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Original Research Article

Influence of psychological and symptom burden on disease activity scores in patients with rheumatoid arthritis

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ABSTRACT

Background: Joint disease activity indices such as DAS28, CDAI, and SDAI are important for the treatment of rheumatoid arthritis (RA). Yet, indices are influenced by subjective components, which are likely to be reflective of impaired psychological and symptom burden with the former possibly confounding true calculation of inflammatory activity. Objective was to assess the impact of psychological factors and symptom burden on composite disease activity scores in patients with RA.

Methods: This cross-sectional analytical study selected 150 patients who fulfilled the criteria for diagnosis of RA by the ACR/EULAR in 2010. Clinical assessment comprised tender joint count and swollen joint count, patient global assessment, physician global assessment, ESR, and CRP. Depression and fatigue were measured by clinical examination and patient self–report. Disease activity was assessed based on DAS28, CDAI, and SDAI.

Results: The mean age was 52.02±12.13 years, and 81.3% were women. In the 36.0% and 48.0% of patients, depression and fatigue were detected, respectively. The average value of DAS28 was 4.28±1.25 (mean±SD)." Depressed patients also had a higher DAS28 (4.82±1.19 versus 3.97±1.18, $p<0.001$), CDAI and SDAI scores. Similar results were observed for individuals reporting fatigue ($p<0.001$). VAS-patient correlated most closely with DAS28 ($r=0.49$, $p<0.001$), and ESR and CRP demonstrated weak but not significant degree of correlation.

Conclusions: Psychosocial and symptom burden strongly contribute to the composite disease activity measures in RA. Disease activity scores must be interpreted in the context of psychosocial factors to prevent misclassification and unnecessary treatment step-up.

Keywords: Rheumatoid arthritis, DAS28, Depression, Fatigue, Disease activity, Patient-reported outcomes

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease resulting in persistent synovial inflammation, progressive joint destruction and marked functional incapacity. The disease penetrates around 0.5–1% of the adult population across the world and is more common in females than in males. Over the last two decades, breakthroughs in early diagnosis and targeted therapy have revolutionized the management of RA with the emphasis now firmly on early intervention and tight control of disease. These changes have been brought about by a better understanding of past perception was that the only effective treatment for RA was glucocorticoids. According to the treat-to-target concept, mutual goal is remission or low disease activity by regular monitoring and medication optimization. In this strategy, the use of composite disease activity indices is key. The disease activity score in 28 joints (DAS28) is still one of the most adopted tools for this purpose both in clinical settings and trials. The DAS28 comprises TJC, SJC, patient global assessment and an inflammatory marker such as ESR or CRP.[1] While these indices are intended to represent inflammatory disease activity, they have significant subjective components. Tender joint count (TJC) and patient global assessment (PGA) are inherently driven by pain perception, emotional status and overall symptom experience. Therefore, the DAS may not purely reflect synovial inflammation. Some researchers have worried that the patient-reported elements are likely to overly affect composite measure;; if so, there will be a mismatch between clinical judgment and objective inflamed burden.[2] Psychiatric comorbidities are very common in patients with RA. Depression affects 30–40% of RA patients and is associated with higher pain sensitivity, worse functional status, and poorer quality of life. Chronic fatigue is another common and disabling symptom that can persist despite control of inflammatory markers. These may further exaggerate the perception of disease severity and affect patient reported outcomes irrespective of actual inflammatory activity.[3] There is some evidence to suggest that pain sensitisation of the central nervous system and symptom amplification may play a role in high tender joint counts and greater global assessment scores.[4] In such instances, composite disease activity measures might exaggerate inflammatory burden. Found distress was associated with increased disease activity, despite no significant difference in objective inflammation.[5] The difference in these findings has significant clinical implications. Treat-to-target approaches primarily use composite measures to inform provider decisions for escalation of therapy. There is also the potential risk that psychological or symptombased factors, rather than synovitis, may be driving high scores and unnecessary exposure to medication risks would occur with aggressive immunosuppressive therapy escalation for little tangible clinical gain. On the other hand, underestimating psychosocial factors can lead to continued symptom burden in spite of successful inflammation targeting.[6] In addition, patient global assessment has been shown to be a predominant determinant of remission status. These findings imply that patients with seemingly low-titres (swollen joint counts and markers of inflammation) fail to meet remission criteria, but have high patient-reported scores as per studies, giving rise to accumulating evidence.[7,8] The relationship between psychological factors, symptom burden and disease activity indices are crucial for the valid assessment of RA severity. A more discriminative expression between inflammation activity and subjective exaggeration of the symptoms may increase the precision of treatment and individualization for patients. Accordingly, the purpose of this study is to explore how psychological and symptom burden (e. g., depression or fatigue, as well as patient-reported end points) might impact composite disease activity scores in patients with RA. By investigating these associations, we aimed to further characterize the relative impact of subjective and objective components in the overall measurement of disease activity.

