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The Effect of Body Mass Index of Asia-Pacific Classification and Gender On Serum Uric Acid Level in A Selected Population from Sri Lanka

Pemarathne R. A. R. P.[1], Karunarathna M. W. A. N.[1], Dias P.[2] and Priyadarshani A. M. B.[1*]

[1] Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, University of Sri Jayewardenepura, Sri Lanka
[2] Department of Statistics, Faculty of Applied Sciences, University of Sri Jayewardenepura, Sri Lanka

ABSTRACT

Uric acid is the end product of purine nucleotide catabolism pathway. In humans, uric acid production and excretion proceed as a balanced process. Serum uric acid concentration is influenced by age, gender, body mass index (BMI), state of hydration and ethnicity. Increased concentration of serum uric acid indicates risks towards renal and cardiovascular diseases, gout, type 1 diabetes mellitus and hypertension. The present study was aimed to investigate the correlation between serum uric acid level and BMI of Asia-Pacific categorization in healthy individuals. A descriptive cross-sectional study was conducted recruiting 120 Sinhala males and females within 20-25 years. BMI was calculated according to the standard protocols. The serum uric acid level was measured using the Uricase method. Serum uric acid level was positively and moderately correlated with BMI ($r=0.516$, $p<0.001$). The mean serum uric acid level reported from the underweight group was 199.7µmol/L, whereas from the obese group, 319.5µmol/L. The normal and overweight groups had relatively similar serum uric acid levels; 275.4 and 256.6µmol/L, respectively. However, the mean serum uric acid concentration in males was significantly higher than in females in all four BMI categories. There was a significant positive moderate linear correlation between serum uric acid level and BMI in the study population.

KEYWORDS: *Body mass index, Serum uric acid, Underweight, Obese, Overweight*

Corresponding author: Priyadarshani A. M. B., Email: priyadarshani@sjp.ac.lk

1 INTRODUCTION

Uric acid is a weak organic acid and it is the final product of purine nucleotide catabolic pathway in humans and higher primates. Serum uric acid level is governed by urinary urate excretion, dietary purine intake, endogenous purine metabolism, and intestinal uricolysis (Barr, 1990).

Serum uric acid reference range without clinical evidence of gout is 3.5-7.2 mg/dL for males and post-menopausal women and 2.6-6.0 mg/dL for pre-menopausal women. In asymptomatic hyperuricemia, <6.0 mg/dL (360 μmol/L) of serum uric acid level is the threshold value for all subjects (Desideri et al., 2014). However, serum uric acid level before puberty is known to be 3.6 mg/dL for both females and males. After puberty, the serum uric acid levels change according to the gender where the adult women's level is normally 1 mg/dL less than that of adult males (Barr, 1990).

Consumption of purine rich food elevates serum uric acid (Choi et al., 2004; Choi et al., 2005). On the other hand, coffee consumption lowers serum uric acid level (Choi, 2007). Further, it has been reported that the risk for gout is decreased with increased consumption of coffee (Choi & Curhan, 2010). Besides, the variations in levels of serum uric acid have been observed among different ethnicities and different body mass index (BMI) categories (De Boer et al., 2012; Tanaka et al., 2015; Wang et al., 2014; Duan et al 2015).

Hyperuricemia exists as asymptomatic and symptomatic states (George & Minter, 2020). Asymptomatic hyperuricemia has the possibility of converting to symptomatic hyperuricemia. Hyperuricemia can eventually lead to other disease conditions such as gout, cardiovascular diseases, hypertension, renal diseases and type 2 diabetes mellitus (Conen et al., 2004; Bhole et al., 2010; Cho et al., 2016; Hisatome & Kuwabara, 2016; Shoizawa et al., 2017).

Generally, people do not care for testing serum uric acid level unless they get symptoms such as inflammation, pain and swelling of joints and renal problems. In most instances, hyperuricemic status is being notified when clinical laboratory investigations are done for other illnesses. Therefore, it is important to screen serum uric acid level in early stages so that people can receive appropriate treatment prior to developing risk.

