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Electrolyte Disturbances and Their Significance in Late Stage Chronic Kidney Disease: A Cross-Sectional Study

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Abstract
The kidneys play a vital role in maintaining electrolyte and acid-base balance. Progressive loss of kidney function inevitably leads to electrolyte disturbances, which adversely affect patient outcomes. As chronic kidney disease (CKD) becomes increasingly prevalent worldwide, this study aimed to evaluate serum electrolyte variations and their significance in pre-dialysis and dialysis patients with CKD. This cross-sectional study was conducted including 156 participants aged 30-85 years. The cohort comprised 78 CKD patients in the pre-dialysis stage and 78 in the dialysis stage. Each participant's medical history was thoroughly documented according a pre-designed proforma, peripheral venous blood samples (5 mL) were collected and analyzed biochemically using automated chemistry analyzer and immunoanalyzer. An independent sample t-test was employed to compare serum electrolyte levels between pre-dialysis and dialysis stages. Data analysis was done using SPSS 20.0. Most patients maintained normal serum levels of potassium, chloride, sodium and calcium. However, the dialysis group exhibited significantly higher serum phosphate and serum calcium levels compared to the pre-dialysis group ($P<0.05$). No significant differences were observed for sodium, bicarbonate, chloride and potassium levels between the groups. Electrolyte disturbances in CKD patients vary based on medical management, diet, comorbidities and lifestyle. Variations in serum phosphate and calcium levels were significant between pre-dialysis and dialysis patients. Careful monitoring and prediction of electrolyte disturbances can help delay CKD progression and reduce associated complications.

INTRODUCTION

End-stage renal disease (ESRD) arising from diabetic kidney disease (DKD) has swiftly emerged as the foremost cause of ESRD within a relatively short timeframe. As the glomerular filtration rate (GFR) declines, manifestations of complications related to DKD, both renal and non-renal, become evident. During the advanced stages of chronic kidney disease (CKD), DKD typically presents with anemia and disturbances in bone and mineral metabolism earlier than other CKD types. CKD, a significant non -communicable metabolic disorder, is associated with elevated rates of morbidity and mortality[1].

Pressure natriuresis, a process where increased renal perfusion pressure triggers an increase in salt and fluid excretion, ensues subsequent to the rise in blood pressure induced by sodium. Conversely, in essential hypertension, there is effective impairment in renal sodium excretion. Essential hypertension is postulated to be primarily a genetic disorder involving several distinct genes that regulate renal sodium handling. This condition clinically manifests within an unfavorable nutritional milieu, especially with excessive salt intake. Electrolyte imbalances play a pivotal role in the progression of disease and mortality among ESRD and dialysis patients[2,3].

Hyperkalemia in ESRD is predominantly attributed to dietary factors, medication and reduced potassium excretion. A translocation from intracellular to extracellular compartments leads to a post-dialytic potassium surge during late-stage dialysis and the initial hours thereafter. Urinary calcium excretion diminishes in CKD stage 2 and drastically declines in stage 5, fostering calcium retention and vascular calcification due to net calcium inflow into the extracellular fluid. Conversely, net calcium outflow may exacerbate secondary hyperparathyroidism and diminish bone mass. Maintaining calcium balance necessitates a net-zero calcium flow concerning the extracellular fluid. Furthermore, independent of established CKD risk factors, elevated blood chloride levels are strongly associated with a modest decline in estimated GFR (eGFR)[4].

Electrolyte abnormalities are commonplace in CKD, with hyperkalemia being one of the most prevalent. Dysnatremia occurs more frequently due to impaired renal water control. Although the prevalence of dysmagnesemia in the CKD population remains uncertain, it is likely underdiagnosed[5]. These electrolyte disturbances lead to significant complications as secondary consequences in CKD. Attaining electrolyte homeostasis is paramount in the management of CKD, making the evaluation of electrolyte significance in pre-dialysis and dialysis patients a focal point of this study.

