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Analysis of Clinical and Demographic Predictors of Anxiety and Depression in Rheumatoid Arthritis Patients

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A B S T R A C T

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease with substantial physical and psychological impact. Anxiety and depression are common comorbidities that may affect disease outcomes, but their association with disease activity remains inconsistent, particularly in Indonesia. This study aimed to analyze clinical and demographic predictors of anxiety and depression in RA patients, with emphasis on their association with disease activity measured by DAS28-CRP. **Methods:** A cross-sectional study was conducted on 58 RA patients at Royal Prima Hospital, Medan. Demographic and clinical variables were recorded. Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS), and disease activity was measured with DAS28-CRP. Associations were tested using logistic regression, and correlations were analyzed with Spearman's rank test. **Results:** The mean age was 47.9 years, and 91.4% were female. Anxiety was identified in 19.0% and depression in 17.2% of participants. High DAS28-CRP was significantly associated with anxiety (OR 5.07; 95% CI 1.26–20.37; p=0.016). In multivariate analysis, DAS28-CRP remained the strongest predictor of anxiety (AOR 3.89; p = 0.073), although not statistically significant. Depression was not associated with demographic or clinical characteristics. Spearman correlation showed a positive association between DAS28-CRP and anxiety scores (r = 0.304; p = 0.020), while the correlation with depression was weaker and not significant. **Conclusion:** Anxiety, but not depression, was associated with higher disease activity in RA patients. Routine psychological screening, particularly for anxiety, should be incorporated into RA management.

1. Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by persistent synovial inflammation, joint destruction, and functional disability. Globally, RA affects approximately 0.5–1% of the adult population, with a higher prevalence in women and individuals between the fourth and sixth decades of life.[1,2] Advances in disease-modifying antirheumatic drugs (DMARDs) and biologic therapies have improved disease control; however, extra-articular manifestations, including psychological comorbidities, remain highly prevalent and have a significant impact on quality of life and treatment outcomes.[3-5]

Psychological distress, particularly anxiety and depression, is increasingly recognized as a major concern in RA. Recent meta-analyses estimate that approximately 20–40% of patients with rheumatoid arthritis experience clinically significant symptoms of anxiety or depression, highlighting the substantial psychological burden associated with the disease.[6-8] These conditions adversely affect treatment adherence, increase pain perception, and worsen disability.[9-11] Moreover, anxiety and depression may

influence disease activity through behavioral and biological pathways, including neuroimmune interactions involving pro-inflammatory cytokines such as IL-6 and TNF-α.[12-14] Despite this, the relative contributions of anxiety and depression to RA disease activity remain unclear, with studies reporting inconsistent findings across populations and settings.[15-18]

In Indonesia, research on the interaction between psychological factors and RA disease activity is still limited. Existing evidence suggests that cultural background, socioeconomic status, and access to healthcare services may influence the prevalence and impact of anxiety and depression among RA patients.[19-21] Therefore, further studies in local contexts are warranted. This study aimed to analyze the association between demographic and clinical characteristics with anxiety and depression in RA patients, with a specific focus on the relationship between psychological outcomes and disease activity measured by DAS28-CRP.

2. Methods

Study Design and Setting

This was a cross-sectional study conducted at the Rheumatology Outpatient Clinic of Royal Prima Hospital, Medan, Indonesia, between March and September 2025. The study was approved by the institutional ethics committee, and written informed consent was obtained from all participants prior to enrollment.

Study Population

The study included 58 patients diagnosed with rheumatoid arthritis according to the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria. Patients aged 18 years and above who attended the rheumatology outpatient clinic during the study period were eligible. Exclusion criteria were patients with overlapping connective tissue disease, severe psychiatric disorders unrelated to RA, or incomplete clinical and laboratory data. Participants were recruited using a consecutive sampling method from eligible rheumatoid arthritis patients attending the rheumatology outpatient clinic during the study period.

Sample Size Calculation

The minimum required sample size was calculated using a single-proportion formula. The minimum sample size was estimated to be 58 participants. The final study included 58 patients, thereby fulfilling the minimum sample size requirement.

