Clinical reaudit on management of diabetic ketoacidosis in Assiut University Children Hospital

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Introduction
Diabetic ketoacidosis (DKA) is one of the most common causes of admission in emergency unit and pediatric ICU in Assiut University Children Hospital. It is one of the important causes of mortality and morbidity in children with diabetes. DKA is a complex metabolic state of hyperglycemia, ketosis, and acidosis resulting from absolute or relative insulin deficiency.

Patients and methods
The study includes pediatric patients presented with DKA to emergency unit and pediatric ICU of Assiut University Children Hospital. It was done on 100 pediatric patients over 1 year from March 2017 to February 2018. This reaudit was done to evaluate the degree of compliance of management of DKA in relation to the guidelines in comparison with the previous study on the same topic that applied the same guidelines (International Society for Pediatric and Adolescent Diabetes Clinical Practice Consensus Guidelines 2014).

Results
Overall, 63% were females and 39% were in the age group older than 10 to 15 years. Resuscitation fluids were administered in 95% of cases on admission. All cases received insulin therapy with the start of resuscitation fluids. Glucose 5% was correctly added to intravenous fluids when blood glucose had fallen to ~14–17 mmol/l (250–300 mg/dl) in all cases.

Conclusion
Guidelines have been followed in the management of DKA in the studied cases, but there were some defects that can affect the outcome of management of DKA. The study recommends avoiding these defects.

Keywords:
diabetes mellitus, fluids, insulin, ketoacidosis, pediatric

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Introduction

Diabetic ketoacidosis (DKA) is one of the important causes of mortality and morbidity in children with diabetes. DKA is a complex metabolic state of hyperglycemia, ketosis, and acidosis resulting from absolute or relative insulin deficiency [1].

DKA is biochemically defined as follows [2]:

(1) Hyperglycemia: blood glucose (BG) of more than 200 mg/dl (11 mmol/l).
(2) Metabolic acidosis: defined as a venous pH less than 7.3 or plasma bicarbonate less than 15 mEq/l (15 mmol/l).
(3) Ketosis: determined by the presence of ketones in the blood or urine.

The severity of DKA can be categorized according to the degree of acidosis [2].

(1) Mild: venous pH more than 7.2 and less than 7.3, and bicarbonate less than 15 mmol/l.
(2) Moderate: venous pH more than 7.1 and less than 7.2, and bicarbonate less than 10 mmol/l.
(3) Severe: venous pH less than 7.1, and bicarbonate less than 5 mmol/l.

DKA is the most common cause of hospitalization, mortality, and morbidity in children with established type 1 diabetes mellitus [3].

The risk of DKA in children with established type 1 diabetes is 1–10% per patient per year [4].

Although less common, ketosis and DKA can occur in children with type 2 diabetes mellitus, particularly in African-American children [5].

Classically, patients will complain of polyuria, polydipsia, weight loss, abdominal pain, nausea, and vomiting. On physical examination, patients may present with dry mucous membranes, tachycardia, signs of delayed capillary refill and hypoperfusion, Kussmaul respirations, a fruity odor on the breath, and diffuse abdominal tenderness [6].

Cerebral edema accounts for most deaths (60–90%) caused by DKA [3,7].

Aim

The aim was to evaluate the degree of compliance of management of DKA in emergency unit and pediatric ICU in Assiut University Children Hospital in relation to the guidelines.

Patients and methods

The study includes pediatric patients presented with DKA to emergency unit and pediatric ICU of Assiut University Children Hospital. It was done on 100 pediatric patients over 1 year from March 2017 to February 2018. The study was approved by the Institutional Ethics Committee of Assiut University.

Inclusion criteria

All pediatric patients presented to emergency unit and pediatric ICU with DKA age group 1 month–18 years were included.

Exclusion criteria

The following were the exclusion criteria:

(1) Neonate age group.
(2) Patient with other causes of hyperglycemia such as stress hyperglycemia.
(3) Patient with other causes of acidosis such as acute gastroenteritis and salicylate overdose.

Tools of study

An observational checklist based on International Society for Pediatric and Adolescent Diabetes (ISPAD) Clinical Practice Consensus Guidelines 2014 was developed by the investigators to assess the management of patients with DKA.

The parameters to be assessed were as follows: investigations needed for diagnosis of the case of DKA, proper management, and clinical and biochemical monitoring as recommended by the guidelines.

