THE EPIDEMIOLOGY OF HYPERURICAEMIA AND GOUT IN TAIWAN ABORIGINES

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SUMMARY

To determine the prevalence of hyperuricaemia, gout and gout-related factors in Central Taiwan Atayal aborigines, 342 subjects over 18 yr old were interviewed and examined. A questionnaire was designed to screen for signs and symptoms of gout and gout-related risk factors. Serum uric acid, triglyceride and creatinine were measured in all subjects. The prevalence of hyperuricaemia was 41.4% and that of gout 11.7% in aborigines. The uric acid level was 7.9 ± 1.7 mg/dl in males and 5.7 ± 1.5 in females, and differed significantly under age 70 yr (P < 0.001). Significantly increased triglyceride, creatinine and alcoholism was found in gouty patients compared with non-gouty patients. In 40 cases with gout, 54% had tophi and 35% of their first-degree relatives had gout. The high prevalence of hyperuricaemia and gout in Taiwan Atayal aborigines, a significant family predisposition, increased creatinine level and alcoholism suggest multiple factors affecting the hyperuricaemia.

KEY WORDS: Epidemiology, Atayal aborigine, Risk factors, Hyperuricaemia, Gout, Tophi.

Depending on its case definition, the prevalence of gout varies between 3 and 38 per 1000 in European and North American populations [1–6]. Our study in Taiwan showed a prevalence of gout of 0.16% in a rural area, which was significantly different from suburban (0.67%) and urban (0.67%) areas [7].

The major inhabitants of Taiwan are Taiwanese whose ancestors migrated from the Fukin Province 400 yr ago. Taiwanese and people (include Hakka) from mainland China are Han and Mongoloid. The minority are the aborigines, the original inhabitants of the island who probably evolved from Austro-Tai >4000 yr ago [8]. The Taiwan aborigines consist of nine tribes, each with their own district lifestyle and language [9, 10]. A survey of a small population [11] indicated a prevalence rate of 94.4% for hyperuricaemia and 44.4% for gout in Atayal aborigines, one of the nine tribes, compared to rates reported in Caucasians.

The present study was undertaken to identify potential risk factors for hyperuricaemia and gout, and to evaluate the quality of medical care.

MATERIALS AND METHODS

Sampling frame

Ho-Ping County in Central Taiwan is composed of six villages. By 1982, the total population in Ho-Ping County was 10 149. Among them, 5846 were female and 4303 were male. Aborigines comprise 32% of the total population (3253) and ~90% of aborigines belonged to the Atayal tribe. In contrast, the rest (68%) of the local residents were Han people, consisting of Taiwanese, Hakka and Chinese who came from mainland China in 1949.

Aborigines live largely mixed with other races and random sampling would not be appropriate to study the epidemiology of disease in this group. However, >90% of aborigines are Christians and regular church attendees. In this study, we studied 342 subjects who were going to church at weekend to maximize participation of employed individuals, to study a cross-section of the population and to minimize the costs of the survey.

Case identification

With the help of the health authority in Ho-Ping County, all subjects were contacted by the local public health nurse who arranged the evaluation. Health workers were trained in conducting a standard interview designed to identify individuals known or suspected to have gout, and to document risk factors. Two doctors, three nurses, four laboratory technicians and two health workers were involved in the study.

The interviewers asked the following questions. (a) Have you ever had pain or stiffness in any joint or bone? If yes, where is it? (b) Have you ever been told that you had gout or other rheumatic diseases? The diagnosis of gout was made by identification of monosodium urate crystals in the synovial fluid, the presence of tophi or Wallace criteria [12]. Further information included: the clinical presentation (first involved joint, presence of tophi, disease duration and medications); family history of relatives with gout; risk factors (hypertension, hyperlipidaemia, diet, alcohol and drugs); 15 questions on knowledge about gout. More than 95% of the aborigines interviewed also agreed to undergo a physical examination and blood sampling.

