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# SERUM CORTISOL AND CORTICOTROPIN LEVELS AMONG HYPERTENSIVE PATIENTS IN KANO, NIGERIA

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## ABSTRACT
Hypertension remains the leading single cause of morbidity and mortality worldwide, and a growing public health problem in sub-Saharan Africa (SSA). Few studies have estimated serum cortisol and corticotrophin (ACTH) levels in a metropolitan city of Kano-Nigeria. A total of 300 adult participants consisting of 200 hypertensive patients and 100 apparently healthy individuals as control were recruited as the study subjects. Serum cortisol and ACTH were analysed using competitive ELISA method, electrolytes ($Na^+$ and $K^+$) by flame photometric method and plasma glucose by glucose oxidase method. The result showed significant ($p < 0.05$) increase in serum cortisol (22.16 ± 11.01µg/L) while, ACTH (9.07 ± 5.5 ng/L) and HDL-C (1.02 ± 0.23 mmol/L) significantly ($p < 0.001$; p=0.016) decrease in hypertensive patients compared to controls (1.94 ± 2.38 µg/L, 16.47 ± 12.8 ng/L and 1.09 ± 0.24 mmol/L respectively). There were no significant ($p > 0.05$) differences in plasma glucose, TC, LDL-C and TG between hypertensive patients and controls. There was a significant ($p < 0.001$) increase in the levels of serum sodium (144.96 ± 9.62 mmol/L) and potassium (4.32 ± 0.70 mmol/L) in hypertensive patients compared to controls ( 136.27 ± 5.84 mmol/L and 3.86 ± 0.36 mmol/L respectively). Serum cortisol was negatively correlated with HDL-C ($r = - 0.298$; $p = 0.001$) and positively correlated with sodium ($r = 0.175$; $p = 0.013$). Cortisol was also found to be directly correlated with the rising hypertension ($r = 0.294$; $p = 0.001$). There is a need for routine evaluation of serum cortisol and ACTH for the management of hypertension.

**KEYWORDS:** ACTH, Cortisol, Lipids, Hypertension, Kano, Nigeria.

## INTRODUCTION
Hypertension or high blood pressure (BP) is a sustained elevation of resting systolic blood pressure (SBP) ≥ 140 mm Hg, diastolic blood pressure (DBP) ≥ 90 mm Hg or both.[1] It is a level of BP at which there is increased risk of morbidity and mortality from cardiovascular disease (CVD), it is divided into primary and secondary according to whether the cause is unknown or known. Secondary hypertension is the one in which the cause is known, it is more common in children and occurs in less than 5% of people living with hypertension.[1]

Cortisol is a steroid hormone produced in humans by the zona fasciculate of the adrenal cortex within the adrenal gland. It is released in response to stress and low blood glucose. The release of cortisol is controlled by the hypothalamus.[2] Corticotrophin-releasing hormone (CRH) is secreted by the hypothalamus triggers cells in the neighboring anterior pituitary to secrete another hormone, the adrenocorticotrophic hormone or corticotrophin (ACTH), into the vascular system, through which blood carries it to the adrenal cortex. ACTH stimulates the synthesis of cortisol.[3]

Cortisol, the major human glucocorticoid, is essential for maintenance of normal blood pressure and in excess, either general or local, produces hypertension.[4] The widely used clinically, synthetic glucocorticoids are said to cause hypertension in some 20% of patients, but steroids invariably raise blood pressure in experimental studies.[3] There is considerable interest in the notion that cortisol may play a role in some forms of essential hypertension and it has been suggested that cortisol may contribute to around 30% of all cases of hypertension.[5] There is interest in the role of cortisol in determination of cardiovascular risk.[6] It has been shown that ACTH reproducibly increases blood pressure in both healthy normotensive and hypertensive subjects, but not in patients with Addison's disease on steroid replacement. This indicates ACTH hypertension is adrenal dependent.[3] Although ACTH receptors have been demonstrated in human aortic endothelial cells.[2] It seems unlikely that direct actions of ACTH are involved in ACTH hypertension in humans. There is some evidence that cortisol excess may be a feature of essential hypertension. Litchfield and colleagues (1998) found higher urinary free cortisol excretion in 153 white

patients with essential hypertension than 18 normotensive controls.[7] The authors of the Four Corners Study observed higher plasma cortisol concentrations in 50 young people with high blood pressure and high parental blood pressure compared with similar numbers of people with lower pressure.[8] Walker *et al*. (2000) examined 226 Swedish subjects in a cross-sectional study and found higher plasma cortisol was independently associated with higher diastolic blood pressure in men, but not women.[9] In another study of 593 English subjects, higher cortisol under the curve during oral glucose tolerance testing was associated with higher systolic blood pressure.[10]

## AIM

This study measured serum cortisol and corticotrophin among hypertensive patients in Kano.

