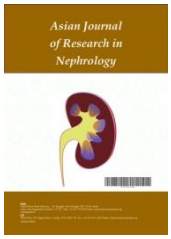

Asian Journal of Research in Nephrology

4(2): 33-38, 2021; Article no.AJRN.74812

The Relationship of Chronic Kidney Diseases Stages and Dipstick Proteinuria for Bangladeshi Patients

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Dr. P. Kiranmayi, GITAM University, India.
Reviewers:
(1) Sabah Mohamed Alharazy, Malaysia.
(2) Celso Eduardo Olivier, Instituto Alergoimuno de Americana, Brazil.
Complete Peer review History: https://www.sdiarticle4.com/review-history/74812

Original Research Article

Received 20 July 2021
Accepted 29 September 2021
Published 12 October 2021

ABSTRACT

Background: It is established that proteinuria is associated with kidney dysfunction. The endeavor in this study was to observe whether the degree of dipstick proteinuria was related to the progressive stages of chronic kidney disease (CKD) for Bangladeshi patients.
Methods: This observational study was carried out on a total of 100 patients above 18 years of either sex with chronic kidney disease in the Department of Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Data were collected through semi-structured questionnaire. p-value <0.05 was considered statistically significant. The data were analyzed by SPSS version 25.
Results: The mean age of the study population was 43.26 ±13.07 years with male predominance (63%). Serum creatinine increased with ages. The major symptoms were swelling of face, feet and ankle; nausea, vomiting and loss of appetite; breathlessness, urinary complaints, and also weakness. The causes for CKD were diabetes, hypertension, glomerular disease, systemic

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Inflammatory disease, previous history of kidney disease, and tubulointerstitial disease. The number of CKD patients in stage 3 was 16%, in stage 4 was 32% and in stage 5 was 52%. The dipstick proteinuria increased significantly with progressive stages of CKD.
Conclusion: The range of proteinuria increased with the progressive stages of CKD.

Keywords: Chronic kidney disease (CKD); proteinuria; glomerular filtration rate (GFR).

1. INTRODUCTION

The burden associated with CKD includes the impact on the health of an individual and the health expenditure of a country. The global death of CKD was 1.2 million in 2017[1].The dialysis costs estimated is 40,000 to 80,000 euro /year/patient based on country[2].Treatment including dialysis cost is a huge burden in the developing country (e.g, Bangladesh). As CKD cannot be detected only with serum creatinine in most of the cases (90%) [3], urine testing for protein can be a great independent tool for diagnosis of CKD in a developing country.

Common benign causes of proteinuria are orthostatic proteinuria, dehydration, vigorous activity or exercise, and fever. Among others, the pathological causes of proteinuria include glomerular dysfunction and multiple myeloma. False-positive proteinuria results in alkaline urine, when urine is highly concentrated; with gross hematuria; in the presence of some antibiotics; and urine contamination with semen or vaginal secretions[4].

The postulated pathological mechanism shows that excessive filtration of proteins across the glomerular basement membrane bring enormous protein in contact with the mesangium and the tubular cells that can mediate inflammation through activation of complement and production of cytokines and mediators by tubular cells and thus may stimulate interstitial inflammation and scarring [5]. Therefore, proteinuria was always target to address for diagnosis and staging of CKD.

The updated KDIGO (Kidney Disease Improving Global Outcome) classification of CKD is based on cause, GFR category and albuminuria category(CGA)[6]. The stages of Chronic Kidney Disease based on GFR are- Stage 1: GFR >90 (normal function): Stage 2: GFR 60-89 (mild CKD); Stage 3A: GFR 45-59 (Mild to Moderate CKD); Stage 3B: GFR 30-44 (Moderate to Severe CKD); Stage 4 – GFR 15-29 (Severe CKD); and Stage 5: GFR<15 or dialysis (Kidney Failure). But GFR has limitations as less reliable at extremes of body composition, wide confidence intervals, estimation need stable creatinine level over days; controversy for the elderly, not valid in under-18 or during pregnancy, and ethnicity consideration[7].

