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Original article

Serum electrolyte levels in Libyan patients with type II diabetes mellitus

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Abstract: The incidence of diabetes mellitus has increased globally making it a major public health concern. Diabetes mellitus is the most common metabolic disorder that causes an imbalance in the electrolytes which regulate essential metabolic mechanisms of the body. This study aimed to estimate the electrolyte levels in Libyan patients with type II diabetes mellitus and to investigate their relations to glycemic control and body mass index. A total of 122 Libyan subjects whose ages ranged between 35 years and 60 years for both sexes were included in this study, 77 patients were type II diabetic patients (37 males and 40 females) and 45 subjects were healthy individuals (23 males and 22 females) live in Tripoli area, Libya. The levels of blood glucose, HbA1c, sodium, potassium, chloride, magnesium and calcium were estimated in this study along with the measurement of body mass index, systolic and diastolic blood pressure. All the findings were statistically analyzed by one-way ANOVA test. Significant increases in glucose, HbA1c, potassium, chloride, calcium, blood pressure and BMI among diabetic patients were observed as compared to the healthy individuals. On the other hand, significant decreases in sodium and magnesium levels among the diabetic patients were observed as compared to the control group. In addition, significant alterations in all the biochemical parameters in uncontrolled diabetic patients as compared to the controlled diabetic patients, and in unhealthy weight diabetic patients as compared to the healthy weight patients. It is concluded that diabetes mellitus results in an imbalance of electrolytes. Poor glycemic control and obesity have adverse effects on electrolyte balance among diabetic Libyan patients. Good glycemic control, maintaining a healthy weight and regular evaluation of electrolytes among diabetics can reduce the fatalities associated with electrolyte rearrangements.

Introduction

Diabetes mellitus (DM) is a heterogeneous group of metabolic disorders characterized by high blood glucose levels (hyperglycemia) due to relative or absolute deficiency of insulin resulting in changes in carbohydrate, lipid, protein, water and electrolyte metabolism [1, 2]. Now, the prevalence rate of DM has increased and has become a major pandemic and an alarming issue worldwide.

According to the International Diabetes Federation, the number of patients affected by DM reached 463 million in 2019 and is expected to reach 578 million in 2030, and perhaps 700 million in 2045. North Africa and the Middle East had the highest prevalence of DM in the adult population aged between 20 years and 79 years in 2019 (12.2%) and are expected to be the highest in 2030 and 2045

(13.3% and 13.9%, respectively). In 2019, the prevalence of DM in Libya was estimated at around 9.7% [3]. Electrolytes play an essential role in many of the body's processes, such as controlling fluid levels, maintenance of acid-base balance (pH), nerve conduction, blood clotting, and muscle contraction [4, 5]. Moreover, they play a crucial role in cellular function and metabolism including enzyme activity. Imbalance of electrolytes is associated with DM [6, 7], and has been implicated as one of the contributing factors towards the development of complications that are observed in DM [8 - 10]. This correlation may be due to impaired and reduction in insulin action which results in the movement of electrolytes between intra- and extra-cellular causing osmotic diuresis [11, 12]. Moreover, hyperglycemia causes the disturbance of cell surface receptors and transport channels which move the fluid and electrolytes from the intracellular to the extracellular space which will result in cellular dehydration causing changes in the metabolism machinery of cells and contributing to the progress of DM complications [13, 14]. Several studies have reported the association of electrolyte disturbance with type II DM and the adverse effects of glycemic control and obesity on the levels of electrolytes which could be a leading cause of morbidity and mortality to the patients. The data regarding the adverse effects of glycemic control and obesity on electrolyte levels among diabetics in Tripoli, Western Libya are unavailable, which could be one of the contributing factors to morbidity and mortality among diabetics in Libya. Therefore, the study aimed to estimate serum electrolyte levels among patients with type II DM. Secondly, evaluating the extent effect of glycemic control on electrolyte homeostasis among diabetics. It also evaluates the effect of obesity on electrolyte homeostasis among diabetic patients.

Materials and methods

Study population: A case-control study was conducted on Libyan subjects from May to July 2023 at Janzur Hospital, Tripoli, Western Libya. A total of 122 subjects whose ages ranged between 35 years and 60 years for both sexes were included in this study, 77 subjects were type II diabetic patients (37 males and 40 females) and 45 subjects were healthy individuals (23 males and 22 females). Both groups were matched for age and sex. The study protocol was approved by the Ethical Committee at Tripoli College of Medical Sciences (2022). All the participants presented their verbal agreement and signed the consent forms. They were informed of the purpose of the study and requested to complete the questionnaires.

