# Epidemiology of Gout: Is the Incidence Rising?

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***ABSTRACT.*** ***Objective.*** To determine whether the incidence of gout is higher in 1995-1996 compared to 1977-1978.

***Methods.*** Using the Rochester Epidemiology Project computerized medical record system, all potential cases of acute gout in the city of Rochester, Minnesota during the time intervals of 1977-1978 and 1995-1996 were identified. The complete medical records of all potential cases were screened and all who fulfilled the 1977 American College of Rheumatology proposed criteria for gout were included as incidence cases. Demographic data, body mass index, clinical presentation, and associated comorbid conditions were abstracted. The overall and age-gender adjusted incidence rates from the 2 cohorts were calculated and compared.

***Results.*** A total of 39 new cases of acute gout were identified during the 2 year interval 1977-1978 representing an age and sex-adjusted annual incidence rate of 45.0/100,000 (95% CI: 30.7, 59.3). For the interval 1995-1996, 81 cases were diagnosed, representing an annual incidence rate of 62.3/100,000 (95% CI: 48.4, 76.2). There was a greater than 2-fold increase in the rate of primary gout (i.e., no history of diuretic exposure) in the recent compared to the older time periods ($p = 0.002$). The incidence of secondary, diuretic related gout did not increase over time ($p = 0.140$).

***Conclusion.*** Our results indicate that the incidence of primary gout has increased significantly over the past 20 years. While this increase might be a result of improved ascertainment of atypical gout, it may also be related to other, as yet unidentified, risk factors. (J Rheumatol 2002;29:2403–6)

*Key Indexing Terms:*
GOUT EPIDEMIOLOGY

Gout is one of the most common rheumatic diseases worldwide. The prevalence of gout varies widely reflecting both the ethnic and environmental influences affecting its occurrence[1-3]. Recent observations suggest that the prevalence of gout may be increasing in certain populations. A multicenter study of general practices in the United Kingdom caring for 300,000 persons found that the prevalence of gout in 1991 had increased 3-fold compared to the estimates from the 1970s[4]. Similar observations have been reported from New Zealand in both the native Maori and European populations[5]. We sought to determine whether the incidence of gout (i.e., the number of newly diagnosed cases in the general population) is also rising.

## MATERIALS AND METHODS

*Data collection*. Using the Rochester Epidemiology Project computerized medical record system, all potential cases of acute gout in the city of Rochester, Minnesota during the time intervals of 1977-1978 and 1995-1996, were identified. This medical record system is designed to ensure that all diagnoses resulting from episodes of medical care provided by practitioners at either the Mayo Clinic, its affiliated hospitals, the Olmsted Medical Clinic and Olmsted Community Hospital are recorded. Thus, this data resource ensures virtually complete ascertainment of all clinically diagnosed disease[6]. The complete medical records (i.e., inpatient and outpatient by all local healthcare providers) of all potential cases were screened by a rheumatologist (EA), using a structured data collection form and all who fulfilled the 1977 American College of Rheumatology proposed criteria for gout were included as incidence cases[7]. Demographic data, body mass index (BMI) at the time of first diagnosis of gout, clinical presentation, and associated comorbid conditions were abstracted. The overall and age-gender adjusted incidence rates from the 2 cohorts were calculated and compared.

*Statistical analysis*. Crude incidence rates for the 2 cohorts were calculated using the 1977 and 1995 Rochester populations respectively. The rates were adjusted using the US white 1990 population. Incidence rates for both primary gout and gout occurring in patients taking diuretics, secondary gout, were calculated separately. Confidence intervals were obtained for all incidence rates. Demographic characteristics and variables of interest were described using appropriate summary statistics. Continuous variables were compared between the 2 groups using the Wilcoxon rank-sum test. Categorical variables were compared using a chi-square test or Fisher's Exact test. Results were considered significant at the $p < 0.05$ level. The relationship of incidence rates to calendar year was assessed using generalized linear models assuming a Poisson error structure[8]. Such models fit the natural logarithms of the crude rates as linear combinations of age-group (in 9 categories, 0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80+), gender and calendar year using the SAS procedure, GENMOD.

