

ASSOCIATION OF SERUM URIC ACID WITH BLOOD UREA AND SERUM CREATININE

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Background: Hyperuricemia can cause serious health problems including renal insufficiency. Hyperuricemia is associated with many diseases including Hypertension, Diabetes Mellitus, Hypertriglyceridemia and Obesity. Objective of the present study was to study the Association of Serum Uric Acid with Blood Urea and Serum Creatinine. **Methods:** Eighty subjects, aged above 40, having blood urea more than 40 mg/dl and serum Creatinine more than 1.3 mg/dl were selected. 52.5 % subjects were male. Eighty subjects were selected as control group matching the age and sex with study group with normal blood urea and serum Creatinine. **Results:** Serum Uric Acid was found to be raised in 33 patients. Mean Serum Uric Acid value was 6.98 ± 2.021 in males ($p < 0.05$) and 5.054 ± 2.324 in females ($p < 0.05$). **Conclusion:** Serum Uric Acid is raised in patients with impaired renal function ($p < 0.05$). Levels of increased Serum Uric Acid were not significantly associated with the cause of renal disease.

Keywords: Serum Uric Acid, Blood Urea, Serum Creatinine

INTRODUCTION

Uric acid is the end product of purine metabolism in humans. Humans convert the major purine nucleosides, adenosine and guanosine to uric acid via intermediate.¹

Normal range for serum uric acid is 2.4–7.4 mg/dL (140–440 $\mu\text{mol/L}$) in males and 1.4–5.8 mg/dL (80–350 $\mu\text{mol/L}$) in females.²

Overproduction of Uric Acid causes gout.³ It may also lead to progressive renal insufficiency.⁴ Hyperuricemia is also associated with Hypertension⁴, Diabetes mellitus⁵, Hypertriglyceridemia⁶ and Obesity⁶.

Overproduction of uric acid and extreme hyperuricemia may also lead to a rapidly progressive form of renal insufficiency. Patients with less severe but more prolonged forms of hyperuricemia are predisposed to a more chronic tubulointerstitial disorder, often referred to as gouty nephropathy. Since other conditions associated with hyperuricemia, such as hypertension, nephrolithiasis, pyelonephritis, and even lead poisoning may contribute to renal damage, the effect of chronic hyperuricemia on renal function is unclear. Nevertheless, the severity of renal involvement in this disorder correlates well with the duration and magnitude of the elevation of the serum uric acid concentration.⁴ Hyperuricemia leading to hyperuricaciduria may also result in increased prevalence of nephrolithiasis.⁷

Glomerular filtration rate is the best estimate of number of functioning nephrons and functional renal mass. Accurate measurement of glomerular filtration rate is time-consuming and expensive, but a number of filtered substances may be measured to estimate glomerular filtration rate, including Blood Urea and Serum Creatinine.⁸

Objective of the present study was to study the Association of Serum Uric Acid with Blood Urea and Serum Creatinine.

MATERIAL AND METHODS

Eighty subjects were selected for study from outpatients department of Khyber Teaching hospital and clinics of general practitioners of Peshawar. All the patients were above 40 years of age. 42 (52.5%) of the subjects were males and 38 (47.5 %) were females. All of the subjects were having blood urea more than 40 mg/dl. Serum Creatinine more than 1.3 mg/dl in male subjects and more than 1.0 mg/dl in female subjects.⁸ The cause of the abnormal renal function was also noted.

Eighty subjects were selected as control group. All the subjects in the control group were more than 40 years old; 42 (52.5%) of the subjects were males and 38 (47.5%) were females. Blood Urea and Serum Creatinine were normal in control group subjects.

RESULTS

The cause of the abnormal renal function is summarized in Figure-1. Serum Uric Acid was found to be raised in 33 patients. Mean Serum Uric Acid value was 6.98 ± 2.021 in males ($p < 0.05$) and 5.054 ± 2.324 in females ($p < 0.05$). The results are summarised in Table-1 and 2.

