

Is Major Depression More Commonly associated with Widespread Pain? A Cross-sectional Study to identify Any Relation

¹Pavana Nagaraj, ²Gautam Das, ³Ravi S Sharma, ⁴Snehil Gupta

ABSTRACT

Introduction: Major depressive disorder (MDD) is one of the most common mental disorders and frequently associated with chronic pain. This chronic pain can be widespread or localized and regional. Questions have been raised whether severity of major depression is more associated with widespread pain, or it can be equally associated with localized and regional pain. The purpose of this study is to identify the association of depression with areas of pain and whether depression is more severe in widespread pain.

Materials and methods: A cross-sectional study was conducted on patients attending Daradia Pain Clinic, Kolkata. Patients suffering from both chronic pain and depression of any age and sex who attended this clinic between April 2015 and March 2017 were selected. The patients were divided into two groups: Group I comprised patients with widespread pain with widespread pain index (WPI) ≥ 4 and group II comprised patients with regional pain with WPI ≤ 3 . All the clinical and demographic variables were analyzed and severity of depression was compared between the two groups.

Results: Variables like age, Patient Health Questionnaire 9 (PHQ-9), and numerical rating scale (NRS) scores showed comparability (p -value > 0.05) in both the groups (in group I, $n = 246$; in group II, $n = 125$), while the gender distribution was found highly significant (p -value = 0.0003) for females in chronic widespread pain (CWP) (73.79% in group I vs 52.76% in group II). The subgroups of moderate (PHQ-9 ≤ 14) and severe (PHQ-9 ≥ 15) depression showed no statistical significance (p -value > 0.05).

Conclusion: Our study concluded that severity of depression is equally common with chronic pain whether it is regional and localized or widespread. Females suffer more from widespread pain with depression.

Keywords: Chronic widespread pain, Depression, Patient health questionnaire-9, Severe depression.

How to cite this article: Nagaraj P, Das G, Sharma RS, Gupta S. Is Major Depression More Commonly associated with Widespread Pain? A Cross-sectional Study to identify Any Relation *J Recent Adv Pain* 2018;4(1):25-31.

^{1,3,4}Fellow, ²Director

¹⁻⁴Department of Pain Management, DARADIA: The Pain Clinic Kolkata, West Bengal, India

Corresponding Author: Ravi S Sharma, Fellow, Department of Pain Management, DARADIA: The Pain Clinic, Kolkata, West Bengal, India, Phone: +919993116929, e-mail: drravishankar-sharma4u@gmail.com

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Chronic widespread pain is frequently associated with increased health care use, poor social performance, and increased work absenteeism. Similar occurrences are seen in patients with depression. Major depressive disorder is one of the most common mental disorders and is the second most common cause of disability in industrial countries. Although fibromyalgia and depression are known to coexist, many other systemic diseases that involve multiple pain areas and of chronic nature are also seen to be associated with depression. The female population has shown increased prevalence in patients of both depression and chronic pain.

Compared with the general population, patients attending pain clinics, rheumatology, and fibromyalgia clinics have an excess of psychiatric disorders.^{1,2} The reason for this has been explained by the sharing of common pathways for depression and pain.³ The pain and depression interaction is yet to be fully understood. If pain precedes the depressive illness in as many as 40% of cases, then the reverse is also true, and depressive illness often precedes physical pain.⁴ And we frequently fail to diagnose their coexistence. It is also observed in a few studies that depression is more common when pain is severe.³ This is an important finding since severe depression patients have low compliance to treatment and show dissatisfaction to medical therapy, which in turn may result in increased health care use. Recognizing the need for general approaches to pain management, rather than treating each syndrome as a regional problem of pain, may improve the outcome in such patients.²

Whether pain precedes depression or the opposite, the nature and areas of pain in depressive patients had always been questioned. A common myth among physicians and laypeople is that major depression is more commonly associated with widespread pain. Aim of this study is to identify any association between widespread pain and severity of depression, whether major depression is more commonly associated with depression.

