Hyperuricemia and Serum ADA Levels in Psoriasis and their Correlation to Severity of Disease

Mir Nadeem[1], Bilal Ahmad Mir[2], Tabinda Ayub Shah[3], Mir Waseem[4], Aqib Hassan Dar[5]

ABSTRACT

Introduction: Psoriasis is a chronic inflammatory autoimmune disease characterized by hyperproliferation of keratinocytes with multifactorial pathogenesis including genetic, and environmental factors. The aim of this study was to evaluate serum ADA, SUA, and ESR in psoriatic patients and their correlations with PASI score.

Material and methods: Our study was a case–control study. The sample size was calculated using the Cochran formula and 50 patients of psoriasis who attended the out patient clinic at SMHS and Government medical college, srinagar were included in the study. These patients were divided according to PASI scores into three groups (mild, moderate, and severe). PASI score <10 defined psoriasis as mild, between 10 and 20 as moderate, and >20 as severe. A group of 50 healthy subjects of matched age and sex were included as a control group who were taken from amongst volunteering hospital staff and relatives.

Results: This study included 50 psoriatic patients classified according to PASI score into mild, moderate, and severe psoriatic group and 50 age and sex matched controls. Out of these four patients had mild psoriasis, twelve patients had moderate psoriasis and thirty four patients had severe psoriasis according to PASI. Fifty healthy subjects were included as a control group. There were no statistically significant differences of age and sex between different patients and the control group.

Conclusion: ESR, Serum Uric Acid and serum adenosine deaminase levels are significantly raised in patients with psoriasis. However there was no association with severity of disease in these patients, however, larger studies are needed to elucidate the mechanism and whether this hyperuricemia predisposes these patients to gout and increased risk of cardiovascular disease.

Keywords: Hyperuricemia, Serum ADA Levels, Psoriasis, Severity of Disease

INTRODUCTION

Psoriasis is a chronic inflammatory autoimmune disease characterized by hyperproliferation of keratinocytes with multifactorial pathogenesis including genetic, and environmental factors.[1] It can occur at any age, and is most common in the age group 50–69.[2] The reported prevalence of psoriasis in countries ranges between 0.09%[3] and 11.4%[4], making psoriasis a serious global problem. The etiology of psoriasis remains unclear, although there is evidence for genetic predisposition.[5] The role of the immune system in psoriasis causation is also a major topic of research.

In 1958, Walkerin first suggested that psoriasis may be associated with hyperuricemia. Hyperuricemia has been detected more frequently in patients with psoriasis and has also been associated with cardiovascular diseases and metabolic syndrome. Specifically, the prevalence of CVD has been linked with higher levels of uric acid[6] In addition, hyperuricemia has been reported to cause adverse cardiovascular outcomes, especially sudden cardiac death.+ Adenosine deaminase (ADA) is an enzyme involved in purine metabolism and is essential for the breakdown of adenosine from food and the turnover of nucleic acids in tissues. It is considered as a marker of nonspecific T-cell activation.[8] The epidermis of psoriatic patients showed high levels of ADA which correlated with the hyperproliferative states of the keratinocytes with pronounced DNA synthesis.[9] In addition, plasma ADA activity was higher in psoriatic patients compared to controls and decreased after treatment with propylthiouracil (PTU), PUVA, or cyclosporine.[10] Several studies have found correlation between serum uric acid (SUA) level, and the severity of psoriasis and increased risk of cardiovascular mortality.[11] Erythrocyte sedimentation rate (ESR) increases with the severity of psoriasis pointing out the chronic inflammatory nature. It was found as a strong predictor for the presence of psoriatic arthritis [PsA].[17] However, others showed variable ESR between psoriatics with and without subclinical arthritis.[13]

The aim of this study was to evaluate serum ADA, SUA, and ESR in psoriatic patients and their correlations with PASI score.

MATERIAL AND METHODS

Our study was a case–control study. The sample size was calculated using the Cochran formula and 50 patients of psoriasis who attended the out patient clinic at SMHS and Government medical college, srinagar were included in

[1]Assistant Professor, Department of Medicine, SGT, Gurgoan, Haryana, [2]Senior Resident, Department of Medicine, GMC, Srinagar, J&K, [3]Senior Resident, Department of Medicine, GMC, Srinagar, J&K, [4]Senior Resident, Department of Medicine, SKIMS, Soura, J&K, [5]Senior Resident, Department of Dermatology, GMC, Srinagar, J&K, India

Corresponding author: Dr Tabinda Shah, Doctors Quarters, GMC Baramulla, Kashmir, India pin 193101, India

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the study. These patients were divided according to PASI scores.[14] into three groups (mild, moderate, and severe). PASI score <10 defined psoriasis as mild, between 10 and 20 as moderate, and >20 as severe.[15] A group of 50 healthy subjects of matched age and sex were included as a control group who were taken from amongst volunteering hospital staff and relatives. All participants signed an informed consent before being included in the study.

