An observational study on Assessment of disease activity in Rheumatoid Arthritis patients using Patient based Disease Activity Score 2 (PDAS 2)

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Abstract

Objective

To assess the utility of Patient Based Disease Activity Score 2 (PDAS 2) in assessing the disease activity in Rheumatoid arthritis (RA).

Methods

A prospective cohort study was conducted on 80 patients of RA. The demographic and clinical characteristics of the patients were recorded. They were assessed for disease activity using “Disease Activity Score 28” (DAS 28), “Clinical Disease Activity Index” (CDAI) and PDAS 2 score at baseline (M0), at 2 months (M2) and at 4 months(M4) while they were on treatment. Data was analyzed for correlation of PDAS-2 with other scores and internal reliability. P < 0.05 was considered for statistical significance.

Results

The mean age was 40.13 ± 11.74 years with 70 females and 10 males. There was significant reduction in DAS28, CDAI and PDAS 2 score over 4 month follow up (all scores’ p values < 0.001). Internal reliability (as assessed by Cronbach's Alpha) of PDAS 2 was 0.578. PDAS 2 showed significant correlation with DAS28 at M0, M2 and M4 (r = 0.792, 0.757 and 0.669 respectively, p value < 0.001) and CDAI (r = 0.861, 0.832 and 0.695 respectively, p value < 0.001). Overall there was a significant agreement between DAS 28 and PDAS 2 (K = 0.788,p < 0.001) and between CDAI and PDAS 2 (K = 0.766,p < 0.001).

Conclusion

PDAS-2 score can be routinely used in the clinical practice owing to its correlation with DAS-28/CDAI and because of the advantage that it assessed the patients’ daily living activities.

Introduction

The disease activity in Rheumatoid arthritis (RA) needs regular assessment due to regular fluctuations and guidance of treatment. Clinically, the physicians have the prime focus of controlling the ongoing inflammation, to achieve a low disease activity.

For disease activity, the applied tools in the current scenario include DAS 28, CDAI which are physician dependent and outpatient department (OPD) based. But since the Indian rheumatology are too busy with time constraints, the physician gets little time to assess the disease holistically. So there is an increasing focus on patient-centered care. This has shifted the focus on the tools which are patient dependent rather than physician dependent.
Patient–reported outcome measures (PROMs) have been found to be patient-friendly, non-specific to location and time efficient. The domains generally considered for assessment by patient himself are pain, physical functions, functional disability, patient’s global assessment, emotional and physical well being and sleep disturbances.11–14

Previous studies on the psychometric properties of composite indices based purely on PROMs, such as Patient Activity Scale (PAS), the RADAI11,12 or RAPID-313,14 index, have demonstrated adequate reliability, validity and responsiveness of these indices among patients with RA and proven them to be feasible, informative quantitative measures in busy clinical settings12,14. In RA, self-monitoring of disease at home can make patient self-aware in availing medical advice during increasing disease activity. These considerations inculcated in the development of an index, termed Patient Based Disease Activity Score (PDAS)15.

Earnest H. Choy et al developed and validated PDAS 1 (with ESR) and PDAS 2 (without ESR) in 200815,16. The application of PDAS 2 without any laboratory parameter increases the feasibility of its use by the patients themselves at home15. However there is paucity of data on the correlation of DAS 28 and CDAI and PDAS 2 in RA in Indian population. Thus the current study was undertaken to assess the correlation of PDAS-2 with the routinely applied DAS28 and CDAI.

Methods

The study was a prospective observational cohort study over a period of one year where a total of Eighty patients of RA as per ACR criteria (1987)17 and on regular treatment reporting to the Out Patient Department of Rheumatology Clinic of a tertiary care hospital, Rohtak were enrolled. Patients with severe anemia, hypothyroidism, renal, hepatic, cardiac, or pulmonary disease were excluded. A written informed consent was obtained from all eligible patients. The detailed history and clinical examination along with relevant hematological and biochemical evaluation was done. The patients were primarily on treatment with steroids and conventional synthetic Disease-modifying antirheumatic drugs (csDMARDs) such as sulfasalazine, methotrexate, gold salts, lefunomide and hydroxychloroquine (HCQ). No intra-articular injections or biologicals were given to the study patients. Among all patients, DAS28, CDAI and PDAS-2 scores were calculated (Annexure I) using the formulas:

\[
\text{a) DAS28 score} = 0.56\sqrt{TJC} + 0.28\sqrt{SJC} + 0.70 (\log \text{ESR}) + 0.014 (\text{GH})^{8,9}
\]