MATERIALS AND METHODS

Design and Population

A cross-sectional study was designed with patients of depression with chronic pain, whether widespread and regional. After approval from the ethical committee, patients who attended pain clinic between April 2015 and March 2017 of any age and either sex were included if they fulfilled the inclusion criteria. After taking informed consent, each patient underwent necessary questionnaires and clinical evaluation was done about areas of pain, pain scores, and other necessary examination. Psychological evaluation in these patients was done with PHQ-9. Areas of pain were noted and counted as WPI. Data were collected and compiled by a computer-based data collection system.

Inclusion Criteria

- PHQ score ≥ 10 .
- Patients with chronic pain, i.e., >3 months pain duration.

Exclusion Criteria

- PHQ score <10.
The patients were categorized into two groups:
Group I comprised patients with WPI ≥ 4 .
Group II comprised patients with WPI of 1 to 3.

Each group was further subdivided into two categories based on PHQ-9 score: PHQ-9 score of 10 to 14 was considered as moderate depression group and PHQ-9 score of ≥ 15 was considered as severe depression group.

Baseline Assessment of CWP

Subjects were asked about the distribution of their pain areas and whether the pain had been present for more than 3 months. Two manikin drawings of the body were included (front, back, and sides), on which subjects were asked to indicate the sites of pain to assess the location and duration of pain.^{1,5} Based on this information, a trained observer categorizes the subjects as presence (≥ 4 WPI) or absence (<3 WPI) of CWP and then were grouped in either group I or II. Widespread pain index and CWP were defined using the American College of Rheumatology (ACR) 1990 and 2010 criteria for fibromyalgia.^{6,7} As head was not included in the WPI definition of ACR 1990 criteria, we have given one score to pain in head area for convenience.

Pain Assessment

The assessment of intensity of pain was based on NRS. It is the most commonly used scale as it has good sensitivity and generates the data that can be statistically analyzed

for audit purposes.⁸ It is a numerical scale between “no pain (0)” and “excruciating pain (10).”

Psychiatric Assessment

The 9-item version of the PHQ-9 was used to identify potential cases of mental illness, serving as the initial screening process. This scale has comparable sensitivity and specificity and consists of actual nine criteria upon which the diagnosis of depression as described by the Diagnostic and Statistical Manual of Mental disorders IV) is based.⁹ Maximum score is 27, score of 1 to 4 indicates minimal depression, 5 to 9 mild depression, 10 to 14 moderate depression, 15 to 19 moderately severe depression, and 20 to 27 severe depression. All the subjects having PHQ-9 ≥ 10 were included in the study as PHQ-9 ≥ 10 has a sensitivity of 88% and specificity of 88% for major depression.

Statistical Analysis

The sample size was calculated assuming that moderate-to-severe depression is more commonly associated with CWP patients than in regional pain and localized pain and we considered the difference between two groups to be >20%. For our study, the alpha error of the sample was taken as 0.05 and beta error was 0.2. Power of study was 0.8. Based on the above parameters, the minimal sample size needed was 81 in each group.

Initial descriptive analysis compared various parameters like age, sex, PHQ-9 scores, and NRS scores between two groups. Age distribution in two groups was analyzed using independent sample Student's t-test after assuming equal variance. The sex distribution, PHQ-9 score, and NRS score were compared using independent variable testing by chi-square analysis.

RESULTS

On completion of our study, data were analyzed and clinical and demographic variables were summarized.

At the end of our study period, total number of patients in group I was 246 with mean age of 45 years. In group II, the total patients was 125 with mean age of 46 years. Table 1 shows the age distribution in both the groups.

Statistical analysis was applied using independent Student's t-test after assuming equal variance in the study population. The analysis has shown that age in both groups is comparable with $p > 0.05$ and will not interfere with our results.

Table 2 shows gender distribution in the two groups. It was statistically analyzed using chi-square test. Total females in group I were 181/246 (73.79%) (Graph 1), whereas in group II were 65/125 (52.76%) (Graph 2).