## MATERIALS AND METHODS

**Study area:** This study was conducted at Hypertensive Clinic of Murtala Mohammed Specialist Hospital (MMSH), Kano. Kano State is located in the North-Western Nigeria. It is one of the reference hospitals in the state where people from various parts of the state and neighbouring states of various backgrounds attend.

**Subjects:** A total of 300 participants consisting of 200 hypertensive patients and 100 apparently healthy individuals as control were recruited as the study subjects. Subjects were selected from a population of hypertensive patients attending MMSH Hypertensive Clinic. An interviewer administered Questionnaire was used to elicit the subjects' socio economic and Demographic data and relevant clinical information. Physician on-duty helped the selection process of the patients.

**Ethical Consideration:** Ethical clearance for the study was obtained from Murtala Mohammed Specialist Hospital (MMSH), Kano and an informed consent was obtained from each subject prior to the commencement of the study.

**Collection of blood:** From each selected subject, 3 ml of venous blood sample was collected using a sterile disposable syringe and needle and allowed to clot at room temperature after which it was centrifuged at 3000 rpm for 5 minutes to obtain a clear unhaemolyzed serum. The sera were harvested and placed in another plain tube and rapidly stored at -20 $^0$C until the time for analysis.

**Estimation of biochemical parameters:** Serum cortisol and ACTH were estimated using competitive ELISA method. Serum total cholesterol (TC) and high density lipoprotein-cholesterol (HDL-C) levels were estimated using enzymatic method of Roeschlan *et al*.[11] Serum triglyceride (TG) was estimated using enzymatic method of Trinder.[12] Serum low density lipoprotein-cholesterol (LDL-C) was calculated as described by Friedewald *et al*.[13] Serum glucose was estimated using enzymatic method (Glucose oxidase) as described by Trinder.[12]

**Statistical Analysis:** The data generated was analyzed using statistical package for social sciences (SPSS) version 20. The results were expressed as mean plus/minus standard deviation (Mean ± SD). The results of both the clinical and biochemical parameters obtained from hypertensive patients were compared with those of controls using paired two-tailed student's t-test for matched samples. Pearson correlation was used to correlate data. The p value less than or equal to 0.05 ($p \leq 0.05$) was considered to be significant.

## RESULTS

Table 1 shows the clinical variables of hypertensive patients and controls. Table 2 shows serum cortisol and ACTH in hypertensive patients and controls. There were no significant ($p = 0.155$) differences between the ages, whereas the mean BMI of hypertensive patients was significantly ($p = 0.001$) higher than that of control. Mean serum cortisol significantly ($p = 0.001$) increase in hypertensive patients compared to controls, while mean serum ACTH of hypertensive patients significantly ($p = 0.001$) decrease compared to controls. Table 3 shows the serum lipids, electrolytes and glucose in hypertensive patients and controls.

The results of correlation study between serum cortisol and various biochemical parameters in hypertensive patients are shown in Table 4. There were significant positive correlation between the serum cortisol and TG ($r = 0.130$, $p = 0.019$), sodium ($r = 0.175$, $p = 0.013$) and potassium ($r = 0.307$, $p < 0.001$) (Figs. 1-2), whereas serum HDL-C showed negative correlation with cortisol concentration ($r = - 0.298$, $p = 0.001$). Serum cortisol was also found to be directly correlated with the rising hypertension ($r = 0.294$; $p = 0.001$) (Fig. 3).

