EVALUATION OF EFFICACY OF INDICES IN PSORIASIS IN RELATION TO SEVERITY AND IMPROVEMENT IN THERAPY

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BACKGROUND

Psoriasis is a chronic disfiguring, inflammatory and proliferative condition of the skin in which both the genetic and environmental factors have a critical role. Many environmental factors like the trauma, infection, drugs, sunlight, metabolic factors, psychogenic factors, alcohol and smoking have been linked to psoriasis and have been implicated in initiation of disease process and exacerbation of pre-existing disease treatment.

ABSTRACT

METHODS

The present study is conducted on a total of 40 patients, who presented with chronic plaque psoriasis to Department of DVL, Osmania General Hospital, Hyderabad, from September 2014 to July 2015. All the 40 cases were subjected to thorough clinical examination and investigations. We performed the calculations of BSA, PGA, PASI, PLASI in the cases.

RESULTS

The mean results of BSA, PGA, PASI, PLASI before and after 8 weeks of treatment with methotrexate were calculated. The mean score before and after treatment therapy differed significantly (p <0.0001). Largest absolute difference was found with PLASI (35.1) followed by PASI (19), BSA (12.8), PGA (4). Largest relative difference was found with PLASI (86.32%), PASI (84.16%), PGA (80%) and BSA (75.75%).

CONCLUSIONS

Strength of each correlation was compared. The correlation between PLASI and PASI (r=0.932) was significantly stronger than correlation between any other two indices. Correlation between PLASI and BSA (r=0.593) was found to be weakest among all other indices. Correlation with PGA with PASI, PLASI was weaker than correlation between PASI and PLASI. In our study, the slope of the regression for PLASI (b = 3.319) vs. PASI (b = 2.462) indicates that PLASI is more accurate than PASI. In the regression analyses, all other slopes were less than unity indicating that the severity differentiation was inferior, especially when BSA was involved in the analysis.

KEYWORDS

Psoriasis, BSA, PGA, PASI, PLASI.

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INTRODUCTION

Psoriasis is a chronic disfiguring, inflammatory and proliferative condition of the skin in which both the genetic and environmental factors have a critical role. Many environmental factors like the trauma, infection, drugs, sunlight, metabolic factors, psychogenic factors, alcohol and smoking have been linked to psoriasis and have been implicated in initiation of disease process and exacerbation of pre-existing disease. Many measures are established to evaluate severity of skin disease. In psoriasis clinical trials, the most common measure is Psoriasis Area Severity Index (PASI).

Financial or Other, Competing Interest: None. Submission 09-08-2016, Peer Review 01-09-2016, Acceptance 08-09-2016, Published 15-09-2016. Corresponding Author: Dr. Venkata Krishna Ananthula, H. No. 21-41, Vivekananda Nagar, Dilsukhnagar, Hyderabad-500060, Telangana. E-mail: drvkananthula@gmail.com DOI: 10.14260/jemds/2016/1244 Several years later psoriasis log based area and severity index (PLASI) were introduced. This study investigates the strengths of these individual measures and aims to select best fitting measure to describe the severity and improvement after treatment.

Measures to Assess Psoriasis

To measure disease severity and effectiveness of therapies, good clinical psoriasis measures are a necessity. The purpose of this study was to identify all clinical measures of psoriasis severity and outcome in use and to evaluate the quality of these measures. We identified 53 separate clinical measures, which were regrouped into 4 measures for quality analysis.

The Psoriasis Area and Severity Index is the most commonly used clinical measure in research, but it has substantial limitations such as low response distribution, no consensus on interpretability, and low responsiveness in mild disease. Nevertheless, because of its widespread use the Psoriasis Area and Severity Index permits some degree of comparison of results among clinical trials.

All Retrieved Clinical Outcome Measures Re-Grouped in 4 Main Clinical Severity and Outcome Measures for Analysis 1. Body Surface Area (BSA).

- 2. Physician's/Psoriasis Global Assessment (PGA) Static assessment.
- 3. Psoriasis Area and Severity Index (PSI).
- 4. Psoriasis Long Based Area and Severity Index (PLASI).

