

Risk Factors of Diabetic Ketoacidosis among Type 1 Diabetic Patients in Abha City, Saudi Arabia

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Abstract

Aim of Study: To assess prevalence of ketoacidosis and to identify risk factors associated with it among patients with type-1 diabetes mellitus (T1DM) in Abha City, Saudi Arabia.

Methods: A cross-sectional study was conducted among 385 type-1 diabetics in Abha City, Saudi Arabia.

Results: Our study included 228 males (59.2%), 44.2% were diabetic for more than 5 years, 48.3% had positive family history of diabetes, while 70.9% reported past history of DKA. Last recorded HbA1c levels for 53.5% were >9%. The main predisposing factors for DKA were being first presentation (59%) or treatment discontinuation (53.1%). DKA occurred significantly more in patients with family history of diabetes ($p<0.001$), in patients with poor glycemic control ($p<0.001$), and in patients whose parents were less educated or unemployed. However, its occurrence did not differ significantly according to patients' age or their duration of disease.

Conclusion: Most T1DM patients experience DKA, mainly with their first presentation of disease or due to discontinuation of treatment. DKA tends to occur more frequently among patients with poor glycemic control, those with less educated or unemployed parents, and those with positive family history of diabetes.

Key words: Type 1 diabetes, ketoacidosis, HbA1c, risk factors, Saudi Arabia.

Introduction

Diabetes mellitus (DM) is a chronic endocrine disorder associated with abnormal blood glucose metabolism. It results in both short-term and long-term complications, such as diabetic ketoacidosis (DKA) (1). Due to hyperglycemic emergencies, case fatality ranges from 4% to 40% in developing countries (2).

It is the most common acute hyperglycemic emergency in people with DM. It is the consequence of an absolute or relative lack of insulin and concomitant elevation of counter-regulatory hormones, usually resulting in the triad of hyperglycemia, metabolic acidosis and ketosis, often accompanied by varying degrees of circulatory volume depletion (3).

DKA occurs mostly in people with uncontrolled type 1 diabetes mellitus but can also occur in adults with poorly controlled type 2 diabetes mellitus under stressful conditions, such as acute medical or surgical illnesses, and, in adolescents, in new-onset T2DM. Although any illness or physiological stress can precipitate DKA, the most frequent causes are infections, particularly urinary tract infections and gastroenteritis (1).

DKA presents with several vague symptoms, e.g., nausea, vomiting, and abdominal pain, excessive thirst and polyuria. Kussmaul breathing and fruity odour are specific signs present on examination of a patient with DKA (4). It is the presenting manifestation of diabetes in about one-third of type 1 diabetics, mainly in children (5). Its incidence is as high as 5.6 events per 100 person-years, with a prevalence of up to 12.8 per 100 people (6-7), depending on the clinical setting, region of the world, state of development of a country, and level of income inequality (8-9).

There are several precipitating factors of DKA, especially missed insulin dose and an ongoing infection. The clinical outcomes of DKA depend upon the patients' response to initial medical intervention, the precipitating factor for DKA, and biochemical values (10).

It is necessary to identify risk factors of DKA. For the prevention of DKA, interventions that address its modifiable risk factors or target management of ketosis are largely needed. Such preventive strategies should be tailored to the non-modifiable risk factors to match the needs of these risk groups to increase their effectiveness in preventing DKA. This approach also includes specific interventions, such as peer support and community-based approaches that actively seek populations at high risk, with little access to health care (11).

Advances in technology have provided more efficient means of monitoring diabetes and maintaining glycemic control in an outpatient setting. The use of real-time continuous glucose monitoring in patients with T1DM has been shown to significantly lower hemoglobin A1c.

Real-time continuous glucose monitoring also has the advantage of signaling to patients the early detection of glucose abnormalities, allowing for prompt intervention (12).

At-home use of ketone meters that detect blood β -hydroxybutyrate has also been shown to aid in early detection and management of ketosis, which may decrease the need for specialized care. Short-acting insulin can be administered with fluids early on to prevent DKA (13).

Atkilt et al. (14) reported that the odds of developing DKA in newly diagnosed T1D children was 49% lower for children whose parents knew its signs and symptoms than parents' who didn't know. They explained their finding by that parents who know its signs and symptoms seek health care before their children develop DKA.

Study rationale

DKA is the most severe health problem among diabetic children (15). It is typically caused by treatment non-compliance, i.e., shortage of insulin and may be precipitated by several factors, e.g., infections. Although DKA can be a life-threatening event for type 1 diabetics, it is a preventable condition. Recent advances in diabetes management could not minimize prevalence of DKA among children with T1DM (6).

This study aimed to assess prevalence of ketoacidosis and to identify risk factors associated with it among patients with type 1 diabetes mellitus (T1DM) in Abha City, Saudi Arabia.

