Study of relationship between Serum electrolytes status and Glycated Hb in Diabetes Mellitus Type-II Patients

Soumili Banerjee[1], Sudeshna Behera[1*] Meghanad Meher[2], Itishri Jena[1], Sangeeta Sanghamitra Bhanja[1], Bandana Thakur[1], Subhashree Ray[1]

[1]Department of Biochemistry, IMS and SUM Hospital Siksha 'O' Anusandhan University, Bhubaneswar, Odisha, India.*
[2] Department of General Medicine, IMS and SUM Hospital Siksha 'O' Anusandhan University, Bhubaneswar, Odisha, India.

*** Corresponding Author:** Dr. Sudeshna Behera
*Professor, Department of Biochemistry IMS and SUM Hospital Siksha 'O' Anusandhan University Bhubaneswar Odisha India. E mail Id: sudeshnabehera@soa.ac.in

Abstract
Introduction: Diabetes Mellitus (DM) is an endocrine metabolic condition marked by insulin resistance or inadequate insulin production resulting in disruptions in the metabolism of fats carbohydrates and proteins. India holds the second position worldwide in diabetes mellitus prevalence with millions of individuals. The chronic consequences of diabetes mellitus encompass major health issues. Diabetes Mellitus Type II is significantly linked to electrolyte abnormalities are essential for regulating acid-base equilibrium muscle contractions fluid homeostasis and haemostasis. Concurring with above scenario the present study attempts to assess the concentrations of serum electrolytes (Na^+ K^+ Cl^- and Ca^{2+}) and HbA1c in individuals with managed and uncontrolled Type II diabetes mellitus.
Material Methods: The study was comprised of 150 individuals 75 of were managed and 75 uncontrolled diabetic patients.
Result and Conclusion: The results of our findings highlight the importance of serum electrolyte and its association with FBS PPBS & HbA1c levels in DM type 2 patients that can control and avert problems. This highlighted insight improves our comprehension of the biology of diabetes mellitus and facilitates the creation of targeted therapies to prevent the detrimental consequences of electrolyte imbalance in our future endeavours.

Keywords: Diabetes Mellitus, Electrolyte Imbalance, HbA1c, Glycemic Status, Pathophysiology

1. Introduction

Diabetes Mellitus (DM) is a chronic endocrine metabolic disorder caused either by insulin resistance or lack of insulin secretion in the body leading to disturbances in metabolism of fat carbohydrates and protein. Considering the global epidemics of diabetes mellitus India ranks 2nd only after China where 77 million people suffer from diabetes mellitus. In India prevalence of diabetes has surged from 7.1% in the year 2009 to 8.9%in 2019 [1]. Various long-term usually grave complications related to this disorder include foot ulcers stroke cardiovascular disease chronic renal diseases and retinopathy. DM type-II also shows a strong association with electrolyte imbalance. Electrolytes play a considerable role in maintenance of acid-base balance muscle contractions managing body fluid and blood coagulation [2]. Along with this serum electrolyte status plays crucial role in maintenance the overall homeostasis of whole body along with protection of cellular function and helps in tissue perfusion. Diabetic patients very commonly develop a plethora of e disorders related to electrolyte imbalance. There are also rising evidences that imbalances in electrolytes are among the earlier biochemical events those contribute to long-term complications associated with DM type-II [2]. Imbalances in electrolytes also determine course the disorder and has profound effect in its management [3].

There is a complex relationship between electrolytes and blood sugar which also influences the course and management of DM type-II. Both Fasting Blood Sugar (FBS) and Post Prandial Blood Sugar (PPBS) both are age-old and commonly used methods to determine glycemic status but glycated hemoglobin (HbA1C) is the gold standard to know glycemic status of patient also indicates the mean plasma glucose in last three months which is crucial to provide optimal care to DM type-II [4]. Value of HbA1c that is under 6% is considered normal while risk of complications due to DM proportionately increase with elevated values as shown by various previous researchers. Complications like diabetic retinopathy neuropathy and nephropathy are the micro angiopathies normally associated with long term DM. Thus the inter relationship of HbA1c and DM would serve as preventive care due to irreversible complications [5].