Body Surface Area (BSA)

Most commonly used to estimate the BSA is the "rule of nines" (Ramsay and Lawrence, 1991).¹ It is defined as 9% coverage for the head and neck, each arm, anterior and posterior leg as well as the four trunk quadrants respectively, leaving 1% for the genitalia. The BSA can also be estimated by the number of patients' hand areas affected, assuming that one "handprint" reflects approximately 1% of BSA.

BSA is arithmetic mean of the affected skin surface based on assumption that Head (H), the Upper Limbs (UL) 20%, Trunk (T) 30%, Lower Limbs (LL) 40% of total body surface area.

The Formula for Calculation of BSA is:

 $BSA = 0.1*BSA_{H} + 0.2*BSA_{UL} + 0.3*BSA_{T} + 0.4*BSA_{LL}$

PHYSICIAN GLOBAL ASSESSMENT

Generally speaking, the PGA is an average assessment of all psoriatic lesions based on erythema, scale and induration. Typically, the PGA is a 5, 6 or 7-point ordinal rating ranging from "clear" to "very severe psoriasis." In addition to the different approaches to PGA, the PGA tool described in clinical trials varies widely. This variation has the potential to produce non-standardised results. The scales used range from 4 points to 10 points and although all typically evaluate the average erythema, plaque elevation and scale of all involved lesions.

Grade	Description	Response	
0	Completely Clear	No evidence of disease;	
0	completely clear	100% improvement CR	
		Very significant	
		clearance	
1	Almost Clear	(≥ 90% to < 100%);	
		only traces of disease	
		remain PR	
		Significant improvement	
2	Marked Improvement	(≥ 75% to < 90%);	
2	Markeu improvement	some evidence of disease	
		remains PR	
	Moderate Improvement	Intermediate between	
3		slight and marked	
3		improvement;	
		(≥ 50% to < 75%) PR	
	Slight Improvement	Some improvement	
4		(≥ 25% to < 50%);	
т		significant evidence of	
		disease remains SD	
		Disease has not changed	
5	No Chango	from	
5	No change	baseline condition	
		(+ <25%) SD	
		By ≥ 25% or more PD CR	
6	Worse Disease is Worse than at Baseline	= complete response;	
		PR = partial response; SD	
	Evaluation	= stable disease;	
		PD = progressive disease.	
Supplementary Table 1: Physician's Global Assessment of			
Clinical Condition (Dynamic)			

STATIC PGA

Rate Psoriasis Severity at each Time Point, for each Patient using Static PGA

- 6 Severe psoriasis.
- 5 Moderate-to-severe psoriasis.
- 4 Moderate psoriasis.
- 3 Mild-to-moderate psoriasis.
- 2 Mild psoriasis.
- Psoriasis almost cleared.
- Clear (no lesions).

Psoriasis Area and Severity Index (PASI)

In 1978, the PASI was developed to assess the effects of retinoids in psoriasis (Fredriksson and Pettersson, 1979).^{2,3} The affected area and lesion characteristics are entered in a formula that results in a score from 0 to 72.

A patient's Psoriasis Area and Severity Index (PASI) is a measure of overall psoriasis severity and coverage. It is a commonly-used measure in clinical trials for psoriasis treatments.

PASI consists of Two Major Steps:

- 1. Calculating the BSA (Body Surface Area) covered with lesions.
- 2. Assessment of the severity of lesions. The second step in turn consists of assessing lesions erythema (Redness), induration (Thickness) and scaling.

All calculations are combined into a single score (PASI Score) in the range of 0 (no psoriasis on the body) and up to 72 (the most severe case of psoriasis). Typically, the PASI would be calculated before, during and after a treatment period in order to determine how well psoriasis responds to the treatment.

These Values are Finally Entered in the Following FormulaPASI=0.1(Eh+lh+Dh)*Ah+0.2(Eu+lu+Du)*Aul+0.3(Et+It+Dt)*At+0.4(El+ll+Dl) Al

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Psoriasis Log Based Area Severity Index (PLASI):

The PLASI uses six BSA groupings (47 - 100% - 6, 12 - 46% - 5, 11 - 12% - 4, 6 - 10% - 3, 3 - 5% - 2, 1 - 2% - 1, 0% - 0) with finer partitioning for smaller extents of BSA affected.

This is supposed to reduce the error resulting from inaccurate estimation of BSA in patients with less extensive disease, also to increase sensitivity among patients with mild-to-moderate disease in detecting changes in psoriasis severity. PLASI calculation is identical with PASI, but for a different score for extent of skin lesions, which is mentioned above. These values are a result of the logarithms of x/3(x=1-6) eg $10^0/3=0$, $10^1/3=2$, $10^2/3=5$, ... $10^6/3=100$.

