

Association of Serum Potassium Disorders with Chronic Kidney Disease

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ABSTRACT

Introduction: Chronic kidney disease (CKD) may be associated with a variety of electrolyte disturbances. One such disturbance, hyperkalemia, is of great concern to care providers, who are treating patients with CKD. This is because of its possible implications for patient safety, related to the potential for associated adverse cardiac outcomes. The aim of this study was to find out the association between serum potassium disturbance and CKD patients. **Methods:** This descriptive type of cross-sectional study was conducted in the department of physiology in Mymensingh Medical College over a period of one year from January to December, 2016. A total number of 140 subjects participated in this study. On the basis of selection criteria, study subjects were divided into case and control groups. Serum potassium levels were measured in all study subjects by using same Auto-analyzer. **Results:** Serum potassium level was observed in CKD patients (case group) and healthy person (control group) were 5.57 ± 1.04 mmol/l and 4.13 ± 0.42 mmol/l respectively. In case group, serum potassium level was significantly ($p < 0.03$) increased with the comparison of control group. **Conclusion:** This study revealed that mild degree of hyperkalemia is a common feature in CKD patients. It emphasizes the need for regular checking of serum potassium level in CKD patient.

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INTRODUCTION

Chronic kidney disease (CKD) refers to an irreversible deterioration in renal function which usually develops over a period of years that initially shows some biochemical abnormalities but eventually, it causes loss of the excretory, metabolic and endocrine functions of the kidney.¹ It is a worldwide public health problem with an increasing incidence and prevalence, poor outcomes and high cost. Outcomes of CKD include not only kidney failure

but also complications of decreased kidney function and cardiovascular diseases.²

CKD results from progressive and irreversible loss of huge numbers of functioning nephrons which leads to ill health. It is associated with significant morbidity and mortality.^{3,4} Serious clinical symptoms often do not occur until the number of functional nephrons decrease at least 70 to 75 percent below normal. In fact, relatively normal blood concentrations of most electrolytes and normal body fluid volume can still be maintained

until the number of functioning nephrons reduces below 20 to 25 percent of normal.⁵ Therefore, electrolyte disturbances are common features of CKD patients. Among them hyperkalaemia is most important because of its' adverse cardiac outcomes, which is a great challenge for care providers of these patients.⁶

In a healthy person, serum potassium (K⁺) level is maintained in a narrow range, typically between 3.5 and 5.0 mEq/L.^{7,8} This homeostatic maintenance of serum K⁺ is important for many physiologic processes, such as nervous signaling, cardiac conduction, smooth muscle tone etc. In CKD, less K⁺ is excreted through urine and ultimately causes hyperkalaemia. Some medications (ACE inhibitors, diuretics) are commonly used for CKD patients who might cause hyperkalaemia or hypokalaemia.^{9,10}

Individuals with CKD and those with end-stage renal disease (ESRD) may experience both hyperkalaemia and hypokalaemia, in which the former typically occurs due to reduced kidney function or as a consequence of drugs such as Angiotensin Converting Enzyme Inhibitors (ACEIs) or Angiotensin-Receptor Blockers (ARBs), whereas the later is typically a consequence of diuretic administration.^{11,12}

As this type of study yet not done in Bangladesh, this study aimed to establish the association between serum potassium disturbance and CKD patients.

METHODS

This descriptive type of cross-sectional study was conducted in the department of physiology of Mymensingh Medical College, Bangladesh over a

period of one year from January to December, 2016. A total number of 140 subjects participated in this study. Among them 70 were healthy and 70 were diseased. In each group, male and female ratio was equal (1:1). Exclusion criteria for the study was; age <40 years and >70 years, pregnant woman, gouty arthritis, chronic liver disease, endocrine disease and malignancy, alcohol consumption, history of taking some drugs such as furosemide, thiazide, allopurinol. During visit, the presented age matched CKD patients (case group) and healthy persons (control group) were interviewed, examined and sample of blood was collected with due permission. The subjects were selected on the basis of history and clinical examination. Serum potassium level was measured by using Auto-analyzer (Electrolyte Analyzer, Biolyte 2000, Germany). All statistical analyses were done by using Statistical Package for Social Science (SPSS), version-20. Results were expressed as Mean±Standard Error (SE). Statistical significance of reference between two groups was evaluated by using students unpaired *t*-test and *p*<0.05 was considered as statistically significant.

