MALAYSIAN JOURNAL OF BIOCHEMISTRY & MOLECULAR BIOLOGY

The Official Publication of The Malaysian Society For Biochemistry & Molecular Biology (MSBMB)
http://mjbmb.org

EVALUATION OF ELECTROLYTES IMBALANCE AMONG TYPE2 DIABETIC MELLITUS IN SOUTH GAZA STRIP-PALESTINE

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History
Received: 13th March 2021
Accepted: 7th May 2021

Keywords:

T2DM, Electrolytes Imbalance, Sodium, Potassium, Calcium, Magnesium, Phosphorus

Abstract

Diabetic patients may suffer from imbalanced electrolytes due to complications such as thrombosis, hypertension, neuropathy and cardiomyopathy. Early detection can prevent the complications that occur due to the imbalance distribution. This study was carried out to evaluate the electrolytes imbalance in T2DM. A case-control study consisted of 200 subjects: 105 patients with T2DM collected from primary health care centers and 95 healthy persons as control group gathered from the community. A questionnaire interview was applied. Blood samples were collected in plain tubes. The serum levels of electrolytes: sodium, potassium, calcium, magnesium, and phosphorus were determined. The data were statistically analyzed by SPSS and p-value < 0.05 was considered significant. We found that 61% of cases had a family history of DM but in control was 9.9% which is statistically significant (p=0.000). The means of potassium and phosphorus were not significantly different between both groups, but the potassium and calcium levels were slightly elevated when compared with controls. The means of sodium, calcium and magnesium were statistically significant between both groups (P = 0.012, P = 0.013 and P =0.000 respectively). The percentage of hypomagnesaemia was increased in patients to reach statistically significant (26.67% in DM group and 1.05% in the control with p=0.0006). Hypomagnesaemia is more prevalent in our study in the diabetic population than the other electrolyte abnormalities. Screening for electrolyte imbalances should be considered in the diabetic population and necessary steps might be taken to prevent its consequences. Additional research is suggested for accurate assessment of the association of diabetes and electrolyte imbalance.

INTRODUCTION

Electrolytes play a crucial role in several body processes, such as regulating fluid levels, acid-base stability (pH), and maintenance of the transmission of nerve pulses, coagulation and muscle contraction [1]. Calcium (Ca^{+2}), Sodium (Na^{+}) and Potassium (K^{+}) are essential for appropriate electrolyte balance. Electrolyte imbalance ensuing from dehydration, kidney failure, vomiting and fever has been prompt mutually of the tributary factors toward complications determined in diabetic mellitus patients and different endocrine disorders [2]. The foremost common electrolyte imbalance is hyponatremia; others are hypokalemia, hypomagnesemia, and hyperkalemia[3]. Hyponatremia, known as a plasma Na^{+} concentration <130 mmol/L, frequently reveal a hypotonic state. Nevertheless, the normal or increased level of plasma osmolality could be found in some cases of hyponatremia. Hypertonic, which occur in hyponatremia cases, are usually due to hyperglycemia; due to insulin deficiency glucose cannot enter into muscle cells [3].

The decrease in magnesium level leads to elevated free radical development and reduction in the antioxidant characteristic next to the oxidative stress in T2DM [4]. The

intracellular Mg^{+2} levels are regulated by Insulin which activates the Na^{+}, Mg^{+2} exchange at the cell membrane and this might justify the prevalence of low cellular Mg^{+2} levels as a result of insulin resistance [5].

The major sources of phosphate in the blood are dietary sources absorbed within the intestine, lost from cells into the blood, and released from bone. In healthy people, all these processes are comparatively constant and simply regulated by excretion or reabsorption of phosphate by kidneys [6]. Disturbances to any of those processes will alter phosphate concentration within the blood; but, the loss of regulation by the kidneys can have the foremost profound impact. Though different factors like vitamin D, calcitonin, growth hormone (somatotropic hormone), and the acid-base event will affect renal regulation of phosphate, the most important factor is parathyroid hormone (PTH), which overall lowers blood concentrations by increasing the renal excretion of phosphate [6].