Laboratory tests

All subjects gave blood for the determination of uric acid (Uricase method, Teco Diagnostics, USA), triglyceride, cholesterol and creatinine carried out in our hospital. The uric acid level in normal healthy Chinese subjects ranges from 3 to 7 mg/ml in men and from 2...
to 6 mg/ml in women before the menopause and from 3 to 7 mg/ml after the menopause. Hyperuricaemia was defined as uric acid >7 mg/ml in men and >6 mg/ml in women before the menopause and >7 mg/ml after the menopause.

Statistical analysis

Proportions with their 95% confidence interval were used to estimate the prevalence of gout among aborigines. Analysis of covariance (ANCOVA) was then used to compare the differences in clinical features between gout and non-gout, adjusting for the effect of age. Finally, logistic regression was carried out to examine the independent effect of clinical features on the prevalence of gout.

RESULTS

The study was carried out between July through December 1994. There were 342 subjects from four different aboriginal villages. Among them, 145 (42.4%) were male and 197 (57.6%) were female (Table I). There were no significant differences between males and females with respect to age distribution ($P > 0.05$).

Gout was confirmed in 40 subjects and most were male (95%). The diagnosis of gout was based on the typical clinical presentation. In three cases, urate crystals were identified in the synovial fluid. Age and sex distribution in cases with gout is shown in Table I. There were two peaks in male patients: one is from the age of 31 to 40 yr (29.0%) and another is from 61 to 70 yr (31.6%). Only two cases with gout were seen in women and both were post-menopausal.

The mean uric acid level in males was $7.9 \pm 1.7$ mg/ml, whereas in females it was $5.7 \pm 1.5$ mg/ml. These differences ($P < 0.001$) were significant overall and in each age group (Fig. 1), except those over 70 yr ($P = 0.0656$). In aborigines, the uric acid started rising in young adulthood in males. The uric acid was similar in pre- and post-menopausal women.

The prevalence rate of gout in aborigines was 11.7% (95% confidence interval 0.08–0.15) and was more common in male aborigines than in females (26.2% vs 1.0%, $P < 0.001$). Hyperuricaemia occurred in 41.4% of all aborigines (95% confidence interval 0.36–0.47) and 53.8% in male aborigines in contrast to 30.7% in female ($P < 0.001$).

Among 40 cases with gout, 38 were male and two were female. The mean age of these patients was 51 yr.

**TABLE I**

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>M (%)</th>
<th>M (%) gout</th>
<th>F (%)</th>
<th>F (%) gout</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30</td>
<td>19 (5.6)</td>
<td>1 (2.6)</td>
<td>30 (8.8)</td>
<td>0 (0)</td>
<td>49 (14.3)</td>
</tr>
<tr>
<td>31–40</td>
<td>40 (11.7)</td>
<td>11 (29.0)</td>
<td>45 (13.2)</td>
<td>0 (0)</td>
<td>85 (24.9)</td>
</tr>
<tr>
<td>41–50</td>
<td>22 (6.4)</td>
<td>6 (15.8)</td>
<td>33 (9.7)</td>
<td>0 (0)</td>
<td>55 (16.1)</td>
</tr>
<tr>
<td>51–60</td>
<td>30 (8.8)</td>
<td>7 (18.4)</td>
<td>36 (10.5)</td>
<td>0 (0)</td>
<td>66 (19.3)</td>
</tr>
<tr>
<td>61–70</td>
<td>26 (7.6)</td>
<td>12 (31.6)</td>
<td>40 (11.7)</td>
<td>0 (0)</td>
<td>66 (19.3)</td>
</tr>
<tr>
<td>&gt; 70</td>
<td>8 (2.3)</td>
<td>1 (2.6)</td>
<td>13 (3.8)</td>
<td>1 (50)</td>
<td>21 (6.1)</td>
</tr>
<tr>
<td>Total</td>
<td>145 (42.4)</td>
<td>38</td>
<td>197 (57.6)</td>
<td>2</td>
<td>342 (100)</td>
</tr>
</tbody>
</table>

*Statistics for difference of age by sex ($\chi^2$ test, test of homogeneity), $P = 0.875$.
†$P < 0.01$ (comparison between male and female with gout).
‡$P < 0.05$ (comparison between male and female with gout).
and the mean disease duration was 6 yr. The first metatarsophalangeal joint was the most frequently involved during the first attack of gout (53%). Tophi were seen in 54% of the subjects with gout and were large and generalized in 70% of patients. The mean duration from the first gouty attack to the development of tophi was 4.1 yr. Thirty-five per cent of the first-degree relatives in the 40 cases had gout.

