International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 27-12-2018; Accepted: 29-01-2019
www.medicalsciencejournal.com
Volume 5; Issue 2; February 2019; Page No. 120-123

Evaluation of albuminuria and reduced estimated glomerular filtration rate between first-degree relatives of chronic kidney disease patients from Bihar region

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Abstract
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.
The present study was planned in the Department of Nephrology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar. Total 100 individuals were enrolled in the present study. from July 2018 to Dec 2018.These were divided in to the two study groups as 50 cases of the first degree relatives of CKD patients and 50 are control cases. The inclusion criteria control group is the patients 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.
The present study concludes the data regarding relatives of patients with CKD found a greater prevalence of CKD, albuminuria, and reduced eGFR among the first degree relatives of patients with CKD. It can also be concluded that 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

1. 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].
Albuminuria is a pathological condition wherein the protein albumin is abnormally present in the urine. It is a type of proteinuria. Albumin is a major plasma protein (normally circulating in the blood); in healthy people, only trace amounts of it are present in urine, whereas larger amounts occur in the urine of patients with kidney disease. For a number of reasons, clinical terminology is changing to focus on albuminuria more than proteinuria [4].
It is usually asymptomatic but whitish foam may appear in urine. Swelling of the ankles, hands, belly or the face may occur if losses of albumin are significant and produce low serum protein levels (nephrotic syndrome). The amount of protein being lost in the urine can be quantified by collecting the urine for 24 hours, measuring a sample of the pooled urine, and extrapolating to the volume collected. Also a urine dipstick test for proteinuria can give a rough estimate of albuminuria. This is because albumin is by far the dominant plasma protein, and bromophenol blue the agent used in the dipstick is specific to albumin.
Albuminuria is a sign of kidney disease and means that you have too much albumin in your urine. Albumin is a type of protein that is normally found in the blood. Your body needs protein. It is an important nutrient that helps build muscle, repair tissue, and fight infection. But it should be in your blood, not your urine. A healthy kidney doesn't let albumin pass from the blood into the urine. A damaged kidney lets some albumin pass into the urine. The less albumin in your urine, the better. When you have albumin (protein) in your urine, it is called "albuminuria" or "proteinuria."
Transient proteinuria is the temporary excretion of protein and can be caused by strenuous exercise, a high fever, exposure to cold, stress and other conditions. Pregnant women may also excrete more protein in their urine. Transient proteinuria does not involve underlying kidney

disease and requires no treatment. Orthostatic proteinuria means an increased amount of protein is excreted when a person is in the upright position. It's most often found in tall, thin adolescents and young adults less than 30 years of age. The kidneys are usually healthy. Proteinuria can be caused by diseases not involving the kidneys, such as multiple myeloma, a cancer of the plasma cells in the bone marrow. In this case, the blood is flooded with too many proteins that are then filtered into the urine. The condition is known as overflow proteinuria [5].

The other type of proteinuria is due to kidney disease, such as glomerulonephritis, primary focal segmental glomerulosclerosis (FSGS) or kidney damage due to a systemic disease. Micro albuminuria means low levels of albumin are detected in the urine. Micro albuminuria can indicate that people with diabetes or hypertension are developing early stages of kidney disease.

Glomerular filtration rate (GFR) is a test used by physicians and other medical professionals to see if the kidneys are working correctly. In basic terms, it is a measurement of how much liquid and waste is passing from the blood through the tiny filters in the kidney, called the glomeruli, and out into the urine during each minute. The test measures how much creatinine is in the blood. This shows how well the kidneys are performing. In a normal healthy person the GFR stays close to the same value all of the time. The test is done by taking blood from a person and sending it to a laboratory. Normal values are between 90ml/min and 110ml/min. A value below 60ml/minute means the person has chronic renal disease and a value below 15ml/minute means the person's kidneys have stopped working.

Measurement of the GFR can be very helpful to medical professionals. It helps them decide if a person has a disease of the kidneys or not. A normal value for GFR is between 90-110ml/min. This will normally go down in older people. It will also go down in people with kidney disease. As well as helping a medical professional diagnose a kidney disease, the GFR is also used to monitor the progress of a disease.

