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Biochemical markers of liver and kidney functions in Nigerian hypertensive patients

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ABSTRACT

Plasma albumin, total protein, total globulin, urea, creatinine and uric acid, concentrations were assayed by standard spectrophotometric methods as simple biochemical indicators of liver and kidney functions of 103 hypertensive patients (44 males; 59 females) and 88 apparently healthy subjects (40 males; 48 females). Additionally Plasma sodium (Na^+) and potassium (K^+) were determined by flame photometry. The healthy and the hypertensive subjects were recruited from Abeokuta and Ibadan (South-Western Nigeria). The subjects were classified into male and female subgroups. The mean age of the hypertensive patients was 41.9 ± 10.3 (range 21-68) years, while the mean age of the healthy subjects was 37.8 ± 8.6 (range 18-52) years. The weight and height of all subjects were measured and their body mass indices (BMI) computed. The levels of plasma albumin, urea and uric acid were significantly higher in the hypertensive patients than in healthy group ($P<0.05$, $P<0.001$ and $P<0.001$ respectively). The mean levels of plasma Na^+, K^+, total protein and creatinine were not significantly different in both groups. Raised albumin levels in hypertensives probably reflected the total antioxidant defence system that may be increased due to oxidative stress associated with this disorder, while higher level of urea and uric acid in hypertensives were probably due to extra-renal causes, since creatinine a better index of renal pathology is similar in both groups.

Keywords: Liver, Kidney, Biochemical markers, Hypertensives.

INTRODUCTION

The liver is the largest organ in the body. It is involved with almost all of the biochemical pathways that allow growth, fight disease, supply nutrients, provide energy, and aid reproduction (Bock et al., 1993; Babalola et al., 2003). Both the liver and kidney are important organs of metabolism, detoxification, storage and excretion of nutrients, xenobiotics and their metabolites, and are especially vulnerable to damage (Brzóska et al., 2003).

The study was designed to evaluate the liver and kidney functions in clinical condition known as essential hypertension. There is increased incidence of this disease in this environment. (Babalola et al., 2007).

In most pathologic conditions, the two organs are usually affected; in fact indices of renal function, such as, serum urea and creatinine have been one of the numerous routine biochemical tests for hypertensive patients. This study is expected to advance our understanding of the different complications associated with the disease, and probably, come up with new approaches to its diagnosis, management and treatment.

MATERIALS AND METHODS

Selection of hypertensive patients

One hundred and three adult Nigerians of both sexes aged between 21 and 68 years with essential hypertension were selected for the study. All patients were examined by the

consultant physicians and their complete medical history and physical examination were documented. The diagnosis of essential hypertension was based on at least two separate blood pressure readings within a minimum of two weeks intervals and laboratory examinations. The patients were considered to be hypertensive as defined by an average of two or more diastolic blood pressure in the range of 90-120 mmHg and/or the average of multiple systolic blood pressures in the range of 140-200 mmHg in the sitting position, on two of more subsequent visits to the clinic.

They were recruited from Federal Medical Centre (F.M.C), Abeokuta, Abi Memorial Hospital, Abeokuta and University College Hospital (U.C.H), Ibadan. These comprised of newly diagnosed patients and those that were previously on antihypertensive agents such as Propranolol and Moduretic.

The following exclusion criteria were employed in this study:

(i) All cases of hypertension secondary to other diseases were excluded from the study.

(ii) Patients with history of alcoholism, cigarette smoking, drug abuse or any form of mental disorder.

(iii) Patients with angina pectoris.

(iv) Female patients were neither pregnant nor lactating mothers nor on any oral contraceptives at the time of the study.

(v) All obese patients (BMI of patients not $\geq$ 27 kg/m^2).

(vi) Patients with diabetes mellitus.

(vii) Patients with evidence of renal disease.

The following Inclusion Criteria was also adopted:

Participation in the study was purely voluntary. Informed consents were obtained from patients after they were properly educated about the benefit of the study. .

Selection of healthy subjects group (controls)

These consist of eighty-eight apparently healthy subjects of both sexes, aged between 18 and 52 years. The subjects were all apparently healthy with their blood pressure in the normal range. They were all non-smokers and non-alcoholics and were mainly students, office workers and traders. They were not taking any medication during the period of the study. The control group was selected as much as possible to match the hypertensive group in age, sex and BMI. Their blood pressure and pulse rates were similarly measured at the time of sample collection. Also, none of the apparently healthy subjects was obese. They were also classified into male and female subgroups. Inform consents were obtained from all participants after being educated on the benefit of the study.