Table 1: Age distribution

	Group I (with widespread pain)	Group II (with regional pain)
Sample size (n)	246	125
Range	14–65 yrs	17–65 yrs
Arithmetic mean	45.2967 yrs	46.52 yrs
95% CI for the mean	43.7617–43.2234	44.3263–48.7137
Median	45 yrs	48 yrs
Mode	60 yrs	60 yrs
Standard deviation	12.3330	12.6131
Statistical difference between two groups	p = 0.370784 [#]	

CI: Confidence interval

Table 2: Gender distribution

	Group I (with widespread pain)	Group II (with regional pain)
Sample size (n)	246	125
Male	65 (26.21%)	60 (47.24%)
Female	181 (73.79%)	65 (52.76%)
Statistical difference between two groups	p = 0.000032 [#]	

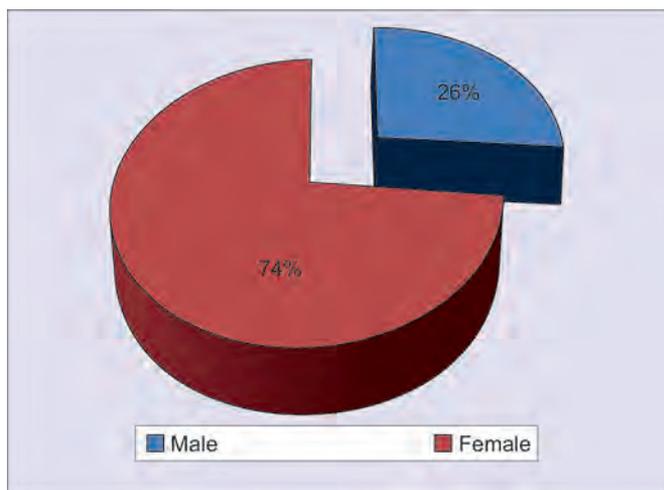
Statistically significant difference was noted in sex distribution and females suffer more from CWP; p-value of 0.0003 is highly significant.

Other variables like PHQ-9 scores and NRS scores showed comparability (p-value > 0.05) in both the groups with mean PHQ-9 score in group I being 15.07 (Graph 3), and in group II being 14.2 (Graph 4). Mean NRS scores in both the groups were 6.8 and 6.4 respectively (Graphs 5

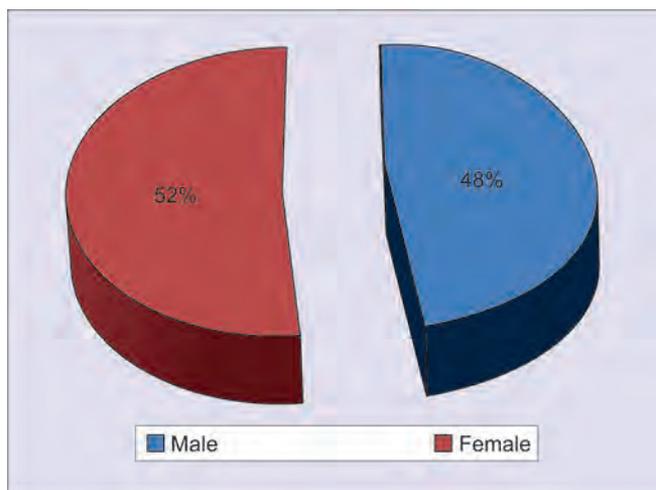
and 6). Tables 3 and 4 compare the PHQ-9 scores and NRS scores between the two groups.

The PHQ-9 scores were further analyzed and divided into moderate and severe subgroups (PHQ-9 = 10–14 and PHQ-9 ≥ 15 in groups I and II) (Graphs 7 and 8). On comparing the two groups, no statistically significant difference could be demonstrated, indicating severe depression may occur equally in CWP or regional and localized pain patients (Table 5).

