Recent Trends in Hyperuricemia and Gout in Japan

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Abstract

The prevalence of hyperuricemia amongst Japanese adult men is now estimated to be nearly 30%. Although it had been increasing continuously until a few years ago, it now seems to have reached a plateau. In women, the prevalence of hyperuricemia is much lower than in men: 1–2% among those aged younger than 50 years and around 3% amongst those aged 50 years or older. A population-based study conducted in 2003 in a small district in Wakayama Prefecture, the age distribution of which was representative of Japan, found that the prevalence of gout was 1.7% in adult men who were older than 30 years. In that study, all 14 of the gouty patients detected were male. The results of research on the prevalence of gout in the same area conducted 30 years ago were about half of the 2003 results, suggesting that the gout prevalence may have increased. Since the number of tablets of urate-lowering drugs sold in Japan has continued to increase, the number of patients with hyperuricemia or gout that are being treated is thought to be increasing. Since hyperuricemia can cause chronic kidney disease and urolithiasis as well as gout, proper management of serum uric acid levels is warranted.

Key words Hyperuricemia, Management, Gout, Obesity

Introduction

Hyperuricemia is a pathological condition with a high frequency, affecting approximately 30% of adult males in Japan. In addition to being a direct cause of gout, it is also closely related to both renal damage and urinary tract stones.[1] In Japan, hyperuricemia has tended to increase in the past, but it is possible that there has been a recent change in this trend. In addition to describing trends in hyperuricemia and gout, this paper also considers the background to these trends.

Frequency of Hyperuricemia

According to a report by Tomita et al.[2] that analyzed serum urate levels in the results of occupational group health checkups conducted on approximately 400,000 people working in the Tokyo Metropolitan area, the frequency of hyperuricemia has fluctuated between 25 and 30% amongst men aged in their 30s, exceeding 30% in 2006 (**Fig. 1**). That is, one in every three to four men in this age group have hyperuricemia. In the 40–50 year age group, the frequency of hyperuricemia becomes slightly lower, but even so it is above 20%, and so by no means can the frequency of hyperuricemia be said to be low (**Fig. 1**). Furthermore, amongst men aged in their 20s, the frequency of hyperuricemia is higher than that for men aged in their 50s, and so it can be said that hyperuricemia is a common disease even amongst members of the younger generation. In a survey conducted in Nagano Prefecture, the frequency of hyperuricemia amongst junior high school boys (age 12 to 15) was already close to 10%.[3]

One possible reason why the frequency of hyperuricemia is lower amongst people aged in the 40s and older than amongst people aged in

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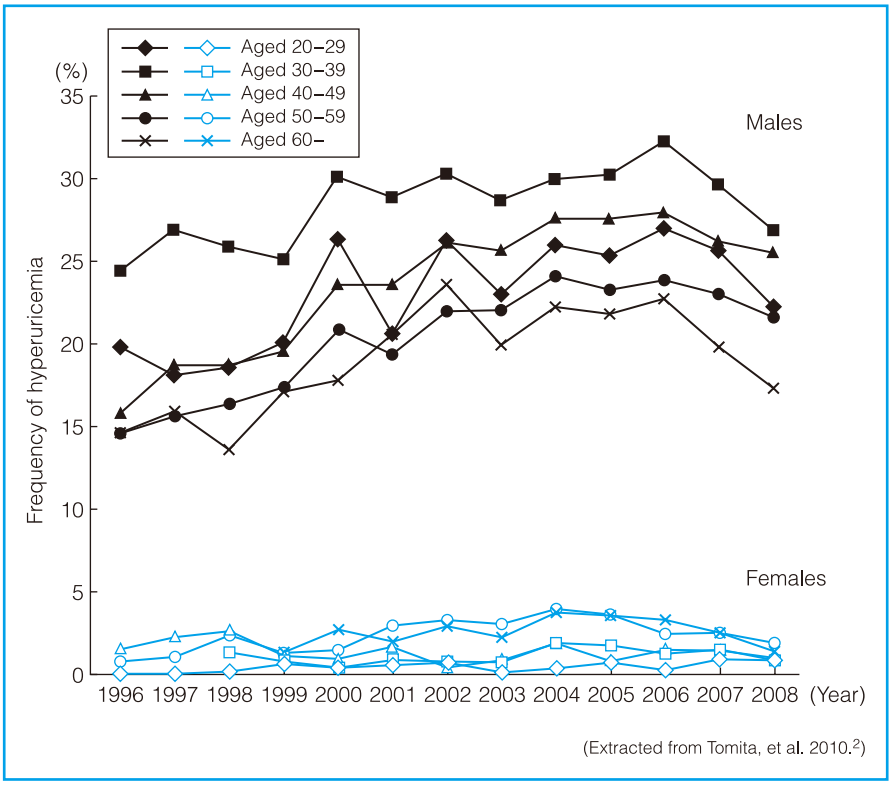

