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COMPARATIVE EVALUATION OF BIOCHEMICAL PARAMETERS IN HEALTHY CONTROLS AND PATIENTS WITH CHRONIC KIDNEY DISEASE

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Abstract

Background: Chronic kidney disease (CKD) affects about 5-10% of the global population. As there is decline in renal function, alterations can be observed in acid base balance, fluid and electrolyte homeostasis and decrease in clearance of metabolic wastes like urea, creatinine and uric acid; all of which results in unwanted health complications.

Aim: To estimate serum urea, creatinine, uric acid and minerals (calcium, phosphorus, sodium, potassium and chloride) in patients with CKD and to compare that with the healthy controls.

Methods: This study was conducted with inclusion of 50 CKD patients and 50 age and sex matched healthy control group. Biochemical investigations such as serum urea, creatinine, uric acid, calcium, phosphorous, chloride, sodium and potassium were carried out. The findings were recorded and results were analyzed using SPSS version 20.

Results: Hypertension and diabetes mellitus were the common etiologies of CKD while general weakness, pallor, pedal edema and anorexia were the commonest clinical signs presented. Serum urea, creatinine, uric acid and phosphorous were significantly increased while the levels of calcium, sodium, chloride and potassium were not altered significantly. The levels of significantly altered biochemical parameters showed progressive and significant increase as the renal impairment progressed.

Conclusion: CKD is associated with altered blood levels of several biochemical parameters. Hence routine analysis of these parameters aids in the management of CKD patients.

Key words: Chronic kidney disease (CKD), Glomerular filtration rate (GFR), End stage renal disease (ESRD), Urea, Creatinine, Electrolytes

Introduction

Chronic kidney disease abbreviated as CKD is also known as a silent killer because the symptoms of renal damage do not occur at an early phase [1]. There is a gradual loss of renal function characterized by decrease in glomerular filtration rate (GFR) which is less than 15mL/min for the period of three months in an individual with body surface are of $1.73m^2$ [2]. CKD is one of the leading causes of global mortality and morbidity [3]. In India, the prevalence of CKD is around 13-15.04% [4]. CKD is further categorized into five stages based on GFR as follows [5]:

Stage I→ GFR>90 mL/minute
Stage II→ GFR 60-89 mL/minute
Stage III→ GFR 30-59 mL/minute
Stage IV→ GFR 15-29 mL/minute
Stage V→ GFR <15mL/minute

CKD has multiple etiologies such as old age, unhealthy living, malnutrition, anemia, hypertension, obesity, diabetes etc [6]. As CKD progresses, it results in an inevitable loss of functional nephrons leading to end stage renal damage (ESRD), a condition in which the endogenous renal function is lost irreversibly [7]. During CKD, a number of regulatory mechanisms of body are affected such as electrolytes balance, acid base balance, energy balance etc all of which contribute to the increased susceptibility to cardiovascular diseases and mortality [8].

Kidney disease can be diagnosed by analysis of various biochemical parameters like urea, creatinine and electrolytes such as sodium, potassium, chloride, calcium, phosphorous and magnesium [9]. Creatinine is an anhydride of creatine made up of glycine, methionine and arginine while urea is a catabolic end product of amino acids and proteins. As the renal function decreases gradually, urea and creatinine are retained back to the circulation and their levels in blood increase [10]. Serum uric acid is an end product of purine nucleotide catabolism. Elevation in the level of uric acid is one of the common manifestations of CKD [11].

Minerals are important for growth and development of body. They are involved in various metabolic regulatory functions such as enzymatic reaction (as cofactors), bone formation, muscle contraction, nerve impulse conduction etc. Therefore, their concentrations in blood should be maintained within the normal range [9]. However, in CKD, there is marked impairment in the metabolism and homeostasis of these minerals that leads to associated complications of CKD and increases the mortality rate if not controlled in time. Diagnosis at an early stage along with adequate treatment strategy can prevent the progression of CKD to the successive stages, minimize complications and decreases the risk of mortality; hence the current study was put forth with an aim to evaluate biochemical parameters like serum urea, creatinine and electrolytes in the patients with CKD and compare that with the healthy controls. The value of these biochemical parameters were also compared among the patients at various stages of CKD.