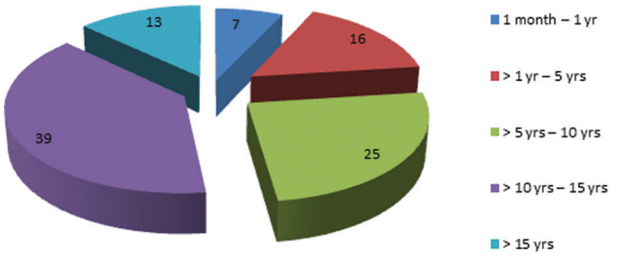
Results

The study included 100 pediatric patients admitted with DKA in emergency unit and pediatric ICU of Assiut University Children Hospital over 1 year.

Demographic data

Incidence was the highest in the age group (>10 yrs–15 yrs) by 39% and was the lowest in the age group (1 month–1 year) by 7%. According to the sex, 63% was females and 37% was males. Forty three percent of cases was from Assiut city. Most cases were old diabetic (68%) while 32% was newly diagnosed. Most of old diabetic had recurrence of DKA (88%) [Figs. 1 and 2].

Figure 1



The age distribution of the studied cases with diabetic ketoacidosis.

Clinical history

More frequent symptoms were abdominal pain, vomiting, polyuria, and polydipsia by percentage of 92%, 91%, 72%, and 65% respectively [Fig. 3].

Clinical signs

Kussmaul respiration and acetone odor of breathing were detected in all the cases. Tachycardia, lethargy, and low blood pressure were detected in most cases by percentage of 96%, 90%, and 74% respectively [Fig. 4].

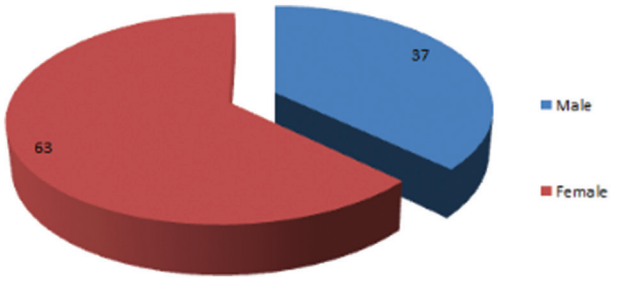
Investigation

Most cases had BG > 400 mg/dl on admission (54%). Fifty four percent of cases had +4 ketonuria. Severe acidosis was presented in 45% of cases. Some cases were presented with electrolyte disturbance. Few cases were associated with raised renal chemistry (5%). WBCs were increased in 65% of cases [Table 1].

Management

Resuscitation fluids were administered by percentage of 95% on admission and administered with correct dose and type of fluid in all cases. Deficit replacement and maintenance fluids were started with 0.9% saline in the 1st 4-6 hours in all cases but were changed to ≥0.45% after that according to serum Na level in only 6% of cases. Amount of fluids was correctly calculated in all cases. All cases received insulin therapy with the start of resuscitation fluids. Dose of the starting insulin was correctly calculated in all cases. Insulin dose was decreased when BG < 200 mg/dl in all cases. Glucose 5% was correctly added to intravenous fluids when BG had fallen to approximately 14-17 mmol/l (250-300 mg/dl) or when BG had fallen rapidly >

Figure 2



The sex distribution of the studied cases with diabetic ketoacidosis.

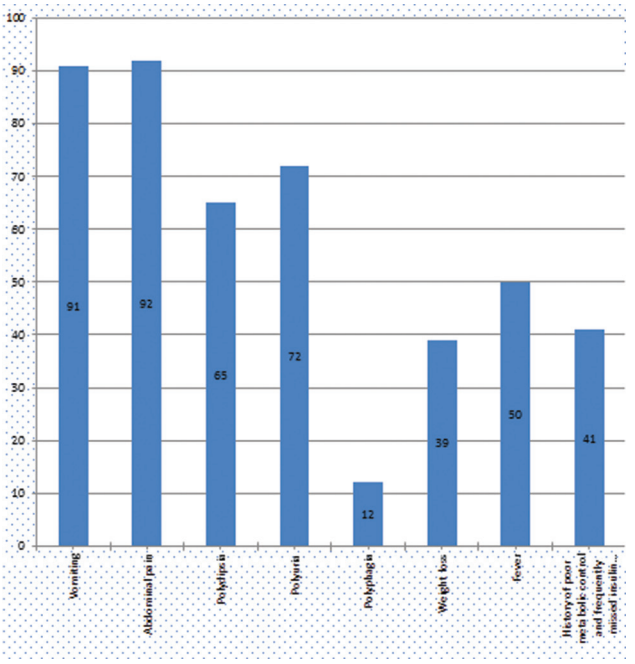
Table 1 Investigations of the studied cases with diabetic ketoacidosis

