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.[1] Clinically, the physicians have the prime focus of controlling the ongoing inflammation,[2] to achieve a low disease activity.[3,4]

For disease activity, the applied tools in the current scenario include DAS 28, CDAI which are physician dependent and outpatient department (OPD) based.[5–10] 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 RADAI[11,12] or RAPID-3[13,14] 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 settings[12,14]. 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 2008[15,16]. The application of PDAS 2 without any laboratory parameter increases the feasibility of its use by the patients themselves at home[15]. 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, leflunomide 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:

a) DAS28 score = $0.56\sqrt{TJC} + 0.28\sqrt{SJC} + 0.70\ (\log ESR) + 0.014\ (GH)$[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)[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)[15]

Where,

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

HAQ – Health Assessment Questionnaire[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 PDSA 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 baaed test.[20]

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)[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 PDSA 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[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[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

References

1. Marjonne CW, Creemers, Leo BA, Isenberg DA, Maddison PJ, Woo P ,et al Rheumatoid Arthritis. Oxford Text Book of Rheumatology. 3rd New York: Oxford University Press; 2008. p. 697-710.
2. Wolfe F,Cush JJ, O'Dell JR, Kavanaugh A, Kremer JM, Lane NE**,** et al. Consensus recommendations for the assessment and treatment of rheumatoid arthritis. J Rheumatol. 2001;28:1423-30.
3. Fransen J,Stucki G, van Riel P. The merits of monitoring: should we follow all our rheumatoid arthritis patients in daily practice? Rheumatology (Oxford). 2002; 41:601-4.
4. Kiely PD,Brown AK, Edwards CJ, O'Reilly DT, Ostör AJ, Quinn M, et al. Contemporary treatment principles for early rheumatoid arthritis: a consensus statement.Rheumatology (Oxford). 2009;48:765-72.
5. Klinkhoff AV, Bellamy N, Bombardier C, Carette S, ChalmersA, Esdaile JM, et al. An experiment in reducing interobservervariability of the examination for joint tenderness. J Rheumatol. 1988;15:492–4.
6. Scott DL, Choy EH, Greeves A, Isenberg D, Kassinor D, RankinE, et al. Standardising joint assessment in rheumatoid arthritis. ClinRheumatol. 1996;15:579–82.
7. Thompson PW, Hart LE, Goldsmith CH, Spector TD, Bell MJ, Ramsden MF. Comparison of four articular indices for use inclinical trials in rheumatoid arthritis: patient, order and observer variation. J Rheumatol. 1991;18:661–5.
8. Van der Heijde DMFM, van ‘t Hof MA, van Riel PLCM, Theunisse LAM, Lubberts EW, Van Leeuwen MA et al. Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. Ann Rheum Dis. 1990;49:916–20.
9. Prevoo MLL, van ‘t Hof MA, Kuper HH, van Leeuwen MA, Van de Putte LBA, van Riel PLCM. Modified disease activity scores that include twenty eight-joint counts: development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum. 1995;38:44–8.
10. Jaclyn K. Anderson, Jimmerman L, Caplan L, and Michaudk K. Measures of Rheumatoid Arthritis Disease Activity Patient (PtGA) and Provider (PrGA) Global Assessment of Disease Activity, DiseaseActivity Score (DAS) and Disease Activity Score With 28-Joint Counts (DAS28),Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), PatientActivity Score (PAS) and Patient Activity Score-II (PASII), Routine Assessment of PatientIndex Data (RAPID), Rheumatoid Arthritis Disease Activity Index (RADAI) andRheumatoid Arthritis Disease Activity Index-5 (RADAI-5), Chronic Arthritis SystemicIndex (CASI), Patient-Based Disease Activity Score With ESR (PDAS1) and Patient-BasedDisease Activity Score Without ESR (PDAS2), and Mean Overall Index for RheumatoidArthritis (MOI-RA).Arthritis Care & Research. 2011;63:14-36.

11. Stucki G, Liang MH, Stucki S, Bruhlmann P, Michel BA : A self-administered rheumatoid arthritis disease activity index (RADAI) for epidemiologic research. Psychometric properties and correlation with parameters of disease activity. Arthritis Rheum. 1995;38:795-8.
12. Veehof MM, Ten Klooster PM, Taal E, van Riel P L C M, van de Laar M A F J: Psychometric properties of the rheumatoid arthritis disease activity index (RADAI) in a cohort of consecutive Dutch patients with RA starting antitumor necrosis factor treatment. Ann Rheum Dis. 2008;67;789-93.
13. Pincus Y. Yazicy, Bergman M, Maclean R, Harrington T: A proposed continuous quality improvement approach to the assessment and management of patients with rheumatoid arthritis without formal joint counts based on quantitative routine assessment of patient index data (RAPID) scores on a multidimensional health assessment questionnaires (MDHAQ). Best Pract Res Clin Rheumatol. 2007;21:789-04.
14. Wolfe F, Michaud K, Pincus T. A composite disease activity scale for clinical practice, observational studies and clinical trails: the patient activity scale (PAS/PAS-2). J Rheumatol. 2005;32:2410-5.
15. Choy EH, Khoshaba B, Cooper D,MacGregor A, Scott DL. Development and validation of a patient-based disease activity score in rheumatoid arthritis that can be used in clinical trials and routine practice. Arthritis Rheum. 2008;59:192-9.
16. Alexander MH. Farewell LD, Lau CS, Ernest HS. Defining criteria for rheumatoid arthritis patient-derived disease activity score that correspond to Disease Activity Score 28 and Clinical Disease Activity Index based disease states and response criteria. Rheumatology. 2016;55:1954-8.
17. Aletaha D, Neogi T, Silman AJ, Funovitis J, Felson DT, Birnbaum NS, et al. Rheumatoid Arthritis classification criteria: An American college of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum. 2010;62(9):2569-81.
18. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum. 1980;23:137-45.
19. Bruce B, Fries JF. Health Assessment Questionnaire HAQ. Clin Exp Rheumatol. 2005;23:S14-8.
20. Pollard LC, Kingsley GH, Choy EH, Scott DL. Fibromyalgia rheumatoid arthritis and disease assessment. Rheumatology 2010;49:924-8.

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/1sthr)	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	0.861	<0.001
M2	18.75±12.05	3.94±0.82	0.832	<0.001
M4	15.13±8.87	3.65±0.62	0.695	<0.001

Table: V. Showing Cronbach's Alpha value

DAS 28	CDAI	PDAS 2
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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