

Is CDAI comparable to DAS 28 and SDAI regarding inter-observer agreement and correlation to MHAQ in Egyptian RA patients?

K. El-Hadidi¹, S.M. Gamal¹, S. Saad², N.Y. Elsaid¹

¹Rheumatology and Rehabilitation Department, Faculty of Medicine, Cairo University, Egypt;

²Rheumatology and Rehabilitation Department, Monera General Hospital, Cairo, Egypt

SUMMARY

Choosing between the different disease activity indices used for rheumatoid arthritis RA evaluation in clinical practice and research is often difficult. The aim of the current study was to compare clinical disease activity index (CDAI) to simplified disease activity index (SDAI), and disease activity score 28 (DAS28) regarding inter-observer reliability and correlation to the modified health assessment questionnaire (MHAQ) in a cohort of Egyptian RA patients. This study included one hundred RA patients. Every patient had an independent clinical evaluation made by two rheumatologists (professor and candidate) to evaluate disease activity using DAS28 with its 4 types, CDAI and SDAI. We used Cohen's weighted kappa coefficient to measure the inter-observer agreement between the professor and candidate in different disease activity measures. Correlation between MHAQ and disease activity measures was made with Spearman's rho test. Inter-observer agreement in CDAI and DAS28 values was almost perfect. A strong positive correlation was found between professor and candidate regarding the tested activity indices ($p < 0.001$), and a positive correlation was found between MHAQ and all Disease Activity Scores made by both professor and candidate ($p < 0.001$). CDAI proved to be comparable to other disease activity scores regarding inter-observer agreement and relation to MHAQ.

Key words: CDAI; SDAI; DAS 28; rheumatoid arthritis; MHAQ; interobserver agreement.

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INTRODUCTION

Rheumatoid arthritis (RA), the most common chronic inflammatory arthritis, typically leads to physical disability and worsened quality of life (1). Thus, according to the current guidelines, diagnosis should be established as early as possible, therapy should be initiated immediately and increased promptly to achieve remission or low disease activity (2).

Current RA treatment guidelines recommend the use of activity indices in the assessment of disease activity and treatment success to achieve tight disease control (3). Assessments of disease activity in RA are important in determining treatment plans and patient response to treatment (4). To accomplish this aim, different measurement tools of disease activity have been

developed. Of the 63 currently available RA disease activity measurement tools, the American College of Rheumatology (ACR) used a multistep process to recommend 6 measures: the clinical disease activity score (CDAI), disease activity score 28 joints (DAS28), patient activity scale (PAS), patient activity scale II (PAS-II), routine assessment of patient index data 3 (RAPID-3) and simplified disease activity index (SDAI). The reasons for this recommendation was that all 6 produce a single index and have defined ranges for indicating low, moderate, or high disease activity or clinical remission. It is suggested that by applying these measures in clinical practice, physicians will be able to *treat to target* and effectively apply the ACR recommendations for the treatment of RA (5). Although the systematic measurement of

Corresponding author:

Nora Y. Elsaid

Department of Rheumatology
and Rehabilitation, Cairo University, Egypt
E-mail: norayousry@kasralainy.edu.eg

disease activity facilitates clinical decision-making in RA, no recommendations currently exist on which measures should be applied in clinical practice. Also, other questions remain unsolved such as the inter-observer reliability of different activity indices and whether simple indices like CDAI are comparable to more composite indices or not. Thus, in this study we aimed to compare the performance of the preferred activity indices by comparing their inter-observer reliability and by correlating different activity indices to the modified version of the health assessment questionnaire (MHAQ) and measuring the time to score.

■ PATIENTS AND METHODS

This study was carried out on one hundred adult RA patients (6% males and 94% females, mean age of 45.12 years) fulfilling the ACR/EULAR 2010 classification criteria of RA (6). All patients were recruited from the outpatient clinic of the Rheumatology and Rehabilitation Department, Faculty of Medicine, Cairo University & Manial Specialized Hospital, Cairo University. Our patients' mean disease duration was 8.14 ± 6.84 years. Exclusion criteria for this study were pregnant females, patients with hepatitis C infection and those with secondary fibromyalgia and overlap syndrome. All patients had full history taking, complete physical examination as well as assessment of disease activity and functional ability.