	n (%)
BG (mg/dl)	
>200-250	6 (6)
>250-300	10 (10)
>300-400	30 (30)
>400	54 (54)
Urine dipstick for ketones	
+2	4 (4)
+3	42 (42)
+4	54 (54)
Blood gases (pH, pCO_2, and HCO_3) and degree of acidosis	
Mild	20 (20)
Moderate	35 (35)
Severe	45 (45)
Serum electrolytes (sodium and potassium)	
Normal	84 (84)
Hypernatremia	6 (6)
Hyponatremia	2 (2)
Hyperkalemia	4 (4)
Hypokalemia	4 (4)
Kidney function tests (done in all cases)	
Normal	95 (95)
Raised chemistry	5 (5)
Complete blood count (done in all cases)	
Decreased Hb	41 (41)
Increased HCT	64 (64)
Increased WBCs	65 (65)
Culture(s)	
Blood	
Done	13 (13)
Not done	87 (87)
Urine	
Done	4 (4)
Not done	96 (96)
ECG	
Done	0 (0)
Not done	100 (100)
Chest radiography	
Done	9 (100)
Not done	0 (0)

BG, blood glucose; Hb, hemoglobin; HCT, hematocrit; WBC, white blood cell.

5mmol/l/hr (90 mg/dl/hr). Glucose concentration was not increased to 10% or even 12.5% when BG < 100-250 mg/dl while continuing to infuse insulin to correct metabolic acidosis in any case of both studies. all cases received potassium therapy after initial volume expansion without special care to hypokalemia or hyperkalemia. All cases with PH < 7.15 received bicarbonate [Tables 2-6].

Figure 3



Clinical history of the studied cases with diabetic ketoacidosis.

Discussion

DKA is one of the most common causes of admission in emergency unit and pediatric ICU in Assiut University Children Hospital. It is one of the important causes of mortality and morbidity in children with diabetes. Our study includes pediatric patients presented with DKA to emergency unit and pediatric ICU of Assiut University Children Hospital to evaluate the degree of compliance of management of DKA. From this study, we recorded the following:

(1) Fever was present in 50% of the studied cases, which make us to search for it and source of expected infection in cases of DKA.
(2) On admission, some of the recommended investigations were not properly done:
   (a) Blood culture was done only in 13% of cases and urine culture was done in 4% of cases. Although 50% of cases had fever, 54% had associated febrile illnesses, and 10% of cases had urinary tract infection. Blood and urine cultures should be done in cases with fever or urinary tract infection according to ISPAD 2014 guidelines.
   (b) Serum chloride was not done in any case,

although it is important in calculating anion gap according to our guidelines.

(c) ECG was not done in any case, but it should be done (according to ISPAD 2014 guidelines) in diagnosed cases of DKA with hyper-or-hypokalemia or when serum potassium level cannot be assessed to detect arrhythmia and changes in T-wave. Flattening of the T waves, widening of Q-T interval, and appearance of U waves indicate hypokalemia. Tall, peaked, symmetrical T waves and shortening of the Q-T interval are signs of hyperkalemia [8].

(3) DKA may be presented even with BG more than 200–250 mg/dl; therefore, high index of suspicion with early symptoms in new or established insulin-dependent diabetic patients and close supervision of established patients should be a major goal to prevent DKA.

(4) Resuscitation fluids were administered to all studied cases with correct dose by recommended type (0.9% saline) with correct rate. These were given on admission in 95% of cases and delayed in the other cases, which was not in agreement with our guidelines that recommend patients with mild DKA usually do not have impaired peripheral circulation and, therefore, do not require a fluid bolus. Resuscitation fluids administration was not recorded in the previous study.

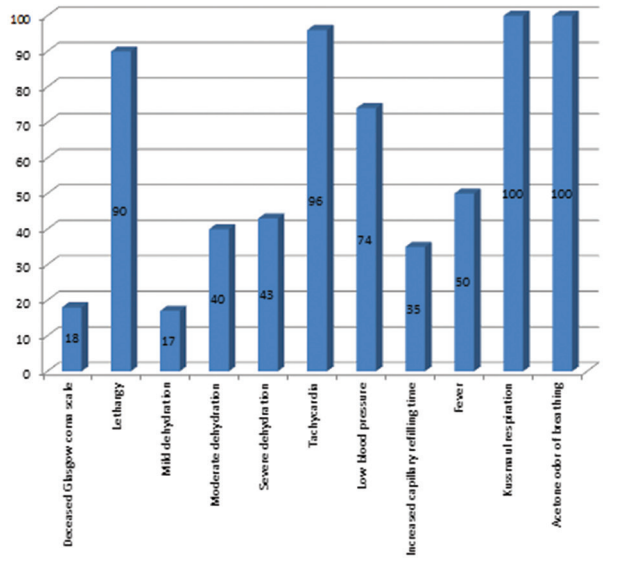
(5) Deficit replacement and maintenance fluids were started with 0.9% saline in the first 4–6 h in all cases, and this is in agreement with ISPAD 2014 guidelines. However, in majority of cases, there was a defect in changing the type of fluid to at least 0.45% saline after first 4–6 h according to follow-up of serum sodium level, and it was only changed in cases that were admitted with associating hypernatremia. This is not in agreement with ISPAD 2014 guidelines. The same defect had been found in the previous study.

