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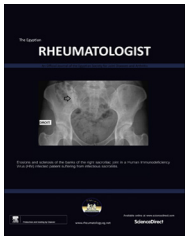

ORIGINAL ARTICLE

Depression and pain in patients with rheumatoid arthritis: Mediating role of illness perception

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Rheumatoid arthritis;
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Abstract *Aim of the work:* Illness perception is considered to be an important contributor in the relationship between physical and psychological factors in rheumatoid arthritis (RA). This study examined the mediational role of illness perceptions in the relationship between depression and pain in RA.

Patients and methods: Illness perception, depression and pain were assessed in 100 adults with RA (72 females and 28 males). Patients were asked to complete 4 questionnaires including socio-demographic data form, depression subscale of Hospital Anxiety and Depression Scale (HADS), Brief Illness Perception Questionnaire (Brief-IPQ) and Rheumatoid Arthritis Pain Scale (RAPS). Using the Baron and Kenny approach and Sobel tests, the mediation of illness perceptions in the relationship between depression and pain symptoms was examined.

Results: Sixty-six RA patients (66%) endorsed a clinically significant level of depression (HADS 12.94 ± 5.39). The mean RAPS was 41.97 ± 23.45 (range = 4–91.93). Depression symptoms were significantly associated with perceived pain ($r = -0.57$, $p < 0.001$). Three illness perceptions significantly mediated the relationship between depression and pain; consequences ($z = 1.39$, $p < 0.05$);

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personal control ($z = 1.47$, $p < 0.05$) and emotional response ($z = 1.51$, $p < 0.05$). Gender and education showed no significant effect on the presented results.

Conclusions: Greater depression symptoms were associated with perceptions that pain negatively affected one's life and emotions and was difficult to control. These negative illness perceptions were, in turn, related to greater pain symptoms. Illness perceptions helped explain the depression-pain link in RA patients. Results suggest that targeting illness perceptions in adults with RA and depression may help reduce pain symptoms.

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1. Introduction

Rheumatoid arthritis (RA) is a systemic auto-immune disease that affects between 0.5% and 1% of the adult population worldwide [1]. The diagnosis of RA may cause stress and uncertainty in patients [2]. The bio-psycho-social model of illness highlights the importance of biological, psychological and environmental contributors to the etiology and treatment of all diseases [3]. Although there is a large amount of evidence pointing to the biological factors related to chronic pain such as RA, there is a growing body of evidence of psychological and social factors affecting the course and outcome of pain [4–6].

RA can affect all aspects of one's life, like social relationships, family life, and psychological well-being in addition to physical symptoms [7–9]. It has been shown that RA patients are either quit or change their jobs in a 2-year period with a rate of 33 and 16%, respectively [8]. In addition to these stressors, pain, restriction of activities and physical handicaps are associated with changes in psychological aspect. RA is related with significant psychiatric morbidity. The main psychiatric disorders reported in RA cases are anxiety, depression, or both [9–13].

While the mechanism underlying the relationship between pain and depression remains unknown, the presence of depression disorder has been repeatedly linked to poor health, increased higher levels of pain, impaired mood and functional disability in RA patients [14–16].

It is important to understand how pain and depression are related in RA patients. Understanding mediating factors of the depression-pain relationship in RA patients may help to improve pain symptoms and ultimately health related quality of life. Although examination of potential mediators is essential to fully understand this association, this study focuses on the role of cognitions.

Cognitive appraisal and illness perceptions are considered to be important contributing factors in relationship between physical and psychological factors in chronic pain. Based on the cognitive-behavioral mediation proposed by kerns and Turk [17], cognitive appraisal factors are one possible pathway through which depression symptoms may be related to pain symptoms. Lefebvre and Keefe [18] showed that catastrophic cognitions were related to the recall of both pain intensity and pain variability in RA patients.

