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ASSOCIATION OF SERUM URIC ACID AND C-REACTIVE PROTEIN LEVEL IN CHRONIC KIDNEY DISEASE PATIENTS

Biochemistry

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ABSTRACT

Increased C-reactive Protein (CRP) and hyperuricemia are both identified as independent markers of inflammation. An increased uric acid level to be associated with endothelial dysfunction. Its role in chronic kidney disease (CKD) has not been explored much.The present study was planned to assess the serum uric acid and c-reactive protein levels in patients suffering from CKD and to explore the association of serum uric acid and c-reactive protein levels in these CKD patients. Hundred patients diagnosed for CKD based on International Classification of diseases (ICD-10) were enrolled for the study. Hundred age and sex matched healthy subjects constituted the control group. Serum uric acid and c-reactive protein levels were estimated for all enrolled subjects. Results obtained were compared statistically among the diseased and healthy control subjects. Mean serum CRP (P=0.00) and uric acid(P=0.00) were significantly higher in CKD patients. Findings of the present study suggest that CRP and serum uric acid level tend to be higher in patients suffering from CKD. Further the study also demonstrates that serum uric acid levels increase with the increasing CRP levels. Since both CRP and uric acid are established independent risk factors of cardio vascular disease (CVD), their association in CKD patients should be explored further.

KEYWORDS

C-reactive protein, chronic kidney diseases, hyperuricemia

INTRODUCTION

C-reactive protein (**CRP**) is an annular (ring-shaped), pentameric protein found in blood plasma, which rise in response to inflammation.[1] It is synthesized by the liver in response to factors released by macrophages and fat cells (adipocytes).[2] It was the first pattern recognition receptor (PRR) to be identified.[3] It is used mainly as a marker of inflammation.

Uric acid is a product of the metabolic breakdown of purine nucleotides, and it is a normal component of urine. It forms ions and salts known as urates and acid urates. Uric acid concentrations in blood plasma above and below the normal range are known as hyperuricemia and hypouricemia.[4]

High uric acid levels in your blood can also indicate of a variety of conditions, including-Diabetes, gout, (which involves recurring attacks of acute arthritis), hyperparathyroidism, acute kidney failure and plays a major role in kidney stones. Elevated levels of CRP have been associated with diabetes and cardiovascular incidence in previous studies. It has been associated with albuminuria and reduced eGFR in cross sectional studies. Elevated levels of CRP have been associated with diabetes and cardiovascular incidence in previous studies. It has been associated with albuminuria and reduced eGFR in cross sectional studies.[5]

Serum uric acid is commonly elevated in patients with chronic kidney disease (CKD), but was not frequently used as diagnostic test. Recently, uric acid has been restored as a potential contributory risk factor in the development and progression of CKD. Most studies documented that an elevated serum uric acid level independently predicts the development of CKD.[6]

CKD is a general term for heterogeneous disorders affecting the structure and function of the kidney. CKD encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR).[7] CKD is highly prevalent in developing countries.[8]Rapid increase in the prevalence of risk factors such as diabetes, hypertension, and obesity will result in an even greater burden of CKD in the future, and is likely to have substantial socioeconomic and public health consequences in resource-poor countries.[9]

The guidelines define CKD as either kidney damage or a decreased glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 for at least 3 months. Whatever the underlying etiology, once the loss of nephrons and reduction of functional renal mass reaches a certain point, the remaining nephrons begin a process of irreversible sclerosis that leads to a progressive decline in the GFR.[10]

Increased CRP and hyperuricemia are both identified as independent maker of inflammation. Several studies have suggested increased uric acid levels to be associated with endothelial dysfunction. However, association of CRP and uric acid has not been studied as such.

The present study was planned to assess the association of serum uric acid and CRP levels in CKD patients.

MATERIAL AND METHOD

The study was conducted in Department of Biochemistry in association with Department of Nephrology of Mahatma Gandhi Medical College &Hospital, Jaipur. Patients diagnosed for CKD, visiting the Outpatient Department (OPD) of Nephrology fulfilling the inclusion criteria were enrolled for the study. 100 age and sex matched healthy subjects constituted the control group. The study was conducted after seeking approval from the Institutional Ethics Committee (IEC).Patients above 65 years of age, CKD patients with overt inflammatory or infectious diseases, Patients suffering from Malnutrition, Estrogen therapy and patients on uric acid lowering medication were not included in the study.

Blood samples were collected by venipuncture using standard aseptic technique. Serum CRP and uric acid levels were estimated on VITROS 4600 Chemistry analyzer using Ortho Clinical diagnostics reagents. Results obtained were presented as mean$\pm$SD and compared statistically in the disease and control groups.

RESULT

This study involved 100 CKD patients and 100 control subjects. The CKD group comprised of 68 males and 32 females. CRP, urea, creatinine, uric acid were significantly higher in CKD group than in control group.

Table 1: Comparison of parameters between CKD and Control groups

PARAMETER	CONTROL	CKD	P-value
Age (years)	46.56±15.24	47.75±14.69	NS
CRP (mg/L)	6.24±1.66	35.23±20.27	0.00
Uric Acid (mg/dl)	3.98±1.15	6.73±1.92	0.00
Creatinine (mg/dl)	0.81±0.47	8.06±3.38	0.00
Urea (mg/dl)	3.98±1.15	6.73±1.92	0.00

Further the patients are sub-divided into 3 groups:
CRP <10mg/L- **Negative ;** n=18
CRP 10-30mg/L – **Mild ;** n=30
CRP >30mg/L – **Strongly positive ;** n=52

Table 2: Distribution of Male and Female ratio among the respective groups of CRP levels

