International Journal of Research in Medical Sciences
Phukan RR et al. Int J Res Med Sci. 2016 Dec;4(12):5405-5410
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20164218

Original Research Article

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

Rashmi Rekha Phukan*, Rohini Kt. Goswami

Department of Biochemistry, Assam Medical College, Dibrugarh, Assam, India

Received: 13 October 2016
Revised: 14 October 2016
Accepted: 11 November 2016

***Correspondence:**
Dr. Rashmi Rekha Phukan,
E-mail: drrashmiphukan@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: chronic kidney disease is a very commonly encountered health problem which if diagnosed and treated at a very early stage can increase the survivability and decrease the morbidity and mortality among these patients.
Methods: The present study is a hospital based study in patients with CKD attending a tertiary care hospital in Assam, India. 71 CKD patients (31 conservatively treated and 40 hemodialysed) and 50 healthy controls were included in the study. Serum sodium and calcium was estimated in all 71 cases and 50 controls after taking written consent for being included in the study. The results were compared statistically with the controls and also between the conservatively treated and hemodialysed group.
Results: Serum Na+ and calcium was significantly lower with p value 0.015 and <0.001 respectively in CKD groups as compared to the controls. Varied ranges of dyselectrolytemia were observed in the CKD group with occurrence of hyponatremia being more prevalent in CKD patients undergoing treatment with prevalence of 28.1%. Whereas prevalence of hypernatremia was found to be 12.6%. Between the conservatively treated and hemodialysed group, hyponatremia was found to be more prevalent in conservatively treated group with prevalence of 41.9%. Hypocalcemia was prominent invariably in both conservative and hemodialysed group. There was significant difference of Na+ values between CKD patients treated by hemodialysis and conservatively with p value 0.0103. Whereas no difference was observed for serum calcium between the two groups.
Conclusions: In the present study, varied range of dysnatremia has been noticed in CKD patients that depend upon the mode of treatment. Early detection of dyselectrolytemia with frequent investigation and adjustment of composition of the dialysate and mode of treatment may decrease the morbidity and mortality in CKD patients.

Keywords: CKD, Dysnatremia, Hemodialysis, Prevalence

INTRODUCTION

Gradual deterioration of the kidney function caused by a varied range of etiology that causes reduction of effective functional 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 apparently

healthy controls. Among the 71 cases, there were 31 conservatively treated predialysed CKD cases and 40 hemodialysed patients and results were compared between these two groups as well.

Definition of CKD[1,2]

Kidney damage for ≥3 months irrespective of the value of GFR along with biochemical and pathological abnormalities 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 presence of kidney damage and level of kidney function (glomerular filtration rate), irrespective of diagnosis.[3] GFR is calculated using cockcroft and Gault formula.[1] Symptoms and biochemical changes occur when the GFR falls below 40 ml per minute. The symptoms of CKD are non-specific and depend 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 neuromuscular 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, and calcium in patients with CKD as compared to controls.
- To study the difference in serum sodium, 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.[4]

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 transported along with glucose or amino acids.[5] Sodium potassium 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 buildup 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.

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.[6]

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.[6]

METHODS

The present study is a randomized case control study including 71 CKD patients attending a tertiary care hospital of Assam, India. 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.

Study was conducted at advanced clinical biochemistry laboratory, Department of Biochemistry, AMCH, Dibrugarh, Assam, India from September 2010 to August 2011.

Inclusion criteria

- Patients of chronickidney 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 and serum creatinine, abnormalities in serum electrolytes) or imaging tests (ultrasonogram) showing loss of cortico medullary differentiation on ultrasonogram.

Exclusion criteria

Diabetes mellitus, Ischemic heart disease, Patients with history of alcohol consumption and smoking

Clinical criteria for chronic kidney disease[4]

The clinical signs and symptoms of chronic kidney disease begin to appear only in the later stages of the disease and depend 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 ultrasonogram is 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 and calcium. Serum sodium was estimated by using Easylite electrolyte analyzer. Serum calcium was estimated by semiautoanalyzer microlab 300. Test procedures and principles are followed as written in the literature of the kit insert.