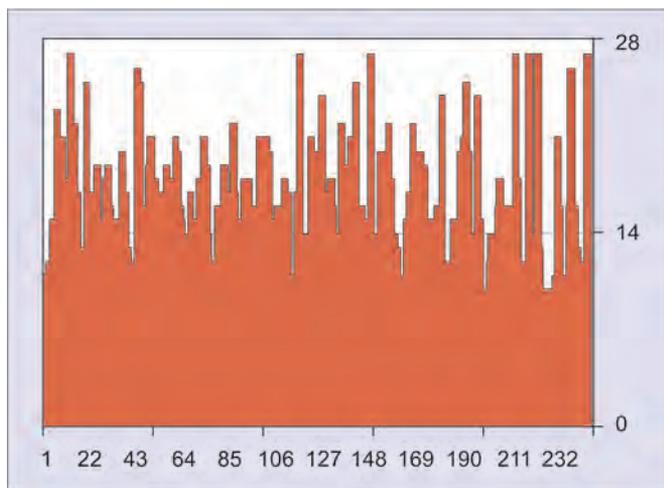
But the data suggested that moderate depression is more common than severe depression in our patient population.



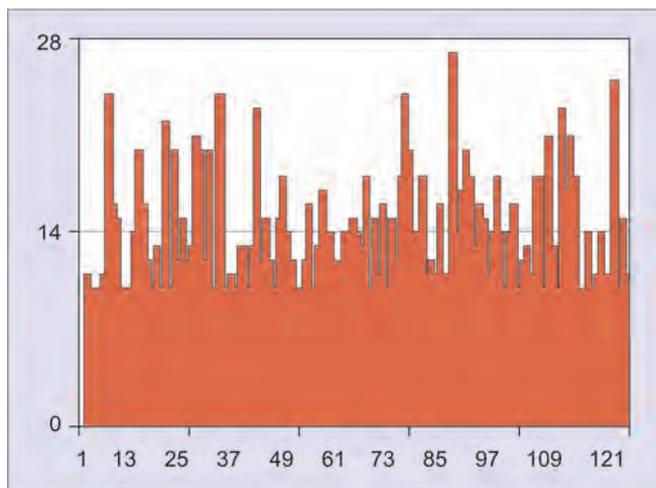
Graph 1: Gender distribution for group I



Graph 2: Gender distribution in group II



Graph 3: Comparison of PHQ-9 scores in group I



Graph 4: Comparison of PHQ-9 scores in group II

Table 3: Comparison of PHQ-9 score

	Group I (with widespread pain)	Group II (with regional pain)
Sample size (n)	246	125
PHQ-9 score range	10–27	10–27
Median PHQ-9	14	13
Mean	15.0772	14.232
Mode	10	10
Standard deviation	4.4673	4.1155
95% CI for the mean	14.5212–15.6332	13.5105–14.9534
Statistical difference between two groups	p = 0.0779 [#]	

CI: Confidence interval

Table 4: Comparison of NRS between two groups

	Group I (with widespread pain)	Group II (with regional pain)
Sample size (n)	246	125
NRS score range	1–10	1–10
Median NRS	7	7
Mean	6.8130	6.408
Mode	8	8
Standard deviation	1.8421	2.0124
95% CI for the mean	6.5828–7.0431	6.0552–6.7607
Statistical difference between two groups	p = 0.0532 [#]	

