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Gout in women: differences in risk factors in young and older women

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Abstract

Aim To describe the clinical characteristics of female patients with gout, assess risk factors in this group and to identify any differences between pre- and postmenopausal women with this diagnosis.

Methods We retrospectively reviewed the case records of all women who were seen with gout in a secondary care setting (inpatient and outpatient) at Counties Manukau District Health Board between July 2007 and July 2008. Demographic data, risk factors for gout and information on urate-lowering therapy was collected. A cut-off of ≤50 years was used to estimate pre-menopausal status.

Results 122/509 (24%) of patients seen with gout were female. Fourteen female patients were ≤50 years of age; all of these patients were either Maori (43%) or of Pacific Island ethnicity (57%). Comorbidities in those ≤50 years old were renal impairment (78.6%), hypertension (64.3%), congestive heart failure (43%) and diabetes mellitus (42.9%). Comorbidities in women >50 years old were similar: hypertension (77%), renal impairment (70%), dyslipidemia (53%) and diabetes mellitus (50%). Ischemic heart disease was more common in older women (43% vs 7%), P<0.01. Mean body mass index (BMI) was significantly higher in the younger women (43.5 vs 33.1), P<0.01. Half of all the female patients were on diuretics, and medication used to lower uric acid level was prescribed in 35.7% of women ≤50 years of age, and 42.59% of women >50 years of age.

Conclusion Women who develop gout are more likely to be over the age of 50, have other comorbidities and be on diuretics. In comparison, younger women who develop gout have similar risk factors but tended to have a higher body mass index and are more likely to be of Māori or Pacific Island ethnicity.

Gout is a form of inflammatory arthritis caused by uric acid precipitation in and around joints. This painful condition was first identified in ancient times by Egyptians around 2640 BC. Hippocrates first wrote about this disorder in 400 BC.[1,2] Prolonged hyperuricemia is the main risk factor for gout.

Hyperuricemia can be caused by either excessive intake of a purine rich diet or inadequate excretion of uric acid by the kidneys. Human beings lack the enzyme uricase which converts uric acid into water soluble allantoin which is more readily excreted.[3] Genetic studies have identified association between polymorphism in the GLUT9 (SLC2A9) gene and URAT1 (SLC22CA12) gene to be key regulators and transporters of uric acid.

Genetic variations in these enzymes are identified as risk factors for hyperuricemia and gout.[4,5] Other well recognised associations for hyperuricemia and gout include

age, diabetes mellitus, hypertension, metabolic syndrome, renal disease, cardiovascular diseases and medications like diuretics.

Gout is predominantly a disease of males, but in recent times, there has been an increase in prevalence in women. The reported male to female ratio is approximately 7:1 to 9:1 but in people over the age of 65 this ratio is reduced to 3:1.[6–8] Gout is considered rare in premenopausal women as the estrogenic hormones have a mild uricosuric effect and therefore protective against hyperuricemia and gout. During menopause the estrogen levels drop and women with risk factors become more likely to develop hyperuricemia and gout.[9] However, in our clinical practice we have noticed an increasing frequency of young women presenting with acute flares of gout.

The objective of this study was to describe the clinical characteristics of female patients with gout, assess risk factors for gout in this cohort and identify any differences between pre- and postmenopausal women with this diagnosis who present to secondary care in South Auckland.

Methods

We retrospectively reviewed the records of female patients with a diagnosis of gout using the International Classification of Diseases-9 (ICD-9 codes 274.0, 274.8, 274.9), who were seen at Counties Manukau District Health Board (CMDHB), South Auckland, New Zealand, between July 2007 and July 2008.

Demographic data, information on relevant comorbidities and diuretic use were collected. Comorbidities of interest were obesity, hypertension, congestive heart failure, dyslipidemia, diabetes mellitus and renal impairment. Obesity was defined as body mass index (BMI) >30kg/m^2; renal impairment was defined as estimated glomerular filtration rate (eGFR) of <60mls/min using the Modification of Diet in Renal Disease (MDRD) formula.[10]

The menstrual status of women was not usually recorded in the hospital medical charts therefore we used an age cut-off of 50 years (average age of menopause in our population) as a surrogate marker for pre-and postmenopausal status.

We collected laboratory data on lipid levels, serum urate and glomerular filtration rate. The use of urate-lowering therapy was determined from the electronic medical records.

Statistical analysis—Statistical analysis was conducted using OpenEpi (version 2.3.1) software. Paired t-test (2 sided) was used to compare differences among means. Chi-squared was used to compare differences in proportions. One-way ANOVA used to compare differences in means when there were more than 2 samples. All reported p values less than 0.05 were considered statistically significant.

Results

Between 1 July 2007 and 31 July 2008, 509 patients presented to CMDHB for management of gout. This included inpatient as well as outpatient visits. Table 1 shows the gender and ethnic distribution of the study population. Among the 509 patients, 122 (24%) were female.

