ASSESSMENT OF SERUM AND URINE URIC ACID LEVEL IN RELATION WITH ANTHROPOMETRIC INDICES IN OVERWEIGHT AND OBSESE UNIVERSITY UNDERGRADUATE STUDENTS

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ABSTRACT

Objectives: Elevated uric acid level is related to a variety of adverse metabolic conditions including gout, obesity, and risk factor for cardiovascular disease. This prospective study designed to assess the serum and urine uric acid level in relation with anthropometric indices in overweight and obese undergraduate students at NAU, Nnewi, Nigeria.

Methods: A total of 302 undergraduate students aged between 18 and 40 years were randomly recruited for the present study. They were grouped based on their body mass index (BMI) as overweight, obese, and control participants. 132 participants were males, of which 21 were obese, 34 were overweight while 77 were normal (control) males. 170 participants were females, of which 56 were obese, 62 were overweight while the remaining 52 were normal (control) females. Fasting blood and 24 h urine sample were aseptically collected from all the participants for determination of serum and urine uric acid.

Results: The study observed significantly higher serum uric acid level in obese and overweight males than female and control counterparts (p<0.000, respectively). Urine uric acid level was significantly higher in obese males and females than in their overweight and control counterparts (p<0.000). This shows increase production and accumulation of monosodium urate with decreased uric acid excretion which may result in hyperuricemia and hyperuricosuria which may result in gout. Serum and urine uric acid levels were significantly higher among age range (26–32) and (33–40) years compared with those among age range (18–25) (p<0.05) signifying that uric acid level increases with age. Serum and urine uric acid were significantly positively correlated with BMI, waist circumference, and waist hip ratio (p<0.05).

Conclusions: High serum uric acid is a prerequisite for gout and also associated with the metabolic syndrome and risk factors for cardiovascular disease. Proper awareness of the implication of hyperuricemia among undergraduate students is necessary.

Keywords: Uric acid, Anthropometric indices, Overweight, Obesity, Undergraduate students.

INTRODUCTION

Uric acid is originated from enzymatic degradation and metabolic conversion of exogenous or endogenous purines in the liver and intestine. It is excreted in urine through the kidney as the by-product of amino acid (purines) metabolism in humans [1]. Uric acid is a weak acid with a high dissociation constant and can exist in plasma as the monovalent sodium salt in the form of monosodium urate [2]. Some studies have indicated that variation in serum uric acid is genetic and could be affected by several genes [3-5]. When the saturation threshold of uric acid in body fluids (serum or urine) is exceeded, hyperuricemia or hyperuricosuria, respectively, occurs. The average urate pool in healthy adults is estimated to be 1200 mg with a mean turnover rate of 700 mg/day. Hyperuricemia was established as serum uric acid level >450 µmol/L for males and >390 µmol/L for females while hyperuricosuria was defined as uric acid level >1000 mg/24 h assuming for normal diets and <600 mg/24 h assuming low purine diets [6-8]. Excessive production and accumulation of monosodium urate with a reduction in the urinary excretion lead to high levels of uric acid in body fluids. This results in the formation and continual deposition of the crystals in and around the joints and tissues thereby causing severe pains and inflammation in the joints and subsequently leads to impaired health [9-11]. Elevation of uric acid is associated with a variety of metabolic diseases including inflammatory gout, hypertension and cardiovascular death, renal disease, atherosclerosis, and ischemic heart disease [12-19]. Several modifiable risk factors have been linked with hyperuricemia; these include starvation, body mass index (BMI), obesity, waist circumference (WC), high purine, and fructose-rich diets [20,21]. Serum uric acid may be grossly elevated in starvation due to accelerated tissue turnover and reduced renal excretion of uric acid [22]. Impaired kidney function leads to impaired uric acid excretion in the urine [23].

