Lipid Abnormalities in Taiwan Aborigines With Gout

C.-T. Chou and P.-M. Chao

An epidemiologic study to determine lipids and biochemical traits was performed in central Taiwan aborigines with and without gout and in the local Han Chinese. The lipid profile included measurement of serum triglyceride, cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein A-I (apoA-I), and apoB. The results showed no significant difference for body mass index (BMI) and cholesterol between the three groups. Greater alcohol consumption was found in aborigines with gout compared with the other two groups. With univariate analysis, serum triglyceride, uric acid, creatinine, LDL-C, and apoB were significantly higher in aborigines with gout versus aborigines without gout or Han people ($P < .001$). By contrast, HDL-C and apoA-I were significantly lower in aborigines with gout ($P < .001$ or .01). However, with multivariate analysis, only serum triglyceride, uric acid, and apoB-1 were significantly different between aborigines with versus without gout. In conclusion, the apparent lipid abnormalities, particularly triglyceride and apoB, in Taiwan aborigines with gout are unlikely secondary to obesity. Instead, excessive alcohol intake or genetic factors may play a role in inducing hyperlipidemia in gout.

GOUT IS A DISEASE characterized by hyperuricemia, acute and intermittent arthritis, and chronic arthritis with and without tophi. Hyperuricemia is caused by either overproduction or undersecretion of uric acid.[1] The common risk factors for overproduction include a genetic enzyme defect, alcoholism, and intake of a high-purine diet. In contrast, factors for undersecretion include a genetic defect with low uric acid clearance, renal disease with low creatinine clearance, alcoholism, and drugs that reduce renal uric acid secretion.

Hyperuricemia and gout are common in Taiwan aborigines, and the estimated prevalence of gout and hyperuricemia is 11.7% and 41.4%, respectively.[2] Aborigines in Taiwan possibly originated from the southern part of mainland China and belong to the Austronesian population.[3] The high prevalence of hyperuricemia and gout in this minority may be attributable to genetic predisposition, alcohol consumption, and low uric acid clearance.[4-7] A report from Ko et al[8] showed that the incidence of cancer, heart disease, and cerebrovascular accident was comparatively higher in Taiwan aborigines than in local Taiwanese. A relationship between hyperuricemia, gout, hypertriglyceridemia, and coronary heart disease has been reported.[9-13] We therefore determined the lipid profile in Taiwan aborigines with gout.

SUBJECTS AND METHODS

Patient and Control Sera

Over the 6-month period from July to December 1995, a survey of the prevalence of hyperuricemia and gout in central Taiwan aborigines (Atayal tribe) was undertaken. All of the aborigines and local Han Chinese who regularly received an annual physical examination for pulmonary tuberculosis (TB) were the subjects of this study. Approximately 90% agreed to undergo the clinical examination and blood sampling for laboratory tests. We obtained blood samples from 83 aborigines without gout and 38 aborigines with definite gout.[14] Among the cases with gout, approximately half had tophi. In the same aboriginal villages, we obtained 100 blood samples from local Han Chinese who had resided there for more than 3 years. They had no history of gout.

To measure serum levels of uric acid, triglyceride, and other lipids, blood was drawn after 12 hours of fasting. After centrifugation, the serum was collected and stored at −70°C. A questionnaire was used to record the amount, frequency, and type of alcoholic beverages consumed in the past 6 months. To determine the body mass index (BMI), the height and weight of each subject were also recorded.

Serum Lipid Measurement

All subjects provided blood for determination of uric acid (uricase method; Teco Diagnostic, Placentia, CA), triglyceride, cholesterol, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) in our hospital. Plasma apolipoprotein A-I (apoA-I) and apoB levels were measured as previously described.[15-17]

Statistical Analysis

An unpaired Student's t test was used for univariate analysis, and logistic regression was used for multivariate analysis. Significance was indicated at a P value less than .05.

RESULTS

Demographic biochemical data for all cases studied are shown in Table 1. The frequency of gout in aborigines, as in Han Chinese, is higher in men than in women. However, for the age- and sex-matched subjects in the three groups shown, we obtained blood samples from 18 female aborigines and 20 male aborigines with gout to perform the laboratory tests. Half of them had multiple tophi, and one third had a family history. There was no significant difference for either age or sex between each group. None of the aborigines with gout have regularly taken antihyperuricemic agents, including allopurinol or probenecid. No TB was found in the 38 cases with gout, and therefore, none of the aborigines used anti-TB drugs. Only two aborigines irregularly took a diuretic for high blood pressure. Dietary habits did not show any difference, except that groups 1 (aborigines with gout) and 2 (aborigines without gout) drank more alcohol daily than group 3 (local Han Chinese) ($P < .001$). Alcohol consumption was even greater in group 1 compared with group 2 ($P < .001$). Aborigines drink two kinds of alcohol: one has a high alcohol content, rice wine, and the other has a

From the Division of Rheumatology, Department of Medicine, and the Department of Nutrition, China Medical College Hospital, Taichung, Taiwan, Republic of China.