If a relationship between serum uric acid level and BMI could be derived, people can be screened for serum uric acid level considering BMI before symptoms arise. Further, assumptions could be made regarding the risk towards hyperuricemia on the basis of BMI, whereby people may control their food intake or life style and may obtain proper treatment. It was found that no studies have been carried out previously to investigate the associations among serum uric acid level, gender and BMI categorization of Asia-Pacific cutoff values in healthy individuals. Therefore, the objective of the present study was to determine the relationship between serum uric acid

concentration and BMI of Asia-Pacific cutoff points in healthy males and females.

2 MATERIALS AND METHODS

This was a descriptive cross-sectional study with laboratory investigations. The appropriate individuals were selected by a self-administered questionnaire. Inclusion criteria considered were being apparently healthy, Sinhala, males and females of 20-25 years; whereas exclusion criteria were being clinically diagnosed with hyperuricemia, having joint pain, kidney and heart diseases, type 2 diabetes and hypertension, having family history of hyperuricemia, being pregnant and lactating women. The self-administered questionnaire comprised information on demographic characteristics, food habits, types of food and beverage consumed and meat consumption.

2.1 Sample size calculation

Sample size calculation was done according to the following formula.

$$n = \frac{Z^2 \times S^2}{B^2}$$

Where,

Z Confidence level - 95%

S Standard deviation

B Minimum detectable difference - 0.5

n Sample size

Thirty subjects were enrolled for each BMI category. Therefore, the study population comprised 120 individuals.

2.2 Collection and processing of blood specimens

All the subjects were informed to fast a minimum of four hours before the venipuncture. Three milliliters of whole blood was collected from each subject. All the blood specimens were protected from direct sunlight and artificial light by using suitable protocols. Blood specimens were collected into the plain vacutainers and were left undisturbed in room temperature for 10-15 minutes. After 10-15 minutes, they were checked for clot formation. All the blood specimens had been clotted after 15 minutes. Then, the vacutainers were smoothly tapped to remove the clots. Next, centrifugation was carried out for 10 minutes at 3000 rpm and the serum was separated.

2.3 Serum uric acid analysis

Uricase method was performed to determine the serum uric acid concentration (Duan et al., 2015) and was measured by the KONE 20XT fully automated biochemistry analyzer. First, the analyzer was calibrated for serum uric acid by multi-calibrator as specified by the manufacturer. Following the calibration, two quality control samples were run as the pathological level and the normal level. The analysis of serum specimens was done after obtaining quality control results.

2.4 Body Mass Index (BMI) calculation

Weight of the individuals was measured by an electrical scale which was pre-calibrated using known weights. The scale was placed on a flat surface. Individuals were instructed to stand, bare foot or with socks, unassisted, with both feet in the center of the scale, after confirming they were wearing light clothing. The weight was recorded in kilograms.

The height of the individuals was measured using a stadiometer which was arranged on a wall against a flat floor. Individuals were asked to remove their shoes, hair ornaments and other items that may interfere with the measurement. It was checked whether head, shoulders and heels touched the wall. Then the head piece of the stadiometer was lowered until it touched the crown of the head firmly at a right angle with the wall. Finally, the height was recorded in metres by keeping the eye of the investigator at the same level as the head piece.

The BMI was determined by following formula (Lim et al., 2017).

$$BMI = Weight/Height^2$$

The BMI of each individual was categorized into the relevant BMI group according to the Asia-Pacific cutoff points; (i) underweight: BMI of <18.5 kg/m^2 (ii) normal weight: BMI of 18.5 - 22.9 kg/m^2 (iii) overweight: BMI of 23 - 24.9 kg/m^2 and (iv) obese: BMI of ≥25 kg/m^2 (Lim et al., 2017).

2.5 Data analysis

Data were analysed using the IBM Statistical Package for Social Sciences (SPSS) version 25 statistical package. The normality test (Shapiro-Wilk) was used to see whether the distribution of serum uric acid level within the study population was normal or not before applying parametric tests. Comparison of mean serum uric levels in males and females was done through independent sample t-test whereas comparison of mean serum uric acid levels between BMI groups was done by Tukey HSD test. The p value was considered statistically significant at the level of <0.05.

