Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy **Dove**press

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ORIGINAL RESEARCH

Assessment of Selected Serum Electrolyte and Associated Risk Factors in Diabetic Patients

This article was published in the following Dove Press journal:
Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

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Purpose: The objective of this study was to assess selected serum electrolytes imbalance and associated factors in diabetic patients attending their follow up appointments in Jimma University Medical Center (JUMC) from February 1 to April 1, 2019.

Patients and methods: A cross sectional study design was used to assess the selected serum electrolytes in diabetic patients attending their follow up appointments at Jimma University Medical Center (JUMC) chronic illness clinic. A convenience sampling technique was used to include 279 diabetic patients in the study and an interviewer based questionnaire was used to include all necessary data from each diabetic patient. Five milliliters of blood were collected from each subject and processed and analyzed for blood glucose and serum electrolyte determination by ABX Pentra400 and Humalyte plus[5] ion-selective electrode (ISE) system clinical chemistry analyzers. Pearson's correlation coefficient model and multivariate logistic regression were used respectively to assess the correlation and significant association between abnormal serum electrolytes and independent variables.

Results: A high prevalence of one or more serum electrolyte abnormalities was determined in diabetic patients. The overall prevalence was 42.0% (n=116/276) in which hyponatremia was the highest followed by hypochloremia and hypercalcemia, 40.6%, 14.9% and 10.9% respectively. Age, type of medication, and high body mass index (BMI) had strong positive correlations with abnormal serum concentration levels of sodium (r=0.611, P=0.731), potassium (r=0.752, P=0.812) and chloride (r=0.645, P=0.459). Being employed (AOR: 3.933, 95% C.I: 1.057–14.637, P value: 0.041), treated with mixed medications (AOR: 2.9, 95% C.I: 1.292–6.441, P value: 0.010) and being unable to control blood glucose level or being hyperglycemic (AOR: 3.2, 95% C.I: 2.179–5.721, P value: 0.000) were statistically identified as risk factors for serum electrolyte abnormalities in diabetic patients.

Conclusion: The serum electrolyte concentration level was highly abnormal in diabetic patients. The prevalence of abnormal concentration was more common in diabetic patients with advanced age, and some variables had strong positive correlation with abnormal serum electrolyte level in diabetic patients.

Keywords: hyperkalemia, diabetic patients, hyponatremia, Jimma University

Introduction

Body fluid is an aqueous solution containing electrolytes and non-electrolytes, consisting of intracellular and extracellular compartments.[1,2] Most metabolic activities primarily occur in intracellular fluid (ICF), due to this, substantial alteration in its ionic strength may occur with adverse effects on body function. Extracellular fluid (ECF) functions efficiently as a conduit and regulates intracellular volume and its ionic strength, because of this, it requires maintenance of optimal volume. Any alteration in extracellular osmolality is followed by an identical change in intracellular

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DovePress
http://doi.org/10.2147/DMSO.S233053

osmolality, which is accompanied by a reciprocal change in cell volume because an osmotic equilibrium exists between the cells and the extracellular fluid.[1,3–6]

Electrolytes are substances that become ions in solution and acquire the capacity to conduct electricity.[7,8] Electrolytes are an essential component in numerous processes including body fluid volume and osmotic regulation (Na^+, K^+ and Cl^-), myocardial rhythm and contractility, and neuromuscular excitability (e.g., K^+) as well as acid-base balance (e.g., K^+, Cl^-).[1,8] Sodium and chloride ions are the main electrolytes in the extracellular fluid whereas potassium; magnesium and phosphate are the main electrolytes in the intracellular fluid. Diffusion of cellular K^+ out of cells and Na^+ into cells is caused by trans-membrane electrical gradients. Sodium-potassium ion (Na^+-K^+) pump, which is stimulated by insulin and catecholamine hormones, reverses the movement of these electrolytes in order to maintain their extracellular and intracellular homeostasis.[1,4,8–10] Alterations of the levels of insulin and catecholamine affect the serum level electrolytes.[1,5] Changes in the total amount of extracellular solute, osmotic dieresis, intake of water driven by thirst, and influences from associated conditions are the mechanisms that have been considered by which fluid and solute abnormalities occur in hyperglycemic patients.[2,11–13]

Hypo- and hyper-secretion of electrolyte disorder is the most common in hospitalized patients. Hypokalemia and hyperkalemia are when the serum concentration of potassium level is below 3.5 mmol/L and greater than 5.1 mmol/L respectively. Hyponatremia is when the sodium serum concentration is less than 135 mmol/L and hypernatremia is when its serum concentration is greater than 150 mmol/L. Shift of electrolytes from the cells to the extracellular fluid or from extracellular fluid into the cells, increased intake and reduced renal excretion are the mechanisms by which their serum elevation may occur.[1,2,8,11,14–19]

Diabetes is a chronic condition that occurs when there are raised levels of glucose in the blood because the body cannot produce any or enough of the hormone insulin or use insulin effectively.[20,21] Hyperglycemic hyperosmolar state is one of the acute complications of diabetes caused by inadequate fluid intake and absolute deficiency of insulin and it is characterized by hypotension, hyperosmolarity, and dehydration, and, with several weeks of polyuria, it may lead to electrolyte disorders in diabetic patients with different durations of hyperglycemia.[2,9,13,16,22–25] Hence, this study was aimed to assess selected serum electrolyte abnormalities and factors associated with the abnormality in diabetic patients.