Decreased Insulin levels have been shown to cause down regulation of Na^+-K^+ ATPase enzyme causing poor metabolism of K^+ and Na^+ and loss of body electrolytes and fluids through osmotic dieresis induced by glucose [6]. Diabetes influences serum as well as bone calcium levels. Previous studies have indicated that

diabetes mellitus is linked with raised risk of osteoporosis as with decreased serum calcium due to osmotic dieresis and hypercalcuria there is bone resorption indirectly influenced by hyperparathyroidism. A dilutional effect on electrolyte concentrations is also seen due to osmotic dieresis. Glucose itself can cause cellular dehydration be decreasing blood volume leading to increased risk of electrolyte disorder [7].
There have been previous studies showing significant hyponatremia hypokalaemia and hyperchloremia [5, 8-9]. Which are inconsistent with the research findings done by Rahiman *et al*. [9] and Ugwuja *et al*.[10]. Similarly the study conducted in Sudanshowed hypocalcemia in diabetic patients [11]. The study at Chennai showed significant hyponatremia but hyperkalaemia and hyperchloremia [5].
Considering the above facts this study aimed to evaluate the levels of serum electrolytes (Na^+ K^+ Cl^- and Ca^+) and HbA1c in both controlled and uncontrolled diabetic patients and investigate the co-relation that exists between electrolyte disorders and HbA1c levels and to provide more information on preventive care in Diabetes Mellitus.

2. Materials and Methods

2.1. Study design

This cross-sectional analytic study included 50 Diabetic mellitus type-II diagnosed according to the ADA criteria (case group) and 50 ages matched healthy subjects (control group). After taking informed consent from all the subjects the study was conducted at IMS & SUM Hospital Bhubaneswar over the allotted time under the ICMRSTS Project 2023.

2.2. Sample Size

Patients with DM type-I severe infections and disorders of respiratory tract cardiovascular system gastrointestinal renal system trauma major surgery pregnant women and age less than 18 years were excluded from study group. The total number of 100 patients was taken for this study.

2.3. Data collection and analysis

Venous blood was withdrawn from patient using aseptic precaution for estimation of the analytes. Plasma collected in EDTA and fluoride tubes were utilized for estimation of HbA1c and blood sugars respectively. Serum collected in clot activator tube was utilized for electrolytes estimation. Glycated Hb level (HbA1c) level was measured by the method of HPLC (high-performance liquid chromatography)in Bio-RadD10 analyzer and electrolytes analysis was done through ISE-Direct method in Medical Easy Lyte automatic analyzer. Blood sugars were estimated by hexokinase method in Cobas Integra 6000. All data were kept confidential and no private or sensitive information were collected.

2.4. Statistical analysis

The data was analyzed using SPSS version 22. Descriptive statistics was expressed in mean and SD. Probability (p) value of ≤ 0.05 was taken as significant statistically. Pearson's coefficient was calculated to determine the inter-relationship between serum electrolytes and glycated Hb levels.

3. Result

In this study a total of 100 subjects were included and categorized into 2 groups. One group containing 50 patients having diabetes mellitus type-II cases and other group containing 50 age and gender matched healthy subjects as control. Mean age of cases was calculated to be 56.16 ± 12.62 with duration of diabetes ranging from 2 yrs to 21 yrs. Gender distribution of cases revealed 28 males (56%) and 22 females (44%). (Table 1), shows the mean serum levels of FBS 2hr PPBS and glycated Hb were significantly raised in type 2 DM patients in comparison to controls.

Table 1: Comparison of biochemical parameters between type2 DM cases and control

Parameters	Case (n=50)	Control (n=50)	p-Value
FBS (mg/dl)	173.8 ± 28.35	87.76 ± 12.93	< 0.001**
2 hr PPBS (mg/dl)	253.8 ± 36.06	104.52 ± 18.89	< 0.001**
HbA1c (%)	8.7 ± 2.55	4.56 ± 0.48	< 0.001**

Each value is expressed as mean ± SD for each group. ** signifies statistically highly significant FBS: fasting blood sugar, PPBS: Postprandial blood sugar, HbA1c: glycosylated Hb,
(Table 2), illustrates the distribution of serum electrolytes in cases and control groups. It was observed that serum Na and K levels were significantly lower in cases in comparison to controls with P value of <0.001 and <0.05 respectively whereas no significant change was reported in case of serum Ca level (8.7 ± 0.74 in cases Vs 8.72 ± 0.81 in controls with p value 0.44) . Serum chloride level was illustrated to be significantly high in cases (99.04 ± 5.49) in comparison to controls (97.35 ±3.37) with significant P value of <0.05.

