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RESEARCH ARTICLE

EVALUATION OF SELECTED RENAL MARKERS IN HYPERTENSIVE SUBJECTS IN EKITI STATE, NIGERIA

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ABSTRACT: Hypertension has become a serious health challenge in the 21st century because it may cause organ damage as it progresses and could result in increased morbidity and mortality. The study evaluated selected renal markers (urea, creatinine, uric acid and cystatin C) in hypertensive subjects relative to control. A total of 92 subjects were investigated consisting of 31 hypertensive subjects on treatment, 31 hypertensives not on treatment and 30 apparently healthy subjects who served as control subjects. The levels of urea, creatinine and uric acid were determined using spectrophotometric methods while cystatin C was analyzed using enzyme linked immunoassay (ELISA) technique. Blood pressure and body mass index (BMI) were also measured in addition to the selected markers. The results showed that urea, uric acid, blood pressure and BMI were significantly higher at $p<0.05$ while creatinine and cystatin C did not show significant difference ($p>0.05$) in hypertensive subjects compared with control. It was concluded that urea, uric acid, blood pressure and BMI were significantly high in hypertension. Measurement of these markers could be helpful in identification of patients at high risk of developing renal complications associated with hypertension.

KEYWORDS: hypertension, urea, creatinine, uric acid, cystatin C

INTRODUCTION:

Hypertension has become a serious health challenge in the 21st century because it is a chronic elevation of blood pressure that, in the long term, causes organ damage and could results in increased morbidity and mortality. It is the end product of cardiac output and systemic vascular resistance.[1] The prevalence of hypertension in Nigeria has been shown to range from 8-46.4% which depends on the study population, type of measurement and the cut-off value used for defining hypertension.[2] Complications from hypertension are usually seen in patients who undergo inadequate hypertensive treatment or patients who discontinue their medications.[3] These complications of hypertension are clinical outcomes that result from persistent elevation of blood pressure.[4] Hypertension affects the structures and

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functions of small vascular arteries, arterioles and other blood vessels and can cause damage at variable rate to various target organs including kidney, brain and eye, related with the end stage of renal disease and to be the cause of stroke.[5,6] Chronic diseases such as hypertension have been shown to be a major cause of death worldwide as a result of changes in the systems and organs of the body.[7] A lot of variations may occur in the levels of blood parameters during hypertension such as changes in the levels of demographic parameters (blood pressure, BMI etc) and renal markers (urea, creatinine, uric acid, and cystatin C).

Urea is used as a marker of renal function, although some researchers believed that it is inferior to other markers such as creatinine because blood urea levels are influenced by other factors such as diet and dehydration. [8,9] The cycling and excretion of urea by the kidneys is a vital part of mammalian metabolism.

Serum creatinine is used in the detection and assessment of acute kidney injury and chronic kidney disease. [10,11] Creatinine is a by-product of energy metabolism that is filtered from the blood by kidneys and is excreted into the urine.[12] Creatinine is removed from the body entirely by the kidneys and if kidney function is abnormal, creatinine level will increase in the blood.[12]

Increased level of uric acid has been associated with the metabolic syndrome and implicated as a risk factor in the etiology of hypertension, atherosclerosis, insulin resistance, diabetes mellitus, and kidney disease. [13,14] Hyperuricemia has been shown to be one of the risk factors for the development of prehypertension, primary hypertension, and resistant hypertension. [15,16,17]

Decrease in cystatin C levels on the other hand has been suggested to predict the risk of developing chronic kidney disease and cystatin C could be used to evaluate and classify kidney diseases.[18,19] Previous studies have also investigated cystatin C as a marker of kidney function in the adjustment of medication dosage.[20] Since there has been increase in renal complications due to hypertension, the study evaluated the levels of selected renal markers and anthropometric parameters (blood pressure and BMI) in hypertension Ekiti State.

