PSORIASIS & HYPERURICAEMIA; A PROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Psoriasis is a chronic dermatologic inflammatory disorder with genetic predisposition playing a strong role. Plaque psoriasis which is the commonest form, affects up to 2% of population and is increasingly associated with high uric acid level.

Objective: We aimed to determine the association of psoriasis and hyperuricaemia, with reference to concomitant occurrence of risk factors that may confound serum uric acid levels in addition to the primary diagnosis.

Methods: This is a cohort study with historical control subjects, who were matched with the study population in terms of age and gender. All patients were investigated about uric acid levels, renal function, and metabolic profile including serum cholesterol, triglycerides, fasting blood sugar and risk factors for metabolic syndromes such as body mass index (BMI).

Results: Overall mean age was 43.7 ± 8.94 years with 94 (72.3%) males and 36 (27.7%) females. Mean symptoms duration since diagnosis was 11.6 ± 4.5 years and mean psoriatic body surface area was 19.8 ± 6.6%. In this cohort study, we observed a significantly higher prevalence of asymptomatic hyperuricemia (63% vs 20%) in the psoriatic population as compared to controls. Obesity was more prevalent (24.6% vs 6.2%, $p = 0.004$, OR: 4.0, 95% CI: 1.4 – 11.3) in the psoriasis group as was the prevalence of metabolic syndrome (55.4% vs 13.8%, $p < 0.001$, OR: 4.0 95% CI: 2.1-7.6).

Conclusions: Psoriasis is a commonly associated with hyperuricaemia. The high prevalence of metabolic syndrome and the association of hyperuricaemia with increased risk of cardiovascular diseases warrants special attention in these patients.

Keywords: Psoriasis, hyperuricemia, metabolic syndrome

INTRODUCTION

Psoriasis is an immune-mediated chronic dermatologic disease which affects up to 4% of population. It is a diverse condition with various sub-types such as erythrodermic, pustular and guttate psoriasis. Psoriasis frequently presents with painful and itchy lesions. The pathogenesis of psoriasis is still a matter of ongoing research, however, inflammatory cells infiltration of the skin layers and abnormal differentiation patterns have been described. Various inflammatory mediators have been described as a possible driving force for the disease process. Psoriasis is frequently complicated by concomitant occurrence of obesity, lipid metabolism disorders, diabetes mellitus, metabolic syndrome and cardiovascular diseases.[1,2,3]

High serum uric acid levels have been observed in patients presenting with psoriasis, which have also been implicated in increasing the risk of cardiovascular diseases and metabolic syndrome. Many other studies have also shown that high serum uric acid levels in psoriasis are associated with increased cardiovascular disease risk. Walker Jr[4] was the first who presented the observation that hyperuricemia might be prevalent in psoriasis patients than the normal population. This was later investigated by other researchers, some of which confirmed this observation while others rejected. Later other studies have shown that the involved body surface area is strongly correlated with serum uric acid levels.[5,6]

A variety of researchers have questioned the association of psoriasis with hyperuricemia, attributing its occurrence to the concomitant presence of metabolic syndrome rather than a direct effect of psoriasis itself.[7,8] This has prompted clinical studies where control of the confounding factors may prevent bias in interpreting study results.[9]

The aim of our study was to analyse in a randomised controlled design the correlation of psoriasis and serum uric acid levels, while controlling for the confounding factors such as concomitant occurrence of the metabolic syndrome, presence of cardiovascular

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disease, diabetes, obesity and other conditions that may increase purine metabolism. Study in such a fashion may reveal better understanding of the association between hyperuricemia and psoriasis. Our secondary objectives include to document the incidence of gout and psoriatic arthritis.

METHODS

This is a prospective case control study conducted at the Department of Dermatology, District Headquarters Hospital, Bannu between January 2014 and December 2015. Approval was obtained of the institutional ethical committee. Informed consent was obtained from all patients before inclusion in the study.

Sample size of 65 for each group (total 130 subjects) was calculated using MedCalc version 14.8.1, taking alpha at 0.05, beta at 0.1 with a 20%[10] prevalence of hyperuricemia in psoriasis patients and 1.16%[11] prevalence of gout in the general population. Two study groups were created, Group A included 65 cases with definitive diagnosis of psoriasis and Group B comprised of 65 historical control subjects who were matched for age and gender.