Type 2 Diabetes Mellitus (T2DM) is a heterogeneous group of syndromes resulting from an increase in the level of blood glucose due to a decrease or complete absence of insulin secretion [7]. T2DM is characterized not by changes in carbohydrate metabolism only, also by changes in the metabolism of lipids, known as diabetic dyslipidemia. Therefore, it is necessary to emphasize the fact that T2DM might exist at the same time and/or synergistically with other systemic diseases, like dyslipidemia, since there's an immediate relationship between indices of glycemic management and the elevation of lipid plasma [8,9]. Diabetic patients commonly develop a group of electrolyte disorders and these disturbances are notably common in diabetics [10].

The most common disturbances due to hyperglycemia in DM patients are impaired electrolyte levels. Hyperglycemia encouraged changing in osmotic fluid osmotic diuresis. Also, the administration of diabetes and the complications of diabetes may cause electrolyte imbalances [11].

Hence, in uncontrolled DM, increased glucose level draws water from muscle cells leading to hyponatremia. Also other conditions like hyperproteinemia and hyperlipidemia caused hyponatremia [12]. Other conditions leading to hyponatremia are due to a primary sodium loss secondary to water gains, such as burns, sweating, gastrointestinal loss (vomiting and diarrhea) and kidney loss (diuretics agents, decrease in aldosterone) [9]. A primary water gain secondary to sodium loss which occurs in inappropriate antidiuretic hormone secretion, hypothyroidism, and polydipsia may also cause hyponatremia. In addition, sodium gained secondary water gain in conditions like heart disease, hepatic cirrhosis and nephrotic syndrome [13]. In this case-control study, the general objective is to assess the electrolytes imbalance in T2DM patients in the Gaza strip.

MATERIALS

Electrolytes measured (Ca^{+2}, Na^{+}, K^{+}) by automated machine (Caretium, China) and P_i, Mg^{+2} by using manual kit were purchased from DiaSys, USA. A professional weighing scale (SECA type) and Stadiometer (SECA type) were used to measure the weight in kilograms and height in centimeters, respectively, of all participants.

METHODS

A total of 105 patients with T2DM older than 35 years of age were collected from Primary Health Care Centers - the Ministry of Health and 95 healthy individuals as control group gathered from the community were incorporated in this comparative cross-sectional study.

The participants contributed to this study after giving a written informed agreement. Authorization to carry out the study was obtained from the Palestinian Ministry of Health. According to the American Diabetes Association [14], patients that have fasting glucose of ≥126.1 mg/dL are considered diabetic. Concerning the age group, the preponderance of the participant patient's age ranged from 36–70 years. Patients who were diagnosed mainly with T2DM less than three years ago and those with conditions like renal disease, other chronic illnesses, and pregnancy were excluded from the study.

Blood Sampling and Analysis

The blood samples were collected from each subject by vein puncture into plain tubes. To obtain serum samples, the serum was separated by centrifugation at 4500 rpm for 5 minutes and stored at -20˚C. After the sampling process was completed, the stored serum was used for measuring electrolytes automatically (Ca^{+2}, Na^{+}, K^{+}) and P_i, Mg^{+2} using a manual kit. A questionnaire was filled out for all subjects by a meeting interview. The body weight in Kilogram and height in centimeter were measured and the BMI was calculated using the formula as (wt in kg/ Ht in m^2). BMI are classified as the following values: <18.5 (underweight), 18.5-24.9 (normal weight), 25-29.9 (overweight), 30- 34.9 (obesity- class 1), 35-39.9(obesity-class 2) and > 40 (obesity-class 3) (World Health Organization (WHO), 2012). For statistical analysis, Independent Samples T-test and Chi-square test were used to compare T2DM patients with reference intervals. P-value < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The study population comprised of 200 samples (105 patients with T2DM, 95 healthy individuals as control). The mean age of subjects was 52.12 ± 11.3 (45.25±8.8 and

58.33±9.6 for control and case groups respectively). The percentage of females was 58.5% (117/200), while that of males was 41.5% (83/200). Around 90% (180/200) of the contributors were non-smokers, while 10% (20/200) were smokers. Approximately 25% (50/200) of the study samples were physically active subjects, while 32.5% (65/200) of them were physically inactive, and 61% (64/105) of the case group had DM complications. Furthermore, 35.5% (71/200) of the study population had a family history of DM.

