SERUM ELECTROLYTES LEVELS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL STUDY

© Shridhar Reshma, Sushith Sushith*, Mangalore Balakrishna Prathima, D'Sa Janice, Gopal R Madan, Pragathi Gowda, Kiran PK Kumar, Mohandas Rai, Bhuvanesh Sukhlal Kalal*

A.J. Institute of Medical Sciences and Research Centre, Karnataka, India

BACKGROUND: Diabetes Mellitus (DM) is a common metabolic disease worldwide. Electrolyte played significant roles in the normal functioning of the body, and deregulation is indicative of different types of disease and electrolyte disturbances are often reported in type 2 DM (T2DM).

AIM: The aim of the study was to estimate the levels of serum electrolytes in outpatients with T2DM and correlate serum electrolytes with random blood sugar (RBS).

MATERIALS AND METHODS: Patients with T2DM visiting the outpatient Departments of Medicine, between April 2016 and March 2017 were included. Of 148 diagnosed T2DM cases, 74 were had RBS level >300mg/dL (group-1) and 74 had RBS level ≤300mg/dL (group-2). Serum sodium (Na^+), potassium (K^+), chloride (Cl^-) levels were measured by using the Roche 9180 electrolyte analyzer.

RESULTS: In this study, there was a significant decrease in serum Na^+ levels in group 1 (131.83±4.36 mmol/L) compared to group 2 (134.15±4.90 mmol/L).The serum levels of K^+ was found to be increased in group 1 (4.51±0.61 mmol/L) in comparison with group 2 (4.26±0.52 mmol/L). In group-1, an inverse relationship was present between serum Na^+ (r=-0.342) and Cl^- (r=-0.538) with RBS which was statistically significant. In group-2, a significant correlation was present between serum K^+ and RBS (r=0.356, p<0.05).

CONCLUSIONS: The study showed lower levels of Na^+ and higher K^+ levels in group-1 compared to group-2 subjects. This study showed that the distribution of serum Na^+ and K^+ levels is dependent on plasma glucose levels in patients with DM and also suggests that monitoring the electrolyte levels in hyperglycemia is pertinent in the management of diabetes.

КЛЮЧЕВЫЕ СЛОВА: diabetes mellitus; hyperglycemia; electrolyte; Na^+; K^+; blood sugar

КОНЦЕНТРАЦИЯ ЭЛЕКТРОЛИТОВ СЫВОРОТКИ КРОВИ У ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ 2 ТИПА: ПОПЕРЕЧНОЕ ИССЛЕДОВАНИЕ

© S. Reshma, S. Sushith*, M.B. Prathima, D. Janice, G.R. Madan, P. Gowda, K.P. Kumar, M. Rai, B.S. Kalal*

A.J. Institute of Medical Sciences and Research Centre, Карнтака, Индия

АКТУАЛЬНОСТЬ. Сахарный диабет (СД) – это частое метаболическое заболевание, распространенное во всем мире. Электролиты играют большую роль в нормальном функционировании организма, нарушение регуляции служит признаком различных типов заболевания. Электролитные нарушения часто выявляют при СД 2 типа (СД2).

ЦЕЛЬ. Целью этого исследования было определение концентрации электролитов сыворотки крови у амбулаторных пациентов с СД2 и выявление корреляции между их уровнями и концентрацией глюкозы в крови при случайном измерении (случайный уровень глюкозы – СУГ).

МЕТОДЫ. В исследование включены пациенты с СД2, посещающие амбулаторное отделение Биохимии и медицины в период с апреля 2016 г. по март 2017 г. Из 148 пациентов с диагностированным СД2 у 74 пациентов СУГ был >300 мг/дл (группа 1) и у 74 пациентов – ≤300 мг/дл (группа 2). Концентрации натрия (Na^+), калия (K^+), хлорида (Cl^-) измеряли с помощью анализатора электролитов Roche 9180.

