

RENAL FUNCTION IN SUDANESE PATIENTS WITH ESSENTIAL HYPERTENSION

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ABSTRACT

Background: The kidney is an important target of hypertension. Understanding of renal function is critical for prevention of hypertension and renal disease. **Objectives:** The main objective of this study was to detect the effect of primary hypertension on renal function in Sudanese male patients. **Material and Method:** This case-control and cross-sectional study assessed renal function in Sudanese male patients with essential hypertension. Hypertensive and normotensive subjects were randomly selected. **Result:** Mean creatinine clearance was 57.8 ± 33.9 ml/min in hypertensive cases. Thirty five percent of hypertensive group had >1.5 mg/dl serum creatinine. Urea was found significantly high in 25.8% of hypertensive cases and coincided with those having serum creatinine > 1.7 mg/dl. Mean uric acid was 7.71 mg/dl and 6.03 mg/dl in hypertensive and normotensive subjects respectively. Serum sodium increased in hypertensive cases insignificantly; potassium elevated in 21.2% and 4.2% in hypertensive and normotensive subjects respectively. Albuminuria, casts and RBCs were present in urine of hypertensive patients. **Conclusion:** Serum uric acid may be a more sensitive test for renal function. Strong association was found between essential hypertension and renal biomarkers.

KEYWORDS: RFT, Sudanese, hypertension.

INTRODUCTION

Blood pressure is the force of blood pushing against blood vessel walls as the heart pumps out blood, and high blood pressure, also called hypertension, is an increase in the amount of force that blood places on blood vessels as it moves through the body. Factors that can increase this force include higher blood volume due to extra fluid in the blood and blood vessels that are narrow, stiff, or clogged.

Blood pressure test results are written with two numbers separated by a slash. For example, a health care provider will write a blood pressure result as 120/80. A health care provider will say this blood pressure result as "120 over 80." The top number is called the systolic pressure and represents the pressure as the heart beats and pushes blood through the blood vessels. The bottom number is called the diastolic pressure and represents the pressure as blood vessels relax between heartbeats.

Most people without chronic health conditions have a normal blood pressure if it stays below 120/80. Prehypertension is a systolic pressure of 120 to 139 or a diastolic pressure of 80 to 89. High blood pressure is a systolic pressure of 140 or above or a diastolic pressure of 90 or above.^[1]

Hypertension is one of the most common diseases worldwide for which treatment is available. Nowadays, the most important causes of renal failure and dialysis in the world are arterial hypertension and diabetes mellitus.^[2]

The kidney is an important target of hypertension-induced organ damage. Understanding of the early stages of the interaction between blood pressure and renal function is critically important for the primary prevention of hypertension and renal disease. A better understanding of the effects of essential hypertension on renal function may help for early detection of the disease, follow-up and management on a scientific base.^[3]

Renal function includes removal of waste and potentially harmful end products of metabolism, such as urea, uric acid, sulphates and phosphates and conservation of substances that are essential to life such as water, sugars, amino acids and electrolytes (e.g. sodium, potassium, bicarbonate, and chloride).

Long-term regulation of arterial blood pressure depends on the maintenance of extracellular fluid volume, a function of the kidneys. The distal segments of the nephron, operating under hormonal control, match the excretion of sodium and anions to dietary intake to ensure regulation of extracellular fluid volume, but to work effectively. These segments require a relatively stable load delivered from more proximal segments.^[4]

Renin-angiotensin-aldosterone- system is linked to the basic mechanism of hypertension. A reduction in renal perfusion pressure can occur leading to decreased glomerular filtration (GF) and reduced sodium and water excretion. Decreased renal perfusion leads to the production of renin which converts angiotensinogen to angiotensin I. This is changed into angiotensin II which stimulates the secretion of aldosterone and further contributes to salt and water retention.^[5]

Glomerular hypertension results in increased protein filtration and endothelial damage, causing increased release of cytokines and other soluble mediators, promoting replacement of normal kidney tissue by fibrosis. An important factor contributing to progressive renal disease is activation of the renin-angiotensin system, which tends to increase blood pressure and also promotes cell proliferation, inflammation, and matrix accumulation.^[6]

The kidney can suffer the consequences of a persistently elevated blood pressure. In fact end-stage renal failure caused by essential hypertension appears to be one of the most prevalent aetiologies in patients entering the dialysis program. Blood pressure control is needed in order to prevent the progressive loss of renal function. Target blood pressure control has been established at values as low as 125/75 mmHg for patients with proteinuria above one gram per day.^[3]

