

## ASSOCIATION OF PSORIASIS AND SERUM URIC ACID LEVELS: A CASE CONTROL STUDY

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### ABSTRACT

**Objective:** To determine the association between psoriasis and serum uric acid levels.

**Study Design:** Case control study.

**Place and Duration of Study:** Study was conducted at Department of Dermatology, Pakistan Air Force Hospital Islamabad, from Jan 2017 to Jul 2017.

**Material and Methods:** This study involved 31 psoriatic subjects of both genders aged between 18-70 years. Subjects were matched with 31 healthy volunteers from PAF Hospital staff. Serum uric acid level was tested in all the study participants. Outcome variable was frequency of hyperuricemia among cases and controls.

**Results:** The age of the subjects ranged from 18 years to 70 years with a mean of  $39.47 \pm 13.92$  years. Majority ( $n=37$ , 59.7%) of the subjects were aged under 45 years. There were 35 (56.5%) male and 27 (43.5%) female subjects with a male to female ratio of 1.3:1. There were 20 (32.3%) obese subjects. Mean serum uric acid was significantly higher among cases ( $5.89 \pm 1.28$  vs.  $4.76 \pm 1.44$  mg/dl;  $p=0.002$ ) as compared to controls. Frequency of hyperuricemia was significantly higher among cases (25.8% vs. 6.5%;  $p=0.038$ ; OR=5.043; 95% CI: 0.975 - 26.086) as compared to controls.

**Conclusion:** Mean serum uric acid and frequency of hyperuricemia was found to be significantly higher among cases (25.8% vs. 6.5%;  $p=0.038$ ) as compared to controls irrespective of age, gender and obesity status of patient.

**Keywords:** Hyperuricemia, Psoriasis, Serum uric acid.

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### INTRODUCTION

Psoriasis is a common, chronic, complex, disfiguring, inflammatory, non-infectious skin disease, with no cure. The exact cause is still not known but it is supposed to be a multifactorial disease initiated by interplay between genetic, environmental, and immunological factors and also triggered by drugs<sup>1</sup>. The reported prevalence of psoriasis in countries ranges between 0.09% and 11.43%, making psoriasis a serious global problem with at least 100 million individuals affected worldwide which can occur at any age, and is most common in the age group 50-69<sup>1</sup>. It is a proliferative disease characterized by the rapid multiplication of skin cells; 10 times faster than the normal. As underlying cells reach the skin's surface and die, their sheer volume causes clinically raised, red plaques covered with white

scales<sup>2</sup>. The need for treatment is usually lifelong and is aimed at remission. So far, there is no treatment that would give hope for a complete cure of psoriasis<sup>1</sup>.

The increased cell turn over in psoriatic plaques can lead to metabolic abnormalities like rise in serum uric acid levels<sup>3,4</sup>. It has been postulated that hyperuricaemia results from increased purine synthesis from the rapid epidermal cell turnover<sup>4</sup>. It has been noticed that serum uric acid levels exacerbate by increase in the severity and duration of psoriasis, in psoriatic arthritis, and in patients with non-plaque type psoriasis.

Historically psoriasis was considered a disease exclusively of the skin with little consideration of systemic sequelae. The identification of psoriatic arthritis as a distinct condition from rheumatoid arthritis and its association with cutaneous psoriasis heralded a new appreciation of psoriasis as more than "skin deep". More recently recognition of metabolic syndrome has raised the profile of psoriasis as a systemic

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inflammatory disease with the need to manage patients holistically<sup>5</sup>. It is also associated with inflammatory bowel disease and depression<sup>1</sup>.

Hyperuricemia appears to be a frequently associated metabolic abnormality in patients with psoriasis and may cause a number of additional health related problems like joint pains, coronary artery disease, hypertension and renal disease. These associated comorbidities can further decrease the quality of life of psoriatic patients who are already upset about the unsightly chronic disfiguring psoriatic plaques on their skin<sup>6</sup>. Routine screening of serum uric acid levels is not being carried out in psoriatic patients, it should however be done in patients presenting with psoriasis so that timely identification and treatment can reduce the health related consequences of this metabolic abnormality. These associated comorbidities tend to worsen the burden of disease, as well as further reduce quality of life indices of the sufferers.

