

Original Research Article

High sensitivity C-reactive protein, a predictor of cardiovascular mortality and morbidity, and psoriasis: a case control study

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ABSTRACT

Background: Psoriasis, a chronic inflammatory disease, is associated with systemic comorbidities. The blood levels of various inflammatory markers are increased in psoriasis. One of them is high sensitivity C-reactive protein (hs-CRP). The serum level of hs-CRP is increased in many inflammatory diseases like psoriasis, cardio vascular diseases, infections, arthritis and others. The objectives of the study were to determine serum level of hs-CRP in psoriasis in relation to its PASI score, which is a subjective method to determine severity of the disease, whereas hs-CRP is an objective and more reliable method. And to have a better idea of systemic inflammatory process caused by psoriasis, serum level of hs-CRP was evaluated in psoriasis patients.

Methods: A case control study was conducted including 38 patients of chronic plaque psoriasis from dermatology outpatient department of Maharaja Agrasen Medical College (MAMC), Agroha, India, and 38 healthy controls.

Results: The serum level of hs-CRP was significantly raised in psoriasis patients ($p < 0.001$). The mean hs-CRP level in psoriasis patients was 6.824 ± 8.562 mg/l whereas it was 1.072 ± 0.929 mg/l in controls. Two observations were noticed, one, the increase in hs-CRP level correlated with PASI score and second, it was much higher in psoriatic patients as compared to controls.

Conclusions: The much higher hs-CRP levels in psoriasis as compared to controls and its correlation with severity of psoriasis has led us to propose that this much high hs-CRP is a biomarker of systemic inflammatory process of psoriasis as well as inflamed cutaneous lesions.

Keywords: Psoriasis, High sensitivity C-reactive protein (hs-CRP), Cardiovascular disease

INTRODUCTION

Psoriasis is a chronic inflammatory disease of the skin with systemic inflammatory repercussions. Its prevalence is high in western population ranging from 2-3% as reported by systematic review of published population based studies.^{1,2} Its prevalence in developing countries has not been established. In United States, it has been

reported to be around 1%, whereas in Norway as 8.5%.³ Its recurrent nature i.e. recurrent inflammation of skin causing more recurrent systemic inflammatory damage and along with adverse quality of life, it causes systemic comorbidities with every relapse.

Psoriasis is a multifactorial and complex disease with interplay of genetics and environmental factors.² Psoriasis

area and severity index (PASI) score is used to evaluate the severity of psoriasis which is highly subjective method. We need an objective and more reliable method to determine the severity of psoriasis. High sensitivity C-reactive protein (hs-CRP) may prove one of them.

Psoriasis is characterized by hyper proliferation and defective keratinization in the epidermal layer of skin. Its inflammatory nature leads to excessive secretion of dermal and systemic inflammatory cytokines such as IL-2, IL-6, IL-8, IL-12, IL-17, IL-19, IL-20, IL-22, IL-23, IL-24, IFN- γ and TNF- α .⁴ C-reactive protein (CRP) is an acute phase reactant protein which is an inflammatory biomarker induced by TNF- α through IL-6.⁵ CRP being a reflection of systemic inflammatory pathway, may guide treatment of the disease and prevention of mortality and comorbidities. hs-CRP is a very sensitive biomarker of inflammation. Its level is directly related to the severity of the disease activity. Psoriasis has been studied widely viz-a-viz systemic organs. It has been reported to be associated with metabolic co-morbidities including cardiovascular diseases, obesity, non-alcoholic fatty liver disease (NAFLD) and diabetes.⁶⁻⁸

