ORIGINAL ARTICLE

Serum glucose, sodium and potassium concentrations in patients with diabetic ketoacidosis

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ABSTRACT

Aim To investigate possible differences in serum glucose and sodium and potassium concentrations with respect to age, gender and severity of diabetic ketoacidosis.

Methods Medical records from 1 January 2017 to 31 December 2019 were reviewed and patients with the diagnosis of diabetic ketoacidosis were selected.

Results The study included 52 patients. Glucose concentration was significantly higher in the age group of 25-44 and >65 years compared to the group of 18-24 years (p=0.02). Sodium concentration was significantly higher in the age group 18-24 and >65 years compared to groups 25-44 and 45-65 years (p=0.002). Females had significantly higher sodium concentration than males (p=0.002). Potassium concentration was significantly higher in the age group 25-44 years compared to other groups (p=0.01). Males had significantly higher potassium concentration (p =0.01).

Conclusion This study showed that significant differences exist in electrolyte concentration between specific age groups, male and female gender as well as DKA severity. Knowing these differences could help clinicians to promptly recognize and treat electrolyte derangements, leading to better outcome of patients with DKA.

Key words: diabetes complication, electrolyte, emergency medicine, hyperglycemia

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INTRODUCTION

Hyperglycemic crises as complications of diabetes including diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state; both are acute conditions that need to be identified and taken care of as soon as possible. Namely, DKA is one of the most common causes of death in young adults and children with type 1 diabetes (1). In addition to patients with type 1 diabetes, DKA also occurs in patients with type 2 diabetes, whose number has been increasingly growing (2,3).

The onset of DKA is associated with precipitating factors, the most common of which are infections (pneumonia, urinary tract infections and gastrointestinal infections) and omission of insulin therapy or dose reduction (4). Other causes include cerebrovascular accident, myocardial infarction, pancreatitis, use of drugs that oppose insulin action such as corticosteroids and the use of sodium-glucose co-transporter 2 inhibitors (5,6).

In the pathophysiology of DKA, the most important role is played by the relative or absolute lack of insulin, which is associated with elevated levels of hormones that oppose insulin action, i.e. glucagon, cortisol, growth hormone and catecholamines. (7). Due to lack of insulin and the consequent inability to utilize glucose, hyperglycaemia occurs causing osmotic diuresis leading to glucosuria, hypovolemia and decreased glomerular filtration rate (8). Patients with DKA most often present at the emergency department with polydipsia, polyuria, and weight loss (9).

In patients with suspected DKA, detailed laboratory work should be performed including glucose, electrolytes (sodium and potassium), urea and creatinine, complete blood count with differential blood count, urine analysis and arterial blood gas analysis with acid-base status (10). Glycated haemoglobin (HbA1C) concentration helps to distinguish an acute episode in a well-controlled patient (HbA1C <7%) from the culmination of a long-term condition due to poorly controlled or undiagnosed diabetes (11). Diagnostic criteria for DKA according to the American Diabetes Association (12) include plasma glucose concentration higher than 13.9 mmol/L, arterial blood pH less than 7.3, bicarbonate concentration less than 18 mmol/L, anion gap greater than 10, ketonemia, ketonuria (positive acetoacetate in urine by nitroprusside test) and acute altered mental status. Depending on the pH and bicarbonate concentration there are three types of DKA: mild, moderate and severe (13).

Hyperglycaemia is one of the key diagnostic criteria. However, a wide range of glucose concentrations from normal to extremely high are possible (1). Patients with DKA often have mild hyponatremia. In the hyperglycaemic state fluid leaks out of the cells, which leads to an increase in the volume of extracellular fluid and dilution hyponatremia (14). A major problem is total potassium deficiency due to osmotic diuresis and ketonuria in patients with DKA, while their laboratory findings imply normal or higher potassium concentrations. This occurs because potassium is displaced outside of the cell due to insulin deficiency, hyperosmolarity and acidaemia (15).

The majority of studies on DKA focus on precipitating factors, as well as clinical presentation, while data on electrolyte disturbances in certain population are lacking (9, 16–18).

The aim of this study was to determine possible differences in patients with DKA in serum glucose, sodium and potassium concentration with respect to DKA severity, age and gender. Results of this study could prove to be useful, especially for emergency physicians by providing information on what to expect in different groups of DKA patients.