(6) Another defect was that the estimated fluid deficit was replaced over 23 h in all studied cases compared with the previous study, where it had been correctly replaced over 48 h in most cases,

Table 2 Fluid therapy in the studied cases with diabetic ketoacidosis

	This study [*n* (%)]	Previous study (%)
Resuscitation fluids		
Start on admission	95 (95)	Not included
Type is 0.9% saline	100 (100)	
Dose 10-20 ml/kg	100 (100)	
Within 1-2 h	100 (100)	
Deficit replacement plus maintenance fluids		
Type is 0.9% saline in first 4-6 h	100 (100)	100
Change type to ≥0.45% saline after 4-6 h according to follow-up of serum sodium level	6 (6)	12
Correct dose [deficit+maintenance - resuscitation fluids (if needed)]	100 (100)	92
Replace the estimated fluid deficit over		
48 h	0 (0)	97
23 h	100 (100)	3

Figure 4



Clinical signs in the studied cases with diabetic ketoacidosis.

Table 3 Initial insulin therapy and adding glucose to fluids in the studied cases with diabetic ketoacidosis

	This study [*n* (%)]	Previous study (%)
Time of starting insulin		
1-2 h after starting fluid therapy	0 (0)	100
With the resuscitation fluid	100 (100)	0
Dose and rate of insulin		
Start with 0.1 μ/kg/h	100 (100)	100
Decreasing to 0.05 μ/kg/h. if BG <200 mg/dl	100 (100)	95
Added glucose 5% to intravenous fluids (0.9 or 0.45%) saline when blood glucose had fallen to~14-17 mmol/l (250-300 mg/dl) or when BG had fallen rapidly >5 mmol/l/h (90 mg/dl/h) by concentration of 1: 1	100 (100)	100
Glucose concentration was increased to 10% or even 12.5% when BG <100-250 mg/dl while continuing to infuse insulin	0 (0)	0

BG, blood glucose.

Table 4 Potassium replacement therapy in the studied cases with diabetic ketoacidosis

	This study [*n* (%)]	Previous study (%)
Start replacing potassium at the time of initial volume expansion and before starting insulin therapy in case of hypokalemia	0 (0)	0
Start replacing potassium after initial volume expansion and concurrent with starting insulin therapy	100 (100)	100
Defer until urine output is documented in case of hyperkalemia	0 (0)	0
Adding potassium phosphate together with potassium chloride	0 (0)	0

Table 5 Bicarbonate administration in the studied cases with diabetic ketoacidosis

	This study [*n* (%)]	Previous study (%)
Bicarbonate administration in life-threatening hyperkalemia (1-2 mmol/kg over 60 min) or in profound acidosis (pH<6.9)	15 (100)	Not included
Bicarbonate administration when pH<7.15 (not profound acidosis or life-threatening hyperkalemia)	30 (100)	92

Table 6 Transition to subcutaneous insulin injections and introduction of oral fluids in the studied cases with diabetic ketoacidosis

	This study [*n* (%)]	Previous study (%)
Subcutaneous insulin		
Transition when ketoacidosis has resolved	100 (100)	97
Start 15-30 min before stopping the insulin infusion	0 (0)	Not included
Started after stopping infusion by 6 h	100 (100)	Not included
Type was short acting	100 (100)	100
Introduction of oral fluids		
When substantial clinical improvement has occurred (mild acidosis/ketosis may still be present)	100 (100)	Not included
Subtract oral fluids from total fluid intake	0 (0)	

in agreement with ISPAD 2014 guidelines and many other studies and guidelines [9–12].

(7) It was found that all cases received correct amount of fluids, whereas in the previous study, some cases (8%) had received incorrect amount.

