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Full Length Research Paper

A study of serum electrolytes and calcium status in both hemodialysed and conservatively treated chronic kidney disease patients attending a tertiary care hospital of Assam

[1]Rashmi Rekha phukan and [2]Rohini Kt. Goswami

[1]Department of Biochemistry, Sikkim Manipal Institute of Medical Sciences, Gangtok, Sikkim, India, [2]Department of Biochemistry, Assam Medical College, Dibrugarh, Assam, India.

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The present study is a hospital based study in patients with CKD attending a tertiary care hospital in assam. 71 CKD patients (31 conservatively treated and 40 hemodialysed) and 50 healthy controls were included in the study. Serum Na+ and calcium was significantly lower with p value 0.015 and <0.001 respectively in CKD groups as compared to the controls. The difference of serum potassium between the cases and controls was statistically not significant. Varied ranges of dyselectrolemia is observed in the CKD group with incidence of hyponatremia and hypokalemia being more prevalent in CKD patients undergoing treatment with prevalence of 28.1% and 53.5% respectively. Whereas prevalence of hypernatremia and hyperkalemia was found to be 12.6% and 11.2% respectively. Between the conservatively treated and hemodialysed group, hyponatremia was found to be more prevalent in conservatively treated group with prevalence of 41.9%, whereas hypokalemia was more prevalent in the hemodialysed group with prevalence of 60%. Hypocalcemia was prominent invariably in both conservative and hemodialysed group. There was significant difference of Na+ and K+ values between CKD patients treated by hemodialysis and conservatively with p values 0.0103 and 0.0258 respectively. Whereas there was no differences found for calcium between the two groups. Varied range of dyelectrolemia has been noticed in CKD patients that depend upon the mode of treatment.

Keywords: CKD, hemodialysis, dyselectrolemia, prevalence.

INTRODUCTION

Gradual deterioratin of the kidney function caused by a varied range of etiology that causes reduction of effective fuctional unit of kidney leads to chronic kidney disease. Electrolyte disturbances are frequently observed in patients with CKD both in treated and untreated cases. Kidney is the major organ for water and electrolyte homeostasis. Deterioration of kidney function leads to different forms of electrolyte imbalances which increase morbidity and mortality in CKD patients. In the present study, we have investigated 71 randomly selected CKD cases attending a tertiary care hospital of Assam within 1 year time frame and compared it with 50 apparantly healthy controls. Among the 71 cases, there were 31 conservatively treated predialysedckd cases and 40 hemodialysed patients and results were compared between these two groups as well.

Definition of ckd[4,5]

Kidney damage for≥ 3 months irrespective of the value of GFR along with biochemical and pathological abnormalities

*Corresponding author E-mail: drrashmiphukan@gmail.com

or GFR < 60ml/min/1.73m^2 for ≥ 3 months, with or without kidney damage.

The presence of chronic kidney disease should be established based on the presence of kidney damage and level of kidney function (glomerular filtration rate), irrespective of diagnosis.

GFR is calculated using cockcroft and Gault formula [4]

Symptoms and biochemical changes occur when the GFR falls below 40 ml per minute. The symptoms of CKD are non specific and depends upon the underlying cause of the disease.

Estimation of serum electrolytes and calcium is an important part of management of CKD as electrolyte disturbances often leads to neurmascular and cardiovascular complications and even death in these patients. Timely correction of electrolyte imbalance increases the survivability and decreases the morbidity in CKD patients.

Aims and objectives

To study the status of serum sodium, potassium, and calcium in patients with CKD as compared to controls.

To study the difference in serum sodium, potassium, and calcium in hemodialysed and conservatively treated CKD patients.