**Table 1: Clinical variables (Mean ± SD) of hypertensive patients and controls.**

| Clinical variables | Subjects | | P-value |
|---|---|---|---|
| | Controls | Patients | |
| N | 100 | 200 | |
| Age (yrs.) | 54.47 ± 14.43 | 56.45 ± 12.74 | 0.155 |
| Weight (Kg) | 66.83 ± 16.10 | 69.02 ± 15.63 | 0.040 |
| Height (m) | 1.61 ± 0.10 | 1.53 ± 0.89 | 0.081 |
| BMI (Kg/m$^2$) | 25.10 ± 6.26 | 29.23 ± 6.94 | 0.001 |
| SBP (mmHg) | 122.96 ± 11.86 | 140.36 ± 22.33 | 0.001 |
| DBP (mmHg) | 84.00 ± 8.63 | 87.95 ± 11.87 | 0.005 |

SBP=Systolic blood pressure; DBP=Diastolic blood pressure; N=number of subjects.

**Table 2: Serum cortisol and ACTH (Mean ± SD) in hypertensive patients and controls.**

| Parameters | Controls (n =100) | Patients (n =200) | p-value |
|---|---|---|---|
| Gender | (M=50; F=50) | (M=100; F=100) | |
| Cortisol (µ/ml) | 1.94 ± 2.38 | 22.16 ± 11.01 | 0.001 |
| ACTH (ng/ml) | 16.47 ± 12.85 | 9.07 ± 5.50 | 0.001 |

ACTH=Adrenocortical trophic hormone; M=mail; F=female.

**Table 3: Serum lipids, electrolytes and glucose (Mean ± SD) in hypertensive patients and controls.**

| Parameters | Controls (n =100) | Patients (n =200) | p-value |
|---|---|---|---|
| Gender | (M=50; F=50) | (M=100; F=100) | |
| TC (mmol/l) | 3.91 ± 3.20 | 3.75 ± 0.88 | > 0.05 |
| TG (mmol/l) | 11.39 ± 0.70 | 11.22 ± 0.77 | > 0.05 |
| HDL-C (mmol/l) | 1.58 ± 0.62 | 1.09 ± 0.24 | 0.016 |
| LDL-C (mmol/l) | 2.31 ± 0.62 | 2.31 ± 0.62 | > 0.05 |
| $Na^+$ (mmol/l) | 136.27 ± 5.84 | 144.96 ± 9.62 | 0.001 |
| $K^+$ (mmol/l) | 3.86 ± 0.36 | 4.32 ± 0.70 | 0.001 |
| Glucose (mmol/l) | 4.48 ± 2.35 | 4.31 ± 0.85 | > 0.05 |

TC =Total cholesterol; TG= Triglycerides; HDL-C=High Density Lipoprotein Cholesterol; LDL-C= Low Density lipoprotein Cholesterol.

**Table 4: Correlation between serum cortisol and biochemical parameters in study subjects.**

| Group | | | TC (mmol/L) | TG (mmol/L) | HDL-C (mmol/L) | LDL-C (mmol/L) | $Na^+$ (mmol/L) | $K^+$ (mmol/L) |
|---|---|---|---|---|---|---|---|---|
| | Cortisol | Vs | | | | | | |
| I (100) | | R | 0.002 | 0.017 | 0.083 | 0.102 | 0.000 | 0.110 |
| | | P | 0.987 | 0.199 | 0.411 | 0.311 | 0.997 | 0.274 |
| | Cortisol | | | | | | | |
| II (200) | | R | 0.040 | 0.130 | -0.298 | 0.028 | 0.175 | 0.307 |
| | | P | 0.574 | 0.019 | 0.001 | 0.699 | 0.013 | 0.001 |

Values are correlation coefficients (r) and p-values which are statistically significant at $p < 0.05$ using Pearson correlation analysis. Group I = controls and Group II = patients.