PATIENTS AND METHODS

Patients and study design

Research was organized as a cross-sectional study with historical medical data. Data were collected from the hospital information system of the Clinical Hospital Centre Osijek in the period from 1 January 2017 to 31 December 2019. Data were collected from patients admitted to the Emergency Department of the Clinical Hospital Center Osijek with the diagnosis of DKA provided they met the criteria for DKA from the American Diabetes Association (13). All patients were registered under a unique number for anonymity.

The study was approved by the Ethics Committee of the School of Medicine, Josip Juraj Strossmayer University in Osijek, Croatia.

Methods

By searching the hospital information system, basic demographic data (age and gender), type of

diabetes, precipitating factor and outcome were collected. Reviewing the laboratory findings data on arterial blood gas analysis and acid-base status (pH, bicarbonates, oxygen saturation, partial pressure of oxygen and carbon dioxide in arterial blood), renal and hepatic function (urea, creatinine, aspartate transaminase, alanine transaminase, gamma-glutamyl transferase), inflammatory parameters (C-reactive protein - CRP, leukocytes), serum glucose, HbA1c, sodium and potassium concentration were collected. Data on the presence of ketones in urine and the presence of signs of urinary tract infection were also monitored. Patients were divided into groups according to DKA severity, age and gender. The division according to the severity of DKA is defined according to the guidelines of the American Diabetes Association (13): mild DKA (pH 7.25-7.3; bicarbonates 15-18 mmol/L), moderate DKA (pH 7.0-7.24; bicarbonates 10-15 mmol/L) and severe DKA (pH <7.0; bicarbonates <10 mmol/L) (13). Age groups were: 18-24, 25-44, 45-65 and >65 years.

Statistical analysis

Categorical and numerical data were used for statistical analysis. Categorical data were presented as absolute and relative frequencies. Numerical data were presented in the form of arithmetic mean and standard deviation in case of normal distribution and median and interquartile range for data that do not follow the normal distribution. Differences in category variables were tested by $\chi 2$-test. The Student's t-test for independent samples and One-way ANOVA test were used in the case of normal distribution and the Mann Whitney U test and Kruskal-Wallis test in the case of deviations from the normal distribution to test numerical data. All p-values were two-tailed. The significance level was set to p=0.05.

RESULTS

Research included 52 patients, of which 23 (44.2%) were males and 29 (55.8%) were females. The median age of patients was 34 years (interquartile range 21–56 years) ranging from 18 to 85 years. The largest number of the patients belonged to the age group 18-24 years, 19 (36.5%) (p<0.001). Most male patients belonged to the age group of 25-44 years, whereas the largest number of females belonged to the age groups of 18-24 and 45-65 years. All patients over the age of 65 were females (Table 1).

Table 1. Frequency of diabetic ketoacidosis in different age groups with regard to gender

Age (years)	No (%) of patients			p
	Males	Females	Total	
18 – 24	7 (36.8)	12 (63.2)	19 (36.5)	< 0.001
25 – 44	11 (91.7)	1 (8.3)	12 (23.1)	
45 – 65	5 (31.3)	11 (68.7)	16 (30.8)	
> 65	0	5 (100)	5 (9.6)	
Total	23 (44.2)	29 (55.8)	52 (100)	

Moderate DKA severity was the most common, in 34 (65.4%) patients (p=0.005). The median of overall glucose concentration was 27.1 mmol/L (interquartile range 21.9-36.7 mmol/L). Higher glucose values were found in patients with moderate DKA and in females, but without statistical significance. Significantly higher glucose values were recorded in the age groups 25-44 and >65 years (p=0.02) (Table 2).