РЕЗУЛЬТАТЫ. В этом исследовании в группе 1 выявлено значимое снижение концентрации Na^+ в сыворотке крови (131,83±4,36 ммоль/л) по сравнению с группой 2 (134,15±4,90 ммоль/л). Концентрация K^+ в сыворотке крови была выше в группе 1 (4,51±0,61 ммоль/л) по сравнению с группой 2 (4,26±0,52 ммоль/л). В группе 1 отмечена статистически значимая обратная корреляция между Na^+ (r=-0,342) и Cl^- (r=-0,538) сыворотки крови и СУГ. В группе 2 значимая корреляция обнаружена между концентрацией K^+ в сыворотке крови и СУГ (r=0,356, p<0,05).

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ЗАКЛЮЧЕНИЕ. Исследование показало, что в группе 1 концентрации Na^+ были ниже, а K^+ выше, чем в группе 2. Результаты исследования показали, что у пациентов с СД распределение концентраций Na^+ и K^+ в сыворотке крови зависит от концентрации глюкозы в плазме крови, и также свидетельствуют об обоснованности контроля концентраций электролитов при гипергликемии в лечении СД.

KEYWORDS: сахарный диабет; гипергликемия; электролит; Na^+; K^+; глюкоза крови

Diabetes mellitus (DM) is a metabolic disorder with heterogeneity that is characterized by the common feature of chronic hyperglycemia and disturbances in carbohydrate, fat and protein metabolism [1, 2]. Approximately 1% of the global population suffers from DM. The incidence is rising in the developed countries of the world, especially of type 2 DM (T2DM), due to the rising incidence of obesity and reduced physical activity levels. Diabetes Mellitus is expected to continue as a major health problem owing to its serious complications, especially end-stage renal disease, ischemic heart disease, gangrene of the lower extremities and blindness in the adults [3].

T2DM is characterized by both insulin resistance and defective insulin secretion. The chronicity of hyperglycemia causes damage to blood vessels and nerve cells through the body, producing microvascular complications such as retinopathy, neuropathy, and nephropathy [4].

Electrolytes play an important role in many of the body processes, such as controlling fluid levels, maintenance of acid-base balance (pH), nerve conduction, blood clotting, and muscle contraction. Imbalance in the electrolyte levels that results from kidney disease, dehydration, fever, diarrhea, vomiting has been implicated as one of the contributing factors towards the development of complications that is observed in diabetes mellitus and other related endocrine disorders [5, 6]. The electrolytes in serum include sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), and magnesium (Mg^{2+}). These electrolytes play an important role in intermediary metabolism and cellular function, including enzyme activities and maintenance of electrical gradients [7]. The levels and concentration of serum electrolytes have a correlation with the levels of plasma glucose levels. Disturbance in the levels of some electrolytes are associated with diabetes mellitus (DM) and can prove to be crucial [8, 9].

Recent studies implicate the vascular etiology for diabetic-related complications like neuropathy, nephropathy, and hypertension. An inverse relationship between serum Na^+ and K^+ levels in a diabetic coma has been reported [10]. This dissociation may be on the basis of the movement of electrolytes between intra- and extracellular spaces that are dependent on impaired and reduced insulin action [11]. Na^+ K^+ ATPase pump in the red blood cells play a crucial role in the maintenance and regulation of intracellular and extracellular cationic homeostasis [12]. The alterations of this transport enzyme are linked to the various complications of DM [8, 13]. The decrease in this enzyme activity has been implicated in the pathogenesis of diabetic polyneuropathy.

Electrolyte imbalance is common in diabetic patients and this may be associated with increased complications along with raised morbidity and mortality. This kind of disturbances is frequently seen in decompensate DM, in the geriatric group, as well as in the presence of renal impairment. The patients with DM receive complex drug regimens of which some of them may be associated with electrolyte disorders. Careful monitoring of these medications along with strict control of glycemia is of utmost importance in order to prevent electrolyte abnormalities in diabetic patients. In general, the electrolyte imbalances are seen in hospitalized patients but studies have shown that community subjects are also frequently affected [11]. Thus for the successful management of these disorders in the best interest of the patients, the underlying pathophysiologic mechanisms should best be elucidated [14].