CI: Confidence interval

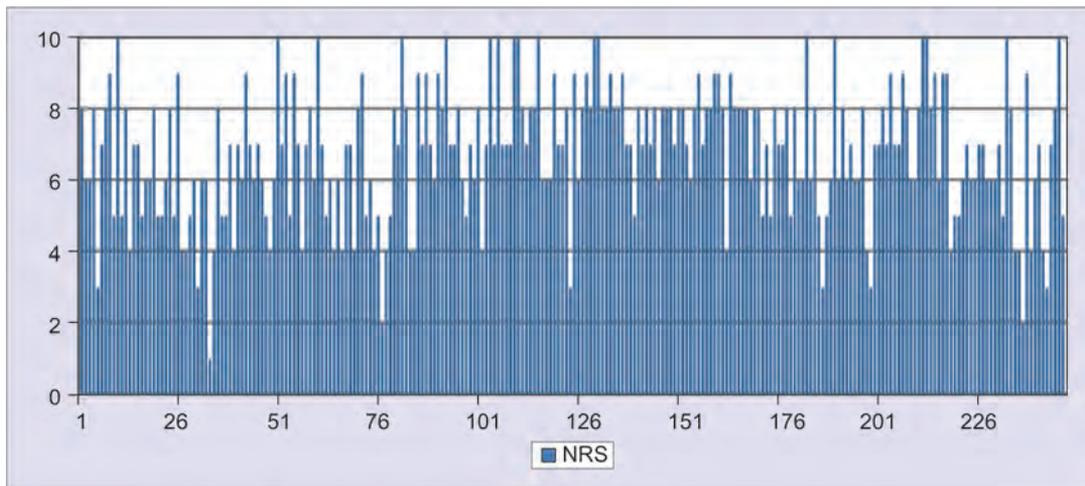
Table 5: Comparison of severity of depression between two groups

	Group I (with widespread pain)	Group II (with regional pain)
PHQ-9 ≥15 severe depression	116 (47.15%)	46 (36.8%)
PHQ-9 = 10–14 moderate depression	130 (52.84%)	79 (63.2%)
	p = 0.057	

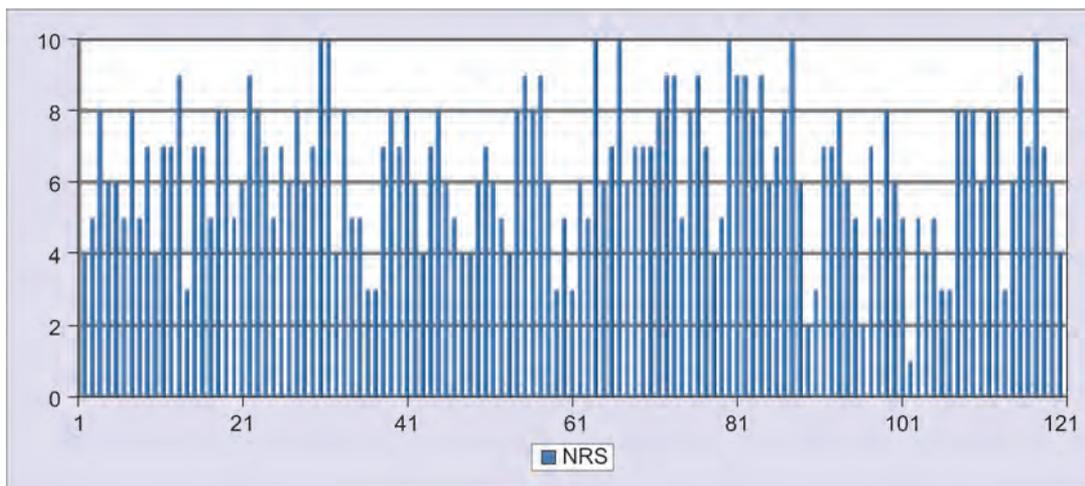
DISCUSSION

Our study was designed to identify the relationship between depression and widespread pain. Depression was assessed with PHQ-9 score and pain by NRS score. We began with a hypothesis that patients with depression suffer more from widespread pain.