Materials and Methods

This study was commenced in the Department of Biochemistry, Prasad Institute of Medical Sciences, from November 2021 to June 2022. After obtaining ethical approval from the institute, 50 patients with CKD and 50 age and sex matched healthy controls were enrolled for the study. Details of the patients such as age, gender, family history, dietary habits and clinical history were recorded. Before commencement, an informed consent was obtained from all the participants who were willing to volunteer this study. The patients selected for this study fulfilled following inclusion and exclusion criteria.

Inclusion criteria

- Elevated serum urea and creatinine
- Decreased creatinine clearance
- Ultrasound evidence of chronic renal failure
- Changes in serum electrolytes, low specific gravity which provided supportive laboratory evidences

Exclusion criteria

Patients with bleeding disorders, chronic inflammatory disease, malignancies, liver diseases, cardiovascular diseases and acute illness were excluded from the study.

Blood samples were collected from the patients and controls groups; and then transported to the laboratory for analysis. Serum urea and creatinine were analyzed by Urease-GLDH method and modified Jaffe's method respectively. Calcium, phosphorus, sodium, potassium and chloride were measured by ion selective electrode method. Serum uric acid was measured by Uricase method.

After the analysis, the values of each parameter were documented and analyzed using SPSS version 20. The comparative analysis between the patient group and the control group was done using students' t-test while the comparative analysis within the different stages of CKD was done using ANOVA. The p value less than 0.05 represented statistical significance.

Results

In this study, most of the patients were from the age group 40-60 years (44%) (figure 1). With respect to gender, 70% of patients wee males while 30% were females with male:female ratio of 2.3:1 (figure 2). The most common etiology of CKD in this study was hypertension (48%) followed by diabetes mellitus (22%) and renal stones (12%) (figure 3). All the patients enrolled in this study showed the clinical signs of general weakness. Other common signs presented by the patients were pallor (96%), pedal edema (88%), hypertension (88%), anorexia (80%) and oligouria (72%) (table 1). Most of the patients enrolled in this study had stage II CKD (36%) followed by stage V (30%) (figure 4).

When biochemical parameters were compared between healthy controls and CKD patients, it was observed that the levels of serum urea, creatinine, uric acid and phosphorous were significantly high in the patients while the serum level of calcium was significantly low. There was no significant difference in the serum level of sodium and chloride though the levels decreased in the patient group compared to the control group. Likewise the serum level of potassium was marginally high in the patients group but it was not significant statistically (table 2).

Table 3 shows the comparative analysis of biochemical parameters (urea, creatinine, uric acid, calcium and phosphorous) at different stages of CKD. It was found that the levels of urea, creatinine, uric acid and phosphorous increased significantly as the patients progressed from stage I to stage V CKD while there was no significant change in the level of calcium.