Test principles

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

The Easylyte analyzer measures sodium 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:

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

Where

- E = ISE potential developed in sample solution
- E° = 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

Serum calcium was estimated by arsenazo III method[8]

Principle

Calcium+Arsenazo III → Blue Purple coloured complex

Normal reference range

Serum/ plasma: 8.7-11.0 mg / dl

RESULTS

Results are analyzed using windows Microsoft excel software.

Table 1: Serum sodium and calcium in controls and CKD patients (Mean±SD).

Groups	Serum sodium Mmol/lit	Serum calcium Mg/dl
Controls	141.43±3.94	9.56±0.52
Patients	138.36±8.12	8.54±0.49
p-value	0.015	<0.001

Table 2: Comparison of serum sodium and calcium in conservatively treated and hemodialysed CKD patients.

Group	Na+ mmol/L	Ca++ mg/dl
Conservatively treated Mean±SD	135.583±8.320	8.532±0.462
Hemodialysed Mean ± SD	140.507±7.372	8.54±0.517
P value	0.0103	0.9321

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 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, and calcium value between conservatively treated and hemodialysed groups was compared. The difference of sodium between the two groups was found to be statistically significant.

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%

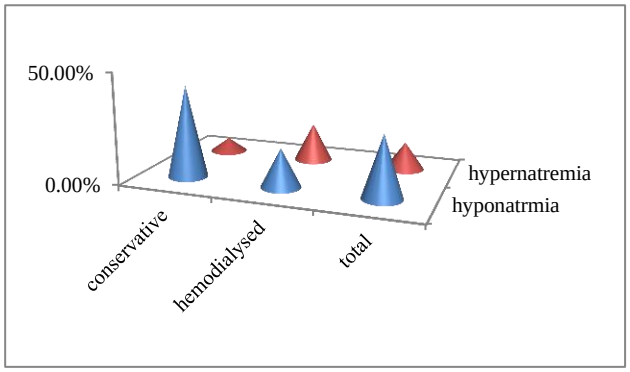

Figure 1: Prevalence of hypo and hypernatremia in conservatively treated and hemodialysed CKD patients.

Masahiko Nagahama, MD, et al in their study found that prevalence of hyponatremia varied according to CKD stage. It was 11.5%, 9.3%, 6.0%, 9.8%, 11%, and 15.1%, among patients with CKD stage 1, 2, 3a, 3b, 4, and 5, respectively.[9] Kovesdy CP et al in their study observed point prevalence of hyponatremia is 13.5% and that of hypernatremia is 2% in non-dialysis dependent CKD patients.[10]

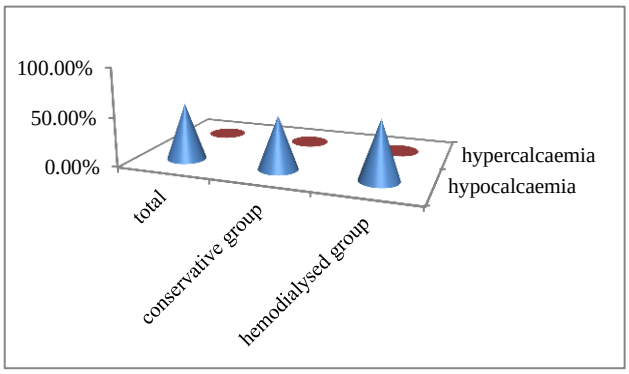

Figure 2: Prevalence of hypocalcaemia and hypercalcaemia in conservatively treated and hemodialysed CKD patients.

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%

From the Table 5 and Figure 2, it has been observed that the prevalence of hypocalcaemia in CKD patients is as high as 57.7%. None of the patients in the present study was hypercalcaemic.

The prevalence of hypocalcaemia in both conservatively treated and hemodialysed group was high with 54% and 60% respectively. Sanjay vikrant et al in their study of 462 patients of CKD observed hypocalaemia in (23.8%) and hypercalcemia in (5.4%) of patients.[11]

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 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 prevelant 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.[12] 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.[13] 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 etc.[14] severe symptoms include confusion, seizure, coma, even death.[15,16]

Hypernatremia lead to shrinkage of neuronal cells and resultant brain injury. Loss of volume may lead to tachycardia, hypotension. Rapid free-water replacement can cause cerebral edema.[17] 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. Salt and water intake or restriction should be advised judiciusly and dialysate sodium content should be adjusted according to the patients' electrolyte status. Rusul Arif Abd Ali AL-Hisnawi et al in their study observed statistically nonsignificant decreased in serum sodium in the CKD patients 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 was observed both in conservatively treated and hemodialysed patients. None of the patients in the present study had calcium value more than 11 mg/dl (hypercalcaemic).

