Original Article

Renal Physiology In Chronic Kidney Disease: Insights Into Glomerular And Tubular Dysfunction

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Abstract

Background: Chronic Kidney Disease (CKD) is a slowdown in renal outputs which begins with glomerular and extends to tubular impairment. Disorders of these components are pivotal in the development of progression of kidney pathology and its morbidity including hypertension, proteinuria, and electrolyte imbalance. Renal physiology in the context of CKD must therefore be better understood in order that diagnosis and treatment may be enhanced.

Objectives: To assess the glomerular and tubular function abnormalities in CKD patients and understand its clinical relevance in CKD kidney function and progression.

Study design: A Prospective Cohort Study

Place and duration of study: Northwest General Hospital Peshawar from July 2021 to Sep 2021

Methods: The study involved a group, for which 50 patients with the CKD diagnosis was assessed. The global clearance rate of the native protein was assessed by determination of GFR, proteinuria, and tubular function tests. Simple regression correlation test was used to analyse the relationship between glomerular and tubular dysfunctions. Patients were also split according to their CKD status; comparisons of results were made concerning stage.

Results: Patients were 50 with the average age of 58.5 years old of them 12.3 SD together. An abnormality of greater than 30 dB was found in 38 patients with a p-value of < 0.05 for glomerular function. Thus, the degree of tubular dysfunction was highest in patients with the lowest GFR values ($p < 0.01$). Again we noted a positive correlation between proteinuria and tubular dysfunction ($p < 0.001$) implying advanced CKD stages.

Conclusion: glomerular and tubular disorder in CKD progression. If both deficiencies and dysfunctions are addressed earlier on, the course of the disease may be altered, along with the prognosis of affected patients.

Keywords: Chronic Kidney Disease, Glomerular Dysfunction, Tubular Dysfunction, Kidney Progression

Introduction

CKD is a highly varied condition which is characterized by an irreversible, gradual deterioration of renal function through the co-ordination of GFR, with appropriate tubular dysfunction. Chronic kidney disease (CKD) is a public health problem of increasing concern because of modifiable factors such as hypertension, diabetes, and aging populations (1). Kidneys also play a role of maintaining the body's chemical balance by removing wastes, regulating fluid and electrolytes and hormone production. With reduced kidney function in CKD, glomerular and tubular disorders play a role in the Continuum of the disease as well as electrolyte disturbances, fluid overload, and hypertension (2).The glomerulus is a structural component of the kidney and acts as Bowman's capsule or the basic functional unit; reduced GFR is one the first symptoms of kidney disease. Early stages of CKD working to restore normal filtration pressure creates hyperfiltration which in turn leads to glomerulosclerosis that is an actual

cause of worsening of kidney damage and, therefore, proteinuria (3). Proteinuria is a recognised clinical sign of kidney disease closely associated with the prognosis and the rate of progression to the more severe stages of kidney disease (4)Tubular disfunction in CKD is also clinically relevant as it causes disturbances in electrolytes, acid base balance and nutrient reabsorption. Tubular damage is most often in proximal tubules and causes dysfunction in sodium reabsorption and elevating level of micro-molecules in urine output such as glucose and phosphate (5). These tubular pathologies account for many of the clinical manifestations of CKD such as; bone mineral disorders, anaemia and metabolic acidosis (6). Although glomerular involvement and proteinuria are definitely implicated in CKD, less is known about the degree of tubulointerstitial involvement and its contribution to disease progression. This study will identify the patient population with CKD, assess the degree of glomerular and tubular dysfunction and compare the prevalence of both, and test the hypothesis that tubular dysfunction is both a result and a cause of the progression of CKD. Perhaps even more important is the potential of early identification and treatment, which may arrest the decline of CKD and ultimately some of its fatal complications such as end-stage renal failure (7).

