Original Article

# Prevalence of Hyperuricaemia in a Rural Population of Nigerian Niger Delta Region

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### ABSTRACT

**INTRODUCTION:** Hyperuricemia is a cardiovascular disease risk factor that has been poorly researched into in Africa and its prevalence is largely unknown in the rural areas in Nigeria and in the Niger Delta region of Nigeria in particular.

**METHODS:** A cross-sectional rural survey involving 500 subjects aged 15 years and above. Demographic and social data were obtained using a questionnaire. Anthropometric (height, weight, waist circumference) and blood pressure measurements were taken. Blood samples were taken for blood uric acid, glucose and lipid check.

**RESULTS:** The mean age of the study subjects was 41.32±17.0 (males, 42.84±17.8; females, 40.62±16.6) with a range of 15 years to 95 years. The male to female ratio was 1:2.3. The mean serum uric acid was 337.58±94.59 mmol/l with a significant higher mean for females (males 333.20±88.70, females 339.56±97.21, p<0.001). Hyperuricemia was found in 86 subject giving a prevalence of 17.2 % with higher prevalence in males (males 25%, females 13.7%;  $x^2 = 7.75$ , p = 0.006). Correlational analysis of serum uric acid with other parameters revealed that waist circumference, total cholesterol, low-density lipoprotein and gender had significant association with uric acid. Male gender was found to be a significant predictor for hyperuricaemia following a logistic regression.

**CONCLUSION:** The prevalence of hyperuricemia is high in this rural community of study. There is need for more research considering the cardiovascular and other implications of hyperuricaemia.

**KEY WORDS:** Hyperuricaemia, prevalence, Rural, Niger Delta, Nigeria

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# INTRODUCTION

Serum uric acid level which is a final product of purine metabolism and a function of the balance between the breakdown of purines and the rate of uric acid excretion is beginning to gain prominence globally as both a risk factor for cardiovascular disease and its involvement in metabolic and kidney diseases.<sup>1-3</sup> Several physiologic and environmental factors have been reported to be associated with the prevalence of hyperuricaemia. Among such are geographical location, socio-economic status, age, sex, and race.<sup>4-5.</sup>The increased risk of cardiovascular disease observed with westernization of native peoples, immigration to Western countries, and movement from rural to urban communities also correlates with increased uric acid levels.<sup>6</sup> Women tend to have lower levels (by 0.5 to 1.0 mg per decilitre [30 to 60  $\mu$ mol per litre]) than men, probably because of the uricosuric effect of estrogens.<sup>7</sup>

Hyperuricemia is a cardiovascular disease risk factor that has been poorly researched into in Africa even though it has strong association with the development of cardiovascular diseases.<sup>8</sup> Hyperuricemia is also a major risk factor for gout, <sup>9-10</sup> and is implicated in the etiology of some degenerative diseases.<sup>11-16</sup> There is a growing data on the rising incidence of gout internationally particularly among the middle-aged and older people and westernization of lifestyle is said to be associated with this rising incidence.<sup>17-19</sup> Globally, researchers have reported various prevalence rates ranging from 5% to 62%.<sup>20</sup> The prevalence of hyperuricemia is however largely unknown in Nigeria and in the Niger Delta region of Nigeria in particular. In 2005, Isezuo et al<sup>21</sup> reported a prevalence of 32.3% among diabetic patients in Nigeria which is higher than the 25% reported by Ogbera et al in 2010 among Nigerian diabetics.<sup>22</sup>However there is paucity of data on ruralurban dichotomy as most of the published works were mainly urban and hospital based. Hence there is need to study the prevalence of this increasingly important cardiovascular risk factor in a homogenous rural community setting.

The purpose of this present research is to determine both the prevalence and predictors of hyperuricaemia in a rural community in the Niger Delta region of Nigeria.

### **MATERIALS AND METHODS**

This is a cross sectional survey conducted in Mba, a rural community in Etche local government area of Rivers state in Niger Delta region of Nigeria involving 500 subjects aged 15 years and above. Approval of the Ethics committee of the University of Port Harcourt Teaching Hospital was obtained. Consent from the village Chiefs was also obtained.

