

Research Paper

# The Role of Sex, Perceived Pain, and Illness Perceptions in Disease Activity in Rheumatoid Arthritis



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## ABSTRACT

**Background:** In the “treating to target” strategy for Rheumatoid Arthritis (RA) management, “cognitive” beyond “physical” measures allow a more comprehensive assessment.

**Objective:** This study reported a predictive analysis of patients on disease activity and the degree to which these predictions could be uniquely attributable to Illness Perception (IP), pain, and sex differences.

**Methods:** This cross-sectional study was conducted on 108 patients with Rheumatoid Arthritis aged 18 to 65 years old, selected via convenience sampling. Measurements were done using Disease Activity Score in 28 Joints (DAS28), patient’s Illness Perception Questionnaire (IPQ-R), and Numerical Rating Scale (NRS) for perceived pain. Data were analyzed applying Spearman and Pearson correlation coefficients and Multiple Stepwise Regression (MSR).

**Results:** In correlation analysis, the sex- Disease Activity association (0.40,  $P < 0.01$ ) and Pain-Disease Activity association (0.54,  $P < 0.01$ ) were found. Additionally, we observed stronger and significant associations between IPQ-R subscales and disease activity [Identity ( $r = 0.53$ ,  $P < 0.01$ ) personal control ( $r = -0.40$ ,  $P < 0.01$ ) and emotional representation ( $r = 0.36$ ,  $P < 0.01$ )]. Regression analysis showed that sex differences were a not significant predictor and perceived pain and three IPQ-R items (identity, personal control, and emotional representation) emerged as the strongest predictors ( $P < 0.001$ ).

**Conclusion:** Disease activity was predicted by pain and three illness perception items. By identifying the components affecting Disease Activity, the therapist can adjust complementary treatment according to patients’ needs.

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## 1. Introduction

Rheumatoid Arthritis (RA) is a chronic disease and disabling condition that affects most aspects of the patient's life [1]. The initial treatment of RA includes reducing disease activity and prevention of further disability [2]. The significant document for RA management is based on well-validated Disease Activity Measures (DAMs), but researchers have suggested that clinicians should solve problems through different investigated information taking into account patients' properties [3].

Although many evidence-based inflammatory illnesses reports suggest sex differences may inappropriately affect outcomes and except some research that explains the poorer prognosis for males [4] in greater complexity, prognoses for females are poorer [5-7].

The patients' well-being is influenced by their cognitions, emotions, and body sensations, such as pain. Illness perceptions are cognitive and emotional representations that people have about their condition. In illness perceptions, patients expand their cognitions about the illness to develop a sense of difficulties that their illness causes [8]. IP is not only based on symptoms, but also on illness-related outcomes and past events [9].

In RA patients, IP has been noticed with low functioning, depressive mood, and anxiety disorder [10]. Researchers have investigated individual differences in Illness perception as potential reasons underlying why some patients experience worse conditions [11]. Some researchers have suggested that patients' healthcare should comprise psychological treatment to change or adopt patients' beliefs about their RA [12].

In some research about RA, negative illness perceptions were related to greater pain symptoms, and pain is a factor that increases negative disease effects for people with RA, have a lot of research evidence [13].

Although evidence from inflammatory conditions suggests sex differences may inappropriately affect patients [14], few studies have examined sex differences concerning Illness perception in some chronic illnesses. For example, in a study, females compared with males perceived Allergic Rhinitis (AR) as a significantly more threatening disease, which was associated with worse adherence to treatment and disease outcome [15]. To date, the examination of sex differences concerning IP and disease activity has been done in RA. Moreover,

considering the relative importance of sex difference on disease exacerbation, prior research has not controlled for the importance of sex difference concerning Illness perception on disease activity in people with RA.

Based on past studies, we hypothesized that sex differences, patients' beliefs about their illness, and pain are variously associated with disease activity.

This study aimed to (a) investigate sex differences in disease activity and (b) determine the role of sex differences, illness perception dimensions, and pain perception (as relative predictors of disease activity) in disease activity prediction.

