A Study on Serum Electrolyte Imbalance in Type-2 Diabetes Mellitus - A Hospital-Based Study

Sreenivasulu Uppara[1], Bhagyamma Sollapurappa Narayanaswamy[2], Rama Kishore Akula Venkata[3], Thanuja Ramanna[4], Shyam Prasad B.R.[5]

[1, 2, 5] Department of Biochemistry, Government Medical College, Ananthapuramu, Andhra Pradesh, India.
[3]Department of Paediatrics, Government Medical College, Ananthapuramu, Andhra Pradesh, India.
[4]Masters in Biology, University of Memphis Tennessee, USA.

ABSTRACT

BACKGROUND
The multi-organ disorder, diabetes mellitus (DM) continues to be one of the commonest and challenging health-related problems in the 20th century, prevalent in about 9.3 % of the world's population in 2019 and likely to affect 10.2 % by 2030. Diabetes mellitus is a group of chronic metabolic disorders of multiple aetiology, characterized by chronic hyperglycaemia due to derangement in carbohydrate, fat and protein metabolism. Electrolytes are crucial in maintaining various metabolic functions and play a pivotal role in maintaining a healthy state's body. Diabetic patients are more prone to and frequently develop a constellation of electrolyte disorders due to hyperglycaemia, polydipsia and polyuria.

METHODS
Our study comprised a total of 70 subjects in the age group of 35 - 60 years with age and sex-matched controls. They were grouped into two groups; the first group, group-1 (healthy controls) and the second group was group-2 (patients of diabetes mellitus on oral hypoglycaemic agents with poor control). 5 ml of fasting venous blood was collected in a plain vacutainer tube in the morning after a zero-calorie overnight 08 hours fast. Post collection, the blood sample was used as serum or plasma or whole blood to estimate plasma glucose, blood urea, serum creatinine, serum sodium, serum potassium, serum chloride by kit methods using an auto analyser.

RESULTS
Among the various parameters tested, the mean value of fasting plasma glucose, blood urea, serum creatinine, serum potassium, serum chloride were higher in group-2 (diabetic patients) compared to group-1 (healthy controls) with a p-value of < 0.0001. The value of the mean of serum sodium was lower in group-2 (diabetes mellitus) compared to group-1 (healthy controls) with a p-value of < 0.0001.

CONCLUSIONS
We conclude that electrolyte abnormalities are present in diabetic patients and maybe a root cause for associated morbidity or mortality. These disturbances are generally seen in decompensated Diabetes Mellitus patients, elderly individuals and in the presence of renal impairment.

KEYWORDS
Diabetes Mellitus, Serum Electrolytes, Fasting Blood Glucose

Corresponding Author:
Dr. Shyam Prasad B.R.,
Associate Professor,
301, Hanuman Classic,
2nd Cross, Aravinda Nagar,
Ananthapuramu – 515001,
Andhra Pradesh, India.
E-mail: shyamcapt@yahoo.com

DOI: 10.18410/jebmh/2020/583

How to Cite This Article:
Uppara S, Narayanaswamy BS, Venkata RKA, et al. A study on serum electrolyte imbalance in type-2 diabetes mellitus - a hospital-based study. J Evid Based Med Healthc 2020; 7(48), 2847-2851. DOI: 10.18410/jebmh/2020/583

Submission 29-08-2020,
Peer Review 05-09-2020,
Acceptance 14-10-2020,
Published 30-11-2020.

