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Predictors of Comorbid Depression in Iranian Patients With Knee Osteoarthritis

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Abstract

Background: The correlation between depression and pain is reported in several chronic diseases including osteoarthritis (OA). This depression could lead to more pain perception and is considered as one of the confounding factors of the association between radiographic symptoms and the pain level in patients with OA.
Objectives: Assessment of comorbid depression and its predictors could significantly improve assessment and management of the OA. The current study aimed to evaluate the association between depression and pain in patients with OA and explore the determinants of this depression in Iranian population with OA, as well.
Methods: The study evaluated the clinico-socio-demographic predictors of depression in 100 patients with OA. Depression was recorded using Beck depression inventory-II (BDI-II) and pain was measured by self-reporting visual analogue scale (VAS).
Results: Depression score was significantly higher in younger (P = 0.04), unmarried (P = 0.01), physically inactive (P = 0.03) and patients with higher grade of OA (P = 0.02). In addition, a significant correlation was observed between comorbid depression and pain (r = 0.381, P = 0.008, 95% confidence interval), OA grade (r = 0.332, P = 0.009, 95% CI) and age (r = -0.259, P = 0.024, 95% CI).
Conclusions: Given the confounding role of comorbid depression in the assessment and management of OA, and the high prevalence of depression in patients with OA, the predictors of comorbid depression in these patients should be considered to improve the outcome of therapeutic interventions.

Keywords: Osteoarthritis, Pain, Comorbid Depression

1. Background

Osteoarthritis (OA) is considered as the most common disorder of musculoskeletal system in both developed and developing countries (1). Since OA mostly affects the elderly, a population with high prevalence of depression, the coexistence of OA and depression is frequent (2, 3). According to the great body of evidence, depression significantly affects the quality of life of the patients with OA (2, 4). Individuals with depression report more severe pain and unfortunately more than half of the patients with chronic pain end up with depression (2, 5, 6). In other words, the pain causes more depression and the depression causes more pain and this interaction finally leads to the sooner end stage of the disease (7). Theoretically, patients with depression exhibit decreased brain serotonin function and elevated cortisol secretion (8). Serotonin is a pain modulator and its decline is associated with increased pain perception (9). In addition, the higher amount of cortisol weakens the immune system, leading to the lower anti-inflammatory and higher pro-inflammatory cytokine release which finally results in higher pain perception (10, 11).

The link between depression and pain was previously evaluated in several chronic diseases (5, 12, 13). Nearly all of the former studies reported a positive correlation between depression and pain. Such positive correlation between pain and depression is also found in OA (2, 14), leading to the inconsistency between radiographic symptoms and the amount of declared pain. This inconsistency adversely affects the assessment of OA and results in inappropriate management of the disease (15, 16). However, considering this association in the OA assessment and management would diminish its adverse effect. In addition, since the higher depression level could be associated to the higher pain perception, the depression management

could lead to less pain level which results in an improved quality of life of such patients (17).

2. Objectives

The current study aimed to evaluate the depression and pain level in patients with OA in the society to elucidate their potential correlations. In addition, the study aimed to evaluate the effect of clinico-socio-demographic variables in OA comorbid depression. It was hypothesized that the OA caused by depression might be predicted by these variables. In that case, more attention is needed to manage OA in the patients presenting depression risk factors, especially in those who clinical and radiological symptoms do not accord.

3. Methods

In a cross-sectional study, a total of 100 patients with knee OA referred to the medial center from 2012 to 2014 were selected and enrolled to the study after confirming the OA according to the Kallgren and Lawrence osteoarthritis grading system (18, 19). Patients with any other comorbid diseases, which could affect the pain and depression levels, including diabetes, cardiovascular and psychiatric disease were excluded from the study. Each patient signed the written informed consent. In addition, Iran University of Medical Sciences institutional review board reviewed and approved the waiver of authorization to use protected health information (PHI) for research purposes for this study.

Totally, 80 (80%) females and 20 (20%) males were evaluated. The mean age of the patients was 58 years, ranging from 42 to 75 years. Table 1 contains the detailed demographic characteristics of the patients.

