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## RESEARCH ARTICLE

# ASSESSMENT OF EFFICACY OF PATIENT REPORTED OUTCOME CLINICAL ARTHRITIS ACTIVITY INDEX (PROCLARA) IN EVALUATING DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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**ABSTRACT**

***Background*:** Patient reported Outcome - Clinical Arthritis Activity Index (PRO-CLARA) is a new, continuous and feasible index to assess the impact on activity of daily living (which is the patient's prime concern) so it could be useful in regular clinical practice for monitoring Rheumatoid Arthritis (RA) patients. ***Objective*:** Assessment of disease activity in Rheumatoid Arthritis using Patient reported Outcome - Clinical Arthritis Activity Index (PRO-CLARA). ***Material and method:*** The present study was a cross sectional study done on hundred RA patients as per American College of Rheumatology criteria (ACR criteria) who presented in Rheumatology clinic at PGIMS, Rohtak (Haryana). Patients were assessed for disease activity using Disease activity score-28 (DAS28), Clinical disease activity index (CDAI) and PRO-CLARA at baseline thereafter two months and at four months on therapy. ***Results*:** The mean age was 44.4±11.8 yrs with 84 females and 16 males. At baseline the mean DAS28, CDAI and PRO-CLARA score was 6.65±0.68, 36.5±9.7 and 8.78±0.64 respectively, at two months 4.58±0.81, 18.36±6.58 and 6.62±1.31 respectively while at four months was 3.33±0.96, 9.69±6.69, and 4.21±1.59, respectively. At baseline, 2 months and 4 months Pearson's Correlation Coefficient of PRO-CLARA with DAS28 was 0.931, 0.889 and 0.893 respectively, and with CDAI was 0.517, 0.674 and 0.682 respectively (all P value <0.001). Reliability index (as assessed by Cronbach's alfa) at baseline, 2 months and 4 months for DAS28 was 0.662, 0.569 and 0.685; for CDAI was 0.574, 0.586 and 0.767 for PROCLARA was 0.862, 0.980 and 0.987 respectively. ***Conclusion*:** PRO-CLARA was found to be significantly correlated with DAS28 and CDAI. The components of PRO-CLARA include all important measures of disease activity, so it could be useful in regular clinical practice for monitoring RA patients.



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## INTRODUCTION

Rheumatoid Arthritis is a disease with highly variable presentation and disease course so attempts have been made, especially in the last decade, for consensus about a minimal set of variables for assessing disease activity. A wide variability of instruments (variables including such as various types of joint counts (SJC, TJC), acute phase reactants (ESR, CRP), global assessment scales (PGA, EGA)) and general measures such as hemoglobin or body weight. Amongst the currently available composite disease activity indices that provide a single snatcher on a continuous scale, the two most widely used variables are the Disease Activity Score using 28 joint count (DAS28) and Clinical Disease Activity Index (CDAI) (Aletaha and Smolen, 2005). Recently Patient Reported Outcome Measures (PROMs), have been used to assess the disease activity, based on the assessment done by patient himself (Fransen *et al.,* 2005; Laure Gossec, 2010). PROMs provide knowledge about patient's health, functional status, symptoms, treatment preferences, satisfaction and quality of life from patients's personal perspective. Health Assessment Questionnaire Disability Index (Bruce and Fries, 2003), Rheumatoid Arthritis Disease Activity Index (RADAI) (Fransen *et al.,* 2001) and Routine Assessment of Patient Index Data (RAPID) (Pincus *et al.,* 2008), are the effective PROMs used for RA assessment of disease activity, and they have been demonstrated adequate reliability, validity and responsiveness of these indices among patients with RA and proven them feasible, informative quantitative measures in busy clinical settings (Bruce and Fries, 2003; Fransen *et al.,* 2001; Pincus *et al.,* 2008). These considerations have led on to development of an index, termed Patient reported Outcome - Clinical Arthritis Activity Index (PRO-CLARA). PRO-CLARA is a new PROM for assessment of disease activity in Rheumatoid Arthritis.It is a short and easy to complete self administered index, without formal joint counts, combining three items a) patient's physical function (as measured by ROAD questionnaires), b) self administered TJC and c) patient global disease activity(PGA) into a single measure of disease activity. There are very few studies and little experiences with PRO-CLARA worldwide and there is no Indian experience till date, so it was worthwhile to evaluate the disease activity by using PRO-CLARA in RA patients (Salaffi, 2005).