BACKGROUND

Diabetes mellitus (DM) has become one of the common and challenging health-related problems in the 20th century. The prevalence of diabetes mellitus is estimated to be around 9.3 % of the world's population, approximately around 463 million.[1] Diabetes mellitus is established as a group of chronic metabolic disorders of multiple aetiologies characterized by chronic hyperglycaemia due to derangement in carbohydrate, fat and protein metabolism. Poor glycaemic control, sedentary lifestyle, dietary habits, genetic mutations, high blood pressure, elevated cholesterol levels, genetic mutations, obesity and lack of regular exercise are considered the risk factors that may have led to a dramatic rapid increase in the incidence of diabetes mellitus.[2] It is proved to be due to either the pancreas not producing enough insulin as required for the body or the body's cells not responding correctly to the insulin produced. Type 1 diabetes mellitus is diagnosed based on the fact that the pancreas fails to produce enough insulin. This type is referred to as type-I or insulin-dependent diabetes mellitus or juvenile diabetes mellitus. The type 2 DM category starts with insulin resistance; a condition where the cells fail to respond to insulin appropriately. The symptoms of high blood sugar (hyperglycaemia) include frequent urination (polyuria), increased thirst (polydipsia) and increased hunger (polyphagia). If not treated, diabetes mellitus can lead to complications. The acute complications are diabetic ketoacidosis; the hyperosmolar hyperglycaemic status may lead to death. The long-term complications are mostly due to the effects on organs and may cause kidney disease, cardiovascular disease, foot ulcers and damage to the eyes.[3] Diabetes mellitus remains as one of the major causes of renal failure. Diabetic nephropathy affects 30 % of diabetics, and it is a leading cause of nephritis, leading to end-stage renal disease in many countries.[2] The complications of diabetes have been labelled as different entities, based on the organ affected like diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, diabetic foot, etc. It is also implicated as a predisposing factor for early onset of presbyopia, cataract, metabolic disorders like atherosclerosis, cardiovascular diseases, cerebrovascular disorders etc.

Electrolytes play a pivotal role in maintaining the homeostasis of the body and are in balance.[4] In the intracellular fluid, potassium is the major cation, and phosphates and proteins are the predominant anions. Extracellular fluid mainly contains sodium as the cation and chloride and bicarbonate as anions. Approximately 75 % of sodium is present as exchangeable sodium. Approximately 90 % of the exchangeable sodium is in the extracellular fluid. Approximately 25 % of sodium is present as non-exchangeable sodium. Non-exchangeable sodium is present as sodium incorporated in tissues such as bones and other tissues. The plasma concentration of sodium is in the range of 135 - 145 mEq / L. Sodium contributes to the acid-base balance as sodium bicarbonate. In a sodium-potassium pump, three ions of sodium are pumped out of the cell through the sodium-potassium pump for every two ions of potassium pumped into the cell. The sodium-potassium pump is essential for the maintenance of cell membrane potential. Sodium transport is coupled to the transport of potassium, glucose, galactose, or amino acids. This belongs to the type of secondary active transport. This mechanism is responsible for absorbing glucose, galactose and amino acids from the proximal jejunum and reabsorption of these molecules from the proximal renal tubules. Potassium is a major cation of intracellular fluid. Total body potassium is about 3600 mEq. About 95 % is in cellular water. The plasma concentration of potassium is in the range of 3.5 to 5.0 mEq / L.

The Na-K-ATPase pump maintains high intracellular potassium. Intracellular potassium is required for several enzyme reactions, ex: pyruvate kinase reaction, glycogen synthase reaction. Potassium is an essential determinant of excitable cells' resting membrane potential, such as nerve and muscle. Chloride is a major extracellular cation. The average plasma concentration is 95 – 105 mEq / L. The serum chloride levels vary in direct proportion to the serum sodium concentration in hypo osmolar states and hyperosmolar states in the absence of acid-base abnormalities. Chloride plays a vital role in regulating fluid and electrolyte balance, regulation of gastric acid secretion, chloride shift in acid-base balance and has a role in bicarbonate transport in erythrocytes.

Diabetic patients frequently develop different types of subclinical electrolyte disorders. They are due to insulin deficiency or resistance manifesting as hyperglycaemia and, if not corrected, will lead to hyperketonaemia.[5] The most frequently seen electrolyte abnormality in DM in clinical practice is hyponatremia, which is associated with increased morbidity and mortality. However, potassium, chloride, calcium and magnesium disturbances are not uncommon[4]. Potassium becomes a crucial marker in diabetic nephropathy. It is monitored in diabetic nephropathy cases as one of the markers in evaluating end-stage renal disease and planning of dialysis. The present study aimed to evaluate the electrolyte imbalance in type 2 diabetes mellitus.

