Female Gout: Clinical and Laboratory Features

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ABSTRACT. ***Objective.*** To evaluate and compare clinical and laboratory features of gout in men and women.

Methods. Twenty-seven women and 31 men with gout underwent clinical and laboratory evaluation and review of medical records.

Results. Disease onset in women was a mean of 7 years later than in men. There were no differences between women and men regarding systemic hypertension, diabetes mellitus, hyperlipidemia, chronic renal failure, renal stones, ischemic heart disease, or heavy alcohol consumption. Tophaceous gout was similar in both groups, although female gender seemed to be protective against risk of developing tophi (odds ratio: 0.449; 95% confidence interval: 0.151–1.330). Podagra was more common in men, and women showed a higher frequency of upper limb joint involvement. Most patients had low urate excretion rates. Achieving disease control was similar in women and men. Of the 8 women who were premenopausal at disease onset, 7 had secondary causes for gout; 5 of the 8 had high serum urate despite treatment.

Conclusion. Gout in women had a later onset and higher frequency of upper limb joint involvement in comparison to men. Those with premenopausal onset tended to be refractory to standard therapy. (J Rheumatol 2005;32:2186–8)

Key Indexing Terms:
GOUT FEMALE URIC ACID HYPERURICEMIA

Gout is a clinical syndrome secondary to the inflammatory response elicited by the deposition of monosodium urate crystals inside and around joints. It is common among adult men older than 40 years[1-2] and women comprise only 5.1% of gout cases. Gout is rare in premenopausal women, but after menopause, the rise in serum urate increases its risk[3]. We analyzed both women and men with gout to compare their clinical and laboratory features.

MATERIALS AND METHODS

Inclusion criteria. Twenty-seven women and 31 men with gout under regular followup at the Rheumatology Outpatient Clinic in the Federal University of São Paulo were selected. Inclusion criteria were fulfillment of the American College of Rheumatology Classification for acute gouty arthritis[4] and/or the presence of urate crystals by polarized optic microscopy in synovial fluid or tophus.

Study design. Patients were clinically evaluated and their medical records were reviewed. A blood sample was collected after a 12 h fast for glucose, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, triglycerides, uric acid, and creatinine determination. Uric acid urinary excretion on an unrestricted purine diet and creatinine clearance were measured in 24 h urine samples.

Disease control was defined as serum urate level lower than 6.0 mg/dl and absence of arthritis in the last 6 months. Alcohol abuse was defined as intake above 300 g per week for the last 6 months[5]. Systemic hypertension, diabetes mellitus, and hyperlipidemia were diagnosed according to established criteria[6,7]. Serum creatinine above 1.4 mg/dl or creatinine clearance below 40 ml/min defined renal failure[8]. Urinary urate levels lower than 200 mg, between 200 and 700 mg, and above 700 mg were considered as under, normal, and hyperexcretion of urate, respectively. Polyarticular gout was defined as the presence of acute arthritis in 2 or more joints with evidence of sodium monourate crystals in at least one joint.

Statistical analysis. The 2-sample t test was used for quantitative values. Chi-square and Fisher's exact tests analyzed categorical variables. Results were significant when $p \leq 0.05$. Two univariate logistic regression models analyzed associations of gender with tophi and gender with disease control. Results were expressed as odds ratio (OR) with 95% confidence intervals (95% CI).

RESULTS

The mean age was 63.8 (± 10.8) years for women and 61.4 (± 9.2) for men ($p = 0.380$). Nineteen women (70.3%) and 25 men (80.6%) were white ($p = 0.361$). Disease onset was earlier in men 47.5 (± 11.9) than in women 55.0 (± 12.3) ($p = 0.022$). Disease duration was lower in women 8.7 (± 6.6) versus 13.9 (± 8.9) years in men ($p = 0.014$). The mean age at onset of gout in women was 7 years later than in men. Family history of gout occurred in 40.7% of women and in 25.8% of men ($p = 0.226$). There were no differences between genders concerning the frequency of systemic hypertension, diabetes, hyperlipidemia, chronic renal failure, renal stones, ischemic heart disease, alcohol abuse, or the presence of tophi. Osteoarthritis was more common in women ($p = 0.021$) (Table 1). The frequency of podagra was similar in both genders at the time of gout onset ($p = 0.118$). During the disease course, podagra was more common in men ($p = 0.009$). Women had more upper limb involvement ($p < 0.001$). No significant differences were found when analyzing other joints.

