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RESEARCH ARTICLE

SIGNIFICANCE OF RAISED SERUM URIC ACID LEVELS IN PATIENTS WITH CHRONIC KIDNEY DISEASE.

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Abstract

Background: Hyperuricemia is common in chronic kidney disease (CKD). The present study evaluated the associations between baseline serum uric acid levels with mortality and end-stage renal disease (ESRD). Chronic kidney disease (CKD) is a serious condition associated with premature mortality, decreased quality of life, and increased health-care expenditures. Chronic kidney disease occurs when one suffers from gradual and usually permanent loss of kidney function over time.

Material and Method: This is a prospective observational study conducted in Nephrology Dept affiliated to Biochemistry Dept, Govt. General Hospital, Kurnool From June 2018 to May 2019. In this study, 158 CKD patients were studied with detailed clinical and laboratory examination and divided into two groups: one group included 60 CKD patients with raised serum uric acid and another group containing 98 CKD patients with normal serum uric acid. Both groups were age matched.

Results: In our study, prevalence of raised serum uric acid in CKD patients was found to be 38.4%. It is observed that, CKD patients with raised serum uric acid were predominantly male and presented mainly in later part of life. There is statistically significant ($p < 0.05$) positive correlation is found between serum uric acid and stages and severity of CKD, hypertension, diabetes mellitus, serum BUN, serum creatinine, urine albuminuria, anaemia, cardiovascular disease, mortality and negative correlation with eGFR.

Conclusion: In CKD patients, higher serum uric acid levels were associated with higher degree of renal dysfunction, hypertension, diabetes, urine albuminuria, anaemia, cardiovascular disease and mortality. It is found that most common cause of mortality in CKD patients with raised serum uric acid was cardiovascular disease/events.

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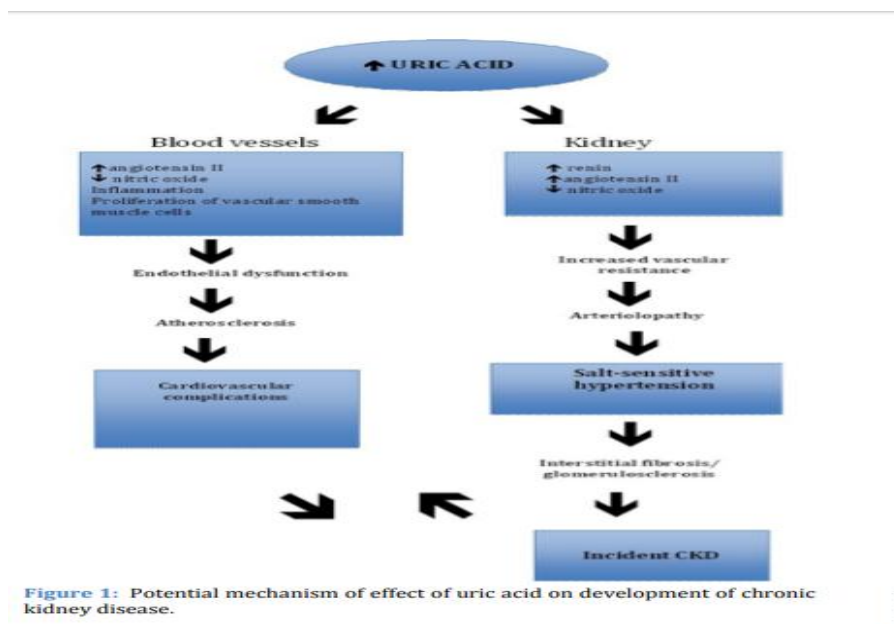
Introduction:-

Hyperuricemia is common in chronic kidney disease (CKD). The present study evaluated the associations between baseline serum uric acid levels with mortality and end-stage renal disease (ESRD). Chronic kidney disease (CKD) is a serious condition associated with premature mortality, decreased quality of life, and increased health-care expenditures. Chronic kidney disease occurs when one suffers from gradual and usually permanent loss of kidney function over time. This happens gradually, usually over months to years.¹

The lineage of kidney disease as a subject of study generally is traced to 1827, when Richard Bright (1789-1858) described his eponymous disease of the kidneys in albuminuric dropsical patients who died in kidney failure. By middle of 19th century, kidney disease was defined, its diagnosis by urinalysis was established, and its structural changes were characterized, but speciality of nephrology went unborn and patients continued to seek urologic care for their hematuria, proteinuria and uremia.³ It was a return to the roots of nephrology at the turn of the 21st century that refocused attention on kidney disease not as a fatal condition requiring replacement therapy, but as a clinical entity that is common, harmful, early to diagnosed and potentially treatable.⁴

Chronic kidney disease (CKD) prevalence is increasing world-wide and the prevalence of end-stage renal disease (ESRD) is expected to rise by 44% from 2000 to 2015.