Presently, there is not much work being done in Pakistan to assess the association between psoriasis and hyperuricemia. Very few studies have been conducted in our region to look at serum uric acid levels in psoriatic patients<sup>4</sup>. However it did not look into the parameters of age, gender and obesity. Aim of our study was to determine the serum uric acid levels in adult psoriatic patients and also determine their baseline characteristics of age, gender and obesity.

## **MATERIAL AND METHODS**

It was a case-control study. Study was conducted at the department of Dermatology, Pakistan Air Force Hospital Islamabad after approval from the Institutional Ethical Committee. Duration of study was 6 months, from 15<sup>th</sup> January 2017 to 14<sup>th</sup> July 2017.

Sample size of 62 (31 cases, 31 controls) was calculated with 80% power of test and 95% confidence level while taking expected frequency of hyperuricemia to be 25% and 1% in adult patients with psoriasis and healthy controls respectively<sup>4</sup>. Patients were selected by non-probability, consecutive sampling.

Patients of both genders aged between 18-70 years, those presenting with psoriasis diagnosed during the last 6 months and healthy adults without psoriasis (members of PAF Hospital Staff) as controls were included in the study.

Patients with alcohol consumption, diabetes mellitus, chronic liver disease, chronic kidney disease, those taking any of following medications for the preceding 2 weeks period were also excluded; Diuretics, Salicylates, Ketoconazole, Theophylline, Pyrazinamide, Ethambutol, pregnant women and lactating mothers, psoriatic arthritis and gout and data collection procedure were excluded from the study.

Thirty one subjects presenting in the Dermatology Outpatient Department of Pakistan Air Force Hospital, Islamabad meeting the inclusion criteria of the study and 31 healthy adults without psoriasis who are members of PAF hospital staff were enrolled into this study. Detailed history and written informed consent was obtained from each patient. Following 2 groups of subjects were assimilated. Presenting with psoriasis diagnosed during the last 6 months

Healthy adults without psoriasis (members of PAF Hospital Staff).

Hyperuricemia was labeled upon a serum uric acid level  $\geq 7$  mg/dl in men and  $\geq 6$  mg/dl in women. Serum uric acid level was acquired after an overnight fast. 5ml of venous blood was sampled by venepuncture and sent for analysis. The test was done by enzymatic calorimetric reaction on fully automated chemical analyzer, Cobas® modular 8000 (Roche/Hitachi), using Roche/Hitachi calibrators and controls. Patient's demographic details along with serum uric acid levels were recorded.

All the collected data was entered and analyzed through SPSS version 21.0. Numerical variables; Age and serum uric acid level have been presented as mean  $\pm$  SD. Categorical variable i.e., gender and hyperuricemia have been presented by frequency and percentage. Frequency of hyperuricemia has been compared between the two groups using chi-square test

taking  $p \leq 0.05$  as significant. Data has been stratified for age, gender and obesity to address effect modifiers. Post-stratification chi-square test has been applied taking  $p$ -value  $\leq 0.05$  as

Frequency of hyperuricemia was significantly higher among cases (25.8% vs. 6.5%;  $p=0.038$ ) as compared to controls as shown in table-III.

**Table-I: Baseline characteristics of study groups.**

Characteristics	Cases (n=31)	Controls (n=31)	<i>p</i> -value
Age (years)	40.29 ± 13.10	38.65 ± 14.86	0.645
<b>Age Groups</b>			
18-44 years	18 (58.1%)	19 (61.3%)	0.796
45-70 years	13 (41.9%)	12 (38.7%)	
<b>Gender</b>			
Male	18 (58.1%)	17 (54.8%)	0.798
Female	13 (41.9%)	14 (45.2%)	
<b>Obesity</b>			
Yes	11 (35.5%)	9 (29.0%)	0.587
No	20 (64.5%)	22 (71.0%)	

Independent sample t-test and chi-square test, observed difference was statistically insignificant.

statistically significant.

