



STUDY OF PRECIPITATING FACTORS OF DIABETIC KETOACIDOSIS AMONG TYPE I DIABETES MELLITUS CHILDREN

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ABSTRACT

Diabetic ketoacidosis (DKA) is a common complication among children with diabetes mellitus (DM), and the risk of DKA in established type 1 diabetes mellitus is 1–10% per patient per year. This study aimed to determine the frequency of the precipitating factors of DKA admissions to emergency room in Amiriya general hospital – Al-Anbar/Iraq. This case-control study was conducted from January to December 2019 on 40 children with diabetic ketoacidosis (DKA) (19 males and 21 females; between 1 and 15 years of age) and 42 children with type 1 diabetes mellitus, as a control group (21 males and 21 females; between 1 and 15 years) who were admitted to Amiriya general hospital, Al-Anbar - Iraq. Data regarding history, full physical examination, and laboratory investigations (presence of glucose and/or ketones in urine, serum potassium (mEq/l), blood bicarbonate (mmol/L), venous pH, blood glucose (mg/dl), and the treatment given were recorded. The frequency of DKA was not significantly higher in girls than in boys 21(52.5%) vs. 19 (47.5%) (P > 0.05). In 22(55%) of cases, it was the first time they were discovered to be diabetic, and 10 (55.5%) of known diabetic patients had history of previous attacks of DKA and previous attacks of hypoglycemia were encountered in 15 (83.3%) of cases. The most common precipitating causes of DKA was infection, which occurred in 18 (45%) of the episodes, no identifiable cause for the episode was encountered in 10 (25%) of cases, missing the usual dose of insulin, and stress were identified in 6 (15%) for each, while increased food intake was documented as a precipitating factors in 2 (5%) of cases. Infection, missing the usual dose of insulin, stressful conditions and increased food intake were the main precipitating factors for DKA. Newly discovered DM presenting for the first time as DKA involved a significant proportion of the cases of DKA. It can be concluded that the main precipitating factors for the episodes were infections, missing the usual dose of insulin, infections, stressful conditions and increased food intake especially sweets. Newly discovered DM presenting for the first time as DKA were a significant proportion of the cases of DKA.

INTRODUCTION

Diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality in children with type 1 diabetes mellitus. Less commonly, it can occur in children with type 2 diabetes mellitus. DKA is caused by absolute or relative insulin deficiency.

The incidence and prevalence of type 2 diabetes mellitus have increased across all ethnic groups. This has been coupled with an increasing awareness that children with type 2 diabetes mellitus can present with ketosis or DKA, particularly in obese African American adolescents.^[1-3]

Standard qualitative measurements of ketones (as acetoacetate) can underestimate severity of ketosis.

Serum beta-hydroxybutyrate is a more accurate measure of ketosis and should be used whenever available. Beta-hydroxybutyrate concentrations ≥ 3 mmol/L (31 mg/dL) are consistent with DKA.^[4]

Factors that increase the risk that a child will have DKA at the initial presentation of type 1 diabetes include young age (<5 years of age and especially <2 years), low socioeconomic status or lack of health insurance, ethnic minority, delayed diagnosis, lower body mass index, children living in countries with low prevalence of type 1 diabetes.^[5]

Common precipitating factors for DKA include poor metabolic control or missed insulin doses,^[6] Stress,^[7] vomiting and dehydration, medications as well as drugs

and alcohol.^[8]

Signs and symptoms of DKA are related to the degree of hyperosmolality, volume depletion, and acidosis.^[9] The earliest symptoms of DKA are related to hyperglycemia older children and adolescents typically present with polyuria, polydipsia, tachycardia and fatigue. Other findings include weight loss, nocturia, daytime enuresis and vaginal or cutaneous moniliasis. Hypovolemia may be severe if the urinary losses are not replaced.

In infants, the diagnosis is more difficult because the patients are not toilet trained and they cannot express thirst. As a result, polyuria may not be detected and polydipsia is not apparent. However, decreased energy and activity, irritability, weight loss, and physical signs of dehydration are common findings. In addition, severe Candida diaper rash or otherwise unexplained metabolic acidosis or hypovolemia should heighten the suspicion for diabetes [9]. A number of other clinical findings may be seen such as polyphagia, hyperventilation and deep (Kussmaul) respirations, extracellular volume depletion Neurologic findings, ranging from drowsiness, lethargy, and obtundation to coma, are related to the severity of hyperosmolality and/or to the degree of acidosis.^[10]

PATIENTS AND METHODS

The current case control hospital-based study was conducted in Amiriya general hospital, district of Al-Anbar during the period from January to December 2019. All the (40) children with DKA admitted to the hospital were studied in addition to a control sample comprising the (42) diabetic children admitted to the hospital during the same period of the study.