Exclusion criteria: No history of systemic or topical steroid medication, methotrexate, biologics, or phototherapy treatment for at least 2 months before inclusion. No history of medical disorders that might affect the serum levels of ADA,CRP, such as lymphoid malignancies, infectious and noninfectious systemic diseases with chronic T-cell activation such as pulmonary and pleural tuberculosis, sarcoidosis, typhoid fever, and cutaneous anthrax. patients with connective tissue diseases, including progressive systemic sclerosis, morphea, dermatomyositis, and lupus erythrematosis, were also excluded from the study.

A detailed history including age, drug history, and history of medical diseases with stress on age, duration of illness, quality of life, severity and joint affection. A careful physical examination was also noted.

Blood sample was collected after an overnight fast of 8 hours. ESR was assayed using Westergren method. SUA was assayed by enzymatic colorimetric uricase method using SPINREACT, S. A/S. A. U Ctra. Santa Coloma, 7 E-17176 SANT ESTEVE DE BAS (GI) SPAIN according to the instructions of manufacturing company.

ADA was assayed through kinetic method using Ben Biochemical Enterprise (BEN) ADA quantitative ultraviolet assay kit, Milano, Italy.

STATISTICAL ANALYSIS

Statistical analyzes were carried out using SPSS for Windows, release 20 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were presented as mean ± standard deviation or median and range, and qualitative data were presented as frequency and percentage. Chi-square and Fisher's exact tests were used to determine the relationship between qualitative data. Quantitative data were compared with oneway ANOVA The data was represented in graphs and barcharts. Spearman's correlation was used to assess the correlation of PASI scores and other variables in psoriatic patients. P<0.05 was considered statistically significant.

RESULTS

This study included 50 psoriatic patients classified according to PASI score into mild, moderate, and severe psoriatic group and 50 age and sex matched controls. Out of these four patients had mild psoriasis, twelve patients had moderate psoriasis and thirty four patients had severe psoriasis according to PASI. Fifty healthy subjects were included

	Mild	Moderate	Severe
Age range [median]	52-54yrs[53]	28-66y[60]	28-64y[52]
Sex			
Male(%)	0	4(33.3%)	20(62.5%)
Female(%)	4(100%)	8(66.6%)	12(37.5%)

Table-1: Shows the demographic data of psoriatic patients studied.

Parameter	Patients	Controls	P value
	Mean (range)	Mean (range)	
ADA(U/L)	22.57(6.1-55)	8.58(1-19)	<0.00001
ESR(mm/hr)	25.68(6-75)	11.64(4-22)	<0.00001
SUCA(mg/dl)	6.584(5.4-7.8)	4.13(2.0-6.6)	<0.00001

ADA: Adenosine deaminase, SUA: Serum uric acid, ESR: Erythrocyte sedimentation rate

Table-2: Comparison of adenosine deaminase, serum uric acid, and erythrocyte sedimentation rate between psoriasis and controls

Parameters	Pasi		
	Mild	Moderate	Severe
ADA			
R	0.173	0.15	0.124
P	0.2	0.44	0.566
ESR			
R	0.335	0.17	0.05
P	0.13	0.44	0.567
SUA			
R	0.01	0.177	0.005
P	0.55	0.47	0.044

r: Spearman correlation coefficient, ADA: Adenosine deaminase, SUA: Serum uric acid, ESR: Erythrocyte sedimentation rate, PASI: Psoriasis area severity index

Table-3: Correlations of psoriasis area severity index score with laboratory results in psoriatic patients

Arthritis	Mild	Moderate	Severe
Present	0(0%)	2(16.67%)	8(25%)
V	4(100%)	10(83.33%)	24(75%)

Table-4: Psoriatic arthritis according to psoriatic group

as a control group. There were no statistically significant differences of age and sex between different patients and the control group. Table 1 shows the demographic data of the studied groups Of the studied patients, 24(48%) patients had chronic plaque psoriasis, 8(16%) patients had pustular psoriasis, 6(12%) had guttate psoriasis, 6 (12%)had nail psoriasis, 4(8%) had inverse psoriasis and 2(4%) patient had erythrodermic psoriasis.