Figure 1: Distribution of patients and control group according to age

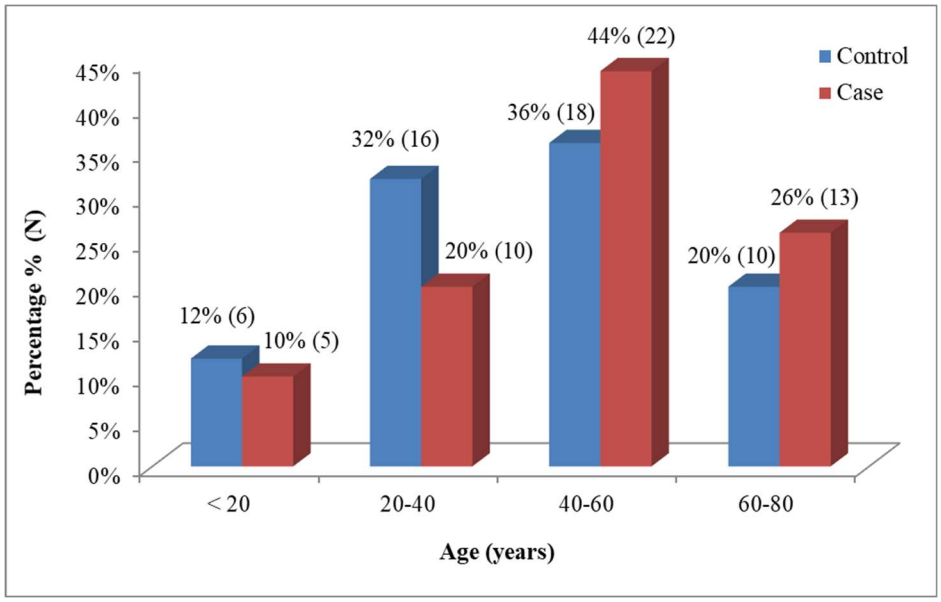

Figure 2: Distribution of patients and control groups according to gender

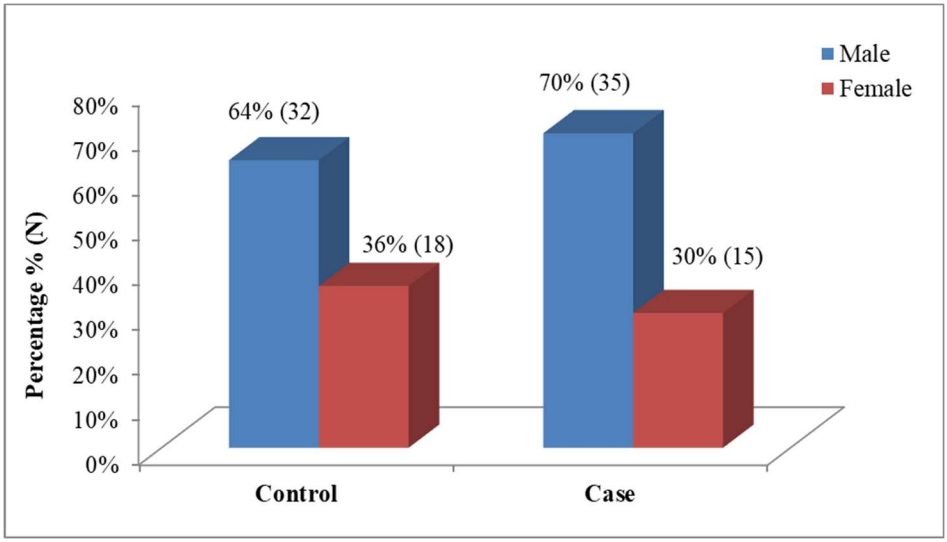

Figure 3: Distribution of patients based on etiologies of CKD

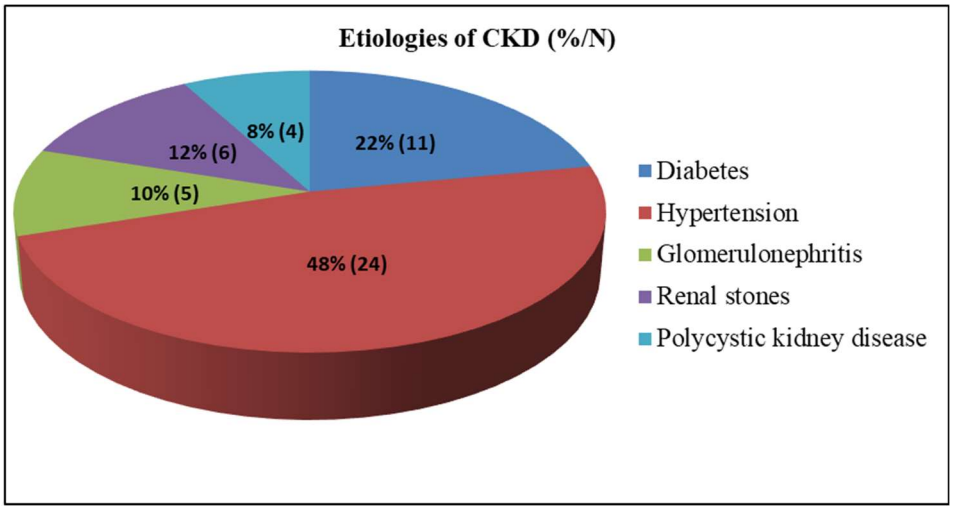

Figure 4: Distribution of patients according to the stage of CKD

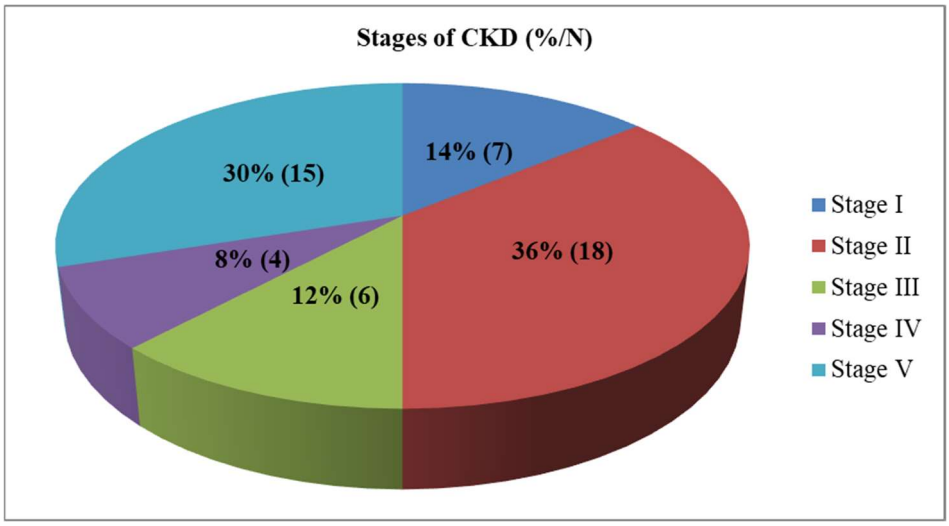

Table 1: Clinical sign of CKD presented by the patients

Clinical signs	**N (%)**
General weakness	50 (100)
Breathlessness	26 (52)
Anorexia	40 (80)
Vomiting	32 (64)
Oligouria	36 (72)
Pedal edema	44 (88)
Facial edema	10 (20)
Hematuria	3 (6)
Pallor	48 (96)
Ascites	15 (30)
Abdominal distension	7 (14)

Flaps	20 (40)
Convulsion	2 (4)
Hypertension	44 (88)

Table 2: Comparison of biochemical parameters among cases and controls

Parameters	Control	Cases	P
Urea (mg/dL)	26±5.4	130.18±30.6	< 0.05*
Creatinine (mg/dL)	0.8±0.2	7.8±3.1	< 0.05*
Uric acid (mg/dL)	5.3±1.2	10.3±2.8	< 0.05*
Calcium (mg/dL)	10.5±0.8	8.4±0.9	< 0.05*
Phosphorus (mg/dL)	4.4±0.4	6.6±1.2	< 0.05*
Sodium (mEq/L)	138.7±5.4	134.7±7.2	> 0.05
Potassium (mEq/L)	3.8±0.2	4.5±0.8	> 0.05
