

# Gout In Women

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**Gout has long been associated with old men with red faces who imbibe heavy alcohol and eat rich meats.** Because of this, it was dubbed “the disease of Kings.” These misconceptions persist, and many people continue to believe that gout is a condition that is self-inflicted by overindulgence, occurs only in men, with symptoms confined to the foot.

## WOMEN GET GOUT TOO

Gout is not rare in women. Although women comprise approximately 5% of all gout patients, the incidence has risen. According to Arromdee, et al, the incidence of gout in men and women has doubled over the past 20 years.<sup>1</sup> Because it is principally a disease seen in men, gout is often misdiagnosed in women, and/or the diagnosis is often delayed.

In this article we will discuss some of the epidemiological, clinical and treatment aspects that distinguish female from male gout patients.

Women are older than men at the time of diagnosis of gout. In several studies, the mean age at diagnosis of gout was 7-12 years greater in women than in men.<sup>2-6</sup> In patients older than 60 years with newly diagnosed gout, approximately half will be women. The incidence of females with gout peaks at age 80 years and older.

One important difference between women and men with gout is the change in urate levels that occurs in women after menopause. Serum urate concentrations in men average about 1mg/dl higher than those in adult women until after menopause, at which time the serum levels of uric acid in women approach or equal those in men. In 2008, Hak and Choi reviewed data from the Third National Health and Nutrition Examination Survey, and published their findings on menopause, postmenopausal hormone use, and serum uric acid levels in women.<sup>7</sup> They concluded that menopause was associated with higher serum uric acid levels, and that postmenopausal hormone replacement was associated with lower serum uric acid levels, suggesting that estrogen plays a key role in pro-

tecting women from hyperuricemia and gout.

Pui et al found further evidence of the role of estrogens in regulating serum uric acid: they found early onset hyperuricemia and gout following hormone treatment given for the purpose of female to male gender reassignment.<sup>8</sup> Estrogen may enhance renal uric acid excretion. During gender reassignment, testosterone treatment likely dampens the effect of estrogen, and causes increased serum urate concentrations by reducing renal excretion of uric acid. It was also suggested that sex hormones may also influence the expression of acute gout through effects on the inflammatory response to monosodium urate crystals.

## ...gout is often misdiagnosed in women

Another important risk factor for gout in women is the use of diuretics. Both loop and thiazide diuretics increase serum uric acid. Meyers, et al., analyzing 92 women with gout, found that 78% of them were receiving diuretic treatment.<sup>6</sup> Although many of the women who were taking diuretics were postmenopausal, diuretic use appears to be an independent risk factor. Yu, et al found that 18% of premenopausal women had “diuretic-induced acute gouty arthritis.”<sup>9</sup> In a case report Hayem et al. showed that diuretic abuse for the purpose of weight loss was implicated in three premenopausal women with tophaceous gout.<sup>10</sup> Another case report described a 32-year-

old woman with anorexia nervosa who developed tophaceous gout. This case was also attributed to diuretic abuse, as she had been taking furosemide to lose weight since age 18.<sup>11</sup>

Several studies have shown an increased incidence of renal insufficiency in women with gout. Renal insufficiency can reduce the serum uric acid excretion, thereby increasing risk for hyperuricemia and gout.<sup>12</sup> Puig, et al. found that more than 50% of women with gout had renal insufficiency, whereas approximately 11% of men with gout had renal insufficiency. This report described four of five premenopausal women with gout, none of whom were taking diuretics. Also, Yu’s study noted some form of renal disease in 85% of premenopausal women with gout.<sup>9</sup> Many of the reports that showed higher prevalence of renal insufficiency in gouty women also showed a higher prevalence of hypertension and diuretic use.

A widely observed association in female gout is the presence of pre-existing joint disease, in particular, **osteoarthritis (OA)**. (Figure 1) Lally, et al. found pre-existing joint disease in 70% of women and in only 37% of men. This paper described 6 women with tophi and/or acute gouty arthritis in association with Heberden’s or Bouchard’s nodes.<sup>2</sup> Similarly, Puig et al. reported 76% of women with gout had OA compared to 40% of men.<sup>5</sup> The latter study also found a relationship between nodal OA and monosodium urate crystal deposition in women with gout and nodal disease in the hands. The presentation of acute or subacute gout in the fingers of a woman with nodal OA may contribute to a delayed or in-

**Table 1. Differences between Women and Men with Gout**

	Women	Men
<b>Age at presentation</b>	<b>Older (50s-60s)</b>	<b>Younger (40s)</b>
Renal insufficiency	More (~28%)	Less (~16%)
Alcoholism	Less	More
Family history	More	Less
Pre-existing joint disease	More (~50%)	Less (~25%)
Obesity	Less	More
Diuretic use	More (~30%)	Less (~13%)



Figure 1: The hand of a 90-year-old woman with her first presentation of gout. Inflammation occurring in a joint with preexisting nodal osteoarthritis may obscure the correct diagnosis.

correct diagnosis.

