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Evaluation of Serum Uric Acid and C- Reactive Proteins in Sudanese with Hypertension in Khartoum State

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***Abstract*—Uric acid is commonly associated with hypertension; recent experimental and clinical studies suggest that uric acid could have a contributory role in the pathogenesis of elevated blood pressure. Individuals at risk for developing hypertension and cardiovascular disease, frequently have evidence for a systemic inflammatory response, often marked by elevations of C-reactive protein (CRP) in their blood. Elevated levels of CRP have emerged as one of the most important predictors of myocardial infarction, stroke, and vascular death, with prognostic value exceeding that of LDL cholesterol.**

Aim: To evaluate, serum uric acid and CRP levels in Sudanese hypertensive patients in Khartoum state.

Material and methods: 100 subjects in the age group of 25- 60 years, divided into two groups of hypertensive and control healthy normotensive group. (54) Patients suffering from hypertension and (46) ages matched non hypertension subjects, who were volunteered to be included in the study. Blood samples were collected in plain container for estimation of Serum C-RP and uric acid levels, Serum CRP levels were detected (qualitatively) using latex agglutination method (Spinreact Kit; 2016). Uric acid was estimated by quantitative commercial kit method (on Autoanalyzer Mindray. BS200). Venous blood sample was drawn from all subjects, allowed to clot at room temperature for 1–3 hours and serum was separated by centrifugation for 15 min at 3000 r. p. m. Data were analyzed using statistical package for the social sciences (SPSS).

Result: The patients of hypertension under study comprised of 51.9% males and 48.1% females while the control comprised of 52.2% males and 47.8% females, the age range between 25 years to 60 years. Uric acid levels were high in 66.7 % of patients and normal in 33.3 % of patients. However uric acid levels observed within normal range in all normotensive subjects (control). CRP in 63 % of patients was positive while 37 % were negative and all control was negative. There was strong significant positive correlation between uric acid and CRP with P- value 0.000.

Conclusion: Serum uric acid levels were found higher in hypertensive patients than in healthy individuals. Serum CRP in hypertensive patients shows higher percentage than in healthy individuals.

I INTRODUCTION

Essential or primary hypertension, the world's leading risk factor for global disease burden is expected to cause more than half of the estimated 17 million deaths per year resulting from cardiovascular disease (CVD) worldwide [(1)]. Defined as an elevation of blood pressure (BP) beyond 140/90 mmHg, hypertension is strongly correlated with adverse outcomes such as stroke, ischemic heart disease, heart failure, and end stage renal disease. The challenges of managing hypertension and preventing the development of these latter outcomes are unlikely to relent; the global burden of hypertension is projected to increase by 60% to affect approximately 1.6 billion adults worldwide by 2025 [(1)]. Uric acid levels vary significantly within humans as the result of factors that increase generation (such as high purines or protein diets, alcohol consumption, conditions with high cell turnover, or enzymatic defects in purines metabolism) or decrease excretion. Reduction in glomerular filtration rate (GFR) increases serum uric acid, although a significant compensatory increase in gastrointestinal excretion occurs [(2)]. Hyperuricemia also may result from increased net tubular absorption. After filtration, uric acid undergoes both reabsorption and secretion in the proximal tubule, and this process is mediated by a urate/anion exchanger and a voltage-sensitive urate channel [(3)].

Uric acid is also commonly associated with hypertension, It is present in 25% of untreated hypertensive subjects, in 50% of subjects taking diuretics, and in >75% of subjects with malignant hypertension [(4)]. The increase in serum uric acid in hypertension may be due to the decrease in renal blood flow that accompanies the hypertensive state, since a low renal blood flow will stimulate urate reabsorption [(5)]. Hypertension also results in micro-vascular disease, and this can

lead to local tissue ischemia [6]. In addition to the release of lactate that blocks urate secretion in the proximal tubule ischemia also results in increased uric acid synthesis [7]. With ischemia, ATP is degraded to adenine and xanthine and there is also increased generation of xanthine oxides [8].

