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Serum Uric Acid Levels among Nigerians with Essential Hypertension

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Summary: There is an ongoing debate on the role of serum uric acid as an independent risk factor for hypertension and renal disease. This study determined the serum uric acid levels of Nigerians with essential hypertension and also evaluated the association between serum uric acid levels and blood pressure of these patients. A retrospective case-control study of three hundred and fifty one patients with essential hypertension seen at the hypertension clinic of Aminu Kano Teaching Hospital, Kano between January 2004 and December 2008. The control group comprised of one hundred apparently healthy non hypertensive subjects. The clinical characteristics including blood pressure measurement, serum uric acid, urea, creatinine, lipid profile and glucose were evaluated.The mean systolic and diastolic blood pressures of the male patients were 156mmHg and 101mmHg respectively, while those of the male controls were 120 ± 6.0 and 80 ± 5 respectively. The mean serum uric acid, fasting blood glucose, urea and creatinine were 483umol/L, 5.7mmol/L,6.61mmol/L, 93umol/l respectively compared to those of the male controls which were 326 ±10µmol/l, 5.0± 0.5mmol/l, 4.2± 0.12mmol/l, 5.16mmol/l ± 0.12 and 69±2.71µmol/l respectively. The mean systolic and diastolic blood pressures of the female patients were 158mmHg and 101mmHg, while those of the female controls were 101±2 and 62±9 respectively. The mean serum uric acid, fasting blood glucose, urea and creatinine of the female patients were 434umol/L, 5.3mmol/L 6.20mmol/L, and 88umol/L respectively while those for the female controls were 290±9µmol/l, 4.8±0.5mmol/l, 5.02±0.28 mmol/l, 62±0.36µmol/l respectively. Hyperuricaemia was observed in 59.3% of the male study patients and 62% of the female study patients. Serum uric acid correlated positively with both systolic blood pressure ($r=0.192$, $p<0.001$) and diastolic blood pressure ($r=0.216$; $p<0.001$). Hyperuricaemia is common among Nigerian patients with essential hypertension and there is an association between serum uric acid level and blood pressure. Further studies on the pathophysiologic significance of hyperuricaemia in these patients are recommended.

Keywords*:* Essential hypertension, Hyperuricaemia, Nigeria

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INTRODUCTION

High blood pressure has emerged as one of the major health problems in Nigeria. The prevalence rate among Nigerians was put at up to 15% and this rate may not be a true representation of the magnitude of the problem (Akinkugbe,2000). Studies have shown that Serum Uric Acid (SUA) levels play a very important role in the development of cardiovascular morbidity and renal disease progression both in the general population and in patients with hypertension (Liese et al.,1999; Alderman et al.,1999; Verdecchia et al., 2000; Franse et al., 2000; Puddu et al., 2001; Niskanen et al., 2004). Some studies have observed that an elevated SUA level is an independent risk factor for hypertension and renal disease after controlling for confounders, while findings from another study doubted the contribution of uric acid as an independent risk factor for hypertension (Hunsicker et al.,1997; Johnson et al., 1999; Appel et al., 2003; Mellen et al., 2006; Oppathan et al., 2008). Increases in SUA have been reported elsewhere in hypertensive patients. For example in some studies, it was observed that about 20- 89% of hypertensive individuals have increased SUA (Oppathan et al., 2008). A more strong association between hyperuricaemia and the development of hypertension has been reported in blacks (Mellen et al., 2006). The relationship between the SUA level and the blood pressure in our hypertensive patients have not been previously studied, hence the basis for this study. Our objective was to determine the serum uric acid levels of Nigerians with essential hypertension and to evaluate the association between SUA levels and blood pressure of these patients.

MATERIALS AND METHODS

Three hundred and fifty one patients with essential hypertension were retrospectively studied over a

period of 5 years (January 2004 to December 2008). They were patients referred to hypertensive clinic of Aminu Kano Teaching Hospital who were above 18 years of age and their initial laboratory assessment done at the chemical pathology laboratory included serum uric acid levels among other investigations. The medical records of the patients were reviewed to retrieve other information including the medical history, age, sex and blood pressure at the time of the laboratory assessment. Those patients with diabetes mellitus and those on any antihypertensive medication known to affect SUA level were excluded. Fifty apparently healthy males and fifty females with normal blood pressure and of similar age group were used as controls. Five milliliters of fasting veinous blood was collected from the antecubital vein. The blood specimens were allowed to clot at room temperature for 30 minutes and sera were obtained after centrifugation at 1000g for 10minutes. The sera were used for the evaluation of uric acid, glucose, urea, creatinine, triglycerides, total cholesterol and HDL cholesterol using *Chiron express plus chemistry* autoanalyser by *Chiron diagnostics,* USA. The LDL cholesterol was calculated using Friedewald's formula (Friedewald et al.,1972).