Where, TJC = tender joint count (range, 0–28)

SJC = swollen joint count (range, 0–28)

ESR = Erythrocyte sedimentation rate in mm first hr by Wintrobe method

GH = General health as assessed by physician (0-100 mm)
b) CDAI score = SJC + TJC + PGA (VAS, 0 to 10 cm) + EGA (VAS, 0 to 10 cm)\textsuperscript{10}

Where, SJC = swollen joint count (range, 0–28)

TJC = tender joint count (range, 0–28)

PGA = patient global assessment of disease activity (on VAS, 0 to 10 cm)

EGA = evaluator global assessment of disease activity (on VAS, 0 to 10 cm)

c) PDAS 2 score = 2.667 + 0.021*(PGA) + 0.483*(HAQ) + 0.033*(patient 28 SJC) + 0.002*(EMS)\textsuperscript{15}

Where,

PGA – Patient Global Assessment of disease activity (0-100 mm)

HAQ – Health Assessment Questionnaire\textsuperscript{18,19}

Patient 28 Self SJC – Swollen Joint Count of 28 joints as assessed by the patient him/her-self (Supplementary Fig. 1).

EMS – Early Morning Stiffness (in minute).

All subjects were on their medication and all the three mentioned scores were reassessed at baseline (M0) and at follow up of two months (M2) and four months (M4). During the follow up ongoing therapy was changed according to the disease activity (CDAI scores).

**Statistical analysis**

Data was collected, plotted on Microsoft excel sheet and analyzed statistically by using SPSS software. The PDAS 2 score was compared with DAS-28, CDAI score; and with disease activity variables of DAS28 and CDAI. Pearson Correlation test was used to assess the correlation between two quantitative variables. Cronbach’s alpha test was used to check the internal consistency of the indicators used in PDAS-2. Inter class correlation co-efficient was measured to assess the agreement between PDAS-2 and DAS-28/CDAI. For all tests confidence interval was kept at 95 percent. Statistical significance was measured by p-value < 0.05.

**Results**

The mean age of study group was 40.13 ± 11.74 year and there 70 females and 10 males. (Table I). The mean duration of the disease was 67.5 ± 57.8 months.

**Assessment of disease activity**
Disease activity was assessed using DAS 28, CDAI and PDAS 2 score at baseline (M0), at 2 months (M2) and at 4 months (M4) follow up (Table II). There was a statistically significant reduction (all p values < 0.001) in DAS28, CDAI and PDAS 2 score over 4 month duration of therapy (Table-III). This may be because of the introduction of steroids in the early phase of the treatment.

PDAS 2 score showed significant (all p value < 0.001) correlation with DAS28 and CDAI score at M0, M2 and M4 as assessed by Pearson's coefficient (Table IV). Cronbach's Alpha was used to calculate internal reliability of scores. It was 0.799 for DAS28, 0.794 for CDAI and 0.578 for PDAS 2 score. (Table V). It was noticed that if early morning stiffness was excluded from PDAS-2, its Cronbach's Alpha value turned to be highly significant 0.757 (Table VI). To measure the agreement between disease activity categories of PDAS 2, DAS28 and CDAI, the inter-class coefficient (ICC) was used. The agreement between DAS 28 and PDAS 2 was 0.788 (p < 0.001) and between CDAI and PDAS 2 was 0.766 (p < 0.001) (Table VII), which is comparable to agreement between DAS 28 and CDAI, that is, 0.757 (p < 0.001).

Discussion

The ongoing advancements in therapeutics require continuous upgrade in disease activity measurement tools. The present study holds strength in showing the positive correlation of PDAS-2 with the currently applied physician centered clinical tools (DAS-28 and CDAI).

