

Serum uric acid levels among thirty-four thousand people in Japan

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SUMMARY During 1978 a survey was carried out on 34 036 people in Nagano Prefecture, Japan, in an epidemiological study of hyperuricaemia; 15 712 males and 18 324 females were examined by means of our health examination car. The subjects of the survey were all volunteers. The results have shown that the serum uric acid (SUA) levels were related to sex and age. The male group had a mean SUA level of 5.82 mg/dl (range 0.9 to 11.8 mg/dl, standard deviation 1.14 mg/dl) (0.35, range 0.05–0.7, SD 0.07 mmol/l), and the female group had a mean of 4.33 mg/dl (range 0.5 to 9.7 mg/dl, standard deviation 0.91 mg/dl) (0.26, range 0.03–0.58, SD 0.05 mmol/l). The distribution curve for SUA was almost normal in both sexes. Lower levels of SUA were found in males from the 2nd to the 6th decade, but they increased again after the 7th decade. In females they gradually decreased and were at the lowest in the 4th and 5th decades, and then increased again. The values were always lower in females than males with the difference ranging from 1.84 to 0.81 mg/dl (0.11–0.05 mmol/l).

In Japan the number of patients with gout has been steadily increasing in recent years.^{1–3} It is believed, however, that there are several times more patients with asymptomatic hyperuricaemia. At present no definite criteria are available on which to decide whether these patients should receive medical treatment. An epidemiological study of serum uric acid (SUA) levels in a well defined population may help to provide an answer. Some reports show that the SUA level and the prevalence of hyperuricaemia vary with physiological factors such as race, sex, and age, and with environmental factors such as geographical area, social class, occupation, and the year of investigation.^{4–14} In Japan smaller studies than the one reported here have been made in some districts.^{1–3}

The authors have recently carried out a survey of SUA levels in Nagano Prefecture, which is located in the centre of Japan about 200 km west of Tokyo. Surrounded by high mountains, it is an inland district, 500 to 1200m above sea level, with relatively limited movement of population. This survey is the most extensive study of SUA levels conducted in a particular geographical district inhabited by a homogeneous race.

Materials and methods

A total of 15 712 adult men and 18 324 adult women were examined by means of our health examination car in Nagano Prefecture. This health examination was conducted to take care of the health chiefly of members of the farm co-operative in Nagano Prefecture, their families, their relatives, and their acquaintances. The farm co-operative in Japan is a co-operative society which is organised by farmers and those who are engaged in industries related to farming, and the farm co-operative of this prefecture is composed of about 210 000 households. The health examination was made on those people who wished to have it, but we encouraged in advance all the members through the office of the co-operative, regardless of their history of gout, to respond to our call for the examination, and we also made other efforts to gain as many participants as possible in all districts of the prefecture. The number of people examined represents approximately 5% of the adult members and their families, or 2.5% of the total adult population of the prefecture (Table 1).

The survey consisted of the following items: (1) questioning about the occurrence of adult diseases such as arthralgia; (2) study of daily routines and habits such as drinking, smoking, and diet; (3) measurement of height, weight, and blood pressure,

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Table 1 Number of subjects examined

Age	Male	Female
15-19	231	560
20-	3054	3368
30-	3356	2798
40-	4190	4695
50-	3029	4629
60-	1499	2053
70-	353	221
Total	15 712	18 324

Table 2 Analysis of variance

		SS	DF	MS	F values
Male	Age	377.12	6	62.854	49.486
	Error	19 947	15 705	1.2701	
Female	Age	891.25	6	148.54	188.55
	Error	14 429	18 317	0.7877	

SS: Sum of squares, DF: Degrees of freedom, MS: Mean square.

and (4) chemical analysis of blood by the Auto-Analyzer technique. The blood sample was centrifuged to separate the serum, which was then refrigerated, transported to a central laboratory, and submitted to automatic analysis in the Technicon SMA-12160 the next day. The SUA level was determined by the phosphotungstic acid method.

Results

Distribution of SUA levels by sex (grouped into 0.5 mg/dl classes)

The mean SUA was 5.82 mg/dl (range, 0.9 to 11.8

mg/dl, standard deviation, 1.14 mg/dl) (0.35, range 0.05-0.7, SD 0.07 mmol/l) for men and 4.33 mg/dl (range, 0.5 to 9.7 mg/dl, standard deviation, 0.91 mg/dl) (0.26, range 0.03-0.58, SD 0.05 mmol/l) for women. The distribution pattern in both sexes was nearly normal, and the range was narrower for women than for men (Fig. 1).

