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Assessing disease severity by hsCRP as a biochemical marker for psoriasis

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ABSTRACT

Background: For a complex chronic disease like psoriasis, having a biomarker to objectively assess the clinical severity can be very helpful in disease management.

Methods: In a hospital based prospective study, 70 patients of psoriasis diagnosed clinically, were studied. The extent of disease severity was assessed using PASI and BSA and patients were grouped into having mild, moderate and severe disease using these scores. Serum high sensitivity C-reactive protein (hsCRP) levels were then estimated for each group.

Results: Of the 70 psoriasis cases enrolled, 46 patients were male and 24 females. Patients with early onset psoriasis were associated with higher values of hsCRP than those with late onset (r=-0.063; p=0.012). A positive correlation was seen between the PASI score and hsCRP levels (r=0.891; p \leq 0.001). On comparing mean PASI and mean hsCRP in severity groups (mild, moderate and severe), hsCRP was higher in the group with maximum severity (p \leq 0.001).

Conclusions: A negative correlation between the age of onset and hsCRP implies that, earlier the age of onset, higher is the value of hsCRP. Our study shows a positive correlation between the body surface area and PASI score both of which varied linearly with hsCRP values. The findings also suggest that patients with severe psoriasis have higher mean serum hsCRP levels than patients with mild psoriasiss. We proposed hsCRP as a useful marker of psoriasis severity that could be used to monitor psoriasis and, together with PASI, as a global index of disease severity.

Keywords: Psoriasis, PASI, BSA. High sensitivity CRP

INTRODUCTION

Psoriasis is a complex chronic inflammatory systemic disease, with environmental and genetic components, that affect the skin, scalp, nails and occasionally the joints, with periods of exacerbation and remission. It is an immune-mediated, multifactorial disease characterized by phenotypic diversity and genetic heterogeneity.

Psoriasis is a clinical diagnosis. The basic characteristics of psoriatic lesions-erythema, induration and scaling-

provide a means of assessing the severity of psoriasis. The current gold standard for assessment has been the Psoriasis Area and Severity Index (PASI).² The score can vary from 0 to 72. Limitation of PASI score lies in its inter-observer variation, which makes subsequent evaluation by the same physician necessary.

C-reactive protein (CRP) is a member of the class of acute phase reactants, which is synthesized exclusively in the liver. Its level has been shown to rise by many folds following acute inflammation.³ Accordingly, CRP has

been suggested to be a marker of inflammation in several conditions including psoriasis.⁴

Conventional CRP assays cannot detect low levels of rise in CRP due to subtle causes of inflammation in various diseased states particularly cardiovascular disease.⁵ The high sensitivity C-reactive protein (hsCRP) assay is a quantitative analysis of very low level of CRP in blood (<10mg/L). The high-sensitivity CRP (hsCRP) test accurately measures low levels of C-reactive protein to identify low but persistent levels of inflammation. Previous studies have attributed CRP as a prognostic disease marker in psoriasis.^{6,7} However, studies attributing the elevated levels of hsCRP to events in psoriasis are scarce.

The present study is thus designed to assess the association of inflammatory marker hsCRP with disease severity (as measured by the psoriasis area and severity index) in Indian patients with psoriasis.

METHODS

A hospital based, prospective study involving 70 patients of clinically diagnosed psoriasis, was conducted in a tertiary care hospital in Uttar Pradesh. Patient selection was done by simple random sampling of individuals coming to the outpatient department of Dermatology. The study was conducted between January 2016 and April 2017 (16 months). Patients were included in the study based on the following criteria

Inclusion criteria for patients

Inclusion criteria were a clinically confirmed case of psoriasis consenting to undergo required investigations; age 18 years or older.

Exclusion criteria for patients

Exclusion criteria were 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, or taking active systemic therapy; subjects with known chronic diseases. i.e. tuberculosis, any apparent sign of acute or chronic inflammation (hepatitis or auto immune disease), Liver or renal problems, alcohol dependence.

After explaining purpose and contents of the study to subjects, written informed consent was obtained from each. A detailed history with special emphasis on psoriasis including age at onset, total duration, duration of present episode, remitting and relapsing factors, history of joint and nail involvement along with family history was recorded on a pre-designed case record form. Dermatological examination including morphological type of psoriasis, body surface area (BSA) involvement

in percentage and psoriasis area severity index (PASI) were calculated for all patients.