## RESULTS

The age of the patients ranged from 18 years to 70 years with a mean of  $39.47 \pm 13.92$  years.

## DISCUSSION

Our study has shown significantly frequent increase in serum uric acid levels in patients of psoriasis as compared to the controls which is

**Table-II: Comparison of mean serum uric acid among study groups.**

Characteristics	N	Cases (n=31)	Controls (n=31)	<i>p</i> -value
Overall	31/31	5.89 ± 1.28	4.76 ± 1.44	0.002*
<b>Age Groups</b>				
18-44 years	18/19	5.86 ± 1.40	4.76 ± 1.36	0.020*
45-70 years	13/12	5.93 ± 1.15	4.76 ± 1.62	0.047*
<b>Gender</b>				
Male	18/17	5.89 ± 1.26	4.79 ± 1.48	0.024*
Female	13/14	5.89 ± 1.36	4.71 ± 1.44	0.040*
<b>Obesity</b>				
Yes	11/9	6.22 ± 1.27	4.81 ± 1.57	0.040*
No	20/22	5.71 ± 1.28	4.74 ± 1.42	0.026*

Independent sample t-test, \*Observed difference was statistically significant.

Majority (n=37, 59.7%) of the patients were aged under 45 years. There were 35 (56.5%) male and 27 (43.5%) female patients with a male to female ratio of 1.3:1. There were 20 (32.3%) obese patients as shown in table-I.

Mean serum uric acid was significantly higher among cases ( $5.89 \pm 1.28$  vs.  $4.76 \pm 1.44$  mg/dl;  $p=0.002$ ) as compared to controls. Similar significant difference was observed across age, gender and obesity groups as shown in table-II.

consistent with the metabolic abnormality reported in literature with psoriasis<sup>3,4</sup>. Our mean age of the subjects with psoriasis was  $40.29 \pm 13.10$  years. This finding is in line with that of Haider *et al* (2014) who observed similar mean age of  $40.0 \pm 12.0$  years among psoriatic patients presenting at Civil Hospital Karachi<sup>7</sup>. Ejaz *et al* (2013) reported similar mean age of  $39.8 \pm 7.9$  years among psoriatic patients presenting at Combined Military Hospital, Sargodha<sup>8</sup>. Gisoni *et al* however reported much higher mean age of

51.1 ± 10 years and 54.1 ± 12.5 years in Italian patients<sup>9</sup>. So our patient's age group is more in line with those reported in literature for our ethnic sub-population.

In the present study, there were 35 (56.5%) male and 27 (43.5%) female patients with a male to female ratio of 1.3:1. A similar male predominance among such patients in local population has been reported by Haider *et al* and Ejaz *et al*<sup>7,8</sup>. Gisondi *et al* (2014) also reported much higher male predominance among Italian patients with a male to female ratio of 2.8:1<sup>9</sup>.

In the present study, there were 20 (32.3%) obese patients. A similar frequency of obesity among psoriatic patients has been reported by Gisondi *et al* who observed it to be 30.2%<sup>9</sup>. These findings have strengthened the results of baseline

A meta-analysis of 14 observational studies and 170 identified reports found a significant higher serum uric acid level (MD 0.68, 95% CI 0.26–1.09;  $p=0.002$ ) in patients with psoriasis in Western Europe, but no significant differences were found between the East Asia and India subgroup (MD 1.22, 95% CI -0.13–2.56;  $p=0.08$ ) or the Middle East subgroup (MD 0.48, 95% CI -0.49–1.44;  $p=0.33$ )<sup>12</sup>. Our study has however shown results which are different from this large meta-analysis for our geographical location. These differences can be attributed to different lifestyles, eating, and social behaviors between the regions. Therefore, it is not surprising to assume that the correlation between psoriasis and hyperuricemia displays a region-dependent pattern. This factor was however not being considered as a confounding factor in the above mentioned

