Hyperuricemia in patients with chronic plaque psoriasis

Paolo Gisondi, MD, a Giovanni Targher, MD, b Anna Cagalli, MD, a and Giampiero Girolomoni, MD a
Verona, Italy

Background: Few studies have examined the association between elevated serum uric acid (SUA) levels and psoriasis, and their results have been inconclusive because most of these studies did not take into account the confounding effects of coexisting features of the metabolic syndrome.

Objective: We compared the prevalence of hyperuricemia and SUA levels between psoriatic patients and control individuals.

Methods: Levels of SUA were measured in 119 consecutive psoriatic patients and 119 control individuals matched for age, sex, and body mass index.

Results: Compared with control subjects, psoriatic patients had higher SUA levels (5.61 ± 1.6 vs 4.87 ± 1.4 mg/dL; P < .001) and a remarkably greater prevalence of asymptomatic hyperuricemia (19% vs 7%; P < .001). Multivariate logistic regression analysis revealed that psoriasis was the strongest predictor of hyperuricemia (odds ratio 3.20; 95% confidence interval 1.32-7.58; P < .01) after adjusting for age, sex, and metabolic syndrome features.

Limitations: The cross-sectional design of this study does not allow us to draw any conclusion about a causal relation between psoriasis and hyperuricemia.

Conclusions: Hyperuricemia is a common finding in psoriatic patients. Its treatment might be clinically useful for the global treatment of patients. (J Am Acad Dermatol 2014;70:127-30.)

Key words: body mass index; cardiovascular risk; hyperuricemia; psoriasis; psoriatic arthritis; uric acid.

Psoriasis is a chronic inflammatory disease that is often associated with features of the metabolic syndrome, including obesity, dyslipidemia, and type 2 diabetes.1-3 Psoriasis is also linked to an increased risk of incident cardiovascular disease (CVD).4,5 Similarly to psoriasis, growing epidemiologic evidence suggests that elevated levels of serum uric acid (SUA) are strongly associated with features of the metabolic syndrome and predict increased risk of CVD mortality and morbidity.6,7 Few studies have examined the relationship between psoriasis and hyperuricemia and their results have been inconclusive as most of these studies did not take into account the confounding effects of coexisting features of the metabolic syndrome.8-11

The aim of this study was to compare circulating levels of SUA and the prevalence of hyperuricemia between psoriatic patients and control subjects.

METHODS

Participants
We enrolled 119 psoriatic patients, who consecutively attended our joined dermatology and rheumatology outpatient clinic, specifically dedicated to

Abbreviations used:
BMI: body mass index
CVD: cardiovascular disease
PASI: Psoriasis Area and Severity Index
PsA: psoriatic arthritis
SUA: serum uric acid

From the Department of Medicine, Section of Dermatology, a and Section of Endocrinology, Diabetes, and Metabolism, b University of Verona.
Supported by the Ministero della Salute, and the Ministero dell'Istruzione, Università e Ricerca Scientifica (Programmi di Ricerca Scientifica di Rilevante Interesse Nazionale), and by the Association for Dermatological Research.
Conflicts of interest: None declared.
Accepted for publication September 6, 2013.
Reprints not available from the authors.