BSA

BSA was calculated using the number of patient's hand areas affected. One hand area is equivalent to patient's one palm and fingers, and represents 1% of his entire body surface area.⁸

Calculation of PASI

The body was divided into 4 sections (head (H) (10% of a person's skin); arms (A) (20%); trunk (T) (30%); legs (L) (40%)). For each section, the percent of area of skin involved was estimated and then transformed into a grade from 0 to 6:

- 0% of involved area, grade: 0
- <10% of involved area, grade: 1
- 10-29% of involved area, grade: 2
- 30-49% of involved area, grade: 3
- 50-69% of involved area, grade: 4
- 70-89% of involved area, grade: 5
- 90-100% of involved area, grade: 6

Within each area, three clinical signs estimated the severity: erythema (redness), induration (thickness) and desquamation (scaling). Severity parameters were measured on a scale of 0 to 4, from none to maximum.

Hence, the final formula for calculating PASI score is as follows:

$$PASI = 0.1(Eh + Ih + Dh) A + 0.2(Eu + Iu + Du) A + 0.3(Et + It + Dt) A + 0.4(El + Il + Dl) A$$

The score can vary from 0 to 72.

In our study: PASI <7 was graded as mild; 7-12 was graded as moderate; >12 was graded as severe.⁹

Serum HsCRP level was measured by immunoturbidimetric method using commercially available kit on semi-automated analyzer of "Nephlostar"

Statistical analysis

Results on continuous measurements have been presented as mean±SD and results on categorical measurements are presented in number and percentage (%). The significance of study parameters was calculated by student's t test for continuous data.

The relationship between disease variables (age at onset, disease duration, clinical severity scores) was examined using Pearson's correlation coefficients. The correlation coefficient ranges from -1 to 1. A value of 1 implies that a linear equation describes the relationship between X

and Y perfectly, with all data points lying on a line for which Y increases as X increases. A value of -1 implies that all data points lie on a line for which Y decreases as X increases. A value of 0 implies that there is no linear correlation between the variables. The level of significance was taken as 0.05.

The statistical software used was Microsoft excel and SPSS software version 16.0 for analysis of data and Microsoft word to generate graphs, tables etc.

RESULTS

Of the 70 psoriasis cases that were enrolled for the study, 46 (65.7%) were males and 24 (34.3%) were females. The ratio of males and females in our study group was 1.92:1. We found no variation in hsCRP with the gender of the patient, as there was no significant difference in the mean hsCRP levels of males and females.

Descriptive characteristics

We observed a negative correlation of age of onset with hsCRP (r=-0.063; p=0.012). Thus, patients with earlier age of onset of psoriasis were associated with higher values of hsCRP than those with late onset of psoriasis. There was a negative correlation of duration of current episode with hsCRP (r=-0.202; p=0.011), indicating that patients with shorter duration of current episode had a higher value of hsCRP implying that hsCRP is an acute phase reactant. These results are shown in Table 1.

Table 1: Correlation of hsCRP with descriptive features.

Score	R value	P value
Age of onset with hsCRP	- 0.063	0.012
Total disease duration with hsCRP	0.055	0.611
Duration of current episode with hsCRP	- 0.202	0.011

Correlation of BSA with hsCRP

BSA, though not related to PASI, is an important parameter to assess the clinical involvement of the disease. Hence, we studied its association with our biochemical marker, hsCRP. The correlation was found to be a positive one with a high statistical significance. (n=70; r=0.880; p \leq 0.001)

Correlation of psoriatic area severity index (PASI) with hsCRP

We found a positive correlation between the PASI score of patients at the time of presentation with their levels of serum hsCRP with a highly significant p value (Figure 1). Also, when compared taking the mean PASI in each severity group (mild, moderate and severe) to the mean hsCRP in that group, the results were statistically highly significant in patients with moderate and severe psoriasis. It was also observed that the mean hsCRP was higher in the group with maximum severity of psoriasis. This data has been shown in Table 2.

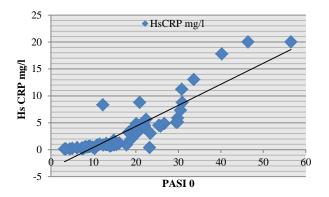


Figure 1: Correlation of hsCRP with PASI in psoriasis patients (n=70).