3 RESULTS AND DISCUSSION

3.1 Gender distribution within the study population

The study was conducted using 120 healthy Sinhala, individuals aged 20-25 years. Of 120 individuals, 90 were females and 30 were males.

3.2 Serum uric acid concentration distribution within the study population

The minimum serum uric acid concentration reported from the study population was 94.8 µmol/L while the maximum uric acid concentration was 446.7 µmol/L. The serum uric acid level distribution within the study population was normal.

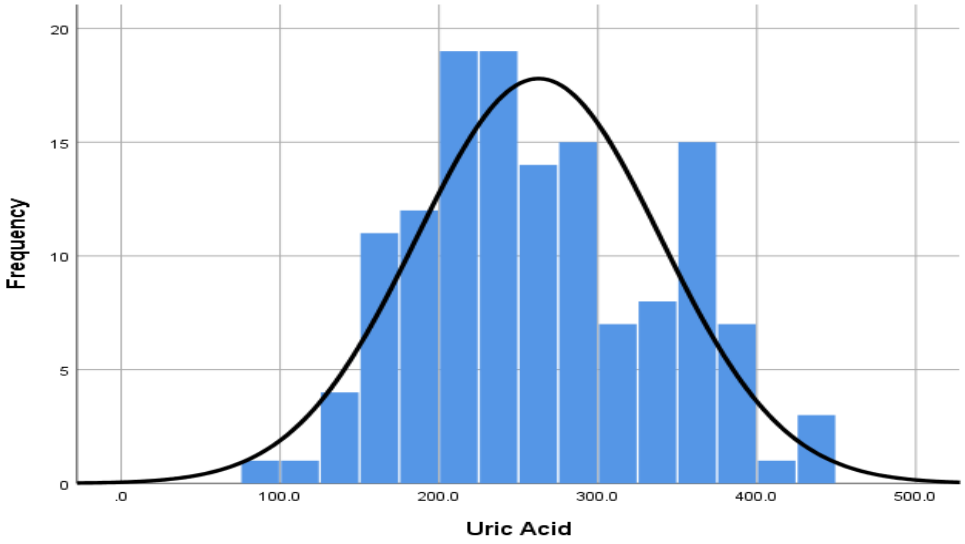

Figure 1. Distribution of serum uric concentration within the study population
Note: Serum uric acid concentration is given in µmol/L

3.3 Serum uric acid concentration distribution according to gender

Table 1 shows the serum uric acid level distribution with respect to gender. According to the independent sample t test, the mean serum uric acid concentration in males is significantly higher than that of females, with a p value < 0.05.

Table 1. Distribution of serum uric acid level with respect to the gender

Gender	Mean±SD	Minimum value	Maximum value
Female	234.7 ±66.67	94.8	404.6
Male	316.37 ±66.1	199.0	446.7

Note: Serum uric acid concentration is given in µmol/L.

Independent sample t-test was used and the p value was considered statistically significant at level of < 0.05.

3.4 Serum uric acid concentration distribution according to the BMI

Distribution of serum uric acid concentration according to the BMI is shown in Table 2. The results showed that the underweight group has the lowest mean level and the obese group has the highest mean level of serum uric acid. However, the normal and overweight groups had comparatively similar values.

Table 2. Distribution of serum uric acid level within BMI groups

BMI Group	Mean±SD	Minimum value	Maximum value
Under weight	199.7±56.0	94.8	338.9
Normal	275.4±54.1	194.8	446.7
Over weight	256.6±68.8	153.3	377.7
Obese	319.5±72.9	173.9	446.2

Note: Serum uric acid concentration is given in µmol/L.

3.5 Distribution of serum uric acid concentration within BMI groups according to the gender

The distribution of serum uric acid concentration across the four BMI categories according to gender is shown in Table 3.

Table 3. Mean serum uric acid concentration according to the gender and BMI

Gender	Mean ± SD	p Value
Underweight female (n=25)	175.5±35.73	<0.0001
Underweight male (n=11)	262.7±50.6	
Normal female (n=20)	257.8±42.3	0.012
Normal male (n=13)	306.2±60.4	
Overweight female (n=25)	229.9±58.1	0.0014
Overweight male (n=7)	307.7±59.3	
Obese female (n=20)	287.2±67.5	0.0007
Obese Male (n=16)	370.1±49.2	

Note: Serum uric acid concentration is given in µmol/L.