GROUP	n	Male	%	Female	%
CRP <10 mg/L	18	11	61.0	7	39.0
CRP 10-30 mg/L	30	21	70.0	09	30.0
CRP >30 mg/L	52	36	69.0	16	31.0

Table 3 – Comparison of all the parameters among the respective groups of CRP levels

PARAMETER	CRP<10 mg/L (n=18) NEGATIVE	CRP 10-30 mg/L (n=30) MILD	CRP >30 mg/L (n=52) STRONGLY POSITVE	F= value	P-value
Age(Years)	38.27±8.36	37.17±11.37	40.88±7.36	1.72	NS
CRP (mg/L)	5.66±1.14	16.41±5.38	47.46±15.78	114.57	0.00
Uric Acid (mg/dl)	5.84±1.88	6.34±1.75	7.27±1.81	4.41	0.015
Creatinine (mg/dl)	5.80±1.87	7.47±2.97	7.27±8.90	5.38	0.006
Urea (mg/dl)	111.61±35.92	194.13±59.01	149.90±74.53	2.42	0.094

Table 2 represents the gender based distribution of patients in present study represents that the prevalence of kidney diseases in male is higher (68%) than the females (32%). The study group with CRP10-30mg/L has the higher (52%) percentage of occurrence of kidney disease in comparison with other two study groups.

Table 1 shows the comparison of parameters among disease group and control group, the mean serum CRP levels in control group and study group 6.24±1.66 mg/L and 35.23±20.27 mg/L.

It was observed that mean serum creatinine was progressively higher with increase in CRP levels (p=0.006).On applying one way ANOVA the variation was statistically significant. The mean serum urea level in the study sub-groups. Though the mean level show a non-significant variation on applying one way ANOVA, but serum urea level seem to be higher in the CRP positive patients as compare to CRP negative CKD patients(P=0.094).

Serum Uric acid levels were shown to increase with the increasing level of CRP. The variation was significantly higher on applying one way ANOVA test (p=0.015). In the sub-group with CRP >30mg/L, uric acid levels were as high as 7.27±1.81mg/dl, but in the other two subgroups the levels of uric acid remains under the normal range.

DISCUSSION

CKD has been defined as the presence of markers of kidney damage for more than 3 months with or without reduction in GFR or as the presence of GFR less than or equal to 60ml/min/1.73m^2 for 3 months with or without other signs of kidney damage.[10]

Several studies have shown the relation between serum urea and creatinine as the marker of kidney disease. But CRP and uric acid are always neglected by physicians to assess CKD stages in patients.

Recently C-reactive protein (CRP) is in vogue for its utility in assessing cardiovascular risk. Elevated plasma CRP level, the prototypic marker of inflammation, has been shown to be strongly predictive of an increased risk of future myocardial infarction and predicts mortality in apparently healthy people as well as in patients with established coronary artery disease.[11]

The mean serum CRP levels in lower in control group than that of study group. In a review by Oluseyi A. Adejumo et.al,[12] reported that the median serum level of CRP was significantly higher in the CKD group compared to the controls who did not have CKD (p=<0.001). Similarly, a study by Ervin R Fox, et. al,[13] states that mean CRP concentrations in CKD patients was observed to be 3.2±1.1 mg/L which is almost same as that of the current study.

Hyperuricemia is an independent risk factor for CKD and contributes to kidney fibrosis. Increased uric acid (UA) is strongly linked to cardiovascular disease. However, the independent role of UA is still debated because it is associated with several cardiovascular risk factors including obesity and metabolic syndrome.[14]Christin Giordano et al.,[15] have demonstrated that uric acid does indeed affect endothelial function and can contribute to worsening renal disease.

Previously published data reveals that, there are controversial reports on the association between SUA levels and CKD. Ching-Wei Tsai et.al.,[16] study showed a higher UA level was significantly associated with a greater decline in renal function and a higher risk of progressing to kidney failure in a Chinese population.The results of Tokiko Miyaoka et.al.[17] study showed that hyperuricemia but not serum uric acid levels were associated with all-cause mortality, CVD mortality after adjustments with CVD risk factors, kidney disease factors, and allopurinol in stage 2–4 CKD patients.

The present study states that the mean age was highest in than the group with CRP >30mg/L. of groups CRP>30mg/L. The difference was however statistically not significant (P=NS).Mary Mallappalli et.al.,[18] stated that age is a significant risk factor for chronic kidney disease (CKD).

Serum Uric acid levels were shown to increase with the increasing level of CRP. The variation was significantly higher on applying one way ANOVA test (P=0.015). The uric acid levels were as high in of groups CRP>30mg/L, but in the other two subgroups the levels of uric acid remains under the normal range. Ching-Wei Tsai et. al.,[16] study showed a higher UA level was significantly associated with a greater decline in renal function and a higher risk of progressing to kidney failure in a Chinese population. In another study by Salvatore De Cosmo et.al.,[19] presented that mild hyperuricemia is strongly associated with the risk of CKD in patients with type 2 diabetes.

It was observed that mean serum creatinine was progressively higher with increase in CRP levels (p=0.006).On applying one way ANOVA the variation was statistically significant. Pravin N. Baravkar et.al.,[20] demonstrated that CRP levels were higher in the CKD stage 5 patients as compared to CKD stage 4 patients. Serum creatinine is reliable marker of renal function.

CONCLUSION

Findings of the present study suggest that CRP and serum uric acid level tend to be higher in patients suffering from CKD. Further the study also demonstrates that serum uric acid levels increase with the increasing CRP levels. Since both CRP and uric acid are established independent risk factors of CVD, their association in CKD patients should be explored further.

The study recommends that screening of CKD patients for CRP as well as uric acid can be helpful in identifying patients at risk of developing CVD. Early risk assessment of such patients can be helpful in providing timely patient care.

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