REVIEW OF LITERATURE

Water and sodium homeostasis

With normal renal function, the tubular reabsorption of sodium and water is maintained and reabsorption and excretion matches dietary intake so that total body water and sodium is balanced. But in chronic kidney disease, this homeostasis is impaired and varied forms of fluid and electrolyte imbalances are seen which depends upon the stage of CKD and also the mode of treatment.[2]

Sodium is mostly (70%) reabsorbed in the proximal tubule. Reabsorbed sodium enters the cytosol of the epithelial cells either by diffusion through the sodium channel or cotransported along with glucose or amino acids.[17]

Sodium popassium ATPase in the basolateral surface drives three sodium out and two potassium in, which is done against the concentration gradient and is an energy dependent process. This mechanism prevents build up of sodium inside the cells. This process leads to high concentration of potassium inside the cells and is corrected by the potassium ion channels that allow potassium to move out of the cells in the basolateral surface. As a result the inside of the cells becomes negative and more sodium is reabsorbed.

Potassium homeostasis

Potassium is excreted in the distal nephron by aldosterone mediated mechanism. In CKD gradually GFR declines and as a result, potassium is expected to be increased with gradual deterioration of renal function but this scenario is not everytime observed. This may be because of potassium retention in these patients is defensed by augmented potassium excretion in the GI tract. Even though hyperkalemia may be precipitated in some patients with CKD in certain conditions like increased dietary potassium intake, increased protein catabolism, hemorrhage, hemolysis, transfusion of stored red blood cells, and metabolic acidosis. Hypokalemia is not commonly seen in CKD patients but may occur because of reduced dietary intake, GI losses and simultaneous diuretic therapy[2].

Calcium and phosphorous homeostasis

With gradual decrease in functional renal nephrons, the GFR decreases and so the excretion of phosphate which causes reciprocal decrease in serum calcium. To maintain serum phosphate and calcium homeostasis, parathyroid hormone level increases. Parathyroid hormone causes excretion of phosphorus and retention of calcium leading to normal serum calcium and phosphate. But with further progression of the disease, this homeostatic mechanism does not work leading to hyperphosphatemia and hypocalcaemia.[3]

As nephron mass decreases, there is also decrease in 1 α hydroxylation of 25-hydroxy cholecalciferol leading to decrease in level of active form of vitamin D which helps in absorption of calcium from the gut. As a result, there is further decrease in calcium level as the disease progresses[3].

MATERIALS AND METHODS

The present study is a randomized case control study including 71 CKD patients attending a tertiary care hospital of assam. Among the 71 CKD patients, 31 were conservatively treated and 40 were treated by hemodialysis. 50 apparently healthy controls were also included in the study and investigated for the same parameters as done in the CKD patients.

Place of study: Advanced clinical biochemistry laboratory, Department of Biochemistry, AMCH, Dibrugarh.

Duration of study : One year from September 2010 to August 2011.

Inclusion criteria

Patients of chronic kidney diseases.

Diagnostic criteria for chronic kidney disease included were Clinical signs and symptoms of uremia, level of GFR, abnormalities in the composition of blood (elevated blood urea & serum creatinine, abnormalities in serum electrolytes) or imaging tests (ultrasonogram) showing loss of cortico medullary differentiation on ultrasonogram

\diabetes mellitus, Ischemic heart disease, Patients with history of alcohol consumption and smoking.

Clinical criteria for chronic kidney disease:[2]

The clinical signs and symptoms of chronic kidney disease begins to appear only in the later stages of the disease and depends upon the etiology.
The signs and symptoms of CKD include that of uremia in the form of lethargy, headache, muscular cramps, irritability, asterixix, seizure, myoclonus, coma.
Pulmonary and cardiovascular disturbances like pericarditis, congestive cardiac failure, arrhythmias and pulmonary oedema.
Hematological and GI disturbances like anemia bleeding diathesis, nausea, anorexia, peptic ulcer, gastroenteritis, GI bleeding, vomiting etc.
Complications of hyperparathyroidism e.g. osteomalacia, . myopathy, gait disturbance, bone pains etc were noted.

Laboratory Findings

The presence of Chronic Kidney disease was established based on the markers of kidney damage which includes abnormalities in the composition of blood (elevated blood urea, serum creatinine), level of GFR or abnormalities in imaging tests (ultrasonogram).