Some of the proposed mechanisms of kidney damage are from uric acid include induction of afferent arteriopathy, inflammation and activation of the renin-angiotensin system.²



The pattern of disease morbidity and mortality throughout the world is changing both in the developed and the emerging world. The major cause of end-stage renal failure in most countries worldwide is now diabetes. India has the largest number of people with diabetes in the world, with the projected figures of 57.2 million cases in 2025. This will make India the reservoir of CKD.⁹

The annual incidence of ESRD differs between developed and developing countries, 34 — 240 per million population (pmp) to 98 — 198 per million populations, respectively.¹⁰

Classification of CKD:

The KDOQI definition (2002) of CKD was accepted worldwide and given as follows:⁵

Table 1:-Classification on severity of CKD

Stage	Description	GFR ml/min/1.73m ²	Related items
1	Kidney damage with normal or increased GFR	>90	Albuminuria, proteinuria, hematuria
2	Kidney damage with mild reduction in GFR	60-89	Albuminuria, proteinuria, hematuria
3	Moderate reduction in GFR	30-59	Chronic renal insufficiency or early renal insufficiency
4	Severe reduction in GFR	15-29	Chronic renal insufficiency or late renal insufficiency or pre ESRD
5	Kidney failure	<15 or dialysis	Renal failure, uremia, ESRD

Criteria for the Definition of Chronic Kidney Disease(CKD):

Kidney damage for 3 months as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, that can lead to decreased GFR, manifest by either:

1. Pathological abnormalities; or
2. Markers of kidney damage, including abnormalities in imaging tests
3. GFR <60ml/min/1.73 m² for 3months, with or without kidney damage

Materials And Methods:-

The present study is a prospective study carried out on 158 CKD patients in ICU and Nephology Dept of Govt. General Hospital , Kurnool From June 2018 to may 2019. Formal approval of hospital ethical committee and written consent of the CKD patients were obtained for this study.

Patients satisfying the inclusion and exclusion criteria were enrolled into the study. Detailed clinical, biochemical, haematological examinations were conducted to establish the diagnosis and stage of CKD.

The present study was carried out on 158 adult patients of CKD (Chronic Kidney Disease). Out of which 60 CKD patients with raised serum uric acid were placed in study group were compared with age matched 98 CKD patients with normal serum uric acid.

Inclusion Criteria:

1. All the patients of both the sexes >18 years of age
2. All the diagnosed cases of chronic kidney disease.

Exclusion Criteria:

1. All the patients <18 years of age.
2. All HIV Positive individuals.
3. All the patients having history of gout and/or
4. Hyperuricemia.
5. Patients who are on anti tubercular drugs and thiazide diuretics.

Diagnostic Criteria:

All the patients were evaluated for chronic kidney disease (CKD) as per the KDOQI criteria (2002) by National Kidney Foundation for diagnosis of CKD.5

After confirmation of diagnosis from the above parameters, blood samples are drawn from these patients for the estimation of serum uric acid by Uricase method.

The study was designed to include the Demographic, clinical data, biochemical and haematological changes observed in CKD patients. The data was entered into a structured proforma separately. Management was done as per standard guidelines.

Detailed clinical examination was done in all CKD patients. All these CKD patients were evaluated clinically for history of fever, easy fatigability, facial puffiness, swelling over extremities, nausea and vomiting, generalized bodyache, breathlessness, altered sensorium, convulsions, decreased urine output, haematuria, haematemesis/melaena, pallor, pedal oedema, blood pressure and other vitals.

The laboratory investigations done in all CKD patients included a complete haemogram, fasting and postprandial blood sugar level, serum BUN, creatinine, eGFR, Serum potassium, calcium, serum uric acid, 24hrs urine albuminuria, HIV, Hepatitis B and C.

Detailed ultrasonography of abdomen and pelvis was done to check the size, shape and echo texture of the kidney.

Statistical Analysis:-

Data was analyzed by statistical Package for social sciences Version -16 (SPSS 16) software. Data was presented in frequency and percent distribution form. Association in between the parameters was tested using Pearson's chi square test. Mean values of parameters were compared between normal and raised uric acid levels in CKD patients using unpaired t-test. Mean comparisons of values of parameters in between patients with 5 stages of CKD were done by using ANOVA (Analysis Of Variance Test). P value less than 0.05 was considered as significant

