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PASS As A Benchmark Among Outcome Measures In Rheumatoid Arthritis – How Well Does It Fare ?

James E[1], Suseem S R[2*]

[1,2*]Vellore Institute of Technology, Vellore Email: srsuseem@vit.ac.in

***Corresponding Author:-**, Suseem S R
*Vellore Institute of Technology, Vellore Email: srsuseem@vit.ac.in

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ABSTRACT:
PASS acronym stands for Patient Acceptable Symptomatic State and is a simple global dichotomous question, the response to which determines the PASS status of a Rheumatoid Arthritis (RA) patient whether – satisfied or unsatisfied. An affirmative response indicates a patient perceived satisfactory state of this disease/symptoms while a negative response is an indication of patient dissatisfaction. RA symptoms are known to alleviate in remission hence a PASS positive response is also likely to be associated with clinical remission. Here we have assessed the 2 subsets of PASS patients i.e PASS positive and PASS negative and correlated the clinical reported outcomes with patient reported outcomes including PASS. Our study indicates a significant correlation between majority of clinical outcome measures and PASS states , however this was found not to be the same in the case of (Clinical Disease Activity Index) CDAI, (Rheumatoid Arthritis Disease Activity Index) RADAI and Visual Analogue Scale (VAS). Our study also investigated the persistence of symptoms in PASS positive status patients who were also identified to be in clinical remission. using a modified PASS questionnaire. 68% of the patients defined to be in clinical remission acknowledged the persistence of bothersome symptoms of the disease even in their remission state. Only 32% of the patients having clinically remission status were completely liberated from nagging RA symptoms. Hence, it is of therapeutic significance to address the needs of such patients though labelled to be in clinical remission and support them to achieve a complete remission including remission from the patient perspective.

INTRODUCTION: A well-managed rheumatology clinic involves the patient as an informed decision maker in his healthcare needs. Patient responses to questionnaires can generate data which help the clinician in the decision making process to determine the future course of therapy. Patient education can improve health outcomes and reduce health-care costs[1]. There are several patient reported outcome measures that are developed to tap into this cheap, readily available patient resource. Patient-reported outcome measures (PROMs) are questionnaires that collect health outcomes directly from the people who experience them. However patient bias, time constraints and lack of reliability of such measures can hamper such data from being put to good use.[2] Evidence directly linking collection of PRO measures to improvements in performance is conflicting or lacking [3,4,5,6,7].

Patients with rheumatoid arthritis (RA may experience persistent pain or discomfort despite being declared in clinical remission. While physicians primarily focus on specific RA-related outcomes, patients are more concerned about the overall impact of RA on their general health. Addressing and managing the ongoing symptoms reported by patients is crucial, as clinical and laboratory

evaluations may not identify these issues, particularly when inflammatory markers or joint counts appear normal, especially in remission cases. Therefore, the evaluation of patient-reported outcomes becomes highly significant, offering a perspective that unveils aspects overlooked by clinical and lab assessments. This approach can greatly alleviate the patient's experience and contribute to achieving effective remission from the patient's viewpoint.

Many measures of outcome are being used in the assessment of RA. These include the traditional well established CROs (Clinical Reported Outcomea) which measure the clinical outcomes, disease activity and functional status of the patient. In this cross-sectional analytical study, we have attempted to collect patient responses using numerous PROMs such as PASS, RADAI, Health Assessment Questionnaire (HAQ), Patient Global Health (PGH), Visual Analogue Scale VAS (pain), Tender Joint Count (TJC) and Swollen Joint Count (SJC). Clinically generated data like CDAI, Disease Activity Score (DAS 28) ESR, VAS (pain) ,TJC and SJC on physical examination were also determined. The PASS states of the patient were of particular interest in this study.