To analyze the depression level, Persian version of Beck depression inventory-II (BDI-II) (20) was applied. Briefly, the BDI-II contains 21 questions and each answer is scored on a scale of 0 to 3; while higher total scores indicate more severe depression symptoms. In this regard, it is divided into four levels including 0 - 13, 14 - 19, 20 - 28 and 29 - 63 which correspond to minimal, mild, moderate and severe depression, respectively (20).

Visual analogue scale (VAS) was used to assess pain severity. VAS is a self-reported criterion, in which the respondent is asked to place a perpendicular line on the VAS line according to the pain he/she is experiencing. VAS is the most common scale in pain evaluation and represents the intensity of pain on a scale of 0 - 10, where 0 indicates no pain and 10 indicates the worst pain ever felt (21).

Previously reported prevalence of OA was considered to determine the required sample size (22). Regarding the prevalence of 15.4% in the urban area of Tehran, reported by Davatchi et al. and at type I error of 10%, the minimum sample size of this study was 50.

Statistical analysis was performed using IBM SPSS for windows, version 21. Central tendency and variability of numeric variables were evaluated using the mean and standard deviation, respectively. Independent sample T-test, one-way ANOVA, Chi-square test, Pearson and Spearman correlation coefficient tests were used to analyze the significant associations and correlations between the variables. P values ≤ 0.05 were regarded as statistically significant.

4. Results

The results were provided in two separate sections including the analysis of associations showed by P-value and analysis of correlations indicated by r-value. The mean and standard deviation (SD) of pain and depression scores were calculated according to the aforementioned criteria. In this regard, the mean $\pm$ SD of depression and pain scores were 10.06 ± 4.36 and 4.12 ± 1.6, respectively. The detailed mean $\pm$ SD of pain and depression scores according to the corresponding variables are demonstrated in Table 2.

Totally, 60 negative or minimal depressions, 30 mild depressions and 10 moderate depressions were observed in the population with OA. Bivariate analysis of variables showed a significant association between depression score and factors including age (P = 0.04), marital status (P = 0.01) and regular sport activity (P = 0.03). In this regard, patients who were married, employed and physically active had significantly lower depression scores. The mean depression score was also significantly high in higher grades (P = 0.02). Correlation analysis showed a significant positive correlation between depression and pain (r = 0.381, P = 0.008, 95% CI) and OA grade (r = 0.332, P = 0.009, 95% CI). In addition, a significant negative correlation was observed between depression score and age (r = -0.259, P = 0.024, 95% CI). No other significant correlation was observed between depression score and variables including gender, marital status, etc.

As expected, the mean pain score was significantly higher in higher grades of OA (P = 0.015). The pain score was also significantly higher in patients with higher BMI (P = 0.03). Moreover, a significant association was observed between pain score and age group. In this regard, patients aged less than 50 years old reported higher pain, which was significantly different from those of older age groups (P = 0.04). No other significant association was observed between pain and other variables including gender, education, etc. The correlation of pain and OA grade was also significantly positive (r = 0.512, P = 0.001, 95% CI), as expected.

The detailed results of association and correlation analyses are also demonstrated in Table 2.

Table 1. The Socio-Clinico-Demographic Characteristics of Patients

Variable Group	N, %
Age	
< 50	18
≥ 50	82
Gender	
Male	20
Female	80
OA grade	
I	15
II	24
III	38
IV	23
Body mass index (BMI), Kg/m^2	
< 25	12
25 - 29.9	36
29.9	52
Education	
Undergraduate	62
Graduate	20
Postgraduate	18
Occupation status	
Working	54
Retired	46
Regular sport activity	
Yes	18
No	82
Marital status	
Married	58
Single/divorced/widow	42
Financial satisfaction	
Totally satisfied	17
Relatively satisfied	71
Dissatisfied	12
Smoking	
Yes	19
No	81

Abbreiation: OA, osteoarthritis.