**Table-III: Comparison of frequency of hyperuricemia among study groups.**

Hyperuricemia	Cases (n=31)	Controls (n=31)	OR	95% CI	p-value
Yes	8 (25.8%)	2 (6.5%)	5.043	0.975 - 26.086	0.038*
No	23 (74.2%)	29 (93.5%)			
Total	31 (100%)	31 (100%)			

Chi-Square test, \*Observed difference was statistically significant

characteristics of our study which is in line with the global epidemiological data of psoriasis<sup>1</sup>.

In the present study, mean serum uric acid was significantly higher among cases as compared to controls. Our observation match with that of Gisondi *et al* who also observed similar significant difference in the mean serum uric acid level in Italian psoriatic patients ( $5.61 \pm 1.6$  vs.  $4.87 \pm 1.4$  mg/dl;  $p<0.001$ ) as compared to controls<sup>9</sup>. However Agravatt *et al* (2013) didn't observe any significant difference in the mean serum uric acid levels between Indian psoriatic patients ( $5.42 \pm 2.2$ mg/dl vs.  $5.7 \pm 0.57$ mg/dl;  $p>0.05$ ) and healthy controls<sup>10</sup>.

Frequency of hyperuricemia was also significantly higher among cases as compared to controls. Similar difference was observed across all age, gender and obesity groups. Similar results have been reported by Puri *et al* and Gisondi *et al* who reported the frequency of hyperuricemia to be 16% and 20% respectively among patients presenting with psoriasis in Indian population<sup>11,9</sup>.

meta-analysis and can be a potential factor for consideration while designing such studies.

There is substantial evidence in literature suggesting that chronic hyperuricemia is an independent risk factor for metabolic syndrome, hypertension, cardiovascular diseases and chronic kidney disease<sup>13-15</sup>. The putative toxic mechanisms of hyperuricemia include mediation of inflammation, induction of endothelial cell dysfunction, stimulating vascular smooth muscle proliferation, and increasing oxidative stress<sup>14</sup>. This highlights the need for greater attention to serum uric acid levels when profiling patients with psoriasis.

It can be thus advocated on the basis of the results of the present study that in future while consulting patients of psoriasis screening should routinely be carried out for serum uric acid levels so that timely identification and management can be offered thereby reducing the morbidity and potential mortality associated with raised serum uric acid levels.

A larger prospective study indicated that psoriasis patients with extensive involvement of the skin tended to have a higher incidence of hyperuricemia<sup>16</sup>. This aspect of extent of skin disease and its correlation with the rise in serum uric acid levels has not been checked in our study, which can be limitation of this study. Also we did not take into account the confounding effects of coexisting features of the metabolic syndrome (BMI, Diabetes Mellitus, Hyperlipidemia), a condition again strongly associated with Psoriasis<sup>17,18</sup>.

Future studies can be planned to correlate the extent of psoriasis, through various indices like Psoriasis Area Severity Index (PASI scoring) or body surface area (BSA) calculation, and the rise in serum uric acid levels. Also studies can be designed to assess the impact of various topical and systemic psoriasis therapies on pre and post therapy serum uric acid levels. This will allow to early picking up this associated metabolic abnormality in patients of psoriasis thereby eliminating further risks like gout, hypertension, cardiovascular and renal diseases.

## CONCLUSION

Frequency of hyperuricemia was found to be significantly higher among cases as compared to controls irrespective of age, gender and obesity status of the patient. Its treatment might be clinically useful for the global treatment of patients. In fact management of associated hyperuricemia should be made essential part of psoriasis routine management to avoid the related morbidity and mortality risks.

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## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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