Fig. 1 Trends in the frequency of hyperuricemia

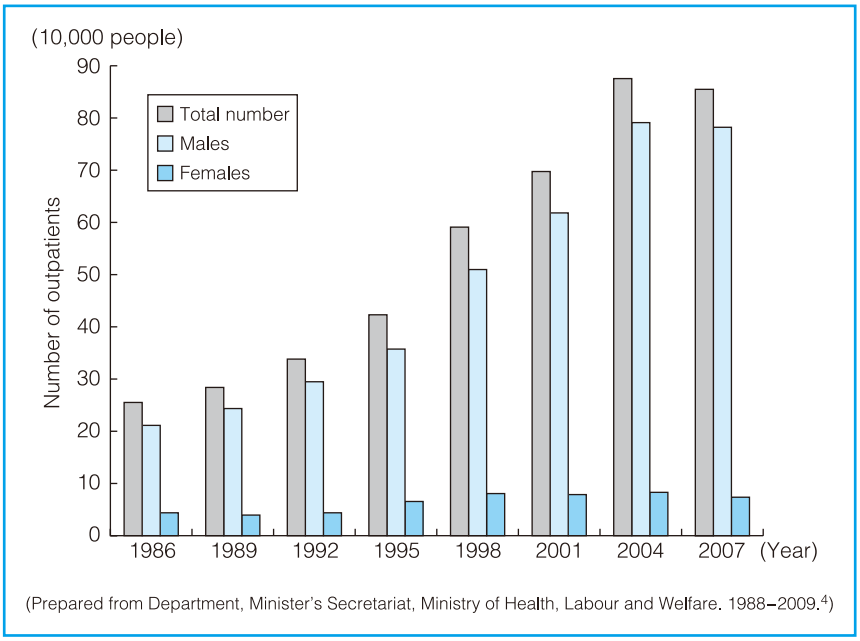

Fig. 2 Trends in the number of gout patients estimated from the number of survey respondents answering that they were "receiving outpatient treatment for gout"

