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Research Article

Assessment of C-Reactive Protein in Psoriasis Patients

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Abstract

Psoriasis is a global burden of disease characterized by the presence of well circumscribed erythematous papule & plaque of various size & shape, covered by silvery scales and has an inflammatory nature demonstrated by excessive secretion of dermal, systemic, pre-inflammatory cytokines. Furthermore, liver stimulation and the production of acute phase reactants such as C-reactive Protein (CRP), which is considered an inflammatory biomarker, are believed to stem from IL-6 secretion induced by TNF-a. CRP is an acute phase reaction protein biomarker that is identifiable within 24 to 48 hours after tissue damage or infection. To assess role of CRP in psoriasis patients is the objective of the present study. It was a cross sectional observational study, conducted in department of Dermatology and Venereology, Bangladesh Medical University, Dhaka among diagnosed cases of chronic plaque psoriasis. Sample was selected by purposive sampling technique. Data were collected from the informant and recorded in structured case report form. Clinical examination and relevant investigation were done meticulously. Mean age of the patient was 39.42±8.5 years. Study shows that maximum patients (37.0%) had CRP value 3.1-6.0. The average CRP value was 4.2±1.2. On correlation between severity of psoriasis with CRP value revealed that, out of 24 patients of severe disease, 13(54.1%) cases was ≥9.1 and 8(33.3%) cases was 6.1-9.0 CRP. On the other hand maximum patients [34 (44.7)] of mild cases had CRP 3.1-6.0. CRP was significantly elevated (>6 mg/L) in severe psoriatic patients with severe disease than those with mild disease. The mean CRP values in mid disease (PASI<10) was 0.9±0.2 and in severe cases (PASI>10) was 7.5±2.1. There was a significant difference in CRP values with PASI score. So, CRP shows a significant association with severity of psoriasis. From this study, we suggest that CRP value is a good predictor in the diagnosis and disease severity of psoriasis. Patients with moderate to severe psoriasis had active systemic inflammation, which was demonstrated by increased levels of C-reactive Protein.

Keywords: c-reactive protein; psoriasis patients

Introduction

Psoriasis is an immune-mediated genetic skin disease. The underlying pathomechanisms involve complex interaction between the innate and adaptive immune system. T cells interact with dendritic cells, macrophages, and keratinocytes, which can be mediated by their secreted cytokines. In the past decade, biologics targeting tumor necrosis factor-a, interleukin (IL)-23, and IL-17 have been developed and approved for the treatment of psoriasis.1 These biologics have dramatically changed the treatment and management of psoriasis. In contrast, various triggering factors can elicit the disease in genetically predisposed individuals. Recent studies suggest that the exacerbation of psoriasis can lead to systemic inflammation and cardiovascular comorbidity. In addition, psoriasis may be associated with other auto-inflammatory and auto-immune diseases. Despite its systemic nature, the quantification of the burden of systemic inflammation in psoriatic disease is challenging. Hence, the levels of C-reactive protein (CRP), which is commonly used to quantify systemic inflammation, are increased in psoriatic disease.2-3 Psoriasis is a chronic, recurrent inflammatory cutaneous disease. Psoriasis patients alternate between periods of remission and periods of exacerbation of the disease. Usually, psoriasis severity is clinically

evaluated using tools like Psoriasis Area and Severity Index (PASI) that present some limitations and subjectivity. Clinicians select the therapy according to psoriasis severity, aiming that patients achieve longer remission periods and improve their quality of life. Biological markers for diagnosis and prognosis of psoriasis help to establish its severity and to monitor the therapeutic response; moreover, collaboration of Psoriasis Area and Severity Index (PASI) score with biomarkers of psoriasis assists clinician's precise evaluation, therapeutic decision to treat psoriasis and to choose earlier and more adequate therapeutic strategies, avoiding or minimising worsening of psoriasis. C-reactive protein (CRP) has special importance for psoriasis due to its relation with cytokines which are responsible for skin inflammation. CRP is cheap, available and common biomarkers. The plasma half-life of CRP is constant under all conditions of health and disease, so that the sole determinant of circulating levels of CRP is the synthesis rate, which thus directly reflects the intensity of pathological process stimulating CRP production. With this marker, it would be able to monitor therapeutics, avoiding unnecessary therapeutic surcharge or changes to a more aggressive therapy.

Materials and methods

Study design: Cross sectional observational study

Place of study: Outpatient Department of Dermatology and Venereology, Bangladesh Medical University, Dhaka

Study period: This study was conducted over a period of six months from February 2021 to August 2021.