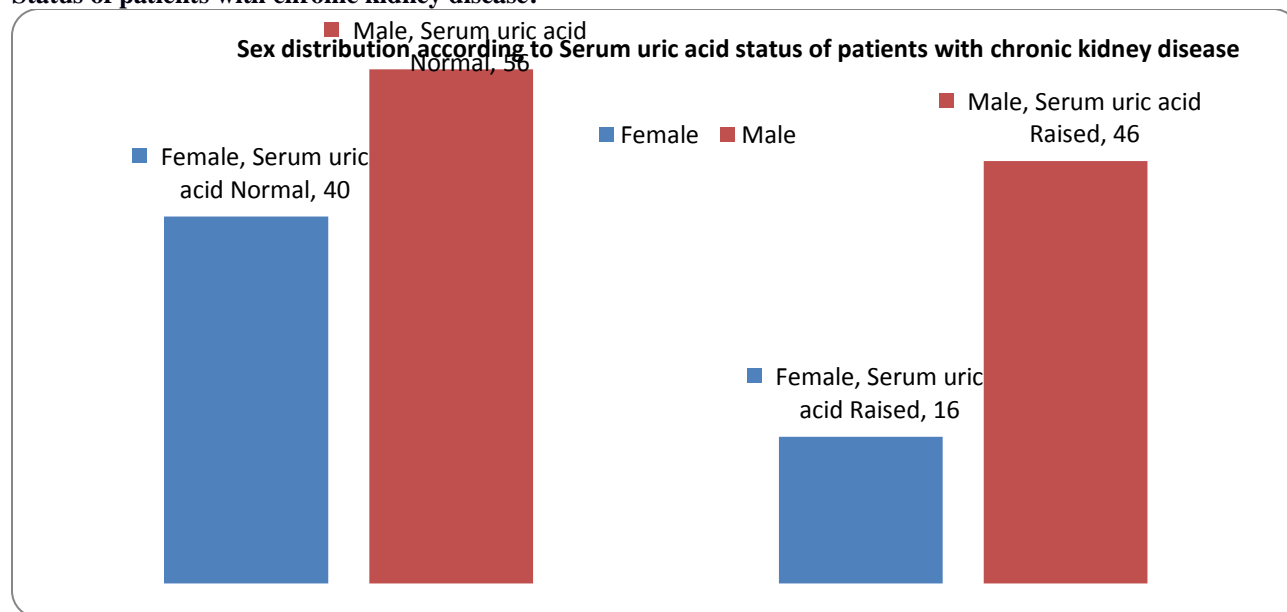
Results:-

158 patients of documented CKD were taken and divided into 2 groups of which study group included 60 CKD patients with raised serum uric acid levels and comparison group included 98 CKD patients with normal serum uric acid levels. Statistical analysis showing results of study is given as follows:

Table 2:-Sex distribution according to Serum uric acid

Sex	Serum uric acid		Ttotal
	Normal	Raised	
Female	40	16	56
Male	56	46	95
Total	96	62	158

Status of patients with chronic kidney disease:



Stages of CKD:

In those with raised uric acid level, Maximum i.e. 54% CKD patients had stage 5 CKD, 30% had Stage 4 and 10% had Stage 3 CKD, 5% had Stage 2 and 1% has Stage 1 CKD. Of Normal uric acid level patients 28% were in stage 5, 26% were in stage 4 and 15% in Stage 3 while 16% in Stage 2 and 15% in Stage 1. There was statistically highly significant ($p < 0.01$) difference with higher proportion of patients in higher Stage of CKD in raised uric acid group compared to normal uric acid group.

Table 3:- Stage of CKD according to Serum uric acid status of patients

Stage of CKD	Serum uric acid		Total
	Normal	Raised	
1	15	1	16
2	16	3	19
3	15	6	21
4	25	18	43
5	27	32	59
Total	98	60	158
	100.00%	100.00%	100.00%

Table 4:- Associated disorders according to Serum uric acid status of patients with chronic kidney disease

Parameters	Serum uric acid		Total	X2	P value
	Normal	Raised			
CKD with cardiovascular Diseases					
No	69	23	92	18.767	<0.001
	75%	25%	100%		
Yes	21	33	54		
	38.9%	61.1%	100%		
CKD with anemia					
No	21		21	15.262	<0.001
	23.3%		14.4%		
Yes	69	56	125		
	76.7%	100.0%	85.6%		

Table 7:- Comparison of different parameters in CKD patients with raised and normal serum uric acid

Parameter	Uric acid		P value
	Normal	Raised	
Age (yrs)	52.97	54.07	0.604
Sex(% Male)	58.9%	78.6%	0.027
SBP on admission (mmHg)	140	162	<0.001
DBP on admission (mmHg)	87	96	<0.001
Hypertension	70%	85.7%	0.031
Fasting Glucose (mg/dl)	102	134	<0.001
Postprandial glucose (mg/dl)	174	220	<0.001
HbA1C	5.47	7.25	<0.001
Diabetes mellitus	24.4%	44.6%	0.011
Urine albuminuria (mg/dl)	390	1112	<0.001
S BUN (mg/dl)	44.42	72.11	<0.001
Creatinine (mg/dl)	2.774	4.93	<0.001
eGFR (ml/min/1.73m2)	44.16	15.15	<0.001

Anemia risk	76.7%	100%	<0.001
Cardiovascular risk	23.3%	58.9%	<0.001
Death	0	14.3%	<0.001

Discussion:-

Previous studies have shown that serum uric acid is having independent role in progression of CKD and is also cause and predictor of associated morbidities in CKD.