(8) It was found that initial insulin therapy was started with resuscitation fluids in all cases. According to ISPAD 2014 guidelines, it should be started 1–2 h after starting fluid therapy to decrease incidence of cerebral edema, as was correctly done in the previous study. However, another study was done supporting this recommendation [10].

(9) Insulin dose, rate, and decreasing dose to 0.05 μ/kg/h when BG is less than 200 mg/dl were properly done in all cases in our study, whereas there had been defect in decreasing dose in 5% of the previous ones.

(10) Adding glucose 5% to intravenous fluid when BG had fallen to ~14–17 mmol/l (250–300 mg/dl) or when BG had fallen rapidly more than 5 mmol/l/h (90 mg/dl/h) by concentration of 1: 1 was properly done in all cases in both studies.

(11) There was defect in increasing glucose concentration to 10% or even 12.5% with continuation of insulin infusion when BG had fallen to less than 100–250 mg/dl to prevent hypoglycemia and correct metabolic acidosis in all cases of both studies. Other than ISPAD 2014 guidelines, BSPED 2015 Guideline supported this recommendation [12].

(12) In potassium therapy (according to ISPAD 2014 guidelines), it should be started after initial fluid therapy in eukalemic cases and from the start in hypokalemic cases and postponed in cases with hyperkalemia until urine output is documented. There was defect in potassium therapy in both studies, as it was started after initial volume expansion without special care to hypokalemia or hyperkalemia in all cases. There was another defect in potassium therapy as potassium phosphate was not added to potassium chloride in any case and this is not in agreement with ISPAD 2014 guidelines.

(13) Bicarbonate should not be given except in life-threatening hyperkalemia or in profound acidosis (pH < 6.9). In our study, all cases with pH less than 7.15 received bicarbonate for correction of acidosis and the same had occurred in most cases (92%) with pH less than 7.15 in the previous study. There are other studies that were done supporting this recommendation [13,14].

(14) Transition to subcutaneous insulin was properly planned in all studied cases with short-acting insulin as recommended, but there was defect in time of starting subcutaneous insulin injection.

(15) It was started after stopping infusion by 6 h, whereas it should be started 15–30 min before stopping infusion to allow sufficient time for insulin absorption.

(16) There was a defect in subtracting the amount of introduced oral fluids from total fluid intake.

(17) Regarding clinical and biochemical monitoring, the results revealed the following:

(a) Vital signs were monitored in all cases of our study and majority of cases (80%) of the previous one every 2 h instead of hourly monitoring, and this is not in agreement with our guidelines.

(b) Mental status was monitored by Glasgow Coma Scale and warning signs and symptoms of cerebral edema every hour in 18%, which

were presented with decreased Glasgow Coma Scale on admission and every 2 h in the rest of cases in this study, whereas in the previous study, it had been hourly monitored in 90% of cases. It should be hourly monitored in all cases according to our guidelines.

(c) BG was monitored every 2 h in all studied cases not hourly according to recommendations; in the previous study, it had been hourly monitored in majority (60%) of cases.

(d) Urinary ketones were never monitored in any case in our study, and it had not been included in the previous study.

(e) Serum sodium and potassium were not routinely monitored in both studies and only monitored in cases presented with electrolyte disturbance on admission; it was not in agreement with our guidelines which recommend routine monitoring in all cases to select type of fluid according to serum sodium level to prevent cerebral edema and also to prevent potassium disturbance, which has many complications. Serum chloride was not monitored in any case in both studies; it should be routinely monitored in all cases to calculate the anion gap and to avoid hyperchloremic acidosis. Effective osmolality and corrected sodium were not monitored in any case, which is not in agreement with guidelines.

(f) According to guidelines, blood gases should be monitored every 2–4 h; this had happened in most cases in the previous study but did not happen in any case of our study. In our study, blood gases were monitored every 6 or 12 h.

(g) Amount of administered insulin and accurate fluid input and output should be monitored according to guidelines, but it was not monitored in cases of our study and had not been included in the previous study.

(18) Cerebral edema occurred in 9% of cases in our study, and all of them received proper management.

(19) Hypoglycemia occurred in 21% of cases in our study. British Society for Paediatric Endocrinology and Diabetes 2015 guidelines recommend giving bolus 2 ml/kg of 10% glucose and reducing insulin less than 0.05 μ/kg/h without stopping insulin, which is not included in our guidelines. All cases with hypoglycemia received bolus 2 ml/kg of 10% glucose, but insulin was stopped in all these cases.

Conclusion

ISPAD Clinical Practice Consensus Guidelines 2014 have been followed in the management of DKA in the studied cases, but there were some defects that can affect the outcome of management of DKA. The study recommends avoiding these defects.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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