Variables and Measurements

Demographic characteristics included age, sex, education level, and ethnicity. Clinical variables comprised body mass index (BMI), disease activity, and psychological status. Disease activity was measured using the Disease Activity Score with 28 joint counts and C-reactive protein (DAS28-CRP), categorized as remission, low, moderate, or high activity.

Psychological status was assessed using the validated Indonesian version of the Hospital Anxiety and Depression Scale (HADS), a validated screening tool consisting of two subscales: HADS-A for anxiety and HADS-D for depression. Each subscale ranges from 0–21, with higher scores indicating more severe symptoms. A cut-off value of ≥8 was used to classify clinically relevant anxiety or depression.

Statistical Analysis

Statistical analyses were performed using SPSS version 25. Descriptive statistics were presented as mean ± standard deviation, median (minimum–maximum), or frequency and percentage, as appropriate. Associations between categorical variables and anxiety or depression status were evaluated using Chi-square test or Fisher's exact test. Variables showing potential association with anxiety were entered into multivariate logistic regression analysis to identify independent predictors. Correlations between DAS28-CRP and HADS scores were assessed using Spearman's rank correlation coefficient. Statistical significance was defined as $p < 0.05$.

3. Results

A total of 58 patients with rheumatoid arthritis were included in this study. The mean age was 47.97 ± 11.87 years, with an equal distribution between patients younger than 50 years (50.0%) and those aged 50 years or older (50.0%). The majority of participants were female (91.4%). Half of the patients had a high school education or lower, while the other half had higher education (Diploma–S2). Batak ethnicity was predominant (60.3%), followed by Javanese (12.1%), Chinese (10.3%), and other ethnic groups (17.2%). The mean BMI was 24.16 ± 4.42 kg/m², with 60.3% classified as obese.

The mean DAS28 score was 3.29 ± 1.15, with 29.3% in remission, 17.2% with low activity, 27.6% with moderate activity, and 25.9% with high activity. The median HADS-A score was 3 (0–15), with 19.0% classified as anxious. The median HADS-D score was 3 (0–13), with 17.2% classified as depressed (Table 1).

Bivariate Analysis of Anxiety

Bivariate analysis showed that high disease activity (DAS28) was significantly associated with anxiety (OR 5.07; 95% CI 1.26–20.37; p = 0.016). Younger age (<50 years) and obesity were also associated with a higher risk of anxiety (OR 3.30 and OR 3.39, respectively), but these did not reach statistical significance (Table 2).

Multivariate Analysis of Anxiety

In multivariate logistic regression, high DAS28 remained the strongest predictor of anxiety (AOR 3.89; 95% CI 0.88–17.23; p = 0.073), although not statistically significant. Younger age (<50 years) and obesity also showed positive associations (AOR 3.64 and 3.51, respectively), but the effects were not significant (Table 3).

Bivariate Analysis of Depression

No significant associations were observed between demographic or clinical characteristics and depression. Although female sex and high DAS28 appeared more frequent in the depression group, the results were not statistically significant (Table 4).

Correlation Analysis

Spearman's rank correlation revealed a weak-to-moderate positive correlation between DAS28 and anxiety scores (r = 0.304; p = 0.020). The correlation between DAS28 and depression scores was weaker and not significant (r = 0.246; p = 0.062). No significant correlations were found between age or BMI and either anxiety or depression (Table 5).

Figures

Scatter plots further illustrated these findings: anxiety scores increased with higher DAS28 (Figure 1), while depression scores showed a similar but weaker trend that did not reach significance (Figure 2).

Table 1. Baseline Characteristics of Patients with Rheumatoid Arthritis (n = 58)

Variable	n (%) / Mean ± SD / Median (Min–Max)
Age (years)	47.97 ± 11.87
≥ 50 years	29 (50.0)
< 50 years	29 (50.0)
Female	53 (91.4)
Male	5 (8.6)
≤ Senior high school	29 (50.0)
Higher education (Diploma–S2)	29 (50.0)
Batak	35 (60.3)
Javanese	7 (12.1)
Chinese	6 (10.3)
Others	10 (17.2)
BMI (kg/m²)	24.16 ± 4.42
Non-obese (<25)	23 (39.7)
Obese (≥25)	35 (60.3)
DAS28	3.29 ± 1.15
Remission	17 (29.3)
Low	10 (17.2)

Moderate	16 (27.6)
High	15 (25.9)
HADS-A Median (0–15)	3
Anxiety	11 (19.0)
No anxiety	47 (81.0)
HADS-D Median (0–13)	3
Depression	10 (17.2)
No depression	48 (82.8)

Values are presented as mean ± SD, median (min–max), or n (%).