## MATERIALS AND METHODS

A total of hundred patients of RA as per American College of Rheumatology criteria (ACR criteria 1987) reporting to the Out Patient Department of Rheumatology Clinic of Pt. B.D. Sharma PGIMS, Rohtak were enrolled in the study from. A written informed consent was taken from all patients of Rheumatoid Arthritis (RA) selected for being subjects in the study. All those patients of RA who were severely anaemic, any evidence of malignancy, hypothyroid, having evidence of severe renal, cardiac, liver or pulmonary disease were excluded from the study. Patients with any evidence of recent infections or developing infections during the study period were excluded from the study. All the subjects included in the study were detailed for their history and clinical examination. All these subjects underwent routine laboratory investigations including radiographic examination and biochemical evaluation at baseline. All the subjects were assessed for disease activity using DAS28, CDAI, and PRO-CLARA at baseline using the formula mentioned below:

DAS28: $DAS28 = 0.56\sqrt{TJC} + 0.28\sqrt{SJC} + 0.70 (\log ESR) + 0.014 (GH)$

where, TJC = Tender Joint Count, SJC = Swollen Joint Count, ESR=Erythrocyte Sedimentation Rate (in mm/1st hr), GH = Global Health on visual analog scale(VAS), in 0 to 100 min

CDAI: CDAI = TJC + SJC + PGA + EGA

where, TJC = Tender Joint Count, SJC = Swollen Joint Count , PGA = Patient Global Assessment of disease activity (as per VAS - 0 to 10 cm), EGA = Evaluator Global Assessment of disease activity (as per VAS - 0 to 10 cm)

PRO-CLARA: was calculated by summing the scores of three individual measures and dividing by three, and range from 1-10 (Annexure-I)

All subjects continued with their medications and all three mentioned scores were reassessed at follow up at two months and four months.

### Statistical analysis

Data was collected and analyzed by using the Statistical Package for social sciences version 11 and compared the PRO-CLARA score with DAS28 and CDAI score. Pearson's correlation was used, for all tests with p value of less than 0.05 and confidence interval kept at 95 percent. Values were expressed as numbers, percentage, mean±SD. Statistical significance was measured by p-value <0.05= significant.

## RESULTS

In the present study, the mean duration of illness was 67.5 ± 59.8 months. The mean age of study group was 46.17±11.47 years and there were 84 females and 16 males. Eighty two were rheumatoid factor positive.

**Assessment of disease activity:** Disease activity of the study group were assessed using PRO-CLARA, DAS28 and CDAI score at baseline (M0), 2 months (M2) and at 4 months (M4) follow up (Tables I and II). The mean change in PRO-CLARA, DAS28, and CDAI from the base line was statistically significant (all p<0.001). Correlation of PRO-CLARA with DAS28 and CDAI: was studied at baseline (M0) and at follow up 2 months (M2),4 months (M4) using Pearson's correlation coefficient (r). All correlations were found to be statistically significant (p<0.001) (Table IV). Cronbach's Alpha was calculated to measure the reliability of indices. It was 0.662 for DAS28, 0.574 for CDAI and 0.862 for PROCLARA (Table V)

**Table I. Mean values of the disease activity characteristics of the study population**

| Variable | Mean at M0 (± SD) | Mean at M2 (± SD) | Mean at M4 (± SD) | P value |
|---|---|---|---|---|
| TJC | 18.45±6.2 | 8.75±3.97 | 3.78±2.99 | <0.001 |
| SJC | 4.57±3.54 | 2.01±2.1 | 0.98±1.79 | <0.001 |
| PGA | 7.28±1.24 | 4.38±1.58 | 3.01±2.05 | <0.001 |
| EGA | 6.12±1.42 | 3.19±1.09 | 1.77±1.21 | <0.001 |
| ESR | 43.35±11.87 | 25.52±8.45 | 18.43±7.71 | <0.001 |
| GH | 70.10±11.84 | 40±10.15 | 24.20±12.4 | <0.001 |

TJC-tender joint counts; SJC-swollen joint counts;PGA-patient global assessment; EGA- evaluator global assessment; ESR-erythrocyte sedimentation rate; GH-Global health; M0-baseline ; SD- standard deviation; M2-two months; M4-four months.

**Table II . Showing disease activity variables of PROCLARA at M0, M2 and M4**

| | M0 | M2 | M4 |
|---|---|---|---|
| Mean ROAD | 8.24±0.72 | 6.34±1.37 | 4.07±1.58 |
| Mean SELF-TJC | 8.65±0.71 | 6.65±0.91 | 4.13±1.62 |
| Mean GH | 9.46±0.74 | 6.99±1.45 | 4.35±1.78 |

**Table III. Table showing Mean values of disease activity scores at M0, M2 and at M4**

| | M0 | M2 | M4 | p Value |
|---|---|---|---|---|
| DAS28 | 6.65±0.68 | 4.58±0.81 | 3.33±0.96 | <0.001 |
| CDAI | 36.5±9.7 | 18.36±6.58 | 9.69±6.69 | <0.001 |
| PROCLARA | 8.78±0.64 | 6.62±1.31 | 4.21±1.59 | <0.001 |