The primary aim of this study was to investigate the disruption of serum electrolyte levels among pre-dialysis (CKD stage 4) and dialysis (CKD stage 5) patients. The specific objectives were to evaluate the frequency and percentage of serum electrolyte abnormalities in pre-dialysis and dialysis stages of CKD, identify the types of serum electrolyte abnormalities commonly observed in CKD and assess the clinical significance of serum electrolyte abnormalities in both pre-dialysis and dialysis stages of CKD.

MATERIALS AND METHODS

A total of 156 patients with diagnosed CKD were selected from the outpatients and wards. This included 78 patients in the pre-dialysis stage and 78 patients in the dialysis stage. The diagnosis was based on an estimated glomerular filtration rate (eGFR) of 60 mL/min/1.73 m², according to the criteria established by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative[6]. The study objectives and procedures were explained to each participant before commencement and informed consent was obtained, ensuring confidentiality.

Each participant's medical history was thoroughly documented according a predesigned proforma, and relevant investigations were conducted. Peripheral venous blood samples (5mL) were collected from each participant under strict aseptic conditions and placed in appropriate vacutainer tubes. The samples were centrifuged to separate the serum from the plasma. The serum samples were then analyzed biochemically using automated chemistry analyzer and immunoanalyzer.

RESULTS AND DISCUSSIONS

(Table 1) presents the electrolyte levels of the study participants as measured in milliequivalents per liter (mEq/l) for sodium, potassium, chloride, bicarbonate, phosphate and in milligrams per deciliter (mg/dl) for calcium. The table includes the ranges for each electrolyte level along with the corresponding number of participants (n) and the percentage (%) within each range.

(Table 2 and fig. 1) displays a comparison of electrolyte levels between the Pre-Dialysis and Dialysis stages of CKD. In the Dialysis stage, the mean sodium level was 1.53±0.53, while in the Pre-Dialysis stage, it

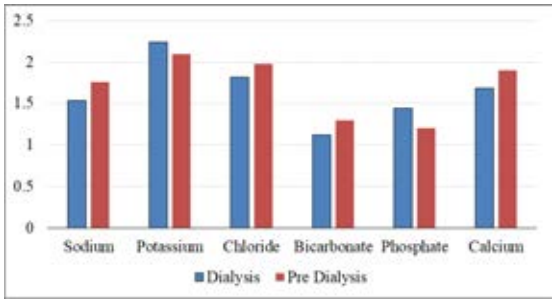

Fig. 1: Graphical comparison of serum electrolyte levels

Table 1: Electrolyte levels of the study participants

Electrolyte	Range (mEq/l)	n	Percentage
Sodium	<134	62	39.74
	134-145	93	59.62
	>145	1	0.64
Potassium	<3.6	20	12.82
	3.6-5.2	84	53.85
	>5.2	52	33.33
Chloride	<96	17	10.90
	96-106	122	78.21
	>106	17	10.90
Bicarbonate	<22	117	75.00
	22-28	36	23.08
	>28	3	1.92
Phosphate	<2.7	115	73.72
	2.8-4.5	40	25.64
	>4.6	1	0.64
Calcium (mg/dl)	<8.9	36	23.08
	9-11	117	75.00
	>11	3	1.92

Table 2: Comparison of electrolyte levels in Pre Dialysis vs Dialysis stage of CKD

Electrolyte	Dialysis (Mean±SD)	Pre Dialysis (Mean±SD)	p-value
Sodium	1.53±0.53	1.76±0.52	0.61
Potassium	2.24±0.66	2.10±0.59	0.38
Chloride	1.82±0.48	1.98±0.48	0.10
Bicarbonate	1.12±0.41	1.29±0.51	0.47
Phosphate	1.44±0.47	1.20±0.45	<0.01
Calcium	1.68±0.47	1.90±0.38	<0.01

was slightly higher at 1.76±0.52, with a non-significant P value of 0.61. For potassium, the Dialysis stage had a mean of 2.24±0.66 compared to 2.10±0.59 in the Pre-Dialysis stage, with a P value of 0.38, also not statistically significant. Similarly, chloride levels were lower in the Dialysis stage with a P value of 0.10. Bicarbonate levels were higher in Pre-Dialysis, with a p-value of 0.47.