Psoriasis patients have an increased risk of cardiovascular diseases (CVD) and reduced life span.⁹ There may be a role of cofactors like obesity, sedentary life style, dyslipidemia for increased CVD, but evidence indicates that psoriasis itself may be an independent risk factor for cardiovascular mortality and morbidity.¹⁰ Underlying mechanism to this is platelet hyper-reactivity, hyperhomocysteinemia, increased levels of c-reactive protein (CRP) and other proinflammatory cytokines, along with obesity, dyslipidemia and life style (sedentary life style because of disease related poor quality of life and depression).¹¹⁻¹⁴ Though psoriasis is more apparent on skin as erythematous scaly plaques, various studies have shown its association with other comorbid condition like arthritis, osteoporosis, uveitis, inflammatory bowel diseases metabolic syndrome, obesity, type-2 diabetes and NAFLD.⁶⁻⁸ Psoriasis is a T-cell mediated disease, Th-1 and Th-17 playing a major role, which in turn produce pro-inflammatory cytokines like IL-6, IL-17, IL-22, TNF- α and IFN- γ resulting in inflammatory changes.^{15,16}

All these diseases add to comorbidities and cause of mortality in psoriasis and hs-CRP is raised in all these inflammatory systemic diseases which are consequence of chemokine cascade originating from psoriasis plaques in psoriatics. So we chose to detect the serum level of hs-CRP in psoriasis with its relation to PASI score and controls, in this case control study to propose that hs-CRP levels may not be related only to severity of psoriasis but also to its associated systemic inflammatory diseases, so that we can manage the psoriasis patient as a whole.

METHODS

The present case-control study recruited 38 patients of chronic plaque type psoriasis attending our outpatient

department of Maharaja Agrasen Medical College (MAMC), Agroha, India, and 38 healthy, age and sex matched controls between September and November of year 2018. The psoriasis patients who were aged 18 years and older, and clinically diagnosed were included in the study. The approval from the ethical committee of the institution was taken before initiating the study.

Patients having any symptom or sign of acute or chronic infection, any inflammatory skin disorder, autoimmune diseases, previous history of myocardial infarction or any severe cardiovascular disease, chronic renal disease, arthritis including psoriatic arthritis, carcinoma, chronic smokers/alcoholics, pregnant and lactating mothers, recent surgery, bony fracture within last 3 months were excluded from the study.

All details of the patients were recorded in a standard proforma and a written informed consent was taken from all the participants of the study. Psoriasis Area and Severity Index (PASI) score was used to measure the severity of psoriasis and body surface area (BSA) was calculated with the help of rule of nine.

A 5 ml venous blood sample was taken from all the participants of the study and sent to the laboratory. Serum hs-CRP levels were measured by immunoturbidimetric method. For cardiovascular risk assessment based on hs-CRP level, patients having levels <1.0 mg/l were considered as 'low risk', between 1.0 to 3.0 mg/l as 'moderate risk', and >3.0 mg/l as 'high risk'.

SPSS (Statistical package for Social Science) version 17.0 software was used to analyze the data. The continuous variables were compared using student's t-test of independence and Chi-square test of significance was used to compare the categorical variables. Pearson's correlation coefficient (r) was used for correlation of continuous variables. In all assessments for statistical significances, level of significance was confidence interval at 95% level of confidence (P value <0.05).

RESULTS

Thirty eight psoriasis patients and thirty eight healthy controls were included in this study. The average age of patients was 40.605 ± 11.253 years with 7.934 ± 5.509 years as duration of the disease. The mean BSA involved was 45.00 ± 18.083 and mean PASI was 21.321 ± 8.312 (Table 1).

The mean serum hs-CRP level was 6.824 ± 8.562 in psoriasis patients while it was 1.072 ± 0.929 in control group. The serum levels of hs-CRP were significantly higher in the psoriasis patients ($p < 0.001$). A significant percentage of psoriasis patients (68.4%) were found to have a value of hs-CRP suggesting high risk of cardiovascular disease (Table 2).

Table 1: Basic characteristics of psoriasis patients (n=38) and controls (n=38).