Table II lists factors associated with gout. In univariate analysis, the body mass index (BMI), triglyceride and serum cholesterol levels were not different in aborigines with gout and aborigines without gout. Factors associated with gout were increased uric acid and creatinine level, and the percentage of hypertriglyceridaemia (serum triglyceride > 140 mg/dl) and renal function impairment (serum creatinine > 1.5 mg/dl) (P < 0.001 or 0.01). In stepwise logistic regression analysis, the presence of hypertension did not show a significant difference between the two groups. However, for alcoholism, there was a statistical difference between the two groups (odds ratio 2.07, P < 0.01, 95% confidence interval 0.49–2.18). Both age and sex also had a significant difference between the two groups (odds ratio 1.03, 22.83; 95% confidence interval 1.01–1.06, 5.05–103.2; P < 0.05, P < 0.001, respectively). The survey of dietary habit in the past years showed that, over the years, people of aborigine and Han descent have mixed thoroughly and there were no apparent dietary differences.

**DISCUSSION**

In 1990, Taiwan had ~330,000 aborigines and 20 million people of other ethnic background. The ancient aborigines in Taiwan probably moved from the Southern Provinces of mainland China and then migrated to Taiwan from the Philippines, Timor, the Marinas through Micronesia island and New Zealand [8]. From our previous study and S.-J. Chen’s research (unpublished), the high frequency of HLA-A24, B13 and B60 in Taiwan aborigines (including Atayal), compared to Taiwanese, suggests that the Taiwan aborigines are probably more similar to Oceanian populations than to Taiwanese.

This epidemiological survey was a cross-sectional study and cases investigated were small numbers of aborigines living separately in different mountain areas. It was impossible to carry out random sampling since the populations have not been fully documented by census. Therefore, we had to take advantage of when those aborigines were going to church at the weekend (they are not working at the weekend) to obtain enough samples. In fact, a pilot study was carried out and we did not find a significant difference in dietary habits (including alcohol), living standard, education level, and disease pattern and severity between those who were going to church and those who were not. Thus, the data on the number of gouty cases over the number of investigated cases can represent the prevalence of gout in this population.

In this study, a high prevalence of hyperuricaemia was observed in male aborigines. Significantly, hyperuricaemia in males starts at or before the age of 20 yr and on average is >2 mg/dl as compared with females (7.8 vs 5.7). Together with a family history of gout in 35% of first-degree relatives, a genetic defect [13], such as overproduction of uric acid or a renal tubular defect for uric acid secretion, may be responsible. A study on 115 Maori men in New Zealand by Gibson et al. [14] demonstrated that the high percentage of hyperuricaemia (23%) and gout (8%) in Maori people was attributable to the lower uric acid clearance. Other reports [18–22] have documented that Polynesians, including Maoris, Cook Islanders and Samoans, have an increased frequency of hyperuricaemia. The uric acid level in South Pacific aborigines ranges from 6.1 to 7.3 mg/100 ml [17]. Healey et al. [18], Healey and Bayani-Sison [23] and Decker and Lane [24] reported that Filipinos in the USA had a higher rate of hyperuricaemia than Filipinos in the Philippines, and postulated that it was due to the intake of a more high-purine Western diet and a defect in the renal excretion of uric acid. Likewise, Simmonds et al. [25] demonstrated that a high prevalence of hyperuricaemia among Polynesian women (Maoris, Cook Islanders, Samoans, Tongans) resulted from a reduced fractional uric acid clearance. In Taiwan aborigines, three of 342 (0.9%) cases had a creatinine >1.5. However, when cases with gout were compared with non-gout, a significant increase in serum creatinine was also noted in gouty patients [26, 27]. Evaluation of renal function using more sensitive techniques is needed.