5. Discussion

Pain is the most primary reason of seeking health care in patients with OA. The pain level is usually correlated with radiographic changes, where higher OA grade is accompanied by higher pain experience (23). However, in a considerable number of patients with OA, pain and radiographic symptoms do not accord with each other and radiographic signs without pain or pain without radiographic signs are frequently reported (15, 16, 24). This strong variability in the patients with OA makes it difficult to properly identify the affected individuals and subsequently evaluate the disease progression. Several psychosocio determinants may explain the different pain perception in the patients with OA (25) and predispose patients to report more or less pain. Among them, depression is a common condition in the elderly, which affects a considerable number of patients with OA (26, 27). A significantly higher association of knee pain and radiographic signs was observed in patient without depression symptoms (28). As a result, a comprehensive understanding of interactive pain/depression correlation in the patients with OA could optimize the assessment and management of OA.

According to the study analysis, a significant correlation was observed between pain and depression level. Such correlation was also reported in many former studies. Kim et al. reported that the presence of depression was associated with an increased risk of knee arthritis and suggested that the assessment of comorbid depression should be integrated to the assessment and management of OA (29). Leite et al. showed a high frequency of depression in patients with OA, which can impact the pain and physical function of such patients, and proposed the depression control along with OA management to reach superior outcomes (2). Creamer and Hochberg reviewed the relationship between OA pain and psychological variables and proposed that better understanding of this complex interaction improves the effectiveness of many pharmacologic interventions (14). In this regard, the current study also evaluated the effect of clinical, social and demographic variables on comorbid depression in patients with OA. According to the study analysis, depression score was significantly higher in younger patients and higher OA grades. Moreover, depression score was significantly lower in married and physically active patients with OA. In addition, depression was significantly correlated with the pain, OA grade and age of patients with OA. Interestingly, OA grade was simultaneously correlated with both depression and pain, which could confirm the study hypothesis. As higher OA grade generally causes more pain and pain triggers depression, correlation of OA grade and depression could be expected.

The determinants of comorbid depression were also evaluated in other investigations (30-32). Miller and Cano investigated the risk factors of comorbid pain and depression in chronic disorders including OA. They suggested that certain demographic groups including younger and female patients were more likely to have comorbid depression and chronic pain and proposed that such groups may benefit from depression screening (33). However, correlation of comorbid depression with age is debating and even

Table 2. The Statistical Analysis of Correlation and Association Between Socio-Clinico-Demographic Characteristics of Patients With Pain and Depression Score[a,b]

Variable Group	Pain, Mean (SD)	Association (P-Value)	Correlation (r, P-Value)	Depression (Mean ± SD)	Association (P-Value)	Correlation (r, P-Value)
Age		0.04*	0.115, 0.09		0.04*	-0.259, 0.024*
< 50	4.41 (1.5)			10.41 (5.4)		
≥ 50	3.98 (1.6)			9.9 (5.1)		
Gender		0.06	0.076, 0.31		0.06	
Male	3.88 (1.6)			9.82 (5.6)		0.164, 0.08
Female	4.36 (1.4)			10.3 (5.3)		
OA grade		0.01*	0.512, 0.001*		0.02*	0.332, 0.009*
I	2.62 (1.2)			8.89 (5)		
II	3.36 (1.3)			9.25 (4.8)		
III	4.4 (1.5)			10.3 (5.6)		
IV	6.1 (1.5)			11.2 (4.1)		
Body mass index(BMI) (kg/m^2)		0.03*	0.175, 0.09		0.1	0.011, 0.4
< 25	3.8 (1.4)			9.51 (4.2)		
25 - 29.9	4.06 (1.3)			10.7 (5.3)		
> 29.9	4.5 (1.6)			9.97 (5.5)		
Education		0.22	-0.022, 0.42		0.11	-0.066, 0.23
Undergraduate	4.1 (1.3)			9.43 (4.8)		
Graduate	4.08 (1.4)			10.43 (5.8)		
Postgraduate	4.18 (1.7)			10.32 (5.2)		
Occupation status		0.08	0.112, 0.12		0.18	0.085, 0.2
Working	4.01 (1.3)			10.1 (4.6)		
Retired	4.23 (1.5)			10.02 (5.7)		
Regular sport activity		0.11	0.155, 0.1		0.03*	0.122, 0.09
Yes	4.16 (1.6)			9.08 (5.5)		
No	4.08 (1.6)			11.04 (5.7)		
Marital status		0.09	0.101, 0.15		0.01*	0.141, 0.07
Married	4.02 (1.5)			7.86 (4.8)		
single/divorced/widow	4.22 (1.4)			12.26 (6.1)		
Financial satisfaction		0.9	0.055, 0.35		0.06	-0.051, 0.34
Totally satisfied	4.12			10.21		
Relatively satisfied	4.18			10.08		
Dissatisfied	4.06			9.89		
Smoking		0.2	-0.036, 0.46		0.31	0.013, 0.5
Yes	4.16			10.08		
No	4.08			10.04		

