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Original Research Article

Correlation of Serum Fasting Blood Glucose, Hba1c & Serum Electrolytes in Type 2 Diabetes Mellitus

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Abstract

Objective: The study aims to identify the relationship of serum electrolytes Na+, K+ Mg+ and Ca+ with FBG and HbA1c levels in T2DM patients treated with insulin, oral hypoglycemic agents.

Methodology: The study was done on 239 type 2 Diabetes mellitus patients selected randomly aged between 18 and 65 years for both Group- I (FBG >100 mg%; HbA1c % >6.5) and Group-II (FBG <100 mg%; HbA1c % <6.5). HbA1c, fasting blood glucose (FBG), Sodium (Na+), potassium(K+), magnesium (Mg+) and calcium (Ca+) were assessed in all samples and compared between two groups.

Results: In the present study, 149(62.3%) were male and 90 (37.7%) were female cases. The use of oral hypoglycemic agents was found in 145 subjects (60.6%) and insulin therapy was in 62 (25.9%) and 32 (13.5%) were newly diagnosed cases. In Group-I Na+ and Mg+ negatively correlated with FBG and HbA1c. K+ & calcium showed insignificant relation with FBG & HbA1c for both groups respectively, but it was significant when taken as a total of both the groups with a P value of 0.001. The K+ showed negative correlation with HbA1c alone when taken as a total of both groups.

Conclusion: The present study showed significant reduction in serum Na+ and Mg+ level among T2DM patients especially when FBS >100 mg% and HbA1c % >6.5. Serum K+ also demonstrated significant association with HbA1c. Therefore, the FBG, HbA1c and serum electrolytes, considering the multifactorial origin of electrolyte imbalance, a cause-specific treatment is required to avoid any risk.

Keywords: Type 2 diabetes mellitus, electrolyte imbalance, HbA1c, hyponatremia

Introduction

Diabetes mellitus (DM) is now one of the most common non-communicable and endocrinal diseases worldwide [1]. Type 2 diabetes mellitus (T_2DM) refers to a group of metabolic disorders. The Complex interactions of genetics and environmental factors play role in the etiopathology of this entity. Deregulations resulting from these interactions cause secondary pathophysiologic changes in multiple organ systems [2]. Hyperglycemia sets the inner environment for osmotic diuresis while causing a dilutional effect on electrolyte concentrations [3]. The osmotic effect of glucose results in fluid shift from the intracellular spaces and decreased circulating blood volume causing cellular dehydration. Insulin has been shown to decrease extracellular potassium concentration as well likely through activation of Na-K-ATPase [4]. The synergistic action of cationic imbalance and osmotic effect of glucose could very well impact the course of DM [5]. However, resistance to insulin action or deficiency of insulin may contribute to the development of electrolyte abnormalities. Considering all these factors, the altered distribution of sodium (Na^+) and potassium (K^+) between the intracellular and extracellular compartments may affect the course of DM as well as its management [6]. Studies on electrolyte imbalances in association with diabetes have reported an inverse relationship between serum electrolytes level in diabetic coma [7]. This association may be based on the movement of electrolytes between extra and intracellular space dependent on impaired insulin action [8]. A significant direct association was reported between hyperkalemia and hyperglycemia in diabetic patients. It was observed that elderly uncontrolled diabetics are at higher risk of hyperkalemia. Until now, no studies have been performed to correlate serum electrolyte concentrations with fasting blood glucose (FBG) and Hemoglobin A1C (HbA1c) levels. This study aims to identify the relationship of serum electrolytes Na^+, K^+ Mg+ and Ca+ with FBG and HbA1c levels in T_2DM patients treated with insulin, oral hypoglycemic agents.

Materials & Methods

This cross-sectional descriptive randomized clinical study has selected 239 T_2DM patients from outpatient department of Biochemistry at Mahatma Gandhi Memorial Medical College (MGM), Indore (M.P.) during the period of May 2021 to April 2022.

Inclusion criteria: Patients were selected randomly from both gender aged between 18 and 65 (mean 49.24±23.2) years for both Group- I (FBG >100 mg%; HbA1c % >6.5) and Group-II (FBG <100 mg%; HbA1c % <6.5).

The patients were classified according to FBS and HbA1c% levels. There were 117 Group-I and 122 Group-II patients with T_2DM with mean disease duration of 10.1± 2.1 years. HbA1c, fasting blood glucose (FBG), Sodium (Na^+), potassium(K^+), magnesium (Mg+) and calcium (Ca+) were assessed in all samples.

Exclusion criteria: post-operative patients, diabetic neuropathy and retinopathy, smokers, chronic alcoholics, cardio vascular disease, hypertension, pregnant women were excluded. Since all above conditions alter the levels of serum electrolytes.

