Serum Uric Acid as an Obesity-Related Indicator in Early Adolescence

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In adults, serum uric acid levels are positively correlated with body mass index (BMI) and hyperuricemia is considered to be a common lifestyle disorder related with obesity. However, the relation of serum uric acid levels with obesity has not been elucidated in children and adolescents. Serum uric acid levels were determined in 1,729 healthy children, consisted of 923 boys and 806 girls, aged 9.1 - 15.0 years. The incidence of hyperuricemia (defined as more than 7.0 mg/dl) in boys and girls were 8.8% and 0.6%, respectively. In 1,281 children out of all subjects, including 684 boys and 597 girls, height, weight, aspartate aminotransferase, and alanine aminotransferase were also determined and the correlations between serum uric acid levels and obesity were analyzed. BMI is popularly used as a standard indicator of obesity in adults. However, BMI increases without fat accumulation as children grow. In Japan, percentage of overweight (POW) is usually used as an alternative indicator for obesity. In general, children are evaluated as obesity, when POW is equal to or more than 20% (≥ 20%). Serum uric acid levels are positively correlated with obesity-related indicators, BMI and POW, in both boys and girls. Serum uric acid levels of the subjects with high POW (≥ 20%) are significantly higher than those of the subjects with low POW (< 20%) in both boys and girls. These results suggest that serum uric acid levels are significantly increased with obesity and could be used as one of obesity-related indicators even in early adolescence.

Disorders of uric acid metabolism are often seen in conjunction with various genetic conditions, as well as factors associated with lifestyles such as an unbalanced diet abundant in purine, obesity, and alcohol consumption (Nakanish and al. 2001; Wortmann 2002). Recent studies have reported that high uric acid levels were often found in sera from patients with cardiovascular disease in adults with a coexisting cluster of metabolic abnormalities, including obesity, glucose
intolerance, hypertension, and hyperlipidemia (Klein et al. 1973; Schmidt et al. 1996; Costa et al. 2002). Serum uric acid levels are also positively correlated with body mass index (BMI) in adult. However, the correlation between serum uric acid levels and obesity has not been determined in children and adolescents.

In the present study, we investigated the incidence of hyperuricemia in a population of healthy Japanese children. We also attempted to determine the relations between serum uric acid levels and obesity-related indicators in children and early adolescents.

**Subjects and Methods**

A cross-sectional study was performed in children aged 9.1-15.0 years in Akita Prefecture, Japan, between April and May 2003. The subjects tested for serum uric acid levels consisted of 923 boys and 806 girls (Table 1). Besides the serum uric acid, weight, height, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were also measured in 1,281 children, who agreed with additional tests, including 684 boys and 597 girls (Table 1). Sera taken from the children were stored at –20°C until assayed, and serum uric acid levels, AST, and ALT of all subjects were determined at the same time. Serum uric acid levels were determined by the uricase method (Uricase F-DAOS method, Wako, Tokyo). None of the subject in this study had any chronic disease or any medications. A written consent form was obtained from each child’s parents.

Based on these data, we calculated the mean serum uric acid levels grouped by age and sex. We next determined the incidence of hyperuricemia (defined as more than 7.0 mg/dl) in a population of healthy Japanese children. Statistical analysis was performed by Mann-Whitney’s U-test. Furthermore, we analyzed the correlations between serum uric acid level, ALT, and BMI. The ALT was evaluated as an indicator of fatty liver due to obesity. In addition to BMI, percentage of overweight (POW), calculated from an age-height-related standard of weight for Japanese children, was used as an alternative indicator for obesity in children. The age-height-related standard of weight was on the basis of 1990 school year data in Japan and POW was defined as percentage of weight difference from the standard to the standard weight (Yamazaki et al. 1994; Okada et al. 2005). In general, children are evaluated as obesity, when POW is ≥ 20%.

A p-value less than 0.05 was considered significant. Statistical calculations were performed using Statview v5.0 (Abacus Concepts, Berkeley, CA, USA).