Uric acid level in body fluid can vary with height, body weight, kidney function, and alcohol intake in healthy men [24]. Reports have associated elevated serum uric acid levels with BMI and WC [2,19,25]. However, Sivakumar et al. reported that serum uric acid was not significantly correlated with BMI [2]. BMI is an index of weight and height which is used in classifying overweight and obesity in the adult population and individuals. Overweight and obesity are defined as abnormal or excessive fat accumulation due to excess calorie intake; several authors have reported a significant positive association between elevated serum uric acid levels, overweight, and obesity [18,26-28]. Obese individuals, due to excess calorie intake, get impaired kidney excretion leading to the hyperuricemia [29]. The pathogenic factors responsible for the elevated uric acid level in obesity have been implicated to lecithin concentration
and decreased urinary excretion of its metabolites [30,31]. However, the mechanism behind impaired urate excretion in obese individuals and its improvement during weight reduction remains to be determined.

The average urate pool in healthy adults is estimated to be 1200 mg with a mean turnover rate of 700 mg/day. It has been indicated that the level of serum uric acid is lower in women than in men [29,32,33]. However, a study has shown that obesity-related hyperuricemia can be treated with only appropriate diet therapy without drugs in most cases [34]. The present study, therefore, sets to assess the serum and urine uric acid levels in relation with anthropometric indices among overweight and obese university undergraduate students at Nnamdi Azikiwe University Nnewi Campus Nigeria.

METHODS

Study design
This is a cross-sectional prospective study designed to assess the serum and urine uric acid levels in relation with anthropometric indices among overweight and obese undergraduate students at Nnamdi Azikiwe University, College of Health Sciences, Nnewi Campus, Anambra State, Nigeria.

Study population
The study population consisted of 302 apparently healthy male and female students. They were randomly recruited and grouped based on their BMI as obese >30 kgm², overweight 25-29.9 kgm², and control <25 kgm² [35]. The study was conducted between March and May, 2017.132 participants were males, of which 21 were obese, 34 were overweight while 77 were normal (control) males. 170 participants were females of which 56 were obese, 62 were overweight while the remaining 52 were normal (control) females.

Inclusion criteria
Apparently healthy adult male and female undergraduate students aged between 18 and 40 years were recruited for the study.

Exclusion criteria
Students with any known disease conditions, for example, liver and kidney disease diabetics or those taking alcohol, medications that may affect the level of uric acid in serum and urine, for example, diuretic. Pregnant women and lactating mothers were excluded.

Sample collection
5 ml of blood was collected by venepuncture from the subjects following overnight fasting on the morning of completing urine collection and dispensed into a plain container for centrifugation at 5000 rpm for 5 min. Serum was extracted for the estimation of serum uric acid. The samples were refrigerated at −20°C until the analysis of serum uric acid. After centrifugation, the serum samples were separated and stored frozen until analysis serum uric acid.

Anthropometric measurement
The BMI was calculated by dividing the weight (kg) by height square (m²) [37]. WC was measured twice in millimeters, using the smallest circumference between the lower ribs and iliac crests. WC <80 cm for females and <90 cm for males were defined as the reference values [38]. Hip circumference was measured using the greatest circumference between the iliac crest at the level of the umbilicus and thigh at the level of maximal protrusion of the gluteal muscles at the widest circumference. Waist-hip ratio (WHR) was calculated as the ratio of WC to hip circumference.

Sample processing and storage
The blood sample was withdrawn from the antecubital vein by means of sterile plastic syringes into a plain container and was allowed to clot. Later, the tubes were centrifuged for 10 min for proper separation of the serum. After centrifugation, the serum samples were separated and used stored frozen at −20°C until the analysis of serum uric acid. 24 h urine sample was collected with the universal container and was stored frozen until analysis urine uric acid.

Levels of serum uric acid and urine uric acid in obese overweight and control male and female participants
When the mean serum uric acid and urine uric acid levels were compared among all the participants, the mean serum uric acid level in obese and overweight males (382.83±87.64 and 356.63±85.40) was significantly higher when compared with obese female (277.78±78.90), overweight female (220.80±68.30), control male (289.72±66.96), and control female (193.70±56.83) participants (p=0.000, respectively).

Statistical analysis
Data generated from the study were subjected to statistical analysis using the Statistical Package for the Social Sciences version 20.0. The result was expressed as a mean±standard deviation; the statistical difference between groups was done using analysis of variance (ANOVA) with post hoc (least standard deviation). Pearson’s correlation analysis was used for association between variables. The differences were considered significant at p<0.05.