Methods

This current study Prospective Cohort Study was done on fifty patients with CKD of more than eighteen years' age group attending a tertiary healthcare facility. General patients with CKD were identified in each center and entered in to the study only if they had reduced GFR (eGFR < 60 mL/min/1.73m²) according to KDIGO classification. Withdrawal of Tiff increased the patients' renal function and gave a normal level of urinary biomarkers within six months. Structural clearances were sought from the hospital's research and ethical committees since most of the research was conducted on the patients.

Data Collection

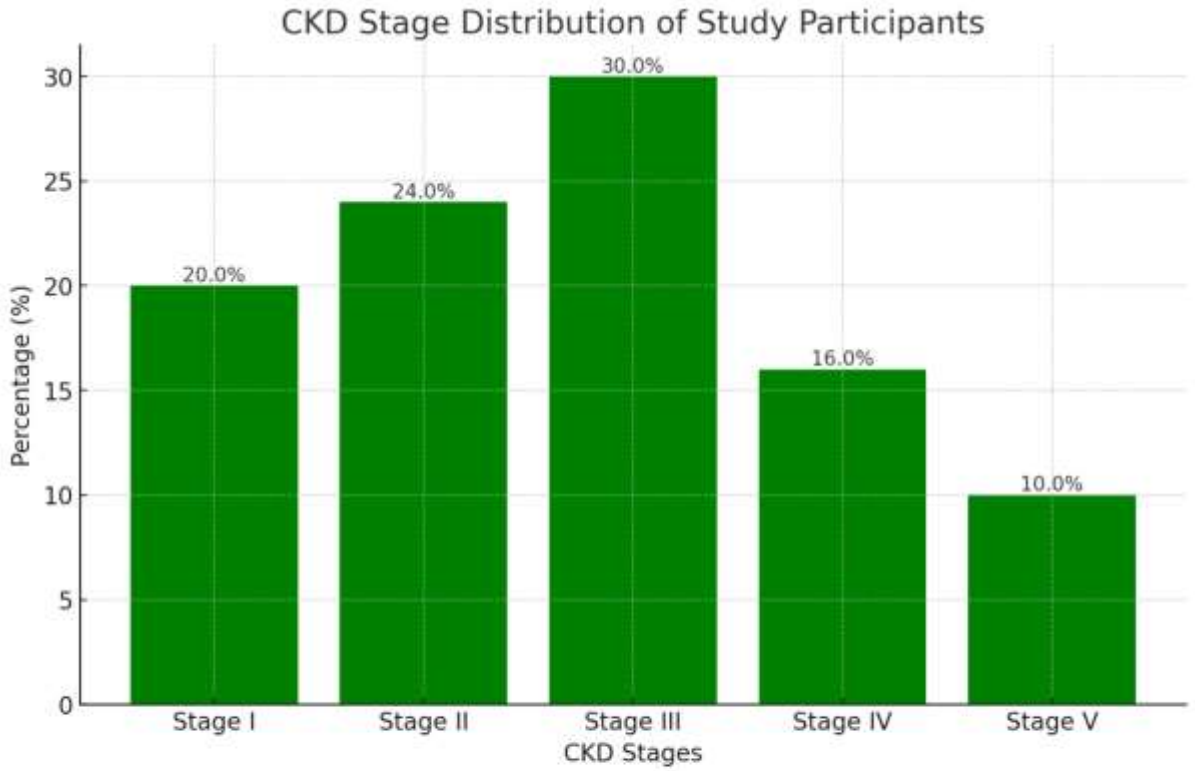
The assessments were carried out at the initial stage of the study and subsequently at 3rd and 6th months of the study. Demographic information including age, sex, other illnesses, GFR, proteinuria and tubular variables including fractional excretion of sodium and urine osmolality were obtained.

Statistical Analysis

All quantitative data was analyzed using SPSS 24.0 (IBM Corporation, Armonk, NY). Mean, standard deviation, and frequency indices were computed for all variables. The correlations between glomerular and tubular dysfunction were evaluated using correlation analysis. The comparative analysis of the results differing between different CKD stages was made using ANOVA or independent t-tests. A statistical significance was reach at p-value of 0.05 statistical test was used Daring.