Sample collection: Five milliliter of venous blood was collected after fasting for 8 - 12 hours from each participant for the measurement of glucose, glycosylated hemoglobin (HbA1c), sodium (Na), potassium (K), chloride (Cl), magnesium (Mg) and calcium (Ca). The blood was collected in sodium fluoride to estimate blood glucose and ethylene-diamine-tetraacetic acid (EDTA) to estimate glycosylated hemoglobin (HbA1c). The blood was allowed to clot and centrifuged at 4000 rpm to 15 min for obtain serum. Serum was used to estimate Na, K, Cl, Mg and Ca levels. Body Mass Index (BMI) (kg/m^2) was calculated for all the patients. Blood pressure (systolic and diastolic pressure) was recorded in both arms after five min of sitting. Demographic characteristics of the study population, including (name, age and sex), family history, medical history, medication, occupation, physical activity and lifestyle patterns were all obtained by a structured questionnaire.

Biochemical parameters: Blood glucose, HbA1c, Na, K, Cl, Mg and Ca levels were all biochemically estimated in the current study. The method used for measuring blood glucose was GOD-PAP method by photometer 4040 Fulfils. While HbA1c was a sandwich immunodetection method by Ichroma made in Korea. Na, K and Cl levels were analyzed using ISE in Beckman Coulter AU 680 analyzer. Mg and Ca levels were estimated by the calmagit complexometric method and complexometric dye methods, respectively.

Inclusion criteria: 77 subjects were known type II diabetic patients whose ages ranged between 35 years and 60 years for both sexes and 45 healthy subjects without any history of diseases were included in this study.

Exclusion criteria: Patients suffering from type I DM, gestational DM, or any kind of chronic disease affecting electrolyte disturbance such as kidney, heart and endocrine diseases. Patients who are suffering from a history of complications of DM. Patients suffering from vomiting and diarrhea. Taking any kind of medication or supplementation affects the value of electrolytes such as thiazide diuretics. Pregnant or lactating women were excluded from the study.

Statistical analysis: All data were presented as means and standard deviations and analyzed by using Statistical Package for Social Sciences (SPSS-version 25). An analysis of variance by one-way test (ANOVA) was used to compare the means of the variables among the groups. Statistical difference between variables was considered at $p < 0.01$ was considered significant.

Results

Table 1 illustrates means and standard deviations of age and biochemical parameters of blood glucose, HbA1c, Na, K, Cl, Mg, and Ca levels for both groups (patient and control groups). Total mean ages were statistically not significant (44.05 ± 6.77 and 44.73 ± 7.19 for the patients and control groups, respectively). Total blood glucose levels significantly differed in both groups (173.28 ± 27.89 mg/dl and 92.91 ± 10.32, while HbA1c were 7.51 ± 1.93 and 5.12 ± 0.69 for patient and control groups, respectively). The total mean levels of electrolyte (Na, K, Cl, Mg, Ca) were also found significantly changed (122.24 ± 9.78, 7.10 ± 1.54, 116.37 ± 10.24, 1.51 ± 0.41 and 10.80 ± 1.90 for diabetic patients, respectively, and 140.06 ± 3.20, 4.12 ± 0.48, 98.15 ± 3.36, 2.08 ± 0.29, and 9.11 ± 0.35 for healthy subjects, respectively). The total mean of BMI levels were higher (28.28 ± 4.70 and 22.62 ± 1.46 for the patient and control groups, respectively). The means of systolic pressure were also high (115.71 ± 23.36 and 99.72 ± 11.56, and diastolic pressure was 87.94 ± 13.68 and 73.85 ± 5.63 for patient and control groups, respectively). Thus, an overall analysis of the data by one-way ANOVA showed statistically significant difference in biochemical variables (blood glucose, HbA1c, Na, K, Cl, Mg, Ca, BMI, systolic and diastolic blood pressure) between patients and control groups at $p < 0.01$.