Ultrasonogram

Shrunken kidneys bilaterally with loss of corticomedullary differentiation as seen on ultrasonogramis taken as evidence for chronic kidney disease.
Detailed history and physical examination was done in all selected patients and data collected was noted.

Collection and processing the samples

Under proper aseptic conditions, 4 ml of blood is collected and transferred to red capped vacutainer. Samples were centrifuged at 3000rpm for 5 minutes and serum separated was transferred to disposable sample cups using micropipette within half an hour. Tests were done as soon as possible on the same day.

Investigations done

All 71 cases and 50 controls were tested for serum sodium, potassium, and calcium. Serum sodium, potassium was estimated by using Easylite electrolyte analyzer. Serum, and calcium was estimated by semiautoanalyzermicrolab 300.

Test principles

Sodium and potassium was estimated by ion selective electrodes[7]:

The Easylyte analyzer measures sodium, potassium, in biological fluids using ion selective electrode technology. It has different electrodes which are specific for a particular type of ion to be measured. An ion selective electrode develops a voltage that varies with the concentration of the ion to which it responds. The potential of each electrode is measured relative to a fixed, stable voltage established by the silver/ silver chloride reference electrode. A comparative method of measurement is utilized. The analyzer can calculate the concentration of the ions in the sample solution, in accordance with the Nernst equation:

$E - E^{o} = S \text{ Log } \{Ci (x) / Ci (s)\}$ or $Ci (x) = Ci (s) \times 10^{\wedge} (E - E^{o}) / S$

where: E = ISE potential developed in sample solution
E^{o} = ISE potential developed in the standard solution
S = Electrode slope calculated during calibration
Ci (x) = Concentration of ion "I" in the sample
Ci (s) = Concentration of ion "i" in the standard solution
"S", the slope, is determined during calibration using Standards A and B, which have known levels of ions[7].

Normal reference range:

Sodium	135–145 mEq/L
Potassium	3.5–5.0 mEq/L

Serum calcium was estimated by arsenazo III method[6]:

Principle

Calcium + Arsenazo III ⟶ Blue Purple coloured complex

Normal reference range

Serum/ plasma : 8.7 – 11.0 mg / dl

RESULTS AND OBSERVATIONS

In table 1, serum sodium in patients was 138.36 ± 8.12 and in controls was 141.43 ± 3.94 with p value 0.015, which is statistically significant.
Serum potassium value in patients was 3.83 ± 0.99 and in controls was 4.10 ± 0.48 with p value 0.083 which was not significant.
Serum calcium in cases was 8.54 ± 0.49 and in controls was 9.56 ± 0.52 with p value <0.001 which is highly significant.
In table 2, serum sodium, potassium, and calcium value between conservatively treated and hemodialysed groups was compared. The difference of sodium and potassium

Table 1. Serum sodium, potassium, and calcium in controls and ckd patients (mean±sd).

groups	Serum sodium Mmol/lit	Serum potassium Mmol/lit	Serum calcium Mg/dl
controls	141.43 ± 3.94	4.10 ± 0.48	9.56 ± 0.52
patients	138.36 ± 8.12	3.83 ± 0.99	8.54 ± 0.49
p-value	0.015	0.083	< 0.001

Table 2. Comparison of serum sodium, potassium, and calcium in conservatively treated and hemodialysed ckd patients.

GROUP	Na^+mmol/L	K^+mmol/L	Ca++ mg/dl
Conservatively treated Mean±SD	135.583±8.320	4.123±1.159	8.532±0.462
Hemodialysed Mean ± SD	140.507±7.372	3.609±0.773	8.54±0.517
P value	0.0103	0.0258	0.9321

Table 3. prevalence of hypo and hypernatremia among ckd patients.

Group	No of hyponatremic patients with sodium <135 mmol/L	prevalence	No of hypernatremic patients with sodium >145 mmol/L	prevalence
Conservatively treated	13	41.9%	2	6.4%
Hemodialysed	7	17.5%	7	17.5%
Total	20	28.1%	9	12.6%

between the two groups was found to be statistically significant.