The increased availability of substrate (xanthine) and enzyme (xanthine oxidase) results in increased uric acid generation as well as oxidant (O2−) formation. The finding that ischemia results in an increase in uric acid levels may also account for why uric acid is increased in preeclampsia (8) and congestive heart failure (9). Other factors may also contribute to why uric acid is associated with hypertension including alcohol abuse, (10) lead intoxication, (11) obesity and insulin resistance, and diuretic use (12). An elevated serum uric acid (UA) in humans is also associated with systemic inflammation, increased CRP levels (13), endothelial dysfunction (14, 15) hypertension (16) and cardiovascular disease (17). Much of the early work on CRP biology focused on its interaction with ligands expressed on bacteria and damaged tissue. CRP binding to the C-polysaccharide was shown very early on to occur through phosphocholine (PC) moieties, which are found on the cell wall teichoic acid and lipoteichoic acid (18). PC is expressed on a variety of pathogenic organisms to which CRP has been shown to bind (19). PC is also the polar head group of phosphatidyl choline a component of the mammalian cell membrane. This PC head group of phosphatidyl choline is not exposed on normal healthy cells (20). However damage to cell membranes by enzymatic action or complement attack leads to extensive binding of CRP to the damaged membrane. Thus CRP can target dead and damaged cells for processing by the innate immune system.CRP also binds to PC exposed on oxidized LDL, which may account for its presence in atherosclerotic lesions. The damaged cell can present and/or release various nuclear antigens that can stimulate the immune system and some of these are the targets of auto antibodies in connective tissue diseases (21).

II MATERIAL AND METHODS

This study is cross–sectional study, was done in Sudan heart center in Khartoum state. Hypertensive patients, who were presented to the hospital for follow- up, (100) subjects in the age group of 25- 60 years, divided into two groups of hypertensive and control healthy normotensive group. (54) Patients suffering from hypertension and (46) ages matched non hypertension subjects, who were volunteered to be included in the study. Blood samples were collected in plain container for estimation of Serum, C-RP and uric acid levels Serum CRP levels were detected (qualitatively) using latex agglutination method (Spinreact Kit; 2016). Uric acid was estimated by quantitative commercial kit method (on Autoanalyzer Mindray.BS200). Venous blood sample was drawn from all subjects, allowed to clot at room temperature for 1–3 hours and serum was separated by centrifugation for 15 min at 3000 r.p.m. Data were analyzed using statistical package for the social sciences (SPSS). Inclusion Criteria: Patients whose BP more than 140 ⁄ 90 mm Hg, and don't complain of gout and renal problems. Exclusion Criteria: The individual suffering from Type-2 diabetes mellitus, tuberculosis, renal disorders, cardiac failure tumor of any type, malaria, the subjects who were consuming drugs like Aspirin statin, fib-rates and phenytoin were excluded from the study. Informed consent was taken verbally from patient and their guardians in the study population and participation was entirely voluntary. Approval was ensured from the University of Medical Sciences and technology and Sudan heart center.

III RESULTS

The study was carried out on 54 patients diagnosed as having essential hypertension and 46 healthy apparently as control group Table (1). The patients of hypertension under study comprised of 51.9% males and 48.1% females while the control comprised of 52.2% males and 47.8% females Table (2), the age range between 25 years to 60 years. Uric acid levels were high in 66.7 % of patients and normal levels were be found in 33.3 % of patients. However uric acid levels observed within normal range in all normotensive subjects (control) Table (3). Table (4) show the percentage of CRP in patients and control, 63 % of patients were positive CRP while 37 % were negative and all control were negative. Table (5) show correlation between uric acid and CRP in patients with hypertension, it was strong significant positive correlation between uric acid and CRP with P- value 0.000.

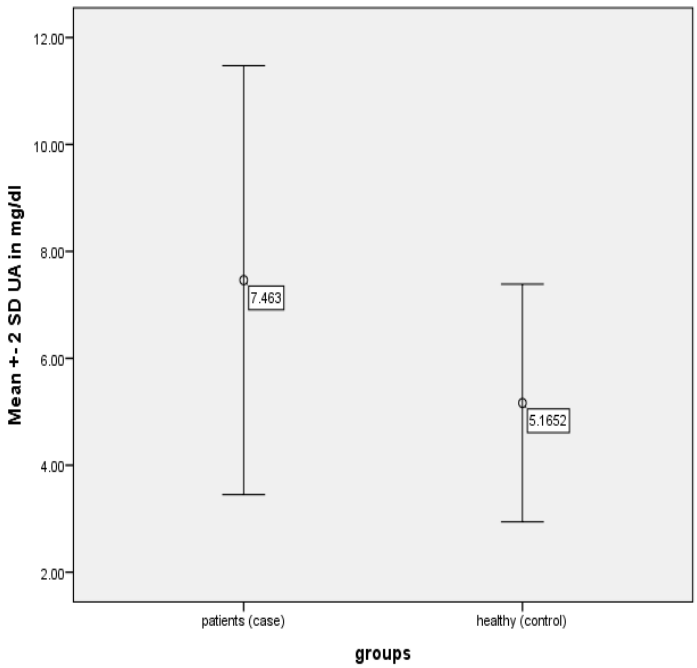

Figure (1) show the mean con of uric acid in patients and control

Fig (1) show the mean con of uric acid in patients and control, the mean con of uric acid in patients were higher than control.