Statistical analysis

The data was analyzed using SPSS version 11. Student's t test was used to compare the means of the study group with the control and level of significance set at $p< 0.05$. Serum uric acid levels were correlated with both systolic and diastolic blood pressure using Pearson's correlation.

RESULTS

There were one hundred and seventy seven males and one hundred and seventy four females. The ages of the males ranged from 27 years to 75years with a mean of 51.2 ± 12.1 years, while the ages of the females ranged from 18 years to 84 years with a mean of 51.8± 16.4 years. The mean age of the male controls was 50 ± 8.4 years, while that of the female controls was 51.2± 7.2 years. Table 1 depicts the blood pressure and laboratory features of both the patients and the controls. Statistically significant differences were observed when all the variables apart from glucose were compared with the controls in male subjects ($p<0.001$). Statistically significant differences were also observed when all the variables but glucose and urea were compared in the female patients with the control subjects (table 1). Out of the 177 male patients, 105 (59%) had serum uric acid above the upper limit of the reference range (202-

Table 1: Blood Pressure, Serum Uric Acid, Lipid profile in patients with essential hypertension and control subjects (Mean± SEM)

	Male		Female	
Variables	Patient	Controls	Patient	Controls
SBP (mmHg)	156± 6*	120± 6.0	158 ±15*	78 ±9
DBP (mmHg)	101± 6*	80± 5	101± 2*	62± 9
SUA (µmol/L)	483± 20.3*	326± 10	434± 21.8*	290± 9
Urea (mmol/L)	6.61± 0.21*	5.16± 0.12	6.20± 0.36	5.02± 0.28
Creatinine (µmol/L)	93± 2.12*	69± 2.71	88± 1.21*	62± 1.81
TC (mmol/L)	5.16± 0.16*	4.20±.0.12	5.25± 0.16	4.4± 0.14
TG (mmol/L)	1.38± 0.09*	1.0 ± 0.08	1.10± 0.06	1.0± 0.08
HDLC (mmol/L)	1.17± 0.05*	1.2± 0.06	1.26± 0.06	1.31± 0.03
LDL C (mmol/L)	3.33± 0.13*	2.52± 0.16	3.44± 0.12*	2.68± 0.04

* $p<0.001$, SBP = systolic blood pressure, DBP= Diastolic blood pressure, SUA= serum uric acid, TC= total cholesterol, , TG= Triglycerides, HDLC= High density lipoprotein cholesterol, LDLC=Low density lipoprotein cholesterol.

Table 2: Characteristics of Study Patients on the basis of Uric Acid levels and Gender

	Male		Female	
Variables	Abnormal	Normal	Abnormal	Normal
SBP (mmHg)	157± 8	156± 6	157± 12	156±10
DBP (mmHg)	102± 4	101± 5	101± 2	101± 4
SUA (µmol/L)	576± 23.3*	348± 10.3	490± 20.9*	253± 15.7
Urea (mmol/L)	7.81± 0.07*	5.22± 0.12	7.22± 0.21*	5.1 ±0.08
Creatinine (µmol/L)	113± 2.16*	72± 2.07	110± 2.21*	69±1.16
Glucose (mmol/L)	5.76± 0.16	5.61± 0.29	5.32± 0.22	5.04± 0.38
TC (mmol/L)	5.05± 0.21	5.33± 0.26	5.36± 0.26	5.04± 0.38
TG (mmol/L)	1.62±0.15***	1.20±0.12	1.04±0.05	1.23±0.19
HDLC (mmol/L)	1.14± 0.07	1.23± 0.06	1.27± 0.08	1.21± 0.12
LDL C (mmol/L)	3.14± 0.02	3.53± 0.21	3.53± 0.14**	3.10± 0.27

* $p<0.001$, ** $p<0.005$, *** $p<0.01$, SBP = systolic blood pressure, DBP= Diastolic blood pressure, SUA= serum uric acid, TG= Triglycerides, TC= total cholesterol, HDLC=High density lipoprotein cholesterol, LDLC=Low density lipoprotein cholesterol.

