

Original Article

## Electrolyte Disturbances and Their Association with Glycemic Status in Type 2 Diabetes Mellitus Patients

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### ABSTRACT

**Background:** Type 2 diabetes milieus (T2DM) is a disorder with complex metabolic and endocrine defects. It results from an alteration in insulin function and its action on peripheral tissue. Genetic and environmental factors also play important roles in the severity of T2DM. Serum electrolytes play an important role in normal body homeostasis. There is also increasing evidence that electrolyte imbalances are early biochemical events responsible for long-term diabetic complications. An imbalance in electrolyte distribution may lead to various clinical disorders, especially if it affects the course of diabetes and its management. So, this study was planned to investigate the electrolyte disturbance and its association with glycemic status in T2DM patients.

**Materials and Methods:** The present study was an observational study conducted in the General Medicine OPD, VIMSAR, Burla, on 200 patients with Type 2 Diabetes Mellitus. Biochemical analyses for glucose and calcium, sodium and potassium, and Magnesium were done using standard procedures. All data were analysed by GraphPad Prism version 5.

**Results:** Serum electrolytes such sodium, potassium, calcium, and magnesium dropped substantially when FBS, PPBS, and HbA1C levels increased in the study group. Most electrolyte abnormalities were hyponatremia (53%), followed by hypomagnesemia (38.5%), hypokalemia (33.5%), and hypocalcemia (31.5%). Patients had 7.5% hypernatremia and 5.5% hyperkalemia.

**Conclusion:** Thus, On careful monitoring to serum electrolyte concentration in DM patients along with glycemic status. Consequently, the assessment of serum electrolytes in diabetic patients must to be included into standard patient care, and any anomalies should be rectified.

**Keywords:** Type 2 diabetes mellitus, Hyponatremia, Hypomagnesemia, Hypernatremia, Hyperkalemia, Hypokalemia, Hypocalcemia.

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### INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a complex metabolic disorder resulting from change insulin secretion in the beta cells of the pancreas and its peripheral action is influence by combination of environmental and genetic variables. [1] In 2024, Globally, around 589 million adults (aged 20–79) were estimated to have diabetes, the number expected to be increase to 853 million by 2050 (a 45% global increase). India contributes significantly to this burden, with 106.9 million cases in 2024 expected to rise by 73% to 184.5 million by 2050.[2] Indians tend to develop diabetes at younger ages and lower body mass index (BMI), partly due to increased insulin resistance, central obesity, and genetic factors.[3] Serum

electrolytes play a key role in maintaining body's acid-base balance, helping blood to clot, enzyme function, nerve conduction muscle movements.[4] Electrolyte imbalance in diabetes mellitus contribute to metabolic instability and long-term complications. Disruptions in electrolyte [sodium (Na<sup>+</sup>), potassium (K<sup>+</sup>), calcium (Ca<sup>2+</sup>), and magnesium (Mg<sup>2+</sup>)] levels can affect cellular metabolism, glucose utilisation and insulin secretion. As a result, a range of clinical issues and significantly influence on both the progression and treatment of diabetes.

The Na<sup>+</sup>/K<sup>+</sup>-ATPase (NKA) is a predominant enzyme that help in maintaining ionic gradients across the cell membrane by extruding 3 Na<sup>+</sup> ions and importing 2 K<sup>+</sup> ions into the cell; is known to be alter in diabetes, influencing glucose transport and cellular excitability. [5] Studies have shown that there is an inverse correlation between serum Na<sup>+</sup> and K<sup>+</sup> levels in patients with diabetes. While, hypokalemia has been linked to an elevated risk of hyperglycemia. [6,7] Disruptions in intracellular Ca<sup>2+</sup> handling can decrease β-cell function and promote insulin resistance, which in turn impacts insulin production and sensitivity when there is a calcium imbalance. [8] High levels of calcium in the cytosol correlate with T2DM. [9]

Similarly, magnesium participates in insulin production and insulin resistance and functions as a cofactor for several enzymes in glucose metabolism. [10] Hypomagnesemia is the predominant electrolyte imbalance seen in ambulatory people with poorly controlled diabetes. A lack of Mg<sup>2+</sup> reduces activity of glucokinase, which in turn affects insulin production, leads to insulin resistance, and increases the cardiovascular risk and blood vessel problems. [2] The increasing prevalence of diabetes, affected by regional food habits, indicates the potential role of electrolytes in its pathophysiology. Assessing these modifications is essential for better clinical management. Therefore, this study aims to evaluate the changes in serum electrolyte levels and their correlation with glycemic status in patients with T2DM.

