Epidemiology and Clinical Manifestation of GOUT in Imam Khomeini Hospital in Tehran, Iran

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Abstract

Background: Gout is an increasingly prevalent condition worldwide, creating a heavy economic burden. Acute gout can be effectively treated with non-steroidal anti-inflammatory drugs and recurrent episodes can be prevented with the uricosuric xanthine oxidase inhibitors. This study was conducted to determine the epidemiology and clinical manifestations of 100 patients with acute or chronic gout in Imam Khomeini Hospital in Tehran, Iran.

Methods: One-hundred patients with gout who referred to the Rheumatology Department were reviewed. Their demographic data, family and drug history, comorbide diseases, body mass index, symptoms and signs at the time of referral to our clinic and lab data were collected.

Results: Among patients, 84 were men and 16 women (mean age=55.8 years and mean Body Mass Index=26.1 kg/m²). Thirty three percent of the patients were smokers and 10% drank alcohol. Seventy cases had previous gout attack of whom, 56 were in the first metotarso-phalangeal joint. The mean serum uric acid was 8.5 mg/dl.

Conclusion: In our study, the mean age and mean body mass index of the patients were similar to those in others studies. Alcohol consumption was low in our study. Hypertension was found to be a risk factor for gout.

Keywords: Gout; Clinical manifestation; Epidemiology; Uric acid; Tophus

Introduction

Gout is a common disorder characterized by acute self-limiting attacks of arthritis or recurrent attack of crystal arthritis and urate tophi sometimes progress in some patients.¹,² Gout is closely associated with purine metabolism hyperuricemia.³ The incidence of the first attacks of gout has been reported about 1.4/1000 annually.⁴ The Community Oriented Program for Control of Rheumatic Diseases (COPCORD) studies demonstrated the incidence of 0.12%–4% in APLAR (Asia and Pacific Area) region.⁵ The incidence and prevalence of gout has increased with the level of serum uric acid over the last 40 years.⁴ Roddy et al. indicated that the prevalence and incidence of gout have increased in the last few decades because of life-style and dietary factors.⁶

The most important risk factor for gout is high levels of serum uric acid that results in urate crystal formation in the articular, periarticular and subcutaneous tissues.⁷,⁸ Other important risk factors in gout are weight gain, hypertension (HTN) and diuretic use adiposity.⁹ Furthermore, Choi et al. established some of the dietary risk factors such as meat, seafood, beer, wine, liquor, and purine-rich vegetables.¹⁰,¹¹

The clinical manifestations of gout can be categorized in four stages: asymptomatic hyperuricemia, acute/recurrent gout, intercritical gout, and chronic tophaceous gout.¹² More than 50% of gout attack episodes have appeared in the metotarso-phalangeal joint of the great toe.⁴ The initial attack may be sudden and wake the patient from sleep. The affected joint becomes hot, red, swollen, very painful and tender.⁴,¹³ Very acute attacks may be accompanied by fever; leucocytosis and raised erythrocyte sedimentation rate (ESR), in some cases, may be preceded by anorexia and nausea.¹⁴ Chronic gout is accompanied by
disability, joint damage and organ damage such as renal failure and cardiovascular disease.\textsuperscript{15}

The gold standard for definite diagnosis of gout is the presence of intracellular crystals of monosodium urate (MSU) in aspirated joint fluid or tophi,\textsuperscript{16} but many centers cannot make use of this method; therefore, gout is confirmed by clinical manifestations and lab tests. Treatment of gout is categorised in three phases: treatment of acute attack, prevention of future attack and treatment of hypourisemic phase in some patients. Non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, corticosteroids and corticotropins are administrated routinely for the treatment of different phases.\textsuperscript{17,18} Even though gout is a common condition in rheumatology clinics, few recent clinical data related to the pattern of epidemiology and clinical manifestations of gout are available in Iran.

In this study, we reviewed the results of the epidemiology and clinical manifestations of 100 patients with acute or chronic gout referred to Rheumatology Clinic or emergency ward in Imam Khomeini hospital (Tehran-Iran).

Materials and Methods

From March 2005 to August 2007, in a prospective study 100 gout patients (86 men, 16 women) who referred to Rheumatology Clinic of Imam Khomeini Hospital affiliated to Tehran University of Medical Sciences were enrolled. They were asked for any musculoskeletal disorders. The case histories were obtained by a questionnaire and personal interview, and the clinical examination was performed systematically by rheumatologists to confirm the gout disease.