METHODS

A cross-sectional analytical study was conducted at the Department of Medicine, Chittagong Medical College Hospital, Chattogram, Bangladesh from August 2022 to July 2023. A total of 150 consecutive patients diagnosed with rheumatoid arthritis were enrolled. The objective was to evaluate the influence of psychological and symptom burden on composite disease activity indices in patients with rheumatoid arthritis.

Inclusion criteria

Patient of age ≥18 years, established diagnosis of RA, and capacity to provide informed written consent were included.

Exclusion criteria

Patients with overlapping autoimmune connective tissue disorders, severe psychologic illness other than depression, active infection or malignancy, and incomplete clinical or laboratory data.

Psychological and symptom burden assessment

The 9 item patient health questionnaire 9 (PHQ-9) was used to assess depression, a validated self-administered scale that ranges from 0 to 27. A score ≥10 was considered clinically significant depressive symptoms, with severity defined as mild, moderate and moderately severe or severe. Fatigue was evaluated with the fatigue severity scale (FSS). The FSS includes 9 items which are rated using a 7-point Likert scale, thus a mean score ≥4 was considered as clinically significant fatigue.

Both instruments are validated in RA and were filled out at the time of clinical assessment before DAS28, CDAI and SDAI computing.

Data collection

The data was obtained through a structured case record form developed for this particular study. Consecutive patients who attended rheumatology outpatient department during the study period were approached and enrolled after taking written informed consent, if they satisfied the following criteria.

Statistical analysis

Statistical package for social sciences (SPSS), version 25.0 was used to enter and analyze data. Continuous variables were reported as mean±standard deviation (SD); categorical variables were reporting frequency and percentage. Group comparisons (depression yes versus no; fatigue yes versus no) were tested with independent sample t-tests for continuous variables. The relationship between psychological variables, laboratory parameters and the composite disease activity scores was evaluated with Pearson's correlation coefficient. P value <0.05 is considered statistically significant.

RESULTS

The mean age was 52.02±12.13 years reflecting a largely middle aged population The majority of the patients were female in number being 122 (81.3%) with men being represented by only 28 patients (18.7%) The mean disease duration was 6.84±4.91 years indicating predominantly long-standing disease Depression was observed in 54 patients (36%) and fatigue experienced by 72 patients (48%), denoting a significant psychological and symptomatic burden in this cohort (Table 1).

Table 1: Baseline sociodemographic and clinical characteristics (n=150).

Variables	Mean±SD/N (%)
Age (years)	52.02±12.13
Female	122 (81.3)
Male	28 (18.7)
Disease duration (years)	6.84±4.91
Depression present	54 (36.0)
Fatigue present	72 (48.0)

The mean tender joint count was 9.82±6.11 and the mean swollen joint count was 6.47±4.32. Patient mean VAS was 5.68±2.01 and physician mean VAS was 4.91±1.88. ESR, CRP was available in 120 (74.5%) samples of the study where ESR and CRP level with mean±SD were calculated as 38.24±19.57 mm/hour and 18.61±12.74 mg/l, respectively suggesting moderate inflammatory activity cumulatively (Table 2).

The overall mean DAS28 was 4.28±1.25. The mean CDAI was 18.74±9.63 and the mean SDAI was 20.36±10.52 (Table 3).

Table 2: Clinical and laboratory parameters.

Variables	Mean±SD
Tender joint count (28)	9.82±6.11
Swollen joint count (28)	6.47±4.32
Patient VAS (0–10)	5.68±2.01
Physician VAS (0–10)	4.91±1.88
ESR (mm/hour)	38.24±19.57
CRP (mg/l)	18.61±12.74

Table 3: Disease activity scores.

Disease activity index	Mean±SD
DAS28	4.28±1.25
CDAI	18.74±9.63
SDAI	20.36±10.52

Remission was seen in 12 patients (8.0%) Low disease activity was noted in 28 patients (18.7%) Moderate disease activity was present in 74 patients (49.3%) and high disease activity was demonstrated by 36 patients (24.0%). Almost half of the cohort was classified as moderate activity and almost one-quarter as high disease activity (Table 4).