The questionnaire, included items such as sex, age, whether the child is known to be diabetic, past history of

previous attacks of DKA and/or hypoglycemia as well as questioning them about the possible precipitating factors. Treatment including insulin, fluid and electrolyte replacement and treatment of the cause of DKA (such as infection) was given as required. All patients were followed until discharge from the hospital.

Immediate intravenous access and fluid and electrolyte replacement regimen were established to all patients. All patients had their blood glucose documented on arrival; the biochemical profiles that were documented for the patients included blood PH, HCO₃, Serum potassium, Serum Sodium, Serum Blood Urea Nitrogen, together with the urine sample examination for the presence of glucose and ore ketones. The same investigations were applied to the 42 control patients who were admitted to control of their DM.

All patients were given an intravenous insulin regimen with blood glucose monitoring at appropriate intervals; together with fluid and electrolyte replacement; all received potassium and antibiotics were given to those in whom an illness was identified prior to admission.

Statistical analysis

Statistical analysis was performed by using SPSS version 23 program. The level of significance was set to 5%. $P < 0.05$ was considered significant, while $P > 0.05$ was considered as a non-significant.

RESULTS

The results of our study showed no significant difference ($P > 0.05$) between the mean age of patients with DKA and those of the control group (10.18 ± 3.02) years (range between 11 months and 15 years), and 10.51 ± 4.72 years (range 2.1 - 15.6 years of age respectively).

Table (1): Demographic characteristics of the study groups.

Variables	Cases = 40		Control = 42	
	Frequency	Percentage	Frequency	Percentage
Gender				
Male	19	47.5	21	50.0
Female	21	52.5	21	50.0
Age group (years)				
< 5	5	12.5	6	14.3
5- 10	17	42.5	15	35.7
> 10	18	45.0	21	50.0
Total	40	100	42	100

The frequency of DKA was not significantly higher in girls than in boys (52.5 vs. 47.5 %; $p > 0.05$), also no gender difference was encountered among members of the control group as shown in table (1), and 18 (45%) of the episodes of DKA were in patients with known DM; in the other 22 (55%) of the cases, it was the first time they were discovered to be diabetic; newly discovered DM was encountered in 34 (80.95%) of the control group as illustrated in table (2).

Table (2): Diabetic history of the study groups.

Diabetic history	Cases		Control	
	Frequency	Percentage	Frequency	Percentage
Previously Diabetic	18	45.0	8	19.1
Newly diagnosed	22	55.0	34	80.9
Total	40	100	42	100

Table (3) showed that 10 (55.5%) of the known diabetic patients in DKA group had history of previous attacks of DKA ranging from 1-5 attacks, 3 (37.5%) of the diabetic patients in the control group had a history of an attack of

DKA; Previous attacks of hypoglycemia were encountered in 15 (83.3%) of them, and 4 (50.0%) of the control group in patients those who were known to be diabetic as seen in table (4).

Table (3): Previous attacks of DKA among known diabetics within the study groups.

	Cases		Control	
	Frequency	Percentage	Frequency	Percentage
Yes	10	55.5	3	37.5
No	8	44.5	5	42.5
Total	18	100.0	8	100.0

Table (4): Previous attacks of hypoglycemia among known diabetics within the study subjects.

	Cases		Control	
	Frequency	Percentage	Frequency	Percentage
Yes	15	83.3	4	50.0
No	3	16.7	4	50.0
Total	18	100.0	8	100.0

Frequent urination with thirst for a day or more and fatigue, were the most common presenting symptoms for members of both cases of DKA and the diabetic patients of the control group accounting for more than 70% of patients in both groups with no statistical difference between them; while the occurrence of rapid breathing

and/or shortness of breath, abdominal pain, fever and nausea and vomiting were significantly higher among patients with DKA. The frequency of occurrence of the different symptoms among DKA cases and control group on admission is illustrated in table (5).

Table (5): Frequency distribution of different symptoms among the study subjects.