MATERIAL AND METHODS

The material for this study constituted 40 patients selected from Department of DVL, Osmania General Hospital, Hyderabad, from September 2014 to July 2015. The patients were selected based on following inclusion and exclusion criteria.

Inclusion Criteria

Extensive plaque psoriasis not responsive to conventional therapy. Psoriasis that adversely affects the ability to maintain employment.

Exclusion Criteria

Active infectious disease or history of serious infection that could reactivate (such as TB). Man or woman contemplating conception Hepatic disease, abnormal liver function tests, active hepatitis, history of liver disease cirrhosis.

Severe haematologic abnormalities pregnancy lactation.

The patients fitting the criteria were selected and detailed history, clinical examination was carried out in all cases as per proforma attached.

All Patients were Subjected to Detailed Investigations as Follows

- Haematological investigations.
- Total leucocyte count.
- Differential leucocyte count. •
- Erythrocyte sedimentation rate. •
- Haemoglobin estimation. •
- Blood sugar. •
- Serological investigation. •
- Liver function tests.
- Renal function tests.
- Serum proteins.
- Serum electrolytes.
- Radiological investigation.
- Chest X-ray.
- Ultrasonography in relevant cases.

METHODOLOGY

The patients taken into study were explained and consent was taken. The photographs of patients were taken before starting treatment in systemised manner shown as follows and 8 weeks following treatment.

The following 4 Indices were applied on each Patient **Before and After Treatment**

- Body surface area.
- Physician global assessment.
- Psoriasis area severity index.
- Psoriasis Log-Based Area Severity Index (PLASI).

Body Surface area Calculated as Follows:

Head (H) represents 10%, upper limbs (U) represents 20%, trunk (T) 30% and lower extremities (L) 40% of total body surface area.

The Formula for Calculation is

 $BSA = 0.1 \times BSA_{H} + 0.2 \times BSA_{U} + 0.3 \times BSA_{T} + 0.4 \times BSA_{L}$

PGA (Physician Global Assessment) was given a Score each Point of Time, i.e. at Each Visit

- 6 Severe psoriasis.
- 5 Moderate-to-severe psoriasis.
- 4 Moderate psoriasis.
- 3 Mild-to-moderate psoriasis.
- 2 Mild psoriasis.
- 1 Psoriasis almost cleared.
- 0 Clear (no lesion).

PASI (Psoriasis Area Severity Index)

The index is calculated as explained below.

Psoriasis Area and Severity Index

First introduced in 1978 (Fredriksson & Pettersson)

Combines assessment of:

Area involved of 4 parts

- 1. Head & Neck
- 2. Upper extremities
- 3. Trunk
- 4. Lower extremities

Characteristics of lesions in each of those 4 parts:

- Erythema (Redness)
- Induration (Thickness)
- Scaling

As different body areas may have different quality of lesions, the PASI treats the different areas as separate units The body is divided into four regions Each of these regions is scored by itcolf Head and Neck Upper extremities Trunk Lower extremities The neck is included as part of the head Head and Neck = 10% (10 palms) Total BSA = 100% (100 palms) Upper extremities Upper extremities = 20% (20 palms) Total BSA = 100% (100 pal The axillae and genitals are included with the trunk Trunk (axillae and groin) = 30% (30 palms) Total BSA = 100% (100 palms)



The inguinal canal separates the trunk and legs anteriorly Lower extremities (buttocks included) = 40% (40 palms) Total BSA = 100% (100 palms) We need to specify the percentage of surface area covered by plaques in each region and then assign the score accordingly: No involvement 1-9% affected 10-29% affected Area Score explained 30-49% 50-69% 70_80% 90-100% Now we need to grade (0-4) EACH of the four body regions (head/neck, arms, trunk, legs) for AVERAGE: Erythema(0-4) Hyperpigmentation does NOT count Induration (0-4) (0-4) Scaling Scoring explained Scoring:

Scoring: 0 - None 1 - Mild 2 - Moderate 3 - Severe 4 - Very Severe

Induration = 3 (1 mm) SEVERE

The following scoring system for erythema, induration, desquamation was used in study.