Patients in clinical samples, and in general population satisfying criteria for CWP, have been described as having

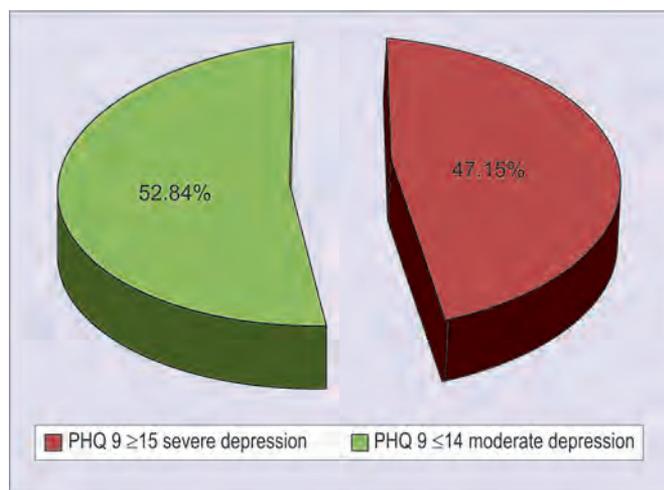


Graph 5: Comparison of NRS score in group I

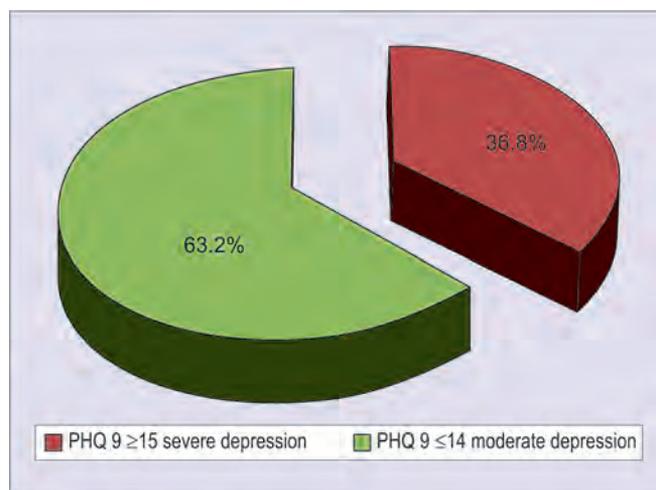


Graph 6: Comparison of NRS score in group II





Graph 7: Comparison of moderate and severe depression in group I



Graph 8: Comparison of moderate and severe depression in group II

greater psychological distress particularly depressive disorders and somatoform disorders than would be expected in the general population without CWP.^{1,10}

There are several studies that have identified the correlation of depression and pain, but few studies have been able to relate the severity of depression with pain. Emptage et al¹¹ in their study on 8,280 participants showed that when depression and pain exist as a comorbidity, it leads to significant functional impairment and financial burden. And as the severity of pain increased, the outcome was worse.

Nicholl et al¹⁰ demonstrated the occurrence of multisite pain in patients of both MDD and bipolar disorder (BD) and also suggested that the patients with chronic and multisite pain are at risk of developing MDD and BD.

In a population-based case-control study conducted by Benjamin et al,¹ the association of CWP and depression was studied. This study also was unable to demonstrate a cause-and-effect relationship, but showed that 16.9% of those with CWP had a psychiatric diagnosis. They suggested that CWP and depression should be identified and treated.

Our result is consistent with this study, and the PHQ-9 scores of both the groups were comparable, indicating that the patients with depression may present with both widespread pain and regional pain or localized pain.

The total number of patients who had widespread pain appeared more frequently as compared with regional pain. This is evident with the difference of sample size between the two groups (group I n = 246 and group II n = 125). The reason for this difference may be because the regional pain patients visit specific specialties,¹² hence they get filtered and may not attend the pain clinic. Their tolerance to pain may be better as compared with widespread pain, and dissatisfaction to treatment may be less as compared with widespread pain patients.

Williams et al¹³ in their study in neurology were able to identify the increased prevalence of pain among

female patients, although the areas of pain have not been specified. Similar gender distribution was established by Munce and Stewart.¹⁴

Our study also was able to demonstrate the findings that among the patients who consult for pain, CWP is higher in female population.