PASS: Remission is not attainable for all patients and therefore a useful measure of outcome is whether patients have achieved a level of health that is deemed 'acceptable' by the patient, the 'patient acceptable symptom state' (PASS).[9,10, 11,12] PASS is a popular PROM used in various rheumatological conditions. PASS acronym stands for Patient Acceptable Symptomatic State and is a simple global dichotomous question, the response to which determines the PASS status of the patient, an affirmative response indicating a patient perceived satisfactory state of his disease/symptoms while a negative response is an indication of patient dissatisfaction. RA symptoms are known to alleviate in remission hence a PASS positive response is also likely to be associated with clinical remission. Various clinical disease activity indices like CDAI and DAS28 ESR have established cut-off values for remission. [13, 14, 15, 16,17]

Hence, it is our objective to compare the PASS status of our study population vis a vis the clinical remission status. A modified and validated PASS question was also developed to probe into the persistence of worrisome symptoms even in remission patients. The responses were correlated with clinical disease activity score DAS 28 ESR.

AIM: To study the PASS patients with respect to their clinical, lab and other outcomes.

PRIMARY OBJECTIVE:

To categorise the patients as PASS positive and PASS negative based on response to the dichotomous PASS question and correlate the PASS status obtained with other composite scores like CDAI, DAS 28 ESR and functional scores as well as lab parameters.

SECONDARY OBJECTIVE: To study a modified PASS question to ascertain the persistence of symptoms in clinically remission patients. (PASS Q 2)

To study the change in PASS response with DAS 28 ESR scores.

METHODOLOGY: The ethical clearance for the study was obtained prior to the study from the VIT Ethical Committee for studies on human subjects (VIT/IECH/006) as well as the independent ethical committee at Sree Sudheendra Medical Mission (IEC/2020/17), Kochi, Kerala. The study included 280 consecutive patients who attended the RA clinic or RA OP at Dr Shenoy's CARE, Kochi, Kerala, India from September 2020 to August 2021, Kochi after fulfilling inclusion- exclusion criteria. Patient Information Sheet and Informed Consent was obtained from the patients and other ethical concerns fulfilled. Data Collection Forms and other documents

A one-time evaluation of their lab values, clinical evaluation and patient reported outcomes was done. PASS a patient tool is used to distinguish between patients who have a self-reported acceptable state of their disease symptoms and those not satisfied with their symptomatic state. The PASS question *"Considering all the different ways your diseases is affecting you, do you consider your present state satisfactory?"* The response to this question was then correlated with the clinical outcomes particularly DAS 28, ESR and CDAI. [18,19 20] The modified PASS Question 2 viz *"Are you free from all the worrisome symptoms of your disease?"* was also answered by the patients and responses were similarly analysed. The modfied PASS questionnaire was intended to investigate whether a completely symptom free state existed or not among the remission patients and whether this correlated well with clinical reported outcomes.

RESULT AND DISCUSSION: It was found that the PASS positive group fared better in most of the disease outcome measures compared to the PASS negative group. The mean scores of each outcome measures was found to significantly different in the two groups (Table1) thus indicating that the PASS tool can be effectively used to identify and differentiate the two population sets.

The difference in the 2 groups is highly significant indicating that PASS positive response can be comparable to a clinical remission state. This difference was not found to be significant in disease activity scores viz. CDAI and RADAI

Table 1: PASS states of the population and the mean scores obtained of various tools.

TOOL	PASS STATUS	NUMBER	MEAN SCORE
RADAI	YES	100	1.9060
	NO	180	1.9450
CDAI	YES	100	4.0204
	NO	180	4.1591
HAQ	YES	100	0.5724
	NO	180	0.7144
DAS28	YES	100	2.2006
	NO	180	3.0427
ESR	YES	100	15.990
	NO	180	27.283
TJC	YES	100	1.4600
	NO	180	2.7500
TJC (Patient reported)	YES	100	1.6800
	NO	180	3.3000
SJC	YES	100	1.0400
	NO	180	2.3944
SJC (Patient reported)	YES	100	1.3100
	NO	180	2.9611
VAS	YES	100	3.0950
	NO	180	3.6139
VAS (Patient reported)	YES	100	3.1850
	NO	180	3.6583

Table 2: Significance in Mann Whitney U test Comparison of various parameters when compared to traditional PASS questionnaire

Sr. No	Variables	P value

1	RADAI	0.655
2	CDAI	0.858
3	HAQ	0.037
4	DAS 28	0.000
5	ESR	0.000
6	TJC	0.000
7	TJC (Patient Reported)	0.000
8	SJC	0.000
9	SJC (Patient reported)	0.000
10	VAS	0.018
11	VAS (Patient reported)	0.025