Disease activity was assessed by using the DAS 28 (3 values and 4 values) (7), SDAI (8) and CDAI (9). RA functional ability was assessed using the MHAQ (10). Assessment of disease activity measurements by DAS 28, SDAI and CDAI was made by the two rheumatologists. The first was a skilled rheumatology professor (Prof), widely experienced in joint evaluation, with more than thirty years of experience in university hospitals. The second was a young rheumatology fellow (candidate) who had been trained by different rheumatology professors and has performed more than 500 supervised joint count ex-

aminations in about three years' training in a university hospital. Both assessed joints for tenderness and swelling in our previous study and in the same setting of our previous study (11).

Data management and statistical analysis were performed using Statistical Package for Social Sciences version 21 (SPSS Inc, Chicago IL). Numerical data were summarized using mean and standard deviation or median and range. Categorical data were summarized as percentages. Correlations were determined by using Spearman's rho test. As a measure of reliability, we used Cohen's weighted kappa coefficient to assess the degree of agreement between the professor and the candidate. In order to support our results, we used Maxwell's chi-square and McNemar test for asymmetry to test for disagreement to see if the assessors significantly disagreed. All p-values are two-sided. p-values < 0.05 were considered significant.

Correlation

Local ethical committee approval was taken.

■ RESULTS

The results concerning the degree of agreement between the professor and the candidate regarding different disease activity measurements are described in the following paragraphs.

DAS28 4 values using ESR

According to DAS28 4V ESR, we observed that remission was found in 1 patient by the professor and in 0 patients by the candidate, mild activity in 8 patients by the professor and in 13 patients by the candidate, moderate activity in 50 patients by the professor and in 46 patients by the candidate, severe activity in 41 patients by the professor and 4 in 1 patients by the candidate. The degree of agreement by weighted kappa measurement was almost perfect agreement (0.84).

DAS 28 4 values using CRP

By using DAS28 4V. CRP we observed that remission was found in 3 patients by the professor and in 2 patients by the can-

didate while mild activity was found in 32 patients by the professor and 31 patients by the candidate, moderate activity in 42 patients by professor and 41 patients by the candidate and severe activity in 24 patients by professor and 25 patients by the candidate. The degree of agreement by weighted Kappa was almost perfect (0.838).

DAS28 3 values using ESR

While comparing DAS28 3V ESR values obtained by the professor and the candidate, there was mild activity in 8 patients, moderate activity in 40 patients and severe activity in 52 patients found by the professor while there were 12 patients with mild activity, 38 with moderate and 52 with severe activity found by the candidate. The agreement was almost perfect (0.823).

DAS 28 3 values using CRP

The values of DAS28 3v CRP obtained by the professor and the candidate showed a substantial degree of agreement (0.797). Remission found in 1 patient by the professor and in 0 patients by the candidate, mild activity in 22 patients by the professor and in 25 patients by the candidate, moderate activity in 40 patients by the professor and in 38 patients by the candidate, severe activity in 37 patients by the professor and in 37 patients by the candidate.

Simplified disease activity index (SDAI) and Clinical disease activity index (CDAI)

By using SDAI and CDAI for assessment of disease activity we observed:

- Remission was found in 2 patients by the professor and in 1 patient by the candidate using CDAI while no remission was found by either the professor and the candidate using SDAI.
- Mild activity was detected in 5 patients in SDAI, 12 patients in CDAI by the professor and 6 patients in SDAI, 11 in CDAI by the candidate.
- Moderate activity was determined in 31 patients in SDAI, 28 patients in CDAI by the professor and 31 patients in SDAI and 30 in CDAI by the candidate.
- Severe activity was observed in 64 patients by the professor 63 by the candi-

date in SDAI and 58 patients by both of them in CDAI (Figures 1 and 2).

Accordance in SDAI and CDAI between the professor and the candidate using weighted Kappa measurement was substantial in SDAI (0.788) and almost perfect in CDAI (0.813).