Chloride (mEq/L)	102.3±6.2	99.5±5.1	> 0.05

*→Statistical significance

Table 3: Comparison of biochemical parameters at different stage of CKD

Parameters	Stage I	Stage II	Stage III	Stage IV	Stage V	p
Urea	76.2±5.1	98.3±4.2	115.4±6.8	146.5±6.1	185±5.4	<0.05*
Creatinine	2.7±0.9	3.8±1.06	7.6±2.9	9.1±3.2	12.3±2.8	<0.05*
Uric acid	5.7±1.6	6.8±1.9	8.7±2.1	10.4±2.1	13.6±3.9	<0.05*
Calcium	8.2±1.02	7.5±1.1	8.4±0.8	8.1±0.9	7.8±0.9	>0.05
Phosphorus	4.8±0.8	5.8±1.3	6.3±1.9	6.7±1.2	6.9±1.8	<0.05*

*→Statistical significance

Discussion

Kidneys are the paired organs vital for the removal of body waste and toxins in urine. They are also essential for the maintenance of water and electrolyte homeostasis, regulation of blood pH and blood pressure. Impairment in renal function causes accumulation of metabolic waste in body leading to life threatening complications. It should be noted that despite of having essential role in physiological functions of body, kidney possesses limited ability to recover from the chronic damage. Hence regular monitoring and attention should be given because kidney function reduces approximately by 50% by the time when symptoms of kidney function impairment manifest.

