to point out that the discovered prevalence in our experiment was greater than that which was stated in the published research. The incidence of this syndrome was found to be 57.1% in a recent study that was conducted out in China on patients who suffered from chronic pain and who were being followed up in PTCs . A study that was conducted in Pakistan and was quite similar to ours found that the prevalence of depression in that country was lower than that found in our study. However, the prevalence of depression found in our study was higher than that found in the Pakistan study. On the other hand, this research looked at people suffering from chronic pain in general and did not focus on the neuropathic component of their suffering, whereas we decided to limit our investigation to NP patients only. It's possible that this choice is part of the reason why we received the result that we did. In point of fact, a number of studies have shown that the presence of a pain neuropathic component may be associated with a higher incidence of depression in patients who are enduring pain. This is the conclusion that was reached by the researchers. In addition, the demographic profile of the people who participated in the study might have some bearing on the fact that we discovered such a high rate of depression in our investigation. The vast majority of our patients had previously been admitted to the PTC before coming to see us; they were referred to us due to the complexity and severity of their pain as well as their refusal to be treated. As a consequence of this, a greater proportion of the population is at increased risk for exhibiting symptoms of a mood illness . It is possible that the high prevalence of NP is evidence that there is a relationship between NP and depression. According to the findings of a number of recent research investigations, these two symptoms are the physical and psychological manifestations of the same neurological disorder. Endorphins are the neurotransmitters that are responsible for the natural modulation of pain. They are able to accomplish this by activating the neurons of the periaqueductal substance, which then activates the neurons of the dorsal marrow that are responsible for carrying serotonin. The latter prevents transmissions to the level of the medullary even after it has been freed . In the dorsal horn of the spinal cord, the operation of two adrenergic receptors, a presynaptic affinity neuron, and postsynaptic neuron inhibitors is what causes the noradrenergic descending pathway to limit the input. Because of this, the system that is responsible for relieving pain requires use of neurotransmitters (such as serotonin and norepinephrine), the levels of which are hypothesized to be lower in people who suffer from depression. The dysregulation of these chemical mediators could conceivably explain one of these disorders or another, which would show that there is a continuum between the experience of pain and that of depression. However, the many data that were presented in the research are still incomplete and usually

phenomenological; however, they demonstrate that there has been a rapid increase in knowledge regarding the depressed effects of NP use. In order to hone these neurobiological hypotheses, there is still a need for a number of additional experiments to be conducted.

According to the findings of our study, there is a correlation between the severity of one's current pain and the presence of depressive symptoms. This conclusion is comparable to others that have been published in the literature, where it has been observed that the degree of emotional distress changes with the severity of the pain. This conclusion is that the amount of emotional distress varies with the severity of the pain.

In clinical settings, it can be difficult to determine the direction of causality and the time of the correlation between the intensity of depressed symptoms and the severity of NP symptoms. This can be a challenge because of the close relationship between the two sets of symptoms. On the one hand, research has revealed that depressive disorders can heighten a person's perception of pain by lowering their threshold for experiencing pain. This is due to the fact that people with depressive illnesses have a lower threshold for experiencing pain. Neurobiological changes are responsible for bringing about this result. In point of fact, the areas of the brain that are connected with a faulty regulation of mood are the same structures that are involved in the regulation of pain. This is because mood and pain are both controlled by the same parts of the brain. On the other hand, the severe NP would be the root cause of the depressive symptoms, in addition to the extreme moral agony that would accompany them. In point of fact, the NP displays a nocturnal recrudescence, and this property may assist to explain how the findings of this study might be interpreted in terms of the influence that it has on sleep. This pain, particularly the intense NPs, is typically coupled with a restriction on interests and activities due to the physical handicap it generates. This is especially true in cases where the NPs are particularly intense. This is especially true in situations in which the NPs are of a particularly severe nature.

In the context of this particular investigation, the presence of pain on a persistent basis was found to be associated with an increased likelihood of experiencing depression.

On the other hand, we detected a positive correlation that was statistically significant between the length of treatment and the mean score of depression ($p = 0.014$, $r = 0.32$). This association was found to be correlated positively with the length of treatment. The length of time that patients were treated in therapy for raised the risk that they would display symptoms of depression at some point in the future. Additional explanations could be provided in order to bolster the argument that this connection exists. When a patient uses a substance for an extended period of time, this can have a substantial influence on them and become a source of emotional anguish for them. In addition to this, the NP often exhibits only a partial reaction to analgesics, which requires the utilization of treatment combinations and, as a consequence, may place the patient at a greater risk of experiencing adverse side effects. As a direct consequence of these diseases, the emotional suffering, and particularly the depression, would consequently become even more acute. In passing, I feel obligated to point out that in the studies that we conducted, 65.85 percent of the patients who were treated received a combination of treatments. In addition to this, the past circumstances that our patients had been in will have an impact on the findings that we get from this study. In point of fact, the majority of the people who took part in the research were accepted to the PTC after having gone through a lengthy treatment program during which they had numerous failed efforts at receiving therapy before being included in the study. Failures of this such would make the emotional toll that the NP takes on a person even more difficult to bear.