As shown in Table 2, there is a very significant correlation between PASS states and DAS 28 ESR, TJC, SJC, VAS and also HAQ . However this was found to be not so significant in CDAI, RADAI.
The correlation between the Modified PASS outcomes and various parameters was also studied. HAQ, DAS 28, ESR, TJC (patient as well as clinician reported) and SJC (Patient as well as clinician reported) were found to correlate well with mPASS. Correlation with RADAI, CDAI and VAS were found to be insignificant. (Table 3)

Table 3. Modified PASS states of the population and the mean scores obtained of various tools.

	PASS	N	Mean	SD	*p-value*
RADAI	YES	59	1.84	1.328	*0.552*
	NO	221	1.96	1.339	
CDAI	YES	59	3.03	3.791	*0.202*
	NO	221	4.29	7.254	
HAQ	YES	59	0.52	0.320	*< 0.01*
	NO	221	0.70	0.456	
DAS28	YES	59	2.27	0.410	*< 0.001*
	NO	221	2.87	0.946	
ESR	YES	59	16.0	6.802	*< 0.001*
	NO	221	25.18	15.840	
TJC	YES	59	1.32	1.382	*< 0.001*
	NO	221	2.55	2.158	
TJC (PT)	YES	59	1.61	1.608	*< 0.001*
	NO	221	3.02	2.421	
SJC	YES	59	0.83	0.985	*< 0.001*
	NO	221	2.19	2.116	
SJC (PT)	YES	59	1.15	1.201	*< 0.001*
	NO	221	2.69	2.322	
VAS	YES	59	3.12	2.001	*0.179*
	NO	221	3.51	1.988	
VAS (PT)	YES	59	3.17	1.904	*0.168*
	NO	221	3.57	2.027	

Table 4. Significance in Mann Whitney U test Comparison of various parameters when compared to modified PASS question. (Question 2)

Sl.Nos	Outcome Tools	Significance
1	RADAI	0.567
2	CDAI	0.269
3	HAQ	0.014
4	DAS 28	0.000
5	ESR	0.000
6	TJC	0.000
7	TJC (Patient Reported)	0.000
8	SJC	0.000
9	SJC (Patient reported)	0.000
10	VAS	0.147
11	VAS(patient reported)	0.144

Table 5: Significance values obtained using Mann Whitney and Wilcoxon Test

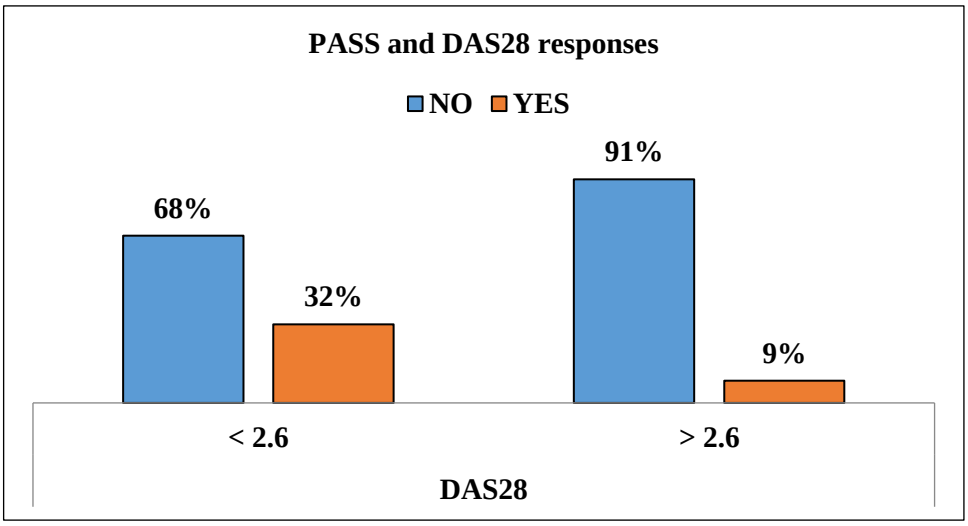
	RADAI	CDAI	HAQ	DAS28	ESR	TJC	TJC (PT)	SJC	SJC (PT)	VAS	VAS (PT)
Mann-Whitney U	6204.000	5927.000	5159.000	3642.000	4064.000	4128.500	4172.500	3775.000	3777.500	5726.000	5721.500
Wilcoxon W	7974.000	7697.000	6929.000	5412.000	5834.000	5898.500	5942.500	5545.000	5547.500	7496.000	7491.500
Z	-.572	-1.106	-2.469	-5.211	-4.469	-4.419	-4.314	-5.104	-5.047	-1.452	-1.460
Asymp. Sig. (2-tailed)	.567	.269	.014	.000	.000	.000	.000	.000	.000	.147	.144