Correspondence to: Paolo Gisondi, MD, Department of Medicine, Section of Dermatology and Venereology, University of Verona, Piazzale Stefani 1, I-37126 Verona, Italy. E-mail: paolo.gisondi@univr.it.
Published online November 1, 2013.
0190-9622/$36.00
© 2013 by the American Academy of Dermatology, Inc.
http://dx.doi.org/10.1016/j.jaad.2013.09.005
psoriasis and psoriatic arthritis (PsA), during the period from January to June 2012. We included all patients with a clinical diagnosis of psoriasis (ie, lasting at least 6 months) who either were never treated or stopped their systemic antipsoriatic treatments at least 3 months before the investigation. Patients with excessive alcohol consumption, advanced chronic kidney disease, and those who were taking any medications known to affect SUA level (except for allopurinol), including diuretics, salicylates, ketoconazole, theophylline, pyrazinamide, and ethambutol, were not included in the study, as per study protocol. Information on daily alcohol consumption was obtained from all participants by a standardized questionnaire. In particular, alcohol consumption was assessed on the basis of the self-reported number of drinks consumed per day. The following amounts of alcoholic beverages were considered 1 drink: 330 mL of beer (containing ~5% alcohol), 150 mL of wine (containing ~12% alcohol), and 40 mL of strong spirits (containing ~50% alcohol). Overall, most of our psoriatic patients were abstainers or drank only minimally (≤2 drinks per day; n = 83; 69.8%), whereas 30.2% of them drank 3 to 4 drinks per day. No participants drank more than 4 drinks per day. Each patient was visited either by a dermatologist and a rheumatologist who assessed the presence/absence of PsA using Classification Criteria for Psoriatic Arthritis (CASPAR) criteria and/or gout. Diagnosis of psoriasis was clinical, and disease severity was scored using the Psoriasis Area and Severity Index (PASI). The control group consisted of 119 adult individuals, who were randomly selected in a 1:1 ratio among a historical cohort of 756 non-psoriatic subjects to be matched for age, sex, and body mass index (BMI) to psoriatic patients.

Clinical and laboratory variables

Venous blood was withdrawn in the morning after an overnight fast. SUA and other biochemical blood measurements were determined by standard laboratory procedures. Obesity was defined as BMI 30 kg/m² or higher. Hypertension was defined as blood pressure greater than or equal to 140/90 mm Hg or hypertension treatment. Diabetes was defined as fasting glycemia greater than or equal to 126 mg/dL, hypoglycemic treatment, or both. Hypertriglyceridemia and hypercholesterolemia were defined as serum triglycerides 150 mg/dL or greater and total cholesterol 240 mg/dL or greater, or lipid-lowering treatment. Metabolic syndrome was defined according to the widely used criteria proposed by the Adult Treatment Panel-III definition. Hyperuricemia was defined as a SUA level 7 mg/dL or higher in men and 6 mg/dL or higher in women or allopurinol use.

Statistical analysis

Data are presented as means ± SD or percentages. Statistical analyses included the paired t test for means and McNemar test for proportions because the 2 groups were matched. A multivariable logistic regression analysis was performed to identify the factors that were independently associated with hyperuricemia. Two forced-entry multivariable regression models were performed: a model adjusted for age, sex, psoriasis, and metabolic syndrome (model 1); and a model adjusted for age, sex, psoriasis, and individual components of metabolic syndrome (model 2). All analyses were performed using a statistical package (SPSS 19.0, IBM Corp, Armonk, NY) and statistical significance was assessed at the 2-tailed .05 thresholds.

RESULTS

Clinical characteristics of participants are shown in Table I. By study design, age, sex, and BMI were almost identical between psoriatic patients and control subjects. Psoriatic patients were more likely to have metabolic syndrome, hypertension, type 2 diabetes, and hypertriglyceridemia whereas smoking and hypercholesterolemia were not significantly different between the 2 groups. Notably, psoriatic patients had significantly higher levels of SUA than control subjects. As shown in Fig 1, the prevalence of hyperuricemia was remarkably greater in psoriatic patients than in control subjects. Results remained essentially unchanged even when those with established diabetes (n = 26), PsA (n = 75), or both were excluded from analysis or when participants were stratified by sex. Also in this case, men and women with psoriasis had significantly higher SUA than their counterparts without the skin disease (6.01 ± 1.6 vs 5.20 ± 1.4 mg/dL in men and 4.47 ± 1.4 vs 3.85 ± 1.0 mg/dL in women).
Similarly, results remained unchanged when participants were stratified by the presence of metabolic syndrome; psoriatic patients, irrespective of the presence of metabolic syndrome, had significantly higher SUA levels than control subjects (Fig 2).

Notably, as shown in Table II, multivariable logistic regression analysis revealed that both psoriasis and metabolic syndrome (included as a categorical variable), independently of each other, were significant predictors of hyperuricemia.