Independent sample t-test was used and the p value was considered statistically significant at level of < 0.05

3.6 Correlation between serum uric acid level and BMI

The distribution of serum uric acid concentration with BMI in the study population is given in Figure 2. As indicated by a Pearson's correlation coefficient (r) = 0.516, p<0.001, there was a significant moderate positive linear relationship between BMI and serum uric acid concentration in the study population.

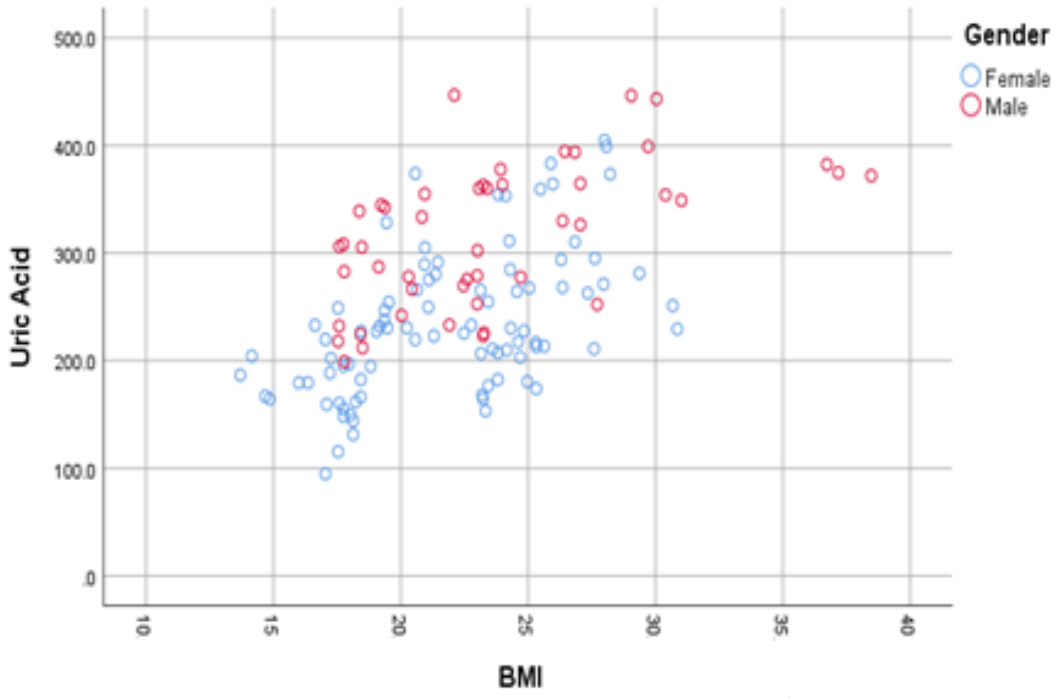

Figure 2. Distribution of serum uric acid concentration with BMI in the study population
Note: Serum uric acid concentration is given in µmol/L

Pearson's correlation coefficients (r) and p values for males and females are given in Table 4. In both genders, p<0.05 and there was a significant moderate positive linear relationship between BMI and serum uric acid concentration.

Table 4. Correlation between serum uric acid level and BMI

Gender	Pearson's correlation coefficient (r)	p value
Female	0.533	<0.001
Male	0.554	<0.001

Note: p Value is considered statistically significant at level of < 0.05

3.7 Comparison of mean serum uric acid levels among BMI groups

The mean serum uric acid level comparison among BMI groups is indicated in the Table 5. A statistically significant difference was observed between the mean serum uric acid levels of underweight and normal groups ($p<0.05$). The mean serum uric acid level of the normal group was 75.69 µmol/L higher than that of the underweight group. There was a statistically significant difference between the mean serum uric acid levels of overweight and obese groups ($p<0.05$). The results showed that the mean serum uric acid level of the obese group was 62.84 µmol/L higher than the overweight group. On the other hand, the mean serum uric acid level of the obese group was 44.05 µmol/L higher than that of the normal group, and the overweight group had a level 56.9 µmol/L higher than the underweight group. As shown by the $p<0.05$, there was a statistically significant difference in the mean serum uric acid concentrations between overweight and underweight groups. Besides, there was a significant difference between the mean serum uric acid levels of underweight and obese groups, where the obese group's level was 119.74 µmol/L higher than the underweight group's. However, the mean serum uric acid level difference between normal and overweight groups was not significant ($p>0.05$) and the mean serum uric acid level of the normal weight group was 18.79 µmol/L higher than that of the overweight group.