Fourteen female patients (11.5%) were either 50 years or younger and 108 (88.5%) were over 50 years of age. Table 2 shows a comparison of the ethnicity, the traditional risk factors and prescribed treatment between the two age groups.

Table1. Gender and ethnic distribution of patients with gout presenting to secondary care at Counties Manukau District Health Board in the period 1 July 2007 and 31 July 2008

Ethnicity	Total n (%)	Males n (%)	Females n (%)	M:F ratio
Māori	129 (25)	87 (22)	42(34)	2:1
Pacific people	237 (47)	190 (49)	47 (39)	4:1
Europeans	115 (23)	86 (22)	29 (24)	3:1
Others	28 (6)	24 (6)	4 (3)	6:1
Total n (%)	**509 (100)**	**387 (100)**	**122 (100)**	**3:1**

Table 2. Description of women with gout stratified by age

Characteristics	Age ≤50 years (n=14)	Age >50 (n=108)	P value
Mean age (range)	41 (23–50)	71.5 (51–95)	
Ethnicity			
Māori n (%)	6 (43)	36 (33.3)	0.67
Pacific n (%)	8 (57)	39 (36.1)	0.22
European n (%)	0 (0)	29 (26)	0.035
Others n (%)	0 (0)	4 (3.7)	1.00
Risk factors			
Mean BMI	43.5	33.1	0.002
Hypertension no (%)	9 (64.3)	83 (77)	0.24
Diabetes mellitus	6 (42.9)	54 (50)	0.41
Renal impairment	11 (78.6)	76 (70)	0.39
CHF	6 (43)	40 (37)	0.44
Dyslipidemia	5 (35.7)	60 (55)	0.13
Ischemic heart disease	1 (7.0)	46 (43)	0.01
Three or more comorbidities	9 (64)	70 (64.8)	0.97
SUA mean (range)	0.54 (0.4–0.8)	0.48 (0.22–0.92)	0.17
Treatment			
Allopurinol no (%)	3 (21.4)	45 (42)	0.12
Uricosuric agent	2 (14.3)	1 (1.0)	0.03

Table 3. Risk factors for the three major ethnic groups

Characteristics	European	Māori	Pacific people	P value
Numbers (%)	29 (24.58)	42 (35.59)	47 (39.83)	
Average age (range)	78.9 (52–95)	60.5 (23–85)	60.93 (27–83)	0.10
Mean BMI (range)	31.6 (20.6–40)	34.1 (24–51.2)	37.1 (21–77)	<0.001
Hypertension No. (%)	19 (65.5)	33 (78.6)	35 (74.5)	0.47
Diabetes mellitus No. (%)	7 (24.14)	21 (50)	23 (48.90)	0.06
Renal impairment No. (%)	18 (62)	27 (64.3)	39 (83)	0.07
CHF no (%)	11 (37.9)	18 (42.9)	17 (36.2)	0.80
IHD no (%)	16 (55)	17 (40.5)	13 (27.7)	0.06
Dyslipidemia No. (%)	20 (69)	19 (45.2)	25 (53.2)	0.14
Diuretic use No. (%)	16 (55)	23 (54.8)	20 (42.6)	0.42
Mean SUA (range)	0.45 (0.22–0.71)	0.51 (0.28–0.92)	0.50 (0.27–0.81)	0.42
Treatment				
Allopurinol No (%)	10 (34.5)	16 (38)	21 (44.7)	0.65
Uricosuric agent No (%)	0 (0)	0 (0)	3 (6.4)	0.10

In the 'pre-menopausal' age group (≤ 50 years), 43% were Māori and 57% were Pacific people. There was no European or people of other ethnic group represented in this age group. In the older age group (> 50 years), 26% of the population were Europeans, 33.3% were Māori, 36.1% were Pacific People and 4% were of other ethnic group (predominantly Asian).

Every patient in the 'pre-menopausal' age group had a comorbidity that predisposed them to gout. Renal impairment (78.6%) and hypertension (64.3%) were the two most common co morbidities in the ≤50 age group. Renal impairment was attributed to hypertensive disease in 57% and glomerulonephritis in 21%.

Congestive heart failure and diabetes mellitus were present in 43% of patients who were ≤50 years old. The underlying cause for congestive heart failure was either rheumatic valvular heart disease or non-ischemic cardiomyopathy.

Comorbidities seen in the older age group were hypertension (77%), renal impairment (70%), dyslipidemia (55%), diabetes mellitus (42.95%) and ischemic heart disease (43%). The presence of ischemic heart disease was more common in older women (43% vs 7%, P<0.01), whereas the mean BMI was significantly higher in the younger age group (BMI 43.5 vs. 33.1, P<0.01).

Diuretic use was similar between the age groups (approximately 50% in both groups). The mean serum uric acid was not statistically different between the 2 age groups. Medication to lower uric acid was prescribed in 5 (35.7%) of patients in the younger age group and 46 (42.59%) of patients in the older age group. Allopurinol was the drug of choice and only 3 (2.68%) received uricosuric agents.