The illness perceptions are the organized cognitive representations that patients have about their diseases and influences the way patients cope with their complaints [19,20]. The self-regulation model suggests that the cognitive and emotional aspects of illness perception guide the response to illness and determine the effectiveness of coping strategies [21]. Furthermore, components of illness perception have been recognized: the identity of the illness (i.e. the symptoms), the perceived consequences of the illness, the illness's causation; the illness's likely time line and the potential for control or cure [22]. Thus, further examination of depression, illness perception and pain symptoms could inform psychological treatment methods for depression in RA patients. Therefore, the purpose of this study was to examine the possible mediation role of illness perceptions in the depression-pain symptoms relationship in RA patients. It was hypothesized that RA patients with increased symptoms of depression would perceive their illness to be more negative, and as a result, experience greater pain symptoms.

2. Patients and methods

2.1. Patients

A cross-sectional study was used to examine the depression and determinants of illness perception (8 components) to identify predictors of pain in RA patients. This study was approved by the research ethics board of Isfahan University of Medical Sciences.

The study included 100 RA patients diagnosed according to the revised American College of Rheumatology (ACR) criteria for classification of RA [23]. These patients were recruited from an outpatient rheumatology clinic affiliated with Isfahan University of Medical Sciences during December 2011 – August 2012. Of the initial sample of 115 patients, 15 (13.04%) were excluded because of incomplete data. The final sample consisted of 100 patients, including 72 females with a mean age of 45.46 ± 12.67 years and 28 males with a mean age of 40.68 ± 13.99 years. The mean length of total education was 13.07 ± 2.72 years (range 9–18 years).

Disease duration ranged between 6 months and 26 years with a mean of 5.67 ± 5.74 years. It was computed from the disease onset to the time of the questionnaires administering. Men and women did not differ in age, duration of disease and education. Inclusion criteria were: (1) receiving the diagnosis of RA by a rheumatologist (the last author), (2) age 18–70 years old, (3) being able to write and read and (4) willingness to participate in the study. Patients were excluded if: (1) they had dementia, mental retardation and fibromyalgia syndrome, (2) inability to write or read and (3) did not agree to participate.

For those who fulfilled the inclusion criteria, the aim and the process of the study along with confidentiality of the gathered information were described. If the patient agreed to continue and was orally consent to participate in the study, then they were asked to complete 4 questionnaires including

socio-demographic data form, depression subscale of Hospital Anxiety and Depression Scale (HADS), Brief Illness Perception Scale (Brief-IPQ) and Rheumatoid Arthritis Pain Scale (RAPS).

The study was approved by the research ethics board of Isfahan University of Medical Sciences. An informed consent was obtained from each participant.

2.2. Methods

Demographic variables such as age, gender and education were obtained via self-report.

2.2.1. Depression (Predictor)

Depression, the primary predictor variable, was assessed using the depression subscale of ***Hospital Anxiety and Depression Scale*** (HADS). It was used to assess current levels of anxiety and depression in non-psychiatric clinical populations [24]. The scale consists of 14 items (7 each for depression and anxiety). Each item is rated on a 4-point Likert-type scale ranging from 0 (not at all) to 3 (very often). The possible scores for each subscale ranges from 0 to 21, with higher scores indicating higher levels of symptomatology. Scores of 11 or above on either subscale are considered to be a significant 'case' of psychological morbidity, while scores of 8–10 represent 'borderline' and 0–7 'normal' [25]. In general the Iranian version of the HADS can be considered reliable and valid. Cronbach's alpha coefficient (to test reliability) has been found to be 0.86 for the HADS depression (HADS-D) sub-scale and 0.78 for the HADS anxiety sub-scale [25]. In the present study, Cronbach's alpha coefficient for the HADS depression sub-scale was 0.84.

2.2.2. Illness perception (Mediator)

The ***Brief Illness Perception Questionnaire*** (Brief-IPQ) was used to assess participant's cognitive and emotional perceptions of RA. The Brief-IPQ is an eight self-report scale designed to rapidly assess perceived consequences, time-line, identity, treatment control, personal control, concern, emotional representation, and coherence of one's illness.