Anthropometric indices

The current ages of the subject were noted. Also the current body weights were measured with minimal clothing using a balance beam scale. Heights were also measured barefooted, using a meter rule. Height (m) and Weight (kg) were used to calculate the body mass index (BMI) (kg/m^2).

Collection of blood

About 10ml of venous blood was obtained from the antecubital fossa vein using disposable pyrogen-free needle and syringes, blood sample was dispensed into plain vacutainer tube containing EDTA to prevent coagulation. The sample was centrifuged at 450 g in IEC centrifuge, for about 5 min to obtain supernatant plasma, which was transferred with a pipette into plain vacutainer tubes and then frozen. Samples were kept frozen at -70 °C until analyzed.

Albumin determination

The sigma bromocresol purple BCP albumin procedure used in this study is a modification of that of Pinnell and Northam (1978).

Total Protein Determination

The most commonly used methods for total protein determination is based on biuret reaction (Cannon et al., 1974). This method was adopted for this study.

Total globulin determination

Total globulin was calculated by subtracting the albumin value from total protein value. Total globulin (g/l) = Total protein (g/l) - Albumin (g/l).

Determination of urea in plasma

Urea concentration in plasma was determined by the method of Coulombe and Favreau (1963).

Determination of creatinine in plasma

Creatinine concentration in plasma was determined by the method of Taussky (1956).

Determination of uric acid in plasma

Uric acid concentration in plasma was determined by the method of Henry et al. (1957).

Determination of sodium and potassium in plasma

Sodium and Potassium in plasma were determined by Flame Photometry.

Statistical Analysis

Results were expressed as mean ± standard deviation (SD). Student t-test was used to determine significance between means. The 5% ($p<0.05$) level of significance using the two-tailed 't' table was used to compare the calculated and critical 't' value from the table and thus statistical significance.

RESULTS

Table 1 shows the results of the anthropometrics indices of the healthy and the hypertensive subjects. All of the quantities were statistically similar except for slightly higher mean age of the hypertensives. Table 2 shows the comparison of the levels of Plasma Total Protein, Albumin, Total Globulin, Creatinine, Urea, Uric acid, Sodium and Potassium in Healthy and Hypertensive Subjects. The mean values of the plasma albumin, urea and uric acid are significantly higher in hypertensive than in healthy subjects. Table 3 shows the comparison of all these parameters between hypertensive males and females respectively. Table 4 and 5 show the comparison of all the parameters between healthy and hypertensive males: and healthy and hypertensive females respectively. The trend in tables 3, 4 and 5 appear similar to that of table 2 except for table 3 where the mean plasma urea is similar for the two groups that were compared.

DISCUSSION

In this study mean values of total protein, total globulin, creatinine, sodium and potassium were similar for both hypertensive patients and healthy group. However, the mean values of albumin, urea and uric acid were significantly higher in hypertensive patients than in healthy group.

Urea is formed almost solely in the liver from the catabolism of amino acids, and is the main excretory product of protein catabolism. The concentration of urea in blood plasma represents a balance between urea formation from protein catabolism and urea excretion. The reference range for plasma urea in this environment is 2.5-7.1 mmol/l. Renal disease of any kind that is associated with a fall in the glomerular filtration rate will lead to decreased excretion of urea and expected to cause high plasma urea. Plasma urea can also increase with age in absence of detectable renal disease; it can also increase in trauma or as a result of increased protein catabolism.

Table 1: Age, weight, height and body mass index (BMI) of healthy and hypertensive subjects.

	Healthy Subjects (n = 88)	**Hypertensive Subjects (n = 103)**	**P**
Age (years)	37.8 ± 8.6 (18 – 52)	41.9 ± 10.3 (21 – 68)	P<0.01
Weight (kg)	62.2 ±9.3 (42 – 78)	64.3 ± 10.7 (56 – 78)	NS
Height (metres)	1.66 ± 0.09 (1.45 – 1.80)	1.65 ± 0.07 (1.45 – 1.75)	NS
Body Mass Index BMI (kg/m^2)	21.06 ± 2.74 (15.57 – 26.70)	21.57 ± 3.84 (18.83 – 26.92)	NS

Values are in mean ± SD, n = No. of Subjects, BMI = Body Mass Index, SD = Standard Deviation, NS = No significant difference.