The test begins by taking blood from a person's veins. The most common places are the vein in the elbow and the veins on the back of the hands. People usually feel a sharp stinging pain when the needle enters their skin. After the blood is drawn out, it is sent to a medical laboratory where a laboratory technician calculates the GFR. It is possible to calculate an exact value for the GFR but this is rarely done any more. Most of the time, the value is estimated (this is called an eGFR). The basis for this estimate is a chemical in the blood called creatinine. The calculation may also include things such as gender, age, height, weight, and race. Getting an exact measurement needs more tests and special equipment. Doctors now normally use the estimated GFR with signs, symptoms and the medical history given by the patient to come to a diagnosis. A final diagnosis of kidney disease may sometimes be made by a pathologist using tests such as a kidney biopsy.

There are some slight risks when this test is done. These include, too much bleeding from the needle entering the skin and vein, blood collecting under the skin, feeling faint, and infection from the skin being pierced by the needle. There are many functions that make up the GFR. These include: nitrogen based waste, sodium (salt), water, potassium, phosphate, and some medicines dissolved in the plasma such as digoxin and gentamicin. Blood pressure, the balance of acids to bases, the release of erythropoietin (a chemical that tells the body to make more red blood cells). The activation of vitamin D1, the formation of glucose in the fasting state, and the creation of peptide hormones (including insulin) all affect the GFR.

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 [6].

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.

2. Methodology

The present study was planned in the Department of Nephrology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar. Total 100 individuals were enrolled in the present study. From July 2018 to Dec 2018.These were divided in to the two study groups as 50 cases of the first degree relatives of CKD patients and 50 are control cases. The inclusion criteria control group is the patients 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.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

3. Results & Discussion

Although proteinuria/albuminuria is considered a surrogate marker of inflammatory process and abnormal endothelial function, the mechanisms underlying proteinuria/ albuminuria as an independent risk factor of CHD or cardiovascular events remain unclear.5 The possible explanations involve the question of whether proteinuria/ albuminuria is the cause or consequence of generalized endothelial damage. Among apparently healthy individuals a different amount of albuminuria is found, reflecting interindividual variations in renal and systemic micro vascular endothelial regulation. Such inherited distinction would result in varying degrees of individual vulnerability to develop future renal and cardiovascular damage. On the other hand, proteinuria/albuminuria often clusters other cardiovascular risk factors and thus as an early sign of endothelial dysfunction and the presence of proteinuria/albuminuria may just reflect the clinical settings of uncontrolled, unrevealed these risk factors.

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

Proband characteristics	Details
Mean age (years)	33 – 65 years
Gender	
Male	26
Female	24
Proband CKD stages	
Stage III	10
Stage IV	15
Stage V	25
Etiology of CKD in probands	
Hypertension	18
Diabetes mellitus	9
Chronic glomerulonephritis	7
Obstructive uropathy	4
HIVAN	3
Lupus nephritis	2
Analgesic nephropathy	1
Nephrocalcinosis	1
Unknown	5

Table 2: Serum Marker Analysis

Parameters	Cases: First degree relatives of CKD patients	Control patients
Serum uric acid (µmol/L)	140.5 – 342.3	185.6 – 325.6
Serum creatinine (µmol/L)	68.5 – 114.6	67.3 – 109.2
Mean eGFR (ml/min/1.73 m2)	78.3 – 132.9	77.1 – 123.6
Reduced eGFR	3 cases	1 case
Albuminuria	18 cases	11 cases
Dipstick proteinuria	8 cases	2 cases

Following the work of Go *et al*, [7] 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. This was likely for two reasons – (1) the MDRD eGFR equation used at the time was known to be less accurate at levels of eGFR greater than 60 mL/min tending to underestimate true GFR [8], and, (2) clinical practice guidelines at the time, defined chronic kidney disease (CKD) as an eGFR below 60 mL/min and thus this threshold was seen as an important clinical cut-point. However eGFR is a continuous variable and investigators remained interested in whether milder forms of kidney dysfunction also conferred an elevated risk for mortality and cardiovascular disease.

Both issues above were subject to vigorous debate in the nephrology community [9] and drove further research through collaboration of large research groups. The first data to provide a more definitive answer on the mortality effects of mild levels of kidney dysfunction came from the CKD Prognosis Consortium [10]. The CKD Prognosis Consortium [11] was established in 2009 to provide comprehensive evidence about the prognostic impact of eGFR and albuminuria on mortality and kidney outcomes.

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 [13].

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 [14].

4. Conclusion

The present study concludes the data regarding relatives of patients with CKD found a greater prevalence of CKD, albuminuria, and reduced eGFR among the first degree relatives of patients with CKD. It can also be concluded that 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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