

# Clinical Manifestations of Patients with Hyperuricemia

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**Objective :** To study the clinical manifestations of patients with hyperuricemia in King Chulalongkorn Memorial Hospital.  
**Method :** A cross sectional study of 188 hyperuricemic patients was done at King Chulalongkorn Memorial Hospital. History, physical examination, and blood samples were drawn to assess complete blood count (CBC), blood urea nitrogen (BUN), creatinine (Cr), liver function test (LFT), and serum uric acid in all patients.

**Results :** Most of the patients (92%) were male, more than 50 years old (69%), the mean age of the patients was  $56.7 \pm 12.1$  years old. All of the female patients were more than 50 years old. Symptomatic hyperuricemia was found in 93%, the mean duration of symptoms was  $63.2 \pm 66.3$  months. The mean of the serum uric acid level was  $10.0 \pm 2.9$  mg/dl. Associated diseases were found in 46% of the patients, and 30% of these patients had more than one disease. Hypertension was the most common followed in frequency by dyslipidemia, diabetes mellitus, ischemic heart disease, and chronic obstructive pulmonary disease consecutively. Renal impairment was detected in about one-third of the patients.

**Conclusion:** This study shows that hyperuricemia is common in elderly, male patients. Associated diseases and renal impairment can be found frequently, and the patients should be monitored.

**Keywords :** Hyperuricemia, Gout, Renal impairment, Clinical manifestations

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Hyperuricemia is a common biochemical abnormality found in clinical practice. This occurs in an absolute sense when serum uric acid concentration exceeds the limit of solubility in the serum. At 37 °C, the saturation value of uric acid in plasma is about 7 mg/dl. A value greater than this concentration represents supersaturation in the physicochemical sense. In most epidemiologic studies, the upper limit has been rounded off at 7 mg/dl in men and 6 mg/dl in women. Finally, a serum uric acid level in excess of 7 mg/dl begins to carry an increased risk of arthritis or renal stone. For these reasons, hyperuricemia is defined as a serum uric acid greater than 7.0 mg/dl<sup>(1)</sup>.

The incidence of hyperuricemia varies from 2-17 percent based on a study population<sup>(2,3)</sup>, and 13-28 percent in routinely screened hospitalized patients<sup>(4,5)</sup>. Hyperuricemia is frequently associated with other metabolic perturbations, such as hypertension, dyslipidemia, diabetes mellitus, renal disease and obesity. Whether hyperuricemia plays a causal role or is an epiphenomenon is currently unknown. One previous study showed an increased risk ratio for death from

all causes in patients with an elevated serum uric acid level<sup>(6)</sup>. The lowering of the serum uric acid is necessary in patients with clinical symptoms associated with hyperuricemia and occasionally in certain asymptomatic subjects.

Clinical manifestations of hyperuricemia may be gouty arthritis, nodules (tophi), and renal involvement. The present study aimed to evaluate the clinical manifestations of hyperuricemic patients in a tertiary care, medical school hospital.

## Material and Method

A cross-sectional study was done in hyperuricemic patients consecutively who came to the out-patient rheumatology clinic, King Chulalongkorn Memorial Hospital. The patient's baseline data including age, sex, associated diseases, and concomitant medications were recorded. History of hyperuricemia was asked for symptomatic or asymptomatic hyperuricemia (symptomatic hyperuricemia was defined as a previous history of gouty attack or lithiasis<sup>(1)</sup>), duration of hyperuricemia, and oral hypouricemic drugs. Physical examination was performed on all of the patients.

Blood samples were drawn to assess for complete blood count (CBC), blood urea nitrogen (BUN),

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creatinine (Cr), liver function test (LFT), and serum uric acid in all patients. The patients who already took oral hypouricemic drugs were asked to stop the drugs at least one month before checking the blood samples. Colchicine 0.6 mg/day was prescribed to all of these patients for prophylaxis of attack of acute gouty arthritis.

Statistical analysis was performed with a statistical microcomputer using program SPSS. Descriptive statistics were used to characterize the patients. Results were presented as mean, standard deviation (SD), and percent.