416µmol/l). Statistically significant difference was observed when serum uric acid, urea, creatinine and triglyceride of the patients were compared with the 72 patients whose uric acid levels were within the normal limits of the reference range, $p<0.001$ and $p<0.01$ respectively as shown in table 2.

A total of 108 (62%) out of the 174 female patients had SUA above the upper limit of the reference range (162-339µmol/l). Statistically significant difference was observed when SUA, urea, creatinine and LDL cholesterol of the patients were compared with the patients whose uric acid was within the reference limit $p<0.001$ and $p<0.005$ respectively. Significantly positive correlation was observed for both between SUA and systolic blood pressure ($r=0.192$; $p<0.001$) and between SUA and diastolic blood pressure ($r=0.216$; $p<0.001$).

DISCUSSION

This study demonstrates that SUA was significantly increased in patients with essential hypertension in Nigeria, with 59% of male hypertensive patients and 62% of female patients having elevated SUA. This finding is consistent with that observed by others where hyperuricaemia was observed in 50% to 70% of hypertensive patients (Oppathan et al., 2008). Some schools of thought have viewed elevated uric acid as a secondary phenomenon that is beneficial, since uric acid is an antioxidant. Studies have shown that hyperuricaemia is one of the most important risk factors for cardiovascular disease and plays significant role in the development of hypertension. Several mechanisms have been suggested on the role of hyperuricaemia in the induction of systemic hypertension and renal injury. Elevated SUA lowers endothelial nitric oxide levels, reducing neuronal nitric oxide synthase in the macuna densa of the kidney and stimulates the rennin-angiotensin system. This mechanism was demonstrated in animal studies where rats developed high blood pressure in about 3 to 5 weeks after raised uric acid levels was induced by the administration of oxonic acid which is an inhibitor of Uricase (Mazzali et al.,2001).The experimental rats developed renal microvascular disease overtime. Even though several authorities such as the Joint National committee on prevention, Detection, Evaluation and Treatment of high blood pressure and the American Heart Association have not recognized elevated uric acid as an important risk factor for CAD or renal disease, emerging data suggest that hyperuricaemia may in fact be one of the important risk factor for CAD in these patients (Heinig and Johnson, 2006). Elevated SUA was significantly associated with cardiovascular events and mortality in hypertensive patients. Studies in humans with asymptomatic hyperuricaemia have also demonstrated association with essential hypertension, obesity, kidney disease, CAD and metabolic syndrome (Mazzali et al., 2001).In addition, Baker JF *et al.(*2005*)* in a review reported several studies in which elevated uric acid was associated with hypertension. Hyperuricaemia is also associated with the presence of target organ damage in hypertensive patients. Viazzi *et al.(2005)* observed that patients with target organ damage demonstrated by left ventricular hypertrophy, carotid atherosclerosis and microalbuminaemia had significantly higher levels of SUA as compared with those without target organ damage regardless of other known cardiovascular risk factors. One of the limitations of our study is its retrospective nature hence we did not compare the presence of target organ damage and SUA.

Our result has shown that more women than men had elevated SUA in the study population. This is in agreement with other reports (Persky et al.,1979; Ruilope and Garcia-Puig, 2001). However a more robust association of uric acid with electrocardiographic abnormalities and coronary atherosclerosis was reported in women (Persky et al., 1979). An interaction between sex hormones and pathophysiological mechanisms linking uric acid to cardiovascular damage may be implicated. Although total cholesterol, triglyceride and other lipoproteins were within normal limits of the reference ranges, statistically significant differences were observed when compared in those with elevated SUA and those without it. Serum uric acid has been shown to be associated with lipid level even in normal subjects (Russo et al., 1996). It is also known to be associated with lipids and other components of the metabolic syndrome (Nakanishi et al., 2003; Johnson et al., 2003). Studies of possible association between lipid and high blood pressure have yielded different conclusions. This may be due to differences in the patient's characteristics such as age, sex, risk factor levels and geographical location.

This study shows that SUA level is elevated in most patients with essential hypertension irrespective of the sex. We also noted a positive correlation between the SUA level and both the diastolic and systolic BP.

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