Clinical studies demonstrated a correlation between the degree of proteinuria and the rate of progression of renal failure and prognosis. This lead to our hypothesis that proteinuria could be an independent marker of staging of CKD, not simply a marker of prognosis. There was always debate for revising the CKD definition and classification system [8]. This study attempted to find the relation of magnitude of proteinuria with successive stages of CKD. No study was conducted so far our knowledge to see the relationship of dipstick proteinuria and CKD stages.

2. METHODS

In this study, 100 adult patients with CKD were enrolled. Both males and females of 18 years and above and patients with chronic kidney disease of stage 3 onwards were included. Patients having gross hematuria, pregnancy, factors or disease known to affect urinary albumin excretion like patients with urinary tract infection, congestive cardiac failure and acute febrile illness and patients on dialysis were excluded from the study. Data were collected in a structured questionnaire form. Informed written consent was taken.

Overnight fasting serum levels of creatinine was sent. GFR was calculated by the modification of Diet in Renal Disease(MDRD)study equation. Reduced GFR was defined as GFR <60 ml/min/1.73 m^2.

Urine samples were collected from patients and sent for dipstick urine test within 1 hour of collection. The sample was graded as: −negative; ± trace positive; 1+ positive (30 mg/dl); 2+ positive (100 mg/dl); 3+ positive (300 mg/dl); or 4+ positive (>2000 mg/dl) according to the report.

2.1 Statistical Analysis

Quantitative and qualitative data were presented as mean with standard deviation. Data with

number was expressed in percentage. Fisher's exact test on qualitative variables and Student's unpaired T-test on quantitative variables were conducted respectively. A two-sided p-value <0.05 was considered statistically significant and SPSS versions 25 was used for data analysis.

3. RESULTS

The study showed male predominance (63% male versus 37% female). Among 100 patients, mean age was 43.26 ±13.07 years. Majority (27+28=57%) of the respondents were found in the age group of 28-37 and 38-47. (Table 1). Serum creatinine increased with age. The most frequently found symptoms were swelling of face, feet and ankle (31%), nausea, vomiting and loss of appetite (23%), breathlessness (11%), urinary complaints (hematuria, polyuria, nocturia, oliguria) (19%), generalized weakness (7%) and others 9% (Fig.1).

The etiology for CKD were diabetes (31%), hypertension (19%), glomerular disease either primary or secondary (18%), systemic Inflammatory disease (15%), previous history of kidney disease (11%), and tubulointerstitial disease (6%) (Fig. 2).

The mean GFR for the study (100) population was 22.8±4.45ml/min/1.73 m^2. The number of patients with GFR 30-59 ml/min/1.73 m^2 (stage 3) was 16% and with GFR 15-29 ml/min/1.73 m^2 (stage 4) was 32% and with GFR less than 15 ml/min/1.73 m^2 (stage 5) was 52% (Table 2).

For 1+ proteinuria the mean GFR was 43.9±4.98 ml/min/1.73 m^2 (stage 3), for 2+ proteinuria, the mean GFR was 24.2±5.24 ml/min/1.73m^2 (stage 4), and for 3+ proteinuria, the mean GFR was 13.8±4.15 ml/min/1.73 m^2 (stage 5).(Fig. 3).

4. DISCUSSION

In this study male was more than the female, the reason could be explained that the females are neglected regarding treatment and their delayed presentation to the clinician. A laboratory based study for a decade in Bangladesh[9] observed high prevalence of stage-2 to stage-5 renal insufficiency in Bangladeshi populations, especially among the females.

