

# Diabetic Ketoacidosis in Children with Type One Diabetes Mellitus: Risk Factors, Outcome and Complications

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**Abstract:** ***Background:** Diabetic keto acidosis (DKA) is the leading cause of morbidity and mortality in children with type one diabetes mellitus (T1DM). Mortality is predominantly related to the occurrence of cerebral edema. **Objective:** The aim of the study is to identify the risk factors leading to the development of DKA and the complications associated with it to increase awareness of both physicians and general population. **Materials and methods:** Data was collected from 99 patients admitted with the diagnosis of DKA to the pediatric ward at Al- Numan Teaching Hospital from January 2018 to December 2020. Diagnosis was based on both clinical and biochemical criteria. Information was taken regarding risk factors, outcome and complications. **Results:** Risk factors differ in patients with new onset diabetes from those with established T1DM. In new onset cases young age (less than 5 years ) was the most important factor ( 42.8% were in the age group 2 – 6 years ). Regarding established cases insulin omission and poor metabolic control were the most important risk factors (65.3% had poor control with omission of insulin doses). Regarding recurrent episodes of DKA adolescent females with behavioral problems or family problems were the highest risk group (85.7%). There were no deaths in our study, 9% developed complications related to hypoglycemia and electrolyte disturbances. One patient developed cerebral edema and one patient developed acute renal failure. **Conclusion:** like other studies, our study showed that risk factors differ depending on whether the patient had new onset or established T1DM. Young age was the most important risk factor for new onset cases while insulin omission and poor metabolic control was the most important risk factor in established cases. Regarding recurrent episodes of DKA peri pubertal and adolescent females with behavioral problems were the highest risk group. Awareness of these and other contributing factors will help in reduction of the number of DKA episodes. Most of the complications related to DKA or its treatment were due to electrolyte disturbances ( hyponatremia and hypokalemia) and hypoglycemia. Cerebral edema although occurring in less than 1% of patients remains a devastating complication and the main cause of death in DKA.*

**Keywords:** Type one diabetes mellitus, diabetic keto acidosis, cerebral edema , hypoglycemia and electrolyte disturbances

## 1. Introduction

Diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality in children with type one diabetes mellitus (T1DM). It is a metabolic derangement caused by the absolute or relative deficiency of insulin leading to intracellular starvation and stimulating the release of counter regular hormones ( glucagon, catecholamines, cortisol and growth hormone) The combined effect of these two factors lead to the development of hyperglycemia, hyperosmolality, ketonemia, ketonuria and metabolic acidosis.(1). Clinical features of DKA include dehydration, rapid deep sighing respiration (Kussmaul breathing) , vomiting, abdominal pain, progressive obtundation and loss of consciousness and fever if there is infection.

The biochemical criteria for diagnosis include

- 1) Hyperglycemia ( blood glucose >11 mmol/L or 200mg /dl)
- 2) Venous pH < 7.3 or bicarbonate < 15 mmol /L
- 3) Ketonemia and ketonuria

Treatment is with exogenous insulin, fluid and electrolyte replacement, this is done according to DKA treatment protocols.(2)

Diabetic Ketoacidosis Treatment Protocol

TIME	THERAPY	COMMENTS
1st hr	10-20 mL/kg IV bolus 0.9% NaCl or LR Insulin drip at 0.05 to 0.10 units/kg/hr	Quick volume expansion; may be repeated. NPO. Monitor I/O, neurologic status. Use flow sheet. Have mannitol at bedside; 1 g/kg IV push for cerebral edema
2nd hr until DKA resolution	0.45% NaCl: plus continue insulin drip 20 mEq/L KPhos and 20 mEq/L KAc 5% glucose if blood sugar <250 mg/dL (14 mmol/L)	IV rate = $\frac{85 \text{ mL/kg} + \text{maintenance} - \text{bolus}}{23 \text{ hr}}$ If K <3 mEq/L, give 0.5-1.0 mEq/kg as oral K solution or increase IV K to 80 mEq/L
Variable	Oral intake with subcutaneous insulin	No emesis; CO <sub>2</sub> ≥16 mEq/L; normal electrolytes

Frequency and risk factors of DKA

- 1) DKA with new onset T1DM

There is a wide geographic variation in the frequency of DKA at diabetic onset, and rates correlate inversely with regional incidence of T1DM and therefore the level of awareness in the community of pediatric diabetes. The range is from 15% - 67%. Risk factors include young

age, low socioeconomic level, no family history of diabetes and misdiagnosis.(3)

2) DKA in established T1DM

The incidence of DKA is 1- 10% per patient per year.

Risk factors include

- Insulin omission and poor adherence to treatment
- Poor metabolic control
- Previous episodes of DKA
- Age ( peri pubertal and adolescent girls have the highest risk )
- Low socioeconomic level and personal behavioral problems
- Limited access to outpatient diabetic care.(3)

**Morbidity and mortality**

In national population studies the mortality rate from DKA is 0.15 – 0.30 %. Cerebral edema accounts for 60 – 90 % of deaths, it is a devastating and unpredictable complication of DKA and it’s treatment. It’s occurrence is about 7/1000 episodes of DKA and it’s pathophysiology is not well understood.