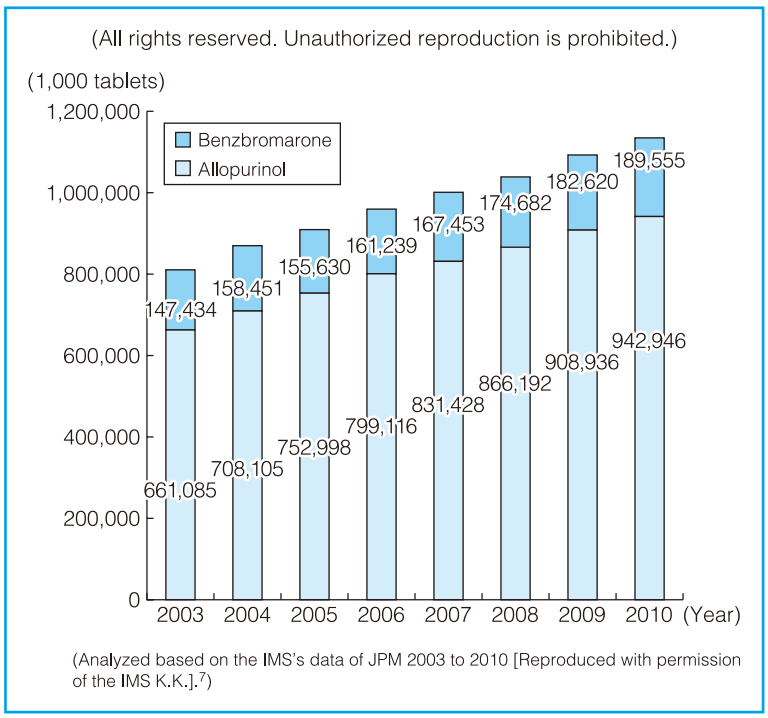

Fig. 3 Trends in the number of uric acid-lowering drugs sold

their 30s could be the effect of treatment using uric acid-lowering drugs. In the National Livelihood Survey conducted in 2007, the 60 to 69 year old age group had the largest number (233,000) of respondents (males) who answered that they were "Receiving outpatient treatment for gout" (believed to also include asymptomatic hyperuricemia), with less than half in male respondents aged in their 40s and less than one-fifth in male respondents aged in their 30s giving this answer.[4]

Amongst these respondents receiving treatment it is possible that there are some whose serum urate levels have been normalized through the administration of uric acid-lowering drugs, and so they may not be diagnosed with hyperuricemia in a health checkup.

Serum urate levels amongst women are gradually lower than those amongst men, and for this reason there are far fewer cases of women with hyperuricemia than men. Although serum urate levels amongst women rise after menopause, there have been no reports published in Japan that separately examined hyperuricemia both pre-menopause and post-menopause. The age on menopause onset for Japanese women is regarded as being between the ages of 45 and 55, and the frequency of hyperuricemia amongst women in the occupation group survey was reported to be 1 to 2% for women aged younger than 50 years and 3 to 4% for women aged 50 years or older.[2]

Is Hyperuricemia Increasing?

According to the investigation conducted by Tomita et al.[2] of occupational groups, up until around 2006 there was a continuous trend for the incidence of hyperuricemia to increase (**Fig. 1**). In addition to this report, other investigations of occupational groups and newly enrolled university students[5,6] showed that from the 1990s through the 2000s, average serum urate levels have tended to increase over time, suggesting that hyperuricemia has tended to increase until recently.

However, what is deeply interesting is that according to the report by Tomita et al.,[2] this increasing trend peaked in 2006, with hyperuricemia tending to decrease from then onward (**Fig. 1**). This trend was also apparent in the National Livelihood Survey, with the number of

respondents answering that they were "Receiving outpatient treatment for gout" increasing rapidly until 2004, but dropping slightly in 2007 to 854,000 from the 2004 figure of 874,000[4] (**Fig. 2**). It is thought that "gout" in this survey also includes a substantial number of asymptomatic hyperuricemia cases. Considering that the number of patients "receiving outpatient treatment for gout" continually increased by more than 100,000 each time the survey was conducted between 1998 and 2004 (the survey was conducted every three years), this is a notable change. Has the trend in hyperuricemia in Japan indeed switched from an increasing tendency to a decreasing tendency, or has the upward trend been stemmed?

Background to Trends in Hyperuricemia

Looking at the number of uric acid-lowering drugs (tablets) sold, the increasing trend from the previous year continues after 2006 until 2010 (**Fig. 3**).[7] Although shifts in the number of tablets prescribed per person are unknown, the increase in the number of tablets sold is thought to reflect an increase in the number of people taking the drugs. In fact, Tomita et al. also reported an increase in the percentage of people receiving treatment for hyperuricemia in the occupational health check-ups.[2] One factor in the decreasing trend for hyperuricemia in occupation fields is thought to be the improvement on test data due to an increase in the number of people taking uric acid-lowering drugs.