Table 1: Biochemical variables in Libyan diabetic patients

Parameters	(Diabetic patients)	(Healthy individuals)
Age (years)	44.05 ± 6.77	44.73 ± 7.19
BMI (kg/m^2)	28.28 ± 4.70 **	22.62 ± 1.46
Blood glucose levels (mg/dl)	173.28 ± 27.89 **	92.91 ± 10.32
HbA1c (%)	07.51 ± 1.93 **	05.12 ± 0.69
Sodium (mmol/L)	122.24 ± 9.78 **	140.06 ± 3.20
Potassium (mmol/L)	07.10 ± 1.54 **	04.12 ± 0.48
Chloride (mg/dl)	116.37± 10.24 **	98.15 ± 3.36
Magnesium (mg/dl)	01.51 ± 0.41 **	02.08 ± 0.29
Calcium (mg/dl)	10.80 ± 1.90 **	09.11 ± 0.35
Systolic pressure (mmHg)	115.71 ± 23.36 **	99.72 ± 11.56
Diastolic pressure (mmHg)	87.94 ± 13.68 **	73.85 ± 5.63

** Significant different by one-way ANOVA ($p < 0.01$, data are mean ± SD)

Table 2 shows the effect of glycemic control on biochemical parameters and blood pressure. The diabetic patients were divided into two groups according to HbA1c levels. The first group in which HbA1c < 06.5% was considered as a controlled blood glucose group and the second group where HbA1c > 06.5% was considered as uncontrolled blood glucose. The means and standard deviations of biochemical parameters of blood glucose, HbA1c, Na, K, Cl, Mg and Ca levels for both groups (controlled and uncontrolled blood glucose groups). Total means and standard deviations of blood glucose levels were 152.5 ± 18.92 and 186.55 ± 24.46, whereas, HbA1c levels were 05.56 ± 0.73 and 8.75 ± 1.33 in controlled and uncontrolled blood glucose levels, respectively. The mean level of Na in the controlled blood glucose group was 129.1 ± 5.33, whereas, in the uncontrolled group was 117.87 ± 9.48. The mean of K levels in the controlled blood glucose was 5.84 ± 0.67, while, in the uncontrolled group was 07.90 ± 1.40, while Cl levels in the controlled and uncontrolled blood glucose were 108.75 ± 8.89 and 121.24 ± 7.83, respectively. Total means of systolic pressure were 103.8 ± 17.77 and 123.31 ± 23.48, whereas, diastolic pressure was 78.36 ± 6.45 and 94.06 ± 13.60 in controlled and uncontrolled groups, respectively. An analysis of the data by one-way ANOVA revealed a highly significant difference of the biochemical parameters (blood glucose, HbA1c, Na, K, and Cl) between controlled and uncontrolled blood glucose groups (**Table** 2).

Table 2: Variables in controlled and uncontrolled blood sugar of Libyan diabetic patients

Parameters Serum levels	Controlled blood sugar HbA1c < 6.5% 5.56 ± 0.73	Uncontrolled blood sugar HbA1c > 6.5% 8.75 ± 1.33
Age (years)	45.66 ± 7.63	43.02 ± 6.02
Blood glucose levels mg/dl	152.5 ± 18.92**	186.55 ± 24.46
Sodium (mmol/L)	129.1 ± 5.33**	117.87 ± 9.48
Potassium (mmol/L)	05.84 ± 0.67**	07.90 ± 1.40
Chloride (mg/dl)	108.75 ± 8.89**	121.24 ± 7.83
Magnesium (mg/dl)	02.07 ± 0.41**	01.38 ± 0.34
Calcium (mg/dl)	9.34 ± 0.96**	11.74 ± 1.75
Systolic pressure (mmHg)	103.8 ± 17.77**	123.31 ± 23.48
Diastolic pressure (mmHg)	78.36 ± 6.45**	94.06 ± 13.60