According to the findings of our study, patients who suffered from depression were more likely to have an NP etiology that was carcinological, poststroke, postoperative, or neuralgia V in origin than patients who did not suffer from depression. The relationship

between depressive symptomatology and the etiology of NP has, as far as we are aware, remained a territory that has not been researched. It would be an intriguing issue to examine whether or not there is a connection between pain and its source and depression. This is because some illnesses may put people at a greater risk for getting depression. The aforementioned conditions are to blame for the emotional anguish that they inflict, as they are debilitating and have a bad outlook on treatment.

One more conclusion from our research is that, according to the SF-12 scales, there is a substantial link between depression and the quality of life of our patients who suffer from pain. This was one of our main hypotheses going into the study. Both our findings and those that have been found by other researchers provide support for the idea that depression has a negative influence on the several dimensions and symptoms that make up quality of life. This result was also supported by the findings of study on the QoL dimensions that was carried out by the BPI. Patients who experience both severe pain and depressive symptomatology have a decreased capacity for walking as a direct consequence of this ($p = 0.001$), as shown by the statistic. If the NP affects the lower limbs, it may result in a handicap for walking, which is added to the depressive symptomatology. This is an additional factor in the depressive symptomatology. The symptomatology of depression includes this as an extra component to consider. In point of fact, depression is characterized by a slowdown of motor function and asthenia in addition to somatic difficulties. These are two of the hallmarks of the condition. As a consequence of this finding, a clinical intersection between these two entities has become clear. According to the findings of our investigation, this depression/NP crossover also takes place for other BPI products. Therefore, neuropathy patients who are suffering a high degree of depression have high averages of pain interference in their "connection with others" ($p=0$), which shows that this may play a substantial role. In addition to this, NP is often a consequence of the underlying disorder (postherpetic pain, diabetes). If the patient continues to endure discomfort even after they have been "healed," the mental suffering of the patient may be prolonged, and it may be difficult to explain why the patient is still experiencing difficulty. It's possible that a member of the family is displaying the same lack of comprehension as well. It is conceivable for the depressive symptoms of a patient to be made worse by a lack of empathy toward the patient's suffering; nevertheless, there are times when the patient's complaint itself can have an influence on the patient's interactions with other people.

In addition, a number of authors have stated that the severity of the pain would be reliant on the interplay between the cognitive, emotional, social, and physical elements. This is an argument that has been presented by a number of authors. They also hypothesized that factors such as stress, worry, and depression, in addition to depression, would be important influencers on the level of pain experienced.

On the other hand, this correlation should not be taken too seriously due to the fact that the core of depression is a change in a person's relationship with the environment in which they live. The symptomatology of depression has an effect on one's mood and is the underlying cause of the person suffering from depression feeling separated from their peers.

In conclusion, the findings of our research shed light on the close relationship that exists between NP, depression, and the quality of life of those who suffer from chronic pain. It is essential to keep this relationship in mind when working with patients who fit the aforementioned profile. In point of fact, a variety of promising psychosocial treatments, such as cognitive restructuring and self-hypnosis training, can alleviate this pain and the negative impact it has on one's quality of life.

CONCLUSION

According to the findings of our study, those who struggle with NP are at a greatly increased risk of acquiring depression; depression is closely tied to the numerous characteristics of NP; and

depression has a detrimental influence on quality of life. When we see a major shift in the quality of life of an NP patient in clinical practice, we should not be content to attribute it exclusively to the patient's feeling of pain or the underlying pathology. Instead, we should be open to exploring other potential explanations for the phenomenon. We should rather look for indicators of depression because it's possible that this is one of the factors that contributed to the worsening of the situation. As a direct result of this fact, screening for the existence of depressive comorbidity should be a crucial component of the first assessment of NP patients. In this context, the HADS is an easy-to-use screening tool that may be applied in a variety of situations. In addition to this, it is of the utmost need to educate the intervening portions of the NP patients about the benefits of making use of this instrument. As a matter of fact, the evaluation of the patient's quality of life ought to be included in the care of any pain sufferer as soon as the NP diagnosis is carried out. This is because the patient's quality of life is directly related to how well they are able to cope with their pain.

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