After obtaining an informed consent from study subjects a thorough study was carried out. 5ml of Venus blood in fasting state was collected; 2 ml blood was transferred in EDTA vials for HbA_1c and 3 ml transferred in a plain tube for electrolytes. Biochemical parameters were estimated based on standard methods approved by IFCC. Plasma glucose was estimated by glucose oxidase peroxidase method. HbA1c levels were estimated by using ion-exchange

HPLC method. Serum Na^+ and K^+ were estimated by electrolyte kit method (Ion selective electrode). Serum calcium was estimated by Arsenazo method and Mg^+ by Xylidyl blue method.

Statistical Analysis

Descriptive statistics were applied for demographic data (i.e., frequency, percentage, mean, and standard deviation). Testing hypothesis was performed using regression analysis. P values less than 0.005 were considered as of statistical significance. Correlation coefficient was used to measure the degree to which two variables are linearly related and coefficient of determination (R^2) was used to measure the relative variation that describes the variation in one value occurring in proportion to variations of another value.

Results

In this study, a total of 239 subjects were recruited with a mean age of 49.24±23.2 years and diabetes duration mean of 10.1± 2.1 years of both groups. Gender distribution revealed 149(62.3%) were male and 90 (37.7%) were female cases. All cases were divided into Group- I (FBG >100 mg%; HbA1c % >6.5) and Group-II (FBG <100 mg%; HbA1c % <6.5). In both groups male percentage was higher in T_2DM patients. The use of oral hypoglycemic agent was found in 145 subjects (60.6%) and insulin therapy was in 62 (25.9%) and 32 (13.5%) were newly diagnosed cases as shown in Table 1.

The mean values of HbA1c (%) and FBG (mg/dl) were 8.9 ± 2.1 and 175 ± 38 in Group-I and 5.6±3.2 and 81±18.0 in group II cases respectively. The mean value of Na^+ was 125±1.4 meq/L in group I and 133±1.21 meq/L in group II. K^+ mean value in group I was 4.6±3.3 meq/L and in group II it was 5.5±3.2 meq/L. The mean value of Ca^+ was 8±0.5 mg/dl in group I and11±0.4 mg/dl in group II. The mean Mg^+ level in group I was 0.9±0.3 mg/dl while in group II it was1.8±0.3 mg/dl. It is observed that the mean values of all the parameters are significantly different in both the groups as shown in table 2.

Table 3 depicts the correlation between FBS, HbA1c and serum electrolytes, although the P values were calculated for each parameter in both groups. The P value was also strongly significant in the Group-I ($P<0.001$) when looking at Na^+ and Mg^+, negatively correlated with FBG and HbA1c. When looking at K^+ it was insignificant for both groups with P value of 0.174, 0.353 (in group I& II respectively) whereas for Calcium it was 0.112 and 0.531, respectively. Association of Na^+ with FBG and HbA1c was insignificant in Group-II individually with P values of 0.114, 0.132, and Mg^+ with FBG and HbA1c was also insignificant in Group-II with P values 0.111 and 0.233, respectively, but it was significant when taken as a total of both the groups with a P value of 0.001. The Ca^+ association with FBG and HbA1c values was insignificant in both groups with a P value 0.112, 0.731, 0.531, and 0.763 respectively, and the total of both the groups also did not show any significant relation. The K^+ is negatively correlated with HbA1c alone when taken as a total with a P value of 0.004. Thus statistically the correlation between FBS, HbA1c and serum electrolytes, although are not significant for both FBS and HbA1c, Na^+ and Mg^+ are negatively correlated with both FBS and HbA1c. K^+ is negatively correlated with HbA1c alone.

Table 1: Comparative average value related with diabetic patients with respect to gender and type of diabetes and treatment given

	Group-I (n=117)	Group-II (n=122)	Total (n=239)
Age (years)	54.23±12.2	49.24±21.2	49.24±23.2
Gender (Male: Female)	78 (66.6%): 39 (33.4%)	71(58.2%): 51(41.8%)	149(62.3%): 90(37.7%)
Duration (years)	12.1± 1.1	10.2± 2.1	10.1± 2.1
Oral medicine	74(63.2%)	71(58.2%)	145 (60.6%)
Insulin	38 (32.5%)	24(19.6%)	62 (25.9%)
Newly diagnosed	5(4.3%)	27 (22.2%)	32 (13.5%)

Table 2: Descriptive statistics of Biochemical parameters

	Group-I (n=117)	Group-II (n=122)	Total (n=239)
HbA1c (%)	8.9±2.1	5.6±3.2	9.5±1.5
FBS (mg/dl)	175±38.0	81±18.0	141.8±2.9
Na+ (meq/L)	125±1.4	133±1.2	130.1±1.8
K+ (meq/L)	4.6±3.3	5.5±3.2	4.8±0.3
Ca+ (mg/dl)	8±0.5	11±0.4	9±0.5
Mg+ (mg/dl)	0.9±0.3	1.8±0.3	1.4±0.3
Fasting blood glucose: FBG, Hemoglobin A1C: HbA1c, Sodium: Na+, Potassium K+, Calcium: Ca+ and Magnesium: Mg+			