Based on past studies, we hypothesized that (a) females would report higher disease activity outcomes, (b) the less pain perception would predict worse disease activity, and (c) higher positive illness perceptions (personal & treatment control and illness coherence) and the less negative illness perceptions (identity, consequences, chronic & cyclical timeline, emotional representation) would display a protective role to predict worse disease activity.

## 2. Materials and Methods

### Setting and participants

This study was conducted from 2017 to 2018 in Shariati hospital in Tehran Province. The statistical population included 264 patients with RA, referring to the hospital in Tehran City, Iran. Using the purposive sampling technique and according to Cohen Table [16], a sample of 151 participants was selected by a rheumatologist diagnosis; after deleting participants who were conflicted with the inclusion criteria, 108 people completed the questionnaires as the final sample. Ten individuals were excluded from the study for lack of adequate literacy, three had a diagnosed psychotic disorder, 13 endorsed substance abuse, and two for self-reported use of alcohol and drugs in the past 24 hr. As described in the exclusion criteria below, 18 participants were classified into depression and anxiety disorders that were not sufficiently controlled by prescribed medicine, and because examining the role of perception was an objective of this research, these participants were excluded from the final analysis.

Also, the final sample was matched to the suggested sample size in the online Sample Size Calculator for Multiple Regression (<https://www.danielsoper.com/statcalc/calculator.aspx>), which is a suitable tool for researchers. A clinical psychologist evaluated patients.

The goal of the study was explained to these patients and their informed consent was obtained and the researchers were committed to protecting the privacy of respondents. Also, 44.5% of the subjects were men and 55.6% were women. The average age of the sample was 38 years. Study inclusion criteria were receiving the diagnosis of RA by a rheumatologist, 18 to 65 years of age, Body Mass Index (BMI) < 35, and reading and writing literacy, and the exclusion criteria included severe psychological damage in the psychiatric axis I that was not sufficiently controlled by prescribed medicine, cognitive impairment, current medication, or substance abuse.

The patient's disease activity score was measured by Disease Activity Score-28 (DAS28). Then, the patient's illness perception score was assessed by the Revised Illness Perception Questionnaire (IPQ-R), and the patient's assessment of pain by the Numeric Rating Scale (NRS); IPQ-R and NRS are more 'subjective' in nature.

#### Materials and measures

##### Demographics questionnaire (sex difference as predictor)

Demographic information was obtained and included self-reported marital status, self-reported years of education, self-reported gender, and self-reported age.

##### Illness perception (predictor)

Patients' perceptions of their RA were measured by the Revised Illness Perception Questionnaire (IPQ-R) [17]. The IPQ-R measures illness perceptions related to the symptoms assigned to the illness (identity), timeline (chronic & cyclical) condition impact on daily life (consequences), and controllability (personal & treatment) of RA, the extent to which patients have a coherent conception about illness (coherence), the emotional impact of their illness (emotional), and the causes of their condition (cause). There has been a lack of good internal consistency for the "cause" subscale in general [18] and specifically in RA [19]. Therefore, in line with other studies on RA [20], perceptions of cause were not measured. In the current sample, the internal reliability for the majority of subscales was acceptable ( $\alpha$  Chronic Timeline=0.81;  $\alpha$  Consequences=0.86;  $\alpha$  Personal Control=0.79;  $\alpha$  Cyclical Timeline=0.85;  $\alpha$  Coherence=0.88;  $\alpha$  Identity=0.88;  $\alpha$  Treatment control=0.90;  $\alpha$  emotional representation=0.78).

##### Pain perception

Pain perception was assessed using the Numeric Rating Scale (NRS). This tool is used as a generic pain scale and assesses pain based on a numeric scale from zero (no pain) to 10 (severe pain) [21]. Based on this scale, patients assessed their pain intensity during the past week. The NRS was suggested by IMMPACT, and Cronbach's alpha for the NRS was reported at 0.89 [22].