METHODS

A prospective study was conducted from October 2019 to December 2019 at Government Medical College, Anantapur. The Institutional Ethical Committee cleared the study design, objective, materials and methods. Consent was obtained from the subjects after duly explaining the purpose of the study, and the sample was collected. The sample size was based on the factors of cost, time and convenience of collecting data. The study comprised a total of 70 subjects attending diabetic clinics and OP services. This study's subjects are in the age group of 35 - 60 years and were age and sex-matched. They were divided into two groups; group 1 contained 35 subjects who were healthy and used as controls; group 2 includes 35 subjects who were confirmed cases of diabetes mellitus.

Inclusion Criteria

Group 1: Controls-apparently healthy individuals without a history of any disease.
Group 2: Cases-confirmed cases of type II diabetes mellitus on oral hypoglycaemics with poor control. The poor control was based on HbA1c of more than 8 %.

Exclusion Criteria

Group 1: History of any disease or treatment affecting electrolyte values was excluded.
Group 2: Type 1 DM, gestational DM, type II DM on insulin therapy, endocrine disorders, patients with cardiovascular disease with or without diuretic treatment, history of any illness or complications of DM affecting electrolyte imbalance were excluded.

Blood samples were collected at the Government General Hospital, Anantapuramu, Andhra Pradesh. Under sterile aseptic standard precautions, 5 ml of venous blood from the median cubital vein was collected in-plain vacutainer for urea and electrolytes and sodium fluoride / potassium oxalate vacutainer for glucose, in the morning after an overnight fast of 08 hours, under sterile aseptic standard protocols. Serum and plasma were separated for estimating plasma glucose, electrolytes and creatinine as per standard procedures.

After collection and separation, the samples were analysed immediately within the stipulated time for serum electrolyte levels (sodium, potassium and chloride) using the electrolyte test kit method.[6] Plasma glucose was quantified by Glucose Oxidase (GOD)- Peroxidase (POD) method.[7] The blood urea was estimated using the Di-Acetyl Monoxime (DAM) method[8] and serum creatinine with an alkaline picrate method.[9] All the analyses were analysed in a semi-auto analyser of ROBONIC make.

Statistical Analysis

The results were entered and tabulated in a Microsoft office excel sheet, and data was analysed. In data analysis, a comparison of parameters between controls and case groups was made by paired t-test. The data obtained are expressed in mean and standard deviation. For determining the statistical significance, the student t-test was used and calculated using graph pad software. A test of the probability of less than 0.05 (< 0.05) was regarded as significant. The correlation was also tested.

RESULTS

The age-wise and sex distribution of the cases and controls are illustrated in table 1 below. A total of 20 males and 15 females were analysed in the cases and control groups. The highest number of subjects were in the age group of 45 – 54 years and comprised of 20 subjects, 60 % of the entire group, and the least was in the age group of 35 – 44 years, 06 subjects – 20 %.

	Group 2						Group 1					
Age Group	Male	%	Female	%	Total	%	Male	%	Female	%	Total	%
35 - 44	3	15	3	20	**6**	17.14	3	15	3	20	**6**	17.14
45 - 54	11	55	9	60	**20**	57.14	11	55	9	60	**20**	57.14
> 55 yrs.	6	30	3	20	**9**	25.71	6	30	3	20	**9**	25.71
Total	**20**		**15**		**35**		**20**		**15**		**35**	

Table 1. Age and Gender Distribution of Cases and Controls

In this present study, the mean value of fasting and postprandial plasma glucose levels in group 2 (DM) patients is higher when compared with group-1 (controls) ($p < 0.0001$), as shown in the table-2. The serum sodium mean value was low, and the serum potassium and chloride were high in group-2 compared to group-1 ($p < 0.0001$), as shown in Table 2. The mean value of blood urea and serum creatinine was high in group-2 compared to group-1, as shown in Table 2.

