



## Original Research Article

## Evaluation of serum electrolytes and their relation to glycemic status in patients with T2DM

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## ABSTRACT

**Introduction:** Diabetes mellitus is a chronic disease that requires long-term medication to limit the development of its ruinous complications. The complications of diabetes are metabolic imbalance, blood vessel degeneration; effect on electrolyte concentration can offset the proportion of electrolytes. Since there is a direct association of serum electrolytes with diabetes mellitus (DM), the study was planned to investigate the electrolytes disturbance and their association with glycemic status in T2DM patients.

**Materials and Methods:** This was cross-sectional hospital-based study; 60 participants who were diagnosed to have T2DM between the age group 30 to 60 years were recruited. Fasting glucose, glycated hemoglobin and serum electrolytes such as sodium, potassium, calcium and magnesium were estimated.

**Results :** Descriptive statistics was expressed as mean & SD. Pearson's correlation analysis was performed to find the association and degree of relationship between serum electrolytes and glycemic status in T2DM. All the biochemical parameters were altered in T2DM patients. There was no significant association between FBS, HbA1c and serum electrolytes.

**Conclusion:** The present study showed an alteration in electrolytes status, but there was no statistically significant association between fasting blood glucose, glycemic control and serum electrolytes consideration of the multifactorial origin of electrolyte imbalance, a cause-specific treatment is required to avoid any risk.

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## 1. Introduction

Diabetes mellitus is a chronic disease that requires long-term medication to limit the development of its ruinous complications. The complications of diabetes are metabolic imbalance, blood vessel degeneration; effect on electrolyte concentration can offset the proportion of electrolytes.<sup>1</sup>

Serum electrolytes play an important role in maintaining acid-base balance, blood clotting, controls the electrical gradient of the body fluids and muscle contractions. There is also increasing evidence that electrolyte imbalances are early biochemical events responsible for long-term diabetic complications.<sup>2</sup> Imbalance in electrolyte distribution may

lead to various clinical disorders; especially it affects the course of diabetes and its management.<sup>3</sup>

Sodium and potassium The Na<sup>+</sup>, K<sup>+</sup>-ATPase (NKA) is an ubiquitous enzyme ensures the maintenance of Na<sup>+</sup> and K<sup>+</sup> gradients across the cell membrane by transporting 3 Na<sup>+</sup> out and 2 K<sup>+</sup> into the cell.<sup>4</sup> Alterations of this transport system are linked to several complications of diabetes mellitus. It has been reported that there is an inverse relationship between serum sodium (Na<sup>+</sup>) and potassium (K<sup>+</sup>) levels in diabetic patients. Moreover, hypokalemia has been clearly shown to be associated with increased risk of hyperglycemia.<sup>5,6</sup>

Calcium plays an important role in biological functions, in recent decades; insulin resistance and its secretion have

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been reported to be dependent on calcium homeostasis.<sup>7</sup> Any alterations in calcium flux can have adverse effects on  $\beta$ -cell secretory function and may interfere with normal insulin release, especially in response to a glucose load. The elevated levels of cytosolic calcium is associated with an increased risk for type 2 diabetes.<sup>8</sup>

Magnesium is involved in insulin secretion, insulin resistance and act as a cofactor of many enzymes in carbohydrate metabolism.<sup>9</sup> Hypomagnesemia is the commonest electrolyte abnormality in the ambulatory and patients with poorly controlled glycemic status.  $Mg^{2+}$  deficiency reduces the affinity of glucose binding to glucokinase and indirectly leads to the impairment of insulin secretion, insulin resistance and increased macrovascular risk.<sup>6,10</sup>

Diabetic patients are more susceptible for development of hypophosphatemia. It is known that increased insulin levels promote the transport of both glucose and phosphate into the skeletal muscle and liver cells.<sup>3</sup>

With this direct association of serum electrolytes with diabetes mellitus (DM), the study was planned to investigate the electrolytes disturbance and their association with glycemic status in T2DM patients.

## 2. Materials and Methods

This was a cross sectional study which was undertaken in adults with T2DM attending the Dept. of General Medicine OPD in a tertiary care hospital setup following approval by the Institute Human Ethics Committee.

### 2.1. Inclusion criteria

Sixty known cases of T2DM between ages 30 to 60yrs who visited the diabetic clinic at MGMCRI were included in this study

### 2.2. Exclusion criteria

Type 1 diabetes mellitus, gestational diabetes mellitus, diabetic neuropathy, diabetic retinopathy, smokers, chronic alcoholics, hypertension, cardiovascular and kidney diseases were excluded from this study since all the above-mentioned conditions will alter the levels of serum electrolytes.

After obtaining an informed consent from the study subjects, a thorough history was taken and 5ml of venous blood in the fasting state (10hrs) was collected under aseptic condition of this 2 ml of blood was collected in ethylenediaminetetraacetic acid vacutainer (EDTA) vials for HbA1c and 2ml collected in a red stoppered plain tube for electrolytes, 1 ml in fluoride tube, for blood glucose. Blood samples were centrifuged at 3000 rpm. Bio-chemical parameters were estimated based on established methods approved by the IFCC. All assays were carried out on fully automated chemistry analyser.