The association of depression with chronic pain is well known and several studies are available in support of the same. It is also proven that chronic pain and depression are best managed in a pain clinic with input from psychiatric specialty.^{15,16}

Higher depression scores imply greater severity of depression, the resultant of which would be lower treatment compliance; hence, the adequacy of therapy cannot be achieved. This was the background for our analysis of occurrence of severe depression in widespread pain.

Kroenke et al¹⁷ in their study were able to demonstrate the relation of severity of depression and severity of pain. The study showed that as severity of depression increases, severity of pain also increases and *vice versa*.

In a large population-based study conducted in Japan by the Japan National Health and Wellness Survey, the relationship between severity of depression and severity of painful symptoms was compared using PHQ-9 and NRS scales. Their results showed that severe pain correlated with severe depressive symptoms (PHQ-9 ≥ 15). It also resulted in worse health-related quality of life, lower health utility, greater impairment at work, and more health care provider visits.¹⁸ They concluded that ameliorating pain among patients with depression resulted in improved outcome.

Several studies have used different modes of assessing psychological health of patients.¹⁹⁻²³ Since PHQ-9 is a questionnaire to be answered by patients, it is a useful tool in clinical setting. We divided each group into subgroups based on PHQ-9 scores (≥15 indicating severe depression and 10-14 for moderate depression)

to identify if patients with CWP have higher depression scores compared with patients with regional pain. Our study could not yield considerable difference in severe depression among CWP patients than regional and localized pain. Though statistically insignificant, we had an observation that moderate depression was more common in both the groups.

At the end of our study, we could not demonstrate any relation between severity of depression with areas of pain; depression scores were similar in both groups of CWP and regional pain. But it surely reasserts the findings with other studies that patients with widespread pain or regional pain may have coexisting depression and females are more prone to develop the same. Thus, chronic pain patients need psychiatric assessment, and adequate management of both the conditions is warranted. It helps in better quality of life, with improved health care utilization.

CONCLUSION

Our study concluded that major depression is equally associated with both regional and widespread pain, with no specific relation to severity of depression and areas of pain. Also, female population has greater prevalence of widespread pain with depression. Hence, the need for psychiatric assessment in all patients is recommended, which will help us in better patient management and improved outcome.

LIMITATIONS OF OUR STUDY

Our study was based on a pain clinic where the people who seek consultation would be mainly those with widespread pain, the ones with regional pain may seek consultation in specific specialties, and hence we lack the actual population size with regional pain. Also severe depression patients may prefer to visit a psychiatry clinic than a pain clinic. The cross-sectional nature of our study hinders analyzing response to therapy since patient follow-up was not a part of our study. A larger sample size may be desired for better results. Our assessment of psychological illness was solely based on PHQ-9 scores, whereas anxiety, the other spectrum of mental illness, was not assessed and not considered as a parameter for the study.

Further multicentric studies involving larger population, more medical specialties, wider psychological assessment tools, and including long-term follow-up may help in better understanding of the relation among the variables.