RESULTS

Among the study subjects (n-140) including case (n-70) and control (n-70) group, male (n-35) and female (n-35) were equally distributed. Age range and mean age of study subjects were 40 to 70 years and 47.44±1.26 years respectively. Maximum number (61, 87.14%) of patients was found within 40 to 50 years of age (Table I).

Table I: Distribution of study subject by age groups

Age group (in years)	Control group (n-70)		Case group (n-70)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
40-50	62	88.57	61	87.14
51-60	3	4.29	7	10.00
61-70	5	7.14	2	2.86

In case group, male and female serum creatinine was significantly (*p*-0.0001) increased and eGFR

was significantly (*p*-0.0001) decreased in comparison with control group (Table II).

Table II: Level of serum creatinine and estimated GFR (eGFR) in study subjects

Variable	S. Creatinine		eGFR		p value
	Control group	Case group	Control group	Case group	
Male	1.03±0.18	3.08±1.38	85.89±2.02	28.65±1.11	0.000†*
Female	0.98±0.16	2.98±1.92	70.58±1.92	30.14±0.92	0.000†*

Student's unpaired 't' test; *Significant

Systolic and diastolic blood pressure of both male and female study groups were increased more than normal which indicates that the CKD patients were hypertensive (Table III).

Table III: Systolic and diastolic blood pressures (in mm of Hg) of different groups

Variable	Systolic blood pressure		Diastolic blood pressure		p value
	Control group	Case group	Control group	Case group	
Male	122.57±8.52	145.86±0.51	75.14±1.14	95.57±1.78	0.00†*
Female	118.43±1.25	143.57±1.35	71.43±1.34	93.86±1.46	0.00†*

Student's unpaired 't' test; *Significant

The mean (±SE) serum potassium level in control and case group of male were 4.14±0.42 mmol/l and 5.62±1.13 mmol/l respectively. The difference between them was statistically significant ($p=0.02$). The mean (±SE) serum potassium level in control and case group of female were 4.12±0.43 mmol/l and 5.51±0.95 mmol/l respectively. Mean (±SE) serum potassium level in case group of female was increased and that was significant ($p=0.04$) (Table IV).

Table IV: Mean serum potassium level in study subjects

Variable	Serum potassium level (mean±SE) mmol/l		t-value	p-value
	Control group	Case group		
Male	4.14±0.42	5.62±1.13	2.35	0.02*
Female	4.12±0.43	5.51±0.95	2.09	0.04*
Total	4.13±0.42	5.57±1.04	2.22	0.03*

Student's unpaired 't' test; *Significant

DISCUSSION

Chronic Kidney Disease (CKD) is a global problem equally affecting the people of developed countries as well as developing countries.¹³ It is recognized as worldwide major public health problem that characterized by progressive deterioration in renal function, which leads to irreversible loss of nephron number and their functions. This worsening of functions can occur over several months or years to progress.¹⁴ In CKD, serum creatinine usually increases and estimated glomerular filtration rate (eGFR) decreases. Our study also shows similar variations in CKD patients. Decrease glomerular

filtration rate (GFR) leads to sluggish flow of the filtered substance through the tubular lumen in CKD patients. This increases reabsorption of the creatinine causes passive back-diffusion from the lumen to the blood and increase serum creatinine in blood.^{15,16} Hostetter et al.¹⁷ suggested that reduced number of functioning nephron in CKD undergoes compensatory hyperfiltration. This adaptive response causes further renal damage by glomerular hypertrophy and glomerulosclerosis. So, filtration is hampered that may result in hyperuricaemia, increased creatinine level. Serum creatinine was increased and eGFR was decreased in both male and female cases in our

study which is consistent with the study of Coresh et al.¹⁸ and Osama et al.¹⁹

In a community-based cohort study done by Culleton et al.²⁰ found that hypertension was significantly higher in patients with renal failure than in those with normal renal function. Sinha et al.²¹ showed that, hypertension and CKD frequently coexist (86%).