The collected data included age, gender, body mass index (BMI; kg/m\textsuperscript{2}), past social history such as smoking and alcohol consumption, family history of gout or kidney stone, accompanying medical conditions such as HTN, diabetes mellitus (DM), dyslipidemia, renal insufficiency, and cancer. Features of gout attacks included the number and location of the involved joints, presence of tophi, and history of urinary stones. All the related biochemical investigations were performed. The routine laboratory screening including complete blood count (CBC), ESR, SGOT, SGPT, triglicerides, cholesterol, glucose, creatinine and serum uric acid were done for all the patients. The 24 hours urinary uric acid and creatinine clearance were undertaken for 48 patients. Medications for gout attack such as non-steroidal NSAIDs, colchicine, and allopurinol. Hyperuricaemia were provided when the serum uric acid level was more than 7 mg/dl in male and 6 mg/dl in female patients. Statistical analysis was performed using SPSS software (version 14.0 for Windows, Chicago, IL, USA). In this study, statistical analyses were performed, using the paired t test or \(x^2\) test and P values <0.05 were considered statistically significant.

Results

The male to female ratio was 5:1. The mean age in men was 54.9±15.0 years (range=20-83 years) and in women 60.44±9.5 years (range: 49-77 years). The age and sex distribution in cases are shown in Table 1. All women but one had their first disease attack before menopausal ages.

The mean of BMI of the patients was 26.1±3.5 kg/m\textsuperscript{2} for men (range=19.7-37.5 kg/m\textsuperscript{2}) and for women 27.7±3.8 kg/m\textsuperscript{2} (range=19.9-35.5 kg/m\textsuperscript{2}). Five percent of the patients (4 men and one woman) had BMI less than 20 kg/m\textsuperscript{2} (less than normal); 36% (33 men, 3 women) had BMI between 20 to 25 kg/m\textsuperscript{2} (normal); 50% (41 men, 9 women) between 25 to 30 kg/m\textsuperscript{2} (overweight); and 9% (6 men, 3 women) had BMI, 30 kg/m\textsuperscript{2} or more (obese). It means that most of our patients were in the overweight group (Table 2).

In our study, 30 men (35.7%) had the history of alcohol drinking, 10 men (11.9%) had the history of smoking and 6 men (7.1%) had positive history for both. Thirty eight male patients (45.3%) had no history of alcohol drinking or smoking. None of the female patients mentioned any history of alcohol drinking, but 3 of them (18.8%) had a history of smoking.

<p>| Table 1: Age and sex distribution in patients with gout |
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<table>
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<tr>
<th>Sex</th>
<th>Age</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Male</td>
<td>&lt; 25</td>
<td>2 (2.4)</td>
<td>6 (7.1)</td>
<td>17 (20.2)</td>
<td>22 (26.2)</td>
<td>14 (16.7)</td>
<td>14 (16.7)</td>
<td>9 (10.7)</td>
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<tr>
<td>Female</td>
<td>&lt; 25</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (6.3)</td>
<td>4 (25.4)</td>
<td>6 (37.5)</td>
<td>4 (25.4)</td>
<td>1 (6.3)</td>
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<td></td>
<td>[25 , 35)</td>
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<td>≥ 75</td>
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<tr>
<td>Total</td>
<td>&lt; 25</td>
<td>2 (2.0)</td>
<td>6 (6.0)</td>
<td>18 (18.0)</td>
<td>26 (26.0)</td>
<td>20 (20.0)</td>
<td>18 (18.0)</td>
<td>10 (17.0)</td>
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</table>
Thirty four patients (34%) had HTN, 19 (19%) had renal stones, 9 (9%) had DM and 7 patients had other less prevalent diseases (CML in one patient, hypothyroidism in one, chronic renal failure in one, Cushing in one, Shihan’s syndrome in one and Kaposi sarcoma in one patient). In this study, 57 patients did not mention any histories of drug usage; 25 patients had the history of aspirin (minimum 80 mg daily) for at least one year; 12 patients had the past medical history of diuretics and 6 patients had used corticosteroids for more than one year. History of radiotherapy was positive in the patients with Kaposi sarcoma.