In the normal outpatient departments it is very difficult and time consuming to assess the RA disease activity using well known score (e.g. DAS28, CDAI). All indices to assess disease activity in RA have some shortcomings. DAS 28 includes 4 variables and it requires complex calculations like square root and logarithm. Further, DAS 28, SDAI, CDAI do not include patient functional status {Health assessment Questionnaire (HAQ)}, which is the best predictor of most severe long term outcomes of RA.

These shortcoming are overcome with the use of PDAS-2 where the clinical symptoms of the disease are self-assessed by the patients at home. It includes all the clinical symptoms of RA like fatigue, early morning stiffness, tender joint count and swollen joint count. In comparison to PDAS-1, PDAS-2 has an advantage of not including ESR measurement which is a laboratory based test.  

In our study PDAS 2 was significantly correlated with DAS28 with Pearson's coefficient 0.792, 0.757 and 0.669 and with CDAI with Pearson's coefficient 0.861, 0.832 and 0.695 respectively at M0, M2, M4 intervals which is comparable to the correlation shown in study done by Earnest H choy et al (2008)\textsuperscript{15} (between DAS28 and PDAS 2 score was 0.76 and between CDAI and PDAS 2 score was 0.73). In our study the agreement between DAS 28 and PDAS 2 was 0.788 (p < 0.001) and between CDAI and PDAS 2 was 0.766 (p < 0.001) which is comparable to agreement between DAS 28 and CDAI 0.757 (p < 0.001). The study by Alexander M.H. Leung et al\textsuperscript{16} depicted similar results (correlation between DAS 28 and PDAS 2 was 0.650; between CDAI and PDAS 2 score was 0.680 and between CDAI and DAS28 was 0.810). In our study, the cronbach's alpha for PDAS 2 was 0.578. It was noticed that if early morning stiffness was excluded from PDAS 2 its Cronbach's Alpha value turned to be highly significant 0.757
suggesting a good internal consistency. In the study of Earnest H Choy et al cronbach's alpha of PDAS 2 was 0.400. They also opined that early morning stiffness score can be omitted without significantly affecting the validity and sensitivity of the instrument\textsuperscript{15}.

The PDAS-2 holds strength since the subjects found it very easy to fill. Subjects, by self assessing their disease activity using PDAS 2 questionnaire, improved their overall understanding of the disease. Many of them agreed that their understanding and involvement helped optimizing medication; as using PDAS 2 they could assess disease activity on that very day; an early and prompt medical attention could be sought which is important in line of management. However the score suffers from the limitation that the it requires the patient to be well educated and with a good common sense. The ignorant behaviour or the lack of understanding of the clinical assessment tool may cause an underestimation of the disease activity as well, leading to worse consequences.

**Conclusion**

Use of PDAS 2 may be a novel approach for RA as the other disease activity scores (DAS28 and CDAI) assess the inflammatory part of disease objectively, but do not assess the impact on activity of daily living. Single- handed practitioners and clinicians working in an environment in which resources are limited could adopt patient-derived measures of disease activity such as the PDAS 2. It could also be used in Web-based recording of disease activity in future years. Nonetheless, it is suggested that larger and longer duration studies are needed to establish the firmness of the above correlation between PDAS 2 (PRO) and DAS 28 and CDAI (conventional method) to assess disease activity.

**Declarations**

The authors report no conflict of interest.

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The ethical clearance was waived off since the study did not affect the patient outcomes.

A written informed consent was obtained from the patients before enrolling them into the study.

The authors give full consent for publication and data.

Code availability: NA

Author contributions:

Conception Of Work ; HS, SG, HK, PY and MK

Design ; HS, SG

Acquisition ,Analysis And Interpretation Of Data : HK, PY and MK
Drafting of work and critical revision; HK, PY and MK

Final version for publication approved by all authors

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**Tables**

**Table I: Showing age distribution.**
| Age group in years | Number of subjects | Total No. | Percent (%) |
|-------------------|--------------------|-----------|-------------|
|                   | Male   | Female |           |             |
| 18-39             | 2      | 43     | 45         | 56.2        |
| 40-59             | 3      | 23     | 26         | 32.5        |
| 60-79             | 5      | 4      | 9          | 11.3        |
| Total No.         | 10     | 70     | 80         |             |