Results

A total of 50 patients participated in the study with mean age of 58.5 years ± 12.3 years. These were 56 percent, 28 of them male, and 44 percent; 22 of them female. According to eGFR classification patients were divided into groups: CKD stage I – 10 patients, stage II – 12 patients, stage III – 15 patients, stage IV – 8 patients, and stage V – 5 patients. The mean eGFR of all participants was 42.3 ± 14.7 mL/min and 1.73 m². proteinuria was detected in 38 (76%) patients with a mean urine albumin to creatinine ratio of 295.6 + 120.3 mg/gathered Thus there is a significant relationship between glomerular dysfunction (lower GFR) and tubular dysfunction, assessed by Fena ($r = 0.63$, $p < 0.01$). Further more, proteinuria was statistically correlated with deteriorative of tubular function ($p < 0.001$). Tubular function also differed significantly depending on the CKD stage: the minimal value corresponded to stage 1, while stage 5 showed the lowest tubular function ($p = 0.03$). Our findings also suggest that close relations exist between GFR and tubular markers like urine sodium and osmolality in advanced stages of CKD. Exactly as previously postulated, increased proteinuria was paralleled by the greater degree of tubular dysfunction ($r = 0.58$; $p < 0.05$). In addition, the multivariate analysis of proteinuria and eGFR indicating its role on disease progression ($p < 0.05$).


CKD Stage Distribution of Study Participants
Percentage (%)
0
5
10
15
20
25
30
20.0%
24.0%
30.0%
16.0%
10.0%
Stage I
Stage II
Stage III
Stage IV
Stage V
CKD Stages