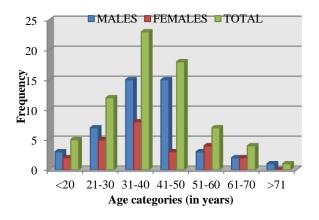


Figure 2: Distribution according to age and sex in the study group.

Table 2: Correlation of severity groups of PASI with hsCRP.

	PASI (mean)	hsCRP (mean) (mg/l)	R value	P value
Mild (n=6) (PASI <7)	4.73	0.229	0.9499	0.002
Moderate (n=20) PASI 7-12	9.7	0.605	0.8488	<0.001*
Severe (n=44) PASI >12	22.159	4.8	0.8894	<0.001*

DISCUSSION

Psoriasis is a distressing chronic and relapsing inflammatory skin disease, characterized by marked inflammatory changes in the epidermis and dermis. Psoriasis patients demonstrate increased inflammatory activity, which is proportional to severity of disease.

Considering the indispensable role of inflammation in development of psoriasis and of studies reporting increased levels of inflammatory markers in psoriasis, present study was undertaken to study the role of hsCRP as a biomarker of severity of the disease.

In our study, the mean age of psoriasis patients was 40.14 ± 13.87 years. The highest incidence of psoriasis in our study was seen in the age group of 31-40 years (32.86%) followed by 41-50 years (25.71%) (Figure 2). In our study, the mean age of onset of psoriasis was 32 ± 14.10 years and the mean total disease duration was 8.18 years with the range varying from 3 months to 26 years. Maximum patients were of chronic plaque psoriasis (90%), which is the commonest type worldwide.

HsCRP

The inflammatory state in psoriasis releases pro inflammatory cytokines, which stimulate liver to produce acute phase reactants. CRP is one such acute phase reactant. Elevated CRP levels result from the interaction between pro-inflammatory cytokines, namely IL -6, TNF – α and IL -1, their receptors and inhibitory factors. CRP concentrations in serum increase with increasing severity of psoriasis and show positive correlation with PASI. 10 Contrary to the previous studies, which have estimated CRP, the present study evaluates the usefulness of the estimation of hsCRP and its correlation with the severity of the disease.



Figure 3: Clinical photograph of classical psoriasis vulgaris over the lower back.

We did not find any significant difference in the mean hsCRP values of males and females, implying there is no variation seen in hsCRP with the gender of the patient. Despite our thorough research, we could not find any previous study either, which has compared the values of hsCRP in psoriatic patients in males to that of females or found a significant difference between them. Hence, emphasizing the fact that the value remains consistent irrespective of the gender of the patient.



Figure 4: Clinical photograph of chronic plaque psoriasis (extensor surface of upper limbs symmetrically involved).

We found a negative correlation of age of onset with hsCRP in our study. The possible explanation for this could be the fact that patients with earlier age of onset of psoriasis are associated with higher values of hsCRP than those with late onset of psoriasis. A negative correlation between duration of current episode and hsCRP indicates that patients with shorter duration of current episode have a higher value of hsCRP implying that it is an acute phase reactant.

A positive correlation between the PASI score of patients at the time of presentation with their levels of hsCRP with a highly significant p value is in concordance with the findings by Keerthana et al, who also had a sample size of 70, like our study. However, the Pearson correlation coefficient (r) had a higher value in our study, thus implying a large positive correlation. In the study done in Gujarat by Agravatt et al also, the correlation between mean PASI and mean hsCRP was found to be a highly significant positive one. 12

When compared taking the mean PASI in each severity group (mild, moderate and severe) to the mean hsCRP in that group, the results were statistically highly significant in patients with moderate and severe psoriasis. It was also observed that the mean hsCRP was higher in the group with maximum severity of psoriasis. Mean hsCRP levels of patients with moderate to severe psoriasis in studies by Keerthana et al and Agravatt et al were 6.26 mg/l and

7.42 mg/l, respectively, with a highly significant correlation with PASI. These are slightly higher than the mean value in our severe psoriasis group, which was 4.5 mg/l. This difference can be explained by the difference in the methods/analyzers used to measure hsCRP levels. Ours was a semi-automated analyzer using kit from "Neplostar", by trubidimetric immunoassay.

We thus propose hsCRP as a useful marker of psoriasis severity that could be used to monitor psoriasis and, together with PASI, as a global index of disease severity.

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institutional ethics committee

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