RESULTS

Levels of serum uric acid and urine uric acid levels were measured by the uricase method [36].

Principle
Uric acid + O₂ + 2H₂O₂ → Allantoin + CO₂ + H₂O

Uric acid is converted by uricase into allantoin and hydrogen peroxide. The hydrogen peroxide initiates the coupling of 4-aminoantipyrine to 3,5-dichloro-2-hydroxybenzene sulfonic acid to form the chromogen which is measured at 520 nm and which is proportional to the amount of hydrogen peroxide generated from uric acid.
The mean serum uric acid level in obese male and female (382.83±87.64 and 277.78±78.97) was significantly higher when compared with their control counterparts (289.72±66.96 and 193.76±56.83) (p=0.000, respectively). Similar observation was made in the mean serum uric acid level between overweight male (356.63±85.40) control male and female (289.72±66.96 and 193.76±56.83) participants (p=0.000, respectively). The mean urine uric acid level in obese males and females (1059.74±399.91 and 1035.22±395.64) was significantly higher when compared with their corresponding control (886.94±349 and 877.62±291.74) participants (p=0.000, respectively). Similar observation was made in overweight males (986.60±352.10) when compared with control male and female (886.94±349 and 877.62±291.74) participants (p=0.000, 0.020, and 0.000, respectively). There was a significantly higher mean level of serum uric acid in control male (289.72±66.96) when compared with the female counterpart (193.76±56.83) (p=0.000) (Table 2).

Levels of serum uric acid and uric acid uric acid according to age ranges

The mean serum uric acid level was significantly higher among the age range 26–32 and 33–40 years (289.00±72.23 and 299.10±83.66) when compared with participants among the age range 18–25 years (238.10±72.69) (p=0.003).

Similarly, the mean urine uric acid level was significantly higher among age range 26–32 years (922.50±324.20) and 33–40 years (999.40±444.80) when compared with participants within the age range of 18–25 years (805.90±82.12) (p=0.000 and 0.003). Furthermore, the urine uric acid level was significantly higher among the age range 33–40 (999.40±444.80) when compared with those within 26–32 (922.50±324.20) years (p=0.040) (Table 3).

Correlation of serum uric acid and uric acid uric acid with the anthropometric parameters

Serum uric acid was significantly positively correlated with age, BMI, WC, and WHR, (r=0.289, 0.313, 0.431, 0.326, and 0.265, p=0.014, 0.032, 0.011, 0.029, and 0.041, respectively). Similarly uric acid was significantly positively correlated with age, BMI, and WC, (r=0.211, 0.351, and 0.549, p=0.008, 0.021, and 0.000, respectively) (Table 4).

DISCUSSION

Participants in this study were classified based on their BMI into obese (>30), overweight (25.0–29.9 kg/m²), and normal control subjects (18.5–24.9 kg/m²) according to the WHO classification of body mass index [35].

The present study observed significantly higher serum uric acid in obese and overweight males when compared with their female counterparts and controls. This is consistent with the other reports [19, 39, 40]. This is an indication of increase formation and deposition of monosodium urate crystals in and around joints suggesting the future risk of development of gout [10] as well as other adverse conditions associated with hyperuricemia [12-18]. Increased serum uric acid levels in these participants may also be due to reduced renal clearance and excessive secretion and production of uric acid by the adipose tissue through xanthine oxidoreductase. Several researchers have also observed elevated levels of serum and urine uric acid level in both men and women [41-43]. In women, the sexual dimorphism in serum uric acid level was thought to be related to higher renal clearance of urate, possibly due to their higher plasma estrogen levels [41,44,45]. However, our study observes that obese male and female participants had significantly higher serum uric acid than the control female. This is similar to the report of Oyama et al. [46]. Our study also observed significantly higher serum and urine uric acid levels in males when compared with females. This shows that variation on the uric acid level is sex-dependent. Increased serum uric acid in apparently healthy males than females have been previously reported [5,41,47].