** Significant different by one-way ANOVA ($p < 0.01$, data are mean ± SD)

Table 3 illustrates the effect of the BMI on the biochemical parameters and blood pressure. The diabetic patient's results were divided into three groups according to BMI levels. The first group was the healthy weight group in which BMI levels were between 19.0 - 24.9 kg/m^2, the second group was the overweight group in whose BMI levels were between 25 and 30 kg/m^2, and the third group was the obese group in whose BMI levels were more than 30 kg/m^2. The means of biochemical parameters of blood glucose, HbA1c, Na, K, Cl, Mg and Ca levels for the three groups (healthy weight, overweight and obese groups). Total means of blood glucose levels were 145.43 ± 43.0, 179.43 ± 22.12 and 189.38 ± 24.6, and of HbA1c levels were 05.5 ± 0.77, 07.5 ± 1.65 and 08.8 ± 1.39 for healthy body weight, overweight and obese groups, respectively. The total means of Na levels were 131 ± 4.3, 123.90 ± 4.8 and 115.09 ± 9.5 and of K levels were 05.5 ± 0.52, 07.4 ± 1.10 and 07.9 ± 1.52 for a healthy body weight, overweight and obese groups, respectively. The Cl levels were found to be 105.90 ± 7.99, 117.03 ± 4.43 and 123.25 ± 8.08 and of Mg levels were 1.92 ± 0.41.99, 1.41 ± 0.25 and 1.30 ± 0.28 for healthy body weight, overweight and obese groups, respectively. The Ca levels were 09.05 ± 0.71, 10.96 ± 1.21 and 11.93 ± 1.94 for healthy body weight, overweight and obese groups, respectively. The means of systolic pressure were 102.86 ± 18.10, 112.14 ± 18.53 and 126.93 ± 1.94, whereas diastolic pressure was 77.95 ± 5.65, 85.14 ± 8.38 and 96.69 ± 14.94 for healthy body weight, overweight and obese groups, respectively. All the biochemical parameters and blood pressure levels were highly statistically different among the three groups at $p < 0.01$.

Table 3: Comparison of variables about body mass index of diabetic patients

Parameters	Body Mass Index			
	Healthy weight 19.0 - 24.9 kg/m^2 n = 23 22.69 ± 1.47	**Overweight 25 - 30 kg/m^2 n = 21** 26.93 ± 1.39	**Obese > 30 kg/m^2 n = 33** 33.03 ± 1.67	**P value Overall difference**
Age (years)	45.04 ± 7.48	44.57 ± 7.52	44.24 ± 7.15	0.90
Blood glucose (mg/dl)	145.43 ± 43	179.43 ± 22.12	189.38 ± 24.60	0.01
HbA1c (%)	05.5 ± 0.77	07.5 ± 1.65	08.8 ± 1.39	0.01
Sodium (mmol/L)	131.0 ± 4.3	123.90 ± 4.8	115.09 ± 9.5	0.01
Potassium (mmol/L)	05.5 ± 0.52	07.4 ± 1.10	07.9 ± 1.52	0.01
Chloride (mg/dl)	105.90 ± 7.99	117.03 ± 4.43	123.25 ± 8.08	0.01
Magnesium (mg/dl)	01.92 ± 0.41	01.41 ± 0.25	01.30 ± 0.28	0.01
Calcium (mg/dl)	09.05 ± 0.71	10.96 ± 1.21	11.93 ± 1.94	0.01
Systolic pressure (mmHg)	102.86 ± 18.10	112.14 ± 18.53	126.93 ± 1.94	0.01
Diastolic pressure (mmHg)	77.95 ± 5.65	85.14 ± 8.38	96.69± 14.94	0.01

** Significant different by one-way ANOVA ($p < 0.01$, data are mean ± SD)

Discussion

Type II DM is an endocrine disease affecting 200 million people around the world and is considered a major global health issue. It is characterized by insulin resistance and defective insulin secretion causing hyperglycemia leading to derangement of water and electrolyte balances [15, 16]. Several studies have reported the association of DM with the disturbance of electrolytes such as Na, K and Cl [17 - 20]. In the current study, there was a decrease in serum Na level 122.24 ± 9.78 among diabetic patients as compared to the control group 140.06 ± 3.20. Many studies were consistent with the current study which all showed a decrease in serum Na levels among type II diabetic patients [21 - 23]. Another study revealed that there are no significant changes in Na levels among type II diabetic patients which was in contrast to our study [24]. Osmotic diuresis caused by hyperglycemia in diabetic patients results in an increase in osmolality leading to the movement of water from intracellular space to extracellular space which dilutes the extracellular Na leading to lower serum Na levels. Furthermore, changes in the rennin angiotensin system in DM lead to alteration in Na concentration [25, 26]. It is reported that the relation between DM and decreased Na may be due to the changed vasopressin regulation [27].