Potassium homeostasis is maintained by kidneys. So, CKD patients are more prone to develop potassium disturbance than others. Both the hyperkalaemia (HK) and hypokalaemia can be experienced by CKD patients. Dangerous cardiac or neuromuscular effects may occur due to slight alteration of serum potassium level and HK is a potentially life-threatening condition which may cause cardiac complications.²¹ Various causes are responsible for HK in CKD patients. Important causes are impaired glomerular filtration rate (GFR) and high dietary potassium intake. Extracellular shift of potassium caused by the metabolic acidosis of renal failure and recommended treatment with renin-angiotensin-aldosterone system inhibitors e.g. captopril, losartan etc. and potassium sparing diuretics e.g. spironolactone, amiloride etc. that inhibit renal potassium excretion.^{6,22} CKD with constipation causes decreased enteral elimination of potassium and therefore lead to hyperkalaemia. In Diabetes mellitus, reduced insulin levels lead to accumulation of potassium in the extracellular space.²³ In this study, most of the patients were hyperkalemic possibly due to end stage renal disease or use of antihypertensive drugs.

Nakhoul et al.²⁴ found HK in 11% of CKD patients and Einhorn et al.⁶ evaluated that, regardless of treatment status, individuals with CKD were more likely to have a hyperkalaemic event than those without CKD. Salem et al.²⁵ established that, in patients with CKD, a compensatory response to chronic HK in which the body eventually develops a new state of potassium level which is often significantly higher than normal. Finding of our study is consistent with the study of researchers.^{6,24,25} This study was done on limited number of patients for a short period of time and no staging of CKD was done. So, further studies with large sample size are needed to evaluate the adverse effects in CKD patients according to stage.

CONCLUSION

It may be concluded that, mild degree of hyperkalaemia is a common feature in patients with chronic kidney disease (CKD). So, this study suggests for regular checking of serum potassium level in CKD patients for the prevention of cardiac complications.

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Conflicts of interest: None

REFERENCES

1. Conway B, Phelan PJ, Stewart GD. Nephrology and urology. In: Ralston SH, Penman ID, Strachan MWJ, Hobson RP, editors. Davidson's Principles and Practice of Medicine. 23rd ed. London, UK: Elsevier; 2018. p.415.
2. Levey AS, Stevens LA, Schmid CH, Zhang Y, Castro AF, Feldman HI, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med.* 2009; 150: 604-612.
3. Khanagavi J, Gupta T, Aronow WS, Tushar ST, Garg J, Ahn C, et al. Hyperkalemia among hospitalized patients and association between duration of hyperkalaemia and outcomes. *Arch Med Sci.* 2014; 10(2): 251-257. DOI:10.5114/aoms.2014.42577.
4. Singh P, Deshwali S, Potey GG, Sharma A. Study of serum sodium and serum potassium level in chronic renal failure. *Int J Adv Res Biol Sci.* 2017; 4(11): 103-111. DOI:http://dx.doi.org/10.22192/ijarbs.2017.04.11.013.
5. Hall JE, editor. Guyton and Hall Textbook of Medical Physiology. 12th ed. Philadelphia, USA: Saunders Elsevier; 2011. p.401.
6. Einhorn LM, Zhan M, Hsu VD, Walker LD, Moen MF, Seliger SL, et al. The Frequency of Hyperkalemia and Its Significance in Chronic Kidney Disease. *Arch Intern Med.* 2009; 169(12): 1156-1162. DOI:10.1001/archinternmed.2009.132.