Table 2. Glucose concentration with regard to age, gender and diabetic ketoacidosis severity

Variable	Glucose median (mmol/L)* (interquartile range)	p	No (%) of patients
Age (years)		0.02	
18 – 24	22.1 (20.8 – 27.8)		19 (36.5)
25 – 44	31.8 (25.6 – 45)		12 (23.1)
45 – 65	28.4 (22.1 – 40.4)		16 (30.8)
> 65	34.4 (27.7 – 47)		5 (9.6)
Gender		0.12	
Male	28.6 (23.9 – 44)		23 (44.2)
Female	25.5 (21.5 – 31.1)		29 (55.8)
Severity		0.65	
Mild	25.6 (19.6 – 30)		10 (19.2)
Moderate	27.8 (22 – 36.5)		34 (65.4)
Severe	29.3 (23 – 41)		8 (15.4)

*Reference range: 4.4 – 6.4 mmol/L

The median of overall sodium concentration was 130 mmol/L (interquartile range 125.8-133.2 mmol/L). The severity of DKA did not significantly affect the sodium concentration. Patients aged 25-65 years had significantly lower sodium values than other patients (p=0.002). In terms of gender, males had significantly lower sodium values than females (p=0.002) (Table 3).

The arithmetic mean of the overall potassium concentration was 4.8 mmol/L (standard deviation of 1 mmol/L). No significant difference in potassium concentration was found with respect to the severity of DKA. Patients in the age group of 25-44 years had the highest potassium values (p=0.01). Male patients had significantly

Table 3. Sodium concentration with regard to age, gender and diabetic ketoacidosis severity

Variable	Sodium median (mmol/L)* (interquartile range)	p	No (%) of patients
Age (years)		0.002	
18 – 24	131 (129 – 136)		19 (36.5)
25 – 44	124.5 (120.5 – 130)		12 (23.1)
45 – 65	128.5 (124.5 – 132)		16 (30.8)
> 65	135 (130.8 – 147.3)		5 (9.6)
Gender		0.002	
Male	128 (122 – 130.8)		23 (44.2)
Female	132 (128.5 – 135.3)		29 (55.8)
Severity		0.92	
Mild	130.5 (125 – 134)		10 (19.2)
Moderate	129.5 (126 – 133)		34 (65.4)
Severe	130 (126 – 136)		8 (15.4)

*Reference range: 137 - 146 mmol/L

higher potassium values comparing to females (p=0.01) (Table 4).

Table 4. Potassium concentration with regard to age, gender and diabetic ketoacidosis severity

Variable	Potassium arithmetic mean (mmol/L)* (SD)	p	No (%) of patients
Age (years)		0.01	
18 – 24	4.7 (1)		19 (36.5)
25 – 44	5.5 (0.6)		12 (23.1)
45 – 65	4.5 (1)		16 (30.8)
> 65	4.1 (0.7)		5 (9.6)
Gender		0.01	
Male	5.1 (1)		23 (44.2)
Female	4.5 (0.9)		29 (55.8)
Severity		0.18	
Mild	4.3 (0.7)		10 (19.2)
Moderate	4.8 (1)		34 (65.4)
Severe	5.2 (1)		8 (15.4)

*Reference range: 3.9 – 5.1 mmol/L
SD, standard deviation

The median of overall pH was 7.2 (interquartile range 7.1-7.3). The lowest pH values were recorded in the age group of 18-24 years, in males and those with severe DKA (Table 5).

Table 5. pH in arterial blood with regard to age, gender and diabetic ketoacidosis severity

Variable	pH median* (interquartile range)	p	No (%) of patients
Age (years)		0.64	
18 – 24	7.14 (7.05 – 7.23)		19 (36.5)
25 – 44	7.19 (7.09 – 7.28)		12 (23.1)
45 – 65	7.23 (7.09 – 7.25)		16 (30.8)
> 65	7.22 (7.18 – 7.24)		5 (9.6)
Gender		0.82	
Male	7.17 (7.06 – 7.27)		23 (44.2)
Female	7.21 (7.09 – 7.25)		29 (55.8)
Severity		< 0.001	
Mild	7.28 (7.25 – 7.33)		10 (19.2)
Moderate	7.18 (7.09 – 7.24)		34 (65.4)
Severe	7 (6.97 – 7.21)		8 (15.4)

*Reference range: 7.35 – 7.45

DISCUSSION

This study investigated differences in glucose, sodium, potassium concentration and pH with respect to DKA severity, age groups and gender. Significant differences in concentration between these groups were observed for glucose, sodium and potassium. Knowing these differences can lead to faster recognition of electrolyte disorders and consequently better outcome of patients with DKA.