Although environmental factors influence gouty arthritis, hereditary factors also play a role. Studies demonstrate an increased prevalence of gout in relatives of patients with gout. Serum uric acid levels are controlled by multiple genes in both genders. However, this seems to be more strongly associated with women. In one example, Yu found a higher familial influence in premenopausal gout patients, citing a positive family history of gout in 59% of premenopausal patients, versus 34% in postmenopausal ones.<sup>9</sup>

There also seems to be a relationship between serum glucose levels and uric acid levels. In the Third National Health and Nutrition Examination Survey, Choi and Ford observed that individuals with moderately elevated hemoglobin A1c levels (6.0-6.9), may be at higher risk of hyperuricemia and gout, particularly in women, however, higher HbA1c levels were associated with a lower risk of these conditions, particularly in men.<sup>13</sup> This observation corresponds to Chou's report in 2001, which states that hyperuricemia in women was correlated with older age, higher fasting serum insulin levels, plasma glucose and hyperinsulinemia.<sup>14</sup> It is suggested that there is a uricosuric effect of glycosuria, which occurs when the blood glucose level is greater than 10 mmol/l.

Several articles on risk factors for hyperuricemia and gout note the association of obesity and alcohol consumption; however, these associations are not as strong in women as they are in men. Puig reported the incidence of obesity seen in his gout population was approxi-

mately 10% less in women, compared with the men in the study. And, in the comparison between women and men with gouty arthritis in Lally's study, that less than 9% of the women had associated alcoholism, compared to 45% of men.<sup>2,5</sup>

### CLINICAL MANIFESTATIONS

The articular findings of gout are similar in men and women. Podagra is commonly the initial manifestation of gout in both genders. However, during the course of the disease, women tend to have more upper extremity joint involvement, and the onset of the gout attack is more often insidious in women. In some studies, women were more often afflicted with polyarticular gout. In fact, in an analysis of 92 women with gout by Meyers, *et al*, 70% of women presented with pauciarticular or polyarticular disease, and only 24% of those patients gave a history of preceding acute monoarticular attacks.<sup>6</sup> In some studies, women were shown to have higher incidence of tophi at presentation. Lally's study, however, did not find a significant difference between tophi in men versus women at presentation.<sup>2</sup>

According to the data reported by Puig, *et al*, the mean serum uric acid levels in women (541 $\mu$ mol/L) with gout has been shown to be significantly higher than those seen in men (476 $\mu$ mol/L). This finding was supported by several other studies, including the studies by Lally and Meyers.<sup>2,6</sup> Puig also noted a lower mean urinary uric acid excretion in women with gout. This finding was

independent of age, renal insufficiency, alcoholism or previous diuretic use.<sup>5</sup>

The diagnosis of gout should especially be considered in postmenopausal women, women who have associated comorbidities, women who are taking diuretics, women who have a positive family history, or women who present with an atypical pattern of inflammatory arthritis. Special attention should be given to women with nodal OA in order that coexisting gouty arthritis not be overlooked.

### TREATMENT CONSIDERATIONS

Once the diagnosis of gout is made, treatment is basically the same in men and women. Recommendations are aimed at decreasing the modifiable risk factors, i.e., avoid alcohol, discontinue diuretics if possible, maintain normal serum glucose levels and blood pressure, maintain ideal body weight and consume a diet low in red meat, fructose, and shell fish.

The use of medications is often required for treatment of acute gout and maintenance of normal serum uric acid. The most commonly recommended therapies for acute gout include **nonsteroidal anti-inflammatory drugs (NSAIDs)**, such as indomethacin or naproxyn, intra-articular corticosteroid injections, oral colchicine, and oral corticosteroids. Uricosuric drugs such as probenecid, and the xanthine oxidase inhibitors allopurinol, and the newly FDA approved drug febuxostat are indicated for the control of hyperuricemia in gouty patients. The proper use of these medications is discussed elsewhere in this journal.

Premenopausal women who are pregnant, or plan to become pregnant require special consideration. Colchicine and allopurinol are both classified as category C. Both enter the breast milk, and should be used with caution. NSAIDs are category C/D. They also enter the breast milk, and use is not recommended in females who are or may become pregnant. Sufficient data on febuxostat is not available for use in pregnant or lactating women, therefore, avoidance is recommended in that group. For acute flares of gout in pregnant or lactating women, prednisone may be the best option for treatment.