The present study revealed that there is a significant increase in serum K (7.10 ± 1.54) among type II diabetic patients as compared to the control group (4.12 ± 0.48). The study was in line with a previous study that showed an elevation in K levels among diabetic patients as compared to the control group [28], and in contrast to other studies which showed a reduction in serum K levels [21, 29], while other studies showed that there is no significant alteration in K status [24, 30]. Increased K levels among diabetic patients can be caused by an increase in the activity of Na-K ATPase pump by promoting K influx into hepatic and skeletal muscle cells due to impaired insulin secretion [12]. Changes in this transport system are associated with several complications of DM [27]. The serum Cl value of the study was significantly higher in diabetic patients at 116.37 ± 10.24 than in the control group at 98.15 ± 3.36. Similar findings were observed in other studies which all showed an elevation in Cl levels among diabetic patients [22, 31]. Ketoacidosis causes alterations in acid-base balance by decreasing blood pH leading to elevation in Cl levels among diabetic patients [12, 31]. The serum magnesium level was significantly lower in diabetic patients 1.51 ± 0.41 as compared to the control group (2.08 ± 0.29). The finding has also been observed by another study which showed a reduction in Mg levels among diabetic patients [32]. Decreases in blood Mg levels are frequently observed in individuals with type 2 DM. It is reported that hypomagnesemia occurs in 13.5 - 47.7% of diabetic patients in comparison to 02.5 - 15.0% of patients without DM. Hypomagnesemia in diabetic patients can be caused by several mechanisms which include poor dietary intake, glomerular hyperfiltration, altered insulin metabolism, diuretic administration and recurrent metabolic acidosis [33, 34], moreover, osmotic diuresis accompanied by the inappropriate magnesiuria can lead to hypomagnesemia in diabetic patients [35]. Serum Ca was significantly higher in diabetic patients at 10.80 ± 1.90 as compared to the control group 9.11 ± 0.35. Elevated intracellular Ca concentration increases the requirement for insulin, resulting in hyperparathyroidism-mediated insulin resistance [36] hypercalcemia observed in diabetic patients could be due to hyperparathyroidism, thiazide therapy or elevated readsorption of renal calcium [11, 37]. A similar finding was observed by several studies [38 - 40]. Ca is mainly reabsorbed in the proximal tubule. Its reabsorption is coupled to Na absorption, and it competes with Mg for transport in the loop of Henle. In the distal convoluted tubule, numerous factors affect the absorption of Ca such as calcitonin, parathyroid hormone, and vitamin D, which can have marked effects on Ca reabsorption and secretion [41, 42]. Mg acts as a Ca antagonist in membrane channels and intracellular regions. Low Mg is associated with high Ca [43]. Another study conducted in 2021 emphasized that high Ca and low Mg levels are risk factors for diabetic retinopathy [44]. The findings of the present study showed an increase in systolic and diastolic pressure in diabetic patients (115.71 ± 23.36 and 87.94 ± 13.68) as compared to the control group (99.72 ± 11.56 and 73.85 ± 5.63). This study showed significant alterations in Na (reduction), K (elevation), Cl (elevation), Mg (reduction) and Ca (elevation) among uncontrolled diabetic patients (HbA1c > 6.5%) as compared to controlled diabetic patients (HbA1c < 6.5%) which could be due to hyperglycemia or insulin deficiency. The findings were consistent with a previous study that showed significant alteration in Na, K, Cl, Mg and Ca among uncontrolled diabetic patients [32]. The incidence of poor glycemic control among diabetic patients is high with hypomagnesaemia [45]. Further, the present study revealed significant changes in all the electrolytes (Na, K, Cl, Mg and Ca) and systolic, diastolic pressure in overweight and obese diabetic patients as compared to healthy-weight diabetic patients. In high BMI (obese or overweight), there is an increase in blood volume leading to an increase in blood pressure and haemodilution which contributes to changes in electrolyte levels. Another study stated that higher BMI can be a determining factor in increasing blood pressure [46, 47].

Conclusion: It may be concluded that diabetes mellitus results in the imbalance of electrolytes. Poor glycemic control and obesity have adverse effects on electrolytes levels among Libyan diabetic patients. Good glycemic control, maintaining a healthy weight with a regular evaluation of electrolyte levels among diabetic patients can reduce the fatalities associated with electrolyte rearrangements.

Author contribution: AAA contributed to data analysis, and interpretation of data & drafted, and revised the manuscript, YNA designed the study, and collected the data. HAS, EMA & AMA collected the data. All authors approved the final version of the manuscript and agreed to be accountable for its contents.
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Ethical issues: Including plagiarism, informed consent, data fabrication or falsification, and double publication or submission have completely been observed by authors.
Data availability statement: The raw data that support the findings of this article are available from the corresponding author upon reasonable request.
Author declarations: The authors confirm that all relevant ethical guidelines have been followed and any necessary IRB and/or ethics committee approvals have been obtained.

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