##### DAS28 (outcome)

**The 4-component DAS28:** In the disease activity score, the severity of the disease was calculated using online methods. That scale has four components (swollen and tender joint counts, C-Reactive Protein (CRP), and patient global assessment) calculated at <http://www.das-score.nl>. The 44-joint swollen joint count ranges from zero to 44. ESR rates from zero to 150 and Patient Global well-being (PGA) rates from zero to 100. The DAS score is scored from zero to 10. In DAS interpretation, the level of disease activity can be changed from low (DAS < 2.4) and moderate (2.4 < DAS < 3.7) to high (DAS > 3.7) [23]. Conforming to the American Rheumatism Association (ARA) criteria, a DAS < 1.6 indicates patient remission [24]. If the DAS score elevates to 1.2, it is assumed a significant elevation [24]. The European League against Rheumatism (EULAR) uses DAS score change and according to this criteria, categorizes patients as medium or non-responders [24].

##### Data statistical analysis strategy

Because the present study aimed to examine sex difference, pain, and illness perception in disease activity prediction, descriptive analyses examined the distribution of sex differences to inform the analytic plan. Fisher's exact test was then used to test differences between the differences in the two sexes and independent samples t-test was used to test differences in age and years of education across the two sexes for descriptive data

Data were analyzed using SPSS software v. 20. The normality of the data was assessed by the Kolmogorov-Smirnov test. Pearson correlation coefficient was used to assess the relationships between illness perception dimensions (perceived consequences, Timeline/cyclical, timeline/acute chronic, identity, treatment control, personal control, emotional representation, and coherence of one's illness) and pain and disease activity. The point-biserial correlation coefficient was used to assess relationships between sex and continuous variables. Then, Multiple Stepwise Regression (MSR) was used to evalu-

ate whether different dimensions of IPQ-R, pain, and sex differences predict Disease Activity Score (DAS-28).

### 3. Results

#### Sample characteristics

In total, 108 participants were entered into this descriptive study. Also, 44.5% of the participants were men and 55.6% were women with a mean age of 37.57 years and 47.2% were single and 52.8% were married. The mean number of education years was 16.78 (Table 1).

#### Comparisons between females and males

Table 2 presents values that statistically compare females and males with respect to disease activity. In a categorical data analysis, disease activity was higher in females than males [ $P < 0.001$  by Fisher's exact test for all comparative levels, low (DAS  $< 2.4$ ), moderate ( $2.4 < \text{DAS} < 3.7$ ) or high (DAS  $> 3.7$ )]. Also, pain severity was higher in females than in males [ $P < 0.001$  by Fisher's exact test for all comparative levels, low (NRS  $< 3$ ), moderate ( $3 < \text{NRS} < 7$ ), or high (NRS  $> 7$ )] and also, independent sample t-test was used to test differences for females and males in the total pain score and the total disease activity score ( $P < 0.001$ ). In addition, based on Table 2, there was a statistically significant difference between males and females in most of the illness perception dimensions ( $P < 0.001$ ), except personal control and cyclical and chronic timeline ( $P > 0.001$ ) (Table 2).

#### Cross-sectional analysis between IPQ-R scores, sex differences, pain severity, and DAS-28 score as outcome measures

The Pearson correlation coefficient ( $r$  values show the best predictor of disease activity score) showed that there was a stronger significant correlation between disease activity and IPQ-R sub-scales of identity ( $r = 0.53^*$ ), personal control ( $r = 0.40^*$ ), illness coherence ( $r = 0.37^*$ ), emotional representation ( $r = 0.36^*$ ), and treatment control ( $r = 0.35^*$ ) compared to the weaker association between disease activity score and consequences ( $r = 0.24^*$ ) and cyclical timeline ( $r = 0.23^*$ ) and also, the chronic timeline was identified with no significant correlation ( $r = 0.18$ ). Other disease activity predictors were pain ( $r = 0.54^*$ ) and sex difference ( $r = 0.40^*$ ).

#### Regression results

Disease activity was considered as the dependent variable in a regression model. First, MSR analysis was used

to evaluate whether sex difference, different dimensions of IPQ-R, and pain predict disease activity.

In the stepwise method, the first variable enters the equation based on the maximum effect, and if other variables can significantly affect the dependent variable, they enter the equation in the next steps.