The study concludes that there was significantly higher serum uric acid level in obese and overweight male than their female counterparts and controls. The mean urine uric acid level was also significantly higher in obese male and females than in their overweight and
control counterparts. This shows that the participants might be predisposing to hyperuricemia and hyperuricosuria which could lead to gout and subsequently results in other adverse conditions such as atherosclerosis, metabolic syndrome, as well as cardiovascular diseases. Serum and urine uric acid levels were significantly higher among the age ranges 26–40 years. The serum and urine uric acid levels were significantly positively correlated with age, BMI, WC, and WHR. This shows that elevated uric acid level is age- and sex-dependent. Proper awareness of the prevalence of hyperuricemia is necessary. Importance of good dietary regimens and physical exercise is highly advocated for weight reduction among university undergraduates in the study area to minimize the risk of gout.

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**AUTHORS’ CONTRIBUTIONS**

1. Conceptualization and study design - Nkiruka Rose Ukibe, Solomon Nwabueze Ukibe.
2. Data collection, sample analysis, and performing the experiment - Nkiruka Rose Ukibe, Emmanuel Ikechukwu Obinwanne Chikamnario Osuagwu.
3. Preparation of manuscript - Nkiruka Rose Ukibe, Solomon Nwabueze Ukibe.
4. Statistical Analysis - Ofia Anya Kalu, Emmanuel Ikechukwu Obinwanne Chikamnario Osuagwu.
5. Proofreading the manuscript - Solomon Nwabueze Ukibe, Emmanuel Ikechukwu Obinwanne Chikamnario Osuagwu.
6. All authors read and approved the final manuscript.

**CONFLICTS OF INTEREST**

All authors have none to declare.

**REFERENCES**

1. Glantzounis GK, Tsimoyiannis EC, Kappas AM, Galairis DA. Uric acid and oxidative stress. Curr Pharm Des 2005;11:4145-51.
2. Sivakumar K, Thamarai R, Praghata RJ. Screening of serum uric acid in obese individuals in rural population. Int J Sci Study 2014;2:1-4.
3. Rao DC, Laskarzewski PM, Morrison JA, Khouy P, Kelly K, Ghucck CJ, et al. The clinical lipid research clinic family study: Familial determinants of plasma uric acid. Hum Genet 1982;60:257-61.
4. Rice T, Vogler GP, Perry TS, Laskarzewski PM, Province MA, Rao DC, et al. Heterogeneity in the familial aggregation of fasting serum uric acid level in five North American populations: The lipid research clinics family study. Am J Med Genet 1990;36:219-25.
5. Voruganti VS, Nath SD, Cole SA, Thameem F, Jowett JB, Bauer R, et al. Genetics of variation in serum uric acid and cardiovascular risk factors in Mexican Americans. J Clin Endocrinol Metab 2009;94:632-8.
6. Lockitch G, Halstead AC, Albersheim S, MacCallum C, Quigley G. Age- and sex-specific pediatric reference intervals for biochemistry analytes as measured with the ektachem-700 analyzer. Clin Chem 1988;34:1622-5.
7. Henry R. Normal values for selected blood and urine tests. J Humber Coll Toronto Canada 2000;2000:11-5.
8. Das M, Borah NC, Ghose M, Choudhury N. Reference ranges for serum uric acid among healthy Assamese people. Biochem Res Int 2014;2014:171053.
9. Underwood M. Diagnosis and management of gout. Br Med J 2006;332:339-42.
10. Roddy E, Zhang W, Doherty M. Is gout associated with reduced quality of life? A case-control study. Rheumatology (Oxford) 2007;46:1441-4.
11. Waring WS, Webb DJ, Maxwell SJ. Uric acid as a risk factor for cardiovascular disease. Quarterly J Med 2000;93:707-13.
12. Lin SD, Tsai DH, Hsu SR. Association between serum uric acid level and components of the metabolic syndrome. J Chin Med Assoc 2006;69:512-6.
13. Kang DH, Park SK, Lee IK, Johnson RJ. Uric acid-induced C-reactive protein expression: Implication on cell proliferation and nitric oxide production of human vascular cells. J Am Soc Nephrol 2007;18:3593-9.
14. Cahn L, Shankar A, Ducatman AM, Steenland K. The relationship between serum uric acid and chronic kidney disease among Appalachian adults. Nephrol Dial Transplant 2010;25:3593-9.
15. Huang SY, Chen VH, Yeh WT, Wu CC, Pan WH. Hyperuricemia and increased risk of ischemic heart disease in a large Chinese cohort. Int J Cardiol 2012;154:316-21.
16. Nagahama K, Inoue T, Kobagura K, Kinjo K, Ohyya Y. Associations between serum uric acid levels and the incidence of hypertension and