Demographic and social information including age, gender, occupation, educational level, cigarette smoking, alcohol consumption and level of physical activity were obtained using a questionnaire administered by face-to-face interview. Anthropometric (height, weight, waist circumference) and blood pressure measurements were done in a standardized manner. Readings were taken to the nearest 0.1 kg for weight and nearest 0.1cm for height. Body mass index (BMI) was calculated as weight in kilogram divided by the square of height in meters. Midway between the uppermost border of the iliac crest and the lower border of the costal margin (rib cage) served as the position for measuring waist circumference.<sup>23</sup> Hip circumference was measured in a horizontal plane at the maximum width over the greater trochanter.<sup>23</sup> Blood pressure was measured using a mercury sphygmomanometer.

Fasting venous blood samples were obtained from study subjects. Plasma samples were conveyed to the Chemical department laboratory of University of Port Harcourt Teaching hospital, subsequently centrifuged. Venous blood Glucose was measured by the Glucose oxidase method. Plasma total cholesterol and triglycerides were determined by the Colorimetric enzymatic methods,(Randox laboratories ltd, Crumlin, Co. Antrim, United Kingdom). Plasma high density lipoprotein cholesterol (HDL cholesterol) were measured by the same enzymatic method after precipitation. Low density lipoprotein (LDL cholesterol) was estimated according to the formula LDL cholesterol = total cholesterol HDL cholesterol triglycerides/2.2. Uric acid was also analysed using enzymatic method.

Hypertension was defined using the JNC 7 (Joint National Committee on Prevention, Evaluation, and Treatment report) criteria of blood pressure = 140/90mmHg or self-reported anti hypertensive medication use.<sup>25</sup> Diabetes mellitus was defined using fasting plasma glucose (FPG) = 7.0 mmol/l  $(126 \text{ mg/dl})^{26}$  and individuals who were previously known to have diabetes based on history of drug medication were also classified to have diabetes. Total cholesterol of > 6mmol/L, TG > 1.8mmol/L, HDL-C <1.0mmol/L and LDL-C = 3mmol/L were taken as abnormal values. Hyperuricemia was defined as =420mmol/L for males and =360 mmol/L for females.<sup>27</sup> Waist Circumference equal to or greater than 102cm in males and 88cm in females were taken as abnormal. Abdominal obesity will be represented or assessed by waist circumference.

Statistical analysis was done using Statistical Package for Social Sciences (SPSS Inc, Chicago,IL) version 17. Results were expressed as either mean values (standard deviation) or proportions. Comparison for statistical significance was by student's t test for Continuous variables and chi-square analysis for categorical variables. Epi info statistical package version 3.5.1 was used for chi-square for trend analysis. Pearson and Spearman' rho correlation test were used to determine the relationship between hypertension and its possible risk factors. Multivariate logistic regression was also done. A p-value of <0.05 was considered statistically significant.

#### RESULTS

The overall mean age of the study subjects was  $41.32\pm17.0$  with a range of 15 years to 95 years. The mean age for males was  $42.84\pm17.8$  and that for females was  $40.62\pm16.6$  with a statistically significant difference (P<0.001) as shown in Table 1.

Table 1: Gender differences in the means of the basic characteristics of the study subjects

variable	All subjects	Male	Female	P value
	N=500	N=156	N=344	
Age (years)	41.32±17.0	42.84±17.8	40.62±16.6	<0.001*
BMI (kg/m <sup>2</sup> )	22.10±3.67	21.80±3.05	22.40±3.84	< 0.001*
WC (cm)	71.68±9.94	72.55±8.78	71.36±9.90	<0.001*
SBP (mmHg)	120.46±21.59	123.57±20.41	119.05±22.36	0.04*
DBP (mmHg)	73.86±12.63	75.52±13.03	73.25±12.30	0.50
FBG (mmol/L)	4.59±1.34	4.58±1.16	$4.60{\pm}1.40$	0.66
TC (mmol/L)	3.93±0.85	$3.80{\pm}0.80$	3.98±0.86	0.16
TG (mmol/L)	1.19±0.43	1.24±0.46	1.17±0.41	0.17
HDL (mmol/L)	1.01±0.19	1.01±0.20	1.01±0.22	0.45
LDL (mmol/L)	2.64±0.78	2.56±0.75	2.71±0.81	0.09
SBP = sys	tolic blood	pressure;	DBP= dia	stolic blood
pressure;	BMI= Bod	ly mass	index; W	C = Waist
circumfer	ence; TC	= total	cholester	ol ; TG=
triglycerides; HDL= High density lipoprotein; LDL=				
Low density lipoprotein; $N=$ number; $P*=$ Significant				

Likewise as also shown in Table 1, mean BMI, mean waist circumference and the mean systolic blood pressure showed significant gender differences amongst the study subjects. The male to female ratio was 1:2.3. The mean age for subjects with hyperuricaemia was not statistical different from those with normal serum uric acid level (P=0.46). Only fasting blood sugar showed a statistically significant difference in mean between subjects with hyperuricaemia and those with normouricaemia (P=0.02) as depicted in Table 2.