Results of the disease activity regression analysis in the final model indicated that the sex difference was not a significant predictor and three dimensions of the illness perception (i.e. identity, personal control, and emotional representation), and pain severity were confirmed as predictors that contributed significantly to disease activity and explaining a total of 48% of its variance ( $R = 0.71$ ,  $R^2 = 0.50$ ,  $R^2$  adjusted = 0.48) in patients with RA. The results of these analyzes are presented in the following tables (Table 3).

As observed from the analysis, pain perception was the strongest significant predictor in the model of disease activity [ $R^2$  change = 0.29,  $F(1, 106) = 43.65$ ,  $\beta = 0.54$ ;  $P < 0.01$ ] (Table 4). It means that increasing pain severity leads to an increase in the level of disease activity and a decrease in pain perception by appropriate treatment in patients with RA resulting in a decrease in the level of disease activity (Table 4).

As apparent from the standardized coefficient ( $\beta$ ), the identity item has the predictive power ( $\beta = 0.38$ ;  $P < 0.01$ ) (Table 4) for the disease activity score of patients with RA and contributed about 0.41% to the disease activity score of patients with RA [ $\Delta R^2 = .41$ ,  $F(1, 105) = 23.40$ ;  $P < 0.01$ ]. This indicates that the patients with stronger symptoms had higher scores in disease activity (Table 4). Personal control also increases the variance by 5.5%, making the prediction to improve further significantly in the expected direction [ $\Delta R^2 = .46$ ,  $R^2$  Change = 0.055,  $F(1, 104) = 11.02$ ;  $P < 0.01$ ] (Table 3) and emerged as the next significant potential predictor ( $\beta = -0.24$ ;  $P < 0.01$ ) of disease activity in patients with RA. It means that in an inverse significant manner, a decrease in beliefs regarding personal control leads to an increase in the level of disease activity score and vice versa (Table 4).

In the same way, the emotional representation emerged as the final significant potential predictor and further increased the variance by 3%, making the prediction improve further in a significant manner [ $\Delta R^2 = 0.48$ ,  $R^2$  Change = 0.030,  $F(1, 103) = 5.92$ ;  $P < 0.01$ ] (Table 3) and displays a positive influence ( $\beta = 0.17$ ;  $P < 0.01$ ) on the disease activity prediction in patients with RA. It means that an increase in negative emotional representation in

**Table 1.** Demographic characteristics in patients with rheumatoid arthritis (RA)

Demographic Characteristics		Mean±SD/%
Age (y)		37.57±9.95
Sex	Male	44.4
	Female	55.6
Marital status	Married	52.8
	Single or divorced	47.2
Years of education		16.78±5.81

the patient leads to an increase in disease activity score and vice versa, and patients had more concern about their illness, and a stronger emotional response to the illness leads to an increase in the level of disease activity. This means that decreasing negative emotions about the disease by psychotherapy or performing enjoyable activities in patients with RA leads to a decrease in the level of disease activity.

#### 4. Discussion

RA is not experienced in a similar way in patients. Females often report worse RA-related experiences [25, 26]. The present study aimed to specify whether these

relative differences of Ra based on disease activity [27, 28], might be at least in part attributable to differences in sex, pain perception, and illness perceptions: personal and treatment control, consequences, illness coherence, identity, cyclical and chronic timeline, and emotional representations.

Consistent with previous studies [26, 27], disease activity was higher in females than males in this study. Besides, compatible with past studies, females endorsed significantly higher levels of pain perception and most of the illness perceptions than males [25]. Compared to males, females identified a higher number of symptoms related to Ra (identity) and judged their illness by

**Table 2.** Comparisons between females and males with Rheumatoid arthritis (RA) in Disease Activity (DASS28), Pain severity (NRS), and Illness perception items (IPQ-R)