## Results

A total of 188 patients were enrolled and completed the study. There were 174 (92%) male and 14 (8%) female patients. Most of the patients (64%) and all of the female patients were in the age group more than 50 years old. The most common age group of the patients was 51-60 years old (30%), followed by 61-70 years old (28%). The mean age of the patients was  $56.7 \pm 12.1$  years old. Table 1 shows the sex and age distribution of the patients.

One-hundred and seventy six patients (93%) were in the group of symptomatic hyperuricemia. The duration of symptoms varied from less than 1 year to more than 10 years, with the mean duration of  $63.2 \pm 66.3$  months. Table 2 shows the distribution of the duration of the symptoms of the patients. All of these patients had arthritis in the onset of their symptoms. One-hundred and fifty of these patients (85%) had monoarthritis at the onset. The other 26 patients (15%) had oligoarthritis. The first metatarsophalangeal joint was the most common joint (75 patients or 42%) at the onset, followed by ankle (67 patients or 38%), and knee joints (30 patients or 17%). Wrist and elbow joints made up the rest of this group. Visible tophi were detected by physical examination in 40 patients (23%). All of these patients had tophi many years after the onset of the first attack of arthritis.

Levels of serum uric acid of the patients are shown in Table 3. The most frequent level was in the range of 9.1-10.0 mg/dl (27%), followed by the range of 10.1-11.0 mg/dl. The mean of the serum uric acid level was  $10.0 \pm 2.9$  mg/dl.

Eighty-six patients (46%) had associated diseases, of which 26 in these 86 patients (30%) had more than one associated disease. Hypertension was the most common associated disease (32%) followed in frequency by dyslipidemia (16%), diabetes mellitus (2%), and each of 1% for ischemic heart disease, stroke,

**Table 1.** Age and sex distribution of the patients

| Age             | Sex        |            | Total (n)  | Percent    |
|-----------------|------------|------------|------------|------------|
|                 | Male (n)   | Female (n) |            |            |
| 30-40           | 22         | -          | 22         | 11         |
| more than 40-50 | 38         | -          | 38         | 20         |
| more than 50-60 | 48         | 8          | 56         | 30         |
| more than 60-70 | 48         | 4          | 52         | 28         |
| more than 70-80 | 18         | 2          | 20         | 11         |
| <b>Total</b>    | <b>174</b> | <b>14</b>  | <b>188</b> | <b>100</b> |

**Table 2.** Duration of symptomatic hyperuricemia

| Duration (years) | Total (n)  | Percent    |
|------------------|------------|------------|
| 1 or less than   | 40         | 23         |
| more than 1-2    | 24         | 14         |
| more than 2-3    | 22         | 12         |
| more than 3-4    | 14         | 8          |
| more than 4-5    | 10         | 6          |
| more than 5-6    | 8          | 4          |
| more than 6-7    | 10         | 6          |
| more than 7-8    | 6          | 3          |
| more than 8-9    | 4          | 2          |
| more than 9-10   | 26         | 15         |
| more than 10     | 12         | 7          |
| <b>Total</b>     | <b>176</b> | <b>100</b> |

**Table 3.** Level of serum uric acid of the patients

| Serum uric acid (mg/dl) | Total (n)  | Percent    |
|-------------------------|------------|------------|
| 7.1-8.0                 | 14         | 7          |
| 8.1-9.0                 | 34         | 18         |
| 9.1-10.0                | 50         | 27         |
| 10.1-11.0               | 42         | 23         |
| 11.1-12.0               | 24         | 13         |
| 12.1-13.0               | 12         | 6          |
| more than 13.0          | 12         | 6          |
| <b>Total</b>            | <b>188</b> | <b>100</b> |

and chronic obstructive pulmonary disease. Most of these patients (93%) had concomitant medication for hypertension and dyslipidemia.

Laboratory assessment showed renal impairment (serum Cr 1.5 mg/dl or more) in 66 patients (35%). Most of these patients (60 patients or 91%) had only mild renal impairment (serum Cr 1.5-2.0 mg/dl). Abnormal LFT (elevated of serum alanine aminotransferase and serum aspartate aminotransferase) was found in 10 patients (5%). All of these patients had a history of concomitant oral hypouricemic drug (allopurinol).