Table (1) Shows the percentage of patients and controls

Type	Frequency	Percent
Patients with hypertension (Case)	54	54%
Normotensive (Control)	46	46%
Total	100	100%

Table (2) Show the distribution of patients and control according to gender

Gender	Patients with hypertension	Normotensive
Male	28(51.9%)	24(52.2%)
Female	26(48.1%)	22(47.8%)
Total	54(100%)	46(100%)

Table (3) Show the percentage of uric acid in patients and control

Serum Uric acid(mg/dl	Frequency	Percent
Patients with high Uric acid	36	66.7%
Patients with high normal acid	18	33.3%
Control	46	0.0%
Total	100	100%

Table (4) Show correlation between uric acid and CRP in patients

C-reactive protein	Frequency	Percent
Patients with Positive CRP	34	63%
Patients with Negative CRP	20	37%
Control	46	00%
Total	100	100%

Table (5) Show correlation between uric acid and CRP in patients

Parameters	R-value	P-value
Uric Acid	0.552**	0.000
CRP	0.552**	0.000

** Correlation is significant at the 0.000

IV DISCUSSION

This study was carried out to evaluate serum CRP and uric acid levels in Sudanese hypertensive patients in Khartoum state. Whether serum uric acid (UA) has an etiologic role in cardiovascular disease continues to be a matter of debate. Whereas several investigators have suggested that, UA contributes to the pathogenesis of atherosclerosis, hypertension and inflammation others have hypothesized that elevation of serum UA is a consequence, not a cause, of vascular disease, since UA is a free radical scavenger, and therefore its elevation could represent a physiologic response to increased vascular oxidative stress. Several studies suggest that increased UA levels may represent a systemic inflammatory state. Our results found that serum uric acid and CRP levels were elevated in hypertensive patients than in control group so, there were positive correlation to hypertension.

Our study and others have shown that serum UA is significantly associated with plasma levels of C-reactive protein (CRP), a marker of systemic inflammation, independent of potential confounders such as the conventional CHD risk factors. Brand, et al (1985), found that among patients with long-standing hypertension, the results of studies examining the association of hypertension with hyperuricemia have yielded inconsistent results, one study noted an inverse relationship between uric acid level and hypertension with increasing age and duration of hypertension, and this suggests that uric acid may be most important in younger populations with early-onset hypertension (22). Kang and park (2005), found serum UA is also commonly associated with different hypertensive conditions such as prehypertension, gestational hypertension, preeclampsia and hypertension in adolescence (23). Xhang and Opatham (2009), found uric acid has been implicated in hypertension via mechanism like inflammation, vascular smooth muscle cell proliferation in renal microcirculation, endothelial dysfunction and activation of the rennin angiotensin aldosterone system (RAS) (24). Peristein and Gumieniak (2006) reported there is relation between serum uric acid and hypertension (25). Kang and park (2005), found an elevation in plasma UA concentration is associated with an increased level of C-reactive protein, which has been identified as an important indicator of myocardial infarction, stroke, and vascular death (23).

Nakahara and Kanemoto (2001), found that patients with hypertension have markedly higher levels of Plasminogen Activator Inhibitor (PAI-1) than normotensive patients, higher levels of CRP play an important role in induction of PAI-1, a marker of impaired fibrinolysis and adhere-thrombosis. This finding that CRP increases PAI expression and activity in human aortic endothelial cells, support a possible mechanism by which association between CRP and development of hypertension is mediated [(26)].

VI CONCLUSION

This study concludes that a serum uric acid level is found higher in hypertensive patients than in healthy individuals. Serum CRP in hypertensive patients shows higher percentage than in healthy individuals. And the raised levels of CRP in hypertension suggest the possibility of inflammatory pathogenesis.

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