Table 2: Comparison of serum electrolytes between type2 DM cases and control

Parameters	Case (n=50)	Control (n=50)	p-Value
Serum Na+ (mmol/L)	130.02 ± 6.93	134.78 ± 5.8	< 0.001**
Serum K+ (mmol/L)	3.93 ± 0.8	4.16 ± 0.51	< 0.05 *
Serum Ca++ (mg/dl)	8.7 ± 0.74	8.72 ± 0.81	0.44
Serum Cl- (mmol/L)	99.04 ± 5.49	97.35 ± 3.37	< 0.05 *

Each value is expressed as mean ± SD for each group *signifies statistically significant, ** signifies statistically highly significant.

(Table 3), depicts correlation of FBS PPBS HbA1c with serum electrolytes. Though the correlations are not significant but we observed positive correlation between serum K+Ca++Cl- with FBS level whereas negative correlation was seen in case of serum Na+ level with FBS.

Table 3: Correlation of serum electrolytes with FBS PPBS & HbA1c level

Parameters	**FBS**		**PPBS**		**HbA1c**	
	P value	r value	P value	r value	P value	r value
Na+	0.85	- 0.03	0.69	0.05	0.22	-0.17
K+	0.19	0.18	0.009*	0.36	0.12	0.22
Ca++	0.78	0.04	0.30	0.15	0.53	-0.09
Cl-	0.65	0.06	0.22	0.17	0.95	0.008

Correlating serum electrolytes with serum PPBS significant positive correlation was reported in case of serum K+ whereas correlation of PPBS with Other electrolytes like serum Na+ Ca++ and Cl- were weak & lacked statistical significance (Figure 1).

On reporting the correlation of serum electrolytes with HbA1c level positive correlation was observed in case of serum K+ and Cl- whereas negative correlation was found in case of serum Na+ and Ca++ level with HbA1c.

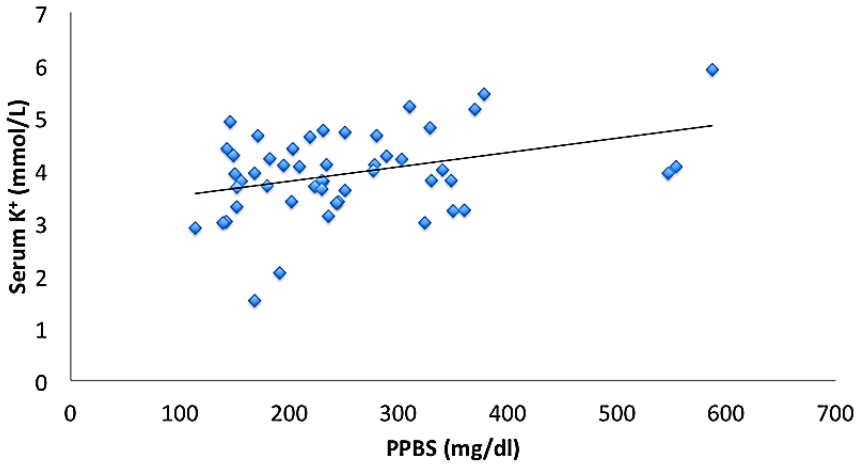

Figure 1: Depicts the outcome results of correlation between serum electrolytes and PPBS with r 0.36 and p value0.009 ** level of significance

4. Discussion

We could find many studies from countries other than India regarding the correlation of serum electrolytes with FBS & glycated Hb in DM patients. But to our knowledge very few data are available in India concerning the relationship of serum electrolyte level with HbA1c level in diabetic patients and it is in conflict with few of the data abroad.