## RESULTS

A total of 39 new cases of acute gout were identified during the 2-year interval 1977-1978 representing an age and sex-adjusted annual incidence rate of 45.0/100,000 (95% CI:

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30.7, 59.3) (Table 1). For the interval 1995-1996, 81 cases were diagnosed, representing an annual incidence rate of 62.3/100,000 (95% CI: 48.4, 76.2) (Table 1). The overall male to female ratio remained the same at 3.3 to 1 for both incidence cohorts. In females, the incidence of gout rose with age, peaking in those 80 years and over. In males, an increase in incidence was observed among elderly men in the 1995-1996 cohort (Figure 1). Compared to the 1977-78 cohort, gout was diagnosed in younger individuals in the 1995-96 cohort (Figure 1).

There was a greater than 2-fold increase in the incidence of primary gout (i.e., no history of diuretic exposure) over the 2 time periods (p = 0.002, Table 2). Recent studies have demonstrated that use of low dose acetylsalicylic acid (ASA) for cardiovascular prophylaxis may be a significant risk factor for gout[9,10]. We identified 16 patients in our study population with documented use of low dose ASA (all of them in the 1995-1996 cohort). Excluding these patients from the analysis yields an age-adjusted incidence rate of 35.4 (95% CI: 25.2, 45.7). The comparison with the 1977-1978 incidence remains statistically significant (p = 0.03). The incidence of secondary, diuretic related gout did not increase over time (p = 0.140).

There was no statistically significant difference observed in the serum uric acid levels at diagnosis, BMI, reported use of alcohol, or the prevalence of comorbid conditions of diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, or hypothyroidism among cases with either primary or secondary gout. In both subgroups, the median BMI was greater than the current definition of overweight (BMI ($\geq$ 25 kg/m$^2$) and approximated the definition of obesity (BMI $\geq$ 30 kg/m$^2$). Age at incidence was similar in both groups (Table 1). Height, weight, and BMI were similar in the 2 time periods, as were comorbidities. In 1977–1978, 53.8% of cases were thiazide users compared to 25.9% in 1995-1996 (p = 0.003). Although newly diagnosed acute gout presented as a monoarthritis in over 85% of both cohorts, classical podagra involving the first metatarsal joint declined in frequency of presentation at diagnosis from 95 to 78% of the cases (p = 0.019). No cases involving the upper extremity joints were diagnosed during 1975–1976, but during 1995-1996, incident cases involving the fingers,

*Table 1.* Characteristics of newly diagnosed cases of gout among Rochester, MN residents in 1977–78 (n = 39) and in 1995–96 (n = 81).

| Variable | 1977–1978 | 1995–1996 | p |
|---|---|---|---|
| n | 39 | 81 | |
| Unadjusted incidence, per 100,000 | 35.1 | 56.4 | 0.015 |
| Adj. incidence, per 100,000 (95% CI) | 45.0 (30.7, 59.3) | 62.3 (48.4, 76.2) | 0.10 |
| Sex, n (% male) | 30 (76.9) | 62 (76.5) | 0.96 |
| Median age at incidence (min, max) | 56.0 (20.0, 86.0) | 60.0 (17.0, 93.0) | 0.260 |
| Follow-up (median, range, yrs) | 16.5 (0.3, 21.8) | 2.4 (0.0, 4.1) | < 0.001 |
| Race, n (%) | | | |
| Caucasian | 36 (92.3) | 75 (92.6) | |
| African American | 1 (2.6) | 1 (1..2) | |
| Oriental | 0 (0.0) | 4 (4.9) | |
| Hispanic | 1 (2.6) | 0 (0.0) | |
| Unknown | 1 (2.6) | 1 (1.2) | |
| Height, cm | 168.0 (147.0, 188.0) | 172.0 (144.0, 189.0) | 0.59 |
| Weight, kg | 83.2 (50.9, 123.2) | 85.0 (50.0, 144.5) | 0.32 |
| BMI, kg/m$^2$ (median, range) | 29.3 (20.9, 40.2) | 29.8 (16.9, 56.5) | 0.36 |
| Comorbidities, n (%) | | | |
| DM | 2 (5.1) | 8 (10.0) | 0.50 |
| HTN | 22 (59.5) | 54 (68.4) | 0.35 |
| Hypercholesterolemia | 23 (76.7) | 53 (75.7) | 0.92 |
| Hypertriglyceridemia | 9 (32.1) | 29 (42.0) | 0.37 |
| Coronary artery disease | 9 (23.1) | 20 (25.0) | 0.82 |
| Hypothyroidism | 3 (7.9) | 10 (13.0) | 0.54 |
| Secondary gout-thiadize use, n (%) | 21 (53.8) | 21 (25.9) | 0.003 |
| Clinical characteristics, n (%) | | | |
| Monoarthritis | 34 (87.2) | 69 (85.2) | 0.89 |
| Unilateral 1st MTP involvement | 37 (94.9) | 63 (77.8) | 0.019 |
| Tophi | 1 (2.6) | 4 (4.9) | 1.00 |
| Fever | 0 (0.0) | 4 (7.4) | — |
| Hospitalized | 2 (5.1) | 8 (10.0) | |
| Uric acid at onset, mg/dl (median, range) | 8.6 (3.0, 14.0) | 8.7 (4.3, 14.5) | 0.54 |
| Alcoholism, n (%) | 5 (12.8) | 6 (7.4) | 0.34 |