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.[19] There is also deficiency of 1, 25 dihydroxycholecalciferol 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. Rusul Arif Abd Ali AL-Hisnawi et obsereved significant hypocalcemia in CKD patients as compared to controls.[18] R. Freethi et all in their study observed significant hypocalcaemia in CKD cases (9.8±0.456 mg/dl) as compared to controls (10.17±0.37 mg/dl).[20]

CONCLUSION

It has been observed in the present study that different forms of dysnatremia 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. 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 have been better study 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.

Funding: The study was conducted with financial help in the form of thesis grant from Dibrugarh University
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Tietz textbook of clinical chemistry and molecular diagnostics. 4th edition. 2006.
2. National kidney foundation. DOQI kidney disease outcome quality initiative. Am J. kidney dis. 2002;39:S1-246.
3. KDOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Available at: https://www.kidney.org/ sites/ default/ files/ docs/ ckd_evaluation_ classification_stratification.pdf
4. Harrison's principle of internal medicine. 18th edition. chapter 280.
5. International Biology Conferences. https://en.wikivet.net/ Reabsorption_and_Secretion _Along_ the_Proximal_Tubule_-_Anatomy _%26_ Physiology
6. Lascano ME, Schreiber MJ, Nurko S. Chronic Kidney Disease. 2010.
7. EasyLyte operators manual. Nov 27, 2014. http://docslide.us/documents/easylyte-manual.html
8. Smith HG Jr, Fager RS, Litman RJ. Light-activated calcium release from sonicated bovine retinal rod outer segment disks. Biochemistry. 1977;16(7):1399-405.
9. Hyponatremia Prevalence in CKD Patients Characterized. Available at: http://www.renalandurologynews.com/ kidney-week-2015-general-news/ hyponatremia-prevalence-in-CKD-patients-characterized/ article/ 452439/
10. Oxford Journals Medicine & Health Nephrology Dialysis Transplantation. 27(3):891-8.
11. Vikrant S, Parashar A. Prevalence and severity of disordered mineral metabolism in patients with chronic kidney disease: A study from a tertiary care hospital in India. Indian J Endocrinol Metab. 2016;20(4):460-7.
12. Arroyo AR. Electrolyte and acid-base balance disorders in advanced chronic kidney disease. Nefrologia. 2008;28(Suppl 3):87-93.
13. Feinfeld DA, Danovitch GM. Factor's affecting urine volume in chronic renal failure. Am J Kidney Dis. 1987;10:231-5.
14. Henry DA. In The Clinic: Hyponatremia. Ann Intern Med. 2015;163(3):ITC1-19.
15. Williams DM, Gallagher M, Handley J, Stephens JW. The clinical management of hyponatraemia. Postgrad Med J. 2016;92(1089):407-11.
16. Ball, SG, Iqbal Z. Diagnosis and treatment of hyponatraemia". Best practice & research. Clinical endocrinology & metabolism. 2016;30(2):161-73.
17. Lukitsch I. Hypernatremia. Medscape, Updated: Aug 24, 2016.
18. AL-Hisnawi RAAA, Salih H. A study of some biochemical changes in patients with chronic renal failure undergoing hemodialysis Int. J. Curr. Microbiol. App. Sci. 2014;3(5):581-6.
19. National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis. 2003;42(4 Suppl 3):S1-201.
20. Freethi R, Raj AV, Ponniraivan K, Khan MR, Sundhararajan A, Venkatesan. Study of serum levels of calcium, phosphorus and alkaline phosphatase in chronic kidney disease. Int J Med Res Health Sci. 2016;5(3):49-56.

Cite this article as: Phukan RR, Goswami RK. A study of serum sodium and calcium status in both hemodialysed and conservatively treated chronic kidney disease patients attending a tertiary care hospital of Assam, India. Int J Res Med Sci 2016;4: 5405-10.