Blood samples for measurement of serum uric acid level and other biochemical assessments were obtained immediately after admission. Uric acid concentration expressed in milligrams per deciliters (mg/dl). Male patients with uric acid concentration >7 mg/dl and female patients with >6 mg/dl were considered as having raised serum Uric acid. Furthermore for studying correlations of serum Uric acid with other clinical and investigational findings, all CKD patients were divided into two groups out of which one group included CKD patients with raised uric acid and other group included CKD patients with normal uric acid. Both groups were age matched.

There were 96 CKD patients with normal UA group and 62 patients in ckd with raised UA group were included in the study.

Serum UA level of ckd patients done on day of admission in both age matched groups were compared by t-test where its value $p < 0.05$ is considered as statistically significant. Thus patients who were having raised serum UA level was because of ckd and in both ckd groups derangement of other clinical and biochemical profiles were due to raised serum UA

The findings which we got in our study are discussed as follows:

Age:

In our study, we found that out of 158 CKD patients maximum that is 54% were within age group of 51-70 yrs. and 46% ckd patients were in age group of 31-50 yrs. This finding is consistent with findings of the study by Punamyadav *et al*, (2014), Madero *et al*, (2009) and George.S *et al*, (2013). It is observed that incidence of CKD reaches its maximum strength in later part of life.12-14

Sex:

In our study, (from Table 2), it is found that 78.6% males and 21.2% females were in ckd with raised UA group which shows statistically significant ($P < 0.027$) difference of male predominance over females in ckd patients with raised UA level. This finding in our study is consistent with findings in the studies by Nacak *et al*, (2014) & Madero *et al*, (2009)

Serum Uric Acid Levels In Relation With Severity Of Ckd

In our study, (from Table 4, 6 & 9), it is found that, there was statistically significant ($p < 0.01$) correlation of raised serum uric acid with increasing stages of ckd, and it's severity. Serum uric acid was statistically significantly ($p < 0.001$) positively correlated with serum BUN, serum creatinine, and negatively correlated with eGFR, . In our study, ANOVA study also showed the statistically significant positive correlation between raised serum uric acid and progressively declining renal functions and severity of ckd. This finding in our study is consistent with the findings of studies by Chen *et al*, (2014)(, Mostafa Kamel *et al*, (2013)16, Nermina Babic *et al*, (2014), J. T. Park *et al*, (2009), where it is found that, this was statistically highly significant positive correlation of serum uric acid with stages and severity of ckd, duration of illness and marker of reduced renal functions like serum BUN and serum creatnine and negatively correlate with eGFR.

Hypertension:

In our study, (from Table 7), it is found that, significant proportion of hypertensive patients had come in CKD with raised UA group i.e., 85.7%, and showing statistically significant positive correlation ($p = 0.031$) of UA with hypertension, this finding is consistent with the findings of studies by J. T. Park *et al*, (2009) , Paul *et al* , (2012) and Liu WC *et al*, (2012). It is found that, there is statistically significant higher systolic BP ($P < 0.001$) and diastolic BP ($P < 0.001$), in raised UA CKD patients than normal UA CKD patients. This findings are consistently matched with findings of studies by B. Satirapoj *et al*, (2010) and Mostafa Kamel *et al*, (2013).

Diabetes Mellitus:

In our study, (from Table 7), it is found that, there was statistically significant positive difference of diabetes ($p=0.011$) in CKD patients with raised uric acid level (44.6%) than normal uric acid level (24.4%) in CKD patients. Also, serum uric acid has statistically significant positive correlation ($p<0.001$) with both fasting and post prandial blood sugar level. This finding in our study is consistently matched with the findings of studies by J. T. Park *et al*, (2009), Adel Gouri *et al*, (2013) and Liu WC *et al*, (2012).15-30

Conclusion:-

In CKD patients, higher serum uric acid levels were associated with higher degree of renal dysfunction, hypertension, diabetes, urine albuminuria, anaemia, cardiovascular disease/ events and mortality. It is found that most common cause of mortality in CKD patients with raised serum uric acid was cardiovascular disease/events.

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