DISCUSSION

The present study is a randomized case control study including 71 CKD patients and 50 apparently healthy controls. Among the 71 CKD patients, 31 were treated conservatively and 40 were hemodialysed. All the cases and controls were tested for sodium, potassium and calcium.

Status of serum sodium

Serum sodium in patients was 138.36 ± 8.12 and in controls was 141.43 ± 3.94 with p value 0.015, which is statistically significant.

There was also significant difference (p value 0.01) of serum sodium between conservatively treated (135.5 ± 8.3) and hemodialysed group (140.5± 7.3).

Among the 71 CKD patients, 20 patients were hyponatremic with serum sodium value <135 mmol/L having prevalence of 28.1 %. Whereas 9 patients were hypernatremic having serum sodium value >145 mmol/L with prevalence of 12.6%.

Among the 31 conservatively treated ckd patients, 13 were hyponatremic with serum sodium value <135 with prevalence of 41.9% and 2 patients were hypernatremic with serum sodium value > 145 with prevalence rate of 6.4%.

Among 40 hemodialysed patients, 7 patients were hyponatremic and 7 patients were hypernatremic with prevalence of both hypo and hypernatremia being 17.5%.

It has been noted that hyponatremia is more prevalent in CKD patients as compared to hypernatremia and it is more prominent in the conservatively treated group.

Decrease serum sodium in the CKD patients may be due to reduced dietary intake, excess excretion, water retention leading to dilutional hyponatremia and due to some medications.

Sodium is mostly present in the extracellular fluid compartment. Kidney has tremendous capacity to maintain water and sodium homeostasis. Dysnatremia is not seen till the requirement of renal replacement therapy[11]. As CKD progresses, and the patient reaches ESRD, the urine osmolality becomes fixed at approximately 300 mOsmol/kg irrespective of water intake. As a result, the chances of both hypernatremia and hyponatremia increases.[10]

Sodium is required for normal nerve cell conduction, muscle contraction, maintenance of blood volume and blood pressure.

Symptoms of hyponatremia varies among different individuals from no symptoms to disorientation, headache, nausea, poor balance[12] etc. severe symptoms include confusion, seizure, coma, even death[13,14].

Hypernatremia lead to shrinkage of neuronal cells and resultant brain injury. Loss of volume may lead to

Table 4. prevalence of hypo and hyperkalemia among ckd patients.

Group	No of hypokalemic patients with potassium <3.5 mmol/L	prevalence	No of hyperkalemic patients with potassium > 5mmol/L	prevalence
Conservatively treated	14	45.1%	7	22.5%
Hemodialysed	24	60%	1	2.5%
Total	38	53.5%	8	11.2%

Table 5. Prevalence of hypo and hypercalcemia in ckd patients.

Group	No of hypocalcaemic patients with calcium<8.7 mg/dl	prevalence	No of hypercalcaemic patients with calcium > 11 mg/dl	prevalence
Conservatively treated	17	54%	0	0%
Hemodialysed	24	60%	0	0%
Total	41	57.7%	0	0%

tachycardia, hypotension . Rapid free-water replacement can cause cerebral edema[15].

Estimation of electrolytes should be frequently carried out in CKD patients to avoid delay in correction of dysnatremias which may lead to serious complications and increase the morbidity and mortality among CKD patients. The same patients may suffer from both hypernatremia and hyponatremia at different times during the course of the disease and during treatment.

RusulArifAbd Ali AL-Hisnawi et al in their study observed statistically nonsignificant decreased in serum sodium in the CKD patients compared to controls.[18]

POTASSIUM STATUS

From table 1 it has been observed that in CKD patients, serum potassium value was 3.83 ± 0.99 and in controls was 4.10 ± 0.48 with p value 0.083 which was not significant.

Among the 71 ckd patients, 38 patient were hypokalemic with serum potassium value less than 3.5 mmol/L with prevalence of 53.5% which is very very high and 8 patients were hyperkalemic with potassium value > 5 mmol/L and the prevalence of hyperkalemia is 11.2%.