Risk factors include young age, new onset T1DM, more sever acidosis at presentation, administration of large amounts of fluid in the first 4 hours of treatment and administration of bicarbonate. Early signs of cerebral edema that should be looked for include headache, irritability, unexplained decrease in heart rate and increase in blood pressure.

Other complications of DKA include hypokalemia, hypoglycemia, hyponatremia , peripheral venous thrombosis, sepsis, acute renal failure and acute pancreatitis.(4)

**2. Methods and Materials**

This is a retrospective study done at Al-Numan Teaching Hospital from January 2018 to December 2020, 99 patients with DKA admitted to the pediatric ward were included. Diagnosis of DKA was made according to both clinical and biochemical criteria other investigations were done according to comorbidities.

Patients were divided into two groups those with new onset T1DM and those with established T1DM, data was taken from their medical records regarding

- 1) Risk factors contributing to DKA development including:
  - a) Age
  - b) Sex
  - c) Compliance with treatment and metabolic control
  - d) ( compliance and metabolic control was considered good if the patient had regular check of his blood sugar at home and regular visits to the diabetic care outpatients )
  - e) Socioeconomic level ( based on educational level of the parents
  - f) Low if illiterate or primary school education, medium if secondary school education and high level if university graduate)
  - g) Personal behavioral problems and family problems

h) Inter current infection

2) Out come and complications of DKA episode

**3. Results**

The total number of patients included in the study was 99, 39 (39.3% ) males and 60 (60.6% ) females.patients with new onset T1DM were 21 ( 21.2% ) and those with established T1DM were 78 (78.7%).

**Table 1:** New or established T1DM and sex distribution

	Male	Female	Total
New onset	15 (15.1%)	6 (6.1%)	21 (21.2%)
Established	24(24.2%)	54 (54.5%)	78 (78.7%)
Total	39 (39.3%)	60 (60.6%)	99 (100%)

**Patients with new onset T1DM and DKA**

Total number of patients was 21 , 15 (71%) males and 6(28.5%) females.

Risk factors for the development of Dka in this group included:

1) Age of patient

**Table 2:** Age and sex distribution

Age	Male	Female	Total
2 – 6 years	6 (28.5%)	3 (14.2%)	9 (42.8%)
7 – 10 years	3 (14.2%)		3 (14.2%)
11 – 14 years	6 (28.5%)	3 (14.2%)	9 (42.8%)
Total	15 (71%)	6 (28.5%)	21 (100%)

2) Family history of diabetes mellitus

**Table 3:** Family history of Diabetes mellitus

Diabetes Mellitus	Present	Absent	Total
	3 (14.2%)	18 (85.7%)	21 (100%)

3) Socioeconomic state of family

**Table 4:** Socioeconomic level of family

Socioeconomic level	Low	Medium	High	Total
	9 (42.8%)	12 (57.1%)		21 (100%)

4) Misdiagnosis of the condition

If the child was diagnosed as having an acute illness before reaching the diagnosis of diabetes and DKA

**Table 5:** Misdiagnosis of DKA

Misdiagnosis	Correct diagnosis from the beginning	Total
12 (57%)	9 (42%)	21 (100%)

**Patients with established T1DM and DKA**

Total number of patients was 78 , 24 (30.7%) males and 54 (69.2%) females .

Risk factors for the development of DKA include

1) Age and sex

**Table 6:** Age and sex distribution in patients with established T1DM and DKA

Age	Male	Female	Total
2 – 6 years	6 (7.69%)		6 (7.69%)
7 – 10 years	6 (7.69%)	24 (30.7%)	30 (38.4%)
11 – 14 years	12 (15.3%)	30 (38.4%)	42 (53.8%)
Total	24 (30.7%)	54 (69.2%)	(100%)

- 2) Insulin omission and poor adherence to treatment 51 (65.3%) had poor adherence to treatment, the majority were females 36 (46.1%).

**Table 7:** Adherence to treatment in patients with T1DM and DKA

Type of adherence	Male	Female	Total
Good adherence	9 (11.5%)	18 (23%)	27 (34.6%)
Bad adherence	15 (19.2%)	36 (46.1%)	51 (65.3%)

- 3) Socioeconomic level, personal and family problems

**Table 8:** Socioeconomic level and sex distribution

Socioeconomic level	Male	Female	Total
Low	18 (23%)	30 (38.4%)	48 (61.5%)
Medium	6 (7.69%)	24(30.7%)	30 (38.4%)
High	0	0	0

- 4) Previous episodes of DKA  
16 (20.5%) patients of the total 78 had more than one episode of DKA during the studied period, 2 (12.5%) were males and 14(87.5%) were Females. 12 (85.7%) of the females were in the adolescent age group.