## MATERIALS AND METHODS

The study was conducted in the Department of General Medicine, from November 2019–October 2021 after obtaining approval from the Institutional Ethics Committee (VIREC-19240/Dt30.11.19/IST-256/19). It was a prospective cross-sectional study. The simple random sampling technique was done to take the study population.

**Sample size calculation.** For estimation of the prevalence of electrolyte abnormality among patients with T2DM we used the single-proportion formula  $n = Z^2 p(1 - p)/d^2$ . Using the prevalence of electrolyte imbalance among diabetic patients reported by Eshetu et al. (83.07%), a confidence level of 95% (Z = 1.96) and an absolute precision (d) of 0.05, the required sample size was 217, which we rounded to 220. Alternatively, at d = 0.07 the required sample size is 111. We enrolled 200 T2DM patients; this sample size provides precision between ±5% and ±7% for an expected prevalence of ≈83%. [11]

**Inclusion criteria:** a. Patients with type 2 diabetes mellitus attending OPD or admitted to the general medicine ward. b. Criteria for the diagnosis of DM were according to American Diabetes Association criteria (symptoms of diabetes plus random blood glucose concentration  $\geq 200$  mg/dl or fasting blood glucose  $\geq 126$  mg/dl or HbA1c  $\geq 6.5\%$  or 2-hour plasma glucose  $\geq 200$  mg/dl during an oral glucose tolerance test). [2]

**Exclusion Criteria:** a. Patients with diabetic ketoacidosis, hyperglycemic hyperosmolar state. b. Patients with acute kidney injury and end-stage renal disease. c. Patients on diuretics.

## Data collection method and analysis:

Patients were enrolled for the study from outdoor and indoor wards of the Department of General Medicine with informed consent. A blood sample of five ml was collected with consent from patients. We estimated the fasting blood glucose (FBS) and postprandial blood sugar (PPBS) levels using the glucose oxidase-peroxidase (GOD/POD) enzymatic method. [12] The latex-enhanced immunoassay is a turbidimetric method used to quantitatively measure glycated hemoglobin (HbA1c) in blood as per standard manufacturer's protocols of Tina-quant HbA1c by Roche Diagnostics. [13] Serum sodium and potassium levels were measured using ion-selective electrode (ISE) technology with the Enlite Automatic Electrolyte Analyzer (Accurex Instruments, India). Serum magnesium was estimated by a colorimetric method employing calmagite dye as the reagent. This study was approved by the institutional ethics committee (VIREC-19240/Dt30.11.19/IST-256/19).

## Statistical Analysis:

All measured variables for the study groups were presented as mean and standard deviation. Data were recorded, and analysis was done using GraphPad Prism version 5. Pearson's linear correlation (r) was used to correlate serum electrolytes (Na<sup>+</sup>, Mg<sup>2+</sup>, K<sup>+</sup>, and Ca<sup>2+</sup>) with FBS, PPBS, and HbA1C. The p-value  $< 0.05$  was considered statistically significant.

## RESULT

A total of 200 patients were enrolled, out of which 115 (57.5%) were male and 85 (42.5%) were female. The mean age of patients was  $56.38 \pm 11.89$ . The maximum number of patients are in the age group of 40-60 years (58%). There were 11 patients under 40 years of age, 116 cases between 41 and 60 years, and 73 cases above 60 years.

Correlation analysis revealed that age showed no significant association with serum sodium (Na), potassium (K), and magnesium (Mg) levels ( $P < 0.05$ ). However, there was a significant negative relationship found between age and serum calcium (Ca) levels, meaning that as age increases, calcium levels tend to go down. (Table 1)

The study demonstrated significant negative correlations between fasting blood sugar (FBS) and HbA1c with all measured electrolytes, including sodium ( $Na^+$ ), magnesium ( $Mg^{2+}$ ), potassium ( $K^+$ ), and calcium ( $Ca^{2+}$ ). As fasting blood sugar ( $160.75 \pm 53.73$  mg/dL) and HbA1c ( $8.84 \pm 2.21\%$ ) went up, the levels of sodium ( $135.03 \pm 7.05$ ), magnesium ( $1.75 \pm 0.41$ ), potassium ( $3.92 \pm 0.77$ ), and calcium ( $0.99 \pm 0.16$ ) went down a lot ( $p < 0.001$  for all). The strongest negative relationship was found between sodium and HbA1c ( $r = -0.5920$ ), showing that having high blood sugar levels is closely linked to problems with electrolytes, especially low sodium, magnesium, and potassium levels. (Table 2) (Figures 1, 2, and 3. All three figures clearly show that high blood glucose (FBS) and HbA1c levels are strongly linked to lower levels of  $Na^+$ ,  $K^+$ , and  $Ca^{2+}$ , indicating that electrolyte imbalance is a common problem in diabetes.)