Interestingly, among psoriatic patients, SUA levels were significantly higher in patients with PASI score 10 or greater than in those with PASI score less than 10 (SUA: 5.9 ± 1.6 vs 5.2 ± 1.5 mg/dL; \( P < .05 \)). In addition, SUA was positively associated with BMI (\( r = 0.34; P < .001 \)), serum triglyceride (\( r = 0.24; P < .01 \)), and creatinine levels (\( r = 0.33; P < .001 \)), but it was not significantly associated with age, sex, and psoriasis duration (data not shown). Finally, no significant difference was found in SUA levels between patients with PsA and those with psoriasis alone (SUA: 5.6 ± 1.6 vs 5.5 ± 1.5 mg/dL; \( P = .60 \)).

**DISCUSSION**

In this case-control study, we found that the prevalence of asymptomatic hyperuricemia was approximately 3-fold higher in psoriatic patients than in matched control subjects (19% vs 7%). Interestingly, and more importantly, the multivariable regression analysis showed that psoriasis was the strongest predictor of hyperuricemia after adjusting for potential confounders, such as age, sex, BMI, and other features of metabolic syndrome.

Although hyperuricemia in psoriatic patients could be simply a consequence of obesity and other coexisting metabolic disorders,\(^6,^7\) our findings suggest that psoriasis itself might, at least in part, contribute directly to hyperuricemia. Kwon et al\(^8\) recently proposed that an increased epidermal cell turnover could be an important cause of raised SUA levels among psoriatic patients. Our findings of a significant, graded relationship between SUA levels

| Table I. Main clinical characteristics of the study participants |
|-----------------|-----------------|-----------------|
| Clinical characteristics | Psoriatic patients (n = 119) | Control subjects (n = 119) | \( P \) value |
| Sex, M/F | 88/31 | 88/31 | Matched |
| Age, y | 54.1 ± 12 | 54.3 ± 8 | Matched |
| BMI, kg/m² | 27.8 ± 4.6 | 27.8 ± 3.1 | Matched |
| Obesity, n (%) | 36 (30.2) | 35 (29.4) | Matched |
| Current smokers, n (%) | 20 (16.8) | 18 (15.1) | .81 |
| Hypertension, n (%) | 61 (51.3) | 45 (37.8) | <.01 |
| Type 2 diabetes, n (%) | 21 (17.6) | 5 (4.2) | <.001 |
| Hypercholesterolemia, n (%) | 15 (12.6) | 17 (14.3) | .76 |
| Hypertriglyceridemia, n (%) | 27 (22.7) | 21 (17.6) | .06 |
| Metabolic syndrome, n (%) | 40 (33.6) | 26 (21.8) | <.01 |
| Serum uric acid, mg/dL | 5.61 ± 1.6 | 4.87 ± 1.4 | <.001 |
| Serum creatinine, mg/dL | 0.92 ± 0.2 | 0.89 ± 0.2 | .86 |
| Psoriasis duration, y | 21.3 ± 13 | NA |
| PASI score | 11.2 ± 9 | NA |
| No. of previous treatments for psoriasis, n | 1.7 ± 0.7 | NA |
| PsA, n (%) | 75 (63.0) | NA |

Data are presented as means ± SD or percentages. Differences are tested by the unpaired t test or the \( \chi^2 \) test (for categorical variables).

BMI, Body mass index; F, female; M, male; NA, not applicable; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis.
and PASI further support this conclusion. However, additional research is required to uncover other specific mechanisms by which psoriasis might contribute to the development of hyperuricemia (possibly through increased uric acid production, decreased urinary uric acid excretion, or both).

Our findings may have important clinical implications. Elevated SUA causes gouty arthritis, which needs to be differentiated from PsA in clinical practice. In addition, elevated SUA is associated with increased carotid-artery intima-media thickness in patients with PsA and independently predicts the development of both CVD events and mortality in nonpsoriatic populations. Although the cross-sectional design of this study does not allow us to draw any conclusion about a causal relationship between psoriasis and hyperuricemia, we believe that SUA levels should be routinely measured in psoriatic patients, and that the pharmacologic treatment of asymptomatic hyperuricemia might also be clinically relevant to the global treatment of patients.

In a cohort study of approximately 7000 individuals aged 60 years or older, the treatment of hyperuricemia with higher doses of allopurinol was significantly associated with lower risks of both CVD events and mortality. However, whether this could be also applied to psoriatic patients needs to be investigated in future large intervention clinical trials.

### REFERENCES