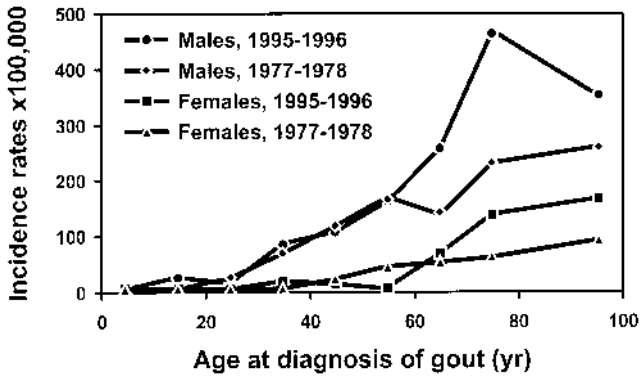


*Figure 1*. Incidence of acute gout in Rochester, MN 1977-78 (n = 39) and 1995-96 (n = 81) according to age at diagnosis.

wrists and elbows were identified.

In addition, diagnostic arthrocentesis increased as a diagnostic tool from 12.8 to 30.9% over the 20 year span between the incidence cohort intervals (p = 0.042). Tophi were noted in newly diagnosed cases of gout in 2.6 and 4.9% of the respective cohort members. Over time the frequency of newly diagnosed gout in cases hospitalized for surgery also increased from 5.1 to 10% (Table 1).

The management of gout in this community has also changed over time. The use of corticosteroids has increased over this time period. In the 1977–1978 cohort, there was no use of oral corticosteroids and only one case with documented use of parenteral corticosteroids, while in the 1995-1996 cohort, there were 10 cases of reported use of oral corticosteroids and none with parenteral. One case of ACTH use and 9 cases of intraarticular corticosteroids were also reported, both in the 1995–1996 cohort. The use of colchicine declined from 47.4% (18 cases) in 1977-1978 to 19.8% (16 cases) in the 1995–1996 cohort. This comparison was highly statistically significant (p = 0.002). Indomethacin was the most frequently prescribed nonsteroidal antiinflammatory drug in both cohorts (35.9 and 58.0% in the 1977–78 and 1995-96 cohorts, respectively). Use of indomethacin was significantly higher in the recent cohort (p = 0.031). The pattern of nonsteroidal antiinflammatory drug (NSAID) use also appeared to change somewhat over time. In the early cohort, there were only 2 cases with reported use of ibuprofen and no cases with reported use of any other NSAID, while in the 1995-1996 cohort, there were 4 cases with reported use of ibuprofen, 6 with reported use of naproxen and 1 with reported use of voltaren. Other NSAID were reported in only 4 cases (10.5%) in the

*Table 2*. Characteristics of newly diagnosed cases of primary gout (i.e., among patients NOT on thiazide diuretics) among Rochester, MN residents in 1977–78 (n = 18) and 1995–96 (n = 60).