Symptom	Cases		Control	
	Frequency	Percentage	Frequency	Percentage
Frequent urination or thirst	33	82.5	35	83.3
Fatigue	30	75.0	30	71.42
Rapid breathing and/or SOB	25	62.5	3	7.14
Abdominal pain	21	52.5	8	19.04
Fever	18	45.0	4	9.52
Nausea and vomiting	15	37.5	8	19.04

The most common precipitating causes of DKA was infection, which occurred before, 18 (45%) of the episodes, no identifiable cause for the episode was encountered in 10 (25%) of cases, missing the usual dose

of insulin, and stress were identified in 6 (15%) for each, and increased food intake was documented as a precipitating factor in 2 (5%) of cases as shown in table (6).

Table (6): Possible precipitating factors of DKA.

Factor	Frequency	Percent
Infection	18	45.0
No identifiable cause	10	25.0
Missing doses of insulin	6	15.0
Stress	6	15.0
Increased food intake	2	5.0
Total	42	100

Signs of dehydration were observed in 26 (96.3%) of the patients with DKA and 2 (7.2%) of the control group;

moderate to severe dehydration was encountered in 16 (59.3%) of the patients (Table 7).

Table (7): Signs of dehydration among DKA cases.

Degree of dehydration	Cases		Control	
	Frequency	Percentage	Frequency	Percentage
None	2	5.0	38	90.4
Mild	15	37.5	2	4.76
Moderate	20	50.0	2	4.76
Severe	3	7.5	0	0
Total	40	100	42	100

Mortality was null. Only 3 (7.5%) patients went into cerebral edema which improved on treatment (Table 8); all patients within the control group improved after the control of their state.

Table (8): Prognosis of patients with DKA.

Prognosis	Frequency	Percent
Improved	37	92.5
Cerebral edema	3	7.5
Total	40	100

DISCUSSION

This study found that there is no significant difference between girls and boys presented as DKA (52.5% vs 47.5%), this was similar to a study conducted by Sandeep Kumar *et al.*, who found that girls and boys are equally affected by DKA.^[11] Table (1).

Similar with a previous study,^[12] our study found that the prevalence of DKA was not related to age in either gender; Rewers A *et al.* (2002) from the University of Colorado, Denver, conducted a cohort study of 1,243 children with T1DM that showed an increased incidence of DKA with age in girls.^[13] Some previous studies,^[14] showed that children < 5 years face an increased risk of presenting in DKA, no similar result was concluded in this study; which can be explained by the small sample size of this study. Table 1.

Newly discovered DM presenting for the first time as DKA involved a significant proportion (55.0%) of the cases of DKA studied which is higher than that concluded by Neu A *et al.* (2003) in their study in Germany which was (26.3%),^[14] and comparable to the results of Lakhdar *et al.* (2005) among Libyan diabetic patients (78% of the episodes of DKA were in patients with known diabetes),^[15] and similar to Sandeep Kumar *et al.* (56.4%),^[11] this might be explained by the better public awareness of symptoms of DM among Germans and, therefore, earlier diagnosis of DM before its possible complication of DKA. Table 2.

The high frequency of previous attacks of complications of DM (i.e. DKA and hypoglycemia) encountered among DKA cases in this study might indicate the importance of the study of the different person variables of diabetic

children (including those of their families) in order to identify those at high risk, and thereafter, planning for prevention measures directed towards patients to avoid complications. Table 3 and 4.

This study found that frequent urination and thirst were the most common symptoms (82.5%), it is comparable with a Sandeep Kumar *et al.* study who found that polyuria and polydipsia were the most common presenting symptoms among cases of DKA studied (54.5%),^[11] Table 5.

In this study, infection was the most common precipitating cause of DKA followed by missing the usual dose of insulin and stressful conditions, followed by increased food intake especially sweets; with no identifiable cause for the episode. In Lakhdar A *et al.* study (2005). The most common cause of DKA was stopping insulin therapy followed by first presentation and infection.^[15] One study conducted in a developing country found that infection was the most common precipitating factor to DKA (37%).^[16] The high prevalence of infection can be explained on the basis of the high prevalence of infections in our country, as in other developing countries, and the health educational level among families of diabetic children.

No death was recorded and the 2 (7.4%) patients with DKA who went into cerebral edema improved on treatment; in Lakhdar A *et al.* study (2005) in Libya the mortality rate was 2%.^[15] The small sample size might explain this difference.

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