ADA, SUA, and ESR were significantly (p value < 0.001) increased in psoriatic patients as compared with the control group Further we compared these markers with respect to severity of psoriasis according to PASI. ADA, SUA, and ESR showed a significant (p value < 0.001) increase in each psoriatic group (mild, moderate, and severe) compared with the control group. The SUA, ADA and ESR were higher in patients with severe psoriasis. However, the difference was not statistically significant (p value >0.05) (table-2). Correlations of psoriasis area severity index score with laboratory results in psoriatic patients are represented in table 3.

Of the studied group of patients 10 (20%) presented with joint involvement. The frequency of arthritis increased with increasing severity of psoriasis ie 0%, 16.67%, and 25% in mild, moderate, and severe psoriasis, respectively [Table 4]

DISCUSSION

Psoriasis is a chronic systemic disease with an immune-inflammatory aetiology, affecting approximately 2%–3% of the world's population, and characterized by T cell-mediated hyper-proliferation of keratinocytes.[16] It is characterised by an exaggerated proliferation of keratinocytes secondary to an activated immune system. The incidence is highest at the age of 20–39 years in males and 40–59 years in females, with an equal male-to female ratio.[17] Hyperuricemia has been detected frequently in patients with psoriasis. We evaluated 50 patients of psoriasis in our study and found that SUA levels were significantly(<0.001) raised than the control group. Similar results have been recorded by many researchers, and a history of psoriasis was associated with an increased risk of gout with increased SUA[16] and this significantly decreased after the treatment of psoriasis.[18] In addition, patients with psoriasis and hyperuricemia showed marked improvement in psoriasis when treated for their hyperuricemia. Psoriasis, like gout, may be, at least partly, a result of a disorder of purine metabolism and monosodium urate crystals may be partially responsible for the cell proliferation that is characteristic of psoriatic plaques Kwon et al[19], found no significant difference between SUA of psoriatic patients and healthy population and reported a positive correlation of SUA with PASI score. This was in contrast to our results of significant increase of SUA in psoriatic patients without a significant correlation with PASI score. They attributed this result to the lower skin involvement in their patients that might not have been sufficient to induce hyperuricemia.[19]

We also studied the serum ADA levels in our patients and correlated these with PASI and found ADA levels were significantly raised than the control group.The increased ADA activity in our psoriatic patients could be a cause of increased SUA because it catabolises adenosine to inosine which is further degraded to uric acid.[20] ADA activity was considered as an indicator of the role of purine metabolism and T-cell activation in the pathogenesis of psoriasis However, the results of studies evaluating ADA level in psoriatic patients are conflicting. Some studies report high ADA in the sera of psoriatic patients than that of the healthy controls.[21,22] Tikhonov et al[9], found double activities of ADA and purine nucleoside phosphorylase (PNP) in the skin of psoriatic patients. In accordance with our results Hashemi et al[21] and Yildirum et al.[22] found no correlation between serum ADA and PASI score. Many studies have also reported a decrease of serum ADA levels after psoriasis treatment with different modalities including cyclosporine, etanercept, PUVA, and PTU.[10,22] On the contrary, one study found normal ADA activity in psoriatic patients.[23] This could be due to the few number of patients (only 18) and the use of a normal laboratory range instead of a control group in that study.

In accordance with our results, many studies reported increased ESR in psoriatic patients than in controls.[24,25]The decrease of RBCs deformability and plasma levels of globulins and fibrinogen with the decrease of albumin could explain the increased ESR in psoriatic patients.[25,26]

We noted in our study that the frequency of arthritis increased with increasing severity of psoriasis ie 0%, 16.67%, and 25% in mild, moderate, and severe psoriasis, respectively. This result supported other studies showing a higher risk of having arthritis with severe psoriasis.[26,27,28,29] The increased frequency of PsA in severe psoriasis is multifactorial. The larger affected body surface area leads to a higher systemic burden of the inflammatory response and wider port of entry for the skin flora to interact with the immune system. These changes under the shared susceptibility genes and/or environmental factors eventually result in triggering of PsA.[30]

CONCLUSION

ESR, Serum Uric Acid and serum adenosine deaminase levels are significantly raised in patients with psoriasis. However there was no association with severity of disease in these patients. Although these findings can be attributed to the increased purine metabolism in these patients, however, larger studies are needed to elucidate the mechanism and whether this hyperuricemia predisposes these patients to gout and increased risk of cardiovascular disease.

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