

The Present Hospital Based Prospective Assessment of the Albuminuria and Reduced Estimated GFR between First-Degree Relatives of Chronic Kidney Disease Patients

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Abstract

Aim: To assess the Albuminuria and reduced estimated glomerular filtration rate among first-degree relatives of patients with chronic kidney disease.

Material & Methods: The present study was planned in the Department of Nephrology, Nalanda Medical College & Hospital, Patna, Bihar, India. Total 60 individuals were enrolled in the present study over a period of six months.

Results: 60 cases were divided in two study groups as 30 cases of the first-degree relatives of CKD patients and 30 are control cases. Hypertension was seen among 10 cases followed by Diabetes mellitus (6) and chronic glomerulonephritis (4).

Conclusion: Presence of hypertension serves as a modifiable independent risk factor for albuminuria while the presence of proteinuria and increasing age were found to predict reduced eGFR in first degree relatives. The prevalence of albuminuria increases with the duration of hypertension. Early screening of essential hypertensive patients for albuminuria and aggressive management of hypertension might reduce the burden of diseases due to renal damage secondary to hypertension in the community.

Keywords: albuminuria, chronic kidney disease, first-degree relatives, reduced estimated glomerular filtration rate

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Introduction

Chronic kidney disease (CKD) is a type of kidney disease in which there is gradual loss of kidney function over a period of months or years. Early on there are typically no symptoms. Later, leg swelling, feeling tired, vomiting, loss of appetite or confusion may develop. Complications may include heart disease, high blood pressure, bone disease, or anemia [1]. Causes of chronic kidney

disease include diabetes, high blood pressure, glomerulonephritis, and polycystic kidney disease. Risk factors include a family history of the condition. Diagnosis is generally by blood tests to measure the glomerular filtration rate and urine tests to measure albumin. Further tests such as an ultrasound or kidney biopsy may be done to determine the underlying cause. A number of different

classification systems exist [2]. Screening at-risk people is recommended. Initial treatments may include medications to manage blood pressure, blood sugar, and lower cholesterol. NSAIDs should be avoided. Other recommended measures include staying active and certain dietary changes. Severe disease may require hemodialysis, peritoneal dialysis, or a kidney transplant. Treatments for anemia and bone disease may also be required [3].

Lower GFR predicts cardiovascular events and mortality in patients with existing cardiovascular disease [4-6], patients at high risk of cardiovascular disease [4], and the general population [7-8]. Most of these studies have relied on the abbreviated Modification of Diet in Renal Disease (MDRD) Study equation to estimate GFR from serum creatinine level, age, sex, and race. In a prospective study of older adults [9], elevated cystatin C, another marker of decreased kidney filtration, predicted cardiovascular and mortality risk more strongly than did creatinine-based estimates of GFR. However, creatinine remains the most widely used marker of decreased kidney function.

None of these large prospective studies of decreased kidney function included quantitative data on albuminuria. Leakage of protein in the urine is a sensitive indicator of early kidney damage, especially in persons with diabetes [10]. Albumin is the recommended marker for detection of proteinuria in adults. Both prevalence and severity of albuminuria are higher at lower GFRs and among persons with diabetes [11-12]. Albuminuria is one of the strongest predictors of GFR decline, and it is associated with a higher risk of cardiovascular disease and mortality in both diabetic and nondiabetic persons [13].

A GFR of less than 60ml/minute for three or more months indicates chronic kidney disease. A GFR of less than 15ml/minute indicates full failure of the kidneys. GFR estimates between 60 and 89 mL/minute do not mean a person has chronic kidney

disease unless there are other signs of disease. People with either higher than normal amounts of muscle mass, such as bodybuilders or people with lower-than-normal amounts of muscle mass, such as amputees or people with muscle wasting disorders (when the muscles become less dense than normal) can have GFR test results that do not appear normal, but may still be normal. A medical professional will explain the meaning of any GFR test done on a patient [14].

The prevalence of hypertension is high in India and hypertensive nephropathy is a common cause of chronic kidney disease. Hence the present study was undertaken to evaluate the association of serum creatinine, albuminuria and eGFR among hypertensive and non-hypertensive individuals to determine the better predictor of renal impairment. Hence the present study was planned to assess the Albuminuria and reduced estimated glomerular filtration rate among first-degree relatives of patients with chronic kidney disease.

Material & Methods:

The present study was planned in the Department of Nephrology, Nalanda Medical College & Hospital, Patna, Bihar, India. Total 120 individuals were enrolled in the present study over a period of six months. The aim and the objective of the present study were conveyed to them

Inclusion and Exclusion criteria

These were divided in to the two study groups as 30 cases of the first-degree relatives of CKD patients and 30 are control cases who do not have family or personal history of the CKD and age above 18 years. The individuals affected by other chronic diseases and on medicine that affects the kidney functions were excluded from the present study.

