

## Association of serum electrolyte with renal function, in diabetes mellitus - a pilot study

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### Abstract

**Introduction:** Decompensated diabetes mellitus with impaired renal function, acid-base disorders are often associated with electrolyte imbalance. Analysis of electrolytes is often advised without a true indication in Diabetes Mellitus. So our objective was to analyze serum electrolyte profile in diabetes mellitus to determine whether routine measurement of electrolytes can be safely avoided in diabetes.

**Study Design:** This was a retrospective study of hospital records of all Diabetes Mellitus cases who were advised kidney function test during the period January 2014 - August 2015. Medical records and laboratory results of 190 Diabetes Mellitus cases could be retrieved and retrospectively viewed for clinical diagnosis, result of Laboratory investigation i.e. Fasting blood sugar, serum urea, creatinine, Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, Ca<sup>2+</sup>, PO<sub>4</sub>. One hundred ninety Diabetes Mellitus cases were divided into 3 groups based on their serum creatinine levels i.e. Group-I (n=98) serum creatinine <1.5 mg/dl, Group-II (n=74) serum creatinine 1.5-3 mg/dl and Group- III (n=18) serum creatinine >3 mg/dl.

**Results:** Out of 190 patients 114 had electrolyte disorder. Serum sodium levels were altered in 45% of Group-I patients, more evident in Group-II (64%) and Group III (89%). Approximately 51% Diabetes Mellitus cases had deranged Serum K<sup>+</sup> levels in Group I. Hyperkalemia and hypochloremia were common electrolyte disorders both in Group-II and Group III. Group- I had hypercalcemia and hyperphosphatemia whereas hypocalcemia and hypophosphatemia were more commonly registered in Group-II (40%, 37% respectively) and Group-III (68%, 61% respectively).

**Conclusion:** So it is concluded that in diabetes mellitus electrolyte derangements occur even with normal renal function. So routine measurement of serum electrolyte could not be avoided in Diabetes Mellitus. However, the frequency of electrolyte derangement is more with deterioration of the renal function in Diabetes Mellitus.

**Keywords:** Retrospective study, Decompensated Diabetes Mellitus, Electrolyte disorders

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### Introduction

Electrolyte disorder occur in a broad spectrum of patients i.e. asymptomatic to terminally ill and often associated with wide range of morbidity and mortality<sup>(1)</sup>. Decompensated diabetes mellitus (especially with diabetic ketoacidosis or non-ketotic hyperosmolar syndrome) with impaired renal function, mal-absorption syndrome, acid-base disorders or multi-drug regimen are often associated with electrolyte imbalance.<sup>(2)</sup> Most serious disorder of Diabetes Mellitus is metabolic acidosis and frequency of metabolic acidosis is higher with the progression of renal failure<sup>(3,4)</sup>. Twelve clinical criteria i.e. poor oral intake, vomiting, chronic hypertension, diuretic use, recent seizure of unknown origin, muscle weakness, age 65 or greater, alcoholism, abnormal mental status, recent history of electrolyte abnormality, history of diabetes mellitus, history of

renal insufficiency or failure have been published for patients that may potentially be at risk for electrolyte abnormalities<sup>(5)</sup>. These are the true indications for rational ordering of the electrolytes in the Emergency departments. However analysis of electrolyte is often advised without a true indication in diabetes cases. So we took up a study to analyse serum electrolyte profile in Diabetes Mellitus cases in order to determine whether routine measurement of electrolytes can be safely avoided in diabetes mellitus. As electrolytes are included as one of the kidney function test parameters, an attempt was made to correlate electrolytes with serum creatinine levels to see whether in Diabetes Mellitus electrolyte derangement can occur even with normal renal function.