Comparative distribution of mean SUA levels by sex and age group (each 10-year age class except the 2nd and the 8th decade)

In men the mean SUA was the highest in teenagers and tended to decrease in older age groups up to the 6th decade, and they increased again after the 7th decade. In women the mean value tended to decrease with age till the 4th decade, and increased again after the menopause, reaching the highest in the 8th decade and over.

A significant difference (by analysis of variance, Table 2) occurred between different age groups except between younger age groups before the 3rd decade and among older age groups after the 6th decade for men, and it was also seen among nearly all age groups except between the 4th and the 5th decade for women.

Larger standard deviations were found in men from the 2nd to the 7th decade. In women they were smaller from the 2nd to the 4th decade, but they increased again after the 5th decade, especially after the 6th decade and over. The range of SUA levels was narrower in younger than in older men, and before the 5th decade than after the 6th decade and over in women (Fig. 2).

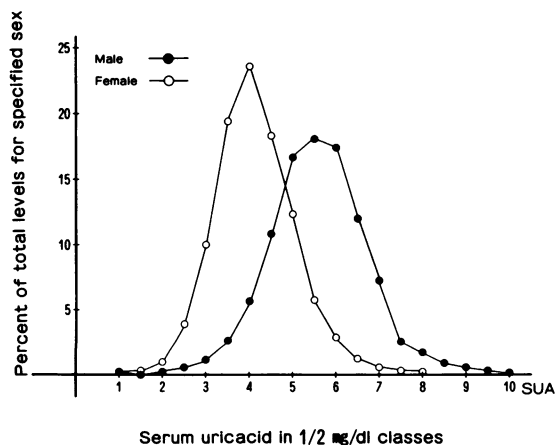


Fig. 1 Distribution of serum uric acid levels. Males: n = 15 712, \bar{x} = 5.82 mg/dl, SD = 1.14 mg/dl. Females: n = 18 324, \bar{x} = 4.33 mg/dl, SD = 0.91 mg/dl. (SI conversion: mmol/l = mg/dl \times 0.0595).

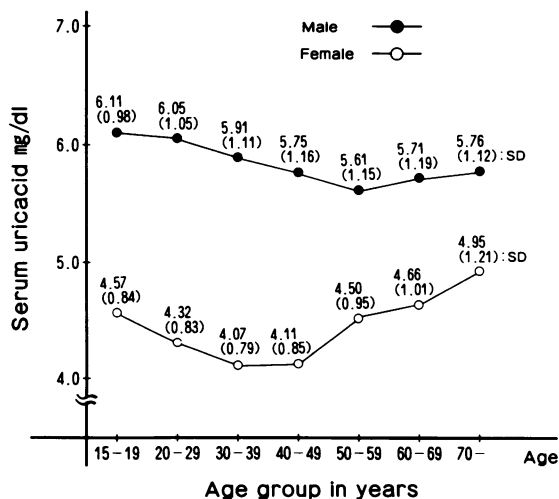


Fig. 2 Sex-age specific mean serum uric acid. (SI conversion: mmol/l = mg/dl \times 0.0595).

Discussion

The sample of this survey is large, but it is one of volunteers rather than a random sample, so it may be biased to an unknown extent and its value for comparison with other studies is limited. However, since the study was conducted as a general health examination in a well defined large population, the results obtained are believed to be worth discussing.

It is well known that gout affects men more than women and SUA levels differ between the sexes. Published studies confirm that men have an SUA level higher by 0.5–1.7 mg/dl (0.03–0.10 mmol/l) in Caucasians,^{4 5 9 10 15} 0.9–1.2 mg/dl (0.05–0.07 mmol/l) in black people of South Africa,^{13 14} and 1.2 mg/dl (0.07 mmol/l) in aborigines of the Mariana Islands¹⁶ than women in these areas irrespective of age in adults. According to 4 Japanese reports^{1–3} together with the present study the sex difference in SUA level of adults (when respective age groups are compared) is within the range of 0.8–1.8 mg/dl (0.05–0.11 mmol/l). It may be concluded that there is a difference of 0.5–2.0 mg/dl (0.03–0.12 mmol/l) between adult men and women without regard to race. The distribution curve for SUA levels is essentially constant for each sex in all investigations dealing with relatively large numbers of subjects. The distribution pattern obtained in these studies was usually normal, with the mean value higher than the median, and there was a narrower range of distribution in women because of the smaller standard deviation.