 Table 2: Comparison of means and standard deviation of parameters between hyperuricaemic and normouricaemic subjects.

parameters	Hyperuricaemic subjects Mean(SD)	Normouricaemic subjects Mean(SD)	P value
Age (years)	42.57(16.43)	41.09(17.08)	0.46
WC (cm)	73.26(8.96)	71.35(10.13)	0.11
$BMI(kg/m^2)$	22.63(3.97)	21.98(3.60)	0.14
SBP	123.79(20.49)	119.81(21.78)	0.12
DBP	75.59(10.99)	73.54(12.92)	0.17
FBS	4.91(2.01)	4.51(1.17)	0.02*
TC	3.87(0.95)	3.95(0.83)	0.39
TG	1.26(0.49)	1.17(0.39) ——	0.07
HDL	0.70(0.25)	0.74(0.23)	0.12
LDL	2.59(0.85)	2.68(0.78)	0.37
*= sioni	ficant		

The mean serum uric acid was  $337.58\pm94.59 \text{ mmol/l}$ with a statistically significant higher mean for females (males 333.20 ± 88.70, females 339.56±97.21,p<0.001).The prevalence of Hyperuricemia was found in 86 out of the 500 subjects giving an overall prevalence of 17.2 %. The males had a statistically significant higher prevalence than the females (males 25%, females 13.7%;  $x^2 = 7.75$ , p= 0.006). In the male sex, the highest rate was noted in the 30-39 years age group with a declining pattern seen with increasing age unlike in the female gender that had the lowest prevalence in the 30-39 years age group and an increasing pattern with increasing age (Figure 1).



Figure 1. Prevalence of hyperuricaemia by Age-group and Gender

According to table 3, a higher proportion of the subjects with hyperuricaemia compared with subjects with normouricaemia had hypertension, diabetes, impaired fasting glucose, hypertriglyceridaemia, abdominal obesity and BMI=25kg/m<sup>2</sup>. However, these differences were not statistically significant except for hypertriglyceridaemia (P=0.03).

Table 3: comparison of percentage of occurrence of parameters between subjects with normal and high uric acid level

Parameter	Hyperuricaemic subiects. (%)	Normouricaemic subiects. (%)	P value
BMI	22.1	16.5	0.67
High WC	4.7	3.1	0.51
Hypertension	25.6	19.6	0.24
FBS =7mmol/l	4.7	1.7	0.14
FBS 6.1-6.9mmol/l	3.5	2.2	0.14
Hypercholesterolaemia	0.0	0.9	0.21
Hypertriglyceridaemia	11.6	5.1	0.03*

\*=significant

Table 4: Pearson and Spearman' rho correlation analysis for uric acid

Parameter	<b>Correlation coefficient</b>	P value
Age	-0.02	0.63
WC	0.22	< 0.001*
BMI	-0 05	0 33
SBP	0.02	0.73
DBP	0.03	0.51
FBS	-0.08	0.10
TC	-0.10	0.03*
TG	-0.01	0.84
HDL	-0 06	0 24
LDL	-0.10	0.03*
Gender	-0.15	0.001*
*=significant		

Pearson and Spearman' rho correlation analysis of serum uric acid with other parameters done for all the study subjects revealed that waist circumference, total cholesterol, low-density lipoprotein and gender had significant association with uric acid . Table 4 depicts this.

Table 5 shows a multivariate logistic regression model for predicting hyperuricaemia. Only male gender was found to be a significant predictor for hyperuricaemia.