Inclusion criteria for Group A included all patients with definitive diagnosis of psoriasis with no past history of psoriatic or gouty arthritis. Psoriatic arthritis or gouty arthritis were excluded by clinical criteria as outlined in CASPAR (Classification Criteria For Psoriatic Arthritis) criteria.

Patients with known comorbids which could affect uric acid levels (gout, haematologic malignancies, renal failure), or drugs that may increase uric acid levels (alcohol, salicylates, ketoconazole, diuretics, antituberculous medications etc.) were excluded from the study.

Serum studies were performed after overnight fasting. These studies were done on venous blood, and included serum uric acid (SUA), serum cholesterol, serum triglycerides, fasting blood sugar and serum creatinine. Cut-off limits for uric acid was 6.5 mg/dL in females and 7 mg/dL in males, for cholesterol it was 200 mg/dL, for triglycerides it was 150 mg/dL and for fasting blood sugar it was 125 mg/dL. Obesity was defined as a BMI of 30 or more while hypertension was defined as systolic BP of over 140 mmHg on different occasions, or those patients who were already on anti-hypertensive treatment.

For the purpose of this study, we adopted the definition of metabolic syndrome as outlined by Adult Treatment Panel-III in the Executive Summary of the Third Report of the National Cholesterol Education Program.[12]

SPSS version 22.0 was used for interpretation and reporting the data. Mean ± standard deviation was used for continuous variables. Independent samples t-test for mean differences and binary logistic regression analysis was used for determining the factors that affect SUA levels.

RESULTS

The demographic and clinical features for the two study groups are listed in Table 1. Overall mean age was 43.7 ± 8.94 years with 94 (72.3%) males and 36 (27.7%) females. Mean symptoms duration since diagnosis was 11.6 ± 4.5 years and mean psoriatic body surface area was 19.8 ± 6.6%. Mean systolic BP was 130.77 ± 15.9 mmHg, mean fasting blood sugar was 123.3 ± 44.8 mg/dL, mean serum cholesterol of 182.7 ± 46.9 mg/dL and mean triglycerides of 153.5 ± 52.1 mg/dL. 45 (34.6%) of patients were obese according to the adopted definition while 20 (15.4%) of patients had findings concurrent with the definition of metabolic syndrome. Overall, mean serum uric acid levels were 6.5 ± 4.0 mg/dL with 54 (41.5%) of patients found to have hyperuricemia according to the cut-off values.

Psoriatic patients were found to have significant differences in serum uric acid levels, fasting sugar, serum cholesterol, triglycerides and BMI. Patients with metabolic syndrome were in significantly higher proportions than the control group. Mean serum uric acid levels were significantly higher in the psoriatic patients as compared to the control subjects. It is worth noting that though fasting blood sugar levels, systolic BP and plasma cholesterol and triglycerides were significantly different between the two study groups, the prevalence of comorbidities such as diabetes and hypertension were not significantly different. Table 2

On Chi-square analysis, moderate to strong associations were observed for psoriatic patients with high BP, FBS, serum cholesterol, triglycerides, obesity, hyperuricemia and metabolic syndrome. Metabolic syndrome was highly prevalent in patient with psoriasis (80% psoriatic vs 20% control subjects had metabolic syndrome).

DISCUSSION

In this cohort study, we observed a significantly higher prevalence of asymptomatic hyperuricemia (63% vs 20%) in the psoriatic population as compared to controls. It is important to note that psoriasis is strongly associated with hyperuricemia in a Chi-square analysis (Phi: 0.43, Cramer's V: 0.43, $p < 0.001$) especially considering the fact that both study groups were matched for age and gender. It is also important to note that obesity was more prevalent (24.6% vs 6.2%, $p = 0.004$, OR: 4.0, 95% CI: 1.4 – 11.3) in the psoriasis group as was the prevalence of metabolic syndrome (55.4% vs 13.8%, $p < 0.001$, OR: 4.0 95% CI: 2.1-7.6). However, by excluding the cases with metabolic syndrome, psoriasis was significantly associated with hyperuricaemia, which suggest that hyperuricaemia is independently associated with psoriasis in a logistic regression analysis ($p = 0.01$, OR: 0.3, 95% CI: 0.12 – 0.7).