| Variable | 1977–1978 | 1995–1996 | p |
|---|---|---|---|
| n | 18 | 60 | |
| Unadjusted incidence, per 100,000 | 16.2 | 41.8 | < 0.001 |
| Adj. incidence per 100,000 (95% CI) | 20.2 (10.7, 29.6) | 45.9 (34.0, 57.8) | 0.002 |
| Age at dx for ACR criteria (median, range) | 43.5 (20.0, 81.0) | 53.5 (17.0, 93.0) | 0.067 |
| Sex, n (% male) | 15 (83.3) | 52 (86.7) | 0.71 |
| Followup (median, range, yrs) | 20.3 (0.3, 21.8) | 2.4 (0.0, 4.1) | < 0.001 |
| Race n (%) | | | |
| Caucasian | 16 (88.9) | 54 (90.0) | |
| African American | 0 (0.0) | 1 (1.7) | |
| Oriental | 0 (0.0) | 4 (6.7) | |
| Hispanic | 1 (5.6) | 0 (0.0) | |
| Unknown | 1 (5.6) | 1 (1.7) | |
| Height, cm | 170.0 (147.0, 188.0) | 172.5 (150.0, 189.0) | 0.78 |
| Weight, kg | 84.5 (62.7, 104.1) | 85.5 (50.0, 144.5) | 0.50 |
| BMI, kg/m$^2$ median, range | 28.8 (24.5, 33.8) | 29.8 (16.9, 56.5) | 0.36 |
| Comorbidities (n, %) | | | |
| DM | 0 (0.0) | 6 (10.2) | — |
| HTN | 6 (37.5) | 33 (56.9) | 0.17 |
| Hypercholesterolemia | 10 (76.9) | 36 (73.5) | 1.00 |
| Hypertriglyceridemia | 4 (36.4) | 20 (41.7) | 1.00 |
| Coronary artery disease | 0 (0.0) | 15 (25.4) | — |
| Hypothyroidism | 1 (5.9) | 7 (12.5) | 0.67 |
| Clinical characteristics n (%) | | | |
| Monoarthritis | 16 (88.9) | 52 (88.1) | 1.00 |
| Unilateral 1$^{st}$ MTP involvement | 17 (94.4) | 48 (80.0) | 0.28 |
| Tophi | 0 (0.0) | 3 (5.0) | — |
| Fever (unknown = 23) | 0 (0.0) | 3 (7.5) | — |
| Uric acid at onset, mg/dl (median, range) | 8.3 (3.0, 11.6) | 8.4 (5.0, 14.5) | 0.28 |
| Alcoholism, n (%) | 4 (22.2) | 6 (10.0) | 0.23 |

1977–1978 cohort, but were reported in 16 cases (19.8%) in the more recent time period. Use of allopurinol for acute attacks seems to have declined substantially with 15.8% reported use in the 1977–1978 cohort and 4.9% in the 1995–1996 cohort. No reports of oxypurinol were evident in either cohort and only 1 case of use of probenecid for treatment of an acute attack was reported in the 1995–1996 cohort.

## DISCUSSION

Our study of 2 incidence cohorts separated by 20 years demonstrates a statistically significant increase in the incidence of primary gout in the community of Rochester, Minnesota. The incidence of secondary gout related to thiazide diuretic therapy did not change over time. The evolving characteristics of the acute gout over the 20 year interval of the study suggests that there is either a change in presentation of gout or a more sophisticated awareness of atypical gout by practitioners in the recent time period compared to the earlier time period or both. The decline in typical podagra and the increase in acute monoarthritis of other joints including the upper extremity observed in this study support this conclusion. The increased use of diagnostic arthrocentesis in the evaluation of acute monoarthritis in this community has likely led to the identification of some of the atypical new cases. Despite this apparent improvement in identifying gout, unrecognized tophaceous gout is still encountered and was found in 5% of the new cases identified in the latter cohort from the mid-1990s.

Although there is an increased awareness of the role of diuretic therapy in the etiology of gout, we found a lower rate of thiazide diuretics exposure among patients first diagnosed with gout in the 1990s compared to the earlier time period. Other risk factors, which have remained stable in the gouty population including obesity, hypertension, diabetes mellitus, and hyperlipidemia, emphasize the role that underlying metabolic risk factors and insulin resistance play in this disorder. Overall, our results indicate that the incidence of primary gout (i.e., unrelated to diuretic exposure) has increased significantly over the past 20 years. While this increase might be a result of improved ascertainment of atypical gout, it may also be related to other, as yet unidentified, risk factors. Clearly, gout will remain a frequently encountered rheumatic disorder in the US, especially as the prevalence of obesity and type 2 diabetes mellitus continues to rise[11,12].


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