Materials and Methods

Study Area and Data Collection Technique

The study was conducted at Jimma University Medical center (JUMC) from February 1 to April 1, 2019. The study was conducted on both type 1 and type 2 diabetic patients attending their follow up at chronic illness clinic of JUMC. An institution-based cross-sectional study design was used to carry out the study and a convenience sampling technique and a single-population proportion formula with P value =0.29 and 95% confidence interval were used to include a sample size of 279 diabetic patients. An interviewer administered questionnaire was used to collect socio-demographic, clinical, and substance use as well as anthropometric data. Diabetic patients with history of renal problems or disease and those on diuresis treatment during data collection period were excluded from the study. Blood pressure measurement was performed based on World Health Organization (WHO) guideline and diabetic patients with abnormal systolic and diastolic blood pressure measurements were considered hypertensive. Anthropometric measurement was carried out based on WHO guideline and body mass index (BMI) for each study subject was calculated by using simple calculation formula, BMI=weight over height square and the diabetic patients were classified as underweight (<18.5 kg/m^2), overweight (25.0–29.9 kg/m^2), obese (≥30 kg/m^2), or abnormal and normal weight (18.5–24.9 kg/m^2) based on WHO guideline category.

Blood Collection and Analysis

Five milliliters over-night fasting blood specimen was collected from each study subject and underwent necessary standardized procedures to separate the serum from the whole blood that is used for serum electrolyte and blood glucose determinations. A clinical chemistry analyzers, ABX Pentra400 and Humalyte plus[5] ion-selective electrode (ISE) system were used for blood glucose and serum electrolyte determinations respectively. The international Federation of Clinical Chemistry (IFCC) recommended cut off values to categorize electrolyte values above and below normal range. Accordingly, the reference interval for sodium concentration level in the blood is 136–145 millimole per liter (mmol/L) and those study subjects whose serum sodium concentration level below 135 mmol/L and greater than 146 mmol/L were considered to be hyponatremic and hypernatremic respectively.

The reference interval for both chloride and potassium concentration levels in the blood are 98–107 mmol/L and 3.5–5.1 mmol/L respectively. Diabetic patients with serum chloride concentration level less than 98 mmol/L and above 107 mmol/L were considered to be hypochloremic and hyperchloremic respectively. Similarly, those study subjects with potassium serum concentration level below 3.5 mmol/L and above 5.1 mmol/L were considered to be hypokalemic and hyperkalemic respectively.

Data Quality Management and Statistical Analysis

All the data from the questionnaire were checked manually for completeness and clarity before any data analysis took place. After that the data were entered into Epidata version 4.1 and then exported to SPSS, IBM, USA version 23. Pearson's correlation was used to assess the strength of correlation between abnormal serum electrolytes and independent variables. Strengeth of correlation was considered very strong, strong, moderate, weak and very weak when the correlation coefficient value, r= 0.8-1.0, 0.6-0.79, 0.4-0.59, 0.2-0.39 and 0.0-0.19 respectively based on the direction of the linear relationship between the dependent and independent variables. Bi-variate and multivariate logistic regression models were used to assess and identify independent predictor variables for serum electrolyte abnormality and those independent variables whose P values less than 0.25 in bivariate logistic model were shifted into multivariate logistic model. Finally, P value less than 0.05 was considered as a statistically significant association between independent variables and serum electrolyte abnormalities.

Results

The total response rate was 98.9% as three study subjects had been excluded before clinical sample analysis due to incomplete information. The age of study subjects ranged from 19–75 years with mean age of 50.9±13.7. Majority of study subjects, 58.7% (n= 162/276), were males and the rest were females. Three major serum electrolytes were assessed for each study subject and the overall prevalence of one or more abnormal serum electrolyte concentration level had been determined among 42.0% (n=116/276) diabetic patients. Hyponatremia, serum sodium concentration level below 135 mmol/L, was the leading abnormal serum electrolyte in diabetic patients followed by hypochloremia or low serum chloride concentration level (40.6% versus 14.9%) respectively and only about 10.9% (n=30/276) of diabetic patients were hyperkalemic or had serum potassium concentration level greater than 5.1 mmol/L. Electrolyte abnormality was determined primarily among 22.8% (n=63/276) male diabetic patients and high prevalence, 15.6% (n=43), was identified among diabetic patients with advanced age group or greater than 58 years. Moreover, the highest prevalence, 30.9% (n=85/276), was determined among married diabetic patients.