Hypertension may lead to glomerular capillary hypertension and result in an accelerated destruction of renal arterioles and glomeruli.^[4]

As GFR declines, the tubules facilitate the excretion of progressively greater fractions of the filtered load of the solutes, either by enhancing their net secretion and/or by diminishing their net reabsorption. The extent of compensation is nearly complete and represents a fundamental adaptation to renal injury.^[7]

The number of patients developing ESRD as a consequence of hypertension is increasing and accounts for 25% of new cases of ESRD in the United States.^[8]

A simple and frequently used method for the estimation of GFR is the determination of creatinine clearance using urine collection periods from 12-24 hours. When renal excretory function is impaired, either acutely or chronically, one or more of the determinants of GFR in affected nephrons is altered unfavourably so that total GFR declines.^[9]

Epidemiological data on the risk of hypertensive patients to develop renal failure offer contrasting results.

In the Baltimore Longitudinal Study of Aging, white middle class hypertensive patients lost renal function at a faster rate with aging than normotensive subjects.

However, the rate of decline was very small and unlikely to result in ESRD.^[9] Furthermore, Rosansky *et al*^[10] in a retrospective study of essential hypertensives followed up for a mean period of 9.8 years found a greater rate of change in serum creatinine over time in hypertensives than in controls but with no statistical significance; the difference was marked for black patients. In addition, autopsy studies on patients with pure essential hypertension suggest that severe renal damage consequent to high blood pressure, in the absence of associated renal parenchymal disease, is either rare or non-existent.^[11]

Reports from the Sudanese Federal Ministry of Health showed that the number of patients with acute chronic renal failure in Sudan is increasing. In 2004, the number of cases with renal failure documented was 2,404 and in 2009, 4,082 cases. Between 2005-2009, the number of renal failure cases increased by 11 %.^[6] and in 2010, the mortality rate with renal failure was 17.4 %.^[12]

GFR reduction is one of the early changes in renal involvement with essential hypertension. The GFR is not frequently investigated in Sudan and no normal range value for GFR in the Sudanese population is estimated. Renal function needs to be investigated in Sudanese patients suffering from essential hypertension.

MATERIAL AND METHODS

This was a cross-sectional and case-control study conducted to detect renal function in Sudanese male patients with essential hypertension. Eighty-one Sudanese patients, aged 25-75 years with essential hypertension were selected randomly from different governmental clinics in Khartoum State, Sudan. Twenty-four healthy normotensive subjects of the same age group were selected randomly as a control group. The hypertensive and normotensive subjects had blood samples and 24-hour urine collection examined. Blood urea, serum creatinine, uric acid, sodium and potassium were measured. Urine was analysed for creatinine, protein and granular casts. Creatinine clearance was calculated.

Renal Function Tests (RFT)

Measurement of serum and urine creatinine was done using Jaffee's reaction (Normal range: Serum creatinine 0.1-1.5 mg/dl, Urine creatinine 1-1.5gm/24 hr).

Calculation of creatinine clearance was done using the following formula:

Creatinine Clearance=

$$\frac{\text{Mg creatinine/dl urine} \times \text{ml urine (24 hours)}}{\text{ml creatinine/dl serum} \times 1440} = \text{ml/min}$$

Measurement of urea was done by colorimetric method using end-point determination Urease-Berthelot Reaction (Normal range: urea = 15 – 40 mg/dl).

Measurement of uric acid was done by the enzymatic colorimetric test Uricase-PAP (normal range: uric acid is 3.5 – 7 mg/dl).

Measurement of sodium and potassium in serum was done using the flame photometer. The technique used measured their concentrations in mmol/l (JENWAY PEP7). Urine was tested using the dipstick (Combur 9 Test BOEHRINGER MANHEIM).

Statistical Methods

Data was entered using SPSS Version 16. Mann-Whitney and Kruskal-Wallis tests were used for comparison of means of continuous variables between groups.

Ethical approval

This study received the ethical approval from our institute. Consent of all subjects was taken prior to entry in the study.

RESULTS

Mean age in years was $55.87 \pm \text{S.E } 1.289$ for the hypertensive cases and $53.05 \pm \text{S.E } 2.72$ for the control group. There was no significant difference between the two groups in age.

Both the systolic and diastolic blood pressure increased with age. (See Table 1).

Fifty four percent of the hypertensive cases had normal values of serum uric acid (3.5-7.0 mg/dl) and 45.9% had values above normal. In the normotensive group 68.2% had normal values of serum uric acid and 31.8% above normal value. (Table 2).

Uric acid is not statistically significant different between cases and control ($P=0.364 >0.05$).