## Discussion

This study demonstrates that hyperuricemia is found more frequently in male than female patients. Most of the patients, especially all of the female patients were over 50 years old. This is in accordance with previous studies<sup>(7-9)</sup>. This may be explained by variation of serum uric acid with the age and sex of the patient. Children normally have a concentration in the range of 3 to 4 mg/dl because of high renal uric acid clearance. At puberty, the levels increase into the adult male range. The lower levels in women of reproductive age compared with their male counterparts have been ascribed to lower renal postsecretory uric acid reabsorption and, thus, increased uric acid clearance in women of childbearing age, but the suspected role of estrogenic compounds remained unclarified. With the onset of menopause, serum uric acid in women approaches or equals those of men of corresponding age<sup>(8)</sup>.

Most of the presented patients (93%) were symptomatic hyperuricemia with the mean duration of more than 5 years, and the onset of symptoms was arthritis. This may be explained by the patient-selection in the rheumatology clinic and tertiary care hospital. The number of asymptomatic cases should be higher in primary care centers, especially in routine physical check up clinics. These patients may be asymptomatic throughout their lifetime. The phase of asymptomatic hyperuricemia ends with the first attack of gouty arthritis or lithiasis. In most instances, this occurs after at least 20 years of sustained hyperuricemia<sup>(1)</sup>. The tendency toward acute gout increases with the serum uric acid level. In the Farmingham study, gout developed in only 12% of patients with a serum uric acid level between 7 and 7.9 mg/dl over a period of 14 years. Values greater than 9 mg/dl had a sixfold greater value<sup>(2)</sup>. In another study, the 5-year prevalence of gout was 30% with a level of more than 10 mg/dl, and only 0.6% in those with a level less than 7 mg/dl<sup>(10)</sup>. The presented patients had the mean level of  $10.0 \pm 2.9$  mg/dl. The frequent pattern of monoarthritis, the commonly attacked joints at the onset, and the visible tophi of the presented patients were not difference from the previous reports<sup>(1,11,12)</sup>.

Most of the patients with hyperuricemia or gout have frequently associated metabolic abnormalities. The present study demonstrates that 46% of the patients had associated diseases. Hypertension was the most common associated disease (32%) in the presented patients. There is a clear association between hypertension and hyperuricemia. One previous study showed that 47% of hypertensive patients (43% with

primary, 44% with renal and 75% with malignant hypertension) had hyperuricemia<sup>(13)</sup>. On the other hand, hyperuricemia may precede and predict the development of hypertension. One large population study demonstrated that baseline serum uric acid level was the strongest independent predictor of new onset hypertension. An increment of 1 mg/dl in serum uric acid was associated with a 23% higher risk of hypertension in a 12 year follow-up<sup>(14)</sup>.

Dyslipidemia is another associated metabolic abnormality in hyperuricemic patients. An association between dyslipidemia and hyperuricemia is well established. Up to 80% of individuals with dyslipidemia have hyperuricemia, and 50-75% of gouty patients have dyslipidemia<sup>(15)</sup>. The present study shows only 16% of the patients had dyslipidemia. This may be explained by the difference of diet, alcohol intake, and culture between the presented patients and patients in Western countries. Apart from dyslipidemia, diabetes mellitus is another metabolic syndrome reported in hyperuricemia. Hyperuricemia is reported in 2-50% of patients with diabetes mellitus, and gouty arthritis in less than 0.1-9%<sup>(16)</sup>. Abnormal glucose tolerance tests have been reported in 7-74% of patients with gout, depending on the criteria used<sup>(17)</sup>. Despite these observations, epidemiologic studies have not demonstrated a relation between gout and diabetes or between serum uric acid level and blood glucose concentrations<sup>(16,17)</sup>. The presented patients demonstrated a 3% history of diabetes mellitus.