One of the most risk factors in the patients with gout was the family history of gout or renal stones; 25 patients (23 men, 2 women) in this study had the family history of gout. Meanwhile, the family history of renal stones was present in 10 patients (9 men, 1 woman). In 3 patients (2 men, 1 woman) the simultaneous family histories of gout and renal stones were mentioned.

In assessing the previous episodes of gout in patients, 70 cases (62 men and 8 women) had the history of previous episode of gout, of which 56 cases (80%) were in the toe joint and 11 patients (15.7%) in the ankle joint. In 3 male patients (4.3%), the knee joint was the affected place. We found tophi in 23 patients (22 men, 1 woman) in ear (18 cases), elbow (12 cases) and hands (4 cases). In 77 patients, no tophi were found (77%).

Physical examination revealed that 36 patients had first metatarsopharyngeal involvement. We found inflammation in 11 patients in other metatarsopharyngeal joints, in 16 patients in the ankle, in 8 patients in the knee and in 29 patients in more than one of the mentioned joints. The involvement manifestations included pain, swelling, redness, tenderness and reduction in movement threshold. The mean serum level of uric acid was 8.3±1.8 mg/100 ml (range=5-13.8 mg/100 ml) in men and 8.7±1.8 mg/100 ml (range=6.4-12.5 mg/100 ml) in women. In gout’s episode, hyperuricemia was documented in 63 (75%) men and 13 (82.25%) women (Table 2). In the laboratory evaluation, 31 patients (31%) had leukocytosis (leukocyte count more than 10000); 43 cases (43%) had elevated levels of ESR (≥20), and 45 (45%) patients had positive C - reactive protein (CRP). Hyperlipidemia (Triglyceride level ≥200 or Cholesterol level ≥250) was present in 64 patients (64%).

**Discussion**

Gout is an arthritic manifestation of chronic/severe hyperuricemia characterized by episodes of intense inflammation. It is a disease whose relation to social and cultural levels has been proved and its clinical manifestations are completely described. Gout is one of the most common forms of inflammatory arthritis in the population and is commonly diagnosed by primary care providers. Nowadays, it is known completely and several drugs are used for acute episodes and also for the prophylaxis and prevention of the future attacks.

Several studies have shown that the prevalence of gout increases with age and between the 4th and 6th decades it has more incidences. In our study, 48% of the patients were between the ages 45 to 65 years. The mean age of the patients in our study was similar to that in other studies performed in other countries.

In our study, the mean ages of the male and female patients were similar to those in the study of Sarawate et al. (men=54.95 vs. 54.1 and women=60.44 vs. 59.6 years). Gout has long been regarded as a male disease and most gout research has focused on men because it is very low in a woman before the menopausal ages. The differences may be due to differences in sex hormones. Various studies have shown that female sex hormones (e.g. estrogen) protect against hyperuricemia, but 50% of patients older than 60 years with

**Table 2: Comparison of BMI, uric acid in our study with other studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>Number of patients</th>
<th>Mean of age</th>
<th>Range of age</th>
<th>Gender</th>
<th>Mean of BMI</th>
<th>Mean of uric acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dessein et al.</td>
<td>2000</td>
<td>South Africa</td>
<td>13</td>
<td>50</td>
<td>38-62</td>
<td>All males</td>
<td>30.5</td>
<td>------</td>
</tr>
<tr>
<td>Heidari et al.</td>
<td>2003</td>
<td>Iran</td>
<td>57</td>
<td>54</td>
<td>38-70</td>
<td>50 males</td>
<td>----</td>
<td>8.5</td>
</tr>
<tr>
<td>Schueller et al.</td>
<td>2006</td>
<td>Austria</td>
<td>19</td>
<td>57.3</td>
<td>47-68</td>
<td>17 males</td>
<td>26</td>
<td>7.4</td>
</tr>
<tr>
<td>Our study</td>
<td>2007</td>
<td>Iran</td>
<td>100</td>
<td>55.83</td>
<td>20-83</td>
<td>84 males</td>
<td>26.8</td>
<td>8.49</td>
</tr>
</tbody>
</table>
newly diagnosed gout are women, and the proportion may exceed 50% in those older than 80 years. \cite{34,35}