| Group                | Serum uric acid (µmol/L) | Urine uric acid (µmol/L) |
|----------------------|--------------------------|--------------------------|
| Obese male (A) n=21  | 382.8±87.64              | 1059.7±399.41            |
| Obese female (B) n=56| 277.8±78.97              | 1035.2±395.64            |
| Overweight male (C) n=34| 356.6±85.40          | 984.6±352.10             |
| Overweight female (D) n=52| 220.8±68.30        | 914.2±352.10             |
| Control male (E) n=77 | 289.7±66.96              | 886.9±349.36             |
| Control female (F) n=52| 193.7±56.83               | 877.6±291.74             |

*p<0.05=Significant. Data were expressed as mean±SD.

**Table 3:** Levels of serum uric acid and urine uric acid according to age ranges

| Age range | Serum uric acid (µmol/L) | Urine uric acid (µmol/L) |
|-----------|--------------------------|--------------------------|
| 18–25 (years) G n=219 | 238.10±57.69               | 905.9±482.12              |
| 26–32 (years) H n=66  | 289.00±72.33               | 922.5±324.20              |
| 33–40 (years) I n=5   | 299.10±83.66               | 999.4±444.80              |

*p<0.05=Significant. Data were expressed as mean±SD.

**Table 4:** Correlation of serum uric acid, urine uric acid with BMI, WC, and WHR in the study participants

| Parameters                       | N   | r value | p value |
|----------------------------------|-----|---------|---------|
| Serum uric acid versus age       | 302 | 0.289   | 0.014   |
| Urine uric acid versus age       | 302 | 0.211   | 0.008   |
| Serum uric acid versus BMI       | 302 | 0.313   | 0.032   |
| Urine uric acid versus BMI       | 302 | 0.351   | 0.021   |
| Serum uric acid versus WC        | 302 | 0.431   | 0.011   |
| Urine uric acid versus WC        | 302 | 0.549   | 0.000   |
| Serum uric acid versus WHR       | 302 | 0.265   | 0.041   |
| Urine uric acid versus WHR       | 302 | 0.045   | 0.659   |
| Serum uric acid versus urine uric acid | 302 | −0.149  | 0.139   |

WHR: Waist-hip ratio; BMI: Body mass index; WC: Waist circumference
metabolic syndrome: A 4-year follow-up study of a large screened cohort in Okinawa, Japan. Hypertens Res 2015;38:213-8.

17. Conen D, Wielandtsch B, Bovet P, Shamlouy C, Riesen W, Paccaud F, et al. Prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country. BMC Public Health 2004;4:9.

18. Liu PJ, Ma F, Lou HP, Zhu YN, Chen Y. Relationship between serum uric acid levels and metabolic syndrome in Chinese postmenopausal women. Clin Endocrinol 2014;71:147-54.

19. Wang H, Wang L, Xie R, Dai W, Gao C, Shen P, et al. Association of serum uric acid with body mass index: A Cross-sectional study from Jiangsu province, China. Iran J Public Health 2014;43:1503-9.

20. Masuo K, Kagawuchi H, Mikami H, Ogihara T, Tuck ML. Serum uric acid and plasma norepinephrine concentrations predict subsequent weight gain and blood pressure elevation. Hypertension 2002;42:474-80.

21. Ishizaka N, Ishizaka Y, Toda A, Tani M, Koike K, Yamakado M, et al. Changes in waist circumference and body mass index in relation to changes in serum uric acid in Japanese individuals. J Rheumatol 2010;37:410-6.