The *consequence component* reflects the individual's beliefs about the illness severity and likely the impact on physical, psychological and social functioning. The *time-line component* indicates their perceptions of the likely duration of their health problems and these have been categorized as acute/short-lasting, chronic, or cyclical/episodic. The *identity* component is concerned with patients' ideas about the label, the nature of their condition and the links between these. The *treatment–control* indicates the extent to which the patient believes their condition is amenable to cure or control. The other items in the scale were *personal control* (how much control the patient has over his or her disease), *concern* (how concerned the patient is about his or her disease), *emotional response* (how much disease affects the patient emotionally) and *coherence* (how well the patient feels he/she understands their disease).

All of the dimensions in the questionnaire are rated using 0 (no effect at all) to 10 (severely affects my life). Items are scored such that higher responses on items 1, 2, 5, 6, and 8 represent more negative illness perceptions. Items 3, 4, and 7 are scored such that higher responses indicate more positive illness perceptions [26]. The items on the Brief IPQ have demonstrated adequate test–retest reliability and predictive validity in samples of adults with various illnesses [26]. The Iranian version of this questionnaire which was used in this study has satisfactory psychometric properties [27].

2.2.3. Pain (Outcome)

The ***Rheumatoid Arthritis Pain Scale*** (RAPS) is a self-report questionnaire. The RAPS was designed to measure pain in RA patients. The content of RAPS is 24 items that measure descriptions of pain. These items constitute the RAPS scale. The items of RAPS include 4 subscales: physiologic component (5 items), sensory-discriminative component (8 items), affective component (4 items), and cognitive component (6 items). Items are scored on a 7-point Likert-type scale from 0 (always) to 6 (never). The scoring in RAPS questionnaire is inverse type. Scores can range from 0 to 144: the higher the score of the patient the lower the degree of pain and vice versa. There is also 1 numerical rating scale of **pain severity** perception. The Numerical Rating Scale has a 0–10 point scale anchored by 0 (no pain) to 10 (extreme pain). After translating the English version of RAPS into the Persian language and its back translation to original language, this revised version was compared with the original version and discrepancies were resolved. The final version was administered to 20 patients and 3 items that were ambiguous were modified. The Cronbach's alpha for the total RAPS was 0.91. Subscale alpha coefficients ranged from 0.64–0.86 [28]. In this sample, Cronbach's alpha coefficient for the total RAPS was 0.83.

Statistical analysis: Data were analyzed with SPSS Version 16.0 for Windows. The results of Kolmogorov–Smirnov tests did not reject normality in the populations. As a result, no parametric tests were used throughout the analysis. As testing of mediational models is warranted if there are significant relations among the primary variables of interest, bivariate correlations were calculated first. In accordance with Baron and Kenny [29], a series of regression analyses were used to examine the hypothesis that illness perceptions mediate the relationship between depression (independent variable) and pain (outcome variable). The first set of regressions examined the relationship between depression symptoms and illness perceptions. The second set of regressions examined the relationship between depression symptoms and pain. Finally, the third set of regressions examined the relationship between depression and pain symptoms with illness perceptions included in the model. Gender, age and pain severity were included as covariates in the regression models. In accordance with guidelines for testing meditational models, post-hoc probing (Sobel test) was used to assess the significance of each [30].

3. Results

Descriptive data for pain, illness perception and depression measures are presented in Table 1. Of the 100 participants, 66% endorsed clinically significant level of depression (score $\geqslant$11). The mean depression score (HADS) (12.94 ± 5.39) indicates severe depressive symptoms. The mean score on the measure of perceived pain symptoms was 41.97 ± 23.45; (range = 4–91.93). Gender and education showed no significant effect on the presented results.