Table 2: Plasma total protein, albumin, total globulin, creatinine, urea, uric acid, sodium and potassium in healthy and hypertensive subjects.

	Healthy Subjects (n = 88)	**Hypertensive Subjects (n = 103)**	**P**
Total Protein (g/l)	76.1 ± 7.3 (61.3 – 85.6)	76.5 ± 8.5 (52.9 – 81.8)	NS
Albumin (g/l)	46.1 ± 10.2 (33.3 – 59.7)	48.6 ± 6.6 (29.3 – 57.8)	<0.05
Creatinine (μmole/l)	28.6 ± 3.2 (27.9 - 30.2)	29.4 ± 5.6 (26.6 - 31.6)	NS
Total Globulin (g/l)	62.5 ± 19.9 (26.5 – 114.9	63.3 ± 16.5 (26.5 – 114.9)	NS
Urea (mmole/l)	4.4 ± 1.6 (2.3 – 7.3)	5.9 ± 1.5 (3.8 – 9.3)	<0.001
Uric acid (mg/l)	43.2 ± 2.8 (31.8 – 49.8)	56.9 ± 3.0 (49.3 – 69.1)	<0.001
Na^+ (mmole/l)	137.3 ± 2.0 (135 – 140)	137.7 ± 2.0 (135 – 148)	NS
K^+ (mmole/l)	4.9 ± 0.5 (3.8 – 5.2)	4.8 ± 0.3 (3.8 – 5.5)	NS

Values are in mean ± SD, NS = No significant difference, n = No of Subjects, Na^+ = Sodium ion, K^+ = Potassium ion.

Table 3: Comparison of plasma total protein, albumin, creatinine, urea, uric acid, sodium and potassium in hypertensive males and hypertensive females.

	Hypertensive Males (n = 44)	**Hypertensive females (n = 59)**	**P**
Total Protein (g/l)	76.6 ± 4.1	75.1 ± 6.1	NS
Albumin (g/l)	46.6 ± 6.8	49.3 ± 6.6	<0.01
Creatinine (μmole/l)	63.4 ± 9.4	63.2 ± 10.6	NS
Urea (mmole/l)	5.8 ± 1.4	5.9 ± 1.6	NS
Uric acid (mg/l)	58.2 ± 2.9	53.4 ± 1.8	<0.001
Na^+ (mmole/l)	136.2 ± 1.8	136.8 ± 2.0	NS
K^+ (mmole/l)	4.8 ± 0.3	4.8 ± 0.3	NS

Values are in mean ± SD, NS = No significant different, n = No of Subjects, Na^+ = Sodium ion, K^+ = Potassium ion.

Table 4: Comparison of plasma total protein, albumin, creatinine, urea, uric acid, sodium and potassium in healthy and hypertensive males.

	Healthy males (n = 40)	**Hypertensive males (n = 44)**	**P**
Total Protein (g/l)	76.4 ± 4.1	76.6 ± 4.1	NS
Albumin (g/l)	43.2 ± 8.4	46.6 ± 6.8	<0.01
Creatinine (μmole/l)	63.2 ± 10.1	63.4 ± 9.4	NS
Urea (mmole/l)	4.8 ± 0.8	5.8 ± 1.4	<0.001
Uric acid (mg/l)	49.2 ± 4.2	58.2 ± 2.9	<0.001
Na^+ (mmole/l)	134.3 ± 2.0	134.2 ± 1.8	NS
K^+ (mmole/l)	4.9 ± 0.5	4.8 ± 0.3	NS

Values are in mean ± SD, NS = No significant different, n = No of Subjects, Na^+ = Sodium ion, K^+ = Potassium ion.

Table 5: Comparison of plasma total protein, albumin, creatinine, urea, uric acid, sodium and potassium in healthy and hypertensive females.

	Healthy females (n = 48)	Hypertensive females (n = 59)	P
Total Protein (g/l)	74.2 ± 4.5	75.1 ± 6.1	NS
Albumin (g/l)	43.6 ± 4.4	49.3 ± 6.6	<0.001
Creatinine (μmole/l)	63.1 ± 14.2	63.2 ± 10.6	NS
Urea (mmole/l)	4.3 ± 0.9	5.9 ± 1.6	<0.001
Uric acid (mg/l)	43.8 ± 4.0	53.4 ± 1.8	<0.001
Na^+ (mmole/l)	137.8 ± 2.2	136.8 ± 2.0	NS
K^+ (mmole/l)	4.8 ± 0.4	4.8 ± 0.3	NS

Values are in mean ± SD, NS = No significant different, n = No of Subjects, Na^+ = Sodium ion, K^+ = Potassium ion.