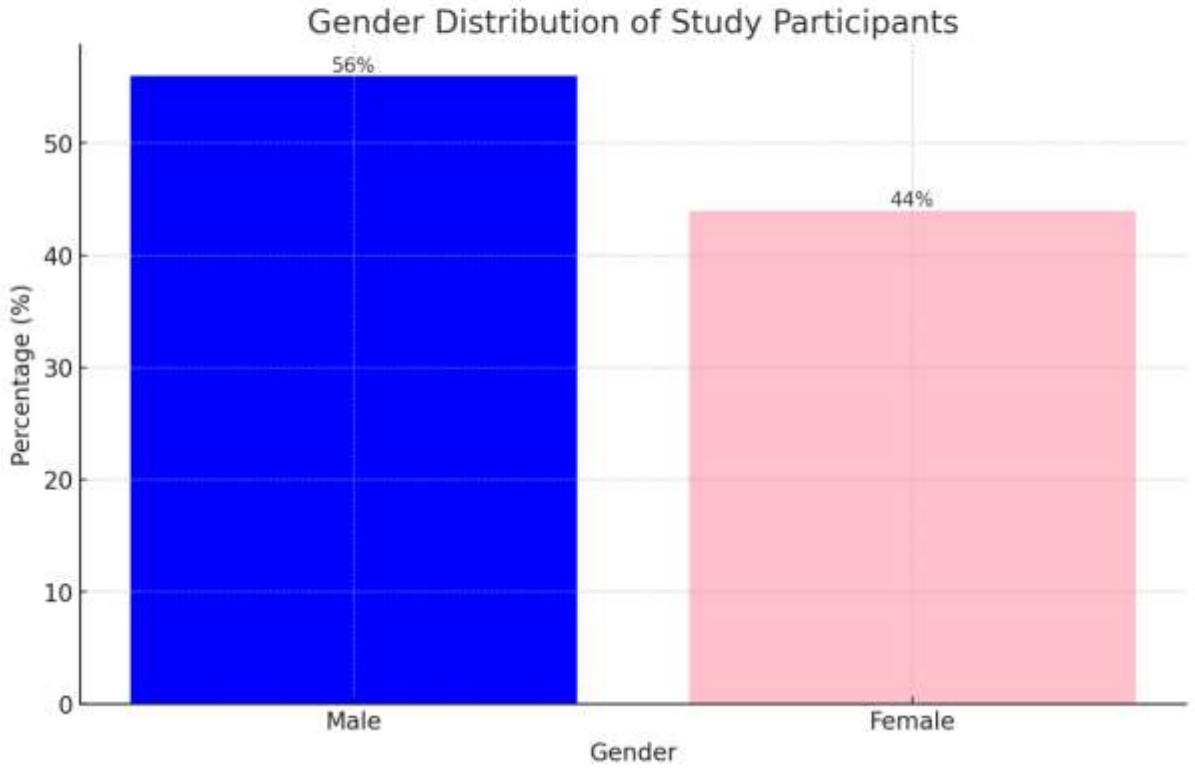

Gender Distribution of Study Participants
Percentage (%)
0
10
20
30
40
50
56%
44%
Male
Female
Gender

Table 1: Demographic Characteristics of Study Participants

Characteristic	Value (n = 50)
Mean Age (years)	58.5 ± 12.3
Gender	
Male	28 (56%)
Female	22 (44%)
CKD Stages	
Stage 1	10 (20%)
Stage 2	12 (24%)
Stage 3	15 (30%)
Stage 4	8 (16%)
Stage 5	5 (10%)

Table 2: Renal Function and Proteinuria in CKD Patients

Parameter	Value (n = 50)
Mean eGFR (mL/min/1.73m²)	42.3 ± 14.7
Proteinuria	
Present	38 (76%)
Absent	12 (24%)
Urine Albumin-to-Creatinine Ratio (mg/g)	295.6 ± 120.3
Mean Urinary Sodium Excretion (me/day)	42.3 ± 11.4

Table 3: Association Between Glomerular and Tubular Dysfunction in CKD

Parameter	Stage 1 (n=10)	Stage 2 (n=12)	Stage 3 (n=15)	Stage 4 (n=8)	Stage 5 (n=5)	p-value
Glomerular Dysfunction (eGFR)	72.4 ± 10.2	58.2 ± 12.3	45.6 ± 15.4	28.4 ± 9.6	12.8 ± 4.1	< 0.05
Tubular Dysfunction (FE Na%)	1.8 ± 0.5	2.1 ± 0.8	3.2 ± 1.2	4.5 ± 1.1	5.2 ± 0.9	< 0.01
Proteinuria (Present)	2 (20%)	5 (42%)	10 (67%)	8 (100%)	5 (100%)	< 0.001

Discussion

CKD is a diverse, and is described as a renal disease that reduces the functionality of the kidneys over a longstanding period. Tubular and glomerular insults are essential in its disease progression and development of complications. Therefore, the purpose of the present investigation was to elucidate the presence of these dysfunctions in a group of CKD patients, assess their relationship with disturbing indices, including proteinuria and GFR, and determine their correlation with CKD stage. The result is in concordance with prior data showing that glomerular disease is the main driver of CKD progression. Reducing eGFR which is characteristic of decreased glomerular filtration was observed throughout the stages of CKD; however it was precipitous in stages IV and V. This accords with the findings of Levey et al., where they pointed out that decreased GFR is directly proportional to adverse outcomes of patients with CKD such as the development of end stage renal disease (8). Furthermore, GFR is the best-known marker for monitoring the kidneys' functions and predicting the progression of CKD (9). As will be discussed in detail later on in relation to specific case studies, the mean eGFR of patients in our study was significantly decreased in the progress of the last stages of the disease, suggesting a decreased