PLASI – PSORIASIS LOG-BASED AREA SEVERITY INDEX The Calculation is Identical to PASI, but a Different Score for the Extent of Lesions is used

- 0 : 0%
- 1 : 1-2%
- 2 : 3 5%
- 3 : 6 10%
- 4 : 11-21%
- 5 : 22 46%
- 6 : 47 100%

Currently, there is still no consensus of what represents mild, moderate or severe plaque psoriasis. The definition proposed in this document to causing on the action to be taken may be considered as operational on,

Mild-to-Moderate Psoriasis: BSA < 10%, PASI < 10, PGA 1 – 3. Moderate to Psoriasis: BSA < 10.20%, PASI 10 or more, PGA – 4. Moderate-to-Severe: BSA > 20, PASI > 20, PGA - 6.

RESULTS

The present study is conducted on a total of 40 patients, who presented with chronic plaque psoriasis to Department of DVL, Osmania General Hospital, Hyderabad, from September 2014 to July 2015. During this period 28495 patients attended OPD with various skin complaints, out of which 10000 patients had papulosquamous disorders and patients had psoriasis. Patients had localised type of psoriasis, patients had chronic plaque psoriasis.

Out of these 40 patients were taken into study out of 40 cases, 15 were new cases, 25 cases took treatment but had relapses. All the 40 cases were subjected to thorough clinical examination and investigations. We performed the calculations of BSA, PGA, PASI, PLASI in the cases.

The results are tabulated as follows.

The different tables show the incidence.

Absolute and Relative Differences

Table 9 shows the mean results of BSA, PGA, PASI and PLASI before and after 8 weeks of treatment with methotrexate. The mean score before and after treatment therapy differed significantly (P <0.0001). Largest absolute difference was found with PLASI (35.1) followed by PASI (19), BSA (12.8), PGA (4). Largest relative difference was found with PLASI (86.32%), PASI (84.16%), PGA (80%) and BSA (75.75%).

Regression Analysis

Each possible correlation between parameters BSA, PGA, PASI and PLASI was calculated (Table 11). Strength of each correlation was compared. The correlation between PLASI and PASI (r=0.932) was significantly stronger than correlation between any other two indices. Correlation between PLASI and BSA (r=0.593) was found to be weakest among all other

Induration = 4 (1.25 mm) VERY SEVERE

Review Article

indices. Correlation with PGA with PASI and PLASI was weaker than correlation between PASI and PLASI. Further analysis of regression lines were carried out involving the b (change in y per unit change in x) and intercept a (value of y when x=0). Y=a+bx, where b is slope and a is intercept. The steepest slope (b) was found for regression between PLASI and PGA (b=3.319). Regression between PLASI and BSA, PLASI and PGA had an intercept (a) greater than 5 (a=9.834, a=5.113 respectively) again in favour of PLASI; all other intercepts were less than 5.

Age in Yrs.	No. of Cases	(%)			
11 - 20	2	5.8			
21 - 30	8	23.52			
31 - 40	14	41.17			
41 - 50	9	26.47			
51 - 60	1	2.9			
61 - 70 0 0					
Total 34 100					
Table 1: Age Distribution in Psoriasis Group					
of Patients					

The age distribution of our study is shown in Table No. 2. Maximum number of cases were observed in 3^{rd} and 4^{th} decade and least in age > 60 years.



Sex	No. of Cases	(%)		
Males	26	76.48		
Females	8	23.52		
Total	34	100		
Table 2: Sex Distribution in Chronic Plaque				
Psoriasis				

Most of the patients in study were males 26 (76.48%) and females are 8 (23.52%).



Score of BSA	No. of Patients BSA 1 (Before Rx)	(%)	No. of Patients BSA2 (After Rx)	(%)
0 - 5	9	26.47	18	52.94
6-10	12	36.30	8	23.52
11-15	9	26.47	8	23.52
16-20	4	11.76	0	0
21-25	0	0	0	0
26-30	0	0	0	0
Total	34	100	34	100
Table 3: Distribution of BSA Before and After Treatment				

Maximum no. of patients before treatment were in BSA score of 6-10: 12 (36.30%). Maximum no. of patients after treatment were in BSA score of 0-5: 18 (52.94%).