Hyperglycemia is the most common metabolic adverse events occurred in acute illnesses and is associated with increased morbidity and mortality. The association of diabetes with hyperglycemia and death are not well established but there are some reports that suggest that the diabetes patients with hyperglycemia (with a blood glucose of ≥300 mg/dL) may suffer worse consequences than those with diabetes patient who has a blood glucose of <300 mg/dL [15].

Hyperglycemia can be mediated by several factors such as stress hormones (e.g., epinephrine and cortisol) and hepatic enzyme. Catecholamines lead to an increase in adipose tissue lipolysis and skeletal muscle proteolysis. The hyperglycemia condition causes the disturbance of cell surface receptors and transport channels which move the fluid and electrolytes from the intracellular to the extracellular space that will result in cellular dehydration [16]. These dehydration conditions cause changes in the metabolism machinery of cells that can progress in several severe complications. Hyperglycemia has been linked to the downregulation of the immune system, inflammatory changes, increased cardiovascular response, thrombosis, poor hippocampal neurons response, and other problems [17]. Therefore, poorly controlled hyperglycemia is associated with increased morbidity and mortality in critically ill patients [18].

AIM

Accordingly, this study was aimed to quantitatively estimate serum electrolytes (sodium, potassium, and chloride) in the outpatients with diabetes mellitus and to correlate their levels in T2DM in the study groups as the electrolyte variation in diabetes mellitus may be helpful in the diagnosis and description of the disease.

MATERIALS AND METHODS

Study Population

The cross-sectional study was conducted between April 2016 – March 2017, in the outpatient departments of Biochemistry and Medicine, on confirmed cases of DM with the age of 25 to 60 years. A total of 148 DM subjects were included in the study, out of which two groups were formed: group 1 (74 were with random blood sugar (RBS) level of more than 300mg/dl [16.7 mmol/L]) and group 2 (74 were with RBS level of less than 300mg/dl). Diagnosis of DM diabetes mellitus was based on the WHO criteria using fasting blood glucose, postprandial blood glucose, and random blood glucose. The RBS cut off point of 300 mg/dl was taken, as mentioned in [15, 19].

The study protocol was approved by the Ethics Committee of the Institution. Voluntary informed consent was taken from the subjects prior to the study (Ref no. ECR/348/INST/KA/2013).

Pregnant women and subjects with renal disease, hepatic disease, cardiac disease, and hypertension were excluded from the study.

Sample collection and analysis:

Blood samples collected with aseptic precaution from patients DM after obtaining written informed consent. 2 ml of blood was collected in sodium fluoride and plain vacutainer. After 30 minutes the blood sample was centrifuged with 3000 rpm for 10 minutes to separate plasma and serum from the cells.

Glucose estimation was done on the plasma sample and electrolytes were processed in a serum sample. All the assays were done in $BiOLiS_2$4i premium Automated Chemistry Analyzer and AVL 9180 Electrolyte Analyzer. The instructions of the manufacturer were followed. The accuracy and precision of the values were ensured by internal and external quality control measures.

Estimation of blood glucose:

Glucose estimation was done on the plasma samples using $BiOLiS2_4$i premium automated chemistry analyzer after the validation of QC.

Method: GOD-POD Method.

$$\text{Glucose} + O_2 \xrightarrow{\text{glucose oxidase}} \text{glucuronic acid} + H_2O_2$$

$$2H_2O_2 + \text{Phenol} + \text{4-aminoantipyrine} \xrightarrow{\text{peroxidase}} \text{red Quinonimine} + 4H_2O$$

The quinonimine is directly proportional to the concentration of glucose and is measured by photometrically by 505 nm using the reference value given in table 1. The assay is a fixed time kinetic/endpoint reaction.

Estimation of serum electrolytes

Serum samples were analyzed by AVL 9180 Electrolyte analyzer after the validation of QC. The 9180 electrolyte analyzer is a sophisticated medical instrument that uses the ion-selective electrode measurement principle to precisely determine electrolyte values using a reference value of table 2.

Statistical Analysis is done by Student t-test & Karl-Pearson correlation test using IBM SPSS Statistics 22.0

RESULTS

The mean age patient was 53.3±8.7 years and 56.5±10.1 years in group 1 and group 2 respectively. There were 61% and 66% male in group 1 and group 2 respectively.