Methodology

Spot urine sample was obtained in the morning, following an overnight fast,

using a clean-catch technique and sterile containers, and was frozen for later analysis. Urinary albumin level was measured by solid-phase fluorescence immunoassay, and urinary creatinine level was measured by the modified kinetic method of Jaffe using a Beckman Coulter Synchron AS/Astra Analyzer (Beckman Coulter, Inc., Fullerton, California). Serum creatinine level was measured by the modified kinetic method of Jaffe using a Roche Hitachi 737 analyzer (Roche Diagnostics Corporation, Indianapolis, Indiana). GFR was estimated on the basis of serum creatinine level, with the most recent expression of the MDRD prediction equation for standardized serum creatinine. Specifically, estimated GFR $\frac{1}{1.75} \times 175 \times 3$ (standardized serum creatinine in mg/dl) 1.154×3 age $0.203 \times (3 \times 0.742$ if female) $(3 \times 1.21$ if Black). The serum creatinine values reported in NHANES III were adjusted to the creatinine assay used in the development of the MDRD equation.

Estimated GFR is reported in ml/minute per 1.73 m² of body surface area.

Results:

60 cases were divided in two study groups as 30 cases of the first-degree relatives of CKD patients and 30 are control cases. Mean age was 31-60 years. Among CKD group, 15 were males and 14 were females. Majority of cases (14) were among Stage V Proband CKD. Hypertension was seen among 10 cases followed by Diabetes mellitus (6) and chronic glomerulonephritis (4). [Table 1]

A total of 10 cases of Albuminuria were seen in First degree relatives of CKD patients while 6 were in control group. Mean Serum uric acid ($\mu\text{mol/L}$) was 162.1-448.3, mean Serum creatinine ($\mu\text{mol/L}$) was 76.2-172.5 while mean eGFR (ml/min/1.73 m²) was 7.80.2-157.6 in First degree relatives of CKD patients. In control group Mean eGFR (ml/min/1.73 m²) was 77.1-123.6. [Table 2]

Table 1: Clinical details of chronic kidney patients (CKD)

Proband characteristics	Details
Age (Range in years)	31-60 years
Gender	
Male	16
Female	14
Proband CKD stage s	
Stage III	6
Stage IV	10
Stage V	14
Etiology of CKD in pro bands	
Hypertension	10
Diabetes mellitus	6
Chronic glomerulonephritis	4
Obstructive uropathy	3
HIVAN	2
Lupus nephritis	1
Analgesic nephropathy	1
Nephrocalcinosis	1
Unknown	2

Table 2: Serum Marker Analysis

Parameters	Cases: First degree relatives of CKD patients	Control patients
Serum uric acid ($\mu\text{mol/L}$)	162.1 – 448.3	185.6 – 325.6
Serum creatinine ($\mu\text{mol/L}$)	76.2 – 172.5	67.3 – 109.2
Mean eGFR (ml/min/1.73 m^2)	7.80.2 – 157.6	77.1 – 123.6
Reduced eGFR	3 cases	1 case
Albuminuria	10 cases	6 cases
Dipstick proteinuria	4 cases	1 cases

Discussion:

Higher risks of cardiovascular and all-cause mortality with decreased estimated GFR and albuminuria were observed in all racial/ethnic groups and in both men and women. Consistent with previous studies, African Americans in this study had higher sex-specific mean serum creatinine levels than Whites, but the MDRD equation used to estimate GFR results in higher sex-specific estimated GFR levels in African Americans than in Whites [15]. Creatinine is a by-product of muscle metabolism and therefore is affected significantly by differences in muscle mass. Muscle mass is, on average, higher in African Americans than in Whites, higher in men than in women, and higher in younger adults than in older adults.

The Modification of Diet in Renal Disease (MDRD) equation was developed to account for average differences in muscle mass by age, race, and sex, but it cannot account for individual differences. The validity of the Modification of Diet in Renal Disease (MDRD) equation was recently demonstrated across 10 studies and several subgroups, including African Americans, though its precision is lower among persons with preserved renal filtration. The MDRD equation also agrees very well with equations developed in African-American study populations [16].

Following the work of Go *et al*, numerous investigators set out to confirm the findings and explore the relationship more comprehensively - in particular, assessing the exact eGFR threshold of the mortality

effect. Go and colleagues chose to assess level of kidney function with the comparison group >60 mL/min. [8]

Dietary protein intake influences the glomerular filtration rate through prostaglandin effects [12]. High protein diets are also associated with elevated renin levels which have been described to be related to nephropathy in adolescents with diabetes. Modest protein restriction (0.6 to 0.8 gm/kg body weight/day) minimizes the waste products the kidney has to excrete [17].

Micro albuminuria and vascular disease are known to occur early in the course of Essential hypertension. MAU is a reversible component that expresses the cellular and molecular status of the renal function. The prevalence of renal disease is severely underestimated when it is defined on the basis of serum creatinine level instead of GFR [18,19].

Conclusion:

Presence of hypertension serves as a modifiable independent risk factor for albuminuria while the presence of proteinuria and increasing age were found to predict reduced eGFR in first degree relatives. The prevalence of albuminuria increases with the duration of hypertension. Early screening of essential hypertensive patients for albuminuria and aggressive management of hypertension might reduce the burden of diseases due to renal damage secondary to hypertension in the community.

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