DETERMINATION OF URINARY PROTEIN TO CREATININE RATIO AS A PREDICTOR OF RENAL INSUFFICIENCY AND END-STAGE RENAL DISEASE

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ABSTRACT:
Renal failure occurs as a consequence of the loss of important homeostatic regulation that the kidneys provide. Moreover, end-stage renal disease (ESRD) and the resulting uremic syndrome may be caused by a wide variety of factors such as chronic glomerulonephritis, chronic pyelonephritis, immunological diseases, hypertension, and toxic and ischemic damage to kidneys. It is reported that in patients with various renal diseases, reducing urinary protein excretion (proteinuria) slows the rate of decline in the glomerular filtration rate (GFR). Analyses have also shown a strong correlation between the degree of proteinuria and the rate of progression of renal failure. It has been observed that in patients with chronic proteinuric nephropathies, the ratio of protein to creatinine predicted the rate of decline in GFR and the progression to ESRD. Several research studies have suggested that patients with a urinary protein:creatinine (P:C) ratio of less than 1.0 had slow pace of renal anomalies with no ESRD where as those with a ratio of 1.0 or greater than 1.0 had decrease in GFR and a higher risk of ESRD. The presented study includes the data of assessment of urinary: creatinine ratio in patients with renal disease such as ARF, CRF. It was observed that those with P:C ratio greater than 1.0 were undergoing dialysis and a decline in renal functions relates to rise in P:C ratio and subsequent manifestation of ESRD.

Key Words: Protein to Creatinine ratio, ESRD, CRF, ARF.

Short Title: Protein to Creatinine ratio in ESRD.

INTRODUCTION
Clinical manifestations of renal disease are divided into well-defined syndromes such as Nephrotic syndrome, Acute (ARF) and chronic renal failure (CRF)1-3. The former is characterized by heavy proteinuria, whereas later two groups are characterized by azotemia and prolonged onset of uremia and azotemia, respectively4-6. Proteinuria is a major determinant of progression of renal disease6. Recent studies have shown that proteinuria itself causes further tubular injury and thus can perpetuate further damage7,8. Furthermore, it is known that CRF that leads to severe illness and required some form of renal replacement therapy (such as dialysis) is called ESRD or end stage renal disease. Moreover, in certain condition, such as Nephrotic syndrome, Chronic renal failure and Acute renal failure, the amount of protein excretion is a reflection of activity of disease leading to ESRD7,9-11.

National kidney foundation (USA) estimated that the number of new cases of ESRD is increasing at a rate of 5% each year [Healthways, Inc, USA]. It is, however, reported that in patients with various renal diseases, reducing urinary protein excretion slows the rate of decline in the glomerular filtration rate (GFR) and reduces the chances of ESRD1. Moreover, it has been observed that in patients with chronic proteinuric nephropathies, the ratio of protein to creatinine predicted the rate of decline in GFR and the progression to ESRD12,13. Studies have shown that patients with a urinary protein:creatinine (P:C) ratio of less than 1.0 had a slow rate of renal abnormalities with no ESRD where as those with a ratio of 1.0 or greater than 1.0 had decrease in GFR and a higher risk of ESRD. The present study describes the assessment of Protein to Creatinine ratio in 112 patients (males 69, females 43) diagnosed with CRF and ARF, for evaluation of renal insufficiency and ESRD.

METHODS AND RESEARCH DESIGN

Patients: 112 patients (69 males, 43 females) aged 52 to 82 years, were included in the study. They were grouped according to gender, type of renal disease and evaluation of ESRD. Clinical history, with related lab diagnoses, renal status, dialysis routine and frequency were taken and logged for assessment. 30 healthy individuals (15 each of males and females) were also included in the study.


Sampling: Random Urine samples from patients admitted in wards, visiting OPDs or labs for routine checkup or tests were collected in sterilized bottles and immediately analyzed for creatinine and protein.
Analysis: Urinary protein (Reference range < 12.00 mg/dl) and creatinine (Reference range 30-260 mg/dl) were analyzed on automated chemistry analyzer 912 (Roche Diagnostics, Basel) with full calibration and both PNU and PPU controls (Roche Diagnostics, Basel). All samples were divided into three aliquots and analyzed. The protein/creatinine ratio were calculated and compared with healthy individuals.

Statistical analysis: Data was analyzed statistically with significance level of P < 0.01 using SSP (version 10) software.

Data presentation: Data is presented in the form of percent onset for clinical stages and numerical figures in P:C values for clarity.