22. Toad JC. Clinical Diagnosis by Laboratory Method, Edited by Israel Davidson and John Bernord Henry. 14th ed. Philadelphia, PA: Saunders; 1969.

23. Seegmiller JE, Grayzel AI, Laster L, Liddle L. Uric acid production in gout. J Clin Invest 1961;40:1304-14.

24. Bandolier. Nurs Older People 2004;16:41.

25. Kuriyama S, Nakano T, Maruyama Y, Sugano N, Takane K, Suetsugu Y, et al. Relationship between serum uric acid levels and muscle strength/volume: A new insight from a large-scale survey. Nihon Jinzou Gakkai Shi 2015;54:1260-9.

26. Chiong WK, Huang DH, Wang MH, Lee YJ, Lin JD. Significance and association of serum uric acid (UA) levels with components of metabolic syndrome (MS) in the elderly. Arch Gerontol Geriatr 2012;55:724-8.

27. Palmer TM, Nordestgaard BG, Benn M, Tybjærg-Hansen A, Davey SG. Uric acid concentration and risk of coronary heart disease: Mendelian randomization analysis of two large cohorts. BMJ 2013;347:f2622.

28. Duan Y, Liang W, Zhu L, Zhang T, Wang L, Nie Z, et al. Association between serum uric acid levels and obesity among university students (China). Nutr Hosp 2015;31:2407-11.

29. Alboqai OK, Odoh AA, Hourani HM, Al-Qudah F. Obesity and serum uric acid. Bahrain Med Bull 2007;29:86-90.

30. Matsuda F, Yamashita S, Nakamura T, Nishida M, Nozaki S, Funahashi T, et al. Effect of visceral fat accumulation on uric acid metabolism in male obese subjects: Visceral fat obesity is linked more closely to overproduction of uric acid than subcutaneous fat obesity. Metabolism 2005;54:1269-73.

31. Jin M, Yang F, Yang J, Yin Y, Luo JJ, Wang H, et al. Uric acid, hyperuricemia and vascular diseases. Front Biosci (Landmark Ed) 2012;17:656-69.

32. Yin X, Zhou J, Yu D, Pan Q, Dong X, Zheng F, et al. The correlation between serum uric acid level and abdominal obesity or metabolic syndrome. Zhonghua Nei Ke Za Zhi 2014; 53: 13-8.

33. Dai X, Yuan J, Yao P, Yang B, Gui L, Zhang X, et al. Association between serum uric acid and the metabolic syndrome among a middle- and old-age Chinese population. Eur J Epidemiol 2013;28:669-76.

34. Yamashita S, Matsuzawa Y, Tokunaga K, Fujioka S, Tarui S. Studies of animal, clinical and epidemiological studies. Physiol Behav 2003;79:929-33.

35. Jin M, Yang F, Yang J, Yin Y, Luo JJ, Wang H, et al. Uric acid, hyperuricemia and vascular diseases. Front Biosci (Landmark Ed) 2012;17:656-69.

36. World Health Organisation. Obesity and Overweight; 2018. Available from: http://www.who.int/mediacentre/factsheets/fs311/en.

37. Brun DE, Goldman PA, Jankowski CB. Elevation of serum uric acid as a clue to alcohol abuse. Arch Intern Med 1981;141:477-9.

38. Bray GA, Paeratakul S, Popkin BM. Dietary fat and obesity: A review of animal, clinical and epidemiological studies. Physiol Behav 2003;83:53-59.

39. Misra A, Chowbey PK, Majumdar MK, Vikram NK, Wasir JS, Chadha D, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for primary care. Ann Rheum Dis 2006;65:1080-3.

40. Lin KC, Lin HY, Chou P. Community based epidemiological study on hyperuricemia and gout in Kin-Hu, Kinmen. J Rheumatol 2000;27:1045-50.

41. Tsushima Y, Nishizawa H, Tochino Y, Nakatsuji H, Sekimoto R, Nagao H, et al. Uric acid secretion from adipose tissue and its increase in obesity. J Biol Chem 2013;288:27138-49.

