Alterations in Serum Electrolyte Homeostasis in Type-2 Diabetes Mellitus Patients - A Cross-Sectional Study in VIMSAR, Burla

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ABSTRACT

BACKGROUND

Type 2 diabetes mellitus is a widely prevalent lifestyle disease associated with high morbidity and mortality due to dead end complications like acute coronary syndrome, chronic kidney failure and acute stroke. Diabetes mellitus patients frequently develop problems of dyselectrolytemia which is common among hospitalised patients with decompensated diabetes. But there is little information on the prevalence of electrolyte disturbances among diabetes patients. Our aim is to find out the pattern of dyselectrolytemia among type 2 diabetes patients and to know if there is any association of blood glucose level with dyselectrolytemia.

METHODS

An analytical cross-sectional study was done among type 2 diabetes patients admitted in the department of medicine. Fasting blood glucose (FBG), glycosylated haemoglobin level (HbA1c), blood sodium (Na+), potassium (K+) and calcium (Ca2+) were analysed. Occurrence of dyselectrolytemia was compared between patients of very much controlled versus uncontrolled blood glucose levels.

RESULTS

Out of 199 patients included in the study, 112 (56 %) had uncontrolled diabetes mellitus (DM) with HbA1c level > / = 7.0 %. Occurrence of hyponatremia, hypokalaemia, hyperkalaemia, hypocalcaemia and hypercalcemia were 35 %, 13 %, 7 %, 16 % and 2 % respectively. In diabetes patients, hyponatremia was seen more commonly in patients with uncontrolled DM than those with very much controlled blood glucose (52.67 % versus 12.64 %, $p < 0.001$). The extent of patients with hypokalaemia or hyperkalaemia didn't vary between the two groups. Patients on insulin treatment were more likely to have hyponatremia than non-insulin patients ($p < 0.001$).

CONCLUSIONS

Type 2 DM patients specifically those who have uncontrolled diabetes mellitus have an increased chance to develop dyselectrolytemia. The most well-known electrolyte disturbances seen were hyponatremia followed by hypocalcaemia in our study and they were generally predominant among patients with uncontrolled DM.

KEYWORDS

Type 2 Diabetes, Dyselectrolytemia, Hyperglycaemia, Fasting Blood Glucose, Hyponatremia

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BACKGROUND

Diabetes is one of the most widely prevalent metabolic disorders characterised by increased level of blood sugar, which progressively leads to serious damage to the cardiovascular system, circulatory system, renal system, neurological system and eyes. The type 2 diabetes is most prevalent type of diabetes, usually found in adults up to old age, occurs due to insulin resistance to the muscle cells leading to hampering normal actions of insulin. If not prevented early by proper diagnosis and management leads to end organ damage and multiple complications including heart attack, kidney failure, blindness, amputations and finally death. About 422 million people worldwide have type 2 diabetes mellitus disease and around 1.6 million deaths are directly attributed to this disease every year. The number of patients and the death due to diabetes has been steadily increasing over the past few years.[1]

As per the review report by 2019 National Diabetes review presented by Ministry of Health and Family Welfare, the predominance was discovered to be 11.8 % in individuals beyond 50 years old.[2] With India having the most noteworthy number of diabetic patients on the planet, this is representing a tremendous medical issue in the nation. The WHO measures overall diabetic patients of 171 million in 2000 is relied upon to develop considerably to 366 million by 2030.[3] According to International Diabetes Federation, the total number of diabetes patients to Diabetes mellitus patients frequently develop problems of electrolyte disturbances.[4]

Electrolytes are substances essential for various physiological and biochemical process including osmotic regulations, renal excretion, myocardial muscle contractility and neuromuscular excitability along with acid base balance. Na+ (sodium) and Cl- (chloride) are the two important ions in ECF (Extra-Cellular Fluid), but potassium (K+), magnesium (Mg2 +), phosphates are found in intracellular fluid predominantly. Sodium–Potassium ion (NA+- K+) pump which is regulated by insulin and catecholamine hormones.[5] Variations in the amount of insulin and catecholamine changes the serum level of electrolytes. Alterations in the total quantity of extracellular solute, osmotic dieresis, intake of water taken by thirst, and impacts from associated conditions are the reasons that have been considered by which fluid and solute alterations takes place in hyperglycaemic individuals.[6]