Study Population: The study population were patients diagnosed chronic plaque psoriasis, above the age of 18 years & both sexes, attended for further management after giving informed written consent

Sample size: The following standard formula is widely used in determining sample size:

n = the desired sample size

Standard normal deviate usually set at 1.96

p = Proportion in the population. Psoriasis affects about 2%-3% of the World population 23. We considered 3%, so 'p' value will be 0.03. q = 1 - p Or 0.97 d = Acceptable error or precision (which is considered as 2%). So acceptable error is 0.02

$$n = \frac{0.111}{0.0004}$$

According to this formula the targeted sample will be 279.3; therefore 100 samples were taken in this study.

Sampling: Purposive sampling was applied for sample selection.

Inclusion criteria

Diagnosed cases of chronic plaque psoriasis, above the age of 18 years & both sexes

Not receiving any systemic treatment for psoriasis for at least one month prior to enrolment

Exclusion criteria

Concomitant other skin infection

Psoriatic arthritis and other inflammatory disorders

Pregnant and lactating females

Patients having acute illness such as fever of unknown origin, diagnosed case of RA or other known arthropathies, malignancy, history of MI, deep fungal or disseminated localized gonococcal infection Data collection procedure: This study was conducted in the Department of Dermatology of BMU, Dhaka. It is a hospital-based, cross sectional study. The study group included 100 patients of chronic plaque psoriasis. All consecutive clinically diagnosed cases of chronic plaque psoriasis (excluding psoriatic arthritis and other inflammatory disorders) above the age of 18 years not receiving any systemic treatment for psoriasis for at least one month prior to enrolment were included in the study. Relevant data included age, gender, weight, height, body mass index, blood pressure, age of onset, and duration of psoriasis. Severity of psoriasis was assessed according to Psoriasis Area and Severity Index (PASI) score, determined by the same investigator in all 100 cases. PASI<10 considered mild and PASI >10 considered severe disease. Investigations carried out included all routine test, and C-reactive protein (immunoturbidimetry) evaluated. Result of CRP correlates with PASI score. Statistical analysis of the data was done using statistical processing software (SPSS) and Microsoft. Quantitative data expressed as mean and standard deviation and qualitative data as frequency and percentage. Comparison was done by tabulation and graphical presentation in the form of tables, pie chart, graphs, bar diagrams, histogram & charts etc. Variables: Main outcome variables: An interview-based questionnaire was used to collect information from the patients or relatives, regarding age, sex, socio-demographic characteristics, educational level, clinical presentation, Severity of disease PASI score, CRP level. The data were analysed by statistical (SPSS) method and presented in the form of tables, figures, graphs, diagrams & charts etc. Data analysis: Data for socio- demographic and clinical variables were obtained from all participants by the use of a pre-designed and easily understandable questionnaire. After collection of all information, these data were checked, verified for consistency and edited for finalized result. After editing and coding, the coded data directly entered into the computer by using SPSS version 22. Data cleaning validation and analysis was performed using the SPSS/PC software and graph and chart by MS excel. The result was presented in tables in proportion. p value <0.05 is considered as significant. Quality assurance strategy: It is extremely important that the data collection procedure, method becomes good in quality, for that purpose at first work manual was made. Then a sample size was selected. A standard questionnaire was made. Then the questionnaire was pretested. The pre-test ensures that the respondents are able to understand the questionnaire and answer accordingly.

Results

Age	Frequency		Total
	male	female	
12-20	9(10.84%)	0	9
21-30	48(57.83%)	9(52.94%)	57
31-40	19(22.89%)	7(41.17%)	26
41-50	7(8.43%)	1(5.88%)	8

Mean ± SD	39.42 ±8.5
M:F	4.88:1

Table 1: Age & Sex distribution of the patients (n=100).

In the study, the maximum incidence was seen in the 3rd decade (57.0%), next to it was the 4th decade (26.0%). Mean age of the patient was 39.42 plus/minus 8.5 years. Out of 100 cases 83% cases were male and 17% were female. Male and female ratio was 4.88:1.