Within the conservative group, 14 patients were hypokalemic with prevalence of 45.1% and 7 were hyperkalemic with prevalence being 22.5%.

Within the hemodialysed group, 24 patients were hypokalemic with prevalence of 60% and only 1 patient was found hyperkalemic with prevalence of 2.5%.

Potassium imbalance is frequently observed in the CKD patients both in conservative and hemodialysed patients and the findings vary with different centres. In the present study we have observed that hypokalemia is more prevalent in patients with CKD as compared to hyperkalemia and it is more so in hemodialysed patients.

98% of potassium is present in intracellular compartment and 2% present in the extracellular fluid.[8] Hypokalemia may occur as a result of reduced dietary intake, excess GI loss, malnutrition, mineralocorticoid use, and use of K-exchange resins[8]. In the dialysed patients, serum potassium level depends upon the composition of the dialysate. Rapid correction of acidosis causes severe hypokalemia due to shift of potassium from the extracellular to the intracellular space.[9]

Therefore in CKD patients, the use of mineralocorticoids, K-exchange rasins, and also potassium sparing diuretics should be used cautiously. Acidosis should be corrected gradually and dialysate composition should be calculated so as to contain adequate potassium concentration.

Both serum sodium and potassium should be continuously monitored in CKD patients. It will help in timely correction of electrolyte disturbances and will help in better prognosis of the disease.

RusulArifAbd Ali AL-Hisnawi et al observed statistically significant increase in serum potassium value in CKD patients as compared to controls.[18]

Status of serum calcium

Serum calcium in cases was 8.54 ± 0.49 and in controls was 9.56 ± 0.52 with p value <0.001 which was highly significant.

In the present study, among the 71 ckd patients, 41 were hypocalcaemic with serum calcium value <8.7 mg/dl. Hypocalcaemia is observed both in conservatively treated and hemodialysed patients. None of the patients in the present study had calcium value more than 11 mg/dl.

Hypocalcemia in CKD is due to hypophosphatemia associated with CKD, decrease in the number of calcium sensing receptor and vitamin D receptor in the parathyroid glands[16]. There is also deficiency of 1, 25 dihydroxychlecalciferol which is the active form of vitamin D that helps in absorption of dietary calcium from the gut.

There was no significant difference of serum calcium value between the conservatively treated and hemodialysed group.
RusulArifAbd Ali AL-Hisnawiet obsereved significant hypocalcemia in CKD patients as compared to controls.[18]

CONCLUSION

It has been observed in the present study that different forms of dyselectrolemia occur in CKD patients both treated by hemodialysis and conservatively. Hyponatremia is more often seen in the CKD patients as compared to hypernatremia which is more prominent in the conservatively treated group.
Although hyperkalemia is seen in few of the patients, hypokalemia is more often seen than hyperkalemia in CKD patients undergoing treatment which is more prominent in the hemodialysed group as compared to conservatively treated group. Dialysate potassium composition should be adjusted so as to maintain the body homeostasis of potassium.
Hypocalcaemia is seen invariably in both conservatively treated and hemodialysed group. Calcium adjustment in dialysate fluid is very crucial as high calcium in dialysate leads to vascular calcification and low calcium causes secondary hyperparathyroidism and bone demineralization.
It is worthwhile to check electrolytes and serum calcium value frequently in CKD patients during the course of the treatment and to treat them accordingly which will decrease their morbidity and mortality.
A more extensive study including larger patient population and longer duration is required to establish the prevalence of different forms of dyselectrolemia in CKD patients. Both pre-dialysis and post-dialysis study in the same patient would be a better one for evaluating the effect of dialysis and conservative treatment on serum electrolytes and serum calcium status in CKD patients. Proper follow up of each patient with serum electrolytes and calcium estimation at different times in the same patient is required to find out the incidence and prevalence of different kinds of dyselectrolemia and its relation with the course of the disease and treatment.

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