When risk factors for different ethnic groups were compared, statistically significant difference was noted in the mean BMI. Obesity, defined as a BMI of greater than 30

was noted in 64 % of the less than 50 age group and 39% in the older age group, with the Pacific People having highest mean BMI (37.1) followed by Māori (34.1) and European (31.6). There was a suggestion that European women were older (mean age 78.9 years) compared to Māori and Pacific women (60.52 and 60.93 years respectively), but this did not reach statistical significance.

Hypertension and renal impairment were the two most common comorbidities in all three ethnicities. Diabetes mellitus occurred more commonly in Māori (50%) and Pacific people (48.9%) compared with European (24%), P=0.06. The mean serum uric acid (SUA) concentration and diuretic use was similar in all three ethnic groups. Therapy to lower uric acid levels was similar in all three ethnicities with no significant statistical difference noted.

Discussion

The Counties Manukau District Health Board (CMDHB) has an estimated population of 464,000 of which 46% are Europeans, 21% Pacific people, 17% Māori and 16% Asians. It has the third highest district health board (DHB) population in New Zealand and has the highest number of Māori and Pacific people. Gout is a common metabolic condition present in this DHB population (11).

This study shows that 24% of patients presenting with gout to secondary care in South Auckland are women, giving an overall male to female ratio of 3:1. The ratio for Māori was 2:1, European 3:1 and Pacific people 4:1. This compares to epidemiological survey conducted by Klemp and colleagues in 1996 which showed that the sex ratio of Māori men to women with gout was 5:1 and European men to women were 8:1.[12]

A potential reason for this discrepancy between our findings and Klemp could be that women are more likely to seek medical attention and attend appointments in secondary care, but alternatively it could mean that the prevalence of gout in women is rising.

Approximately 89% of women with gout in our study were over 50 years of age, confirming that this disease that mainly affects postmenopausal women, but a significant number of women under the age of 50 are now presenting with gout.

Māori and Pacific women have a higher prevalence of gout, similar to their male counterparts, suggesting genetic factors to be involved. Genetic variation in SLC2A9 is shown to increase the risk of gout by 500% in New Zealand Māori and Pacific Island Polynesians as shown in a study by Hollis-Moffatt et al.[13]

European women with gout in our study were on average eighteen years older than Māori and Pacific women. The main traditional risk factors identified for gout were obesity, hypertension, renal impairment and diuretic use similar to those identified in other studies.[14,15]

All the women in the 'pre-menopausal' age group had at least one risk factor for gout and 64% had more than three comorbidities. Similar finding were also noted in women over 50 years of age. The main differences between the risk factors for gout between young and older women were increased body mass index (BMI) in the younger age group and Māori and Pacific Island ethnicity. The Nurses health study showed that women with BMI between 23 and 24.9 kg/m2 had a 1.55 relative risk of gout.

The risk continued to increase with increasing BMI, so that RR was 2.86 for those with BMI of 25-29.9 kg/m^2, RR of 4.69 for BMI of 30 to 43.9 kg/m^2, and RR of 7.25 for BMI exceeding 35kg/m^2.The same study showed hypertension was associated with a RR of 2.26 and diuretic use had a RR of 2.63.[14]

Other important risk factors identified in the women population with gout were diabetes mellitus, congestive cardiac failure and to a lesser extent, ischemic heart disease. A study to determine the prevalence of gout in patients with diabetes mellitus showed a high prevalence (22%) in patients with Type 2 diabetes.[16]

Our study showed that 50% of Māori and Pacific, and 25% of European women with gout had diabetes mellitus. This study highlighted that treatment to lower uric acid was inadequately administered in women with only 40% receiving any form of therapy. This would explain why the mean serum uric acid was elevated in all the study groups.

There are limitations to this study. Firstly only patients who presented to secondary care were included. A large percentage of patients with gout are cared for by their

primary care physicians and it is likely that patients with difficult to treat gout or with multiple comorbidities were more likely to be referred to secondary care.

The prevalence of comorbidities in our study may not be the true reflection of our wider gout population. We only had a small number of patients in the young age group which makes it difficult to interpret the risk factors in this subgroup. Menstrual data was not available and therefore we used an age cut-off as a surrogate marker for menopause. Alcohol and diet history was not reliably recorded, hence the influence of these important risk factors were not included in the study.

In conclusion, women who develop gout are more likely to be over the age of 50 (i.e. postmenopausal), have one or more comorbidity and are more likely to use diuretics. In comparison, younger women who develop gout have similar risk factors but tended to have a higher body mass index and are more likely to be of Māori or Pacific Island ethnicity.

Women with gout seem to be under-treated despite being seen in secondary care. This study highlights important demographic feature of women with gout which can be used as a starting point for larger epidemiological studies and also provides valuable information which can be used in power calculations for future interventional studies to test preventative or therapeutic strategies.

Competing interests: None known.

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