A sex difference in SUA is not present in childhood but appears during adolescence, when SUA values increase more in men than women.^{2 4 11} Many investigators have found that the variation with age of SUA levels is usually negligible in adult men, while in adult women SUA levels show a saucer-shaped distribution, with the lowest values during the period of maturity or fertility, or in the 4th and 5th decades, and increase again after the menopause from about the 6th decade.^{2 4 9 15} The fact that the mean SUA values of men are highest in teenagers in our survey may reflect one of the physiological processes during adolescence. Interestingly, they then showed a slight decrease with age till the 6th decade, followed by an increase again after the 7th decade and over. The reason for this physiological variation with age is not

clear. However, the curvilinear distribution of average SUA levels in both sexes shown in Fig. 2 suggests that both sexes are affected by hormonal factors with only a difference in degree.

References

- Shichikawa K. The prevalence of gout in Japan. In: Bennet P H, Wood P H N, eds. *Population Studies of Rheumatic Disease*. Amsterdam: Excerpta Medica, 1968: 354–7.
- Nishioka K, Mikanagi K, Hirose K. Clinical study of gout and hyperuricemia—1. Epidemiology and pathogenesis. *Ryumachi* 1974; **14**: 95–105 (in Japanese).
- Kato H, Duff I F, Russell W J, et al. Rheumatoid arthritis and gout in Hiroshima and Nagasaki. *J Chronic Dis* 1971; **23**: 659–79.
- Mikelson W M, Dodge H J, Valkenburg H. The distribution of serum uric acid values in a population unselected as to gout or hyperuricemia. *Am J Med* 1965; **39**: 242–51.
- Hall A P, Barry P E, Dawber T R, McNamara P M. Epidemiology of gout and hyperuricemia (a long term population study). *Am J Med* 1967; **42**: 27–37.
- Decker J L, Lang J J, Reynolds W E. Hyperuricemia in male Filipino population. *Arthritis Rheum* 1962; **5**: 144–55.
- Healey L A, Caner J E Z, Decker J L. Ethnic variations in serum uric acid 1. Filipino hyperuricemia in a controlled environment. *Arthritis Rheum* 1966; **9**: 288–94.
- Healey L A, Skeith M D, Decker J L, Bayani-Sloson. Hyperuricemia in Filipinos: interaction of heredity and environment. *Am J Hum Genet* 1967; **19**: 81–5.
- Sturge R A, Scott J T, Kennedy A C, Hart D P, Buchanan W W. Serum uric acid in England and Scotland. *Ann Rheum Dis* 1977; **30**: 171–84.
- Popert A J, Hewitt J V. Gout and hyperuricaemia in rural and urban populations. *Ann Rheum Dis* 1962; **21**: 154–63.
- Munan L, Kelly A, Pettitclerc C. Serum urate levels between ages 10 and 14 changes in sex trends. *J Lab Clin Med* 1977; **90**: 990–6.
- Dun J P, Brooks G W, Mausner J, Roknan G P, Cobb S. Social class gradient of serum uric acid levels in male. *JAMA* 1963; **185**: 431–6.
- Beighton P, Solomon L, Soskolne L, Sweet B. Serum uric acid concentrations in a rural Tswana community in Southern Africa. *Ann Rheum Dis* 1973; **32**: 346–50.
- Beighton P, Solomon L, Soskolne L, Sweet B, Robin G. Serum uric acid concentrations in an urbanized South Africa Negro population. *Ann Rheum Dis* 1974; **33**: 442–5.
- Isomäki H A, Takkunen H. Gout and hyperuricaemia in Finnish rural populations. *Acta Rheumatol Scand* 1969; **15**: 112–20.
- Burch T A, O'Brien W M, Need R, Kurland L T. Hyperuricaemia and gout in the Mariana Islands. *Ann Rheum Dis* 1966; **25**: 114–6.

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