Table 5: Multivariate logistic regression analysis for predictors of hyperuricaemia

P <u>arameter</u>	Odds ratio	95% confidence interval	P value
Age group (years)		r -	
15-29	0.79	0.26-2.41	0.67
30-39	0.66	0.2-2.22	0.51
40-49	0.53	0.17-1.65	0.28
50-59	0.60	0.19-1.91	0.39
60-69	0.52	0.16-1.68	0.28
=70	1.00		
Gender			
Male	0.43	0.26-0.71	0.001*
Female			
BMI			
Underweight	2.09	0.38-11.49	0.40
Normal weight	1.60	0.34-7.50	0.55
Over weight	1.50	0.32-7.06	0.61
Obesity	1.00		
Waist circumference			
High	1.20	0.30-5.0	0.80
Normal	1.00		
Hypertension			
No	0.78	0.42-1.46	0.44
Yes	1.00		
Fasting blood sugar			
Normal	1.87	0.44-7.85	0.39
Diahetic range	1.18	0.16-8.65	0.87
Impaired fasting range	1.00		
Total cholesterol			
Normal	2.91	1.02-8.33	0.05
High	1.00	1102 0100	0.00
Triglycerides			
Normal	2.26	0 95-5 40	0.07
High	1.00	0.99 5.10	0.07
Low density linenuotein			
Normal	0.86	0 51-1 47	0.57
Low	1.00	0.31-1.4/	0.57
LOW	1.00		

\*= significant

#### DISCUSSION

The high prevalence (17.2%) of hyperuricemia found in the present study is lower than previously reported by Isezuo etal and Ogbera et al in Nigeria.<sup>21-22</sup> This may be due to the fact that while the present study is a crosssectional rural community study, the comparative studies were among diabetics, urban and hospital-based. Diabetes is a well established risk factor for development of microvascular kidney disease that can predispose to hyperuricaemia.<sup>28</sup> Urbanisation and development of westernised lifestyle are also important factors implicated in the rising incidence of hyperuricaemia with subsequent development of renal hypertension.<sup>6</sup>

In agreement with previous studies, we found in the present study that the prevalence of hyperuricaemia was significantly higher in males than in females <sup>29-30</sup> with the highest prevalence among the males noted in 30 to 49 years old age bracket similar to the findings by Conen et al.<sup>31</sup> Subsequently, there was a declining prevalence

seen with increasing age in males. This is contrary to what was found among the female group were the lowest prevalence was reported in the 30-39 years age group with an increasing pattern of prevalence seen with increasing age. The increasing prevalence seen in females with advancing age could be associated to the uricosuric effect of oestrogen.<sup>7,31</sup> Oestrogen which is a sex steroid in women is known to lower the plasma concentration of uric acid by enhancing its urinary excretion and as such with advancing age in women, menopause sets in and this uricosuric effect of oestrogen is lost and there is increase in plasma concentration of uric acid.<sup>31</sup> Additional, Adamopoulos et al in their study, focused on the effect of hormone therapy (HT) on uric acid levels in post-menopausal women. In a majority of their study subjects they observed a fall in the plasma uric acid concentration following the administration of conjugated and synthetic eostrogen.<sup>31</sup>

According to the present study, a higher proportion of the subjects with hyperuricaemia compared with subjects with normouricaemia had hypertension, diabetes, impaired fasting glucose, hypertriglyceridaemia, abdominal obesity and BMI=25kg/m<sup>2</sup>. However, these were not statistically significant except for hypertriglyceridaemia (P=0.03). This points to the association of hyperuricaemia with insulin resistance and components of metabolic syndrome. Various researchers have also attributed hyperuricaemia to be a risk factor for the development of Type 2 DM while others see it as a complication of DM. <sup>32-33</sup> In our study, the mean fasting blood glucose was significantly higher in hyperuricaemic subjects. Hypertension was reported in 55 % of hyperuricaemic subjects by Ogbera et al.<sup>22</sup> In the present study, hypertension occurred in 25.6% of the study subjects with hyperuricaemia. This finding in the present study depicts that the prevalence of hypertension is high in hyperuricaemia subjects. The Ogbera et al study was among diabetics as earlier stated and that could account for the higher percentage of hypertension among hyperuricaemic patient as diabetics are at higher risk for microvascular kidney disease and hence hyperuricaemia.28

Various researchers previously have reported a strong relationship between hypertriglycaeridaemia and hyperuricaemia pointing to the role of each of these independently in cardiovascular disease risk.<sup>27,34</sup> This present study demonstrated prevalence of hypertriglycaeridaemia to be significantly higher in hyperuricaemic subjects than normouricaemic subjects.