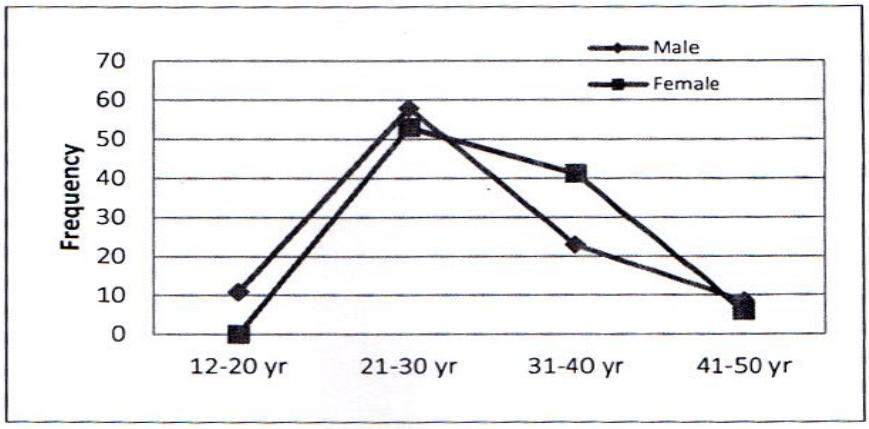

Figure 1: Line chart showing the frequency of disease with age variation (n=100).

Figure-l shows that frequency of disease was predominant at middle age in both sexes, but more female are affected at elder age. Highest incidence of male and female patients were in age group between 21-30 years, 57.83% and 52.94% respectively.

Income classes	Number of patient	Percentage
Low-income class	6	6.0
Lower middle class	18	18.0
Upper middle class	47	47.0
High income class	29	29.0

Table 2: Socioeconomic status (SES) of study population.

Socioeconomically patients were grouped into three classes. Among the patients the upper middle class (47%) comprising the major percentage of the patients, followed by high income class (29%) and remaining were lower middle class (18%), and low income class (6%).

PASI score	Indicator	Number of Patients	Percentage
<10	Mild	76	26.0
>10	Severe	24	31.0

Table 3: Evaluation the severity of the psoriasis according to Psoriasis Area Severity Index (PASI).

Table 3 demonstrated the psoriasis Area Severity Index (PASI). Score revealed that maximum cases (76.0%) were score <10, 24.0% of patients were score >10.

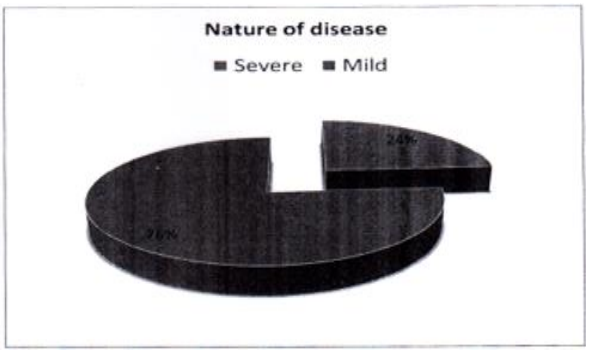

Figure 2: Clinical impression at presentation.

On clinical evaluation, 24.0% of patients considered as severe psoriasis and remaining 76.0% patients revealed that mild psoriasis.

CRP value	Number of patients	Percentage
<0.5	0	0.0
0.6-3.0	16	16.0
3.1-6.0	37	37.0
6.1-9.0	28	28.0
≥9.1	19	19.0
Mean ± SD	4.2±1.2	

Table 4: Assessment of C-reactive protein (CRP) in psoriasis patients.

Table 5 shows the assessment of C-reactive protein (CRP) in psoriasis patients. The CRP was assessed in all patients. Study shows that maximum patients (37.0%) had CRP value 3.1-6.0. The mean CRP value was 4.2±1.2.

CRP value	Severity of disease according to PASI score		
	Mild disease, n = 76	Severe disease, n = 24	p-value
<0.5	0	0	
0.6-3.0	16 (21.0)	0	
3.1-6.0	34 (44.7)	3 (12.5)	
6.1-9.0	20 (26.3)	8 (33.3)	
>= 9.1	6 (7.89)	13 (54.1)	
Mean ± SD	0.9± 0.2	7.5 ± 2.1	0.001

Table 5: Evaluation of validity of CRP to predict the severity of psoriasis (n=100).

In this series correlation was done in between severity of psoriasis with CRP value. Out of 24 patients of severe disease, 13(54.1%) cases were >= 9.1 and 8(33.3%) cases was 6.1-9.0 CRP. On the other hand maximum patients [34 (44.7)] of mild cases had CRP 3.1-6.0. The p-value is <0.05. The difference was significant.