7. Luo J, Brunelli SM, Jensen DE, Yang A. Association between serum potassium and outcomes in patients with reduced kidney function. *Clan J Am Soc Nephrology*. 2016; 11: 90- 100. DOI:10.2215/CJN.01730215.
8. Hoskote SS, Joshi SR, Ghosh AK. Disorders of potassium homeostasis: Pathophysiology and management. *J Assoc Physicians India*. 2008; 56: 685-693.
9. Ishii K, Norota I, Obara Y. Endocytic regulation of voltage-dependent potassium channels in the heart. *J Pharmacol Sci*. 2012; 120: 264-269.
10. Petkov GV. Role of potassium ion channels in detrusor smoothmuscle function and Dysfunction. *Nat Rev Urol*. 2012; 9: 30-40.
11. Palmer BF. Managing hyperkalemia caused by inhibitors of the renin-angiotensin-aldosterone system. *N Engl J Med*. 2004; 351: 585-592.
12. Luo J, Brunelli SM, Jensen DE, Yang A. Association between Serum Potassium and Outcomes in Patients with Reduced Kidney Function. *CJASN*. 2016; 11(1): 90-100. DOI: <https://doi.org/10.2215/CJN.01730215>
13. Saha M, Faroque MO, Alam KS, Alam MM, Ahmed S. Chronic kidney disease specific cardiovascular risk factors among non dialytic patients with chronic kidney disease stage-V an experience of a specialized hospital. *Bangladesh Med Res Counc Bull*. 2012; 38: 18-22.
14. Feig DI. Uric acid - a novel mediator and marker of risk in chronic kidney disease. *Curr Opin Nephrol Hypertens*. 2009; 18(6): 526-530.
15. Brod J, Sirota JH. The renal clearance of endogenous creatinine in man. *J Clin Invest*. 1948; 27: 645-654.
16. Mandell EE, Jonos F, Willis MJ, Cargill WH. Renal excretion of creatinine and inulin in man. *J Lab Clin Med*. 1953; 42: 821-837.
17. Hostetter TH, Olson JL, Rennke HG, Venkatachalam MA, Brenner BM. Hyperfiltration in remnant nephrons: a potentially adverse response to renal ablation. *J Am Soc Nephrol*. 2001; 12: 1315-1325
18. Coresh J, Mcquillan G, Brancati L, Levey A. Prevalence of high blood pressure and elevated serum creatinine level in the United States. *Arch Intern Med*. 2001; 61: 1207-1216.
19. Osama EI, Minshawy E, Bassuoni EI. Anemia and kidney dysfunction in type 2 Diabetic patients. *Nephro Urol*. 2010; 3(4): 543-552.
20. Culeton BF, Larson MG, Wilson PW, Evans JC, Parfrey PS, Levy D. Cardiovascular disease and mortality in a community based cohort with mild renal insufficiency. *Kidney Int*. 1999; 56: 2214-2219
21. Sinha AD, Agarwal R. The Complex Relationship between CKD and Ambulatory Blood Pressure Patterns. *Adv Chronic Kidney Dis*. 2015; 22(2): 102-107. DOI:10.1053/j.ackd.2015.01.003
22. Lehnhardt A, Kempe MJ. Pathogenesis, diagnosis and management of hyperkalemia. *Pediatr Nephrol*. 2011; 26: 377-384. DOI: 10.1007/s00467-010-1699-3r
23. Bianchi S, Aucella F, Nicola LD, Genovesi S, Paoletti E, Regolisti G. Management of hyperkalemia in patients with kidney disease's. 2019; 32(4): 499-516. DOI:10.1007/s40620-019-00617-y
24. Nakhoul GN, Huang H, Arrigain S, Jolly SE, Schold JD, Nally JJV, et al. Serum Potassium, End-Stage Renal Disease and Mortality in Chronic Kidney Disease. *Am J Nephrol*. 2015; 41: 456-463. DOI:<https://doi.org/10.1159/000437151>.
25. Salem MM, Rosa RM, Batlle DC. Extra renal potassium tolerance in chronic renal failure, implications for the treatment of acute hyperkalemia. *Am J Kidney Dis*. 1991; 18(4): 421-440.