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Study of Serum Uromodulin Concenterations Correlate with Glomerular Filtration Rate in Chronic Kidney Disease Patients

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ABSTRACT: INTRODUCTION: Serum uromodulin serve as a marker for kidney function. Uromodulin is found in both CKD and healthy individuals and in patients have faster decline in kidney function.
AIM AND OBJECTIVES: To find out correlation of serum uromodulin concentrations n patients with stages 2 to 4 of Chronic Kidney disease.
MATERIAL AND METHODS: Study involved 120 patients divided in Case group (60 patients) attended medical/ urology OPD or admitted in medical/urology ward of CKD2 – CKD4 while control group – age and sex matched healthy individuals/ stage I CKD patients was taken as control. The plasma/ serum were used for serum urea, creatinine, Cystatin C and uromodulin under all aseptic precaution on receiving consent.
RESULT: The patients of CKD included in study were having glomerulonephritis (46.7%), pyelonephritis (21.7%), diabetic kidney disease (13.3%), polycystic kidney disease (1.7%) and other causes (16.7%). CKD patients demonstrated serum Uromodulin 68.8 ng/ml (range 38.9–108.3) together with a rise in urea 59.9 ± 17.6 mg/dL, serum creatinine 1.56 ± 0.97 mg/dL and Cystatin C 199 ± 113 ng/ml as compared to control have serum Uromodulin209.7 ng/ml (range 153.8 – 312.6), urea 22.3 ± 5.7 mg/dL, serum creatinine 0.75 ± 0.14 mg/dL and Cystatin C 76 ± 17 ng/ml (P value <0.05).
CONCLUSION: Serum Uromodulin closely correlates with serum Cystatin C, creatinine, and eGFR, and serve as a potential early and sensitive marker of impaired kidney function/ chronic kidney disease
Keywords- CKD, GFR, NGAL.

I. INTRODUCTION

Non communicable diseases such as chronic kidney disease are emerging as an important public health problem with its high prevalence, morbidity and mortality. Chronic Kidney Disease (CKD) is found to be one of the causes of mortality in Indian subcontinent. [1, 2] Chronic Kidney Disease was defined by the reduction of glomerular filtration rate (GFR) to less than 60 mL/min/1.73 m^2 and/or evidence of kidney damage, such as proteinuria (albuminuria > 30 mg/g of creatinine), glomerular-based or tubular-based hematuria (not urologic), or abnormal renal imaging and pathologic abnormalities of 3 months duration or longer, irrespective of the cause. According to International Society of Nephrology's Kidney Disease Data Center Study recent report, the prevalence of Chronic Kidney Disease is 17%. In India different regions have prevalence ranges from < 1% to 13%. [3] However GFR is used to determine the stage of kidney disease and its function. Glomerular filtration rate tells about the kidney functions. There are 5 stages in Chronic Kidney Disease which are based on Glomerular filtration rate.

Table: - KDIGO classification of CKD

S. No.	GFR Stages	GFR (mL/min/1.73 m^2)	Terms
1.	G1	>90	Normal
2.	G2	60–89	Mildly decreased
3.	G3a	45–59	Mild to moderately decreased
4.	G3b	30–44	Moderate to severely decreased
5.	G4	15–29	Severely decreased
6.	G5	<15	Kidney failure

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The Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines advocate that serum creatinine is a very sensitive marker for estimating GFR in patients with potential kidney disease and to classify in stage of disease. [4]

Uromodulin (Tamm - Horsfall protein), produced by epithelial cells lining the ascending limb of the loop of Henle and found in urine abundantly under normal conditions,. Uromodulin is released into the lumen of the renal tubules from the apical part of epithelial cells of renal tubules and excreted in urine in amounts of 100 to 200 mg/dl and also present in serum at very low concentrations (70–540 ng/ml). Uromodulin protect tubular cells from ascending urinary tract infections (UTI).

Recent genome wide association studies have shown that modifications in the UMOD gene are associated with an increased risk of chronic kidney disease (CKD) and accelerate its progression. It is believed that uromodulin may be a potential urinary biomarker which reflects renal function, chronic kidney disease, and hypertension. [5]

Various studies suggest that various different kidney parameters are expressed by tubular interstitial damage and atrophy in course of chronic kidney disease. Studies suggested that uromodulin is found in both CKD and healthy individuals while urea, creatinine and Cystatin C raises in acute kidney injury (AKI) and patients who are at higher risk of faster decline in kidney function. Various studies of both serum uromodulin show positive as well as negative correlation with GFR, creatinine and Cystatin C. Reliability; sensitivity and high diagnostic accuracy of uromodulin between healthy individuals and CKD patients were assessed.

