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Assessing Proteinuria in Chronic Kidney Disease: Protein- Creatinine Ratio Vs Albumin-Creatinine Ratio

Divya Dharshini B[1]*, Ganesh M [2], Santhi Silambanan[3]
Dept.of Biochemistry, Sri Ramachandra Medical College and Research Institute, Chennai ,Tamilnadu, India
*Corresponding Author: Divya Dharshini B

Abstract

Quantification of proteinuria is important in the assessment of chronic kidney disease (CKD).Early detection and treatment for CKD can reduce the progression of kidney disease and its complications like cardiovascular disease. The aim of this study was to find out a better parameter to identify proteinuria(albuminuria) in CKD patients. The study design is a case control study with 50 controls (apparently healthy) with normal urine protein to creatinine ratio (uPCR→0.0-0.3) and normal eGFR and 50 chronic kidney disease(CKD) patients as cases with increased uPCR and decreased eGFR (GFR < 60 mL/min/1.73m2).Urine protein is measured by pyrogallal red method. Urine albumin is measured by immunoturbidimetric assay and urine albumin to creatinine ratio(uACR) is calculated. Data were analysed using SPSS software version 22.0. uACR is found to correlate better than uPCR with eGFR values & uACR has p value < 0.005 and significant. uPCR has p value >0.005 and is not significant.Urine albumin to creatinine ratio(uACR) was found to be superior than urine protein to creatinine ratio(uPCR) to identify proteinuria mainly albuminuria in CKD patients.

Keywords : chronic kidney disease, glomerular filtration rate, urine albumin creatinine ratio, urine protein creatinine ratio

Introduction

Chronic kidney disease (CKD) [(1)] refers to decrease in kidney function over a period of 3 months[(2)]. Incidence of CKD is increasing and patients are generally asymptomatic until advanced stage[(3)]. Diabetes mellitus and hypertension are the most common causes of CKD while increasing age, previous h/o Acute kidney injury, family h/o CKD, lower urinary tract obstruction are considered other causes. CKD is detected mainly by measuring serum creatinine and assessing kidney function by calculating glomerular function rate (GFR) [(4)].

GFR is the best measure of assessing kidney function but serum creatinine is considered late indicator of kidney damage[(4)]. Excretion of excessive amounts of proteins mainly albumin in urine is a key marker of damage to kidneys. Many studies have shown that albuminuria and proteinuria are strongly associated with increased risk of CKD and its progression. Proteinuria is increased excretion of urinary proteins mainly albumin and other tubular proteins. Albuminuria is excretion of albumin in urine and its considered as sensitive marker of CKD caused by diabetes mellitus, hypertension and glomerular diseases. Urine protein-to-creatinine ratio (uPCR) and urine albumin-to-creatinine ratio(uACR) are considered as important markers of kidney damage and they are used for diagnosis and prognosis of CKD[(4)].

In this study, we examined the association between uACR, uPCR and eGFR(estimated GFR) in chronic kidney disease patients. We hypothesised that uACR would correlate better with eGFR in Chronic kidney disease patients.

Materials and methods

A total of 100 patients were included in the study. 50 participants between age 30-60 years with Chronic kidney disease fulfilling the inclusion criteria were taken as cases. Patients with other causes of proteinuria(fever, exercise) and other renal causes of proteinuria other than CKD(nephrotic syndrome) were excluded. 50 apparently healthy patients selected from master health checkup at sri ramachandra medical college and research institute were considered as controls. Study protocol was accepted by institutional ethics committee and all the participants gave written consent before perfoming the study. Estimated Glomerular filtration rate(eGFR) calculated by modification of diet in renal diseases (MDRD) method. Urine protein was measured by pyrogallal red method. Urine albumin was measured by immunoturbidimetric method. Urine creatinine measured by jaffes method. uPCR and uACR were calculated.

Statistical analysis were done using SPSS software 16.0 version. A p value of < 0.05 was considered significant.

Results

After statistical analysis it was found that both the groups were similar in age ($p>0.05$). Mean values for serum creatinine, blood urea nitrogen and urine albumin creatinine ratio was higher ($p<0.05$), whereas estimated glomerular filtration rate was lower ($p<0.05$) in the case group when compared to the controls(table1). Urine protein creatinine ratio was higher in case group when compared to controls but it was not statistically significant ($p>0.05$).