In support of our results, Maxwell's chi-square and McNemar tests for asymmetry showed no statistically significant disagreement in all activity measures tested as shown in Table I.

Correlation between the professor and the candidate regarding disease activity measures was made using Spearman's rho test,

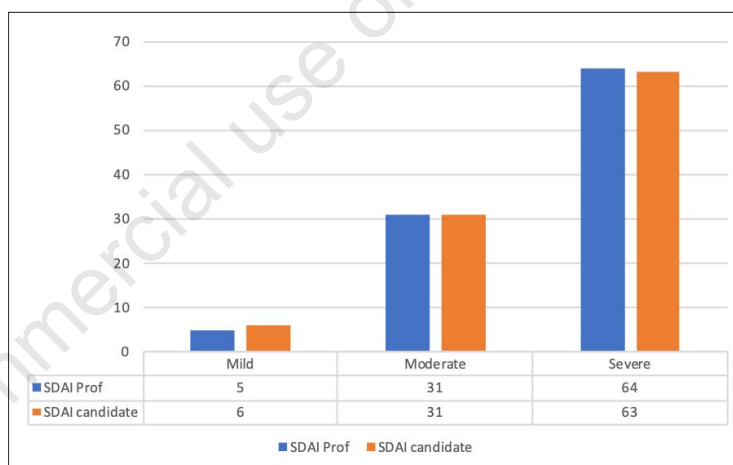


Figure 1 - A comparison between simplified disease activity index (SDAI) made by the Prof and the candidate.

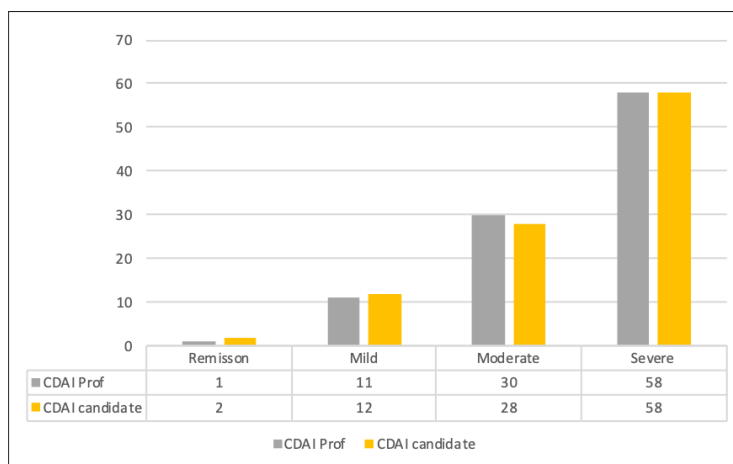


Figure 2 - A comparison between clinical disease activity index (CDAI) made by the Prof and the candidate.

Table I - Maxwell's chi-square and McNemar tests for asymmetry.

Disease activity measures	Maxwell chi square p value	McNemar chi square p value
DAS4VCRP	0.299	0.721
DAS4VESR	0.753	0.976
DAS3VCRP	0.705	0.965
DAS3VESR	0.126	0.246
SDAI	0.842	0.951
CDAI	0.261	0.676

with the highest correlation found in DAS 4V ESR ($p<0.001$) ($r=0.960$), followed by both CDAI and SDAI ($p<0.001$) ($r=0.957$) as in Table II.

Correlation between MHAQ and the other disease activity measures

We made a correlation between the MHAQ and disease activity measurements by both the professor and the candidate included in this study (DAS28 with 4 types: SDAI and CDAI) by Spearman's rho correlation, with highest correlation for the professor found between MHAQ and DAS 28 3V ESR, followed by CDAI ($p<0.001$) ($r=0.626$), ($p<0.001$) ($r=0.611$) respectively, while the

Table II - Correlation between the prof. and the candidate regarding disease activity measurements.

Score	R	P
DAS 28 4v ESR	0.960	<0.001
DAS 28 4v CRP	0.955	<0.001
DAS 28 3v ESR	0.945	<0.001
DAS28 3v CRP	0.956	<0.001
SDAI	0.957	<0.001
CDAI	0.957	<0.001

Table III - Correlation between MHAQ and the other disease activity measurements.