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Address reprint requests to C.-T. Chou, MD, Division of Allergy-Immunology-Rheumatology, Veterans General Hospital, No. 201, Sec. 2, Shih-Pai Rd, Shih-Pai, Tapei, Taiwan.

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Table 1. Clinical and Laboratory Findings in Three Groups

Variable	Group 1 (n = 38)	Group 2 (n = 83)	Group 3 (n = 100)	*P* Posttest (Scheffe)
Sex ratio (female:male)	18:20	42:41	48:52	
Age (yr)	51.4 ± 13.3	50.3 ± 14.2	52.3 ± 15.9	
Cholesterol (mg/dL)	219.9 ± 129.7	207.1 ± 48.3	202.0 ± 41.5	
Triglyceride (mg/dL)	141.5 ± 56.2	109.3 ± 65.4	105.4 ± 62.1	<.001*
Creatinine (mg/dL)	1.061 ± 0.327	0.873 ± 0.166	0.884 ± 0.259	<.001†
Uric acid (mg/dL)	8.34 ± 1.69	6.43 ± 1.81	5.29 ± 1.42	<.001†
HDL-C (mg/dL)	51.4 ± 17.3	61.3 ± 19.5	61.0 ± 19.4	<.01†
LDL-C (mg/dL)	135.8 ± 56.3	107.7 ± 48.0	113.8 ± 44.8	<.01‡
ApoA-I (mg/dL)	144.2 ± 33.5	160.7 ± 33.8	172.0 ± 32.0	<.001†
ApoB (mg/dL)	154.8 ± 53.4	126.2 ± 42.9	124.4 ± 33.5	<.001†
Alcohol (g/d)	25.7 ± 24.3	17.2 ± 15.9	10.7 ± 13.3	<.001†
BMI (kg/m^2)	24.0 ± 6.6	25.4 ± 3.6	24.6 ± 3.3	

NOTE. Groups are as follows: 1, aborigines with gout; 2, aborigines without gout; and 3, normal Han Chinese.

*Comparison between groups 1, 2, and 3.

†Group 1 *v* 2, group 1 *v* 3.

‡Group 1 *v* 2.

low alcohol content, Taiwan beer. There was no significant difference for the BMI between each group.

Multiple variables including cholesterol, triglyceride, creatinine, uric acid, HDL-C, LDL-C, apoA, and apoB were compared in the three groups. There was no significant difference for cholesterol. Serum triglyceride was significantly higher in group 1 versus group 2 or 3. Serum creatinine, uric acid, LDL-C, and apoB were all significantly increased in aborigines with gout versus aborigines or Han people without gout (Table 1). In contrast, HDL-C and apoA-I were significantly lower in aborigines with gout compared with aborigines or Han people without gout ($P < .001$ or .01).

Table 2 shows the multivariate logistic regression analysis in aborigines with and without gout. There were two reasons to include all variables in the multivariate logistic regression analysis: (1) we wished to examine the effects of all variables after controlling for other variables in the model and (2) we sought to detect whether a significant interaction between uric acid and triglyceride was present. Uric acid and triglyceride showed a statistical difference between groups 1 and 2 ($P < .001$). There was a significant difference for alcohol consumption between aborigines with and without gout ($P < .05$). ApoB showed a similar result, differing between the two groups ($P < .01$). In contrast, HDL-C, LDL-C, and creatinine did not discriminate aborigines with gout from aborigines without gout. HDL-C, LDL-C, and apoA in groups 1 and 2 were significantly different (Table 1), but this significance was not apparent using multivariate logistic regression analysis. A good correlation between serum uric acid and serum triglyceride was found ($P < .01$). Since only approximately half of the aborigines had a blood pressure measurement, the hypertension factor was excluded from Table 2. From the available data, the frequency of hypertension did not show a significant difference between aborigines with and without gout (30.6% *v* 24.2%, $P > .05$). For systolic blood pressure, where measured, there was also no significant difference (127.01 ± 20.05 *v* 124.32 ± 21.43 mm Hg, $P > .05$) between the two groups.