Despite the fact that the number of people taking uric acid-lowering drugs can be regarded as being in an increasing trend, the number of National Livelihood Survey respondents answering that they were "Receiving outpatient treatment for gout" showed a slightly downward trend in 2007 (**Fig. 2**). Because the National Livelihood Survey is in a self-answering format, it can be assumed that there was an increase in the number of respondents who were taking uric acid-lowering drugs but did not answer that they were "Receiving outpatient treatment for gout." Behind this is the possibility that in an increasing number of cases in which patients are not aware of what conditions they are taking drugs for due to an increase in long-term prescriptions and to an increase in treatment duration, however, details are unclear. Moreover, because the list of diseases in the National Livelihood Survey did not include hyperuricemia as an option, there is also the possibility that people who had not developed gout and were taking uric acid-lowering drugs for asymptomatic hyperuricemia did not answer that they were "Receiving outpatient treatment for gout."

Adult energy intake in Japan had continuously tended to decrease amongst both men and women, but until recently the percentage of obese men had continued to increase.[8] However, this increasing trend has been slow since 2007.[9] If this is true, it is possible that this decrease affected the trend in hyperuricemia, which is closely related to obesity.

Fujimori et al. reported no change or a slightly decreasing trend in the frequency of hyperuricemia amongst men undergoing comprehensive medical examinations between 1993 and 2003.[10] It is possible that amongst people undergoing comprehensive medical examinations—a group regarded as being highly health-conscious—the effects of uric acid control through medication and improvements to lifestyle habits appeared even earlier than amongst members of other groups.

Gout Prevalence

With regard to the percentage of the population with gout, the recent report in Japan is only that examined the results of a residents survey conducted in one region, Wakayama Prefecture, in 2003.[11] This survey found the overall prevalence rate for gout to be 0.51%, with a prevalence of 1.1% amongst men. All of the 14 gout patients diagnosed were men aged 30 or older, and the prevalence for this age group was 1.67%. The age composition in this region was regarded as being average for Japan, and so it may be possible to say that the gout prevalence for men aged 30 or older in this region is close to the percentage of Japanese men who develop gout over their lifetimes. That is to say, approximately one in 60 Japanese men develops gout.

Is Gout Increasing?

With regard to increases/decreases in the number of people definitely diagnosed with gout, valuable data was reported in the survey conducted in Wakayama Prefecture mentioned above. That

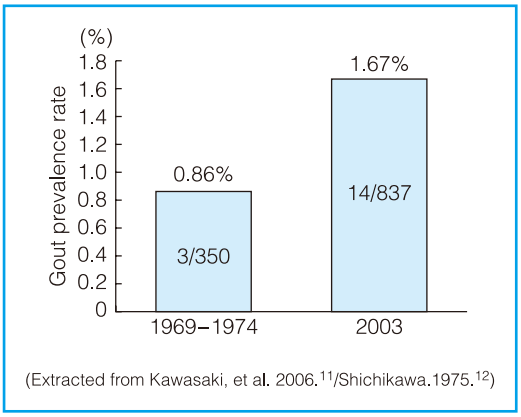

Fig. 4 Changes in the prevalence of gout in Kamitonda Town, Wakayama Prefecture (Males aged 30 years or older)

is, a similar survey was conducted between 1969 and 1974 in the same region as this survey was conducted,[12] and in the earlier survey 3 out of 350 men aged 30 or older were found to have gout. The gout prevalence rate calculated from these values was 0.86%; the gout prevalence rate for the survey conducted in 2003 (1.67%) was approximately twice this value (**Fig. 4**). Because of the small number of patients, there is no statistically significant difference, but the results can be regarded as reflecting the increasing trend in gout at that point in time.

Conclusion

The increasing trend in the number of uric acid-lowering drugs sold is continuing, and the number of hyperuricemia/gout patients receiving treatment is thought to be increasing as well. However, it is possible that the increasing trend towards obesity in men has recently slowed, indicating the possibility that the increasing trend in hyperuricemia has itself slowed. From these circumstances, it is inferred that there is decreasing trend in untreated hyperuricemia/gout. The *Guideline for the Management of Hyperuricemia and Gout* was also revised recently,[1] and expectations are held that more and more hyperuricemia/gout patients will receive appropriate clinical management.

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