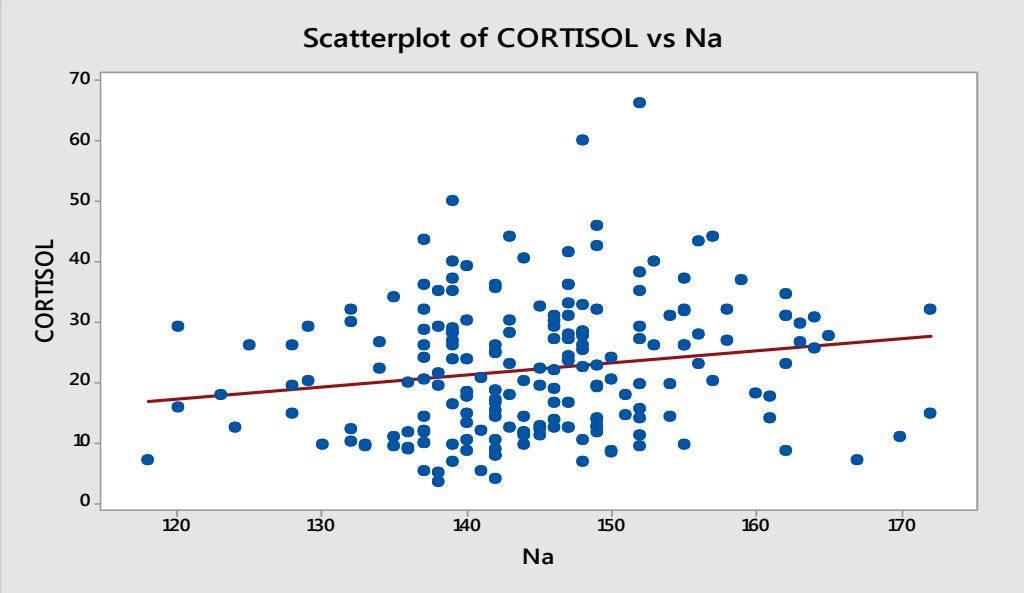


**Fig. 1: Scatter plot between serum cortisol and $Na^+$ in hypertensive subjects (r= 0.175; p= 0.013).**

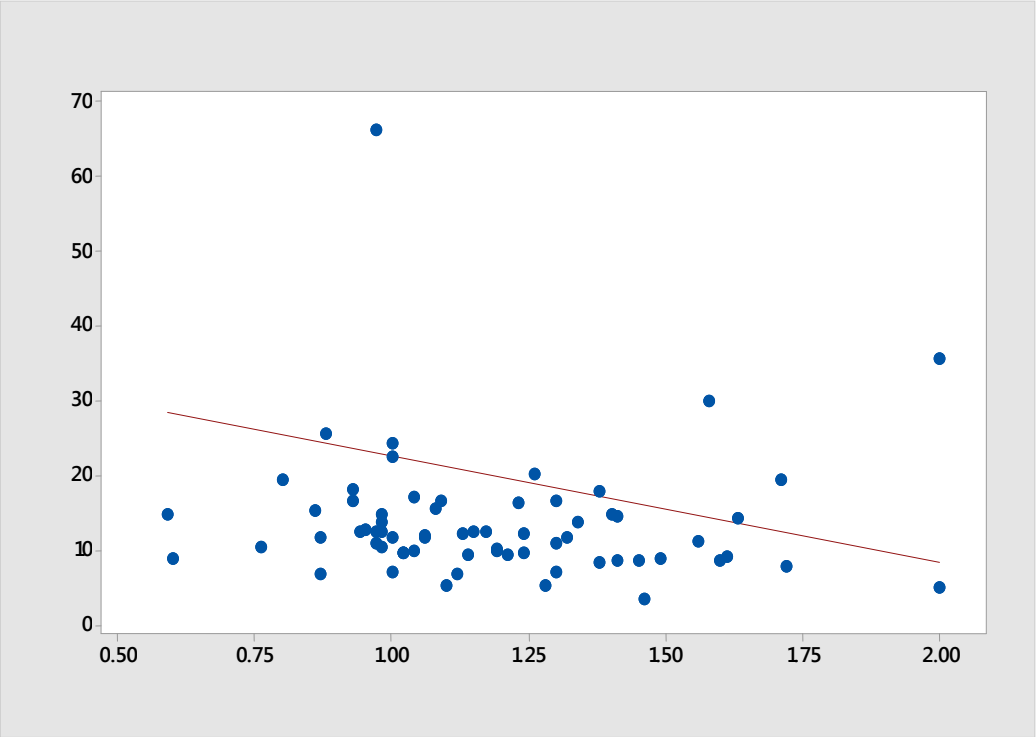


**Fig. 2: Scatter plot between serum cortisol and HDL-C in Hypertensive subjects (r = -0.298; p = 0.001).**

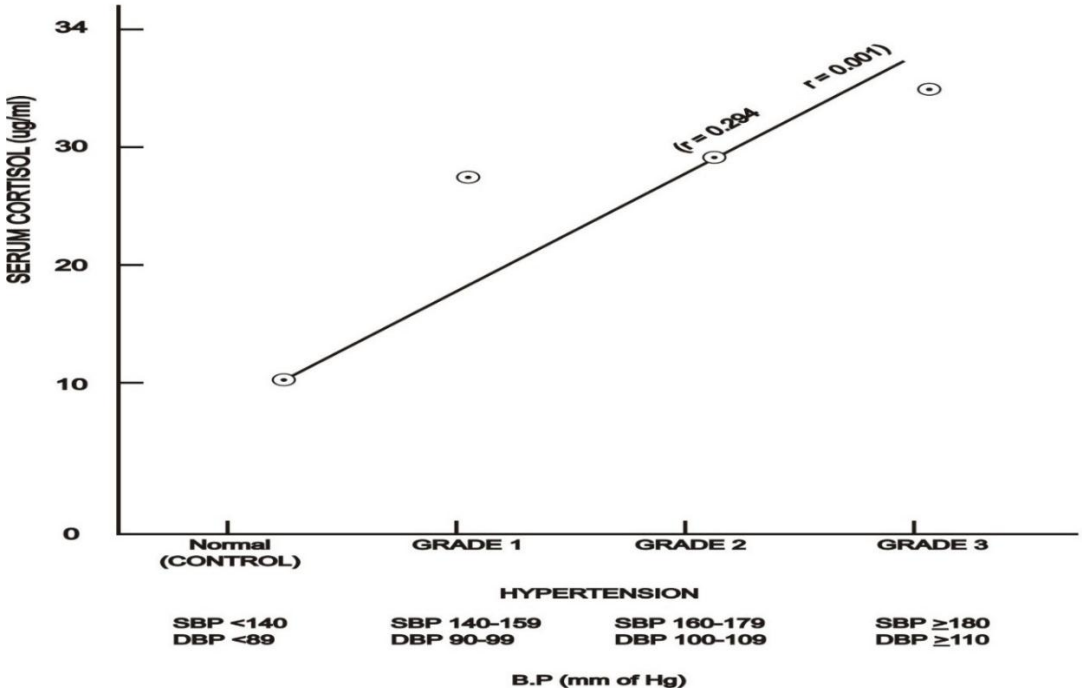


**Fig. 3: Correlation between serum cortisol and advancing hypertension.**

## DISCUSSION

The finding of the present study demonstrated that serum cortisol concentration (22.16 ± 11.00 µg/ml) was significantly higher in hypertensive patients than in controls (10.56 ± 2.42 µg/ml). This is in line with pathophysiology of the human cortisol metabolism. Cortisol is a stress hormone known to be secreted in excess in chronic phase response which may lead to hypertension. The result is in line with the previous work of Litchfield *et al.*,[7] Watt *et al.*[8] and Ward *et al.*[14] There was no significant difference in plasma glucose for both hypertensive patients and controls. This is in line with physiology of the body since the subjects studied were not diabetic. Hypertension is a multifactorial condition which include disturbances in lipid and electrolytes metabolism, derangement of lipid profile (dyslipidaemia) which can predispose to hypertension and metabolic syndrome. But, the result indicate that,