Higher levels of depression symptoms were associated with more perceived pain as measured by RAPS ($r = -0.57$, $p < 0.001$). Six of the eight individual illness perception

Table 1 Illness perception, pain and depression scores in rheumatoid arthritis patients.

Variables	Rheumatoid arthritis patients ($N = 100$)	
	Mean(±SD)	Range
Illness perception questionnaire		
Consequences	4.83 (±2.23)	1–10
How much does pain affect your life?		
Timeline	5.05 (±1.94)	2–10
How long do you think your pain will continue?		
Personal control	5.08 (±1.67)	1–9
How much control do you have over your pain?		
Treatment control	6.62 (±1.99)	0–10
How much do you think your treatment can help your pain?		
Identity	5.17 (±2.03)	1–9
How much do you experience symptoms from your pain?		
Concern	5.22 (±2.1)	1–10
How concerned are you about your pain?		
Comprehensibility	5.1 (±2.52)	0–10
How well do you feel you understand your pain?		
Emotional response	5.33 (±2.23)	1–10
How much does your pain affect you emotionally?		
Pain		
Total Rheumatoid Arthritis Pain Scale (RAPS)	41.97 (±23.45)	4–91.3
Physiologic component	10.1 (±6.47)	1–27
Affective component	9.07 (±5.79)	0–29
Sensory-discriminative component	12.46 (±9.28)	1–51
Cognitive component	10.35 (±6.69)	1–31.49
Pain severity	6.49 (±2.57)	1–10
HADS-D	12.94 (±5.39)	0–21

HADS-D: Hospital Anxiety and Depression Scale Depression subscale.

Table 2 Correlations between illness perception components with Hospital Anxiety and Depression Scale Depression subscale (HADS-D) and pain in rheumatoid arthritis patients.

Illness perception components	RA patients ($N = 100$)	
	HADS-D	Pain
Consequences	0.51**	−0.54**
Timeline	0.44**	−0.41**
Personal control	0.38**	−0.34**
Treatment control	0.16	−0.11
Identity	0.35**	−0.34**
Concern	0.26**	−0.25*
Comprehensibility	0.1	−0.18
Emotional response	0.32**	−0.39**

RA: rheumatoid arthritis; HADS-D: Hospital Anxiety and Depression Scale Depression subscale.
* Significant at $p < 0.05$.
** Significant at $p < 0.01$.

questions were significantly associated with both increased depression and pain symptoms ($p < 0.05$): (1) consequences, (2) timeline, (3) personal control, (4) identity, (5) Concern and (6) Emotional representations (Table 2). Because correlations were significant for these six illness perceptions (potential mediators), a set of three regression analyses was conducted for each illness perception.

The first set of regression analyses included depression and covariates as independent variables and each of the six illness perceptions as the dependent variable. The regression models were significant for five of the six illness perceptions, with greater depression predicting more negative illness perceptions. Greater depression symptoms were linked with perceptions that pain has a greater effect on RA's life and emotion. In addition, increased depression symptoms were related to a longer perceived duration of pain, more symptoms of pain and less perceived control over pain symptoms.

The second set of analyses was one regression analysis with depression at baseline and covariates predicting perceived pain symptoms. The regression model was significant F (4, 93) = 25.62, $p = 0.00$, with increased depression ($\beta = -0.40$, $p = 0.00$), and covariate (increased pain severity, $\beta = -0.32$, $p = 0.001$) associated with more pain symptoms.

The third set of regression models included both depression and the five aforementioned illness perceptions, along with the covariates, as predictors of perceived pain symptoms. All five proposed mediators were significantly related to perceived pain symptoms (Table 3). In the *first model*, greater pain symptoms were predicted by RA's perceptions that pain greatly affected their life ($p = 0.001$), increased pain severity ($p = 0.001$), and increased depression symptoms ($p = 0.01$), F (16, 92) = 16.15, $p = 0.00$, adjusted $R^2 = 0.43$. In the *second model*, greater pain was predicted by longer perceived duration of pain ($p < 0.05$), increased pain severity ($p = 0.001$), and increased depression symptoms ($p = 0.001$), F (5, 92) = 13.73, $p = 0.00$, adjusted $R^2 = 0.39$. In the *third model*, increased depression symptoms ($p = 0.00$), increased pain severity

Table 3 Final regression models predicting pain in rheumatoid arthritis patients.