The correlation analyses for uric acid level showed that waist circumference, total cholesterol and low-density lipoprotein and gender had significant association with uric acid while the logistic regression showed that the male gender was the only significant predictor of hyperuricaemia. In the work by Ebrahimpour et all, waist circumference and total cholesterol among others were also significantly correlated with uric acid in a bivariate analysis.<sup>35</sup>

### CONCLUSION

The prevalence of hyperuricemia is high in this rural community with significantly higher prevalence in males than in females. In males the highest prevalence was noted in the younger age group and declined with advancing age contrary to the female gender that had the lowest prevalence in the younger age group and an increasing pattern with advancing age. A higher proportion of the subjects with hyperuricaemia compared with subjects with normouricaemia had hypertension, diabetes, impaired fasting glucose, hypertriglyceridaemia, abdominal obesity and  $BMI=25kg/m^2$ . However, these were not statistically significant except for hypertriglyceridaemia. This points to the relationship between hyperuricaemia and insulin resistance with other components of metabolic syndrome. Pearson and Spearman' rho correlation analysis of serum uric acid with other parameters revealed that only waist circumference, total cholesterol, low-density lipoprotein and gender had significant association with uric acid and only male gender was found to be significant predictor for hyperuricaemia following a logistic regression. There is need for more research considering the cardiovascular and other implications of hyperuricaemia.

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#### REFERENCE

- 1 Klein R, Klein BE, Cornoni J, Maready J, Cassel JC, Tyroler HA: Serum uric acid, Georgia. Arch Intern Med 1973, 132:401-410.
- 2 Bengtsson C, Lapidus L, Stendahal C, Waldenstrom : Hyperuricemia and risk of cardiovascular disease and overall death. Acta Med Scand 2002, 224:549-555.
- 3 Nakagawa T, Cirillo P, Sato W, Gersch M, Sautin Y, Roncal C: The conundrum of hyperuricemia, metabolic syndrome, and renal disease. Intern Emerg Med 2008, 3(4):313-318
- 4 Mikelson W M, Dodge HJ, Valkenburg H.The

distribution of serum uric acid values in a population unselected as to gout or hyperuricaemia.Am J Med 1965; 39:241-51.

- 5 Hall AP, Barry PE, Dawber TR, McNamara PM. Epidemiology of gout and hyperuricaemia (a long term population study). Am J Med 1967;42:27-37.
- 6 Cannon PJ, Stason WB, Demartini FE, Sommers SC, Laragh JH.Hyperuricemia in primaryand renal hypertension. N Engl J Med 1966; 275:457-464.
- 7 Gertler MM, Garn SM, Levine SA. Serum uric acid in relation to age and physique in health and in coronary heart disease. Ann Intern Med 1951; 34:1421-1422
- 8 Tuttle KR, Short RA, Johnson RJ. Sex differences in uric acid and risk factors for coronary artery disease. Am J Cardiol 2001; 87:1411-1414.
- 9 Terkeltaub RA. Clinical practice. Gout. N Engl J Med 2003; 349: 16471655.
- 10 Mahowald ML. Overview of the evaluation and management of gout and hyperuricemia. Rheumatology &Musculoskeletal Medicine for Primary Care, Gout 2004/10/8 [cited 2005/5/12]; A v a i l a b l e f r o m : http://www.rheumatology.org/publications/primary care/number4/hrh0021498.asp
- 11 Franse LV, Pahor M, DiBari M, et al. Serum uric acid, diuretic treatment and risk ofcardiovascular events in the Systolic Hypertension in the Elderly Program (SHEP). J Hypertens 2000; 18:1149-1154.
- 12 Lai SW, Tan CK, Ng KC. Epidemiology of hyperuricemia in the elderly.Yale J Biol Med 2001;74:151-157.
- 13 Lin KC, Tsai ST, Lin HY, Chou P. Different progressions of hyperglycemia and diabetes among hyperuricemic menand women in the Kinmen study. J Rheumatol 2004; 31: 1159-1165.
- 14 Tseng CH. Independent association of uric acid levels with peripheral arterial disease in Taiwanese patients with Type2 diabetes. Diabet Med 2004; 21: 724-729.
- 15 Langlois M, De Bacquer D, Duprez D, et al. Serum uric acid in hypertensivepatients with and without peripheral arterial disease. Atherosclerosis 2003; 168:163-168.
- 16 Li Y, Stamler J, Xiao Z, Folsom A, Tao S, Zhang H. Serum uric acid and its correlates in Chinese adult populations, urban and rural, of Beijing. The PRC-USA Collaborative Study in Cardiovascular and Cardio-pulmonaryEpidemiology. Int J Epidemiol 1997; 26: 288-296.