The correlation between serum electrolyte concentration level and independent variables was assessed by using Pearson's correlation coefficient model. Based on the assessment, serum electrolyte concentration level of sodium, chloride and potassium showed increment with marital status, duration of diabetes and diastolic hypertension. The age of diabetic patients had strong positive correlation with abnormal serum sodium concentration level (r=0.611, P =0.004) and weak positive correlation with abnormal serum chloride concentration level (r=0.33, P =0.58) and very weak negative correlation with abnormal serum potassium concentration level (r=−0.015, P=0.80). Type of medication used in diabetic patients had strong positive correlation with abnormal serum potassium concentration level (r=0.752, P=0.001) whereas the abnormal serum concentration levels of sodium and chloride had very weak positive and negative correlation with type of medication used by diabetic patients (r=0.05, P=0.408 versus r=−0.06, P=0.321) respectively. Abnormal serum concentration level of potassium had strong positive correlation with higher BMI (r=0.645, P=0.459), whereas sodium and potassium serum concentration levels had very weak correlation with abnormal BMI of diabetic patients (Table 1).

Bivariate and multivariate logistic regression was assessed to identify independent predicator variables that could have a statistically significant association with serum electrolyte abnormalities after the variables whose P values less than 0.25 in binary logistic regression had been shifted into multivariate logistic regression. Based on multivariate logistic regression statistical assessment, three variables were identified as having a statistically significant association with abnormal serum electrolytes. Employed diabetic patients were about 3.9 times more likely to develop abnormal serum electrolytes when compared to unemployed diabetic patients (AOR: 3.933, 95% C.I: 1.057–14.637, P value: 0.041). Similarly, diabetic patients who were treated with both oral anti-hyperglycemic agent and insulin injection were about 2.9 times more likely to develop serum electrolyte abnormality than diabetic patients being treated with insulin alone to

Table 1 Correlation Between Serum Electrolyte Parameter and Independent Variables

Predictor Variables	Na^+		K^+		Cl^-	
	r	P	r	P	r	P
Sex	0.039	0.517	0.33	0.580	−0.015	0.800
Age	0.611	0.004	−0.45	0.454	0.072	0.231
Marital status	0.074	0.218	0.22	0.711	0.025	0.674
Education	0.005	0.929	−0.092	0.128	−0.004	0.943
Occupation	0.103	0.089	−0.004	0.943	0.039	0.520
Duration of diabetes	0.097	0.107	0.057	0.342	0.039	0.520
Type of medication	0.050	0.408	0.752	0.001	−0.061	0.312
Hypertension	−0.076	0.206	−090	0.134	0.023	0.699
BMI	0.145	0.016	−0.003	0.956	0.645	0.459
SBP	0.106	0.078	−0.002	0.976	0.174	0.004
DBP	0.053	0.378	0.003	0.956	0.053	0.385
Alcohol drinking	−0.011	0.852	0.017	0.774	0.033	0.580
Cigarette smoking	0.083	0.167	−0.057	0.343	0.110	0.067
FBG	−0.225	0.000	0.110	0.068	−0.208	0.001

Notes: r= Pearson's correlation coefficient, p= p value for correlation, Na^+ =serum sodium, K^+= serum potassium and Cl^-= serum chloride.
Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar.

monitor their blood glucose level (AOR: 2.9,95% C.I: 1.292–6.441, P value: 0.010). Moreover, diabetic patients who did not monitor their blood glucose level at normal or hyperglycemic diabetic patients were about 3.2 times more likely to develop abnormal serum electrolyte levels when compared to those whose fasting blood glucose level was not well monitored or hyperglycemic during study period (AOR:3.2, 95% C.I: 2.179–5.721, P value: 0.000) (Table 2).