Table 3: Statistical correlation and significance levels on FBS, HbA1c and Electrolytes for different group

	Group-I (n=117)						Group-II (n=122)						Total (n=239)					
	FBG			HbA1c			FBG			HbA1c			FBG			HbA1c		
	" p" value	" R^2" value	" r" Value	" p" value	" R^2" value	" r" value	" p" value	" R^2" value	" r" value	" p" value	" R^2" value	" r" value	" p" value	" R^2" value	" r" value	" p" value	" R^2" value	" r" value
Na+	0.001*	0.32	-0.09	0.001*	0.27	-0.032	0.114	0.11	-0.112	0.132	0.08	-0.142	0.001*	0.38	-0.034	0.001*	0.25	-0.022
K+	0.174	0.07	-0.249	0.111	0.10	-0153	0.353	0.07	0.337	0.643	0.00	0.752	0.008	0.12	-0.245	0.004*	0.05	-0.036
Ca+	0.112	0.10	0.873	0.731	0.04	0.436	0.531	0.00	0.625	0.763	0.18	0.973	0.242	0.08	0.346	0.436	0.35	0.224
Mg+	0.001*	0.22	-0.118	0.001*	0.00	-0.132	0.111	0.11	-0.162	0.233	0.00	-0.121	0.001*	0.35	-0.017	0.001*	0.29	-0.091
"p" value less than <0.005 will be considered as significant, "r" Correlation coefficient "R^2" coefficient of regression, Fasting blood glucose: FBG, Hemoglobin A1C: HbA1c, Sodium: Na+, Pottasium K+, Calcium: Ca+ and Magnesium: Mg+																		

Discussion

To our knowledge, few studies have been performed to investigate the relation between serum electrolytes level with FBS and HbA1c in different diabetic groups. The present study demonstrates a low serum Na^+ levels in T_2DM individuals and is negatively correlated with FBS >100 mg%; HbA1c % >6.5. It has been already known that electrolyte imbalances are the consequences of hyperglycemia, hyperosmolality, and acidosis [9]. Most common electrolyte disturbance in clinical setup is hyponatremia leading to increased morbidity and mortality [10]. The DM is characterized by hyperglycemia, insulin resistance, electrolyte disturbances and acid base disturbances. The electrolyte disturbance is due to hyperglycemia, hypoinsulinemia and acidosis.[11] Hyperglycemia in extracellular compartment draws in water from the intracellular compartment, thus diluting the extracellular compartment and there by the electrolytes. This leads to osmotic diuresis, loss of water pulls in Na^+ to be excreted, which leads to artificial hyponatremia.[12] It is proposed that the correlation between DM and decreased serum Na^+ levels are due to the altered vasopressin regulation, the absorption of water from the gastrointestinal tract is increased due to slower stomach emptying that may play a role in hyponatremia and the expression of vasopressin-induced aquaporin-2 water channels is stimulated by insulin.[13]

The K^+ levels have been positively correlated with FBS but it is insignificant. The serum levels are not significantly altered. Hyperglycemia leads to hyperosmolarity, this in turn lead to dehydration of cells, thus causing an increase in K^+ extrusion from cells into extracellular fluid. [14] This might be the explanation of the inverse relations of serum Na^+ and K^+ with FPG. Na^+/K^+ ATPase plays key role and is involved in trans membrane gradients of Na^+ and K^+, 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^+/K^+ ATPase activity.[15] 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 found between FBG and calcium levels and glycaemic control in the present study. Increase in intracellular Ca^+ leads to defective expression of glucose transporter type 4 receptors in adipose tissue leading to hyperglycemia.[16]

This study demonstrated that there is significant reduction in serum Na^+ level of diabetic subjects with the T2DM regardless of their management type which is similar to findings seen by Saito *et al*. [15]. Similar findings have been established by Parmer *et al* and *Khalid Al et al*. [17,18]. Our study has shown the correlation between HbA1c level and serum Na^+ and Mg^+ expressed by correlation coefficient value and coefficient of determination. These studies have documented that hypomagnesemia is associated with poor glycemic control; this may be due to loss of Mg^+ in urine. [19] 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 [20]. This observation did not show any significance on grouping the cases according to modality of pharmaceutical management or type of diabetes.

Conclusion

The present study showed significant reduction in serum Na^+ and Mg^+ level among T2DM patients especially when FBS >100 mg/dl and HbA1c % >6.5.

Serum K^+ also demonstrated significant association with HbA1c. Serum Ca^+ demonstrated no significant association with FBS and HbA1c. Therefore, the FBG, HbA1c and serum electrolytes, considering the multifactorial origin of electrolyte imbalance, a cause-specific treatment are required to avoid any risk.

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