[a] *, Significant value.
[b] P value < 0.05 was considered significant.

contradictory in some studies. While some studies showed the positive correlation of depression and age, others mentioned an inverse correlation (33-35). The study data also showed an inverse correlation between comorbid depression and age in Iranian patients with OA. This age effect could be interpreted by higher activity limiting impact of OA on this age group. Since the patients aged less than 50 years old need more mobility to take part in their routine activities, the OA imposed restriction could affect their mood more considerably. Surprisingly, both pain and depression scores were higher in younger patients with OA of the study. This also could confirm the interactive effect of pain and depression on each other. In this regard, higher depression score of younger patients with OA could lead to more pain perception, vice versa.

The cross-sectional nature of the study was considered as the biggest limitation of the study. Since the data were collected in a cross-sectional study, it was impossible to explore whether the depression symptoms were the consequence of OA pain or not. The study could not even evaluate which one was earlier, pain or depression. As previously mentioned, the correlation of pain and depression was two-sided, where pain could lead to more depression and depression could cause more pain. Since higher de-

pression is correlated with more pain perception or report, future therapeutic approach of OA needs to be re-evaluated to consider the depression role; especially in patients which the radiographic score and pain level do not accord. In addition, socio-demographic determinants of depression in patients with OA, including age, marital status, physical activity and etc. should be considered to evaluate affected patients.

Footnotes

Authors' Contribution: Study design, Mehdi Moghtadaei and Mehdi Moayedfar; data acquisition, Mehdi Moayedfar, Mohammad Dehghani, Fatemeh Rahmati and Sahleh Mazaheri; manuscript preparation and revision, Mehdi Moghtadaei, Mehdi Moayedfar, Mohammad Dehghani, Fatemeh Rahmati and Sahleh Mazaheri; study supervision, Mehdi Moghtadaei.

Conflict of interest: There was no conflict of interests regarding the current study.