**Table 1. The incidence of hyperuricemia ( > 7.0 mg/dl) grouped by age and sex.**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Hyperuricemia/Boys (%)</th>
<th>Hyperuricemia/Girls (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.1~10.0</td>
<td>1/48 (27*) (2.1)</td>
<td>0/53 (29*) (0.0)</td>
</tr>
<tr>
<td>10.1~11.0</td>
<td>5/215 (147*) (2.3)</td>
<td>1/154 (105*) (0.7)</td>
</tr>
<tr>
<td>11.1~12.0</td>
<td>7/130 (67*) (5.4)</td>
<td>1/110 (46*) (0.9)</td>
</tr>
<tr>
<td>12.1~13.0</td>
<td>13/160 (132*) (8.1)</td>
<td>0/142 (117*) (0.0)</td>
</tr>
<tr>
<td>13.1~14.0</td>
<td>21/199 (172*) (10.6)</td>
<td>2/198 (173*) (1.0)</td>
</tr>
<tr>
<td>14.1~15.0</td>
<td>34/171 (140*) (19.9)</td>
<td>1/149 (128*) (0.7)</td>
</tr>
<tr>
<td>Total</td>
<td>81/923 (684*) (8.8)</td>
<td>5/806 (597*) (0.6)</td>
</tr>
</tbody>
</table>

* Subjects for the relationship between serum uric acid levels, ALT, and POW.
RESULTS

Serum uric acid levels

Fig. 1 shows the mean serum uric acid levels grouped by age and sex. The mean and standard deviation (s.d.) score of serum uric acid levels in boys and girls were determined as 5.3 ± 1.3 mg/dl (range 0.6 - 9.6) and 4.3 ± 0.86 mg/dl (range 0.2 - 7.7), respectively. Between the ages of 11 and 15 years, boys showed significantly higher means than girls ($p < 0.0001$; Fig. 1). Table 1 shows the incidence of hyperuricemia grouped by age and sex. Eighty-one of 923 boys (8.8%) had a serum uric acid value more than 7.0 mg/dl, whereas such a value was present in only 5 of 806 girls (0.6%).

Correlation between serum uric acid and obesity-related indicators

There were positive correlations between BMI and ALT, which is an indicator of fatty liver due to obesity, in boys ($r = 0.52, p < 0.0001$) and girls ($r = 0.25, p < 0.0001$) (Fig. 2). There were also positive correlations between BMI and serum uric acid level in boys ($r = 0.43, p < 0.0001$) and girls ($r = 0.23, p < 0.0001$) (Fig. 3). BMI is commonly used as a standard indicator for obesity in adults. However, BMI increases without fat accumulation as children grow. Some reports suggested limitation of BMI as an individual indicator of fatness in children (Ellis et al. 1999; Widhalm et al. 2001). In Japan, POW is usually used as an alternative index for obesity. In our study, 18.1% and 13.9% of the subjects were evaluated as obese, POW of $\geq 20\%$, in boys and girls, respectively (Fig. 4). There were positive correlations between POW and ALT in boys ($r = 0.54, p < 0.0001$) and girls ($r = 0.28, p < 0.0001$) (Fig. 5). There were also positive correlations between

![Fig. 1](image1.png)

Fig. 1. Mean serum uric acid levels and number for single years of age (mean ± s.d.). At ages between 11 and 15 years, boys showed significantly higher means than girls. * $p < 0.0001$, boys vs girls.

![Fig. 2](image2.png)

Fig. 2. Regression analysis between body mass index (BMI) and alanine aminotransferase (ALT). The ALT was evaluated as an indicator of fatty liver due to obesity. There were positive correlations between BMI and ALT in both boys (a: $r = 0.52, p < 0.0001$) and girls (b: $r = 0.25, p < 0.0001$).
Fig. 3. Regression analysis between BMI and serum uric acid levels. There were positive correlations between BMI and serum uric acid levels in both boys (a: $r = 0.43$, $p < 0.0001$) and girls (b: $r = 0.23$, $p < 0.0001$).