REFERENCES

1. Benjamin S, Morris S, McBeth J, MacFarlane GJ, Silman AJ. The association between chronic widespread pain and mental disorder: a population-based study. *Arthritis Rheum* 2000 Mar;43(3):561-567.
2. Rohrbeck J, Jordan K, Croft P. The frequency and characteristics of chronic widespread pain in general practice: a case-control study. *Br J Gen Pract* 2007 Feb;57(535):109-115.
3. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. *Arch Intern Med* 2003 Nov;163(20):2433-2445.
4. Ohayon MM, Schatzberg AF. Using chronic pain to predict depressive morbidity in the general population. *Arch Gen Psychiatry* 2003 Jan;60(1):39-47.
5. MacFarlane GJ, Croft PR, Schollum J, Silman AJ. Widespread pain: is an improved classification possible? *J Rheumatol* 1996 Sep;23(9):1628-1632.
6. Wolfe F, Clauw DJ, FitzCharles MA, Goldenberg DL, Hauser W, Katz RS, Mease P, Russell AS, Russell IJ, Winfield JB. Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR preliminary diagnostic criteria for fibromyalgia. *J Rheumatol* 2011 Jun;38(6):1113-1122.
7. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. *Arthritis Rheum* 1990 Feb;33(2):160-172.
8. Williamson A, Hoggart B. Pain: a review of three commonly used pain rating scales. *J Clin Nurs* 2005 Aug;14(7):798-804.
9. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001 Sep;16(9):606-613.
10. Nicholl BI, Mackay D, Cullen B, Martin DJ, Ul-Haq Z, Mair FS, Evans J, McIntosh AM, Gallagher J, Roberts B, et al. Chronic multisite pain in major depression and bipolar disorder: cross-sectional study of 149,611 participants in UK Biobank. *BMC Psychiatry* 2014 Dec;14:350.
11. Emptage NP, Sturm R, Robinson RL. Depression and comorbid pain as predictors of disability, employment, insurance status, and health care costs. *Psychiatr Serv* 2005 Apr;56(4):468-474.
12. Mansfield KE, Sim J, Kelvin P. Identifying patients with chronic widespread pain in primary care. *Pain* 2017 Jan;158(1):110-119.
13. Williams LS, Jones WJ, Shen J, Robinson RL, Weinberger M, Kroenke K. Prevalence and impact of depression and pain in neurology outpatients. *J Neurol Neurosurg Psychiatry* 2003 Nov;74(11):1587-1589.
14. Munce SE, Stewart DE. Gender differences in depression and chronic pain conditions in a national epidemiologic survey. *Psychosomatics* 2007 Sep-Oct;48(5):394-399.
15. Surah A, Baranidharan G, Morley S. Chronic pain and depression. *Contin Educ Anaesth Crit Care Pain* 2014 Apr;14(2):85-89.
16. Nekovarova T, Yamamotova A, Vales K, Stuchlik A, Fricova J, Rokyta R. Common mechanisms of pain and depression: are antidepressants also analgesics? *Front Behav Neurosci* 2014 Mar;8:99.
17. Kroenke K, Wu J, Bair MJ, Krebs EE, Damush TM, Tu W. Reciprocal relationship between pain and depression: a 12-month longitudinal analysis in primary care. *J Pain* 2011 Sep;12(9):964-973.
18. Vietri J, Otsubo T, Montgomery W, Tsuji T, Harada E. Association between pain severity, depression severity, and use of health care services in Japan: results of a nationwide survey. *Neuropsychiatr Dis Treat* 2015 Mar;11:675-683.

19. Ang QQ, Wing YK, He Y, Sulaiman AH, Chiu NY, Shen YC, Wang G, Zhang C, Lee KH, Singh P, et al. Association between painful physical symptoms and clinical outcomes in East Asian patients with major depressive disorder: a 3-month prospective observational study. *Int J Clin Pract* 2009 Jul;63(7):1041-1049.
20. Novick D, Montgomery W, Kadziola Z, Moneta V, Peng X, Brugnoli R, Haro JM. Do concomitant pain symptoms in patients with major depression affect quality of life even when taking into account baseline depression severity? *Patient Prefer Adherence* 2013 May;7:463-470.
21. Lee P, Zhang M, Hong JP, Chua HC, Chen KP, Tang SW, Chan BT, Lee MS, Lee B, Gallagher GL, et al. Frequency of painful physical symptoms with major depressive disorder in Asia: relationship with disease severity and quality of life. *J Clin Psychiatry* 2009 Jan;70(1):83-91.
22. Sharma K, Das G, Dey S, Villano EQ, Mandal S. Neuropathic pain and depression: a prospective study to find out any association. *J Recent Adv Pain* 2016 Jan-Apr;2(1):6-10.
23. Navani A, Li G. Chronic pain challenge: a statistical machine-learning method for chronic pain assessment. *J Recent Adv Pain* 2016 Sep-Dec;2(3)82-86.