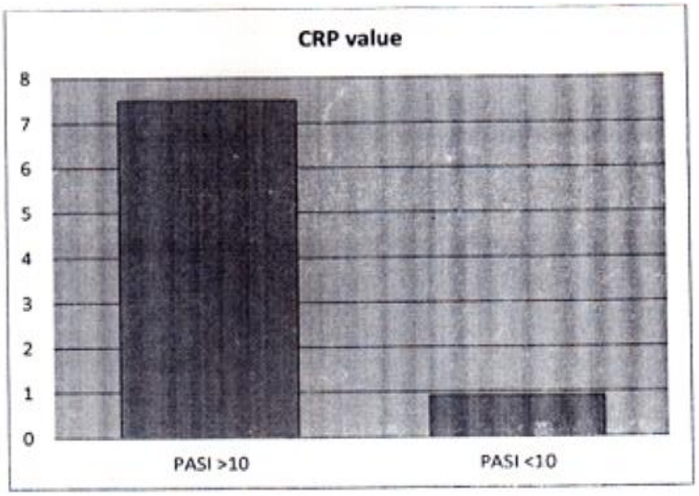

Figure 3: Comparison of CRP value with PASI score.

Figure shows the comparison of CRP value with PASI score. CRP was significantly elevated (>6mg/L) in severe psoriatic patients with severe disease (PASI>10) than those with mild disease (PASI<10) The mean CRP values in mid disease (PASI<10) was 0.9 plus/minus 0.2 and in severe cases (PASI>10) was 7.5 plus/minus 2.1 There was a significant difference in CRP values with PASI score. So, CRP shows a significant association with severity of psoriasis.

CRP Value	PASI score	
	Severe disease (n=24)	Mild disease (n=76)
Significant (n=47)	21(87.5%)	26 (34.2%)
Non-significant (n = 53)	3(12.5%)	50(65.7%)

Table 6: Distribution of adults' behavioral characteristics.

True positive (TP) = 21

False positive (FP) = 26

False negative (FN) = 3

True negative (TN) = 50

Among the 24 cases of severe disease, 21(87.5%) has correlates with significant CRP value, but 3(12.5%) cases proven non-significant in CRP findings. Maximum cases 50(65.7%) of mild disease had non-significant CRP. So effectiveness of CRP finding is valuable in diagnosis of psoriasis.

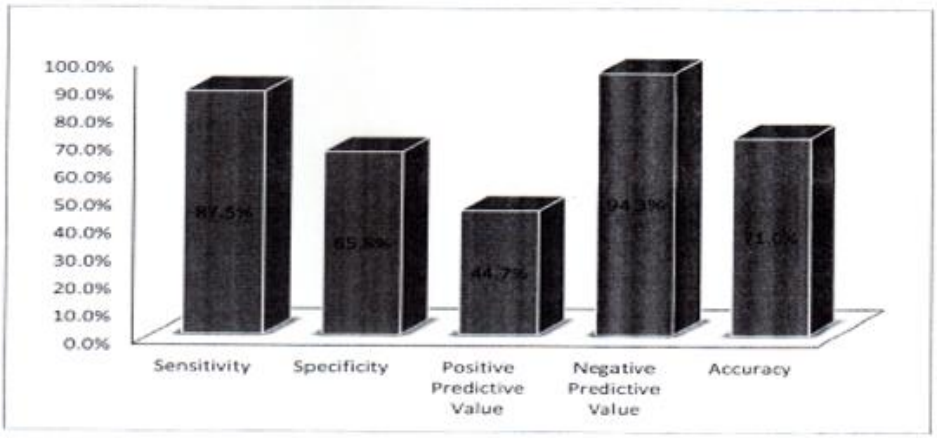

Figure 4: Determination of sensitivity, specificity of CRP.

Statistic	Value	95% CI
Sensitivity	87.50%	67.64% to 97.34%
Specificity	65.79%	54.01% to 76.29%
Positive Predictive Value	44.68%	36.35% to 53.32%
Negative Predictive Value	94.34%	85.10% to 97.99%
Accuracy	71.00%	61.07% to 79.64%

Table 7: Distribution of adults' behavioral characteristics.