Hypersecretion and hyposecretion of electrolyte problems are more common in admitted hyperglycaemic diabetes patients.[7] Hypokalaemia and hyperkalaemia are when the serum level of potassium is below 3.5 mmol / L and more than 5.5 mmol / L respectively. Hyponatremia is termed, when the sodium serum level is less than 135 mmol / L, similarly hypernatremia is when its serum level is more than 145 mmol / L.[5] Likewise Hypercalcemia means when calcium level is below 9 mg / dL and Hypercalcemia is when its level more than 11 mg / dL.[8] Movement of ions from inside cells to the extracellular fluid or from extracellular fluid inside the cells, high intake and decreased kidney excretion are the process by which their serum concentration high may occur.[9-13]

The association between blood glucose and electrolytes is complex and electrolyte disbalance may affect the course of diabetes and its treatment. Diabetic nephropathy is one of the biggest problems in uncontrolled diabetes patients, which ultimately leads to Kidney failure, which is reason of dyselectrolytemia in T2DM patients.[14] Hyper-glycemic hyperosmolar state (HHS) is one of the frequently found problems of diabetes caused by decreased fluid intake and lack of insulin and which results in decrease blood pressure, increase osmolarity and dehydration. Also causes several weeks of polyuria, which may lead to dyselectrolytemia T2DM patients with different periods of hyperglycemia.[15,16]

Production of insulin is a Ca^{2+} ion dependent phenomenon and an increase in Ca^{2+} level is needed for all phases of insulin secretion.[17] T2DM is linked with change from biphasic to monophasic insulin secretion, which may be due to abnormalities of Calcium channels.[18] Type 2 diabetes is a multifactorial polygenic disease. Obviously, polymorphisms in the CACNA1E gene quality alone are not adequate to trigger its significance. Given the present useful information, notwithstanding, it is enticing to guess that broken voltage gated Ca^{2+} channels may vary and again be associated with making the upset β cell phenotype in type 2 diabetes. There is a particular function for voltage gated Ca^{2+} channel diverts in second-stage insulin release, that of interceding the Ca2 + passage required for recharging of the releasable pool of granules just as islet cell separation.[19]

So as there was limited data on patterns of electrolyte disorders, in our setup, this research was planned to know relevant dyselectrolytemia in diabetic patients admitted to Medicine ward in our Medical College VIMSAR (Veer Surendra Sai Institute of Medical Science and Research) of Burla located in Sambalpur District of Odisha state.

Objectives

1. To evaluate various types of electrolyte imbalances in type 2 Diabetes Patients.
2. To know the Glycaemic status of Study population.
3. To find out any Comorbid conditions associated with Study group.
4. To Correlate Fasting Blood Glucose & HbA1C level with various types of electrolyte imbalances.

METHODS

This study was conducted at VIMSAR, Burla, Sambalpur, from August 2019 till July 2020 for a period of one year. Data was collected from patients admitted to Medicine IPD of VIMSAR, Burla. Sample size was estimated at 199 as per standard World Health Organisation sample size calculator based on previous relevant research paper.[20]

Data Collection

Data was collected by standardised format after explaining in local language and receiving informed consent from the patients. Various variables included in the questionnaire were:

- The demographic profile of patients,
- Gender & age,
- Serum electrolyte levels,
- FBS & HbA1c.

Inclusion Criteria

The cases of type 2 diabetes mellitus patients admitted to Medicine IPD, were chosen by non-probability consecutive sampling. Patients were to be called as uncontrolled diabetes with HbA1c of greater than or equal to 7 %.

Exclusion Criteria

Following patients were excluded: Diabetes type 1, chronic liver disease, pregnant women with gestational diabetes mellitus (GDM), and connective tissue disorders, as these patients were more likely to suffer from high blood sugar and dyselectrolytemia.

Sample Collections

Blood samples were collected with all precautionary measures and analysed for sodium (Na +), potassium (K +) and calcium (Ca^{2+}) using ISE electrolyte analyser (Accurex Enlite), blood sugar was analysed by Auto-analyser Cobas C311 Integra and HbA1c was analysed by Nephelometry.

Data Analysis

- Data was analysed by recommended SPSS version 21 software.
- Chi-Square test was applied and p value < = to 0.05 to be taken as significant statistically.

RESULTS

199 participants were included in our study, out of whom 59 % were males and 41 % were females. Age range varies from minimum 22 year to maximum 80 year with a mean age of 45 yrs., maximum 56 % of study population belonged to age group of 40 to 60 years. Similarly, 45 % belonged to urban area and 55 % from rural area as presented in Table number 1 & 2 below.