Table 3 shows the biochemical measurements which include Random blood sugar, Na^+, K^+, and Cl^- ion levels in both the diabetic control groups. Random blood sugar, Na^+, and K^+ ions were significantly elevated in the diabetic with hyperglycemia condition.

In Group 1, an inverse relationship was observed between serum Na+ (r=-0.342) and Cl- (r=-0.538) with RBS which was statistically significant (Fig. 1). In group 2, there was a positive correlation of blood glucose with Na^+, K^+, and Cl^- ions but K^+ had a significant positive correlation with RBS. ($r = 0.356$, $p<0.05$).

Table 1. Reference value of fasting, post-prandial and random blood sugar [20].

Analyte	Sample	Conventional unit	Conversion factor	SI unit
FBS	Plasma	70–100 mg/dl	0.0555	4.1-5.6 mmol/L
PPBS	Plasma	Less than 140 mg/ dl	0.0555	Less than 7.8 mmol/L
RBS	Plasma	100–140mg/dl	0.0555	5.5–7.7 mmol/L

Notes: FBS – fasting blood sugar; PPBS – postprandial blood sugar; RBS – random blood sugar.

Table 2. Reference value of Na^+, K^+, Cl^-[20].

Analyte	Sample	Conventional unite	Conversion factor	SI units
Sodium	Serum	136–145 mEq/L	1.0	136–145 mmol/L
Potassium	Serum	3.5–5.1 5 mEq/L	1.0	3.5–5.1 mmol/L
Chloride	serum	96–107 mEq/L	1.0	96–111 mmol/L

Table 3: Comparison of biochemical parameters between the two groups

Parameter	Group 1(n=74) (blood sugar >300mg/dL)	Group 2 (n=74) (blood sugar ≤300mg/dL)	P value
Random blood sugar (mg/dL)	390.17±95.56	193.65±37.71	<0.001**
Serum Sodium (mmol/L)	131.83±4.36	134.15±4.90	<0.05*
Serum Potassium (mmol/L)	4.51±0.61	4.26±0.52	<0.05*
Serum Chloride (mmol/L)	97.60±4.20	100.70±12.63	0.160

Notes: p value < 0.05 *, p value < 0.01 ** were significant.