- 17 Arromdee E, Michet CJ, Crowson CS, O'Fallon WM, Gabriel SE. Epidemiology of gout: is the incidence rising?J Rheumatol 2002; 29: 2403-2406.
- 18 Chen S, Du H, Wang Y, Xu L. The epidemiology study of hyperuricemia and gout in a community population of Huangpu District in Shanghai. Chin Med J (Engl) 1998;111:228-230.
- 19 Chen SY, Chen CL, Shen ML, Kamatani N. Trends in the manifestations of gout in Taiwan. Rheumatology (Oxford)2003; 42: 1529-1533.
- 20 John Darmawan, Samuel K. Lutalo. Gout and Hyperuricaemia. Bailliere's Clinical Rheumatology.1995:9:83-93.
- 21 Isezuo SA, Ezunu E. Demographic and Clinical Correlates of Metabolic Syndrome in Native African Type-2 Diabetic Patients Journal of the National Medical Association 2005; 97 (4) 563-65
- 22 Ogbera O Anthonia and Alfred O Azenabor. Hyperuricaemia and the metabolic syndrome in type 2 DM. Diabetology & Metabolic Syndrome 2010, 2:24
- 23 Waist Circumference and WaistHip Ratio:Report of a WHO Expert Consultation Geneva, 811 December 2008
- 24 Trinder P. Determination of blood glucose using 4 aminophenazone as oxygen acceptor. J Clin. Path 1969; 22:246.
- 25 Chobanian, AV, Bakris, GL, Black, HR, Cushman, WC. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report. JAMA 2003; 289:2560-72.
- 26 WHO: Definition, Diagnosis and Classification of Diabetes Mellitus and it's Complications. Part 1, WHO,Geneva, 1999
- 27 Nakagawa T, Tuttle KR, Short RA, Johnson RJ. Fructose-induced hyperuricemia as a casual mechanism for the epidemic of the metabolic syndrome. Nat Clin Pract Nephrol 2005; 1:80-86.
- 28 Lee JE, Kim YG, Choi YH, Huh W, Kim DJ, Oh HY. Serum uric acid is associated with microalbuminuria in prehypertension. Hypertension 2006; 47:962-967
- 29 Conen D, Wietlisbach V, Bovet P 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
- 30 Meei-Shyuan Lee, Shih-Chieh Lin, Hsing-Yi Chang, Li-Ching Lyu, Keh-Sung Tsai and Wen-Harn Pan. High prevalence of hyperuricemia in elderly

**Taiwanese.** *Asia Pac J Clin Nutr 2005;14 (3):285-292.* 

- 31 Adamopoulos D, Vlassopoulos C, Seitanides B, Contoyiannis P, Vassilopoulos P. The relationship of sex steroids to uric acid levels in plasma and urine. Acta Endocrinol (Copenh) 1977; 85:198-208.
- 32 Dehghan A, van Hoek M, Sijbrands EJ, Hofman A, Witteman JC: "High serum uric acid as a novel risk factor for type 2 diabetes". Diabetes Care 2008, 31(2):361-362.
- 33 Nakagawa T, Hu H, Zharikov S: "A causal role for

uric acid in fructose-induced metabolic syndrome". American Journal of Renal Physiology 2006, 290(3):625-631.

- 34 Hollister LE, Overall JE, Snow HL: Relationship of Obesity to Serum Triglyceride, Cholesterol, and Uric Acid, and to Plasma-Glucose Levels. American Journal of Clinical Nutrition 1967, 20:777-782.
- 35 Ebrahimpour P, Fakhrzadeh H, Heshmat R, Bandarian F, Larijani B.Serum uric acid levels and risk of metabolic syndrome in healthy adults. Endocr Pract. 2008 Apr;14(3):298-304.