In young female patients with the attack of this disease, we should look for predisposing factors such as, long term usage of corticosteroid and diuretic drugs. It has been reported that the history of drug usage especially aspirin, corticosteroids and diuretics may increase the chance of gout episodes. \cite{19,21} All the female patients in our study had their first attack of the disease after menopause except one patient who had her first attack of gout at the age of 38 years with Cushing syndrome for 3 years. One woman had a history of endocrine disease (Shihan’ syndrome and primary amenorrhea) and one woman had a history of long term usage of corticosteroid drugs. These co-morbidities are a strong risk factor for secondary gout attack. Another important risk factor in the incidence of gout is the increase of weight. Increased body mass index (BMI) also directly correlated with hyperuricemia. \cite{36} Weight gain is a strong risk factor for gout\cite{9} whereas weight loss was protective. \cite{37,38} In the study of Dessein et al.,\cite{24} the mean for BMI was 30.5 kg/m\(^2\). Mc Lachian et al.\cite{39} have reported that 79% of their patients had the mean BMI more than 30 kg/m\(^2\). The mean of BMI was 26.08 kg/m\(^2\) in our study and 59% of patient had BMI ≥ 25 (Table 2).

The consumption of alcohol is another risk factor in gout. Choi et al.,\cite{11} in a study between 1986 and 1998 found that alcohol consumption contributed to an increased risk of gout incidence. In our study, this rate was 16% which was lower than that in other countries, but it may also be because of less confesion of alcohol consumption due to religious and legal prohibitions. The role of smoking has not been obviously demonstrated, but it will increase the rate of heart disease in patients with gout and, indirectly, increases the risk of mortality and morbidity in gout patients. In this study, 33% of patients were smokers, which is higher than that in the study of Mc-Lachian (33% vs. 20%). Among the predisposing diseases, HTN is an important risk factor for gout. Rouhennoff et al.\cite{40,41} reported that HTN increased the risk of developing gout (relative risk, 2.7). This risk may be explained by hypertension-induced renal insufficiency, which can reduce uric acid clearance. In the study conducted by Sarawate et al.,\cite{27} 39.8% of the patients had HTN which is higher than that in our study (39.8% vs. 34%). We had a higher rate of HTN in female patients than that in males (68% vs. 23%). The rate of DM in our patients was less than that reported by Sarawate et al. (9% vs. 18.3%).

The relation between serum uric acid levels and gout is well established. The risk of developing gout is directly related to the degree of hyperuricemia. In a prospective study, the annual incidence of gout was 0.1% in men whose uric acid levels were <7 mg/dL, 0.5% for levels between 7.0 and 8.9 mg/dL, and 4.9% for levels >9.0 mg/dL. \cite{42} In another study, the 5-year prevalence of gout was 0.6% in patients with uric acid levels <7 mg/dL, but 30% in patients with levels >10 mg/dL. \cite{33,35} Although hyperuricemia predisposes patients to the development of gout, it is erroneous to equate hyperuricemia with gout because not all patients with hyperuricemia develop gout, and gout can occur in those with apparently normal urate values. \cite{44,45} The mean level of serum uric acid in our study was 8.49 mg/dL which is similar to that reported by other studies (Heidari et al.=8.5 mg/dL and Schueler et al.=7.4 mg/dL) (Table 2). Another characteristic of this disease is tophus. In our study, 23% of the patients had tophi which were lower than the rate reported by Seze et al. (23% vs. 59%).\cite{46} Among the laboratory findings, hyperlipidemia has been reported to have a strong correlation with gout which also has been the most prevalent abnormal laboratory finding. It may induce hyperuricemia through its negative effect on renal functions.\cite{47,48} Hyperlipidemia has been reported in patients with gout.\cite{47} Genetic (S2 allele of the CIII gene; apo e4 allele) and environmental factors are responsible.\cite{47} In the present study, we found a prevalence of 64%. This shows that hyperlipidemia has a high incidence rate in patients with gout, and due to its affects on different organs especially, cardiovascular system, it deserves special attention.

In conclusion, gout is one of the most inflammatory diseases, especially in older age. With treatment and follow up, its complications would diminish. Consumption of alcohol, high BMI, HTN and high protein food regime are major risk factors for gout attack. The prevalence and incidence of gout seems to demonstrate a similar trend in the different studies that had been done in different countries. In our country, because of no valuable data on gout, some multicenter studies need to performed.

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Conflict of interest: None declared.

References