Table1: patient characteristics

	Case (CKD)	Control	p value
Age (in years)	50.06±11.74	49.83±11.55	0.938
Serum creatinine (mg/dl)	4.22±2.080	.96±0.16	0.000
Blood urea nitrogen (mg/dl)	38.6±12.7	10.4±2.87	0.000
Estimated GFR (ml/min/1.73m²)	30.7±21.2	80.18±15.7	0.047
Urine protein-creatinine ratio (mg/g)	7.4±5.43	0.17±0.09	0.074
Urine albumin-creatinine ratio (mg/g)	146.57±16.88	14.88±6.84	0.000

The sensitivity of uACR is 94.4.3% and specificity is 86.1%. using receiver operator curve analysis(fig1), an Area under curve (AUC) of 0.903 for uACR for detecting microalbuminuria in CKD patients is obtained and it was statistically significant($p<0.05$).

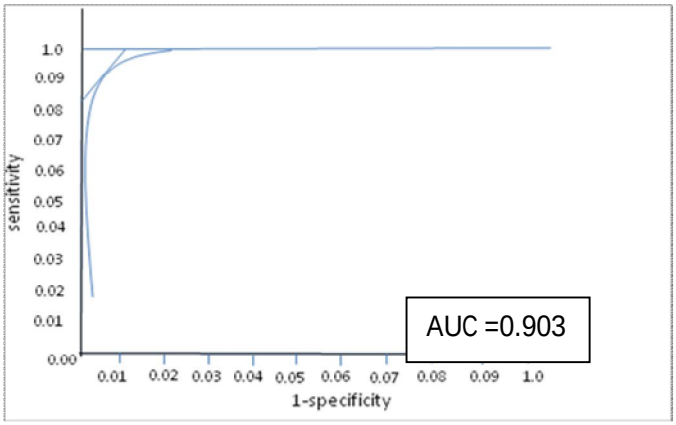

Fig 1 : Receiver operative curve analysis for urine albumin to creatinine ratio

Discussion

Chronic kidney disease is associated with cardiovascular diseases, stroke and even death[6]. Early detection and management of CKD can decrease its progression and the risks associated with it[7]. Routinely used investigations for diagnosis of CKD are serum creatinine and blood urea nitrogen, but they are considered as late indicators because a 33% decrease in GFR can raise serum creatinine from 0.8 to 1.2 mg/dl only. Hence, diagnosis and staging of CKD should be based on evaluation of kidney function by measuring eGFR and presence or absence of kidney damage (by persistent albuminuria, proteinuria, hematuria) after excluding urological causes and structural abnormalities of kidneys by imaging studies[8].Normal GFR is 120-130 ml/min/1.73m² in young adults and it decreases by 1ml/min/1.73m²/year after 30 years. GFR < 60 ml/min/1.73m² strongly predicts risk for CKD and its progression[4]. Measurement of albuminuria, total proteinuria are important in diagnosis, management and prognosis of CKD. Since albumin is a low molecular weight protein and it reflects damage to glomerular vascular endothelium its considered as better marker of kidney damage than total proteinuria[9].Measurement of total protein includes albumin and also non albumin proteins. So it over estimates proteinuria because albumin is the major protein excreted in urine in patients with CKD. Various studies have also shown that measurement of albuminuria is more specific and sensitive than measuring total proteinuria in CKD[5].

The important change in the new KDIGO (kidney disease improving global outcome) guidelines over previous KDOQI (Kidney Disease Outcomes Quality Initiative) is the consideration of uACR as important as eGFR in evaluating severity of CKD[5]. The present study also shows a significant($p<0.05$) increase in uACR in CKD patients when compared with control group. Hence, uACR is the primary laboratory investigation than uPCR in diagnosis of CKD. The present study also showed the significance of uACR over uPCR.

To summarise, this study showed significant correlation between uACR and eGFR when compared with uPCR and eGFR. Thus, uACR is considered earliest and preferred marker over uPCR for diagnosing CKD because albumin appears in urine even before any reduction in GFR and it can lead to earlier intervention and public benefit.

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