In this study, the mean urea concentration of the hypertensive patients was significantly higher than those of healthy subjects. It is probable that the higher level of urea in hypertensive patient was due to extra-renal causes, since creatinine a better index of renal pathology is not significantly different between the two groups, it may be due to the age of the patient, since plasma urea increase with age or due to dehydration or some degree of hemolysis in the hypertensive patients.

Plasma urea was slightly higher in healthy males than healthy females, this is not unexpected, but it was however observed that the mean value of plasma urea was similar for both hypertensive male and female patients.

Uric acid is the principal end product of nucleic acid and purine metabolism in man. It circulates in plasma as sodium urate. Plasma urate represents a steady state between endogenous production and urinary tubular secretion, because filtered urate is normally almost wholly reabsorbed.

Consequently impaired renal function may be responsible for secondary elevation of uric acid level. Thus uric acid may serve as secondary index of renal function. The mean uric acid level of hypertensive patients was significantly higher than those of healthy group, which suggest that there was probably abnormal uric acid metabolism in hypertensive patient.

Urate is also known to be a chain breaking endogenous antioxidant (Rumley and Paterson, 1998), thus increase uric acid level in hypertensive patients may be an antioxidant response due to oxidative stress which can not be ruled out in any pathological states, it may also be due to the use of diuretics by some patients, which is known to raise uric acid.

It was also observed that the male subjects consistently showed higher mean uric acid level than their female counterpart in both groups.

Creatinine is the end-product of creatine metabolism in the muscles. Creatinine diffuses into plasma after synthesis and is excreted by the kidney. Abnormalities in plasma creatinine concentration reflect either change in skeletal muscle metabolism or in renal function. Plasma creatinine is widely used as a primary index for assessment of renal function. The reciprocal of plasma creatinine is a more reliable index than creatinine clearance in monitoring glomerular function in patients with chronic renal disease.

Plasma creatinine is observed to be similar in both hypertensive patients and healthy group. This appears to confirm that there is probably no loss of renal function in both groups. Creatinine is also known to be a measure of muscle mass.

Albumin was used to assess the synthetic function of the liver in the subjects. The liver is central to the metabolism of nutrients and many other substances. Both total protein and albumin may be use as test of nutritional status of the subjects. The mean level of total protein is similar in both healthy and hypertensive patients, in contrast the mean level of albumin is significantly higher in hypertensive group.

Albumin in addition to its transport function is also known to be a preventive antioxidant (Sies, 1993; VanBakel et al., 2000). The relative scavenging activity of albumin is by its non specific binding of

transition metals and by the oxidation of the sulphydryl groups in albumin (Sies, 1993; VanBakel et al., 2000). This may lead to an increased turnover of albumin level. Albumin is probably part of the total antioxidant defence system that was increased due to oxidative stress. However this value fall within the well-known reference values in this environment, which suggest absence of liver disorder, and adequate protein intake, since albumin synthesis is sensitive to amino acid supply and nutritional intake.

Total globulin was measured in this study as a test of immune response in disease. Increase in total globulin level may be suggestive of an inflammatory response; however the level of total globulin was similar for both groups.

Plasma Na^+ and K^+ estimation were expected to provide the most important information about the disturbance of water and electrolyte metabolism. A high plasma Na^+ level (hypernatraemia) occurs when there is excessive intake, failure of the natriuretic hormone, loss of tubular function or increase adrenocortical hormone secretion while a high K^+ level (hyperkalaemia) occurs when there is also excessive intake, diminished excretion or shift of K^+ from the cell to the extracellular fluid.

The increase in the activity of the enzyme Na^+/K^+ ATPase may also increase K^+ permeability, this increasing plasma K^+ level (which is predominantly intracellular cation).

The reference range for plasma sodium concentration in this environment is 135-140 mmol/l while that for plasma potassium is 3.6-5.0 mmol/l. For both healthy subjects and hypertensive patients, the plasma Na^+ and K^+ level are in the upper limit of normal. It is therefore probable that there is no alteration in Na^+ and K^+ homeostasis in hypertensive.

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