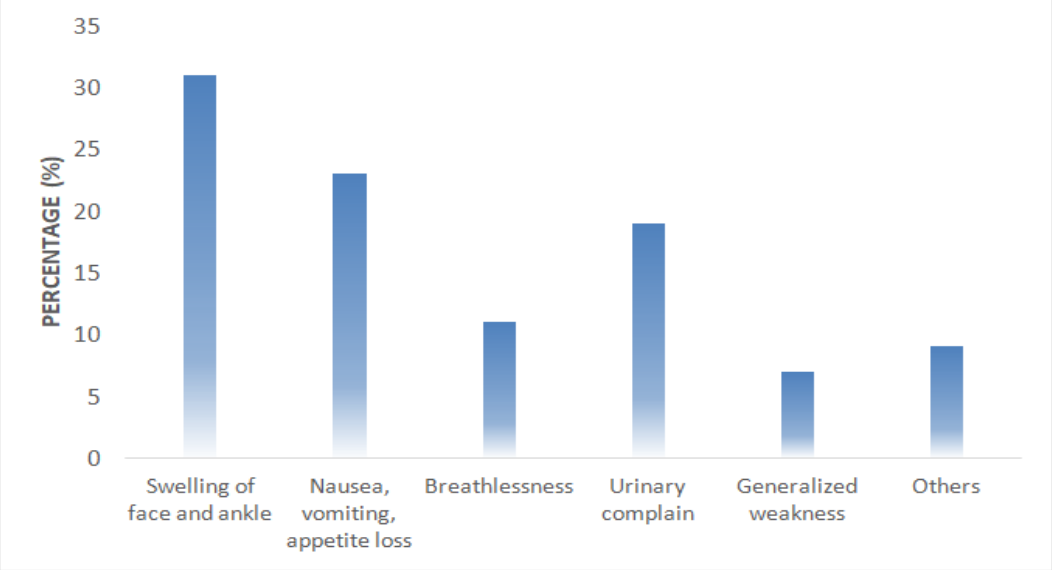

Fig. 1. Clinical presentations of the study subjects (n=100)

Table 1. Age distribution of the study subjects (n=100)

Age Group (yrs)	Number	Mean age	Mean S. Creatinine
18-27	9	23.2±3.49	2.94±1.41
28-37	27	31.70±2.93	5.66±3.65
38-47	28	42.14±2.41	5.41±4.09
48-57	15	52.13±2.70	6.84±2.08
58-67	21	62.33±2.20	7.19±4.21