The median glucose concentration in our study was 27.1 mmol/L. It was observed that patients in the age group of 25-44 years and >65 years had significantly higher glucose values than patients in the age group of 18-24 years. A possible reason for higher glycemic values in the elderly group of patients is the presence of chronic dehydration resulting in higher plasma glucose concentrations (19). In a 2020 study, the prevalence of chronic dehydration was 58.4%. These patients were more likely to have more comorbidities including diabetes and had significantly higher fasting glucose concentrations. Dehydration in the elderly occurs due to decreased fluid intake, comorbidities such as chronic kidney disease and medications such as diuretics (20). In addition to dehydration, the delaying of seeking medical attention and inadequate self-regulation of glucose concentration in elderly patients leads to more severe forms of DKA with higher glucose values (21). Schwarzfuchs et al. found the average glucose concentration significantly higher in patients >65 years, which is consistent with the results obtained in our study (22).

A Newton et al. 2004 study found that patients with type 1 diabetes had higher glucose concentration, taking into consideration that type I diabetes is more common in younger individuals (23) it is not consistent with our result where the glucose concentration was significantly higher in patients >65 years (taking into account that in this age group patients with type 2 diabetes were predominated) . However, the average age of patients with type 2 diabetes in the Newton et al. study was 41 years meaning that that result cannot be compared with the result of the age group over 65 years in our study.

Disorders of sodium concentration are common in DKA. Hyponatremia is the most common, although cases of hypernatremia with impaired

consciousness have been reported (24). The median sodium concentration in our study was 130 mmol/L. Sodium levels were on average lower in males and in the 25–44 and 45–65 age groups. Decreased sodium values are caused by an osmotic gradient where high glucose concentrations draw fluid from the cell which results in dilution hyponatremia (25). Hyperglycaemia and ketonemia lead to increased sodium loss by osmotic diuresis and increased renal sodium loss (26). Therefore, patients with higher glucose concentration would have lower sodium concentration which is consistent with the results obtained in our study. Our results have shown that patients older than 65 years also had significantly higher glucose values, but their sodium values were higher than in other groups. This result could be explained by inadequate fluid intake, which is more common in the elderly, leading to higher-than-expected sodium levels (27). Previous studies have shown that sodium levels were higher in patients with type 2 diabetes and in patients with newly diagnosed diabetes (17,23). Patients with type 1 diabetes are more likely to develop DKA as a first presentation than patients with type 2 diabetes, which could explain the higher sodium concentrations in the 18–24 age group obtained in our study (28). Systemic metabolic acidosis leads to decreased renal reabsorption of water and sodium (15). Males had lower pH values and this could explain the lower sodium values in this group of patients obtained in our study.

Most patients with DKA have a deficiency of potassium in the body (29). Absolute insulin deficiency in type 1 diabetes would lead to higher potassium levels as opposed to type 2 diabetes where there is a relative insulin deficiency (26). This is in line with the results of our research. Newton and Raskin observed lower potassium levels in patients with type 2 diabetes and DKA, which is consistent with our results (23).

Barski et al. found the proportion of patients with hypokalaemia was the lowest in the group of patients with mild DKA and highest in the group of patients with severe DKA (30). On the other hand, in our study, patients with severe DKA had higher potassium values than those with mild DKA. Possible explanations for this difference between studies are different precipitating factors and a small number of participants. The most common precipitating factor in Barski et al. study was omission of insulin therapy, whereas in our study it was an infection and a small number of participants.

No differences were found in concentrations of glucose, sodium and potassium with respect to the severity of DKA in our study. On the other hand, our research indicates the existence of significant differences in the concentration of glucose, sodium and potassium at admission depending on the patients' age and gender.

The main disadvantage of this research is the small number of participants.

Our study confirms the importance of regular check-up of glucose, sodium and potassium concentrations in the setting of DKA. We aimed to investigate the difference in electrolyte concentration between specific age groups, male and female gender as well as DKA severity. This study showed that significant differences exist between these categories. Knowing these differences could help clinicians to promptly recognize and treat electrolyte derangements, leading to a better outcome of patients with DKA.

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TRANSPARENCY DECLARATION

Conflicts of interest: None to declare.

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