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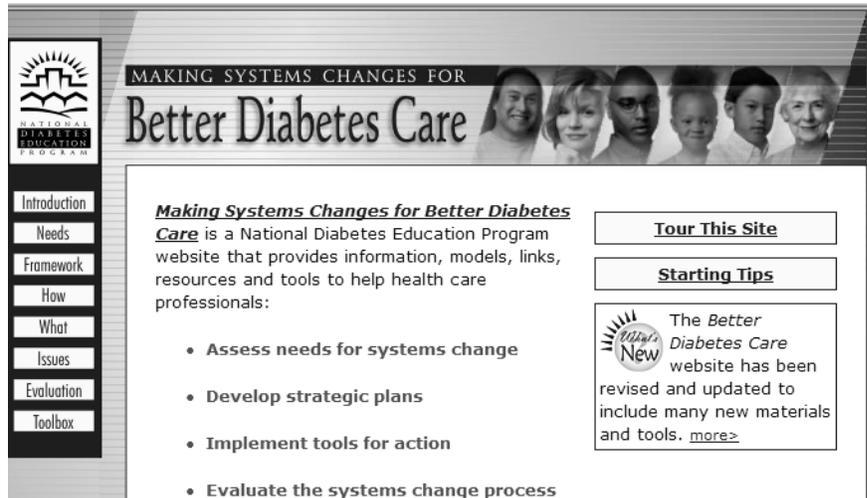
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The authors have no financial interests to disclose.

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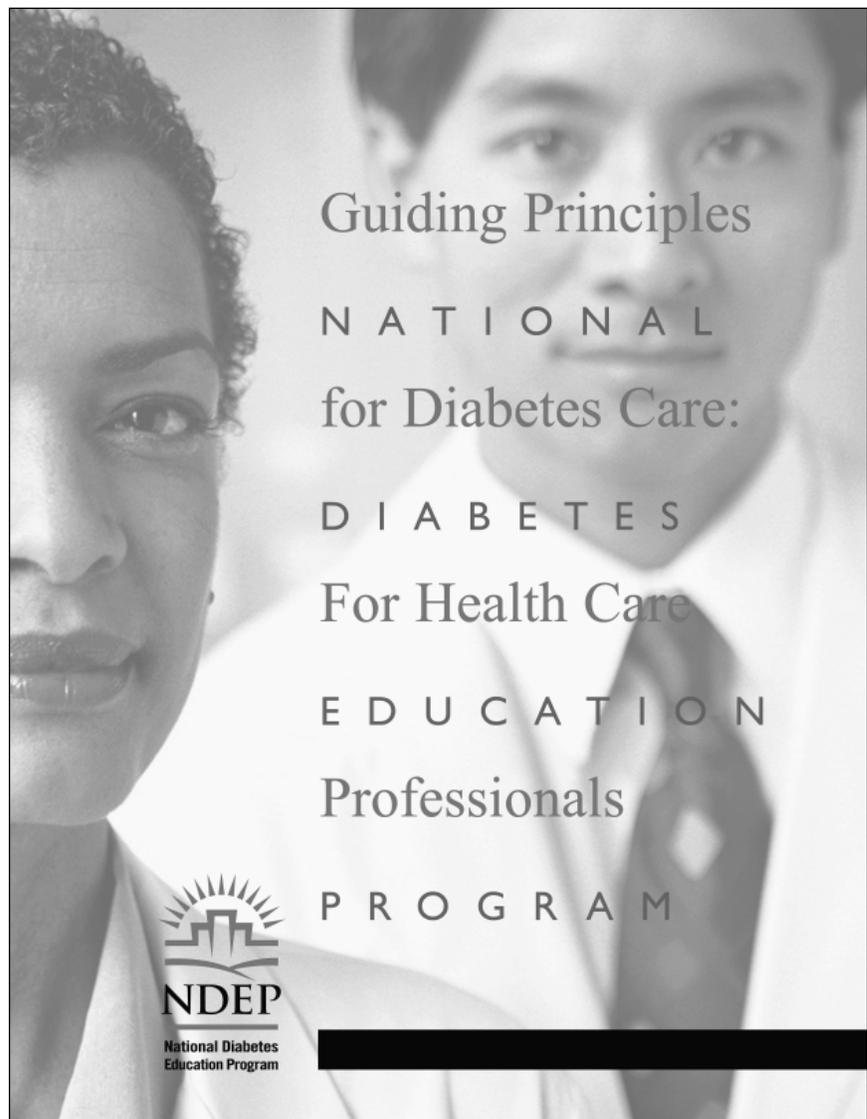
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