### Material and Methods

This was a retrospective study of hospital records of all diabetes mellitus cases attending the OPD/IPD of AIIMS, BBSR who were advised kidney function test. The medical history, age, gender, type of Diabetes Mellitus (DM), complications associated with DM, treatment history i.e., intake of drugs like diuretics, calcium channel blockers were retrieved. Results of serum urea, creatinine, FPG (Fasting Plasma Glucose), 2hr PPBS, Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, Ca<sup>++</sup>, PO<sub>4</sub> of these patients

were also recorded. Estimation of serum urea, creatinine, FPG (Fasting Plasma Glucose) and 2hr PPBS was done in Fully automated Chemistry Analyzer (Beckman Coulter, 5800 Model) using system compatible reagent kits. Electrolytes i.e., Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, Ca<sup>++</sup>, PO<sub>4</sub> were measured in Ecolyte electrolyte analyzer. Depending on the serum creatinine levels, these data were segregated into three groups i.e. group I (Serum creatinine <1.5 mg/dl) group II (creatinine 1.5-3 mg/dl) and Group III (creatinine >3 mg/dl). The electrolyte derangement pattern was analyzed in all the three groups to find out what proportion of diabetes mellitus cases with normal as well as altered renal function were associated with electrolyte derangement. The following cut off limits were used.

Serum Na level > 150 m Eq/L – Hyponatremia

< 135 m Eq/L - Hyponatremia

Serum K level > 5 m Eq/L – Hyperkalemia

< 3.5 m Eq/L - Hypokalemia

Serum Calcium level > 11 mg/dl- Hypercalcemia

< 8 mg/dl - Hypocalcemia

Diabetes Mellitus cases with grossly incomplete medical records or incomplete laboratory results were excluded from this study.

Results were expressed in mean±SD. Statistical analysis was performed using SPSS software 21 version.

The significance of observed differences among the groups were evaluated and P<0.05 was considered as statistically significant.

## Results

The general Characteristics of the study population showed that most of the patients were of Type 2 Diabetes mellitus. There was female predominance in our study groups (Table 1). Hyponatremia, hyperkalemia, hypocalcemia and hypophosphatemia were the common electrolyte derangements associated with Diabetes Mellitus in Group II and Group III (Table 2). The Proportion of Diabetes Mellitus cases with hyponatremia, hyperkalemia, hypocalcemia and hypophosphatemia was significantly higher in Group III as compared to Group II pointing towards the fact that electrolyte derangement is positively associated with dysfunction of the kidneys and with increasing serum creatinine level, the electrolyte disorder is more common (Table 2). Diabetes Mellitus cases with normal renal function i.e. Group I also registered alteration in all electrolyte parameters (Table 3) hyponatremia, hyperkalemia and hypercalcemia being the most predominant electrolyte derangement.

**Table 1: General Characteristics of the study population**

Sl. No.	Characteristics	Group I (n=98)	Group II (n=74)	Group III (n=18)
1	Age	62±5.7	68±7.8	65±6.8
2	Sex (Male)	41	33	7
	Sex (Female)	57	41	11
3	Type-I Diabetes Mellitus	8	5	2
	Type-II Diabetes Mellitus	90	69	16

**Table 2: Proportion of Diabetes Mellitus cases with electrolyte derangement in Patients with renal impairment**

Sl. No	Parameters	Group II (n=74)		Group III (n=18)	
		No. of cases	Proportion	No. of cases	Proportion
1	Normal Sodium	27	36%	2	11%
2	Hyponatremia	18	24%	3	16%
3	Hyponatremia	29	40%	13	73%
4	Normal Potassium	28	37%	3	17%
5	Hyperkalemia	34	45%	14	77%
6	Hypokalemia	12	18%	1	6%
7	Normal Chloride	25	33%	3	16%
8	Hyperchloremia	17	23%	4	23%
9	Hypochloremia	32	44%	11	61%
10	Normal Calcium	30	40%	3	16%
11	Hypercalcemia	14	20%	3	16%
12	Hypocalcemia	30	40%	12	68%
13	Normal Phosphate	31	42%	4	23%
14	Hyperphosphatemia	15	21%	3	16%
15	Hypophosphatemia	28	37%	11	61%