Score	No. of Patients PASI 1 (Before Rx)	(%)	No. of Patients PASI 2 (After Rx)	(%)
0 - 10	5	14.70	26	76.47
11-20	17	50.00	8	23.52
21-30	11	32.35	0	0
31-40	1	2.90	0	0
41-50	0	0	0	0
51-60	0	0	0	0
61-72	0	0	0	0
Total	34	100	34	100
Distribution of PASI Before and After Treatment				

Highest no. of patients before treatment with PASI were with score of 11-20: 17 (50%). Highest no. of patients after treatment with PASI score were in 0 - 10: 26 (76.47%). No patients were with PASI score > 41.



Score	No. of Patients PLASI 1 (Before Rx)	(%)	No. of Patients PLASI 2 (After Rx)	(%)	
0 - 10	0	0	8	23.52	
11-20	5	14.7	20	38.82	
21-30	12	35.29	6	17.64	
31-40	8	23.52	0	0	
41-50	7	20.59	0	0	
51-60	2	5.80	0	0	
61-72	0	0	0	0	
Total	34	100	34	100	
Та	Table 4: Distribution of PLASI Before and After Treatment				

Highest no. of patients before treatment were found in PLASI 21-30: 12 (35.29%) and after treatment were in PLASI 11-20: 20 (38.20%). No patients were in the study having score > 61.



Measures	Mean Before Treatment	Mean After Treatment	P value	Mean Absolute Difference (± SD)	Mean Relative Difference (± SD)
BSA	9.57	6.11	< 10-4	3.6 ± 3.2	34.75± 23.12
PGA	4.68	3.00	< 10-4	1.68± 1.12	35.83± 22.49
PASI	17.27	7.97	< 10-4	9.31± 5.75	51.10± 21.56
PLASI	31.07	15.07	< 10-4	15.12± 8.78	49.20± 19.80
Table 5: Comparison of Various Indices as Measures of Disease Severity					

SD, Standard Deviation.

Highest score of mean before and after treatment; absolute difference and relative difference in study was found with PLASI.

Index	Largest Absolute Difference (Delta)	Largest Relative Difference (Delta %)		
BSA	12.80	75.25		
PGA	4	80.00		
PASI	19	84.16		
PLASI	35.10	86.32		
Table 6: Comparison of Absolute and Relative Differences of Various Indices				

Largest absolute difference and relative difference was found in PLASI, i.e. 35.10 and 86.32 respectively. Least was found in BSA (75.25%).



Moasuros	Regression	Co-Efficient of		
Measures	(y = a + b x)	Correlation (r)		
PLASI	5.113 + 3.319 x PGA	0.676		
PASI	0.585 + 2.462 x PGA	0.760		
BSA	- 0.455 + 2.187 x PGA	0.637		
PLASI	9.894 + 0.848 x BSA	0.593		
PLASI	3.812 + 1.413 x PASI	0.932		
PASI	3.824 + 0.679 x BSA	0.720		
Table 7: Linear Regression and Correlation between				
Each of the Measures				

- y is dependent variable.
- a is intercept
- b is slope
- x is constant.
- r is co-efficient of correlation.

Steepest slope is found in regression with PLASI and PGA indicating that PLASI can differentiate levels of severity more accurately than PGA.

Regression between PLASI and PGA, PLASI and BSA have intercept greater than five (a=5.113, a=9.894) respectively again is in favour of PLASI.

DISCUSSION

BSA and PGA are older measures to grade severity of psoriasis. PASI is the most commonly used measure to investigate the severity and coverage of psoriasis, and the improvement after therapy. The "PASI concept," has made possible many scientific contributions within the last 29 years. All the measures (PASI, PLASI, PGA and BSA) show a very high correlation with each other. In study by Tilo Hensler et al all the measures (PASI, PLASI, SAPASI and BSA) show a very high correlation with each other. The correlation between PASI and PLASI in this study was higher than that found by Hensler et $al_{4,5}$ Feldman et $al_{6,7,8}$ (r = 0.932 vs. r = 0.91 vs. r = 0.77) respectively. In our study, steep regression slope (b = 3.314) indicate PLASI can differentiate levels of severity more accurately than PGA, PASI. For example, one point improvement of PGA is equivalent to 3.314 point improvement of PLASI. In study of Hensler et al,⁴ the steep regression slope (b = 1.48) indicates that PLASI can differentiate levels of severity more accurately than PASI. The better differentiation of PLASI is a result of the logarithmic distribution in the rating of the body area affected. In our study when considering an