After gouty arthritis, renal disease is the most frequent complication of hyperuricemia. Several types of renal diseases have been associated with hyperuricemia, such as urate nephropathy, acute uric acid nephropathy and nephrolithiasis. One previous study demonstrates hyperuricemia may predict renal damage in healthy subjects. The study included 6403 subjects from the general population for 2 years and serum uric acid was the most significant correlate for developing high serum creatinine ( $\geq 1.4$  mg/dl), the adjusted relative risk for those with uric acid levels  $\geq 8$  mg/dl was 2.91 (1.8-4.8) for males and 10.39 (1.9-56.6) for females<sup>(18)</sup>. In addition to these direct effects of hyperuricemia, other causes of renal impairment such as hypertension, diabetes mellitus, alcohol abuse, and nephrotoxic drug therapy also are prevalent in hyperuricemic and gouty populations. The isolation of hyperuricemia or gout as primary risk factors for progressive renal impairment is, thus, exceedingly difficult<sup>(1,19)</sup>. One third of the presented patients demonstrated renal impairment (serum Cr  $\geq 1.5$  mg/dl), most of these patients had

only mild renal impairment (serum Cr 1.5-2.0 mg/dl). These may be combined effects of hyperuricemia, associated diseases, and other nephrotoxic drugs.

In conclusion, the present study shows that hyperuricemia is commonly found in elderly male patients. Associated diseases and renal impairment can be found in hyperuricemic patients. Monitoring for these associated diseases and complications should be done in patients with hyperuricemia.

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### ลักษณะทางคลินิกของผู้ป่วยที่มีภาวะกรดยูริกในเลือดสูง

สมชาย อรรถศิลป์, ยิ่งยศ อวิหิงสานนท์, พันธุ์จิ่ง หาญวิวัฒน์กุล, จีรภัทร วงศ์ชินศรี

**วัตถุประสงค์:** ศึกษาลักษณะทางคลินิกของผู้ป่วยที่มีภาวะกรดยูริกในเลือดสูงที่มารับการรักษาที่โรงพยาบาลจุฬาลงกรณ์

**วิธีการศึกษา:** ทำการศึกษาแบบตัดขวางในผู้ป่วยที่มีภาวะกรดยูริกในเลือดสูงจำนวน 188 ราย ที่มารับการรักษาที่คลินิกโรคข้อ โรงพยาบาลจุฬาลงกรณ์ โดยทำการซักประวัติ ตรวจร่างกาย เจาะเลือด เพื่อตรวจระดับกรดยูริกในเลือด การทำงานของไตและตับ และตรวจนับเม็ดเลือด

**ผลการศึกษา:** ผู้ป่วยส่วนใหญ่ (ร้อยละ 92) เป็นเพศชาย กลุ่มอายุที่พบบ่อยเป็นกลุ่มอายุมากกว่า 50 ปี (ร้อยละ 69) โดยเฉพาะผู้ป่วยเพศหญิงทุกรายอายุมากกว่า 50 ปี โดยอายุเฉลี่ยของผู้ป่วยทั้งหมดคือ  $56.7 \pm 12.1$  ปี ผู้ป่วยร้อยละ 93 จัดอยู่ในกลุ่มผู้ป่วยที่มีภาวะกรดยูริกในเลือดสูงชนิดที่มีอาการ โดยระยะเวลาเฉลี่ยที่มีอาการก่อนเข้าทำการศึกษาคือ  $63.2 \pm 66.3$  เดือน ค่าเฉลี่ยของระดับกรดยูริกในเลือดของผู้ป่วยทั้งหมดคือ  $10.0 \pm 2.9$  ม.ก./ด.ล. ผู้ป่วยร้อยละ 46 มีโรคอื่นร่วมด้วย โดยร้อยละ 30 ของกลุ่มนี้มีมากกว่า 1 โรค โรคที่พบบ่อยเรียงตามลำดับคือ ความดันโลหิตสูง ภาวะไขมันในเลือดสูง เบาหวาน โรคหัวใจขาดเลือด และหลอดเลือดอุดตันเรื้อรัง ผลการตรวจทางห้องปฏิบัติการพบภาวะการทำงานของไตเสื่อม พบได้ร้อยละ 35

**สรุป:** การศึกษาพบว่าภาวะกรดยูริกในเลือดสูงพบบ่อยในเพศชาย อายุค่อนข้างมาก โดยผู้ป่วยมักมีโรคอื่น และภาวะการทำงานของไตเสื่อมร่วมด้วย การตรวจและเฝ้าระวังโรคร่วมและภาวะการทำงานของไตเป็นสิ่งสำคัญที่ต้องคำนึงในผู้ป่วยที่มีภาวะกรดยูริกในเลือดสูง