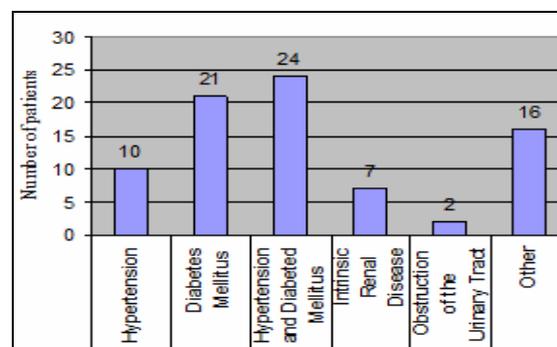


Figure-1: Causes of Abnormal Renal Function

Table-1: Serum Uric Acid levels in study group and control group

Disease	Males (42)	Females (38)	All Patients (80)
Hypertension (10)	6.953±1.756	5.692±1.632	6.165±1.693
Diabetes Mellitus (21)	7.012±1.906	5.726±1.706	6.452±1.832
Hypertension and Diabetes Mellitus (24)	7.101±2.301	5.760±1.089	6.402±1.503
Intrinsic Renal Disease (7)	5.623±1.725	4.935±0.985	5.325±1.423
Obstruction of the Urinary Tract (2)	5.324±1.502	4.534±0.823	4.852±1.326
Other (15)	5.512±1.632	4.561±0.798	4.728±1.136
Total (80)	6.213±2.025	4.956±1.125	5.861±1.132
Control Group	5.361±1.685	3.902±1.012	4.526±1.308

Table-2: Number of subjects with increased Serum Uric Acid

Disease	Males (42)	Females (38)	All Patients (80)
Hypertension (10)	2	1	3
Diabetes Mellitus (21)	6	3	9
Hypertension and Diabetes Mellitus (24)	7	4	11
Intrinsic Renal Disease (7)	2	1	3
Obstruction of the Urinary Tract (2)	0	1	1
Other (15)	4	2	6
Total (80)	21	12	33
Control Group	1	0	1

DISCUSSION

It can be seen from Figure-1, Table-1 and 2 that Serum Uric Acid is raised in patients with impaired renal function ($p < 0.05$). Levels of increased Serum Uric Acid were not significantly associated with the cause of renal disease.

Hyperuricemia is common in elderly, male patients. Associated diseases and renal impairment can be found frequently.⁹ It has been seen that hyperuricemia is commonly associated with obesity, hypertriglyceridemia, diabetes mellitus, development and progression of coronary artery disease^{10,11} and hypertension.¹² Serum Uric Acid is an independent risk factor for development and progression of Coronary Artery Disease.¹¹ Marked hyperuricemia is known to cause acute renal failure via intrarenal crystal deposition.¹³ However, recent studies suggest mild hyperuricemia may have vasoactive and proinflammatory effects independent of crystal formation.¹³

Hyperuricemia is associated with renal disease, but it is usually considered a marker of renal dysfunction rather than a risk factor for progression. Recent studies have reported that mild hyperuricemia in normal rats induced by the uricase inhibitor, oxonic acid (OA), results in hypertension, intrarenal vascular disease, and renal injury. This led to the hypothesis that uric acid may be a true mediator of renal disease and progression.¹⁴

Male gender is associated with a more rapid progression of renal disease independent of blood pressure, dietary protein intake, or serum lipid levels.¹⁴

Although hyperuricemia has long been associated with renal disease, uric acid has not been considered as a true mediator of progression of renal

disease. The observation that hyperuricemia is commonly associated with other risk factors of cardiovascular and renal disease, especially hypertension, has made it difficult to dissect the effect of uric acid itself. However, recent epidemiologic evidence suggests a significant and independent association between the level of serum uric acid and renal disease progression with beneficial effect of decreasing uric acid levels. Furthermore, our experimental data using hyperuricemic animals and cultured cells have provided robust evidence regarding the role of uric acid on progression of renal disease.