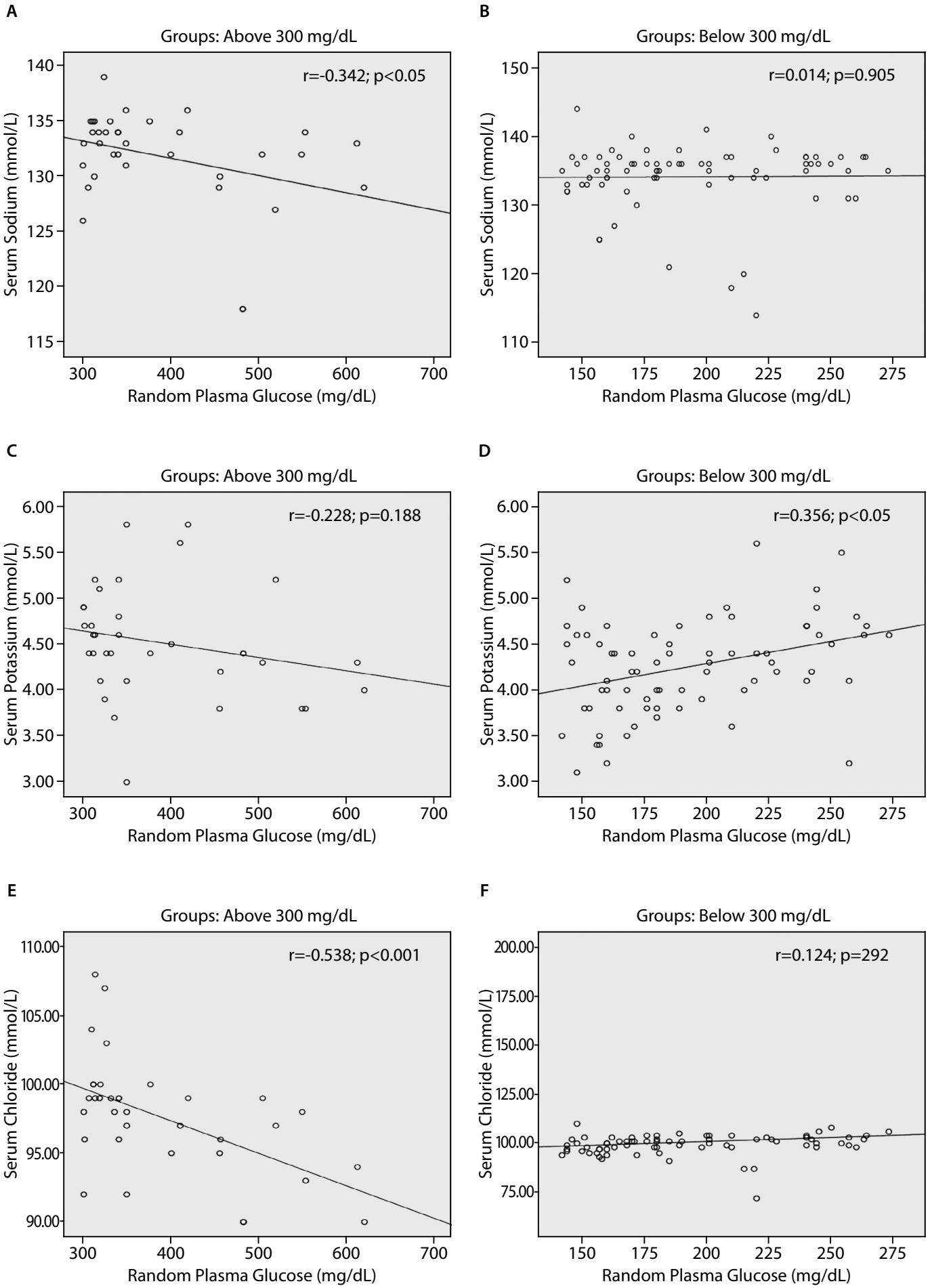

Figure 1: Correlation between the blood glucose and sodium (A, B), potassium (C, D) and chloride (E, F) during severe hypoglycemia (left panel) and diabetes control (right panel).

DISCUSSION

T2DM is an endocrine disease associated with hyperglycemia, characterized by both insulin resistance and defective insulin secretion. T2DM is a major global health problem that affects 200 million individuals globally [21]. The relationship of DM with minerals has been reported by many authors [14, 16, 19, 20]. Among these minerals Na^+, K^+ and Cl^- are of particular interest.

This study was designed to evaluate and compare the serum levels of electrolytes, sodium, potassium, and chloride in the outpatients with DM (group1 and group 2). The study showed a significant decrease in serum sodium level and a significant increase in potassium level in patients in group 1 (RBS >300mg/dl) compared to group 2 (RBS<300 mg/dl). Holkar S, Vaishnav D et.al, also found out a significant (P<0.001) decrease in the levels of serum sodium in cases (126.2±2.7 mEq/L) as compared to controls (139.3±0.8 mEq/L) and significant (P=0.05) increased levels of serum potassium in cases (5.73±0.07 mEq/L) as compared to controls (4.22±0.03 mEq/L) [22]. Similarly, Reza et al., 2015 [13] and, Hasana et al, 2016 [9] also demonstrated the hyperglycemia-induced effects on cellular transport process, dysfunction of Na^+, K^+ ATPase plays a major role in mediating the electrolyte imbalances in diabetes. However, Shahid et al. showed that the levels of serum Na^+ were elevated (142.07 + 42.02 v/s 136.82 + 16.22 mEq/L) in diabetic patients but not significantly (P<0.005) whereas in potassium (7.41 + 1.8 v/s 5.03 + 1.5 mEq/L) was increased significantly (P<0.005) as compared to control subjects [8].