Score	MHAQ prof.		MHAQ candidate	
	R	P	R	P
DAS 28 4V ESR	0.610	<0.001	0.633	<0.001
DAS 28 4V CRP	0.559	<0.001	0.578	<0.001
DAS 28 3V ESR	0.626	<0.001	0.634	<0.001
DAS 28 3V CRP	0.555	<0.001	0.581	<0.001
SDAI	0.589	<0.001	0.602	<0.001
CDAI	0.611	<0.001	0.642	<0.001

highest correlation for the candidate was found between MHAQ and CDAI followed by DAS 28 3V ESR ($p<0.001$) ($r=0.611$), ($p<0.001$) ($r=0.642$) respectively as in Table III.

■ DISCUSSION AND CONCLUSIONS

Quantitative assessment of disease activity over time in patients with RA has been accepted as being necessary to guide treatment decisions in clinical practice (12, 13). The currently available disease composite activity indexes that provide a single number on a continuous scale are the Disease Activity Score (DAS), (DAS-28), SDAI, and CDAI (14). DAS28 is still considered as the gold standard to assess the disease activity in patients with RA (15), although the delay associated with acute phase reactant assessment and the complex formula requiring a calculator make the DAS not always accessible for immediate decision-making at the time of patient-physician interaction because of missing laboratory results (16).

Up till now, it is still debatable whether acute phase reactant (APRs) included in DAS and SDAI make them superior to CDAI. Another question remaining unsolved is inter-observer reliability and whether different disease activity measurements will give the same results when made by different health care professionals with varying years of experience. Therefore, we studied the inter-observer agreement in DAS 28, SDAI, CDAI between two rheumatologists with different years of experience. We found that CDAI and most DAS 28 values showed perfect agreement.

Also, in the current study a strong positive correlation was reported between the professor and the candidate regarding disease activity measurements with the DAS 4V ESR being the best, followed by CDAI and SDAI, while the remaining DAS indices came later. To our knowledge, no previous report has recorded inter-observer correlation of diseases activity indices, although Dhaon et al. 2017 (17) reported strong positive correlation between activity indices by a single observer. Similarly Gaujoux-Viala et al. 2012 (18), after studying 61 reports on activity indices, concluded that DAS, DAS28, SDAI, and CDAI are valid tools for evaluating the activity of RA. In our opinion such results may indicate that CDAI is comparable and it may exceed other acute phase reactant (APRs) including indices. This is in line with Aletaha et al. 2005 (16) as they concluded that APRs add little information on top of the combination of clinical variables included in the SDAI.

Regarding correlation with MHAQ, the highest correlation for the professor was found between MHAQ and DAS 28 3V ESR, followed by CDAI, while the highest correlation for the candidate was found between MHAQ and CDAI followed by DAS 28 3V ESR respectively. Similarly, Eissa et al. 2017 (19) reported strong positive correlation between MHAQ and the previously mentioned activity indices.

CDAI, which is a purely clinical score, is a valid measure of disease activity and has its greatest merits in clinical practice rather than research. The CDAI may help physicians to take immediate and consistent treatment decisions and help to improve patient outcomes in the future (16). In our opinion the added value of composite measures may be helpful in clinical research. However, the simplicity of simple measures may facilitate rapid clinical decision-making in clinical practice and the inter-observer agreement observed shows CDAI to be reliable for use by all practitioners, whether young or experienced.

We can, therefore, suggest its use in daily clinical practice, especially in developing countries where most patients come to phy-

sicians without available laboratory results. Finally, we can say that CDAI score provides good inter-observer agreement, correlation with MHAQ and shortest timing for disease activity measuring in RA patients. These results qualify CDAI for use by physicians with varying degrees of experience, at any time and in the simplest clinical settings and daily practices.

We encourage young rheumatologists, especially in developing countries where resources are limited, to use CDAI as a suitable, validated and reliable measure of disease activity in RA.

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Non-commentary