Methodology

A cross-sectional study design was followed at the Diabetes and Endocrine Unit in the Maternity and Children Hospital, and the Diabetes Center in Abha City, Saudi Arabia. A total of 385 type-1 diabetic children, aged 3-18 years were included.

Based on relevant literature, a study questionnaire was designed in a simple Arabic Language by the researchers.

It comprised the following:

- Personal data: Age, gender, duration of diabetes, parents' education, parents' employment status, and family history of diabetes.
- DKA data: Number of DKA incidents, expected cause(s) related to DKA, HbA1c level.

The study settings were visited by the researchers during the June and July 2019. All type-1 diabetic patients attending the Endocrine Clinic (and their caregivers) were interviewed.

The Statistical Package for Social Sciences (SPSS), version 25, was used for data entry and statistical analysis. Descriptive statistics (e.g., number, percentage, mean, range, standard deviation) and inferential statistics, using chi-square " χ^2 " test was applied. P-values <0.05 were considered as "statistically significant".

Results

Table 1 shows that 59.2% of patients were males, and their age (Mean±SD) was 11.0±4.9 years. Almost two thirds of the fathers had either secondary level of education (34.8%) or university qualifications (32.2%). One-third of fathers (33.2%) and 72.7% of mothers were unemployed.

Table 1: Demographic characteristics of the patients

Characteristics	No.	%
Gender		
• Male	228	59.2
• Female	157	40.8
Age (Mean±SD)	11.0±4.9 years	
Father's education level		
• Primary	25	6.5
• Intermediate	72	18.7
• Secondary	134	34.8
• University	124	32.2
• Postgraduate	30	7.8
Mother's education level		
• Illiterate	34	8.8
• Primary	37	9.6
• Intermediate	60	15.6
• Secondary	108	28.1
• University	137	35.6
• Postgraduate	9	2.3
Father's job		
• Unemployed/Retired	128	33.2
• Teacher	100	26.0
• Military	50	13.0
• Physician	15	3.9
• Others	92	23.9
Mother's employment		
• Unemployed	280	72.7
• Employed	105	27.3

Table 2 shows that most patients were diagnosed since 1-5 years (40.3%) or >5 years (44.2%). Almost half of patients (48.3%) had positive family history of diabetes; diabetes was present in 12.7% of first-degree relatives, in 30.9% of second degree relatives, and in 4.7% of first and second degree relatives. Last recorded HbA1c levels for more than half of patients (53.5%) were >9% and 37.4% had 7-9%, while its level in 9.1% of patients was \leq 7%

Table 2: Clinical characteristics of type 1 diabetic patients

Characteristics	No.	%
Duration of diabetes		
• < one year	60	15.6
• 1-5 year	155	40.3
• >5 years	170	44.2
Family history of diabetes		
• No	199	51.7
• Yes	186	48.3
• First degrees relative	49	12.7
• Second degree relative	119	30.9
• Both first and second degree relatives	18	4.7
HbA1c level		
• \leq 7	35	9.1
• 7-9	144	37.4
• >9	206	53.5

Table 3 shows that 273 patients (70.9%) had history of diabetic ketoacidosis, only once in 43.6%, or twice in 24.5%. Main predisposing factors were being first presentation (59%) or treatment discontinuation (53.1%).

Table 3: Characteristics of ketoacidosis among type 1 diabetics

Characteristics	No.	%
History of ketoacidosis		
• Absent	112	29.1
• Present	273	70.9
Frequency of ketoacidosis (n=273)		
• Once	119	43.6
• Twice	67	24.5
• Three times	39	14.3
• Four times	23	8.4
• Five times	25	9.2
Predisposing factors for ketoacidosis (n=273)		
• First presentation	161	59.0
• Treatment discontinuation	145	53.1
• Non-adherence to diet	42	15.4
• Infectious diseases	25	9.2
• Others	12	4.4

Table 4 shows that diabetic ketoacidosis occurred significantly more in patients with less educated fathers and mothers ($p=0.010$ and $p=0.002$, respectively), and also in patients with unemployed fathers or mothers ($p=0.002$ and $p<0.001$, respectively). Ketoacidosis occurred more frequently among female than male patients (74.5% and 68.4%, respectively). However, diabetic ketoacidosis did not differ significantly according to their gender.