Table 4: Disease activity categories (DAS28).

Category	N (%)
Remission	12 (8.0)
Low activity	28 (18.7)
Moderate activity	74 (49.3)
High activity	36 (24.0)

Disease activity scores were significantly higher in patients with depressive symptoms. Mean DAS28 was 4.82±1.19 in patients with depression and 3.97±1.18 in without depression p<0.001. Mean CDAI was 22.91±8.74 in the depression group versus 16.25±8.92 in the non-depression group p<0.001. The mean SDAI was 24.46±9.33 in depressed patients versus 17.95±9.41 in non-depressed patient's (p<0.001) (Table 5).

Table 5: Comparison of disease activity scores by depression status.

Variables	Depression present (n=54) (mean±SD)	Depression absent (n=96) (mean±SD)	P value
DAS28	4.82±1.19	3.97±1.18	<0.001
CDAI	22.91±8.74	16.25±8.92	<0.001
SDAI	24.46±9.33	17.95±9.41	<0.001

At baseline, patients suffering fatigue exhibited greater disease activity. Average DAS28 was 4.71±1.17 for the fatigue group and, 3.89±1.16 for no-fatigue p<0.001. The mean CDAI was 21.63±8.88 in patients reporting fatigue compared to 16.02±8.94 in non-fatigued patients p<0.001.

Mean SDAI was 23.54±9.76 in fatigue group while it was 17.56±9.44 in non-fatigue group (p<0.001) (Table 6).

Table 6: Comparison of disease activity scores by fatigue status.

Variable	Fatigue present (n=72) (mean±SD)	Fatigue absent (n=78) (mean±SD)	P value
DAS28	4.71±1.17	3.89±1.16	<0.001
CDAI	21.63±8.88	16.02±8.94	<0.001
SDAI	23.54±9.76	17.56±9.44	<0.001

DAS28 (r=0.39, p<0.001) and with depression was moderate positive correlation with DAS28 (r=0.39, p<0.001). Fatigue showed an even better relationship (r=0.42, p<0.001). VAS patient was most strongly correlated with DAS28 (r=0.49, p<0.001). ESR revealed a mild but significant correlation (r=0.21, p=0.04), and CRP showed weak and non-significant relation with r=0.19 (p=0.06). These results demonstrate that clinical symptoms have a greater impact on DAS28 than laboratory inflammatory markers (Table 7).

Table 7: Correlation between psychological/symptom variables and DAS28.

Variables	R value	P value
Depression	0.39	<0.001
Fatigue	0.42	<0.001
Patient VAS	0.49	<0.001
ESR	0.21	0.04
CRP	0.19	0.06

CDAI for depression (r=0.41, p<0.001) and for fatigue (r=0.44, p<0.001) and patient VAS had the strongest association (r=0.52, p<0.001). For SDAI depression had (r=0.38, p<0.001) fatigue showed (r=0.40, p<0.001) and patient VAS showed (r=0.48, p<0.001) (Table 8).

Table 8: Correlation between psychological variables and CDAI and SDAI.

Variable	CDAI (r)	P value	SDAI (r)	P value
Depression	0.41	<0.001	0.38	<0.001
Fatigue	0.44	<0.001	0.40	<0.001
Patient VAS	0.52	<0.001	0.48	<0.001