In this study in group 1, an inverse relationship was observed between serum Na^+ (r=-0.342) and Cl^- (r=-0.538) with RBS which was statistically significant. In group 2, a significant correlation was present between serum K^+ and RBS. (r=0.356, p<0.05). These results concurred with T Saito et al. who reported an inverse relationship between serum Na^+ and K^+ levels in diabetic coma patients and a negative correlation between serum Na^+ levels and fasting plasma glucose (FPG), and positive correlation between serum K^+ levels and FPG. The disorder may be based on the excessive shifting of electrolytes across the cell membrane, dependent on the impaired insulin action as well as hyperosmolality [10]. Cell membrane transporter's dysfunctions have been reported in diabetic patients. impaired ion exchange system can enhance the activity of the transport system that can lead to an increase in Na+ can be secondary to hyperglycemia [23]. Electrolyte disturbance may complicate both acute and chronic metabolic abnormalities of diabetes. Thus, in this study, based on levels of RBS cutoff (more than and less than 300), the serum electrolytes levels of diabetic patients were compared.

Our study shows decreased Na^+, increased K^+ level in T2DM. These alterations of sodium and potassium levels may be pathophysiologic and clinically characteristic of diabetes. The hyperglycemia produces osmotic diuresis causing changes in the distribution of electrolytes between intra- and extracellular spaces. In addition, this effect of hyperosmolality, it may also depend on the effect of insulin on the electrolytes. Increased serum osmolality, resulting in movement of water out of the cells and subsequently in a reduction of serum sodium Na^+ by dilution leads to hypernatremia and hyperkalemia in the serum of the risk group (RBS <300). Osmotic force is a driving force for the movement of water and draws water to the extracellular space. Disturbance in osmotic can change the ions levels across the membrane. vasopressin, is an antidiuretic hormone that is a major regulator of water balance and aberrations can lead to an uncommon condition called diabetes insipidus, in which the kidneys are unable to prevent the excretion of water [24, 25]. Therefore, the management hypernatremia and hyperkalemia in severe cases of diabetes are important.

CONCLUSION

This study demonstrated a significant reduction in blood sugar and serum sodium level while significant elevation of potassium levels among severe T2DM patients compared to diabetes control. Serum sodium and chloride showed significant inverse association while potassium had significant positive correlation with RBS of severe T2DM patients compared to diabetes control.

Alterations of serum electrolytes levels may be pathophysiologic and clinically characteristic of diabetes. Frequent monitoring of electrolytes even in the outpatients will be useful to prevent complications associated with electrolyte imbalance.

ADDITIONAL INFORMATION

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Conflicts of Interest: Authors declare no conflicts of interest.

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AUTHORS INFO

***Sushith Sushith**, MD; address: NH 66, Kuntikan, Mangalore, Karnataka 575004, India; ORCID: https://orcid.org/0000-0001-8047-9127; e-mail: drsushith@yahoo.com

***Bhuvanesh Sukhlal Kalal**, PhD; address: NH 66, Kuntikan, Mangalore, Karnataka 575004, India; ORCID: https://orcid.org/0000-0002-2560-3778; e-mail: bhuvanesh611@gmail.com

Shridhar Reshma, MD; ORCID: https://orcid.org/0000-0002-2168-075X; e-mail: drreshmakiran@gmail.com
Mangalore Balakrishna Prathima, MD; ORCID: https://orcid.org/0000-0002-2302-254X; e-mail: mbprathima@gmail.com
D'Sa Janice, MD; ORCID: https://orcid.org/0000-0003-3002-1649; e-mail: janicedsa@gmail.com
Gopal R Madan, MD; ORCID: https://orcid.org/0000-0002-2678-0303; e-mail: madanbiochem@gmail.com
Pragathi Gowda, MD; ORCID: https://orcid.org/0000-0002-6964-968X; e-mail: gowdap@gmail.com
Kiran PK Kumar, MD; ORCID: https://orcid.org/0000-0003-0144-7341; e-mail: kumarpk@gmail.com
Mohandas Rai, MD; ORCID: https://orcid.org/0000-0002-4654-4332; e-mail: mohandassrao@gmail.com

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