42. Rehman A, Naqui SA. Serum and urinary uric acid in relation to age and sex. J Pak Med Assoc 1980;30:242-4.

43. Brondum E, Micheli CJ, Crosson CS, O’Fallon WM, Gabriel SE. Epidemiology of gout: Is the incidence rising? J Rheumatol 2002;29:2403-6.

44. Bhole V, de Vera M, Rahman MM, Krishnan E, Choi H. Epidemiology of gout in women: Fifty-two-year followup of a prospective cohort. Arthritis Rheum 2016;68:639-46.

45. Antón FM, Garcia Puig J, Ramos T, González P, Ordás J. Sex differences in uric acid metabolism in adults: Evidence for a lack of influence of estradiol-17 beta (E2) on the renal handling of urate. Metabolism 1986;35:343-8.

46. Zhang Q, Lou S, Meng Z, Ren X. Gender and age impacts on the correlations between hyperuricemia and metabolic syndrome in Chinese. Clin Rheumatol 2011;30:777-87.

47. Oyama C, Takahashi T, Oyamada M, Oyamada T, Ohno T, Miyashita M, et al. Serum uric acid as an obesity-related indicator in elderly adolescence. Tokohu J Exp Med 2006;209:257-62.

48. Siła-O A, Pavaró U, Nuchpramool W. Serum and urinary uric acid levels in healthy subjects and in patients with urolithiasis. J Med Assoc Thai 1991;74:352-7.

49. Harris CM, Lloyd DC, Lewis J. The prevalence and prophylaxis of gout in England. J Clin Epidemiol 1995;48:1153-8.

50. Klippe P, Stansfield SA, Castle B, Robertson MC. Gout is on the increase in New Zealand. Ann Rheum Dis 1997;56:22-6.

51. Abbott RD, Brand FN, Kannel WB, Castelli WP. Gout and coronary heart disease: Report of the national heart, lung, and blood institute/american heart association conference on scientific issues related to definition. Arterioscler Thromb Vasc Biol 2004;24:e13-8.

52. Choi HK, Willett W, Curhan G. Coffee consumption and risk of incident gout in men: A prospective study. Arthritis Rheum 2007;56:2049-55.

53. Cohen SD, Kimmel PL, Neff R, Adogola L, Abbott KC. Association of incident gout and mortality in dialysis patients. J Am Soc Nephrol 2008;19:2204-10.

54. Choi HK, Liu S, Curhan G. Intake of purine-rich foods, protein, and dairy products and relationship to serum levels of uric acid. The third national health and nutrition examination survey. Arthritis Rheum 2005;52:283-9.

55. Janssens HJ, van de Lisdonk EH, Janssen M, van den Hoogen HJ, Verbeek AL. Gout, not induced by diuretics? A case-control study from primary care. Ann Rheum Dis 2006;65:1080-3.

56. Zhang H, Tanakoshi K, Yatsuya H, Murata C, Wada K, Osuka T, et al. Long-term body weight fluctuation is associated with metabolic syndrome independent of current body mass index among Japanese men. Circ J 2005;69:1344-7.

57. Onwubuya EI, Ekike MC, Kartu OA, Ekike SN. Prevalence of overweight and obesity and assessment of body fat distribution. Intern Med J 2011;41:408-11.

58. Onwubuya EI, Ukibe NR, Kalu OA, Emelumadu OF, Monago IN, Onwubuya et al. Relationship between serum uric acid levels and muscle strength/ mass and area in the three African populations: Evidence for a lack of influence of uric acid metabolism in adults: Evidence for a lack of influence...
66. Choi HK, Ford ES. Prevalence of the metabolic syndrome in individuals with hyperuricemia. Am J Med 2007;120:442-7.

67. Coutinho Tde A, Turner ST, Peyser PA, Bielak LF, Sheedy PF 2nd, Kullo IJ, et al. Associations of serum uric acid with markers of inflammation, metabolic syndrome, and subclinical coronary atherosclerosis. Am J Hypertens 2007;20:83-9.

68. Fruehwald-Schultes B, Peters A, Kern W, Beyer J, Pflützer A. Serum leptin is associated with serum uric acid concentrations in humans. Metabolism 1999;48:677-80.