Table 2. Bivariate Analysis of Characteristics Associated with Anxiety (HADS-A)

Variable	Anxiety (n=11)	No Anxiety (n=47)	p-value	OR (95% CI)
< 50 years	8 (72.7)	21 (44.7)	0.094	3.30 (0.78–14.02)
≥ 50 years	3 (27.3)	26 (55.3)		
Female	10 (90.9)	43 (91.5)	1.000	0.93 (0.09–9.25)
Male	1 (9.1)	4 (8.5)		
≤ Senior high school	6 (54.5)	23 (48.9)	0.738	1.25 (0.34–4.68)
Higher education	5 (45.5)	24 (51.1)		
Obese	7 (63.6)	16 (34.0)	0.093	3.39 (0.86–13.33)
Non-obese	4 (35.4)	31 (66.0)		
High DAS28	6 (54.5)	9 (19.1)	0.016*	5.07 (1.26–20.37)
Not high DAS28	5 (45.5)	38 (80.9)		

*Chi-square or Fisher's exact test; OR = Odds Ratio; CI = Confidence Interval; *p < 0.05 significant.*

Table 3. Multivariate Logistic Regression of Factors Associated with Anxiety (HADS-A)

Variable	AOR (95% CI)	p-value
< 50 years	3.64 (0.75–17.56)	0.108
Obese	3.51 (0.78–15.82)	0.103
High DAS28	3.89 (0.88–17.23)	0.073

Multivariate logistic regression;
AOR = Adjusted Odds Ratio; CI = Confidence Interval

Table 4. Bivariate Analysis of Characteristics Associated with Depression (HADS-D)

Variable	Depression (n=10)	No Depression (n=48)	p-value	OR (95% CI)
≥ 50 years	6 (60.0)	23 (47.9)	0.487	1.63 (0.41–6.52)
< 50 years	4 (40.0)	25 (52.1)		
Female	10 (100.0)	43 (89.6)	0.575	2.65 (0.14–51.88)
Male	0 (0.0)	5 (10.4)		
≤ Senior high school	6 (60.0)	23 (47.9)	0.487	1.63 (0.41–6.52)
Higher education	4 (40.0)	25 (52.1)		
Obese	4 (40.0)	19 (39.6)	1.000	1.02 (0.25–4.09)
Non-obese	6 (60.0)	29 (60.4)		
High DAS28	4 (40.0)	11 (22.9)	0.265	2.24 (0.54–9.40)
Not high DAS28	6 (60.0)	37 (77.1)		

Chi-square or Fisher's exact test; OR = Odds Ratio; CI = Confidence Interval; p < 0.05 significant. None reached significance.

Table 5. Correlation of Age, BMI and DAS28 with HADS-A and HADS-D scores

Variable	HADS-A (r, p)	HADS-D (r, p)
Age (years)	–0.052, 0.696	–0.019, 0.890
BMI (kg/m²)	–0.076, 0.568	0.078, 0.559
DAS28	0.304, 0.020*	0.246, 0.062

*Spearman's rank correlation; r = correlation coefficient; *p <0.05 significant.*

Figure 1. Scatter plot of DAS28 and HADS-A (anxiety) scores in RA patients (n = 58). A weak-to-moderate positive correlation was observed (r = 0.304, p = 0.020).