**Table 3: Proportion of Diabetes Mellitus cases with electrolyte derangement in Patients with normal renal function**

Sl. No	Parameters	Group I (n= 98)	
		No. of cases	Proportion
1	Normal Sodium	54	56%
2	Hypernatremia	27	28%
3	Hyponatremia	17	17%
4	Normal Potassium	48	49%
5	Hyperkalemia	29	30%
6	Hypokalemia	21	21%
7	Normal Chloride	52	53%
8	Hyperchloremia	29	30%
9	Hypochloremia	17	17%
10	Normal Calcium	56	57%
11	Hypercalcemia	24	24%
12	Hypocalcemia	18	19%
13	Normal Phosphate	57	58%
14	Hyperphosphatemia	21	22%
15	Hypophosphatemia	20	20%

## Discussion

Electrolyte disorders are commonly encountered in a broad spectrum of patients (from asymptomatic to critically ill) in hospital population to community subjects<sup>(6)</sup>. Electrolyte derangements are usually multifactorial and many pathophysiological conditions i.e. coexistent acid-base abnormalities, Drug intake, nutritional status, gastrointestinal absorption, associated renal disease or acute illness, play a key role. Diabetes Mellitus, a common metabolic disorder associated with these pathophysiological conditions often present with a diversity of electrolyte derangements.<sup>(7)</sup> Uncontrolled Diabetes mellitus may be associated with impaired renal function. Diabetic Kidney disease(DKD)/ Diabetic nephropathy is a leading cause of End Stage Renal Disease(ESRD)<sup>(8)</sup>. DKD is considered as a micro vascular complication of diabetes and loss of podocyte, epithelial dysfunction play important role in its pathogenesis. Inflammation, cell hypertrophy, and de-differentiation by the activation of classic pathways of regeneration further contribute to disease progression<sup>(9)</sup>. Many Studies reported a wide variety of electrolyte disorders in diabetes mellitus<sup>(10-13)</sup>. Group II and III documented increased proportion of hyperkalemia in this study. The probable explanations could be: the increased incidence of hyperkalemia in diabetic patients than healthy individuals, reduced glomerular filtration of  $K^+$  (due to acute kidney injury and chronic kidney disease) and many drugs i.e. potassium-sparing diuretics, angiotensin-converting enzyme inhibitors and beta blockers that interfere with  $K^+$  excretion.<sup>(14)</sup> The most common causal factor of chronic hyperkalemia in diabetes is syndrome of hyporeninemic hypoaldosteronism often associated with the reduced tubular secretion of  $K^+$ . In this syndrome, patients typically present with asymptomatic hyperkalemia and

is characterized by mild to moderate renal insufficiency. Diabetes Mellitus and elderly patients with chronic renal impairment more frequently found to have Hyporeninemic hypoaldosteronism. Diabetic nephropathy accounting for significant number of cases could be the most common cause of Hyporeninemic hypoaldosteronism.<sup>(15-17)</sup> Hyperkalemia was more prevalent in Group III as compared to Group II pointing towards the fact that electrolyte imbalance is more profound with deterioration of renal function in diabetes mellitus. Our study registered electrolyte derangements even with normal renal function i.e. in Group I (Table 3). Dysnatremia (hypo and hypernatremia) is the most well-known electrolyte imbalance in diabetes mellitus. Hyperglycemia prevailing in diabetes mellitus is the central mechanism of dilutional hyponatremia. As glucose is an osmotically active substance, hyperglycemia increases serum osmolality, dragging excess of fluid out of the cells and filling inside the serum, resulting in reduction of serum sodium levels ( $[Na^+]$ ) by dilution (Dilutional Hyponatremia). Similarly osmotic diuresis is another important cause of hyponatremia in uncontrolled diabetes. Many studies reported that diabetes mellitus as such independently of drugs or hyperglycemia is associated with hyponatremia<sup>(18)</sup>. Altered vasopressin metabolism, interaction between insulin and vasopressin, both of which act in the renal collecting duct, increase the expression of Aquaporin enhances reabsorption of more hypotonic fluid due to slower stomach emptying, have been proposed as possible underlying mechanisms of this association<sup>(19-20)</sup>. A reduction in serum water fraction (< 80%) may occur in patients with marked hyperlipidemia in uncontrolled DM. In these conditions, there is an artificial reduction in the serum sodium concentration, measured per liter