Variables	Frequency	(%)
1. Age Groups		
< 40 years	62	31
40 - 60 years	111	56
> 60 years	26	13
2. Gender		
Male	118	59
Female	81	41
3. Residential area		
Urban	110	44.7
Rural	89	55.3
4. Treatment received		
Life style modification (LSM) without medication	33	16.6
LSM + Oral Hypoglycaemic agents (OHA)	107	53.8
LSM + Insulin	41	20.6
LSM + OHA + Insulin	18	9
5. Glycaemic status / Glycated Hb / HbA1c		
> = 7 Uncontrolled	112	56
< 7 Controlled	87	44

Table 1. Basic Profile of the Study Samples (n = 199)

Parameters	Mini-mum	Maxi-mum	Mean	Std. Deviation	Total
Age (in years)	22	80	45.2	15.1	199
FBG (mg / dL)	88	720	231	112.1	
HbA1c (%)	5.30	16	8.3	2.2	
S. Sodium (mEq / L)	103	145	135	7.1	
S. Potassium (mmol / L)	2.90	7	4.3	0.79	
S. Calcium (mg / dL)	5	13	9.3	1.26	

Table 2. Baseline Characteristics (Descriptive Statistics) of Quantitative Variables

22 % study populations had no comorbid conditions like hypertension (HTN), cardiovascular diseases (CVD), dyslipidaemia and chronic kidney disease (CKD). A maximum of 33 % suffered from hypertension along with diabetes. Also around 6 % were affected by more than one comorbid conditions. (Figure 1).

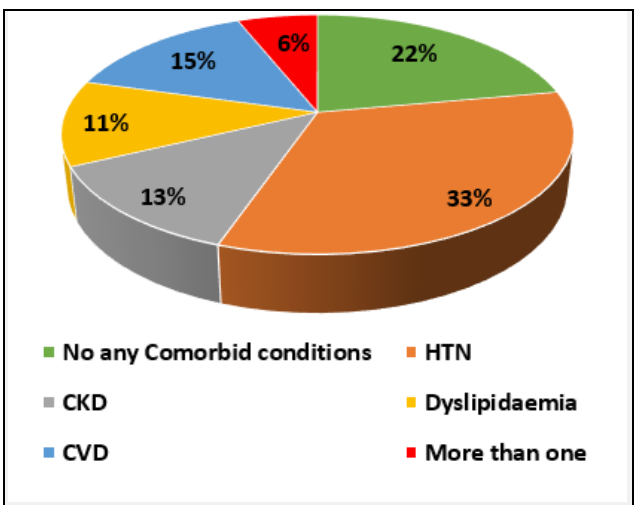

Figure 1. Presence of Comorbidities among Diabetes Patients

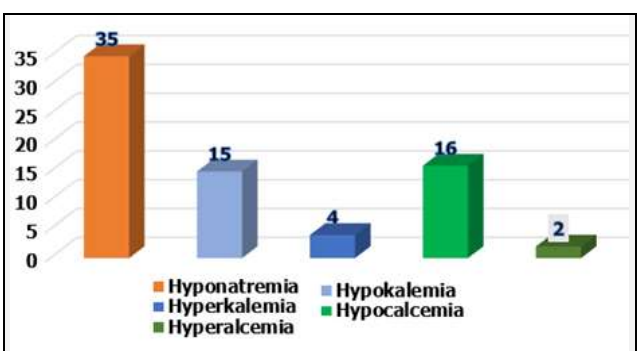

Figure 2. Pattern of Electrolyte Imbalances Observed in the Study

Condition	Uncontrolled DM (n = 112)	Controlled DM (n = 87)	Chi-Square Test P-Value
Hyponatremia (n = 70)	59 (52.67 %)	11 (12.64 %)	0.001
Hypokalaemia (n = 30)	16 (14.29 %)	14 (16.09 %)	0.53
Hyperkalaemia (n = 8)	6 (5.36 %)	2 (2.30 %)	0.53
Hypocalcaemia (n = 32)	20 (17.86 %)	12 (13.79 %)	0.32
Hypercalcemia (n = 2)	2 (1.78 %)	0	0.32

Table 3. Comparison of Electrolyte Disturbances with the Control of Diabetes

The occurrence of hyponatremia, hypokalaemia, hyperkalaemia, hypocalcaemia and hypercalcaemia was 35 %, 1 5 %, 4 %, 16 % and 2 % respectively (Figure 2). In diabetic patients, hyponatremia was seen more commonly in patients with uncontrolled DM than those with well

controlled blood glucose (52.67 % vs 12.64 %, p < 0.001) as shown in Table 3.