MATERIALS AND METHODS:

A total of 92 subjects were investigated in adults who were between ages 18-50 years. Ethical approval was sought for and obtained from the ethical committee of College of Medicine and Health Sciences, ABUAD. The subjects consisted of 31 hypertensives on diuretic treatment (Amiloride hydrochloride 5mg and hydrochlorothiazide 50mg taken once daily for not less than six months), 31 hypertensives not on treatment and 30 apparently healthy subjects who served as control subjects. Convenient random sampling was used to recruit the subjects but excluded pregnant women, nursing mothers, diabetes mellitus subjects and other disease conditions. Systolic and diastolic blood pressure measurements were taken using wrist sphygmomanometer (Hans Dinslage GmbH, Germany). The weight and height were determined using bathroom weight scales and height gauge (Pasco Scale Co., Ltd, India) respectively. The body mass index (BMI) was calculated for each individual using weight/height (kg/m^2). Five milliliters (5ml) of venous blood sample was collected from the subjects, allowed to clot, and centrifuged at 3000 rpm for 5 minutes to separate the serum from cells. The samples were stored at a temperature of -20 ^oC until analysis. All sample analysis was carried out in the laboratory of the Medical Laboratory Science Department, Afe Babalola University.

Analysis of parameter

Urea was estimated using spectrophotometric method.[21]

Creatinine was estimated using spectrophotometric method.[22]

Uric acid was estimated using spectrophotometric method.[23]

Cystatin C was determined using enzyme linked immunosorbent assay technique.[24]

Statistical analysis

Results obtained for both anthropometric and renal parameters were subjected to statistical analysis using statistical package for social sciences version 23 (SPSS Inc. Chicago, Illinois, USA). Analysis of variance (ANOVA) between the three groups was done and results were presented on charts and tables. Correlation analysis was carried out to describe the association or relationship between parameters. All parameters were expressed as mean ±SD and values were found to be statistically significant at $p<0.05$ or $p<0.01$.

RESULTS:

Figure 1 shows anthropometric and renal parameters in hypertensive subjects and control. There was significant increase ($p<0.05$) in the levels of systolic and diastolic Bp, BMI, urea and uric acid but there was no significant difference in the levels of creatinine and cystatin C.

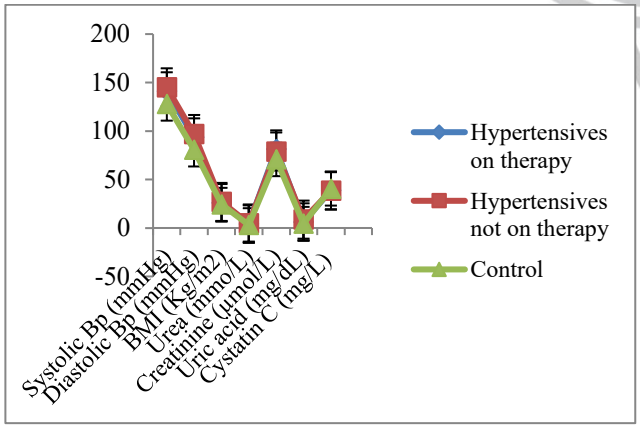

Figure 1 : Anthropometric and selected renal markers in hypertensive and control subjects.

Figure 2 shows the levels of systolic and diastolic Bp, BMI, urea, creatinine, uric acid and cystatin C in hypertensive subjects based on gender. There was no significant difference ($p>0.05$) in the levels of systolic Bp, urea, creatinine, uric acid and cystatin C in females compared with males.