II. MATERIAL & METHODS

The study was conducted on two age and sex matched group of participants attending medical OPD/ urology OPD and Biochemistry Lab of Jawahar Lal Nehru Medical College and Hospital, Ajmer, Rajasthan. The study was conducted in total 120 patients divided in two groups of 60 each. Case group was consist of 60 patients attending medical OPD/urology OPD or admitted in medical/urology ward of CKD 2 – CKD 4 while control group was consist of 60 age and sex matched healthy individuals/ stage I CKD patients were taken as control. Informed and written consent were taken from all the participants. This study was reviewed by the ethical committee.

Inclusion criteria

1. Chronic Kidney disease stage 1 to stage 4
2. Glomerular filtration rate < 90
3. Age > 18 years

Exclusion criteria

1. Pregnancy or lactation
2. Patients with End Stage Renal Disease, dialysis and cardiac conditions
3. Patients on treatment with immunosuppressive drugs
4. Age < 18 years

Blood samples were collected in plain vial for estimation of urea, creatinine, cystatin C, uromodulin and lipocalin 2 by venipuncture, under all aseptic precaution on admission. The samples were collected and serum was stored at – 70^{o} C. The measurement of serum urea by Berthelot enzymatic colorimetric method [6], Serum Creatinine by Jaffe's colorimetric kinetic method [7], Serum Cystatin-C by Enzyme Linked Immunosorbent Assay (Cystatin C Human ELISA Kit, Invitrogen, Thermo Fisher scientific), Serum Uromodulin by Enzyme Linked Immunosorbent Assay (Human Uromodulin ELISA Kit, Invitrogen, Thermo Fisher scientific) was done.

III. RESULT

The patients of CKD included in study were having glomerulonephritis in 46.7% of case, pyelonephritis in 21.7% of cases, diabetic kidney disease in 13.3% of cases, polycystic kidney disease in 1.7% of cases and other causes were found in 16.7% of cases.

CKD patients (case group) demonstrated decreased serum Uromodulin level 68.8 ng/ml (range 38.9–108.3) together with a rise in urea 59.9 ± 17.6 mg/dL, serum creatinine 1.56 ± 0.97 mg/dL and Cystatin C 199 ± 113 ng/ml level as compared to control group have serum Uromodulin209.7 ng/ml (range 153.8 – 312.6), urea 22.3 ± 5.7 mg/dL, serum creatinine 0.75 ± 0.14 mg/dL and Cystatin C 76 ± 17 ng/ml (P value <0.05).

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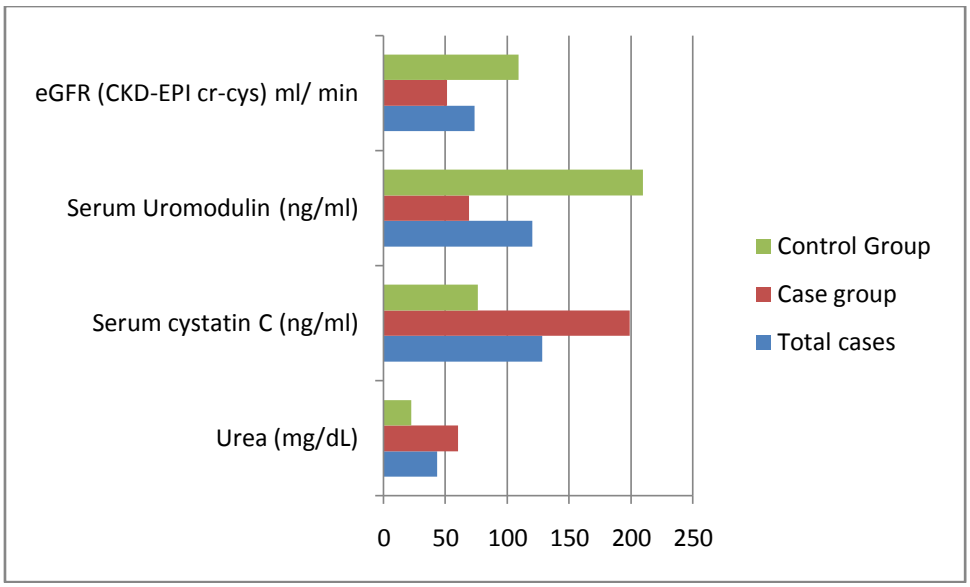
Table 1 – Characteristics of the study group