In this study, risk factors for hyperuricaemia, such as dietary habits, alcohol and hypertension, were assessed. Eleven (30%) of 37 cases with gout have hypertension, which is higher than the 24.9% in aborigines without gout [28, 29]. The prevalence of diabetes

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**TABLE II**

| Difference in clinical features and laboratory findings between aborigines with and without gout after age adjustment |
|---------------------------------|----------------|
| Gout (n = 40)                  | Non-gout (n = 302) |
| **BMI (kg/m²)**                | 25.4 ± 0.7      | 25.0 ± 0.3  |
| Uric acid                     | 8.3 ± 0.3       | 6.4 ± 0.1  | P < 0.001 |
| Creatinine                    | 1.05 ± 0.03     | 0.83 ± 0.01| P < 0.001 |
| Cholesterol                   | 218.1 ± 12.0    | 218.6 ± 4.1| NS        |
| Triglyceride                  | 143.3 ± 12.2    | 126.1 ± 4.5| NS        |
| Hypertriglyceridaemia (%)     | 42.5            | 21.4       | P < 0.01  |
| Creatinine >1.5 (%)           | 7.5             | 0          | P < 0.01  |

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*NS = not significant*
was significantly increased in the aborigines compared with Han people living in other parts of Taiwan [28, 29]. However, there was no difference in hypertension between cases with and without gout. The result is in contrast to the report by Currie [6], who observed a significant increase in hypertension in females with gout, and Roubenoff [30] who found that hypertension was prevalent in gouty patients. In this study, 64% of gouty patients and 42% of non-gouty aborigines took at least one half-bottle of high-alcohol liquor or more than one bottle of beer daily ($P < 0.05$). Although most aborigines started drinking from the age of 20 yr, alcohol seemed not to be the single factor in the development of hyperuricaemia or acute gouty attack since uric acid was elevated before the age of 20 yr. The significant increase in hypertriglyceridaemia in aborigines may be attributable to increased alcohol intake [31, 32] or unknown factors. A good correlation between serum uric acid and triglyceride was demonstrated in aborigines, and is similar to the findings of Takahashi et al. [33].

In this study, BMI did not show a significant difference between the aborigines with and without gout. Obesity is not common in Atayal aborigines, unlike the Maori who have a high prevalence of hyperuricaemia and gout and an increased prevalence of obesity and alcohol consumption [14, 22, 34].

The present report confirms that tophi present early and more severely in aborigines than in Han Chinese. The percentage of tophi in aborigines with gout was 54%, which is much higher compared to other reports (17%, 9.2%) [13]. The rate of formation of tophaceous deposits in primary gout is correlated with the degree and duration of hyperuricaemia. Thus, the prevalent formation of tophi in aborigines with gout was attributed to the genetically higher serum uric acid level. Other possibilities included relatively poor primary health care for the aborigines. Nearly all the patients with gout were not being treated for their disease on a regular basis. We believe that this situation can be improved after patients frequently receive education on gout. The other way is to intensify the ability of local doctors to diagnose and treat gout.

Gout and hyperuricaemia have been recognized as familial disorders, and the reported frequency of familial occurrence ranges from 6% to as high as 80% [35]. The high prevalence of first-degree relative involvement in aborigines with gout raises the possibility of an inborn defect in PRPP synthetase or HGPRT enzyme. A report by Palmer et al. [36] demonstrated that HGPR{Tase deficiency was not an important factor in the development of gout in Maoris. Further research, except for the enzyme study, including the complete renal function profile, may confirm the aetiopathogenesis of hyperuricaemia and gout in Taiwan aborigines.

In summary, gout is severe and prevalent in Taiwan aborigines. Both genetic and environmental factors are suggested, and further studies are indicated. The medical treatment and follow-up appear to be inadequate.

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References