DAS28, Disease Activity Score-28; CDAI, Clinical disease activity index;PRO-CLARA-Patient reported Outcome - Clinical Arthritis Activity Index ; M0-baseline ; SD- standard deviation; M2-two months; M4-four months

**Table IV. Correlation between the DAS28, CDAI and PRO-CLARA at baseline (M0) and follow up of two months (M2), four months (M4)**

| Disease activity score | Pearson's coefficient correlation | | | |
|---|---|---|---|---|
| | M0 | M2 | M4 | P value |
| DAS28 and PROCLARA | 0.931 | 0.889 | 0.893 | <0.001 |
| CDAI and PROCLARA | 0.517 | 0.674 | 0.682 | <0.001 |

DAS28-Disease Activity Score-28;CDAI-Clinical disease activity index;PRO-CLARA-Patient reported Outcome-Clinical Arthritis Activity Index ; M0-baseline ; SD- standard deviation; M2-two months; M4-four months.

**Table V. Table showing the Cronbach's Alpha value of PRO-CLARA, DAS28 and CDAI**

| | M0 | M2 | M4 |
|---|---|---|---|
| PROCLARA | 0.862 | 0.980 | 0.987 |
| DAS28 | 0.662 | 0.569 | 0.685 |
| CDAI | 0.574 | 0.586 | 0.767 |

PRO-CLARA:Patient reported Outcome-Clinical Arthritis Activity Index; DAS28: Disease Activity Score-28; CDAI: Clinical disease activity index

## DISCUSSION

The last two decades has been the major advances in the care of patients with Rheumatoid arthritis (RA). New therapeutics are available that significantly reduce disease activity, improve physical function and reduce damage to the joints that, over time, can reduce to the disability. Critical to accomplishing these important advances has been the development and

refinement of measurement of tools (based on patient reported outcome or physician reported outcomes) to accurately assess the disease activity in clinic/ clinical trials for treatment to target (i.e. to achieve remission). Currently used disease activity measures incorporate some or all core set variables: a) physician assessed measures (tender/ swollen joint count, physician global assessment), b) patient assessed measures (pain, physical function, patient global assessment) and c) laboratory measures (acute phase reactants- erythrocyte sedimentation rate (ESR), C reactive protein (CRP) (Marjonne *et al.,* 2008). Patient reported outcome measures (PROMs) based on the above core set variables and reported by patient themselves have been found to provide knowledge about patients health including functional status of quality of life by their own personal perspectives (Fransen *et al.,* 2005; Laure Gossec, 2010). Patient reported Outcome - Clinical Arthritis Activity Index (PRO-CLARA) (Salaffi *et al.,* 2010) a PROM, measures all components but too few studies are available testing its potential use in RA. This study was planned to find the utility of PRO-CLARA and also its correlation with physician related outcome measures-Disease activity score-28 (DAS28) and Clinical disease activity index (CDAI). Disease activity was monitored by using physician assessed disease activity score (DAS28 and CDAI) and also patient assessed disease activity measure (PRO-CLARA). There was significant reduction of disease activity over 4 months of duration (Table III). PRO-CLARA was compared with CDAI and DAS28 at baseline, and follow up (at 2 months and 4 months). Pearson's coefficient was found to be statistically correlated between PRO-CLARA and DAS28 (0.931; 0.889 and 0.893 respectively) and with CDAI (0.517;0.674 and 0.682 respectively) (Table 4). In a similar study done by Sallaf *et al.* PROCLARA index was compared with DAS28 and CDAI, and was significantly correlated with spearman's correlation coefficient of 0.835 and 0.897 respectively(as our study) showing high reliability factor (Salaffi *et al.,* 2005). The internal consistency (cronbach's alfa) for the three measures used- DAS28, CDAI and PROM was 0.662; 0.574; and 0.86 respectively (Table V). Saffal *et al.* also observed cronbach's alfa for PROCLARA to be 0.893 indicating high reliability. In the present study at baseline and during follow up at 2 months and 4 months, the internal consistency of PROCLARA was found to be highest as compared to DAS28 and CDAI (Table V). In the present study PROCLARA (Patient Reports Outcome-Clinical Arthritis Activity ), an index without formal joint counts, correlated very well and had substantial level of agreement with the DAS28 and CDAI (the time tested clinical tools for assessment of disease activity in clinical trials and practice). Further PROCLARA also doesn't need any Laboratory back up/reports, is short, self administered and easy to calculate so PROCLARA in the present study was found to be effective tool for assessment of disease activity.