Discussion

Electrolytes play a vital role in maintaining homeostasis within the body by regulating fluid balance, oxygen delivery, acid-base balance, heart and neurological functions. However, the level of an electrolyte in the body can be too high or too low leading to an electrolyte imbalance. There was a high prevalence of one or more electrolyte abnormalities in diabetic patients in this study. Among serum electrolytes assessed, hyponatremia or low serum sodium concentration was the most prevalent abnormality in diabetic patients.[2,13,16,21,24,26–31] The low serum concentration of sodium ion in diabetic patients may be due to osmotic diuresis induced hypovolemia. This means glucose is a substance with high osmotic activity, so its high concentration or hyperglycemia leads to increased serum osmolality that causes movement of water out of the cells and causes hypo-natremia by dilution. Hypokalemia or abnormally low blood potassium level was the second electrolyte imbalance assessed in diabetic patients. Other studies also identified abnormally low serum level of potassium in diabetic patients.[2,3,16,26,28,32–35] The main reason for the abnormal level of potassium may be related to insulin treatment. When insulin is administered and glucose is taken up by the cells, potassium passes through the cell membrane along with glucose, decreasing the concentration of potassium both in blood and intracellular fluid. The other possible reason for hypokalemia is related to sodium–potassium pump which reverses the diffusion of cellular K^+ out of cells and Na^+ into cells caused by transmembrane electrical gradients. This sodium–potassium pump is stimulated by two hormones, insulin and catecholamine, through β-2-adrenergic receptors, and alterations in levels of these hormones can affect K^+ transport and its serum levels. Diabetic hyperchloremia or high serum concentration level of chloride ion in diabetics was the third abnormal serum electrolyte assessed in this study. Similar findings were reported from different studies.[2,11,13,23,26]

We also assessed the correlation between serum electrolyte abnormality and independent variables. Based on the finding some variables like cigarette smoking, abnormal BMI and age revealed positive correlation with hyponatremia and diabetic medication also revealed positive correlation with hypokalemia whereas cigarette smoking had positively correlated with hyperchloremia. Bivariate and multivariate logistic regression statistics were analyzed to assess the association between independent and dependent variables. Based on this assessment, three independent variables namely mixed medication (insulin plus

Table 2 Bivariate and Multivariate Logistic Regression and Associated Risk Factors Among Diabetic Patients Assessed for Serum Electrolyte

Variable	Category	COR	95% CI	P value	AOR	95% C.I.	P value
Sex	M F	0.732 1	0.451–1.190	0.208	1.599 1	0.958–2.787	0.097
Age in years	19–28 29–38 39–48 49–58 ≥58	1 1.079 1.349 0.911 0.562	 0.383–3.042 0.633–2.875 0.453–1.830 0.301–1.051	 0.885 0.438 0.793 0.793	1 1.479 1.349 0.911 0.562	 1.383–3.042 0.633–2.875 0.453–1.830 0.301–1.051	 0.885 0.438 0.793 0.793
Occupation	Employed Unemployed	0.305 1	0.092–1.015	0.053	3.933 1	1.057–14.637	0.041
Type of DM	Type 2 Type 1	1.085 1	0.663–1.776	0.746	2.149 1	0.947–4.875	0.067
Diabetes duration	5–15years ≤ 5 years	1 0.800	 0.382–1.677	 0.555	 0.800	 0.382–1.677	 0.655
Medication type	Mixed (oral and Insulin) Insulin alone	0.626 1	0.387–1.013	0.08	2.885 1	1.292–6.441	0.010
Hypertension	Yes No	1.189 1	0.736–1.922	0.480	1.21 1	0.736–1.922	0.490
BMI	Abnormal Normal	1.171 1	0.725–1.891	0.519	1.171 1	0.725–1.891	0.519
Alcohol drinking	Yes No	0.617 1	0.227–1.674	0.343	0.617 1	0.227–1.674	0.343
Cigarette smoking	Yes No	1.386 1	0.192–9.985	0.746	1.386 1	0.192–9.985	0.746
FBS	Hyperglycemic Normoglycemic	3.03 1	0.176–0.524	0.000	3.20 1	2.179–5.721	0.000

Abbreviations: BMI, body mass index; FBS, fasting blood sugar.

oral anti-hyperglycemic), abnormal fasting blood glucose level, and being employed were identified as independent predicator variables for the abnormality of serum electrolyte levels.[23,31]

Limitation

It is difficult to identify the causes of abnormal serum electrolytes in diabetic patients due to the nature of study design which describes only what is happening at a present time. We also did not try to compare the serum electrolyte concentration levels among type 1 and type 2 diabetics.

Conclusion

The overall serum electrolyte concentration level in diabetic patients was highly abnormal and the prevalence of abnormality was highest in diabetic patients with advanced age. The degree of correlations between the abnormal serum electrolyte concentration level and independent variables had great variation in diabetic patients.

Ethical Consideration

Ethical clearance was obtained from ethical review board of College of Health Sciences and then given to Jimma University Medical Center (JUMC) director's office. Next, a permission letter to conduct the study was obtained from the JUMC director's office and provided to the head of chronic illness clinic of JUMC. At the chronic illness clinic, the aim of the study was clearly explained to each study participant and then, informed consent was obtained voluntarily from each study subject before any data collection. The study was conducted in accordance with the Declaration of Helsinki.

Acknowledgments

We would like to thank the study participants for voluntarily participating in this research project, Jimma University Medical Center laboratory for allowing us to use clinical chemistry analyzers, and Jimma University for funding the research project.

Disclosure

The authors report no conflicts of interest in this work.

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