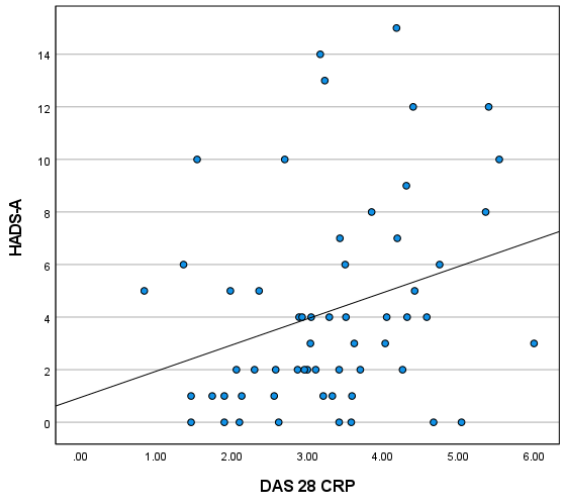
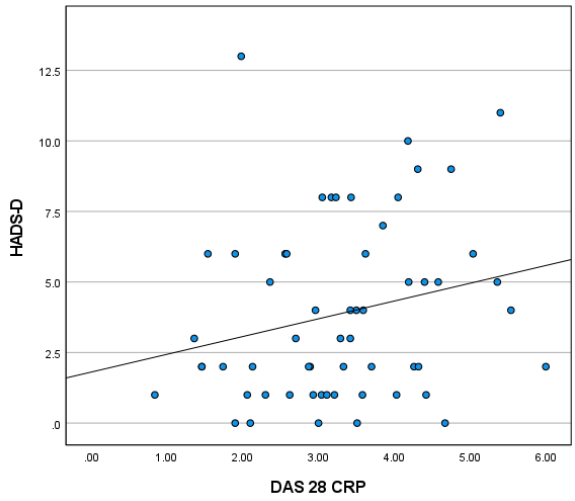


Figure 2. Scatter plot of DAS28 and HADS-D (depression) scores in RA patients (n = 58). A weak positive correlation was found (r = 0.246, p = 0.062).



4. Discussion

The present study demonstrated that anxiety was significantly associated with disease activity in RA patients, whereas depression was not. These findings are consistent with previous reports highlighting the stronger relationship between anxiety and inflammatory activity compared with depression.[19-20] Enginar et al. (2023) reported a higher prevalence of anxiety among RA patients with elevated DAS28 scores,[21] while Cheng et al. (2023) also observed that anxiety was more frequent in patients with active disease compared to those in remission.[22] Similarly, a

meta-analysis by Vestergaard et al. (2024) confirmed that the prevalence of anxiety increases in parallel with higher disease activity.[23]

In contrast, depression did not show a statistically significant association with disease activity in this study. This result supports previous research indicating that depression in RA is more strongly related to functional disability, chronic pain, and psychosocial stressors rather than active inflammation.[24,25] Uda et al. (2022) also demonstrated that while both anxiety and depression are common in RA, only anxiety consistently correlated with markers of systemic inflammation.[26]

Biological mechanisms may explain the stronger association between anxiety and disease activity. Pro-inflammatory cytokines, particularly interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), are central mediators in RA pathogenesis and have also been implicated in the regulation of neuroimmune pathways linked to anxiety.[27,28] These cytokines affect the hypothalamic–pituitary–adrenal (HPA) axis and neurotransmitter systems, which may contribute to heightened anxiety symptoms in patients experiencing active inflammation. Depression, on the other hand, is likely mediated by more complex mechanisms that involve long-term psychosocial and behavioral pathways.

The clinical relevance of these findings underscores the importance of psychological assessment as part of routine RA management.[29] Incorporating standardized screening tools such as the HADS-A into clinical practice may help identify patients at risk of anxiety at an early stage, thereby improving both mental health and disease outcomes. Furthermore, international guidelines increasingly recommend the integration of psychosocial care within RA treatment strategies, highlighting the role of a multidisciplinary approach in optimizing patient outcomes.[30]

Despite these strengths, this study has limitations. The cross-sectional design prevents causal inference. Although the minimum required sample size was achieved, the relatively small sample size may have limited statistical power to detect weaker associations, particularly in multivariate analyses. In addition, data were obtained from a single tertiary referral center, which may limit generalizability to other populations. Psychological symptoms were assessed using self-reported instruments, introducing the possibility of reporting bias. Future multicenter studies with larger sample sizes and longitudinal follow-up are needed to confirm these findings.

5. Conclusion

Anxiety was found to be significantly associated with higher disease activity in patients with rheumatoid arthritis, whereas depression showed no such association. These findings highlight the need for routine psychological assessment, with particular attention to anxiety, as part of comprehensive RA management. Early identification and appropriate intervention may contribute to improved clinical outcomes and quality of life. Further research with larger sample sizes and longitudinal approaches is recommended to validate these results and to clarify underlying mechanisms.

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