of serum, not serum water. Hence, termed as Pseudohyponatremia. The development of hypernatremia is associated with endocrine dysfunction. Hypernatremia and hyperosmolarity are associated with impairment of both insulin-mediated glucose metabolism and glucagon-dependent glucose release. Hypernatremia is implicated in the profound inhibition of gonadotrophin release in postmenopausal diabetic women. Hypokalemia in diabetics could be due to redistribution of potassium [K<sup>+</sup>] from the extracellular to the intracellular fluid compartment (shift hypokalemia). Diabetic-induced motility disorders or chronic diarrheal states often result in gastrointestinal loss of K<sup>+</sup> due to malabsorption syndromes and renal loss of K<sup>+</sup> (due to osmotic diuresis)<sup>(21,22)</sup> are the other common mechanisms of hypokalemia in diabetes. In Diabetes mellitus especially with acidosis redistribution of potassium from the cell to the intravascular space (shift hyperkalemia) can induce hyperkalemia with no net total body K<sup>+</sup> increase. This is frequent in condition of acidosis with altered permeability of the cell membrane resulting in shift hyperkalemia<sup>(23)</sup>. Hyporeninemic hypoaldosteronism being another important condition of hyperkalemia in elderly diabetics<sup>(24)</sup>. Apart from renal causes, these could be the factors responsible for electrolyte disorders prevalent in diabetes *per se* (independently of drugs or complications) that is suggestive of our finding (Table 3).

### Conclusion

In diabetes mellitus *per se*, electrolyte derangement prevail. So routine measurement of serum electrolyte could not be avoided in diabetes. Electrolyte imbalance occur even with normal renal function, however the frequency of electrolyte derangement is more with deterioration of the renal function in diabetes mellitus.