Table 1: Clinical features of the two study groups

Clinical features	Psoriasis patients n = 65		Control subjects n = 65		Significance
	n	%	n	%	
Gender					0.4
Male	49	75.4	45	69.2	
Female	16	24.6	20	30.8	
Obesity	36	55.4	9	13.8	<0.001
High BP	25	38.5	12	18.5	0.01
Hyperglycaemia	26	40.0	7	10.8	<0.001
Hypercholestrolaemia	34	52.3	6	9.2	<0.001
Hypertriglyceridaemia	37	56.9	6	9.2	<0.001
Hyperuricaemia	41	63.1	13	20.0	<0.001
Diabetes	7	10.8	7	10.8	0.9
Hypertension	16	24.6	15	23.1	0.8
Metabolic syndrome	16	24.6	4	6.2	0.004

Table 2: Group-wise statistics

	study group	Mean	SD	Mean diff. (95% CI)	Significance
Patient Age (years)	case	44.17	8.4	0.93 (-2.2 – 4.0)	0.5
	control	43.23	9.4		
Symptoms Duration (years)	case	11.62	4.4	--	--
	control	.	.		
Psoriatic area (%)	case	19.85	6.6	--	--
	control	.	.		
Systolic BP (mmHg)	case	132.25	17.1	2.9 (-2.6 – 8.5)	0.29
	control	129.29	14.5		
Cholesterol (mg/dL)	case	203.48	50.8	41.4 (26.8 – 56.1)	<0.001
	control	161.98	31.3		
Triglycerides (mg/dL)	case	181.17	53.9	55.3 (40.0 – 70.7)	<0.001
	control	125.80	31.6		
BMI	case	29.85	4.7	4.0 (2.6 – 5.4)	<0.001
	control	25.80	3.0		
Uric acid (mg/dL)	case	7.400	2.0	1.7 (0.4 – 3.1)	0.01
	control	5.626	5.1		
Creatinine (mg/dL)	case	.823	.24	-0.06 (0.04 – 0.01)	0.1
	control	.888	.20		

Many studies have confirmed that hyperuricaemia in psoriatic patients might be the result of concomitant metabolic syndrome.[8,13,14,15,16,17] As mentioned above, by excluding cases of metabolic syndrome from both groups, it was observed that psoriasis was strongly associated with hyperuricaemia.

These findings in our study suggest that psoriasis itself is associated with hyperuricaemia. The pathogenesis of hyperuricaemia in psoriasis, however, remains a topic of ongoing research. Some researchers have pointed out that hyperuricaemia might be the result of increased epidermal cell turnover.[9,18,19] These findings have been suggested by the association of psoriatic body surface area with uric acid levels.

Hyperuricaemia is highly prevalent in the general population while gouty arthritis is relatively rare though a highly disabling condition in the young to middle age patients. Studies from various geographic regions have

reported largely similar prevalence.[20] Hyperuricaemia is exceedingly common in obese patients and those who have metabolic syndrome.[21]

The high prevalence of hyperuricaemia in general population as well as the association of psoriasis with hyperuricaemia and psoriatic arthritis, highlight the importance of screening these patients for the presence of the probable cause from all aspects.[10,13] In addition, hyperuricaemia is associated with increased risk of cardiovascular diseases (CVDs) such as hypertension and carotid artery stenosis.[22] These risk factors are individually associated with high mortality in the general population, and it is imperative to determine the health implications for psoriasis patients.[22] Our findings suggest that in order to correctly diagnose and treat concomitant joint disease, it is necessary to investigate patients with psoriasis for hyperuricaemia. This will also lead to reduction in cardiovascular events in these patients. Further studies are required in order to confirm the causal relationship between psoriasis and hyperuricaemia.

CONCLUSIONS

Psoriasis is a commonly associated with hyperuricaemia. Moreover, the high prevalence of metabolic syndrome and the association of hyperuricaemia with increased risk of cardiovascular diseases warrants special attention to determine and treat the asymptomatic hyperuricaemia in psoriatic patients.

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