References

1. Zhang Y, Jordan JM. Epidemiology of osteoarthritis. *Clin Geriatr Med.* 2010;**26**(3):355–69. doi: 10.1016/j.cger.2010.03.001. [PubMed: 20699159].
2. Leite AA, Costa AJ, Lima Bde A, Padilha AV, Albuquerque EC, Marques CD. Comorbidities in patients with osteoarthritis: frequency and impact on pain and physical function. *Rev Bras Reumatol.* 2011;**51**(2):118–23. [PubMed: 21584418].
3. Rzewuska K, Strabel T. Genetic parameters for milk urea concentration and milk traits in Polish Holstein-Friesian cows. *J Appl Genet.* 2013;**54**(4):473–82. doi: 10.1007/s13353-013-0159-8. [PubMed: 23934506].
4. Lin EH, Katon W, Von Korff M, Tang L, Williams JJ, Kroenke K, et al. Effect of improving depression care on pain and functional outcomes among older adults with arthritis: a randomized controlled trial. *JAMA.* 2003;**290**(18):2428–9. doi: 10.1001/jama.290.18.2428. [PubMed: 14612479].
5. Giesecke T, Gracely RH, Williams DA, Geisser ME, Petzke FW, Clauw DJ. The relationship between depression, clinical pain, and experimental pain in a chronic pain cohort. *Arthritis Rheum.* 2005;**52**(5):1577–84. doi: 10.1002/art.21008. [PubMed: 15880832].
6. Rosemann T, Laux G, Szecsenyi J, Wensing M, Grol R. Pain and osteoarthritis in primary care: factors associated with pain perception in a sample of 1,021 patients. *Pain Med.* 2008;**9**(7):903–10. doi: 10.1111/j.1526-4637.2008.00498.x. [PubMed: 18702636].
7. Holmes A, Christelis N, Arnold C. Depression and chronic pain. *Med J Australia.* 2012;**10**:17.
8. Cowen PJ. Cortisol, serotonin and depression: all stressed out?. *Br J Psychiatry.* 2002;**180**:99–100. [PubMed: 11823315].
9. Marks DM, Shah MJ, Patkar AA, Masand PS, Park GY, Pae CU. Serotonin-norepinephrine reuptake inhibitors for pain control: premise and promise. *Curr Neuropharmacol.* 2009;**7**(4):331–6. doi: 10.2174/157015909790031201. [PubMed: 20514212].
10. Irwin MR, Miller AH. Depressive disorders and immunity: 20 years of progress and discovery. *Brain Behav Immun.* 2007;**21**(4):374–83. doi: 10.1016/j.bbi.2007.01.010. [PubMed: 17360153].
11. Herbert TB, Cohen S. Depression and immunity: a meta-analytic review. *Psychol Bull.* 1993;**113**(3):472–86. [PubMed: 8316610].
12. Trivedi MH. The link between depression and physical symptoms. *Prim Care Companion J Clin Psychiatry.* 2004;**6**(Suppl 1):12–6. [PubMed: 16001092].
13. Romano JM, Turner JA. Chronic pain and depression: does the evidence support a relationship? Psychological bulletin. 1985 ;**97**(1):18.
14. Creamer P, Hochberg MC. The relationship between psychosocial variables and pain reporting in osteoarthritis of the knee. *Arthritis Care Res.* 1998;**11**(1):60–5. [PubMed: 9534495].
15. Barker K, Lamb SE, Toye F, Jackson S, Barrington S. Association between radiographic joint space narrowing, function, pain and muscle power in severe osteoarthritis of the knee. *Clin Rehabil.* 2004;**18**(7):793–800. [PubMed: 15573836].
16. Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. *BMC Musculoskelet Disord.* 2008;**9**:116. doi: 10.1186/1471-2474-9-116. [PubMed: 18764949].
17. Unutzer J, Hantke M, Powers D, Higa L, Lin E, D. Vannoy S , et al. Care management for depression and osteoarthritis pain in older primary care patients: a pilot study. *Int J Geriatr Psychiatry.* 2008;**23**(11):1166–71. doi: 10.1002/gps.2048. [PubMed: 18489009].
18. Petersson IF, Boegard T, Saxne T, Silman AJ, Svensson B. Radiographic osteoarthritis of the knee classified by the Ahlback and Kellgren & Lawrence systems for the tibiofemoral joint in people aged 35-54 years with chronic knee pain. *Ann Rheum Dis.* 1997;**56**(8):493–6. [PubMed: 9306873].
19. Brandt KD, Fife RS, Braunstein EM, Katz BR. adiographic grading of the severity of knee osteoarthritis: relation of the Kellgren and Lawrence grade to a grade based on joint space narrowing, and correlation with arthroscopic evidence of articular cartilage degeneration. *Arthritis Rheumatism.* 1991;**34**(11):1381–6.
20. Ghassemzadeh H, Mojtabai R, Karamghadiri N, Ebrahimkhani N. Psychometric properties of a Persian-language version of the Beck Depression Inventory–Second edition: BDI-II-PERSIAN. *Depress Anxiety.* 2005;**21**(4):185–92. doi: 10.1002/da.20070. [PubMed: 16075452].
21. Crichton N. Visual analogue scale (VAS). *J Clin Nurs.* 2001;**10**(5):706.
22. Davatchi F, Jamshidi AR, Banihashemi AT, Gholami J, Forouzanfar MH, Akhlaghi M, et al. WHO-ILAR COPCORD Study (Stage 1, Urban Study) in Iran. *J Rheumatol.* 2008;**35**(7):1384. [PubMed: 18464299].
23. Davis MA, Ettinger WH, Neuhaus JM, Barclay JD, Segal MR. Correlates of knee pain among US adults with and without radiographic knee osteoarthritis. *J Rheumatol.* 1992;**19**(12):1943–9. [PubMed: 1294744].
24. Odding E, Valkenburg HA, Algra D, Vandenouweland FA, Grobbee DE, Hofman A. Associations of radiological osteoarthritis of the hip and knee with locomotor disability in the Rotterdam Study. *Ann Rheum Dis.* 1998;**57**(4):203–8. [PubMed: 9709175].
25. Hawker GA, Gignac MA, Badley E, Davis AM, French MR, Li Y, et al. A longitudinal study to explain the pain-depression link in older adults with osteoarthritis. *Arthritis Care Res (Hoboken).* 2011;**63**(10):1382–90. doi: 10.1002/acr.20298. [PubMed: 20662042].
26. Liew HP. Depression and chronic illness: a test of competing hypotheses. *Health Psychol.* 2011.
27. Axford J, Heron C, Ross F, Victor CR. Management of knee osteoarthritis in primary care: pain and depression are the major obstacles. *J Psychosom Res.* 2008;**64**(5):461–7. doi: 10.1016/j.jpsychores.2007.11.009. [PubMed: 18440398].
28. Pereira D, Severo M, Barros H, Branco J, Santos RA, Ramos E. The effect of depressive symptoms on the association between radiographic osteoarthritis and knee pain: a cross-sectional study. *BMC Musculoskelet Disord.* 2013;**14**:214. doi: 10.1186/1471-2474-14-214. [PubMed: 23875806].
29. Kim KW, Han JW, Cho HJ, Chang CB, Park JH, Lee JJ, et al. Association between comorbid depression and osteoarthritis symptom severity in patients with knee osteoarthritis. *J Bone Joint Surg Am.* 2011;**93**(6):556–63. doi: 10.2106/JBJS.I.01344. [PubMed: 21411706].
30. Barua A, Ghosh MK, Kar N, Basilio MA. Socio-demographic Factors of Geriatric Depression. *Indian J Psychol Med.* 2010;**32**(2):87–92. doi: 10.4103/0253-7176.78503. [PubMed: 21716860].