Table 4: Differences in occurrence of ketoacidosis according to demographic characteristics of patients

Personal Characteristics	History of ketoacidosis				P Value
	Yes (n=273)		No (n=112)		
	No.	%	No.	%	
Gender					0.196
• Male	156	68.4	72	31.6	
• Female	117	74.5	40	25.5	
Fathers' education					0.010
• Primary	23	92.0	2	8.0	
• Intermediate	51	70.8	21	29.2	
• Secondary	102	76.1	32	23.9	
• University	81	65.3	43	34.7	
• Postgraduate	16	53.3	14	46.7	
Mothers' education					0.002
• Illiterate	30	88.2	4	11.8	
• Primary	32	86.5	5	13.5	
• Intermediate	41	68.3	19	31.7	
• Secondary	81	75.0	27	25.0	
• University	82	59.9	55	40.1	
• Postgraduate	7	77.8	2	22.2	
Fathers' job					0.002
• No job	102	79.7	26	20.3	
• Teacher	72	72.0	28	28.0	
• Military	39	78.0	11	22.0	
• Physician	9	60.0	6	40.0	
• Others	51	55.4	41	44.6	
Mothers' employment					<0.001
• Unemployed	223	79.6	57	20.4	
• Employed	50	47.6	55	52.4	

* Statistically significant

Table 5 shows that diabetic ketoacidosis occurred significantly more in patients with family history of diabetes ($p<0.001$) and in patients with higher levels of HbA1c ($p<0.001$). However, its occurrence did not differ significantly according to patients' age or duration of disease.

Table 5: Differences in occurrence of ketoacidosis according to clinical features of the patients

Personal Characteristics	History of ketoacidosis				P Value
	Yes (n=273)		No (n=112)		
	No.	%	No.	%	
Duration of diabetes					0.468
• < One year	41	68.3	19	31.7	
• 1-5 years	106	68.4	49	31.6	
• >5 years	126	74.1	44	25.9	
Family history of diabetes					<0.001
• Yes	110	59.1	76	40.9	
• No	163	81.9	36	18.1	
HbA1c:					<0.001
• ≤ 7	8	22.9	27	77.1	
• 7-9	84	58.3	60	41.7	
• >9	181	87.9	25	12.1	
Age of patient (Mean \pm SD)	10.9 \pm 4.8		11.3 \pm 5.2		0.469

Discussion

Results of this study showed that more than two thirds of the participants experienced DKA at least once. Moreover, 59% attributed their DKA to their first presentation of the disease, while 53.1% attributed their incidents to discontinuation of treatment.

This occurrence is higher than what has been reported in Szybowska et al. (16), in Poland, who reported that one-quarter of type 1 diabetic children presented with DKA at their first diagnosis, while Jefferies et al. (7), in New Zealand, reported that it occurred in 27% of type 1 diabetic patients. Nevertheless, it is lower than that reported by Onyiriuka et al. (17) in Nigeria, where about three-quarters of diabetics presented with DKA.

In Saudi Arabia, Al-Hayek et al. (18) reported all their 103 adolescent T1DM patients had DKA, where 54.4% experienced one episode, and the main reason was the discontinuation of insulin treatment.

Results of our study indicate the pressing need for increasing parents' awareness regarding and premonitory symptoms and signs of diabetes and diabetic ketoacidosis and the need to facilitate prompt access to health care.

Moreover, health education to patients and their parents at primary health care centers is important as it is considered an effective method to prevent DKA. Consequently, every consultation at a health care facility should be used ideally so that diabetic patients can get the maximum benefits from healthcare providers at each visit (16).

Our study showed a significant association between diabetic ketoacidosis and family history. This finding is consistent with those reported in Saudi Arabia by several studies (19-20).

Results of our study did not show significant difference regarding the occurrence of diabetic ketoacidosis according to gender, despite its higher occurrence among females. This finding is in accordance with that reported by Al-Hayek et al. (18) study. Several studies reported that diabetic ketoacidosis is frequently higher among female than male young diabetics. This could be explained by several factors. The first one is attributed to puberty-associated hormonal changes, especially the raising in the serum levels of some counter-regulatory hormones, e.g., estrogen, which is, by far, higher in girls than boys at puberty. The second factor is related to body-image psychiatric problems, including eating problems, since adolescent diabetic girls often miss insulin injections for the sake of losing weight. Moreover, girls with diabetic ketoacidosis may have more behavioral problems, lower social competence, and higher levels of family struggle (17; 20).

Our study revealed significantly higher occurrence of diabetic ketoacidosis among children with poor glycemic control. This finding is in accordance with several other

studies, which reported that patients with high levels of HbA1c had significantly higher risks for diabetic ketoacidosis (20-22).

Conclusion

More than two thirds of type 1 diabetic children aged below 18 years, experience ketoacidosis. The main risk factors for diabetic ketoacidosis include first presentation of disease, and discontinuation of treatment. Female patients are more likely to suffer from ketoacidosis than males. Most cases with history of DKA have uncontrolled HbA1c. DKA is higher among patients with less educated and unemployed parents. DKA is significantly higher among patients with a positive family history of diabetes.

Therefore, primary health care physicians should provide the necessary health education on diabetes care and diabetic ketoacidosis for all T1DM patients and their caregivers during each visit to primary care centers. Health education messages should cover the main points of knowledge, especially how to identify and manage hyperglycemia. Raising the public's awareness regarding DM and DKA through mass media is required.

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