identical clinical improvement, a better differentiation is achieved using PLASI. An improvement by therapy of 50% PLASI corresponds to a change of 13.56% of PGA; when considering with PASI it is 32.69%. In Hensler et al,⁴ DPLASI 50% corresponded to 33.8% of DPASI. In study conducted by C. C. Jackobson et al⁹ and Jemec et al,¹⁰ clinical improvements under the grading systems using PLASI translated into greater percentage changes than calculated using the Delta PASI formula. Specifically, the Delta PASI 50 translated to a Delta PLASI 57·2; Delta PASI 75 was equivalent to Delta PLASI 85·7. Importantly, Delta PASI tended to be systematically lower than patients & #39; self-assessment. While Delta PLASI better matched patients & #39; self-assessments. Based on comparison with two above studies, we conclude that PLASI is better than PASI in showing clinical improvement.

The influence of the logarithmic scale can be demonstrated as follows (Assuming the severity of erythema, infiltration and desquamation does not change). In two patients, if the area affected by psoriasis has been reduced by therapy in all distinct sites from 25% and 80% respectively to 10% in both cases. Using PASI, the improvements are 0% (No change in BSA score) and 20% respectively, whereas PLASI shows improvements of 16.7% (BSA score change from five to three) in the first case and 50% (BSA score change from six to two) in the second case. Therefore, the first case is more accurately measured by PLASI. When improvement is only poor and the patient's BSA remains in the 100-50% interval; however, PASI is able to differentiate therapeutic "success," whereas PLASI cannot. In our study, the slope of the regression for PLASI (b = 3.319) vs. PASI (b = 2.462) indicates that PLASI is more accurate than PASI. In the regression analyses, all other slopes were less than unity indicating that the severity differentiation was inferior, especially when BSA was involved in the analysis. In study of Hensler et al,⁴ the slope of the regression for PLASI (b = 1.48) vs. SAPASI (b = 1.32) indicates that PLASI is more accurate than SAPASI. In the regression analyses, all other slopes were less than unity indicating that the severity differentiation was inferior, especially when BSA was involved in the analysis.

In our study comparison of BSA with PGA (r=0.630) meaning to correlate moderately with PGA. Validity was only tested with the PGA, which correlated strongly (Langley and Ellis, 2004.¹¹ The BSA was least improved after 2 weeks treatment compared with other psoriasis parameters, which is negative for responsiveness. The clinical assessed BSA did not differ statistically from objectively assessed BSA, for instance with computer-based image analysis in two studies (Kanthraj et al 1997 Ormerod et al, 1997).¹²

However, several other studies showed that patients and clinicians significantly overestimate the affected area, especially in mild cases and when untrained (Ramsay and Lawrence, 1991¹; Tiling-Grosse and Rees, 1993¹³; Savolainen et al 1997, 1998^{14&15}; Yune et al, 2003¹⁶; Kreft et al, 2006).¹⁷

The correlation coefficient between BSA assessed by dermatologists and patients ranged from r:0.38–0.82 (Feldman et al 1996, 2005; Fleischer, Jr et al, 1999¹⁰; Szepietowski et al 2001¹⁸; Sampogna et al 2003).¹⁹ In present study, co-efficient of correlation between PASI and PGA was r=0.760, p<0.0001 suggesting moderate strength of correlation.

In study conducted by J. Berth Jones et al 20 found that PGA and PASI moderately correlated (r=0.79, p<0.001)

Dermatology revealed study which studied efficacy of efalizumab in patients with moderate-to-severe psoriasis after 16 weeks of treatment patients with PASI 75 were 71% compared to PGA 0, 1 showing 62% showing that PASI show better improvement than PGA.

CONCLUSION

- 1. There are large no. of indices to assess psoriasis severity and response of which few are in use.
- 2. PASI is one of the most extensively studied and used index.
- 3. PGA is simpler index, but lacks standardisation.
- 4. BSA is simpler and subjective. It is least sensitive in comparison with other indices.
- 5. PLASI is the best sensitive indicator of disease severity in mild-to-moderate psoriasis.
- 6. PASI is better than PLASI in psoriasis when improvement is poor and when BSA is in 100 50% interval.

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