Variables of the 5 models	Rheumatoid arthritis patients ($N = 100$)		
	Standardized β	T	Adjusted R^2
Model 1			
Consequences	−0.30	−3.36***	0.43
How much does pain affect your life?			
Depression	−0.27	−2.83**	
Pain severity	−0.29	3.35***	
Gender	0.005	0.06	
Age	0.008	0.1	
Model 2			
Timeline	−0.177	−2.02*	0.39
How long do you think your pain will continue?			
Depression	−0.33	−3.42***	
Pain severity	−0.31	−3.51***	
Gender	0.04	0.49	
Age	0.006	0.07	
Model 3			
Personal control	−0.137	−1.58*	0.38
How much control do you have over your pain?			
Depression	−0.36	−3.74***	
Pain severity	−0.31	−3.45***	
Gender	0.04	0.59	
Age	0.011	0.136	
Model 4			
Identity	−0.143	−1.69*	0.38
How much do you experience symptoms from your pain?			
Depression	−0.35	−3.74***	
Pain severity	−0.32	3.54***	
Gender	0.05	0.63	
Age	0.01	0.22	
Model 5			
Emotional response	−0.21	−2.54**	0.41
How much does your pain affect you emotionally?			
Depression	−0.34	−3.81***	
Pain severity	−0.31	−3.46***	
Gender	0.01	0.195	
Age	0.003	0.03	

* Significant at $p < 0.05$.
** Significant at $p < 0.01$.
*** Significant at $p < 0.001$.

($p = 0.001$) and lower perceived control over pain ($p < 0.05$), predicted greater pain, $F(5, 92) = 13.03$, $p = 0.00$, $R^2 = 0.38$. In the *fourth model*, increased experience symptoms of pain ($p < 0.05$), increased pain severity ($p = 0.001$) and increased depression symptoms ($p = 0.001$) predicted greater pain, $F(5, 92) = 13.32$, $p = 0.00$, adjusted $R^2 = .389$. In the *fifth model*, increased emotional impact of pain ($p = 0.01$), increased depression symptoms ($p = 0.00$) and increased pain severity ($p = 0.001$) predicted greater pain, $F(5, 92) = 17.94$, $p = 0.00$, $R^2 = 0.41$.

When both illness perceptions and depression were included in the model, the effect of depression symptoms on pain (as indicated by β) was reduced in all five models. Post-hoc examination of these models using the Sobel test indicated three significant mediators: (1) "consequences" $z = 1.39$, $p < 0.05$; (2) "personal control" $z = 1.47$, $p < 0.05$; (3) "emotional response" $z = 1.51$, $p < 0.05$. The fourth and fifth illness perceptions ("timeline" $z = 1.25$, $p = 0.09$; and "identity" $z = 1.32$, $p = 0.08$) approached significance as a mediator.

4. Discussion

According to HADS-D questionnaire, threshold a score of 11 and over, more than 50% of RA patients would be regarded as probable cases of depression disorder. These rates of depression's symptoms are similar to rates obtained in previous studies of patients with RA [31]. In other studies conducted on patients with RA, prevalence of depression has been reported to be from 14% to 46% [15,32,33].

The chronicity of illness as well as the ever-present possibility of patient's suffering pain is the possible cause of psychiatric disorders in RA [9]. Physical disability that develop in the course of the disease leads to dissatisfaction in the family life and work status of patients, who become socially isolated due to inadequacy to fulfill their goals [34,35]. Moreover, patients become hospital-bound due to their deficient functional outcomes [32] and unable to sustain themselves [35], and economic strains and lack of social support [36,37] leads to depression.