The main features of the study groups (control and case) are shown in Table 1. The Body Mass Index [BMI (kg/m^2)] for control was 26.9 ±4.0, whereas BMI= 28.7±4.3 for case group (p value=0.004). According to the family history for DM; 61% of the case group had a family history for DM, but in the control group, the percentage was 9.9% which is statistically significant (p=0.000). In contrast, the mean age of the control group was lower than that of the case group, but the mean BMI was higher in the case group than in the control group. However, the percentage of low physically active in the case group was 35.2%, which was higher than the control group (29.5%). Overall, there were differences between the mean BMI, physical activity, and age between the case and control groups, which were statistically significant.

Table 1. Baseline characteristics of study groups

Variable		Control (n=95)	Case (n=105)	*P*-value
Age (years)		45.25±8.8	58.33±9.6	0.000
Sex, n (%)				
	Male	40 (42.1)	43 (40.95)	0.887
	Female	55 (57.9)	62 (59.05)	
BMI (kg/m^2)		26.9 ±4.06	28.7±4.3	0.004
Family History of DM		7(9.9)	64(61)	0.000
Physical activity, n (%)				
	Low	28(29.5)	37(35.2)	0.000
	Moderate	54(56.8)	31(29.5)	
	High	13(13.7)	37(35.2)	
Smoking, n (%)				
	Non	28(86.3)	98(93.3)	0.24
	Low	4(4.2)	2(1.9)	
	Moderate	8(8.4)	3(2.9)	
	High	1(1.1)	2(1.9)	

The means of potassium and phosphorus were not significantly different in control and case groups: [K^+: 4.4±0.62 versus 4.54±0.39, and Pi: 3.9±1.05 versus 3.8±0.89 respectively]. Still, it was observed that the potassium and calcium levels were slightly elevated when compared with controls. While the means of sodium, calcium, and magnesium were statistically significant between both groups (P = 0.012, P = 0.013, and P =0.000 respectively) (Table 2).

Table 2. Electrolytes levels in study subjects

Variable	Control (n=95)	Case (n=105)	*P*-value
Sodium (mEq/L)	144.47±2.3	143.46±3.2	0.012
Potassium (mEq/L)	4.4±0.62	4.54±0.39	0.142
Calcium (mg/dl)	9.08±0.57	9.28±0.54	0.013
Magnesium (mg/dl)	2.2±0.37	1.8±0.49	0.000
Phosphorus (mg/dl)	3.9±1.02	3.8±0.89	0.431

Based on the duration of T2DM, all the patients were divided into 2 groups: <5 years and ≥5 years. As shown in Table 3, the means of all electrolytes levels were not significantly different in participants who have T2MD duration ≥5 years compared with <5 years duration of disease. Patients were also divided into 2 groups based on the type of glycemic drugs (oral and insulin injection). It is found that 83.81% of T2DM patients were treated with orally glycemic medication, while 13.33% used insulin injection, but the rest of the patients (2.86%) did not receive any medication. It was observed that the mean levels of potassium, sodium, and phosphorus were lower in patients treated with oral medication than patients on insulin injection. In contrast, the means of calcium and magnesium were higher in orally treated patients than those treated with injection therapy, but all differences in electrolytes level were not statistically significant in patient groups (Table 4). We found that the mean electrolytes levels among patients with DM complications were not different from DM who do not suffer from diabetic complications. We also observed that 41 patients of 105 (39.05%) had DM complications. On a comparison between DM patients with and without complications; there was no statistically significant difference in the means of sodium, potassium, calcium, magnesium and phosphorus between the two groups. Additionally, the mean of sodium in DM patients with diabetic complications was higher than in DM patients without complications (Table 5).