In the hypertensive cases, 72.3% had normal serum potassium (3.5-5 mmol/L) and 27.7% had above normal levels. All subjects of the control group had normal serum potassium. (See figure 1).

Serum potassium is not statistically significant different between cases and control ($P=0.924 >0.05$).

In the hypertensive cases 95.3% had serum sodium within the normal range (135-145 mmol/L), and 4.7% had above normal levels; while 100% of the normotensive subjects had normal serum sodium. (Table 3).

Serum sodium is not statistically significant different between cases and control ($P=0.088 >0.05$).

In the hypertensive cases, 35.4% had serum creatinine above normal ($> 1.5 \text{ mg/dl}$), of which 9.2% were borderline (1.5-1.7 mg/dl) and 26.2% had ($> 1.7 \text{ mg/dl}$). The rise in creatinine level was associated with a rise in diastolic blood pressure and duration of hypertension. Serum creatinine level also increased with age and was found to be more prevalent in the age group 45-54years. In the normotensive group, 93.3% had normal serum creatinine and 6.7% had borderline serum creatinine. It should be noted that 80% of the 26.7% hypertensive cases, with renal insufficiency values $> 1.7 \text{ mg/dl}$ serum creatinine, had high blood urea values. (Table 4).

Serum creatinine is not statistically significant different between cases and control ($P=0.539 >0.05$).

In the hypertensive cases, 74.2% had normal blood urea (15-40 mg/dl) while 25.8% showed values above normal. All normotensive subjects had normal blood urea. (Table 5).

Blood urea is a statistically significant different between cases and control ($P=0.000 <0.05$).

Blood Urea Level increased with age and was found more prevalent in the age group 45-54 years. In the hypertensive cases, 68.4% had no RBCs in urine, 26.3% had < 5 erythrocytes/HPF and 8.3% had >5 erythrocytes/HPF. In the normotensive group, 91.7% had no RBCs in urine and 8.3% had < 5 erythrocytes/HPF. (Table 6).

DISCUSSION

This study demonstrated that there is a decrease in renal function biomarkers of Sudanese male patients with essential hypertension. The creatinine clearance had the highest levels in the youngest age group of cases. It decreased gradually with age but with the maximum drop in the age group between 45-54 years. This indicated a decrease of creatinine clearance and ultimately GFR. The GFR is the first biomarker to be affected in renal insufficiency as also shown in the literature. The other renal biomarkers: serum creatinine, uric acid and blood urea levels raised above normal values gradually with increase of age in the hypertensive cases. Surprisingly, matching the greatest drop of creatinine clearance was in the age group between 45-54 years, were the highest rise in levels of serum creatinine,

uric acid and blood urea. This indicated that there might be other factors which had led to a deterioration of renal function in this age group of hypertensive cases. This can be explained by other environmental factors such as smoking, stress etc. The rise in serum creatinine, blood urea and serum uric acid indicated renal insufficiency in these cases. These results match the results found by Cohuet in 2006^[12] regarding blood urea nitrogen reduced GFR and creatinine clearance are well-established biomarkers of renal function. He stated that an increased urinary albumin excretion are manifestations of target organ damage in hypertension. The high level of potassium in the different age groups can be explained by the use of certain drugs as well as physiological factors were the potassium can be retained in the body in exchange of sodium. This area needs further research and investigation. Most of the cases had normal values of sodium. This was observed in other studies as stated by Harrison in 1987 where the serum sodium levels of cases remained unchanged though the kidney plays a central role in sodium control.^[2] In this study, other renal involvement was shown by albuminuria, casts and RBC in the urine of the hypertensive cases. These results add to the results stated by Mihajlov R et al in 2015.^[13] Proteinuria is also demonstrated and shown in cases with chronic kidney disease by Robert G Fassett.^[14] He mentioned proteinuria among other recently used renal biomarkers which include neutrophil gelatinase-associated lipocalin, kidney injury molecule-1, and liver-type fatty acid-binding protein, although none are ready for use in clinical practice. The majority of cases did not take their treatment regularly and had long standing hypertension. This can explain the remarkable deterioration in their renal biomarkers levels.

CONCLUSIONS

The results indicated a high interaction between essential hypertension and renal function in Sudanese male patients. The most affected parameters of renal function are uric acid, serum creatinine, blood urea, serum potassium and albuminuria consecutively. This effect is associated with diastolic blood pressure, duration and control of hypertension

Further studies are needed in the field of renal function and essential hypertension in Sudan to improve early detection, diagnosis, and management of the disease.

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Conflict of interest

No conflict of interest.

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