Consistent with previous findings, higher levels of depression symptoms were related to more pain, more functional impairment, more serious perceived consequences and less control over the illness [38–41]. This is important because these factors may contribute to poor compliance with RA medication. Thus depression screening for individuals reporting numerous pain symptoms despite reported adherence to the prescribed medical regimen could help determine whether or not depression symptoms may be contributing to pain symptoms.

As hypothesized, the relationship between depression symptoms and pain was partially mediated by illness perceptions. Specifically, higher levels of depression were associated with the feeling that one's pain negatively affected one's life and emotions, and difficult to control. These negative illness perceptions, in turn, were related to greater pain symptoms. This study highlights the importance of the patient's beliefs and emotional responses to their symptoms and illness as key factors influencing satisfaction with the consultation and the further use of health care systems.

The findings about the role of illness perception as a mediator between the pain and depression in this study offer support to the existing body of research. In a study by Pilowsky [42], a depressed group of RA sufferers was found to perceive their illness as being more serious and feel hopeless about a cure compared with the non-depressed RA group, even when the actual severity of arthritis was adjusted for.

One of the first longitudinal studies to document the importance of illness perception in RA patients was a study involving a sample of 75 younger female patients [43]. The authors found that depression was consistently predicted by pain, passive coping and beliefs about the consequences of RA. Similar findings were reported by Zyrianova et al. [44] in their study of the complex relationship of illness perception with physical and psychological factors in RA using a structural model. Zyrianova et al. [44] concluded that illness perception was to be a mediator in the relationship between physical disability and depression and anxiety.

Given the high rates of RA and co-morbid depression, it is important to explore interventions that aimed to improve outcomes. The findings of this study suggest that illness perceptions could be tested in a pilot psychological intervention as a means to potentially improve pain symptoms in RA patients. Cognitive behavioral therapy has been shown to effectively reduce symptoms of pain in RA patients [45–47]. Illness perceptions are well identified as a target for treatment [47–51]. No study was found on illness perception focused therapy on RA patients in the related literature. The data of this study suggest that addressing illness perceptions in treatment may result in pain-related changes. For example, if illness perceptions are incorporated as part of the cognition behavior "framework" treatment, it may address co-morbid depression more precisely, thus affecting pain-related outcomes such as symptoms. In particular, the results suggest that addressing patient's perceived control of rheumatoid arthritis and perceived affect of pain on their life and emotions may have the potential to lead to decrease in pain symptoms. These hypotheses are supported by study in other chronic illness populations. For example, in a sample of adults with back pain, treatment of illness perceptions accounted for 14.4% of the variance in improved patient-relevant activities [52].

The results of this study should be interpreted within the context of several limitations. First, this study was cross-sectional and only prospective analyses will give an exhaustive picture of the causal relationships between variables. For example, it is possible that illness perceptions may lead to increased symptoms of depression. Future studies should examine this relationship. Second, because we were interested in investigating specific mediators that clinicians could target in practice, we did not simultaneously examine all variables as mediators. As a result, it is not possible to draw conclusions concerning the combined effect of all three mediators. Third, in this study the self-report questionnaire was used to assess the pain. However, as an alternative to self report questionnaire, it is reasonable to use scales surveying rheumatologist's opinions such as the disease activity scale. Finally, our samples were representatives of the RA patients who live in Isfahan City and the results can be generalized only to similar cultural setting.

Despite these limitations, this study provides additional information regarding the relationship between depression and pain in adult with RA patients. Targeting illness perceptions should be considered when working clinically to improve outcomes in adults with RA and co-morbid depression. Future studies should empirically test whether cognitive behavior interventions that target negative illness perceptions such as perceived control of pain are effective for patients in sustaining both short and long term reduction of pain symptoms.

Conflict of interest

The authors declare no conflicts of interest.

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