Table 3. Characteristics of the patients and levels of electrolytes based on the duration of DM

Variables	<5 years(n=37)	≥5 years(n=68)	*P*-value
Age (years)	53.76±8.19	60.8±9.42	0.000
Body weight (kg)	76.09±10.59	77.64±12.26	0.52
Height (cm)	163.08±7.1	164.85±9.22	0.31
BMI (kg/m^2)	28.70±4.30	28.62±4.40	0.93
Sodium (mEq/L)	143.18±2.6	143.61±3.5	0.51
Potassium (mEq/L)	4.59±0.39	4.52±0.38	0.36
Calcium (mg/dl)	9.23±0.60	9.30±0.51	0.47
Magnesium (mg/dl)	1.89±0.50	1.80±0.47	0.35
Phosphorus (mg/dl)	3.73±0.71	3.85±0.97	0.51

Table 4. The serum levels of electrolytes in patients groups based on glycemic drug type

Variables	Oral (n=88)	Injection (n=14)	*P*-value
Sodium (mEq/L)	143.29±3.16	144.50±3.78	0.199
Potassium (mEq/L)	4.51±0.39	4.72±0.36	0.062
Calcium (mg/dl)	9.29±0.36	9.12±0.58	0.239
Magnesium (mg/dl)	1.85±0.50	1.74±0.38	0.449
Phosphorus (mg/dl)	3.81±0.94	3.88±0.66	0.783

Table 5. The serum levels of electrolytes in patients groups based on the presence of complications

Variables	Without complications (n=64)	With complications (n=41)	*P*-value
Sodium (mEq/L)	142.97±2.94	144.23±3.53	0.050
Potassium (mEq/L)	4.52±0.37	4.57±0.41	0.55
Calcium (mg/dl)	9.27±0.53	9.28±0.56	0.96
Magnesium (mg/dl)	1.83±0.48	1.85±0.50	0.84
Phosphorus (mg/dl)	3.88±0.98	3.71±0.74	0.33

Table 6. Proportions of subjects with electrolyte disturbances in diabetic patients and control group

Variables	Case (n=105)		Control (n=95)		*P*-value
	n	%	n	%	
Hypernatremia(>145 mEq/L)	30	28.57	31	32.63	0.533
Hyperkalemia (> 5.5mEq/l)	1	0.95	2	2.11	0. 51
Hypocalcaemia (<8.8mg/dl)	18	17.14	27	28.42	0.058
Hypercalcaemia (> 10.8mg/dl)	1	0.95	1	1.05	0.943
Hypomagnesaemia (< 1.46mg/dl)	28	26.67	1	1.05	0.0006
Hypermagnesaemia (> 2.6mg/dl)	6	5.71	7	7.37	0.635
Hypophosphatemia(< 2.5mg/dl)	4	3.81	7	7.37	0.17
Hyperphosphatemia (> 4.5mg/dl)	21	20	24	25.26	0.289

Table 6 illustrates the relation between electrolytes imbalance between study groups. The percentage of hypomagnesaemia was sharply increased in patients to reach statistically significant (26.67% in the case group and 1.05% in control with p=0.0006). In contrast, the value of hypernatremia in the case group was lower than the control group and this percentage was not statistically significant. However, there was no statistical difference in the comparison between the two groups in hyperkalemia, hypocalcaemia, hypernatremia, hypercalcemia, and hypermagnesaemia. Additionally, the percentage of hypophosphatemia in control group was nearly double the value in the case group but was still not significant. Nevertheless, no respondents suffered from hyponatremia and hypokalemia. Due to a decrease in insulin secretion and elevation in both glucose and potassium levels, improper fluid and electrolyte levels probably occur in DM patients [15]. To our knowledge, this is the first study conducted on the Palestinian population to determine electrolytes imbalance in diabetic patients in comparison with healthy individuals.

The present study involving 105 patients with T2DM and 95 healthy persons as a control showed that the means of potassium and phosphorus levels were not significantly different in control and case groups, but it was observed that the potassium and calcium levels were slightly elevated when compared with controls. The means of sodium, calcium, and magnesium levels were, however statistically significant between both groups. Our study revealed that there was a significant lowering in magnesium levels in the case group.

Earlier studies had presented the variation in potassium and sodium levels in DM patients [16-18]. The results of our study showed that there is no significant difference in phosphorus and potassium levels in DM patients compared to non-diabetics which is dissimilar to those studies. The difference in magnesium levels was marked in uncontrolled T2DM patients (21/28) compared to controlled T2DM patients (7/28).

The deficiency in magnesium levels may cause alteration in insulin function and endothelial dysfunction as a complication of uncontrolled diabetes. Studies have shown that serum magnesium levels were significantly lower in patients with CVD and diabetes in Caucasians and African Americans [19].