DISCUSSION

The aim of this study was to investigate the contribution of psychological and symptom burden factors in the multidimensional assessments (MDA) of disease activity used in RA patients. The results highlight that depression, fatigue, and patient global assessments are all significant determinants of DAS28, CDAI, and SDAI scores at a level exceeding objective measures of inflammation. The majority of the patients in our cohort were females (122, 81.3%), aged 52.02±12.13 years on AD treatment and had a disease duration of 6.84±4.91 years at study entry. This distribution of demographics is comparable to the reported epidemiology of RA, as it remains more prevalent among women in their middle years of life.[9] Of note, depression was the diagnosis for 36.0% whereas fatigue for 48.0% of the patients. These rates are in keeping with earlier research estimating a 30–40% prevalence of depression among patients with RA.[10] The elevated frequency of fatigue also highlights that symptom burden is still high in the era of contemporary treatment. Shows that the average tender joint count (9.82±6.11) was higher than the swollen joint count (6.47±4.32). This difference is clinically meaningful. The number of tender joints is a subjective measure influenced by pain perception, whereas the swollen joint count better reflects inflammatory synovitis. Analogous discrepancies have been observed in patients with coexistent fibromyalgic features, whereby sore joints are disproportionately high.[10] Patient VAS was higher than physician VAS (5.68±2.01 versus 4.91±1.88) and demonstrated perceptual discrepancy between patient's self-reported burden of disease and physicians' ratings of activity level. Inflammatory indices were slightly elevated (mean ESR was 38.24±19.57 mm/hour and CRP was 18.61±12.74 mg/l) but, when combined with composite scores, laboratory values did not capture well the perceived disease activity extent nor did they correspond to it either way in every case. The mean DAS28 was 4.28±1.25, and CDAI and SDAI were 18.74±9.63, and 20.36±10.52, respectively. In general, these are symptoms of mild to moderate disease activity. Further demonstrates that 49.3% of patients were in the moderate and 24.0% had high disease activity; only 8.0% achieved remission. This pattern indicates an extensive residual disease load in individuals within this cohort despite applied therapeutic strategies, as do the treat-to-target findings in daily care.[11] Disease activity scores were consistently higher in depressed patients at all indices. The mean DAS28 was 4.82±1.19 in the depressed and 3.97±1.18 (p=0.05). These are clinically significant differences which are not only statistical artefacts. Depression has been shown to exacerbate pain perception, induce changes in central pain processing and have an adverse effect on global health perception.[12] Other work has also suggested that psychological distress increases composite disease activity scores irrespective of inflammatory status. Fatigue demonstrated a comparable pattern. Fatigue-reporting patients had higher DAS28 (4.71±1.17 versus 3.89±1.16, p<0.001), CDAI and SDAI scores. Fatigue is a complex symptom that is affected by inflammation, mood, sleep disturbance, and neurobiological processes.[13] Its close association with composite indices confirms these scores reflect the total symptomatic burden and not purely inflammatory activity. Correlation analysis reinforces this observation. Patient VAS correlated most strongly with DAS28 (r=0.49, p<0.001), fatigue (r=0.42) and depression (r=0.39). ESR shows a weak correlation (r=0.21), and CRP

has no level of statistical significance, r=0.19; p=0.06. This implies that subjective variables have a higher impact on DAS28, than do laboratory ones. A similar observation in favor of the impact of FAI on subjective parameters emerged from a study by Pollard et al, who identified the "fibromyalgia RA", with disease activity scores overly determined by patient-reported outcomes.[14] Similar patterns for CDAI and SDAI. Patient VAS correlated best with CDAI (r=0.52) and SDAI (r=0.48), followed by fatigue and depression. As CDAI does not comprise any laboratory values, strong correlations with psychosocial aspects can be anticipated. But even SDAI, including CRP, was more closely related to subjective factors than to inflammation. This is consistent with previous findings that patient global assessment is a predominant driver of remission categorization.[16,17] The clinical implications are substantial. Treat-to-target concepts recommend increasing treatments according to composite disease activity scores. However, in patients with high scores due to depression or fatigue than active synovitis are recommended not increase the intensity of therapy such as possibly worsening adverse events. Central pain sensitization can masquerade as inflammatory disease activity, and make treatment decisions more challenging.[18] Composite indices should, therefore, be interpreted in context. The psychological burden in the present study was assessed through use of standardized and validated instruments, namely the hospital anxiety and depression scale (HADS) and fatigue severity scale (FSS). We used structured tools which increases the reliability of our findings and minimizes subjective misclassification of depressive symptoms and fatigue. We utilized described cut-off values to guarantee that the associations between psychological burden and composite disease activity indices were methodologically valid and clinically interpretable. The subjective components need to be balanced carefully against the objective ones, which are swollen joint count and acute phase reactants. Failure to consider psychological substrates may result in overtreatment, while lack of mental health interventions may sustain a high level of steadily enduring symptom burden despite well-controlled inflammation. A comprehensive model of RA measurement is facilitated by this study. Disease activity scores reflect both inflammation and perceived symptoms. Depression and fatigue are not "secondary" but primary factors in how disease activity is assessed and felt.

CONCLUSION

We show that psychological and symptom burden are strong contributors to the composite disease activity score in patients with RA. The prevalence of depression and fatigue was the most common, which were also linked to significantly higher DAS28, CDAI and SDAI scores (mean±SD difference, p<0.001). Correlation analysis Febuxostat also revealed that the patient-reported measures were more closely related to disease activity indices than inflammatory markers. These results indicate that composite scores do not only measure synovial inflammation, but also subjective symptoms enhancement. Adding psychological assessment to routine RA evaluations could lead to more precise treatment delivery, less unnecessary escalation of immunosuppressive therapy, and disease management that takes into account the whole patient.

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