Discussion

This cross sectional observational study was conducted in Department of Dermatology and Venereology, Bangladesh Medical University, Dhaka, for assessment of C reactive protein in psoriasis patients. In this study maximum incidence was seen in the 3rd decade (57.0%), mean age of the patient was 39.42±8.5 years. Out of 100 cases 83% cases were male and 17% were female. Male and female ratio was 4.88:1. Findings consistent with result of previous study. In a study total of hundred patients with chronic plaque psoriasis and an equal number of age and gender-matched healthy controls were enrolled. The mean age of the patients with psoriasis was 44.71±10.84. Maximum number of patients was in the age group 41-50 years". In another study, out of 25 patients, there were 18 males (72%) and seven females (28%). They were treated by NB-UVB therapy. The ages of these patients ranged from 21 to 67 years, with a mean age of 41.08±14.60 years. In this study Psoriasis Area Severity Index (PASI) score revealed that maximum cases (76.0%) were score <10, 24.0% of patients were score.6 CRP was assessed in all patients. Study shows that maximum patients (37.0%) had CRP value 3.1-6.0. The mean CRP value was 4.2±1.2. On correlation between severity of psoriasis with CRP value revealed that, out of 24 patients of severe disease, 13(54.1%) cases was 29.1 and 8(33.3%) cases were 6.1-9.0 CRP. On the other hand maximum patients [34 (44.7)] of mild cases had CRP 3.1-6.0. The p-value is <0.05. The difference was significant. It is evident that psoriasis is associated with the metabolic syndrome or its components such as obesity, insulin resistance, hypertension, and atherogenic dyslipidemia. The association of psoriasis with enhanced atherosclerosis and risk of cardiovascular disease (CVD) may account for higher morbidity and mortality rates in psoriatic patients. The intensity of inflammation and skin changes in psoriasis may not only indicate the severity of psoriasis but also that of other systemic pathologies.7-8. Previous study demonstrated that psoriasis, metabolic syndrome, systemic arterial hypertension and age share the increase in C-reactive protein Another study reported that patients with moderate to severe plaque-type psoriasis had active systemic inflammation, which was demonstrated by increased levels of C-reactive protein. Furthermore, skin disease severity was correlated with C-reactive protein levels. Elevated C-reactive protein levels result from the interaction between pro-inflammatory cytokines, namely IL-6, TNF-alpha and IL-1. The increased magnitude of CRP seems to be related to the extent of tissue injury and inflammation severity in active stage of psoriasis.2-3 Unlike the earlier rejection of CRP as an empirical test because of its perceived lack of specificity, the current stress over CRP is widely characterized by failure to recognize appropriately the nonspecific nature of the acute phase response". The plasma half-life of CRP is constant under all conditions of health and disease, so that the sole determinant of circulating levels of CRP is the synthesis rate, which thus directly reflects the intensity of pathological process stimulating CRP production.20-21 Several studies have investigated the role of CRP in psoriasis. Two studies by Vanizor et al. have shown that patients with psoriasis have significantly high baseline levels of CRP compared with healthy controls ($p<0.004$ and $p<0.001$).22 Malbris et al. noted that patients with psoriasis had higher levels of CRP compared with controls, with a positive correlation between CRP and total plasma cholesterol.23 In this study CRP was significantly elevated (>6 mg/L) in severe psoriatic patients with severe disease (PASI>10) than those with mild disease (PASI<10). The mean CRP values in mid disease (PASI <10) was 0.9±0.2 and in severe cases (PASI >10) was 7.5±2.1. There was a significant difference in CRP values with PASI score. So, CRP shows a significant association with severity of psoriasis. C-reactive protein is an inflammatory biomarker and its level increases in the serum of psoriatic patients. Its level is also associated with Psoriasis Area and

Severity Index score[2]. In another study, CRP was elevated (>5 mg/L) in 52% of psoriatic patients when compared with 14% of control population and the difference was statistically highly significant (p value 0.001).11 Similar results were observed by Rocha-Periera et al.24 In a study by Kimbell et al25 CRP levels correlated with the presence and severity of disease, with the lowest levels seen in the control group and progressively higher CRP levels observed in patients with increasing disease severity. Compared with controls, patients with mild and severe psoriasis had significantly higher levels of CRP (mean ± standard deviation; 0.31±0.02 mg/dL vs 0.90±0.27 mg/dL; p<0.001). Further comparison indicated that patients with severe psoriasis had significantly higher levels of CRP than those with only mild disease (mean±standard deviation; 0.63±0.03 mg/dL vs 1.16±0.07 mg/dL; p<0.001). In another study, it was found a significant association between disease severity and elevated CRP levels. Psoriatic patients with severe disease (PASI>10) had significantly higher levels of CRP than those with mild disease (PASI<10) (44% vs 25%) (p value=0.003)11. Thus, these results are consistent with the characterization of psoriasis as an inflammatory response that worsens with increasing disease severity. Several other studies have also reported a correlation between increased levels of CRP and PASI.26-28 Thus, CRP can be considered as a useful marker of disease severity that could be used to monitor the disease course and its treatment.

Conclusion

C-reactive protein (CRP) is an important bio marker of inflammation. Present study concluded that CRP values are known to be elevated in a proportion of patients with psoriasis and are associated with disease severity. CRP estimation is inexpensive, widely available, and can be easily carried out in an outpatient clinical setting. CRP along with PASI could be used as a powerful and sensitive blood marker to evaluate psoriasis disease severity, as it is not based on visual evaluation of the lesions. It can be used to monitor the disease course and treatment.

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