DISCUSSION

The prevalence of gout and other rheumatic diseases in three different areas of Taiwan was reported by Chou et al.[18] The increased frequency of gout in Taiwan was thought to be due to the higher standard of living, greater alcohol consumption, increased stress, and possibly the precise diagnosis due to the increased number of rheumatologists over 10 years. During the epidemiological study, the prevalence rate of hyperuricemia and gout in aborigines, the minority group in Taiwan, was roughly four times the rate in the Han people.[2] The results are similar to data in Filipino, Maori, and other Polynesians.[4,5,19-21] The factors contributing to hyperuricemia in this minority group are multiple and may include genetic, obesity, renal, and other causes.[19-21]

Many studies have shown abnormal lipid metabolism in primary gout.[13,22,23] In this study, there was no significant difference in the serum cholesterol level between aborigines with and without gout. However, serum triglyceride was significantly different between the two groups. Hypertriglyceridemia can be attributed to alcohol intake, obesity, or a genetic defect.[23] Nishida et al[22] considered increased serum triglyceride in primary gout to be unrelated to drinking. Jiao et al[23] reported that cholesterol and triglyceride were significantly increased in primary gout. They suggested that the major predictors of serum triglyceride were alcohol intake and uric acid. According to the previous investigation, the prevalence of alcohol abuse and alcohol dependence in Taiwan aborigines was roughly 10 times the rate in local Taiwanese.[24] The increased percentage of hypertriglyceridemia and hyperuricemia in aborigines with gout was probably related to increased alcohol consumption. However, a genetic factor cannot be excluded. A positive correlation between serum triglyceride and uric acid in this study empha-

Table 2. Multivariate Logistic Regression Analysis in Male Aborigines With and Without Gout

Variable	PE	SE	Wald χ^2	OR	95% CI for OR
Intercept	−31.257	8.622	13.142*		
Alcohol	0.038	0.018	4.248‡	1.038	1.002, 1.076
Cholesterol	−0.006	0.006	0.911	0.994	0.983, 1.006
Triglyceride	0.169	0.048	12.500*	1.184	1.078, 1.300
Uric acid	3.452	0.938	13.557*	31.557	5.025, 198.187
HDL-C	−0.024	0.016	2.256	0.976	0.946, 1.007
LDL-C	0.004	0.006	0.413	1.004	0.993, 1.015
ApoA-I	−0.013	0.010	1.713	0.987	0.969, 1.006
ApoB	0.030	0.009	10.683†	1.030	1.012, 1.049
Uric acid-triglyceride	−0.020	0.006	12.181*	0.980	0.969, 0.991

Abbreviations: PE, parameter estimate; SE, standard error; CI, confidence interval; OR, odds ratio.

*$P < .001$.

†$P < .01$.

‡$P < .05$.

sizes their interrelationship. Body weight was not an important factor, since the BMI in the three groups was similar.

Lipoprotein profiles showed that aborigines with gout had lower HDL-C but higher LDL-C, significantly different from the data obtained in aborigines without gout and Han people. HDL can transport cholesterol from tissues and thus reduce cholesterol accumulation in the arterial wall.[11,25] In contrast, the evidence that atherogenesis results from increased LDL-rich hypercholesterolemia is strong.[26] Ko et al[8] demonstrated that the annual death rate in Atayal aborigines due to ischemic heart disease increased from 1981 to 1990. The findings of lower HDL-C, higher LDL-C, and higher triglyceride in many aborigines with gout may explain why there are more individuals with heart disease in this population, particularly those who live in remote areas with relatively poor primary health care.

ApoA is the main protein (90%) of HDL and is subdivided into A-I and A-II. ApoB is found mainly in the chylomicron (5% to 20%), VLDL (37%), and LDL (97%).[27] In the present study, aborigines with gout had significantly lower apoA-I but higher apoB, consistent with another report.[13] Both apoA-I and HDL-C were decreased in aborigines with gout, whereas both apoB and LDL-C were increased. Therefore, quantitation of apoA-I and apoB may be a better index of HDL-C and LDL-C concentrations. Barbir et al[10] showed that apoA-I was better than HDL-C to discriminate cases with coronary heart disease. However, there was no strong evidence to support the proposal that apoB is better than LDL-C in predicting whether subjects are more likely to develop coronary heart disease.[5]

In summary, lipid abnormalities are apparent in Taiwan aborigines with gout. Excessive alcohol intake or a genetic factor may play a role in inducing hyperlipidemia in gout. Early recognition of hyperlipidemia in aborigines with gout and early treatment may prevent vascular heart or brain disease.

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