Parameter	Total cases (120)	Case group (60)	Control Group (60)
Age (years)	45.68 ± 11.08	43.32 ± 12.86	44.18 ± 16.96
BMI (kg/m^2)	25.9 (22.7–29.3)	24.9 (22.1–29.4)	27.5 (23.9–30.9)
Body surface area (m^2)	1.90 (1.71–2.04)	1.72 (1.63–1.87)	2.03 (1.92–2.17)
Systolic blood pressure (mmHg)	133 ±15	131 ±12	132 ±16
Diastolic blood pressure (mmHg)	81 ±7	79 ±8	83 ±10
Urea (mg/dL)	43.2 ± 11.8	59.9 ± 17.6	22.3 ± 5.7
Serum creatinine (mg/dL)	1.02 ± 0.16	1.56 ± 0.97	0.75 ± 0.14
Serum cystatin C (ng/ml)	128 ± 49	199 ± 113	76 ± 17
Serum uromodulin (ng/ml)	120.3 (38.2-312.6)	68.8 (38.9–108.3)	209.7 (153.8-312.6)
eGFR (CKD-EPI cr-cys) ml/ min	73.57 ± 7.93	51.22 ± 8.09	109.13 ± 19.09



Graph 1 – Indicating correlation of eGFR, Urea, Cystatin C, Uromodulin.

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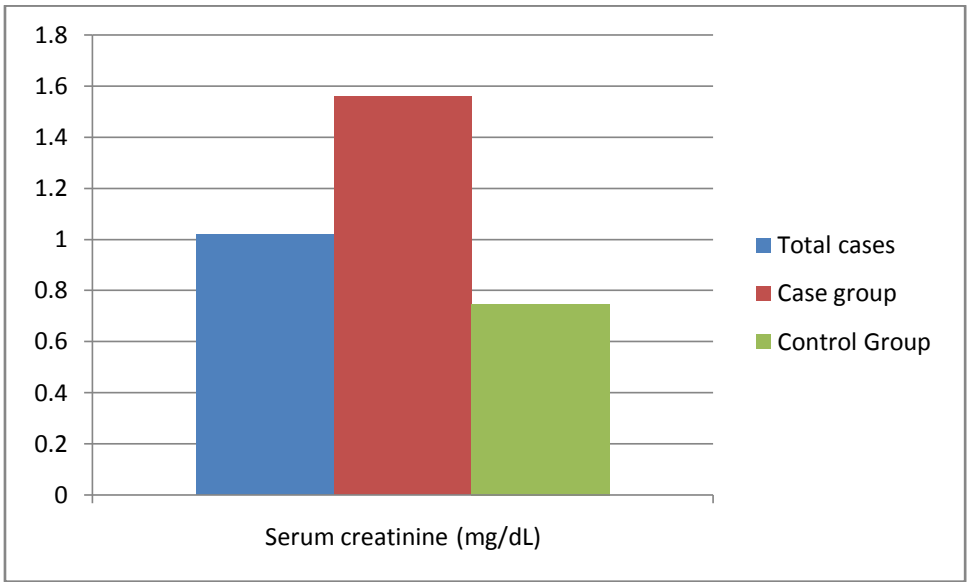

Graph 2 – Indicating correlation of Serum Creatinine with case, control and total patient group.

IV. DISCUSSION

In healthy subjects the serum uromodulin level is high as compared to patients with chronic kidney disease (CKD) in which the excess the degree of CKD the uromodulin level is low means that it is inversely proportional to uromodulin concentration. On the other hand other markers such as creatinine and Cystatin C are increased with deprived renal function due to retention of these along with progressive loss of nephron. Therefore diagnosis of CKD along with its stages can be measured with serum uromodulin concentration with high accuracy. We observed a strong inverse relationship between CKD and blood uromodulin concentration. Most of the studies found the significance of serum uromodulin level with kidney function.[8-12.]

V. CONCLUSION

CKD patients demonstrated elevated serum Uromodulin with a rise in serum creatinine and Cystatin C. Moreover, serum Uromodulin closely correlated with serum Cystatin C, creatinine, and eGFR, and could serve as a potential early and sensitive marker of impaired kidney function/ kidney injury.

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