there were no significant differences in serum total cholesterol, LDL-C and triglyceride between hypertensive patients and controls ($p > 0.05$). Ordinarily dyslipidaemia is expected in hypertension particularly if it couples with diabetes but our results do not fall in line with previous findings by Isezuo *et al*.[15] Choudhury *et al*.[16] and Kanwar *et al*.[17] This may have been due to the fact that the hypertensive patients were educated on the appropriate dietary intake, exercise and the adherence in the intake of lipid lowering drugs which will probably normalize their lipid profile status. The mean serum HDL-C was however significantly ($p=0.016$) lower in hypertensive patients than in controls; this agrees with the previous findings of Bruckert *et al*.[18] Low HDL-C is increasingly recognized as an independent risk factor for adverse cardiovascular disease with increased risk of atherogenic coronary complications. In the current study, mean serum cortisol level was also found to be directly correlated with the rising hypertension ($r = 0.294$; $p = 0.001$) indicating that as the hypertension advances from grade 1 to grade 3, mean serum cortisol also increases.

## CONCLUSION

It could be concluded from the findings of the present study that serum cortisol, sodium and potassium concentrations were elevated with consequent depression of ACTH in hypertension. Routine evaluation of serum cortisol in addition to ACTH and aldosterone is suggested for the investigation of hypertension. This could improve the management of this group of individuals.

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