Fig. 4. The rate of obesity evaluated by percentage of overweight (POW). The results showed that 18.1% and 13.9% of the subjects were evaluated as obesity, defined as POW of $\geq 20.0\%$, in boys (a) and girls (b), respectively.

Fig. 5. Regression analysis between POW and alanine aminotransferase (ALT). The ALT was evaluated as an indicator of fatty liver due to obesity. There were positive correlations between POW and ALT in both boys (a: $r = 0.54$, $p < 0.0001$) and girls (b: $r = 0.28$, $p < 0.0001$).
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POW and serum uric acid level in boys \((r = 0.29, p < 0.0001)\) and girls \((r = 0.23, p < 0.0001)\) (Fig. 6).

Serum uric acid levels were statistically compared between the subjects with low POW \((< 20\%)\) and with high POW \((\geq 20\%)\) (Fig. 7). In boys, serum uric acid levels of the subjects with high POW \((5.9 \pm 1.5 \text{ mg/dl})\) were significantly higher than the subjects with low POW \((5.2 \pm 1.2 \text{ mg/dl})\). In girls, serum uric acid levels of the subjects with high POW \((4.9 \pm 1.1 \text{ mg/dl})\) were also significantly higher than the subjects with low POW \((4.2 \pm 0.8 \text{ mg/dl})\). Significant differences were observed in all groups of separate age in boys and girls, but age of 14.0-15.0 years in girls \((p = 0.25)\).

**DISCUSSION**

Data in the literature indicate that serum uric acid levels increase with age during childhood and show a clear-cut developmental difference between boys and girls during puberty (Passwell et al. 1974; Stapleton et al. 1978). While serum uric acid is described as stabilizing at lower levels in girls around the age of 11 years, uric acid levels in boys show an upward trend throughout adolescence (Costa et al. 2002). These changes have been attributed to a progressive decline in renal uric acid clearance during puberty (Munan et al. 1977; Stapleton et al. 1978), and Garbagnati (1996) suggested that increased renal retention may be the main underlying mechanism enhancing uricemia. Our result showed that serum uric
acid levels began to rise from the age of 11.1 -12.0 years and thereafter in Japanese boys and were higher than those in Japanese girls. The beginning of this difference corresponds with the onset of pubertal development in Japanese boys.

Igarashi (1993) has reported normal serum uric acid concentrations in healthy Japanese children aged between 7 and 18 years in 1993. Compared with these data, the mean serum uric acid levels of boys in our study were somewhat high. We suppose that this would be caused by the increase in obesity over the decade and higher incidence of obesity in Akita Prefecture in contrast with that in Japan overall.

In Japanese, hyperuricemia has been defined as a serum uric acid more than 7.0 mg/dl in both men and women (Japanese Society of Gout and Nucleic Acid Metabolism 2002). These criteria were based on the physical characteristics of urate. Serum uric acid levels differ by sex and age in childhood, so it is very difficult to define hyperuricemia in children and early adolescents. In this study, we defined hyperuricemia as serum uric acid more than 7.0 mg/dl in both boys and girls, the same as that in adults. The incidence of hyperuricemia in Japanese adults has been reported to be about 22% in men and less than 1% in premenopausal women (Japanese Society of Gout and Nucleic Acid Metabolism 2002). Some studies have reported the incidence of hyperuricemia in obese children. However, to our knowledge, there has not been a study in healthy Japanese children. We demonstrated that the incidence of hyperuricemia was 8.8% among Japanese healthy boys aged 9.1-15.0 years. We also demonstrated a sex difference in the incidence of hyperuricemia among children aged 9-15 years. This may reflect a sex difference in renal uric acid clearance, as it does in adults.

We have shown the positive correlations between serum uric acid levels and BMI in Japanese children. In addition, positive correlations were confirmed between serum uric acid levels and POW. There is also significant difference of serum uric acid levels between the subjects with low POW and with high POW. These findings indicate that serum uric acid levels and obesity in children and early adolescents are closely related. Additionally, we have shown the positive correlations between BMI and ALT and between POW and ALT in Japanese children.

References