	Patients	Controls	P value
Age (years) (mean±SD)	40.605±11.253	40.816±9.449	0.930
Sex			
Male (n) (%)	28 (73.7)	25 (65.8)	0.454
Female (n) (%)	10 (26.3)	13 (34.2)	
BMI (mean±SD) kg/m²	24.273±2.486	23.982±2.459	0.608

Table 2: Serum hs-CRP levels in psoriasis patients (n=38) and controls (n=38)

hs-CRP level (mg/l)	Patients	Controls	P value
Mean±SD	6.824±8.562	1.072±0.929	
Minimum	0.45	0.48	<0.001**
Maximum	43.80	3.35	
Low risk (<1.0 mg/l) (n) (%)	5 (13.2)	27 (71.1)	<0.001**
Moderate risk (1.0 to 3.0 mg/l) (n) (%)	7 (18.4)	6 (15.8)	
High risk (>3.0 mg/l) (n) (%)	26 (68.4)	5 (13.2)	

**p<0.001; highly significant.

In this study, we found that serum hs-CRP levels correlated with BSA ($r=0.571$, $p<0.001$) as well as PASI ($r=0.706$, $p<0.001$), but did not correlate with the duration of the disease ($r=0.050$, $p<0.764$).

DISCUSSION

The hs-CRP is a highly sensitive biomarker of inflammation and much more sensitive than CRP. Although many studies have been done to find correlation of serum CRP levels with severity of psoriasis but there are very few which have studied serum levels of hs-CRP in psoriasis patients.

CRP is the most studied proinflammatory biomarker.¹⁷ It is analytically stable and reproducible. CRP is produced in liver (hepatocytes) through action of IL-6 and IL-17 and other chemokines. There is strong evidence supporting CRP as predictor of future cardiovascular events in various clinical settings including healthy subjects.¹⁸ The cause and effect relationship of CRP in CVD is not well understood. Whether CRP is only a biomarker of CVD or does it contribute directly to inflammatory process in CVD is still not studied.

In our study, mean serum hs-CRP level was found to be raised in psoriasis patients than controls (6.824 ± 8.562 vs 1.072 ± 0.929 , $p<0.001$). This was in concordance with other studies done by various authors.¹⁹⁻²³ Our study found high risk value of hs-CRP (>3 mg/l) in 68.4% of psoriatic patients as compared to only in 13.2% of controls ($p<0.001$), which is a highly significant finding. Secondly, raised levels of hs-CRP correlated with PASI ($r=0.706$, $p<0.001$) and BSA ($r=0.571$, $p<0.001$) independent of age, sex, BMI and duration of the disease.

Murari et al found the successive increase in serum CRP levels with increase in severity of psoriasis (1.62 ± 0.39 mg/dl in mild psoriasis, 5.61 ± 0.85 mg/dl in moderate

psoriasis and 10.64 ± 2.23 mg/dl in severe psoriasis with $p=0.001$).²⁴ In another study, Ramay et al have reported that CRP was significantly elevated (>5 mg/l) in psoriatic patients compared to controls (52% vs 14%, $p=0.001$).²⁵ Ibrahimbas et al also found significant correlation between PASI and CRP levels ($p=0.006$).²⁶ Our study results were in concordance with these studies.

hs-CRP level was positively related with severity of psoriasis. The evaluation of psoriasis is dependent on subjective method i.e. PASI score, which varies between observers, whereas hs-CRP is an objective method which can be used as a tool for classifying severity of psoriasis.

hs-CRP, being a highly sensitive biomarker, is raised in all systemic inflammatory diseases associated or caused by chemical mediators of psoriasis. May it be cardiac disease, atherosclerosis, thrombosis, pulmonary embolism; hs-CRP is raised in all. Other comorbidities of psoriasis are diabetes mellitus, insulin resistance, obesity, hypertension, NAFLD which adversely affects the life span of psoriatic patients.

Raised hs-CRP in psoriasis could be a reflection of more serious systemic inflammatory process like cardiovascular diseases, liver involvement, obesity etc.

We thus propose that psoriatic patients with active and moderate to severe psoriasis be screened for hs-CRP and looked for any evidence of hidden cardiovascular diseases and other systemic diseases associated with psoriasis. More research is needed to find the incidence of CVD and other systemic diseases in those psoriatics in whom hs-CRP is raised or if CRP is also a contributing factor in initiating of inflammatory process in vascular endothelium, in psoriatics, leading to cardiovascular mortality and morbidity, and decrease in CRP in these patients reduces the risk of future cardiovascular events, and whether hs-CRP can be used to determine the severity of psoriasis as an objective method.

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