31. Cole MG, Dendukuri N. Risk factors for depression among elderly community subjects: a systematic review and meta-analysis. *Am J Psychiatry.* 2003;**160**(6):1147–56. doi: 10.1176/appi.ajp.160.6.1147. [PubMed: 12777274].
32. Green KM, Zebrak KA, Fothergill KE, Robertson JA, Ensminger ME. Childhood and adolescent risk factors for comorbid depression and substance use disorders in adulthood. *Addict Behav.* 2012;**37**(11):1240–7. doi: 10.1016/j.addbeh.2012.06.008. [PubMed: 22762959].
33. Miller LR, Cano A. Comorbid chronic pain and depression: who is at risk?. *J Pain.* 2009;**10**(6):619–27. doi: 10.1016/j.jpain.2008.12.007. [PubMed: 19398383].
34. Stordal E, Bjartveit Kruger M, Dahl NH, Kruger O, Mykletun A, Dahl AA. Depression in relation to age and gender in the general population: the Nord-Trondelag Health Study (HUNT). *Acta Psychiatr Scand.* 2001;**104**(3):210–6. [PubMed: 11531658].
35. Kessler RC, Foster C, Webster PS, House JS. The relationship between age and depressive symptoms in two national surveys. *Psychol Aging.* 1992;**7**(1):119–26. [PubMed: 1558696].