The risk of CKD increases with the increase of age. According to Rajkondawar AV *et al*, maximum incidences of CKD can be observed at the 6th decade of life. In our study too, maximum incidence was observed in the age group of 40-60 years [12]. Our study showed the preponderance of male in CKD with male female ratio of 2.3:1. The ratio was 2.33:1 and 1.43:1 in the study of Rajapurkar MM *et al* [13] and Modi GK *et al* [14] respectively.

Hypertension (48%) and diabetes mellitus (22%) were the most common etiologies of CKD among the patients involved in this study. While the common clinical signs observed were general weakness (100%), pallor (96%) pedal edema (88%) and hypertension (88%). In the study of Singh AK *et al*, common clinical signs were general weakness, hypertension and pallor which were similar to our study [15].

The mean values of urea, creatinine and uric acid were significantly high in the patients with CKD compared to control groups. Our findings were in accordance to that with Khasawnah N *et al* [16] and Amin N *et al* [17]. Creatinine is obtained from creatine by spontaneous cyclisation. It is continuously synthesized in body and excreted in urine by kidneys. Similarly, urea is synthesized from carbondioxide and ammonia in liver through a sequence of reactions known as urea cycle. It is one of the important mechanisms of detoxification of ammonia released from amino acid and protein catabolism. Like creatinine, urea is also excreted in urine. Decreased renal function affects the rate by which these metabolites are filtered by glomeruli leading to their reduced elimination from the body thereby indicating development of renal failure [18, 19].

Reduced renal clearance also leads to the elevation in the level of uric acid which further facilitates the development as well as progression of CKD. In a systematic review that included 15 cohort studies of 99,205 individuals, the risk of CKD was observed to be 22% high for each increase of uric acid level by 1 mg/dL [20].

Impairment in mineral metabolism can be observed at an early stage of CKD. Hyperphosphatemia and hypocalcemia are the most prevalent disorders related to mineral metabolism. Decrease in GFR leads to increase in serum phosphorus level that consequently decreases the serum calcium level [21]. Hypocalcemia may be due to decrease in receptors for calcium or decrease in the level of calcitriol. 25-OH-cholecalciferol is converted to calcitriol in kidneys. Due to impaired renal function, deficiency of vitamin D (calcitriol) occurs that decreases the renal tubular reabsorption and intestinal reabsorption of calcium [22]. Hyperphosphatemia could be probably due to reduced filtration and excretion of phosphorous with progression to CKD. In the present study, the level of serum calcium was low and that of phosphorus was significantly high. Similar results were also documented by Salih H *et al* [23], Singh S *et al* [24] and Mahdavi MM *et al* [25].

The present study did not demonstrate any significant derangement in the level of sodium, potassium and chloride in CKD patients compared to control. Potassium is the major intracellular cation, the homeostasis of which is maintained by kidneys via monitoring its uptake and removal. However, hyperkalemia due to disturbed potassium homeostasis in CKD increases the risk of cardiovascular events [26]. The level of sodium may be normal or decreased in CKD which is attributed to hemodilution caused by fluid retention [27]. Moreover, both hyperkalemia and hyponatremia are fatal to the patients with CKD. Chloride ion is the predominant extracellular anion. Disturbance in chloride concentration can be observed in 48.8% of patients suffering with CKD. It is the known fact from the literatures that the mechanisms that regulate serum sodium and chloride concentration are similar; hence the patterns of the level of these electrolytes in CKD are comparable [28]. These findings are in accordance to that of Molla MD *et al* who reported

hypernatremia and hyperchloremia in only 2.4% and 5.8% of the patients with CKD respectively [29].

Therefore, from this study, it is apparent that, kidneys are the principal organs for maintenance of fluid and electrolyte homeostasis and clearance of metabolic wastes from the body. Any acute or chronic impairment in kidney function can result in several life threatening complications like hyperkalemia, hyperphosphatemia, hypocalcemia etc.

Conclusion

CKD is linked with abnormal metabolism of a number of biochemical parameters that ultimately increases the risk of several life threatening complications, hence regular evaluation and monitoring of these parameters are necessary so that CKD can be diagnosed at an initial stage and corrected, which will be a great aid in reduction of CKD associated morbidity and mortality.

Conflict of interest:- Nill

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