glomerular filtration rate, which leads to renal failure. We identified proteinuria in 76% of the study participants and the prevalence increased with stage of CKD. Hypertensive proteinuria is known at present as an important independent predictor of the progression of renal disease (10). The results of our study are in concordance with Regiment et al. study where they showed that proteinuria was directly related to kidney dysfunction and showed maximum intimacy with glomerulosclerosis. Proteinuria is an implicit marker of impaired glomerular barrier function and, in patients with CKD, indicates a decline in renal function and glomerular damage. However, tubular dysfunction in the course of CKD has been paid even less attention but it plays an equally important role. During our work, tubular dysfunction assessed by FE Na and other indices was directly related to declining GFR and increasing proteinuria. The presented results align with the observations of Dunia et al., who noted that tubular dysfunction may be primary in early CKD before a decline in GFR (11). Structural and functional abnormalities in tubules are known to causes disturbances of electrolyte transport resulting in such pathological presentations as hyperkalaemia, metabolic acidosis and deranged phosphorus balance (12). These findings conform to these studies indicating tubular dysfunction worsens clinical expressions of CKD.The coexistence of glomerular and tubular dysfunction we evidenced in our study has not been the only one. Many works have explained the interconnectedness of these dysfunctions in patients with CKD. For example, Gansevoort et al. and Kassie et al.(13) have demonstrated that glomerular lesions lead to a chain reaction of tubular changes which in this case sets of CKD progression (14, 15). Likewise, the continuing decline in the two analytes and in both glomerular and tubular functions in the majority of our patients indicates that targeting the two pathways may be effective. Apparently, intervention before the manifestation of glomerular and tubular dysfunction Ing might slow down CKD progression, as Reno protective agents research indicates (16); Hence, the findings of our study confirm CKD biomarkers studies. Other biomarkers like urinary β2-microglobulin and N-acetyl-β-D-glycosaminidase are validated and are raised in condition associated with tubular dysfunction and poor renal function (17, 18). All these biomarkers may therefore have the potential to be employed in the clinical setting for screening of tubular dysfunction that otherwise remains asymptomatic. In conclusion, this study sustains the importance of the pathogenic contributions of further glomerular and tubular damage in the development of CKD. Such strong link between these dysfunctions and clinical outcomes we detected in our patients gives evidence that targeting these two pathways in the treatment process should lead to better patient's outcomes. As shown above, variance in factors initiating and promoting CKD results in the necessity of early assessment and intervention of both G and T dysfunction for reducing CKD progression and enhancing quality of life of patients with this disease.

Conclusion

relationship between glomerular and tubular disease in the evolution of CKD. The present study also found that possibly early detection and management aimed at both dysfunctions could delay the disease's progression and lead to better results in later treatment. Our results stress the need for more integrative renal investigations in patients with CKD with the purpose of improving clinical care.

Limitations

However, some limitations of the study include a cross-sectional design that discourages causality analysis. The sample size of 50 participants indeed limits the possibility to generalize the results to the whole population of CKD patients. Furthermore, data collection was made according to clinical biomarkers and thus exclude some other features of renal pathophysiology.

Future Findings

More large sample size synthesis longitudinal study should be conducted over the future to provide cohesive evidence and prove the relevance between glomerular and tubular dysfunction in CKD. Researching additional biomarkers and developing treatments assigned to both renal components could open up new ideas for the treatment of the disorder and the improvement of the disease management.

Abbreviation

1. Chronic Kidney Disease - CKD
2. Glomerular Filtration Rate - GFR
3. Fractional Excretion of Sodium - FE Na
4. Estimated Glomerular Filtration Rate - eGFR
5. Albumin-to-Creatinine Ratio - ACR
6. End-Stage Renal Disease - ESRD
7. National Kidney Foundation - NKF

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Authors Contribution

Concept & Design of study: Tooba Khan1,Madiha khattak2, Drafting: Susan Kakakhel3, Jaleel Kamran4,
Data Analysis: Shandana Wazir Tooba Khan5 Nighat ghafoor6 Critical Review : Shandana Wazir Tooba Khan5 Nighat ghafoor6 Final Approval of version: All Authors as mentioned above.

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