Parameters	Group-1 (Healthy Controls)	Group-2 (Diabetic Patients)	P-Value	t-Value
Fasting Plasma Glucose (mg / dL)	91.62 ± 7.12	184.05 ± 24.7	< 0.0001	21.21
Post Prandial Plasma Glucose (mg / dL)	122.7 ± 8.56	231.9 ± 28.9	< 0.0001	62.53
Blood Urea (mg / dL)	24.94 ± 5.53	60.6 ± 10.69	< 0.0001	21.13
Serum Creatinine (mg / dL)	0.82 ± 0.1	0.98 ± 0.31	< 0.0001	25.93
Serum Sodium (meq / L)	139.62 ± 2.31	133.02 ± 2.21	< 0.0001	15.91
Serum Potassium (meq / L)	4.102 ± 0.45	5.21 ± 0.234	< 0.0001	12.99
Serum Chloride (meq / L)	99.4 ± 2.82	109.37 ± 2.94	< 0.0001	14.37

Table 2. Comparison of Lab Parameters in the Study Groups

Fasting Plasma Glucose (FPG) showed significant negative correlation with serum sodium ($r = -0.0959$) and positive correlation with serum potassium ($r = 0.1470$) and with serum chloride ($r = 0.3734$), with serum creatinine ($r = 0.19306$) as shown in the Table 3.

Parameters	r-Value	t-Value	P-Value
FPG with Serum Creatinine	0.19306	49.505	< 0.0001
FPG with Serum Sodium	-0.09594	12.61	< 0.0001
FPG with Serum Potassium	0.1470	42.71	< 0.0001
FPG with Serum Chloride	0.3734	17.71	< 0.0001

Table 3. Significant Correlation in the Patient Group

DISCUSSION

Type 2 DM is the most commonly occurring form of diabetes mellitus, affecting almost nearly 90 % of the diabetic population in any country. In diabetes mellitus, the body has a decreased ability to produce insulin or insulin produced may not be sufficient for its action resulting in hyperglycaemia. Defective insulin production causes altered metabolism of carbohydrates, fat, and amino acids. Chronic hyperglycaemia in diabetes leads to cardiovascular, renal, neurological, and ocular complications and increases the risk of recurrent infections. Disturbances in serum electrolytes are found to be associated with diabetes mellitus.[10] Imbalance of electrolytes results from renal failure, fever, dehydration, vomiting. It has been thought to be one of the important contributing factors towards complications developed in diabetes mellitus and other endocrine disorders.[3] In this present study, the mean value of serum sodium in diabetic patients (group-2) is significantly lower compared to controls (group-1) ($p < 0.0001$). The obtained result was consistent with previous studies by Ahmed R et al[5] Das A et al,[10] Rajagambeeran et al.[11]

The most typical electrolyte disturbance in clinical setup is hyponatraemia leading to morbidity and mortality. Na + / k + -ATPase is a ubiquitous enzyme that ensures Na + and k + gradients' equilibrium across the cell membrane and maintains by transporting 3 Na + out and 2k + into the cell. Alterations to this transport system are linked to several complications of types of diabetes mellitus disorders. It is proposed that the correlation between diabetes mellitus and decreased serum sodium may be due to the altered vasopressin regulation. Insulin stimulates the expression of vasopressin-induced aquaporin AQP-2 water channels. The absorption of water in the intestinal tract is increased due to slower stomach emptying that may play a role in hyponatraemia.[11] Hyperglycaemia leads to an increase in serum osmolality, which results in water movement to the extra cellular compartment, out of the cells, and reduces serum sodium levels by dilution. Hyperglycaemic status also induces hypovolemic-hyponatraemia due to osmotic diuresis.[12] In our present study, the mean value of serum potassium was higher in diabetes mellitus patients (group-2) compared to controls (group-1) ($p < 0.0001$). Our study findings are similar to previous studies by Rajagambeeeran R et al.[11] Thivyah Praba AG,[13] Datchanamurthi S et al.[14]

The association of blood glucose and serum electrolytes is multifactorial and is related to several other factors, including age and other associated conditions leading to electrolyte disturbances. The increase in urination results in loss of electrolytes, water and other metabolites and results in imbalance. This disturbs sodium and potassium levels in the body. Exogenous insulin also can induce mild hyperkalaemia as it promotes the potassium influx into the hepatic cells and skeletal muscle cells, thereby increasing the activity of Na^+ and K^+ ATPase pump. Also, hyperkalaemia is associated with impaired insulin secretion, leading to decreased glucose utilization in the peripheral tissues. This results in carbohydrate intolerance and hyperglycaemia.[14]

In our study, the serum chloride mean value was higher in diabetic patients (group-2) when compared to controls (group-1) ($p < 0.0001$). Similar findings were observed with previously published studies by Das A et al. in 2016[10], Thivya praba AG[13], Datchanamurthi S, et al.[14] Elevated chloride levels were detected in patients of diabetes, which might be due to the effect of diabetic ketosis. Ketoacidosis may reduce the pH of blood, which disturbs the acid-base balance leading to elevation of chloride[14] levels.