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Table 1. Clinical features of female and male patients with gout. Results are expressed as percentages unless otherwise stated.

	Female Patients, n = 27	Male Patients, n = 31	p
Age, yrs (mean ± SD)†	63.8 ± 10.8	61.4 ± 9.2	0.380
White race‡	70.3	80.6	0.361
Duration of gout, yrs (mean ± SD)†	8.7 ± 6.6	13.9 ± 8.9	0.014*
Age at onset of gout yrs (mean ± SD)†	55.0 ± 12.3	47.5 ± 11.9	0.022*
Family history of gout‡	40.7	25.8	0.226
Systemic hypertension‡	81.5	77.4	0.703
Diabetes mellitus**	14.8	22.6	0.518
Hyperlipidemia‡	55.6	32.3	0.074
Chronic renal failure**	14.8	25.8	0.348
Renal stones‡	18.5	22.6	0.703
Ischemic heart disease‡	25.9	16.1	0.358
Alcohol abuse**	7.4	16.1	0.432
Osteoarthritis‡	55.6	25.8	0.021*
Tophi‡	29.6	48.4	0.145
Urate underexcretion‡	74.0	58.0	0.200
Urate normoexcretion‡	22.2	38.7	0.175
Urate overproduction**	3.7	3.2	0.920
Use of diuretics**	29.6	12.9	0.116
Disease control‡	59.3	67.7	0.503

† Two tailed t test; ‡ chi-square test; ** Fisher exact test; * significant p value.

Profile of renal urate clearance, use of diuretics, and frequency of disease control achievement was similar in both groups (Table 1). Female gender was protective against risk of developing tophi (OR: 0.449; 95% CI: 0.151–1.330) and was not different from men concerning response to treatment (OR: 1.443; 95% CI: 0.492–4.230).

Premenopausal onset of gout occurred in 8 women (29.6%). All presented with arthritis of the lower limbs at disease onset. Seven premenopausal patients had secondary causes for gout, including heavy alcohol consumption (1), diuretic treatment (4), and renal failure (2), one of whom had prior renal transplantation and was receiving cyclosporine. Abstinence from alcohol, withdrawal of diuretics, and reduction of cyclosporine dose were accomplished in those patients. Nevertheless, 5 patients had no response to treatment with benzbromarone and/or allopurinol. Besides age, no other differences were found between pre and postmenopausal patients.

DISCUSSION

In our study, mean age at onset of gout in women was 7 years later than in men and this is in agreement with the literature[3,9-13]. The low frequency of gout in premenopausal women is thought to be due to enhancing effects of estrogens on renal urate clearance[1]. Osteoarthritis was more prevalent in women than in men with gout; this could be explained by the older age of women at disease onset in our group of patients. Lally, *et al* found a correlation between nodal osteoarthritis and gouty arthritis on interphalangeal joints and/or tophi in women with ages similar to our patients[3]. The frequency of premenopausal gout onset in our study (29.6%) was slightly higher than previously reported (8.6 to 25%)[3,9-10,12-13]. However most of our premenopausal patients had secondary causes for gout, which may explain their failure in achieving disease control.

We found no differences between women and men concerning comorbidities, family history, or other risk factors for gout. Yü found a higher prevalence of family history of gout in premenopausal women[10]. According to some reports, renal insufficiency[3,12], systemic hypertension[12], and use of diuretics[3,10,12,13] were more frequent in women with gout while alcoholism was more frequent in men with gout[3,12]. However, these results may have been affected by the small sample sizes of each of these studies.

In our study, podagra was the most frequent manifestation, but women had more upper limb involvement. Polyarticular gout was similar in both genders, but was lower in women (14.8%) than the 26 to 56.5% previously described[3,9,11-13]. We also found that women with gout presented fewer tophi than men, but this difference was not significant and may be due to their shorter disease duration. Some studies have found a prevalence of tophi significantly higher in women[11,12], but this has not been confirmed by other studies[3,13].

In conclusion, we found that gout in women presents at a later age, and that women have more upper limb joint involvement and higher frequency of osteoarthritis when compared to men with gout.

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