Hyperuricemia increased systemic blood pressure, proteinuria, renal dysfunction, vascular disease, and progressive renal scarring in rats. Recent data also suggest hyperuricemia may be one of the key and previously unknown mechanisms for the activation of the renin-angiotensin and cyclooxygenase-2 (COX-2) systems in progressive renal disease. Although we must be cautious in the interpretation of animal models to human disease, these studies provide a mechanism to explain epidemiologic data that show uric acid is an independent risk factor for renal progression. Although there is no concrete evidence yet that uric acid bears a causal or reversible relationship to progressive renal disease in humans, it is time to reevaluate the implication of hyperuricemia as an important player for progression of renal disease and to try to find safe and reasonable therapeutic modalities in individual patients based on their clinical data, medication history, and the presence of cardiovascular complications.^{15,16}

Hyperuricemia is commonly associated with traditional risk factors such as abnormalities in glucose metabolism, dyslipidemia, and hypertension.

Recent studies have revived the controversy over the role of serum uric acid as an independent prognostic factor for cardiovascular mortality. The authors review clinical and experimental evidence concerning the role of serum uric acid in the development of cardiovascular and renal damage. Results of trials suggesting that serum uric acid variations over time may have a prognostic impact are also discussed.¹⁷

Hyperuricemia is associated with hypertension, vascular disease, renal disease, and cardiovascular events. In this report, we review the epidemiologic evidence and potential mechanisms for this association. We also summarize experimental studies that demonstrate that uric acid is not inert but may have both beneficial functions (acting as an antioxidant) as well as detrimental actions (to stimulate vascular smooth muscle cell proliferation and induce endothelial dysfunction). A recently developed experimental model of mild hyperuricemia also provides the first provocative evidence that uric acid may have a pathogenic role in the development of hypertension, vascular disease, and renal disease. Thus, it is time to reevaluate the role of uric acid as a risk factor for cardiovascular disease and hypertension and to design human studies to address this controversy.¹⁸

Recent studies in both humans and experimental animals have led to renewed interest in uric acid and its association with hypertension, cardiovascular events and renal disease progression. This has also refuelled a longstanding debate regarding the precise role of this ubiquitous breakdown product of purine metabolism in these disease processes. Various lines of evidence suggest that uric acid may have a direct role in the pathogenesis of hypertension and vascular disease. Regardless of this possibility, it is apparent that serum uric acid levels serve as a powerful 'biomarker' or independent predictor of prognosis and outcome in certain renal, cardiovascular and cerebrovascular diseases. Whether these outcomes can be improved by specifically treating asymptomatic hyperuricaemia remains inadequately resolved at this stage. Data from various animal studies suggests that lowering uric acid levels may be of benefit, but the crucial human studies are still lacking. This review examines some of the recent evidence supporting a causal and contributory role for uric acid in cardiovascular and renal disease. How clarification of the role of uric acid may guide future treatment strategies is also discussed.¹⁹

Recent experimental findings have led to renewed interest in the possible role of uric acid in the pathogenesis of both hypertension and vascular disease. Often considered an antioxidant, biochemical and in vitro data indicate that noncrystalline, soluble

uric acid also can react to form radicals, increase lipid oxidation, and induce various pro-oxidant effects in vascular cells. In vitro and in vivo findings suggest that uric acid may contribute to endothelial dysfunction by inducing antiproliferative effects on endothelium and impairing nitric oxide production. Proinflammatory and proliferative effects of soluble uric acid have been described on vascular smooth muscle cells (VSMCs), and in animal models of mild hyperuricemia, hypertension develops in association with intrarenal vascular disease. Possible adverse effects of uric acid on the vasculature have been linked to increased chemokine and cytokine expression, induction of the renin-angiotensin system, and to increased vascular C-reactive protein (CRP) expression. Experimental evidence suggests a complex but potentially direct causal role for uric acid in the pathogenesis of hypertension and atherosclerosis.²⁰

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