		Mean±SD					
Variables		Female	Male	Total	F	t	P
Disease Activity	DAS28	4.44±1.69	3.41±1.28	3.98±1.60	4.75	3.49	<0.001
	NRS	5.20±1.51	4.33±1.09	4.81±1.40	7.70	3.32	<0.001
Pain Perception	Identity	11.8±2.5	8.79±2.7	10.06±2.8	0.07	4.49	<0.001
	Timeline/acute Chronic consequences	14.61±4.8	14.29±3.18	14.47±2.5	0.73	0.56	>0.001
	Treatment control	12.46±3.1	14.08±3.4	13.55±5.4	0.92	-2.68	0.008
Illness Perception (IPQ-R)	Personal control	16.15±4.4	17.60±3.7	16.79±4.3	0.06	-1.74	0.09
	Illness coherence	10.98±4.9	16.77±4.1	13.55±5.4	4.58	-6.49	<0.001
	Timeline/cyclical	12.93±5.1	12.41±3.9	12.70±4.6	4.25	0.56	>0.001
	Emotional representation	20.63±4.24	12.93±5.68	17.21±6.1	2.91	8.20	<0.001

**Table 3.** Summary of Multiple Stepwise Regression (MSR) for predicting disease activity in patients with rheumatoid arthritis

Model	R	R <sup>2</sup>	Δ R <sup>2</sup>	Change Statistics		
				R <sup>2</sup>	F	P
1	0.540 <sup>a</sup>	0.292	0.285	0.292	43.650	<0.001
2	0.649 <sup>b</sup>	0.421	0.410	0.129	23.406	<0.001
3	0.690 <sup>c</sup>	0.476	0.461	0.055	11.021	<0.001
4	0.710 <sup>d</sup>	0.505	0.486	0.030	5.920	<0.001

a. Predictors: (Constant), Pain severity

b. Predictors: (Constant), Pain severity, Identity

c. Predictors: (Constant), Pain severity, Identity, Personal control

d. Predictors: (Constant), Pain severity, Identity, Personal control, emotional representation

Dependent variable: Disease Activity

negative consequences. In addition, females compared to males judged their illness was not controllable with treatment. The female believed that the illness would affect their emotions negatively (emotional representations) and did not understand their illness well (illness coherence) than males. However, both females and males reported their illness as unpredictable in nature belief (cyclical timeline) and chronic (chronic timeline) and believed to have weaker personal control over their RA. Thus, across most illness perception items, males reported more adaptive responses than females. Also, consistent with previous studies, compared to males, females reported a higher score of pain [25].

This finding has potentially important concepts. Given evidence has shown that the negative representations about illness (i.e. personal control, treatment control consequences, illness coherence, identity, cyclical and chron-

ic timeline, and emotional representations) may predict non-adherence, unhealthy behaviors, worse prognosis versus management is possibly related to why chronic illnesses affect patients differently [29, 30]. Further research on that potential is required, as this finding has benefits for related goals in complementary treatments among patients who may represent such inappropriate cognitive contents following RA or other chronic illnesses. In RA literature, females are often found to report worse RA-related experiences. The important aim of the present study was to differentiate cognitive contents, such as illness perception and pain perception, and sex difference, which may influence differently disease activity outcomes. The illness perception dimensions were correlated with expected directions. The positive illness representations, such as personal control, treatment control, and illness coherence were each associated with weaker disease activity and lower pain perception. Also,

**Table 4.** Unstandardized and standardized regression coefficients of variables entered in the disease activity model in patients with Rheumatoid Arthritis

Model	Unstandardized Coefficients		Standardized Coefficients	t	P	
	B	Std. Error	Beta			
(Constant)	1.262	0.812		1.554	<0.001	
Final model	Pain severity	0.427	0.089	0.360	4.795	<0.001
	Identity	0.160	0.046	0.274	3.465	<0.001
	Personal control	-0.094	0.028	-0.246	-3.386	<0.001
	Emotional representation	0.048	0.020	0.179	2.433	<0.001

Dependent variable: Disease Activity

these dimensions were associated with other illness perception dimensions negatively, suggesting these cognitive contents potentially provide a 'barrier' against negative representations. Timeline chronic, timeline cyclical, consequences, identity, and emotional representation items were associated with higher pain perception and greater disease activity. These relationships suggest another document supporting the importance of representations of illness as the cognitive content related to illness.