**Conflict of Interest:** Nil

**Ethical declaration:** Waiver for Ethical Consent obtained.

### References

1. Liam's G, Milionis HJ, Elisaf M. A review of drug-induced hypocalcemia. *J Bone Miner Metab* 2009;27:635-642.
2. Liam's G, Rodenburg EM, Hofman A, Zietse R, Stricker BH, Hoorn EJ Electrolyte disorders in community subjects: prevalence and risk factors. *Am J Med* 2013;126:256-263.
3. Nikolaos Sotirakopoulos, Irini Kalogiannidou, Maria Tersi, Karmen Armentzioiu, Dimitrios Sivridis, Konstantinos Mavromatidis. Acid-Base and Electrolyte Disorders in Patients with Diabetes Mellitus. *Saudi J Kidney Dis Transpl* 2012;23(1):58-62.
4. Liamis G, Liberopoulos E, Barkas F, Elisaf M. Spurious electrolyte disorders: a diagnostic challenge for clinicians. *Am J Nephrol* 2013;38:50-57.
5. Lowe, R.A., Arst, H.F., Ellis, B.K. Rational Ordering of Electrolytes in the Emergency Department. *Annals of Emergency Medicine* 1991;20,16-21.
6. Liamis G, Milionis HJ, Elisaf M. Hyponatremia in patients with infectious diseases. *J Infect* 2011;63:327-335.
7. Liamis G, Milionis H, Elisaf M. A review of drug-induced hyponatremia. *Am J Kidney Dis* 2008;52:144-153 [PMID: 18468754 DOI: 10.1053/j.ajkd.2008.03.004].
8. Filippatos TD, Elisaf MS. Effects of glucagon-like peptide-1 receptor agonists on renal function. *World J Diabetes* 2013;4:190-201.
9. Lindner G, Funk GC. Hyponatremia in critically ill patients. *J Crit Care* 2013;28:216.e11-216.e20.
10. Raebel MA, Ross C, Xu S, Roblin DW, Cheetham C, Blanchette CM, Saylor G, Smith DH. Diabetes and drug-associated hyperkalemia: effect of potassium monitoring. *J Gen Intern Med* 2010;25:326-333.
11. Van den Driessche A, Eenkhoorn V, Van Gaal L, De Block C. Type 1 diabetes and autoimmune polyglandular syndrome: a clinical review. *Neth J Med* 2009;67:376-387.
12. Pham PC, Pham PM, Pham SV, Miller JM, Pham PT. Hypomagnesemia in patients with type 2 diabetes. *Clin J Am Soc Nephrol* 2007;2:366-373.
13. Liamis G, Liberopoulos E, Alexandridis G, Elisaf M. Hypomagnesemia in a department of internal medicine. *Magnes Res* 2012;25:149-158.
14. George Liamis, Evangelos Liberopoulos, Fotios Barkas, Moses Elisaf. Diabetes mellitus and electrolyte disorders. *World J Clin Cases* 2014;2(10):488-496.
15. DeFronzo RA. Hyperkalemia and hyporeninemic hypoaldosteronism. *Kidney Int* 1980;17:118-134.
16. Arruda JA, Battle DC, Sehy JT, Roseman MK, Baronowski RL, Kurtzman NA. Hyperkalemia and renal insufficiency: role of selective aldosterone deficiency and tubular unresponsiveness to aldosterone. *Am J Nephrol* 1981;1:160-167.
17. Liamis G, Milionis H, Elisaf M. Blood pressure drug therapy and Electrolyte disturbances. *Int J Clin Pract* 2008;62:1572-80.
18. Hillier TA, Abbott RD, Barrett EJ. Hyponatremia: evaluating the correction factor for hyperglycemia. *Am J Med* 1999;106:399-403. [PMID: 10225241]
19. Bustamante M, Hasler U, Kotova O, Chivalin AV, Mordasini D, Rousselot M, Vandewalle A, Martin PY, Feraille E. Insulin potentiates AVP-induced AQP2 expression in cultured renal collecting duct principal cells. *Am J Physiol Renal Physiol* 2005;288:F334-F344 [PMID:15494547 DOI:10.1152/ajprenal.00180.2004].
20. Bankir L, Bardoux P, Ahloulay M. Vasopressin and diabetes mellitus. *Nephron* 2001;87:8-18 [PMID:11174201].
21. Yang L, Frindt G, Palmer LG, magnesium modulates ROMK channel mediated potassium secretion. *J Am Soc Nephrol* 2010;21:2109-2116 [PMID:21030597 DOI:10.1681/ASN.2010060617].
22. Kitabchi AE, Umpierrez GE, Murphy MB, Kreisberg RA. Hyperglycemic crises in adult patients with diabetes: a consensus statement from American Diabetes Association. *Diabetes care* 2006;29:2739-2748 [PMID:17130218 DOI:10.2337/dco6-9916].
23. Raebel MA, Ross C, Xu S, Roblin DW, Cheetham C, Blanchette CM, Saylor G, Smith DH. Diabetes and drug associated hyperkalemia: effect of potassium monitoring. *J Gen Intern med* 2010;25:326-333 [PMID:20087674 DOI:10.1007/s11606-009-128-x].

24. Oxlund CS, Henriksen JE, Tarnow L, Schouseboe K, Gram J, Jacobsen IA. Low dose spironolactone reduces in patients with resistant hypertension and Type 2 diabetes mellitus: a double blind randomized clinical trial. *J Hypertens* 2013;31:2094-2102[PMID:20087674 DOI:10.1097/HJH.0b013e3283638b1a.