The mean PPBS (postprandial blood sugar) level of T2DM patients was  $232.18 \pm 88.76$  mg/dL. Pearson correlation analysis revealed that significant negative associations occur between PPBS and all electrolytes measured, like sodium ( $Na^+$ ): ( $r = -0.4666$ ,  $R^2 = 0.2177$ ,  $p < 0.001$ ); potassium ( $K^+$ ): ( $r = -0.2904$ ,  $R^2 = 0.08432$ ,  $p < 0.001$ ); Calcium ( $Ca^{2+}$ ): ( $r = -0.1957$ ,  $R^2 = 0.03831$ ,  $p = 0.005$ ); and Magnesium ( $Mg^{2+}$ ): ( $r = -0.3470$ ,  $R^2 = 0.1204$ ,  $p < 0.001$ ). (Table 3)

**Table 1: Distribution of serum electrolytes according to age**

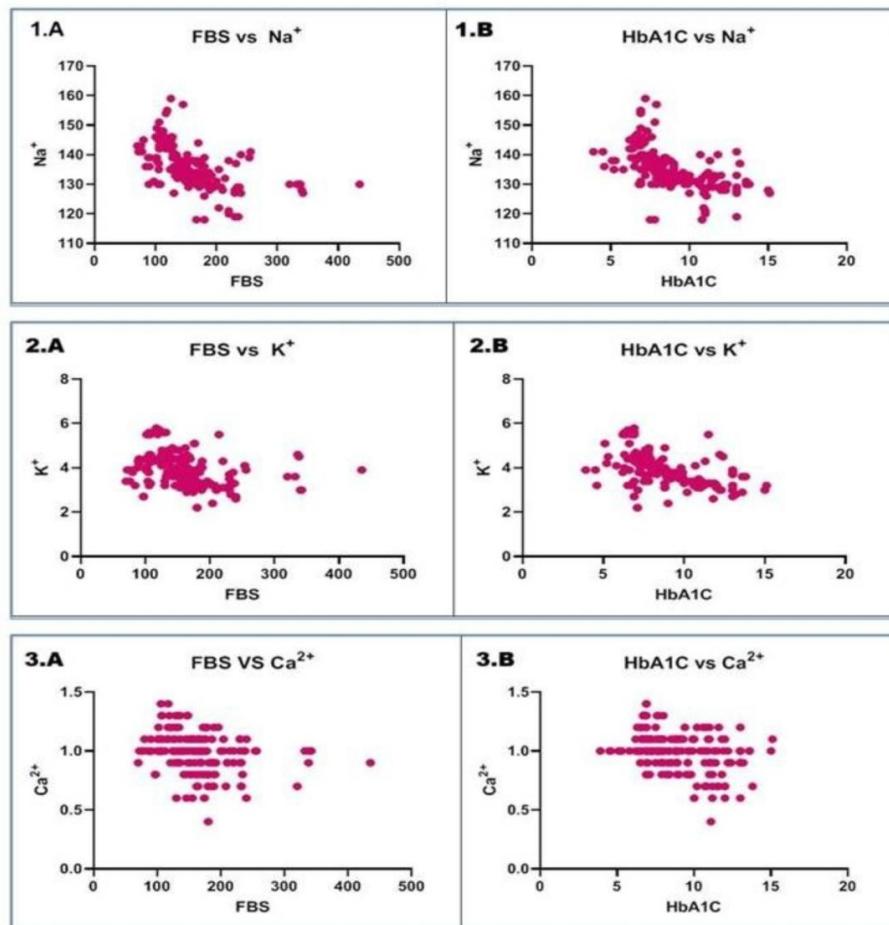
Age	Electrolytes	r	R-squared	p-value
	Na	0.02944	0.0008670	0.679
	K	-0.03242	0.001051	0.649
	Ca	-0.2035	0.04141	0.004
	Mg	-0.04842	0.002345	0.496

**Table 2: Correlation between electrolytes with FBS and HbA1C with a study population (N=200)**

FBS	Electrolyte	Mean $\pm$ SD	Pearson correlation of electrolyte with FBS	p-Value	HbA1C	Pearson correlation of electrolyte with HbA1C	p-Value
$160.75 \pm 53.73$	$Na^+$	$135.03 \pm 7.05$	-0.5192	<0.001	$8.84 \pm 2.21$	-0.5920	<0.001
	$Mg^{2+}$	$1.7455 \pm 0.409$	-0.3652	<0.001		-0.5107	<0.001
	$K^+$	$3.9195 \pm 0.772$	-0.3481	<0.001		-0.5472	<0.001
	$Ca^{2+}$	$0.986 \pm 0.157$	-0.2547	<0.001		-0.3454	<0.001