In pain outcomes, identity item was associated moderately with pain, compared to weaker associations in three positive illness perception dimensions investigated (personal and treatment control and illness coherence), and a significant association was found between emotional representation and pain perception. Therefore, this study provides evidence of the potential role of positive representations of the disease and suggests that personal control, treatment control, and disease coherence provide a "buffer" for pain perception. All three positive illness representations helped to lower pain perception. Also, pain perception was associated significantly with disease activity and moderate effect sizes were found.

In the present study, the effect sizes across these predictive associations were small to medium, providing the lowest contribution of pain to disease perceptions about disease activity in patients with RA. Although there is more evidence suggested that pain is important in relation to elevated conditions in RA [31], it has been shown that illness representations are more important about elevated conditions than pain [32]. Consistent with the predictive approach used in the present study, at least concerning disease activity, it seems that after pain severity some components, such as identity, personal control, and emotional representation, contribute to disease activity outcome.

This study highlights some theoretical considerations about the association between illness representation and disease activity from a cognitive perspective. Based on the partial correlation findings, the results of the regression model showed that beyond the covariates, the three illness perception dimensions and pain together provided a higher level of prediction of disease activity.

In the current study and consistent with the past studies, patients with more representation of illness-related symptoms (identity) reported a higher level of disease activity [33, 34], and after pain severity, the identity component did emerge as the strongest predictor of disease activity, and it was as one of the variables contributed to the explained variance for disease activity. Expli-

cating these deeper, significant associations suggests that weaker representation of symptoms experienced may be protective for patients with this form of illness representation, specifying why some patients demonstrated higher disease activity ratings than others.

According to other observed associations (personal control) between illness perceptions and disease activity in our study, participants reported a smaller ability to provide personal control on their own illness than others and they perceived more impact of illness or consequences on their life than others. These results were equivalent to previous research [35, 36]. Explicating these deeper, significant associations suggests that higher self-report in personal control and lower self-report in negative consequences may be protective for patients, with this form of illness representations, significantly accounting for why some patients demonstrated higher disease activity ratings than others.

Consistent with past research, emotional representation was a strong predictor of disease activity [37, 38] in the current analysis (using steps), emotional representation did emerge as one of the potential predictors of disease activity and it simultaneously has a significant association with sex, pain, and disease activity. Our report is consistent with other previous reports [37, 38].

## 5. Conclusion

The study's findings prepared important new information on the role that different dimensions of illness perception play in RA disease activity. We found that it is possible to differentiate between all dimensions of these cognitive contents and to assess their unique contribution to predicting disease activity. The current findings also acknowledge that sex differences may be associated differently with specific patterns of cognition. For example, while sex differences were associated with identity, consequences, treatment control, illness coherence, and emotional representation, sex differences were not associated with personal control, and cyclical and chronic timeline. As a result, the current findings suggest that higher pain severity, higher experience symptoms (identity), higher personal control, and higher use of negative emotional representations among RA patients, when present, might be influenced by disease activity, as discussed in more detail above. Thus, higher pain severity, higher experience symptoms (identity), higher personal control, and higher use of negative emotional representations were found to significantly account for why patients reported a higher disease activity score. Thus, while RA has been shown to differently affect females,

the illness perceptions assessed in this research demonstrate that the cognitive contents control the impact of illness and enhance healthy strategies despite the experience of chronic illness.

### Limitations

The present research was a cross-sectional study. As a result, cause and effect associations cannot be derived; longitudinal research is needed to more accurately causative relations. A further limitation included that the severity of the association between the variables was small to medium. Hence, the clinical predictability of these variables needs to be investigated in future research.

### Ethical Considerations

#### Compliance with ethical guidelines

The present study was confirmed by the Ethics Committee of the Islamic Azad University, Alborz Branch (Ethical code: IR.IAU.K.REC.1395.9).

#### Conflict of interest

The authors declared no conflict of interest.

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#### Authors' contributions

Conceptualization and Methodology: Mohammad Raza Seirafi; Data collection and Data analysis: Sarah Namjoo; Writing – original draft: Mohammad Raza Seirafi, Sarah Namjoo, Mehrdad Sabet; Writing – review & editing: Mehrdad Sabet.

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