Table II: Mean values of the disease activity characteristics of the study

| Variable                                      | Mean at M0 ±SD | Mean at M2 ±SD | Mean at M4 ±SD | Change in M4-M0 | P value |
|-----------------------------------------------|----------------|----------------|----------------|------------------|---------|
| Tender joint counts (TJC)                     | 7.93±8.40      | 7.51±6.52      | 5.96±4.90      | 0.76             | <0.001  |
| Swollen joint counts (SJC)                    | 4.04±5.98      | 3.74±3.53      | 2.99±2.45      | 1.05             | 0.006   |
| Patient global assessment (PGA in mm)         | 43.0±22.70     | 39.4±23.10     | 32.6±17.40     | 1.04             | <0.001  |
| Evaluator global assessment (EGA in cm)       | 3.79±2.19      | 3.56±1.94      | 2.91±1.46      | 0.88             | <0.001  |
| Erythrocyte sedimentation rate (ESR in mm/1st hr) | 31.74±17.65  | 20.96±10.95    | 22.28±12.09    | 1.96             | <0.001  |
| Early Moring Stiffness (EMS in min)           | 53.00±78.17    | 42.50±60.66    | 39.00±67.49    | 14               | 0.056   |
| General Health (GH)                           | 3.79±2.19      | 3.56±1.94      | 2.91±1.46      | 0.88             | <0.001  |
| Self Swollen joint counts (Self SJC)          | 3.76±5.40      | 3.70±3.54      | 3.01±2.26      | 1.05             | 0.006   |
| Healthassessment Questionnaire (IHAQ):        | 0.97±0.63      | 0.58±0.38      | 0.34±0.24      | 0.04             | <0.001  |

Table III: Table showing values of disease activity score.

| Variable | Mean±SD at M0 | Mean±SD at M2 | Mean±SD at M4 | Change in scores (M4-M0) | P value |
|----------|---------------|---------------|---------------|--------------------------|---------|
| DAS 28 score | 2.84±1.17    | 2.79±0.96     | 2.62±0.83     | 0.22                     | <0.001  |
| CDAI score   | 20.05±17.13  | 18.75±12.05   | 15.13±8.87    | 4.92                     | <0.001  |
| PDAS 2 score | 4.33±1.02    | 3.94±0.82     | 3.65±0.62     | 0.68                     | <0.001  |
Table IV. Correlation between the DAS 28 and PDAS 2 and between CDAI and PDAS 2 score.

| Period | DAS28 Mean± SD | PDAS2 Mean± SD | Pearson's correlation coefficient (r) | p-value |
|--------|----------------|----------------|--------------------------------------|---------|
| M0     | 2.84±1.17      | 4.33±1.02      | 0.792                                | <0.001  |
| M2     | 2.79±0.96      | 3.94±0.82      | 0.757                                | <0.001  |
| M4     | 2.62±0.83      | 3.65±0.62      | 0.669                                | <0.001  |

| CDAI Mean± SD | PDAS 2 Mean± SD |
|---------------|-----------------|
| M0            | 20.05±17.13     | 4.33±1.02     |
| M2            | 18.75±12.05     | 3.94±0.82     |
| M4            | 15.13±8.87      | 3.65±0.62     |

Table V. Showing Cronbach’s Alpha value

|                | DAS 28 | CDAI | PDAS 2 |
|----------------|--------|------|--------|
| Alpha value    | 0.799  | 0.794| 0.578  |

Table VI. Cronbach’s Alpha value of PDAS 2 after deletion of one item one be one.

| Items Deleted | Cronbach's Alpha |
|---------------|------------------|
| PGA           | 0.568            |
| HAQ           | 0.566            |
| Self SJC      | 0.554            |
| EMS           | 0.757            |

Table VII. Showing the Interclass correlation coefficient of DAS 28, CDAI and PDAS 2 scores.

| Agreement between scores | Interclass correlation coefficient | P value |
|--------------------------|-----------------------------------|---------|
| DAS 28 and PDAS 2        | 0.788                             | <0.001  |
| CDAI and PDAS 2          | 0.766                             | <0.001  |
| Overall between all three scores | 0.798                       | <0.001  |
| DAS 28 and CDAI          | 0.757                             | <0.001  |
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