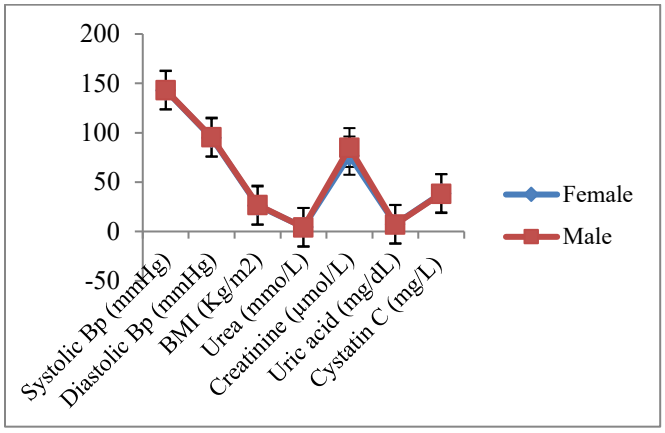

Figure 2 : Anthropometric and selected renal markers in hypertensive subjects according to gender.

Table 1 shows the correlation between anthropometric and renal markers in hypertensive subjects. Systolic blood pressure shows significant positive correlation ($p<0.01$) with diastolic blood pressure. Urea also shows significant positive correlation ($p<0.01$) with creatinine.

Table 1: Correlation between parameters in hypertensive subjects

		BMI	Systolic Bp	Diastolic Bp	Urea	Creatinine	Uric acid	Cystatin C
BMI	r	1.000	0.028	-0.061	0.243	0.074	0.135	0.072
	p	-	0.832	0.636	0.057	0.567	0.297	0.580
Systolic	r	0.028	1.000	0.564**	-0.033	-0.239	0.208	0.044
Bp	p	0.832	-	0.000	0.799	0.061	0.104	0.732
Diastolic	r	-0.061	0.564**	1.000	0.054	-0.068	0.096	-0.041
Bp	p	0.636	0.000	-	0.676	0.600	0.456	0.752
Urea	r	0.243	-0.033	0.054	1.000	0.489**	0.155	0.087
	p	0.057	0.799	0.676	-	0.000	0.230	0.503
Creatinin	r	0.074	-0.239	-0.068	0.489**	1.000	0.025	0.101
e	p	0.567	0.061	0.600	0.000	-	0.848	0.435
Uric acid	r	0.135	0.208	0.096	0.155	0.025	1.000	-0.062
	p	0.297	0.104	0.456	0.230	0.848	-	0.633
Cystatin	r	0.072	0.044	-0.041	0.087	0.101	-0.062	1.000
C	p	0.580	0.732	0.752	0.503	0.435	0.633	-

**= Correlation is significant at $p< 0.01$ level; N = 62

Table 2 shows correlation between anthropometric and biochemical parameters in control subjects. Systolic blood pressure shows significant positive correlation ($p<0.01$) with diastolic blood pressure and uric acid. Urea also shows significant positive correlation ($p<0.01$) with creatinine.

Table 2: Correlation between parameters in control subjects

		BMI	Systolic Bp	Diastolic Bp	Urea	Creatinine	Uric acid	Cystatin C
BMI	R	1.000	0.334	0.137	0.307	0.321	0.013	0.202
	P	-	0.072	0.471	0.099	0.084	0.944	0.285
Systolic Bp	R	0.334	1.000	0.647**	-0.052	0.185	0.452*	-0.222
	P	0.072	-	0.000	0.787	0.327	0.012	0.239
Diastolic Bp	R	0.137	0.647**	1.000	-0.045	0.176	0.198	-0.116
	P	0.471	0.000	-	0.813	0.351	0.294	0.541
Urea	R	0.307	-0.052	-0.045	1.000	0.690**	-0.041	-0.078
	P	0.099	0.787	0.813	-	0.000	0.831	0.680
Creatinine	R	0.321	0.185	0.176	0.690**	1.000	0.026	-0.095
	P	0.084	0.327	0.351	0.000	-	0.892	0.616
Uric acid	R	0.013	0.452*	0.198	-0.041	0.026	1.000	-0.178
	P	0.944	0.012	0.294	0.831	0.892	-	0.348
Cystatin C	R	0.202	-0.222	-0.116	-0.078	-0.095	-0.178	1.000
	P	0.285	0.239	0.541	0.680	0.616	0.348	-

**= Correlation is significant at p< 0.01 level; N = 30

DISCUSSION:

In this study, the analysis of variance (illustrated figure 1) showed that there was no significant difference in BMI, Systolic and diastolic blood pressure, urea, creatinine and cystatin C when hypertensives subjects on therapy were compared with those not on therapies. Significant increases were found in both systolic and diastolic blood pressure in hypertensive subjects on therapy compared with control while there was no significant difference when the other parameters were compared in the subjects. When hypertensive subjects not on therapy were compared with control, there were significant increases in the levels of BMI, systolic and diastolic blood pressure, urea and uric acid but there was no significant difference in other parameters. The systolic and diastolic blood pressures were found to be significantly higher in hypertensive subjects (with or without therapy) compared with control. This research agrees with previous works where systolic and diastolic blood pressures were seen to be significantly higher in hypertensives compared with control. [25,26] Also, there was positive correlation between systolic and diastolic blood pressure which is in line with a previous study.[26] This is expected since the subjects are hypertensive. The BMI of hypertensive subjects on therapy and not on therapy were significantly higher when compared with control subjects. These findings support previous findings where increase in BMI had been obtained. [27,28,29] Increased BMI has been associated with increase in blood pressure and this has been linked with rapid economic development and modernization with changing life styles according to a previous study [29]. The study did not record significant positive correlations between BMI and blood pressure in both hypertensive subjects and control. Thus, this work did not record a strong association like the work which reported a strong relationship between BMI and blood pressure.[29] Serum urea was significantly higher in hypertensive subjects compared with control subjects. Urea has been shown to be a marker of renal function, although some researchers believed that it is inferior to other markers such as creatinine because blood urea levels are influenced by other factors such as diet and dehydration.[30] Serum creatinine was higher in hypertensive subjects compared with control but not significant. This may be an indication of renal involvement because serum creatinine has proven to be useful in the detection and assessment of acute kidney injury and chronic kidney disease. [10,11] The findings are similar to other reports which showed that creatinine levels were significantly higher in hypertensive subjects. [31,32] The study also recorded a positive significant correlation of urea and creatinine in hypertensive subjects and control.

Uric acid showed significant increase in hypertensive subjects compared with control. There was also positive significant correlation between diastolic blood pressure and uric acid in control subjects.

Previous studies showed that increased uric acid is an independent risk factor for cardiovascular disease (CVD) and metabolic syndrome. [33,34] Only uric acid showed significant increase when hypertensive subjects not on therapy were compared with those on therapy indicating that those on therapy have benefitted from the antihypertensive agent. Serum uric acid has been shown to be independently associated with the risk of chronic kidney disease and lowering blood pressure has been shown to reduce the risk of cardiovascular morbidity and mortality.[35,36]

Several studies have shown that serum cystatin C is a better marker for glomerular filtration rate than serum creatinine particularly for individuals with small to moderate decrease in glomerular filtration rate.[32] Cystatin C level did not show significant decrease in hypertensive subjects compared with control. The reason for this may be that the subjects still possess normal glomerular filtrate function. Besides, there was no significant correlation between Cystatin C and other parameters in this study.

The study also assessed the parameters based on gender. There was no significant difference in the levels of systolic and diastolic BP, urea, creatinine, uric acid and cystatin C in females when compared with males.

In all, the increased levels of the renal markers (urea, creatinine and uric acid) and decreased cystatin C in hypertensive subjects compared with control subjects should be well managed so that the subjects do not loss their renal functions or progress to developing kidney disease. This is in line with a previous study where renal profile was carried out in hypertensive subjects.[37] Therefore; the study concluded that there is need for evaluation of these markers (blood pressure, BMI, urea, uric acid, creatinine and cystatin C) in hypertension. Serum urea, uric acid, blood pressure and BMI were significantly high while creatinine and cystatin C did not show significant difference in hypertensive subjects compared with control. Measurement of the selected markers could be helpful in identification of patients at high risk of developing renal complications associated with hypertension.

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