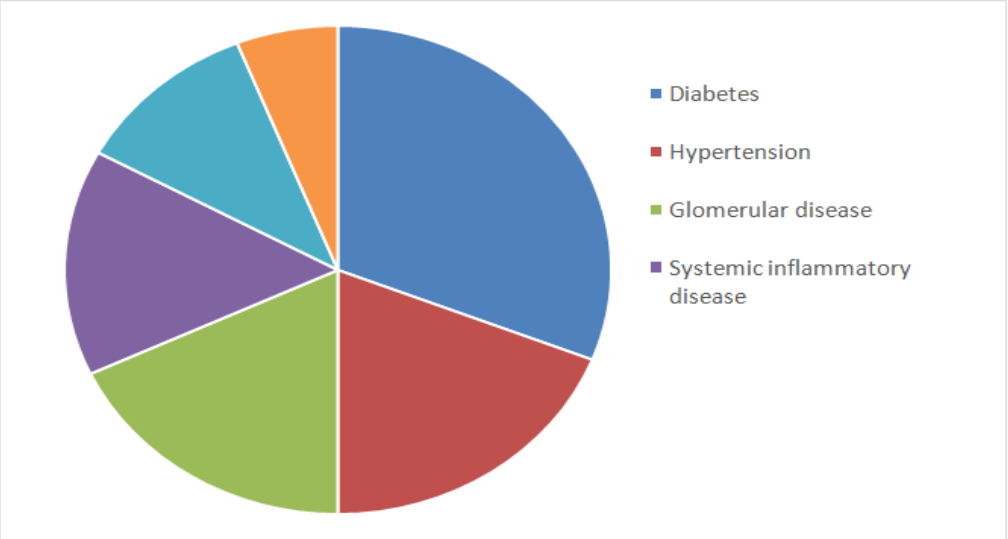

Fig. 2. Etiology for CKD of the study subjects

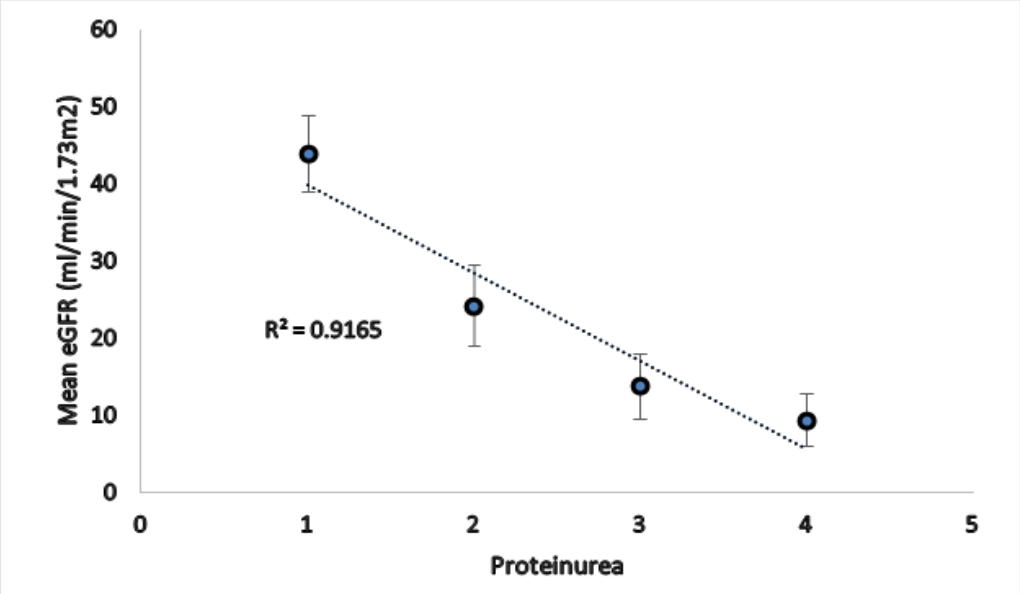

Fig. 3. Relationship between GFR and Proteinuria of the study population showed inverse relationship. r2=0.9165 which was statistically significant

Table 2. Distribution of study subjects by stages of CKD (n = 100)

Stage	GFR	Frequency	Percentage
Stage 3	30-59	16	16
Stage 4	15-29	32	32
Stage 5	<15	52	52

The mean age of the study population was 43.26 ±13.07 years. Majority (27+28=57%) of the respondents was found in the age group of 28-37 and 38-47. Serum creatinine increased with age which was statistically significant. Coresh et al[10] found that the prevalence of CKD increased with age. Douville et al [11] showed that the GFR reduction is progressive after the age of 30 and continue to decline steadily after the age of 60 which supports our findings.

Bangladesh renal registry report [12](1986-1996) noted the etiologies of the chronic kidney diseases were glomerulonephritis (47.0%), diabetic nephropathy (24.3%) and hypertension (30.0%)**.** The major causes of kidney disease and subsequent kidney failure in the US are diabetes (accounting about 44.4%) and hypertension (accounting about 26.8%). Conditions accounting for the remaining 29% include primary glomerulopathies like focal glomerulosclerosis and IgA nephropathy, inherited conditions like polycystic kidney disease, and autoimmune conditions like lupus [13]. Our study reflects the higher prevalence of diabetic nephropathy in Bangladesh, not glomerulonephritis as previous study findings.

In this study, decline in GFR was accompanied with the rise of proteinuria which was statistically significant. Rise of proteinuria was closely linked to the progressive stages of CKD.

5. CONCLUSION

Further study is needed using ACR (albumin creatinine ratio) or PCR (protein creatinine ratio) for quantification of proteinuria as they estimate proteinuria more accurately. In Bangladesh, ACR or PCR is not widely used yet.A multicentric prospective case control study with large sample size and longer duration is recommended to generalize the findings.

CONSENT

Informed written consent was taken from the patients before examination, investigation and data collection.

ETHICAL APPROVAL

Approved by the Medicine Department of Bangabandhu Sheikh Mujib Medical University (BSMMU) and BCPS (Bangladesh College of Physicians and Surgeons).

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle4.com/review-history/74812