The deficiency of magnesium may expedite the development of atherosclerosis through many processes (an increase in lipid oxidation, inflammatory cytokines, endothelial cell growth, and inhibition of cellular DNA repair) [20-22]. Low dietary intake of magnesium, defect in magnesium transportation within the cells, osmotic diuresis, which leads to increased excretion of magnesium by kidneys, or renal tubular dysfunction due to insulin resistance, are reasons for lowering magnesium in DM patients [23, 24]. Hypomagnesemia mechanism in diabetic patients is due to osmotic diuresis that escorted abnormal loss of magnesium in urine. Magnesium is a coenzyme factor in metabolic reactions; therefore, its level deficiency may lead to abnormal clinical conditions [25]. Increased incidence of retinopathy in DM patients was found to be related to hypomagnesemia. Previous studies showed that peoples with a low intake of magnesium are at high risk for developing hypertension, atherosclerosis, and other cardiac diseases [26]. Other studies also stated that although low magnesium levels remained within the normal range are related to increased mortality in T2DM patients [27]. Hypomagnesemia in DM patients increases the rate of uncontrolled DM and complications developing such as neuropathy, retinopathy, and diabetic foot ulcers [28]. Several studies have reported that treating uncontrolled DM patients with magnesium supplementation was very beneficial in protecting and curing the cardiometabolic syndrome [29]. The results of our study are consistent with those of previous studies in China, Pakistan, and India, which showed a decrease in magnesium levels in DM patients [30-32]. In the present study, the differences in the mean levels of calcemia in both study groups were not statistically significant, whereas values lower and higher than the normal level were cancelled due to calculation of the mean. The result of a study conducted in Diwaniya-City in Iraq by Al-Yassin et al. reported that 43% of DM patients had hypocalcemia which is not consistent with our

study which reveals that 17.14% of the case group had hypocalcemia [33]. Similar to our results, a study in Nigeria presented no alteration between the mean levels of serum calcium in DM and control groups [34]. In contrast, other studies showed significantly decreased serum calcium levels in DM patients [31, 32]. According to potassium and sodium levels, our results proposed that 28.57% of the cases may have hypernatremia. In comparison to the control group, the percentage of hypernatremia was lower than case group, but this value does not reach a statistical difference. There was no detectable hypokalemia percentage among case and control groups. The normal or increased level of plasma sodium in the presence of hyperglycemia marked a clinically significant change in whole-body water, so uncontrolled DM was involved in the development of hypernatremia in some cases [11]. Subsequently, in uncontrolled DM patients, the serum concentration of Na^+ is mutable, reflecting the balance between the water movement out of the cells that lower Na^+ due to hyperglycemia, and the osmotic diuresis due to glucosuria, which lead to increase Na^+ [35]. In the present study, levels of serum calcium between patients and control remained unaltered without significant effect of hyperglycemia accompanying diabetes [35]. Levels of serum phosphorus were lower in diabetics in comparison to the control group; this may indicate a possible negative effect of hyperglycemia on serum phosphorus. In addition, low phosphate levels were known to affect those who have T2DM, especially those treated with insulin because insulin has been reported to influence the phosphorus excretion by renal tubules [36]. This could justify our findings as there was low insulin uptake among our study subjects.

Electrolytes show a significant role in regulating fluid levels, acid-base equilibrium, the functions of cardiac muscle and nerves, oxygen transfer, and other several biological processes [37]. Patients with DM are more disposed to develop electrolyte disparities, probably due to the complications they develop and the medications they receive [1]. Hypomagnesaemia is more prevalent in our study in the diabetic population than the other electrolyte abnormalities. Electrolyte imbalances, especially hypomagnesemia, should be considered in treating diabetic patients because a rapid diagnosis would probably prevent the risk of developing many diseases. Detection for electrolyte imbalances should be measured in diabetic cases and essential steps may be taken to avoid its bad outcomes. Additional research is suggested for the proper assessment of a combination of diabetes and electrolyte imbalance.

ACKNOWLEDGMENT

We would like to thank the University College of Science and Technology - Laboratory Medical Science Department for giving us the opportunity and knowledge to achieve this research. We would like to thank all who helped us at the Medical Health Care Centers of the Palestinian Ministry of Health and all participations.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

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