Significant differences were observed in phosphate and calcium levels between the two stages. Phosphate levels in Dialysis were 1.44±0.47 mEq/l, significantly higher than in Pre-Dialysis at 1.20±0.45

mEq/l ($p<0.01$). Similarly, calcium levels in Dialysis were 1.68±0.47 mg/dl, significantly lower than in Pre-Dialysis at 1.90±0.38 mg/dl ($p<0.01$).

In our investigation, a notable discrepancy was observed in serum calcium levels between pre-dialysis and dialysis stages ($P<0.05$). Likewise, there was a highly significant variance in serum phosphate levels between these stages ($P<0.001$). However, no significant differences were noted in serum bicarbonate, sodium, chloride and potassium levels between pre-dialysis and dialysis phases.

Regarding CKD staging, 50% of the patients were categorized as stage 5, 50% as stage 4, with none falling into stages 1, 2, or 3. A comparison with recent Indian clinical studies on CKD revealed that 50.3% of patients were at stage 5, 24% at stage 4 and 19.1% at stage 3[7-9].

In CKD patients, baseline hyponatremia and time-dependent hypo or hypernatremia were independently associated with an increased risk of all-cause mortality. Time-dependent hyponatremia or hypernatremia corresponded to a 41% and 65% elevation in the risk of all-cause death, respectively[10]. The prevalence of hyperkalemia was notably higher in CKD patients compared to all enrolled subjects based on an observational retrospective cohort study utilizing a Japanese hospital claims database[11]. Patients with hyporeninemic aldosteronism, often linked to diabetic nephropathy or tubulointerstitial diseases, may develop hyperkalemia earlier in CKD progression[12]. Post-hemodialysis, serum potassium levels decreased, while sodium and chloride levels were largely unaffected. Hyperkalemia can stem from dietary factors, severe gastrointestinal illness, metabolic acidosis, or medications like angiotensin -converting enzyme inhibitors and potassium-sparing diuretics. Serum phosphorus levels may remain normal in most CKD patients with eGFR >40 mL/min/1.73 m2 due to parathyroid hormone effects., however, renal phosphate excretory capacity diminishes with CKD progression, leading to hyperphosphatemia[13]. Recent studies on calcium balance in adult CKD patients suggest that achieving a neutral calcium balance is feasible with recommended calcium intake but excessive supplementation leads to positive calcium balance[14]. With declining renal function, patients are more likely to exhibit low serum bicarbonate levels, affecting roughly 19% of CKD stage 4-5 patients[15].

Strengths and limitations of our study include its focus on electrolyte variations specifically in stage 4 and stage 5 CKD patients. However, the patient demographics at our study center, predominantly comprising individuals with low socioeconomic and educational backgrounds, may not fully represent the broader population. Additionally, given the dynamic nature of electrolyte homeostasis, a single-time analysis may not comprehensively capture electrolyte variations.

CONCLUSIONS

Electrolyte disturbances vary according to patients' medical management, dietary patterns, comorbid conditions and lifestyle factors. In this study, the majority of patients exhibited normal serum levels of potassium, chloride, sodium and calcium. However, hyponatremia was observed in about 40% of the participants and hyperkalemia was present in about 33% of CKD patients. Hypernatremia was rare among pre-dialysis patients, likely due to severe water intake restrictions. Significant changes were noted in serum phosphate and bicarbonate levels. Variations in serum phosphate and calcium were particularly significant between pre-dialysis and dialysis stages. Careful monitoring and prediction of electrolyte disturbances are essential to delay CKD progression and reduce complications.

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