**Table 3: The distribution of serum electrolytes is categorized based on PPBS levels**

PPBS (Mean $\pm$ SD)	Electrolytes	r	R-squared	p-value
$232.175 \pm 88.763$	$Na^+$	-0.4666	0.2177	<0.001
	$K^+$	-0.2904	0.08432	<0.001
	$Ca^{2+}$	-0.1957	0.03831	0.005
	$Mg^{2+}$	-0.3470	0.1204	<0.001



**Figure 1: Scatter plot showing the relationship between serum sodium with FBS and HbA1C.** A significant inverse correlation between sodium levels and FBS & HbA1c, both glycemic markers ( $p < 0.001$ ). **1.A:** FBS vs.  $\text{Na}^+$ , **1.B:** HbA1c vs.  $\text{Na}^+$ .

**Figure 2: Scatter plot showing the relationship between serum potassium with FBS and HbA1C.** There is a significant negative correlation between the potassium level and both FBS and HbA1c. **2.A:** FBS vs.  $\text{K}^+$ , **2.B:** HbA1c vs.  $\text{K}^+$ .

**Figure 3: Scatter plot showing the relationship between serum calcium with FBS and HbA1C.** There is a significant negative correlation between calcium levels and both FBS and HbA1c. **3.A:** FBS vs  $\text{Ca}^{2+}$ , **3.B:** HbA1c vs  $\text{Ca}^{2+}$

## DISCUSSION

This cross-sectional research included 200 individuals with type 2 diabetes mellitus, including 115 males and 85 females, with a mean age of  $56.38 \pm 11.89$  years. In our study, electrolyte imbalances were quite widespread, affecting 84% of patients. The most common ones were hyponatremia (53%), followed by hypomagnesemia (38.5%), hypokalemia (33.5%), and hypocalcemia (31.5%). Hypernatremia and hyperkalemia were less common. Mixed electrolyte imbalances were widespread, with many patients having low levels of sodium and potassium or magnesium. Fourteen percent of patients had low levels of all four electrolytes.

Our results from multiple linear regression analysis indicated that as glycemic indices (FBS, PPBS, HbA1c) increase, the serum levels of sodium, potassium, calcium, and magnesium decrease significantly. Age did not show a strong connection, except for a slight link with calcium. Age showed no notable association, except a mild correlation with calcium. PPBS explained a small proportion of electrolyte variability, with  $R^2$  values ranging from 8.4% to 30%. Mean electrolyte levels were within low-normal ranges, indicating a tendency toward deficiency in poorly controlled diabetes.

Our results corroborate with Jha et al. (2017) study, which identified reduced blood potassium and sodium levels and elevated calcium and chloride levels in diabetics. [14] Deepti et al. (2017) identified hypomagnesemia as a prevalent complication of diabetes in their investigation. They also found that serum magnesium levels were significantly inversely related to fasting blood sugar (FBS) and hemoglobin A1c values. [15] Karuppan et al. (2018) indicated that a considerable percentage of individuals with diabetes in a Southern Indian population had hyponatremia (33%) and hypokalemia (16%). [16]

Mustahsan et al. (2018) found that young girls with T2DM had significantly lower potassium levels. [17] A study by

Pradhan et al. (2018) found a strong negative relationship between magnesium levels in the blood and different glucose levels in diabetes patients in Odisha. [18] Khan et al. (2019) found that blood sodium levels were inversely related to fasting glucose levels, while potassium levels were directly related. [19] These results were supported by Rajagambeeram et al. (2020), who found a strong negative relationship between serum electrolytes and both FBS and HbA1c. [20]

In our study, lower sodium concentrations in persons with diabetes, which oppose the study of Siddiqui et al. (2019) found that elevated blood potassium and chloride levels. [21] Antony (2019) shows that hyponatremia (75%) is the predominant electrolyte imbalance, with 10% of patients exhibiting concomitant hypokalemia, hyponatremia, and hypomagnesemia. [22]

## CONCLUSION

The present observational research highlighted the necessity of assessing serum electrolytes in T2DM. When fasting, postprandial, and HbA1C levels rise, salt, magnesium, calcium, and potassium levels drop. Low serum electrolyte levels diminish insulin sensitivity and exacerbate hyperglycemia and subsequent microvascular and macrovascular problems. Thus, diabetic patients should have their serum electrolyte levels and glycemic status monitored. Blood electrolyte levels in diabetic patients should therefore be monitored frequently, and any abnormalities should be corrected.

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**Declaration of conflicting interest:** There is no conflict of interest among the authors.

**Data availability statement:** The data of this investigation are available upon request.

**Ethical approval and informed consent statements:** This study was approved by the institutional ethics committee (VIREC-19240/Dt30.11.19/IST-256/19) and informed consent of each patient was taken before the blood sample was taken.

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