Table 5. Comparison of mean serum uric acid level among BMI groups

BMI group considered	Other BMI groups	Mean difference of serum uric acid level (µmol/L)	p Value
Underweight	Normal	-75.690	<0.0001
	Overweight	-56.902	0.0004
	Obese	-119.742	<0.0001
Normal	Overweight	18.788	0.2247
	Obese	-44.052	0.0061
Overweight	Obese	-62.840	0.0005

Note: Tukey HSD test was used and the p value was considered statistically significant at level of < 0.05

3.8 Interaction between gender and BMI related to serum uric acid level

Using ANOVA, the following results were obtained regarding the interaction between gender and BMI with regard to serum uric acid level. As the p value was 0.473, there was no interaction effect of BMI group and gender on uric acid level. Instead, it is possible to discuss the individual effects of gender and BMI on serum uric acid concentration. The gender causes no any interference on the result of serum uric acid level, though it is not kept as a constant variable.

According to the findings of the present study, males had a significantly higher serum uric acid level (316.3 μmol/L) than the females (234.7μmol/L). This finding was supported by the previous studies (Conen, 2004; Liu, 2014; Duan et al., 2015; Tanaka, 2015). Further, the present study showed a significant moderate positive linear relationship between BMI and serum uric acid concentration, which is also supported by the previous research (Oliveira, 2014; Wang, 2014; Duan et al., 2015; Tanaka, 2015).

Our findings showed that the underweight group had the lowest mean value while the obese group had the highest mean value. This is corroborated in the findings of Honggang et al (2014). At the same time, normal and overweight groups had comparatively similar mean values for serum uric acid. However, Wang et al (2014) stated that serum uric acid in subjects within the obese group was significantly higher than the underweight group, while Duan et al (2015) pointed to high serum uric acid levels in overweight and obese groups. Duan et al (2015) further reported that there was a trend of increasing uric acid concentrations with increasing BMI. Yet this was not observed in the present study, with comparatively similar mean values were received for normal and overweight groups. However, Duan et al (2015) had used BMI cut-off points as <18.5 kg/m^2 for underweight and 24 kg/m^2 and 28 kg/m^2 for overweight and obese groups, respectively, and these cut-off points significantly deviated from the Asia-Pacific cut- off points of BMI which were used in the present study.

It has been reported that the activity of the enzyme xanthine oxidoreductase is increased with the obesity. Xanthine oxidoreductase is known to catalyze xanthine and hypoxanthine to uric acid. Adipose tissue is a major site with higher expression and activity of xanthine oxidoreductase. Therefore, with obesity, uric acid production and secretion from the adipose tissues increase, resulting in a higher serum uric acid concentration (Tsushima et al., 2013). A previous study has reported that visceral fat accumulation induces an increased influx of plasma free fatty acids to the hepatic portal vein and liver. This stimulates triglyceride synthesis which activates the uric acid synthesis pathway, leading to an increase in uric acid production. This could be the possible reason for increment of uric acid concentration with increment of BMI (Fox, 1981).

In the present study, the number of females is greater than that of males, which could be mentioned as a limitation.

4 CONCLUSION AND RECOMMENDATIONS

There was a significant positive moderate linear correlation between serum uric acid level and BMI in both genders. In the comparison of mean serum uric acid levels of all four BMI categories, the highest level was found in obese group while the lowest level was found in underweight group. Normal and overweight groups reported comparatively similar concentrations. The mean serum uric acid concentration in males was significantly higher than in females, in all four BMI categories.

A future study could be conducted with the participation of males and females in equal numbers per each BMI category, also ensuring a larger sample size to study the effect of gender on serum uric acid level.

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