Predictor Variables	Na		K		Ca	
	r	p	r	p	r	p
Age	0.512	0.037	- 0.475	0.451	0.075	0.150
FBG	- 0.210	0.000	0.113	0.017	- 0.588	0.557
HbA1c	- 0.394	0.001	0.542	0.588	- 0.132	0.058

Table 4. Serum Electrolyte Parameter and Independent Variables Correlations

There is a statistical strong correlation between fasting blood glucose level and serum sodium (Table 4). Percentage of patients with a hyperkalaemia or hypokalaemia did not differ between the two groups. Insulin therapy patients were more likely to have hyponatremia than non-insulin user. The frequency of hyponatremia was higher in elderly as compared to non-elderly participants, which is statistically significant with p value p < 0.001. as shown in Table 5 below.

Sodium Level	Age Group in Years			Total	Chi-Square Test & P Value
	< 40 Yrs.	40 - 60 Yrs.	> 60 Yrs.		
Hyponatremia	4	47	19	70	
Eunatraemia	58	64	7	129	P < 0.001
Total	62	111	26	199	

Table 5. Distribution of Sodium Level in Different Age Groups

DISCUSSION

Although, it is well known from literature that electrolyte disturbances can possibly occur in diabetic patients, there are limited studies that have documented the magnitude of electrolyte disturbances in western Odisha population. There are substantial differences in the dietary habits, lifestyle and genetics among patients in the Indian sub-continent. Hence, it is worthwhile to perform a region-based study.

In this study, the most common electrolyte abnormality found was hyponatremia. There is a significant variability in the incidence of hyponatremia among hospitalised subjects ranging from 5 to 35 % found in several studies.[7,15-19]

As expected, patients with uncontrolled blood sugar were at a greater risk to develop hyponatremia may due to the inability of kidney to maintain control of normal physiological functions may be due to imbalance of ADH (Antidiuretic Hormone) & Renin angiotensin system.

The frequency of hyponatremia was higher in elderly as compared to non-elderly diabetes participants. Similar findings also observed in other studies 24 by Abhisek Singh et al where hyponatremia was 27 %.

Sometimes hyponatremia due to drugs like insulin, diuretics etc is more common as a chronic presentation and as we measured the sodium levels on admission, the possibility of some of these subjects to have chronic hyponatremia cannot be ruled out. Previous studies have documented that Dyselectrolytemia mostly hyponatremia is a major risk factor with increased mortality in hospitalised patients.[21,16] It may be advisable that the balance of sodium levels during the stay in hospital period could have decrease the potential dangers caused by hyponatremia as a risk factor for mortality in diabetic subjects.

Present study also showed that the frequency of hypokalaemia was 15 % and that of hyperkalaemia was 4 % in the study population. There was no significant changes in the frequency of these electrolyte disturbances between controlled and uncontrolled diabetic subjects. "In a large Swedish health care system, where data was obtained from 364,955 patients, the incidence of hypokalaemia was found to be 13 % and that of hyperkalaemia in 7 % of the population." The study had also reported that the odds of developing hyperkalaemia were 1. 62 in diabetic patients compared to non-diabetic subjects. Previous studies have reported that some of the strong risk factors for hypokalaemia include diuretic usage, losses from the gastrointestinal tract including diarrheal episodes and the use of laxatives and diabetic ketoacidosis.

Present study also revealed that 16 % of the subjects had hypocalcaemia among diabetes patient and 2 % of them presented with hypercalcemia during admission. These findings are in agreement with a study done among critically ill patients with septic shock where the frequency of hypocalcaemia was found to be 35 %.[22,23] Thus, it is pertinent to study the electrolyte disturbances among diabetic subjects admitted in the hospital as they are at a greater chance of developing complications due to the same.

Limitations

The present study did not look for the changes on all days in the electrolyte concentration during the hospital stay and thus those patients who developed electrolyte disturbances after few days of hospital stay were not identified. Authors did not measure the urine concentration of electrolytes and having these variables would help us to characterise patients better.

CONCLUSIONS

Patients with type 2 uncontrolled diabetes have a higher chance of developing dyselectrolytemia. In the present study, the commonest electrolyte disturbance found was hyponatremia. Hence, investigating electrolyte levels should be evaluated in patients suffering from uncontrolled diabetes. Further studies are needed to correlate daily changes in electrolyte levels according to treatment given to the patients.

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