In the present study significant decline in serum sodium was detected in DM type-2 patients in comparison to that of non-diabetic control group. Our findings are in accordance with various other studies demonstrated by Saito et al.[12] Wang et al. [11] and Haglin et al. [13]. The reason for the same could be due to electrolyte loss. Study reports of Liamis et al [3] suggested increase in serum osmolality I hyperglycemic state leads to movement of water out of the cell which in turn results in decrease in serum sodium level by dilution. It is noteworthy that correction of dilutional effect of hyperglycemia on serum serum Na levels could be used as

an important tool for assessing the treatment efficacy in case of hyper glycemic conditions [3]. Abnormal functioning of the kidney dehydration or diabetic nephropathy may lead to this type of electrolyte loss. Dyselectrolytemia can be observed due to inhibition of rennin-angiotensin-aldosterone system that plays a significant role in maintaining water and electrolyte balance. Effect of hypoglycemic drugs such as chlorpropamide insulin diuretics tolbutamide could be considered as another factor that causes drug induced hyponatremia in diabetic patients [3].

We also observed significant low serum potassium levels in diabetic subjects than non- diabetic control groups. This result of our study concurrent with the study results of Ugwuja and Eze [10] and Ramadan R &Abdullah A [5]. High serum glucose boosts the movement of potassium from extracellular fluid into the cells leading to hypokalemia in diabetic patients.

On contrary researchers like Al Ajlan AR [14] & K Al Rubeaan et al. [15] reported hyperkalemia in DM patients in comparison to non-diabetic controls. We also reported significant elevation in serum chloride value in type 2 DM patients in comparison to healthy controls. This report agrees with the study reports of some other researchers [6 15] who also found similar results. This might be due to fall in blood pH as a result of diabetic ketoacidosis which further disturbs acid bas balance.

In this present study we correlated serum electrolyte values with FBS PPBS and HbA1c levels in type 2 DM patients. We obtained positive correlation (non significant) of serum electrolytes like potassium calcium and chloride levels and negative correlation (non-significant) of serum sodium level with FBS level. This is in agreement with the study result of Rajagambeeram et al. [16] who also found similar correlations. They also observed positive but non-significant correlation of serum potassium and calcium levels and negative correlation of serum sodium level with FBS level. Hyperglycemia causes hyperosmolarity which in turn leads to dehydration of cells. This results in K^+ efflux from ICF to ECF. This can be rationale behind positive inter-relationship between serum K^+ with FBS. Insulin is required for the activity of Na^+ /K^+ ATPase that is involved in maintaining transmembrane gradient of Na^+ and K^+. So insufficient insulin or insulin resistance present in type 2 DM could be the reason of diminished Na^+ /K^+ ATPase activity. When serum electrolyte levels were correlated with PPBS level we encountered significant positive correlation of serum K^+ level with PPBS level ($p< 0.05$)

Approaching to correlation of serum electrolytes with glycosylated Hb we noticed positive correlation of serum K^+ & Cl^- levels and negative correlation of serum Na^+ & Ca^{++} levels with HbA1c level though none of them are statistically significant. In the study done by different researchers like Al-Rubeaan K*et al.* [14] and Bagzai DS *et al*. [17] significant negative correlation was encountered between serum Na^+ level with HbA1c level whereas no significant correlation was observed in case of serum K^+ level. In another study conducted among type 2 diabetic Sudanese patients the researchers marked significant negative correlation between serum Ca^{++} and HbA1c level [7 18]. This is in contradictory to our results where we couldn't notice any statistically significant correlation.

5. Conclusion

The findings of our study gives insight and enhances our knowledge about imbalances in electrolyte values and its association with FBS PPBS & HbA1c levels in DM type 2 patients. Though no significant association was noticed in between serum electrolytes and the glycemic status& FBS level electrolyte levels were changed and significant positive correlation was observed between serum K^+ level and PPBS level. Hence prudent evaluation and timely correction would improve the glycemic status. This knowledge paves the way for pathophysiology directed treatment of DM patients that contribute in avoiding the lethal effects of electrolyte imbalance and their treatment. Taking into account the complex origin of electrolyte imbalance a cause-oriented treatment is required.

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7. Ethical Approval

The Institutional Ethics Committee of Institute of Medical Science and SUM Hospital, Siksha 'O' Anusandhan, Deemed to be University, approved this study with reference number Ref.no/IEC/IMS.SH/SOA/2023/622.

8. Conflict of Interest

The authors declare no conflicts of interest.

9. Source of Funding
None.

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