Diabetes mellitus is quite a common disorder nowadays and predisposes or hastens the onset of complications of many types, including inflammatory, infective and degenerative disorders. It has been identified as a risk factor for increased morbidity and mortality in various conditions, including the latest worldwide pandemic of coronavirus infection.[15]

Electrolyte imbalances are also quite common in people with diabetes. They are rarely investigated, leading to chronic irreparable complications or going undiagnosed until a level of severity is reflected in severe conditions.

Our study also increases the importance of identifying electrolytes' disturbances at an early stage, which is supported by other studies mentioned in the discussion.

CONCLUSIONS

In our study, the mean value of serum sodium was low, and serum potassium and chloride were high in cases compared to controls. We conclude that electrolyte abnormalities are present commonly in diabetic patients and may be associated with complications leading to increased morbidity or mortality. These disturbances are generally common in decompensated DM, in the elderly and disorders of renal impairment. Therefore serum electrolytes should be routinely measured in patients with type 2 DM. Serum fasting plasma glucose can be used as a predictor for glycaemic status. Blood urea and serum creatinine levels are also essential tests for helpful in poorly controlled Diabetes to assess renal function. Effective control of blood glucose levels can stop progression to diabetic nephropathy.

Limitations

The sample size of this study is small. So a definitive conclusion is not possible.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.
Authors thank all the study subjects, the staff and faculty of the department of biochemistry.

REFERENCES

[1] Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Research and Clinical Practice volume 2019;157:107843.

[2] Madhusudanao S, Sadhvimani E. A study on diabetes mellitus from Sangareddy District, Telangana, India. International Journal of Medical and Health Research 2017;3(12):132-136.

[3] Jha NK. Study of lipid profile and electrolyte levels in Diabetes. Int J Med Health & Res 2017;3(9):146-148.

[4] Karuppan A, Sahay MI, Ravindranathan R, et al. Elecrolyte disturbances among diabetic patients admitted in a multi-speciality hospital in Southern India. J Clin Diag Res 2019;13(2):OC12-OC15.

[5] Ahmed R, Khandker F, Khanduker S, et al. Electrolyte disturbances in patients with diabetes Mellitus. Bangladesh J Med Biochemistry 2017;10(1):27-35.
[6] Schoenfeld RG, Lewellen CJ. A colorimetric method for determination of serum chloride. Clin Chem 1964;10:533-539.
[7] Trinder P. Enzymatic determination of glucose in blood serum. Ann Clin Biochem 1969;6:24.
[8] Wybenga DR, Giargio JD, Pileggi VJ. Manual and automated methods for urea nitrogen measurement in whole serum. Clin Chem 1971;17(9):891-895.
[9] Slot C. Plasma creatinine determination. A new and specific Jaffe reaction method. Scand J Clin Lab Invest 1965;17(4):381-387.
[10] Das A, Borkotoki S. Evaluation of serum electrolyte levels in type 2 Diabetes mellitus. Indian Journal of Applied Research 2016;6(8):91-93.
[11] Rajagambeeram R, Malik I, Vijayam M, et al. Evaluation of serum electrolytes and their relation to glycemic status in patients with type 2 diabetes mellitus. International Journal of Clinical Biochemistry and Research 2020;7(1):130-133.
[12] Liamis G, Liberopoulos E, Barkes F, et al. Diabetes mellitus and electrolyte disorders. World J Clin Cases 2014;2(10):488-496.
[13] Thivyahprabha AG. Relation between serum electrolytes and serum creatinine levels in diabetes mellitus. Int J Clin Biochem Res 2017:4(3):257-260.
[14] Datchanamurthi S, Vanja R, Rajagopalan B. Evaluation of serum electrolytes in type 2 Diabetes Mellitus. Int J Pharm Sci Rev Res 2016;40(1):251-253.
[15] Rubino F, Amiel SA, Zimmet P, et al. New-onset diabetes in Covid-19. N Engl J Med 2020;383(8):789-790.