Plasma glucose- Fasting blood glucose (venous) was estimated based on glucose oxidase-peroxidase method, HbA<sub>1c</sub> levels were estimated by using ion-exchange high-performance liquid chromatography (HPLC) method, serum Sodium and Potassium was estimated by Electrolyte Kit Method (Ion selective electrode) technology, Serum Calcium by orthocresolphthalin (OCP) method and Serum Magnesium by calmagite method

### 2.3. Statistical methods

Descriptive statistics was expressed as mean & SD. Pearson's correlation analysis was performed to find the association and degree of relationship between serum electrolytes and glycemic status in T2DM

## 3. Observations and Results

**Table 1:** Descriptive statistics of Biochemical parameters

Parameters n=60	Minimum	Maximum	Mean±SD
AGE in yrs.	31	64	49.9±9.49
FBS mg/dl	78	212	147±38.064
HbA1c %	5	14.4	7.9±2.006
Na <sup>+</sup> meq/L	125	141	132±3.842
K <sup>+</sup> meq/L	3.1	5.6	4.3±0.637
Ca <sup>+</sup> mg/dl	7.3	11	9±0.855
Mg <sup>+</sup> mg/dl	0.7	2.5	1.4±0.364

FBS- Fasting blood glucose, HbA1c- glycated hemoglobin, Na<sup>+</sup> - Sodium, K<sup>+</sup> - Potassium, Ca<sup>+</sup> -Calcium and Mg<sup>+</sup> -Magnesium

Table 1 Shows the descriptive statistics of FBS, HbA1c and serum electrolytes, it is observed that the mean values of all the parameters are significantly different the reference range. Table 2 depicts the correlation between FBS, HbA1c and serum electrolytes, although the correlations are not significant for both FBS and HbA1c, sodium and magnesium are negatively correlated with both FBS and HbA1c. Potassium is negatively correlated with HbA1c alone.

## 4. Discussion

The present study demonstrates a low serum sodium levels in T2DM individuals and is negatively correlated with FBS and HbA1c. Similar findings have been established by Parmer et al and Khalid Al et al.<sup>5,11</sup>

Most common electrolyte disturbance in clinical setup is hyponatremia leading to increased morbidity and mortality.<sup>12</sup> Diabetes mellitus is characterized by hyperglycemia, insulin resistance, electrolyte disturbances and acid base disturbances. The electrolyte disturbance is due to hyperglycemia, hypoinsulinemia and acidosis.<sup>13</sup> Hyperglycemia in extracellular compartment draws in water from the intracellular compartment, thus diluting the extracellular compartment (ECF) and there by the

**Table 2:** Correlations between FBS, HbA1c and Electrolytes

Parameters	FBS		HbA1c	
	“p” value	“r” value	“p” value	“r” value
Na <sup>+</sup> meq/L	>0.05	-0.09	>0.05	-0.032
K <sup>+</sup> meq/L	>0.05	0.117	>0.05	-0.01
Ca <sup>+</sup> mg/dl	>0.05	0.067	>0.05	0.136
Mg <sup>+</sup> mg/dl	>0.05	-0.156	>0.05	-0.116

A “p” value less than 0.05 will be considered has significant.

FBS- Fasting blood glucose, HbA1c- glycated hemoglobin, Na<sup>+</sup> - Sodium, K<sup>+</sup> -Pottasium, Ca<sup>+</sup> -Calcium and Mg<sup>+</sup> -Magnesium

electrolytes. This leads to osmotic diuresis, the loss of water pulls in sodium to be excreted, which leads to artificial hyponatremia.<sup>14</sup> It is proposed that the correlation between diabetes mellitus and decreased serum sodium levels are due to the altered vasopressin regulation, the expression of vasopressin-induced aquaporin AQP-2 water channels is stimulated by insulin and the absorption of water from the GI tract is increased due to slower stomach emptying may play a role in hyponatremia.<sup>15</sup>

Potassium levels have been positively correlated with FBS but it is insignificant. The serum levels are not significantly altered. Hyperglycemia leads to hyperosmolality, this in turn to dehydration of cells, thus causing an increase in K<sup>+</sup> extrusion from cells into ECF.<sup>8</sup> This might be the explanation of the inverse relations of serum Na<sup>+</sup> and K<sup>+</sup> with FPG. Na<sup>+</sup>/K<sup>+</sup>-ATPase is the key protein involved in trans membrane gradients of Na<sup>+</sup> and K<sup>+</sup>, which requires insulin for its activity, in T2DM the secreted insulin is inadequate or insulin resistance is present this could result in a diminished Na<sup>+</sup>/K<sup>+</sup>-ATPase activity.<sup>16</sup>

Release of insulin is dependent upon calcium; hence a flux in calcium levels will affect the beta cell function of the pancreas, however there is no significant correlation between calcium levels and FBG and glycemic control in the present study. Increase in intracellular calcium leads to defective expression of Glut4 receptors in adipose tissue leading to hyperglycemia.<sup>7</sup>

Studies have documented that Hypomagnesemia is associated with poor glycemic control; this may be due to loss of magnesium in urine.<sup>17</sup> Although it's been negatively correlated with glycemic control and FBS the strength of association is not strong in the present study. Hypomagnesemia is one of the frequent electrolyte disturbances observed in diabetic patients, the causes include nutritional deficiency, use of diuretics, metabolic acidosis, glomerular hyperfiltration and altered insulin metabolism.<sup>18</sup>

## 5. Conclusion

The present study showed an alteration in electrolytes status, but there was no statistically significant association between fasting blood glucose, glycemic control and serum electrolytes, considering the multifactorial origin of electrolyte imbalance, a cause-specific treatment is required

to avoid any risk.

## 5.1. Limitations

Simultaneous study of serum and urine osmolality of the subjects could have been better. Ionized calcium could be used whenever possible since it is considered as goal of calcium homeostasis. Small sample size is not sufficient to detect minor to modest associations. Thus a study with larger sample size is necessary.

## 5.2. Implications

Although there is no significant/strong association between serum electrolytes and glycemic status. Electrolyte levels are altered; hence judicious assessment and correction would improve the glycemic status.

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## 7. Conflict of interest

None.

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