**Conclusion**

Hence it can be concluded that PROCLARA has similar validity to the other currently employed composite indices such as DAS28 and CDAI. PROCLARA does not include any laboratory measurement and therefore all variables are easily available at point of care in the clinical setting, which can in turn produce more consistency in timing and completeness of disease measurement. It is short, self administered and very easy to calculate and time saving Hence, it is a valid instrument that can be used in routine clinical care to follow patients of RA and to distinguish clinically effective therapies from the ineffective ones. Therefore, PROCLARA should facilitate decision making by physicians and avoid lags in efficient treatment adaptation for patients with RA. However due to paucity of literature, more and larger studies (especially with follow ups) should be designed with PROCLARA index for assessment of disease activity in Rheumatoid Arthritis to test it's utility in day to day practise/research.

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# ANNEXURE-I

**PATIENT REPORTED OUTCOME (PRO) CLINICAL ARTHRITIS ACTIVITY (PRO-CLARA) INDEX :**

Please try to answer each question, even if you do not think it is related to you.
There are no right or wrong answers. Please answer exactly as you think or feel. Thank you.
A)Please check ( ) the one best for your abilities **TABLE I**

| OVER THE LAST WEEK ,were you able to | Without ANY difficulty | With LITTLE difficulty | With SOME difficulty | With MUCH difficulty | UNABLE to do |
|---|---|---|---|---|---|
| 1.Close your hand completely? | ☐ | ☐ | ☐ | ☐ | ☐ |
| 2.Accept a handshake? | ☐ | ☐ | ☐ | ☐ | ☐ |
| 3.Do up buttons? | ☐ | ☐ | ☐ | ☐ | ☐ |
| 4.Open jars which have been previously opened? | ☐ | ☐ | ☐ | ☐ | ☐ |
| 5.Reach up and take down a 2 kg object from above your head? | ☐ | ☐ | ☐ | ☐ | ☐ |
| 6.Stand up? | ☐ | ☐ | ☐ | ☐ | ☐ |
| 7.Walk on a flat ground? | ☐ | ☐ | ☐ | ☐ | ☐ |
| 8.Climb up five steps or stairs? | ☐ | ☐ | ☐ | ☐ | ☐ |
| 9.Get into the car? | ☐ | ☐ | ☐ | ☐ | ☐ |
| 10.Get out of the car? | ☐ | ☐ | ☐ | ☐ | ☐ |
| 11.Wash and dry your body? | ☐ | ☐ | ☐ | ☐ | ☐ |
| 12. Are you still able to work at home or/ and on your job? | ☐ | ☐ | ☐ | ☐ | ☐ |

B) Please place a check ( ) in the appropriate spot to indicate the amount of pain you are having today in each of the joint areas listed below

**TABLE II**

| LEFT | None | Mild | Moderate | Severe | RIGHT | None | Mild | Moderate | Severe |
|---|---|---|---|---|---|---|---|---|---|
| Hand | ☐ | ☐ | ☐ | ☐ | Hand | ☐ | ☐ | ☐ | ☐ |
| Wrist | ☐ | ☐ | ☐ | ☐ | Wrist | ☐ | ☐ | ☐ | ☐ |
| Elbow | ☐ | ☐ | ☐ | ☐ | Elbow | ☐ | ☐ | ☐ | ☐ |
| Shoulder | ☐ | ☐ | ☐ | ☐ | Shoulder | ☐ | ☐ | ☐ | ☐ |
| Hip | ☐ | ☐ | ☐ | ☐ | Hip | ☐ | ☐ | ☐ | ☐ |
| Knee | ☐ | ☐ | ☐ | ☐ | Knee | ☐ | ☐ | ☐ | ☐ |
| Ankle | ☐ | ☐ | ☐ | ☐ | Ankle | ☐ | ☐ | ☐ | ☐ |
| Foot | ☐ | ☐ | ☐ | ☐ | Foot | ☐ | ☐ | ☐ | ☐ |

**TABLE III**

ROAD ☐
**FOR OFFICE USE ONLY**
SELF-TJC ☐

**FOR OFFICE USE ONLY**

1=0.2 2=0.4 3=0.6 4=0.8 5=1.0 6=1.3 7=1.5 8=1.7 9=1.9 10=2.1 11=2.3 12=2.5
13=2.7 14=2.9 15=3.1 16=3.3 17=3.5 18=3.8 19=4.0 20=4.2 21=4.4 22=4.6 23=4.8 24=5.0
25=5.2 26=5.4 27=5.6 28=5.8 29=6.0 30=6.3 31=6.5 32=6.7 33=6.9 34=7.1 35=7.3 36=7.5
37=7.7 38=7.9 39=8.1 40=8.3 41=8.5 42=8.8 43=9.0 44=9.2 45=9.4 46=9.6 47=9.8 48=10.

C) Please place a check ( ) in the appropriate numerical scale to indicate how would you describe your general health today

| Very Well | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Very Poorly |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

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