RESULTS:
A total of 112 patients; 69 males (61.6%), and 43 females (38.39%) aged 52 to 82 years, were tested for P: C ratio in the study (Fig.1). In male group (n = 69), 44.9% (n = 31) were in CRF category and 55.07% (n = 38) were in ARF. Out of CRF category (n = 31), 10 (32.35%) were diagnosed with ESRD designated as MCES (Fig.II). History reveals the onset of CRF in 6 patients for more than 4 years and in 4 patients for more than 3 years. All MCES were undergoing dialysis with a frequency of one per week.

In ARF category (n = 38) (Fig 2), 3 (7.8%) were diagnosed with ESRD and designated as MAES. All were diagnosed with ARF since last three years. Dialysis frequency was one after every 15 days (two per months). In female group (n = 43), 41.8% (n = 18) (Fig.III) were in CRF category and 58.13% (n = 25) were in ARF.

In CRF category (n = 18), 5 (27.7%) (Fig.III) were diagnosed with ESRD designated as FCES. History reveals the onset of CRF in these 5 patients for more than 3 years. All FCES were undergoing dialysis with a frequency of one per week. In ARF category (n = 25), none of the patients were diagnosed with ESRD.

Mean P:C ratio in MCES category was 2.78 ± 0.57 (range 1.22 - 7.05) where as in MAEs 3.78 ± 1.67 (range 1.80-7.12) (Fig 4). Mean P:C ratio in FCES category was 3.94 ± 0.79 (range 1.76 - 5.98). In this study the data concludes that the several patients with> 1.0 of P: C ratio has ESRD (n = 18, [16.07%] w.r.t. total patients n = 112). Moreover, higher the ratio, the more was risk of deterioration of clinical condition and non-responsiveness to Dialysis.

DISCUSSION AND CONCLUSION:
It is known that ESRD and the resulting or proceeding uremic syndrome may be caused by a variety of factors such as chronic glomerulonephritis, chronic pyelonephritis, immunological diseases, hypertension, and toxic and ischemic damage to kidneys. In present study it was found that a total of 13 male patients (10 CRF, 3 ARF) were in the category of ESRD. In female group only 5 patients were categorized as ESRD (all CRF patients). Moreover, P:C ratio in male group was 7.05 and 7.12 for CRF and ARF, respectively, whereas it was 5.98 in female group suggesting a 16% less severity of P:C ratio in females than males.

A study carried out in Indigenous Australians depicts an ESRD incidence of 17.4 times than for non-Aboriginals during 1988-1993. The number of dialysis treatment was also doubling every year.13 The results showed diabetes, glomerulonephritis and hypertension as the prominent cause of ESRD. Diabetes and nephropathy patients have higher risk of ESRD or doubling of serum creatinine levels.12 It is also a well known fact that elevated blood pressure, particularly systolic BP, markedly increases both urinary protein excretion and risk of ESRD in patients with diabetes and nephropathy.12,14 The results of the study also suggest that elevated total and LDL serum cholesterol concentrations are important predictor of the development of ESRD in patients with type 2 diabetes overt nephropathy12. Some goals have been designated and designed after the treatment of CRF and ESRD. The main goal of therapy is to slow down or halt the otherwise relentless process of CRF or ESRD.15 Control of blood pressure and treatment of the original disease, whenever feasible, are the broad principles of management. The prognosis of patients with chronic level of disease has shown that all causes of mortality increases as the level of function decreases. Until renal transplantation, that can maintain patient survival and prolong life, the quality of life is severely affected.16,17 Renal transplantation increases the survival of patients with ESRD significantly as compared to other therapeutic options.15,18,19 It is also recommended that high intensity homehodialysis appears to be associated with improved survival time.20 Finally it is concluded that in present study several patients with> 1.0 of P: C ratio has developed ESRD (n = 18, [16.07%] w.r.t. total patients n = 112). Moreover, it was also suggested that higher the ratio of P:C, the more was risk of deterioration of clinical condition and non-responsiveness to Dialysis subsequently leading to ESRD.
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Fig. I: % Distribution of Patients with Renal Diseases

Females
38% (n = 43)

Males
62% (n = 69)

Fig. II: Group and subgroups of Male patients (n = 69) assessed for P:C ratio and ESRD

Groups

- Males ARF-ESRD
- Males ARF
- Males CRF-ESRD
- Males CRF

Number of Patients

0 5 10 15 20 25 30 35 40
Fig. III: Groups and subgroups of Female patients (n = 43) assessed for P:C ratio and ESRD
Fig. IV: Protein to creatinine ratio in males and female ESRD patients