Table 6. Chi square test showing significance of DAS 28 remission states with PASS response.

PASS	DAS28		Total	$\chi 2$	df	*p-value*
	< 2.6	≥ 2.6				
NO	100 (68%)	121(91%)	221	22.11	1	*< 0.001**
YES	47 (32%)	12 (9%)	59			
Total	147	133	280			

As shown in graph 1 (Table 6) majority of the non remission patients (91%) with DAS28 greater than 2.6 responded as PASS negative using the PASS Questionnaire 2.

Graph 1. PASS (as modified Question 2) in DAS 28 remission non remission states.



From the figure we can conclude that 68% of patients who responded negatively to the modified PASS (PASS Question 2) had a clinical remission state of DAS 28 ESR value <2.6. Only 32% who responded positively were also clinically in remission states. Other studies by Heiberg T, et al have shown that a positive response to PASS, when using the external anchoring question focusing on "satisfactory condition," is associated with a range of moderate disease activity, assessed with several composite indices, such as DAS 28, CDAI, and SDAI [21]. These findings are also in accordance with the study done by Salaffi F et al which demonstrated the discordance between CDAI and PASS scores. [22]

However, in patients who were clinically in active disease state ie DAS value > 2.6, the PASS response also indicated a negative state as shown by 91% responding to be PASS negative. Only 9 % clinically having active disease responded to be in positive PASS state. Thus, the modified PASS question 2 has a greater correlation with disease activity in non remission patients compared to the remission state. The question put forth as PASS 2 was "Are you free from all the worrisome symptoms of your disease?" Studying the response we can pointedly say that though patients were in a clinically remission state as well as PASS positive based on the first PASS question but a major percentage of this population (68%) were not really rid of their disease symptoms, but reported a satisfactory state of disease acceptance. Thus even in the clinically remission group there is need to address the state of symptoms and address the persistence of worrying symptoms. This may also pose the question if the existing threshold for clinical remission by DAS 28 is higher when the patients perspective is taken into consideration. It would be interesting to know if a DAS 28 threshold exists where ALL worrisome symptoms of the disease are non-existent and what would it be?

CONCLUSION:

Rheumatoid Arthritis and its accompanying disability symptoms including pain, swelling in the joints, fatigue can compromise the quality of life of the patients in many ways. The intensity of the symptoms in RA patients show waxing and waning patterns depending on the body's inflammatory status and a total symptom free state is a challenge to achieve and quite rare clinically. The patients of RA have lingering pain or discomfort even though they may be declared to be in clinical remission. Clearly, physicians are most focused on "RA-specific outcomes," whereas patients are more focused on how the general health state is affected by RA [23].

Thus the persistence of worrisome symptoms experiend by the patient needs to be addressed and managed. Clinical and lab evaluation reports do not necessarily detect these issues as inflammatory markers or joint counts appear to be normal especially in the remission patients. However, the

patient continues to experience and suffer . Hence the role of patient reported outcome evaluation is very significant and can be used to assess the disease from the patients perspective which can contribute to reveal aspects ignored by clinical and lab outcomes. This can go a long way to ease the patient and bring about effective remission also from the point of view of the patient.

Author's contribution:

Suseem SR participated in the design of the study and supervised the study and gave final approval of the version of the paper to be published. James Emily made substantial contributions to the conception and design of the study, participated in the acquisition of data, and was involved in revising the paper for important intellectual content. Both authors read and approved the final paper.

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