- 5) Inter current infection precipitating the DKA episode  
18 (23%) patients of the total 78 patients had an infection as a precipitating factor to their DKA episode  
From these 18 patients  
9 (50%) patients had urinary tract infection  
5 (27.7%) patients had gastroenteritis  
4 (22.2%) patients had pneumonia

**Outcome and complications of DKA episodes**

In our study there were no deaths due to a DKA episode .  
The complications were as follows:

- 1 (1%) patient developed cerebral edema (11 year old male with T1DM for one year)
- 1 (1%) patient developed acute renal failure and was referred to a tertiary medical center for dialysis ( 9 year old male ,a known case of T1DM for 4 years, presented with sever dehydration and acidosis)
- 5 (5%) patients developed hyponatremia during treatment  
4(4%) patients developed hypoglycemia during treatment  
4(4%) patient developed hypokalemia during treatment.

**4. Discussion**

DKA is a life threatening condition that requires early recognition and specific management to avoid serious morbidity and mortality.

Management of an episode of DKA is not complete until its cause has been identified and an attempt made to treat it.

Risk factors differ between DKA at the time of diabetes diagnosis and episodes occurring in patients with established diabetes.

At disease onset young age was found to be the most common factor associated with increased risk of DKA especially in children younger than 5 years this was consistent with our study that showed 42.8% of the patients were in the age group 2- 6 years and with other multiple published studies(3), (5), (6). The causes are multiple including awareness of the general population of childhood diabetes(in our study 85.7% of the patients did not have family history of diabetes and therefore had little or no knowledge ) , lower index of suspicion by physicians as the signs and symptoms are similar to many of the acute illnesses of childhood and this was consistent with our study 57% of patients had another diagnosis before reaching the correct diagnosis and was found in other published papers (1) and finally low socioeconomic level as found in multiple published studies (3),(4),(6), in our study both low (42.8%) and medium (57.1%) socioeconomic levels were high risk factors.

In established diabetic cases regarding gender and age our study showed it is more common in females (69.2%) in comparison with males (30.7%). Peri pubertal and adolescent girls are the most common group (38.4%) especially in cases of recurrent DKA( 85.7%) , this was consistent with many published studies (1),(3),(4), (6),(7).

Insulin omission, either inadvertently or deliberately is the main cause in most of the cases. There are many causes for that:

- 1) No adult supervision and the child forgets to take insulin this is seen more in families with low socioeconomic level and this is in consistent with our study (61.5%) and other published studies (1),(3),(5).
- 2) Clinical depression
- 3) A means of escaping intolerable home situation
- 4) Attempt to lose weight in an adolescent girl

The last 3 causes are mostly seen in adolescent females especially in those with recurrent episodes of DKA. (3)

Inter current infection is another cause to precipitate an episode of DKA in our study (23%) of patients had an infection as the cause ,urinary tract infection was found in 50% of those patients this was also found in other published studies (8).

**Outcome and complications:**

There are many guidelines for treatment of DKA, in our hospital the guideline used was that from Nelson textbook of Paediatrics.

Regardless the guideline used the most important thing is correct replacement of insulin, fluid and electrolytes and close monitoring of the patient for early detection of any complications especially cerebral edema.

In our study there was no death, we had one case of cerebral edema (1%) who improved after receiving mannitol . In most studies the incidence of cerebral edema was between

0.5- 0.9% (1), (9). Other complications included hyponatremia (5%), hypoglycemia (4%), hypokalemia (4%) and one patient developed acute renal failure which is a rare complication of DKA and was referred for dialysis.

## 5. Conclusion

- DKA remains a significant complication of T1DM both at diagnosis and in established cases
- It is the most common cause of morbidity and mortality in T1DM
- The only way to prevent DKA is by identifying the risk factors and dealing with them.
- Risk factors for new onset diabetes include age, low socioeconomic level, general population awareness and primary healthcare alertness
- Risk factors for established cases include peri pubertal and adolescent females, poor metabolic control, personal behavioral problems and family conflict, low socioeconomic level and inter current infection.
- Careful replacement of insulin, fluid and electrolytes and close monitoring of the patient to reduce the complications.
- Cerebral edema is the main cause of death therefore early recognition of its signs and symptoms and early intervention will help to reduce it.

## 6. Recommendation

### *Regarding new onset T1DM*

- 1) Programs to increase the general population awareness about childhood diabetes. An example is that of the Italian School and Physician Awareness Program directed to 6 – 14 year age group that reduced the rate of DKA from 78% to nearly 0% over 6 years.(5)
- 2) Increase awareness of primary medical personnel for early detection.

### *Regarding established cases of T1DM*

- 1) Educational programs for both patients and parents regarding
  - Diet control
  - Metabolic control ( regular home checking of blood sugar, ketone in urine and regular visits to outpatient diabetic clinics).
  - Signs and symptoms of DKA for early recognition
- 2) Adult supervision regarding the dose and administration of insulin
- 3) Psychiatric therapy especially for adolescent females with recurrent episodes of DKA
- 4) Proper management of inter current infection

### *Regarding outcome and complications*

- 1) Patients should be treated by experienced medical staff and those with severe dehydration, severe acidosis and distributed level of consciousness should be treated in pediatric intensive care units.
- 2) Close monitoring of the patient using specific flow charts regarding the amount of fluid given, insulin dose and electrolyte replacement to minimize complications.(10)
- 3) Close monitoring of the patient for early signs of cerebral edema (headache, irritability, unexplained fall in heart

rate and increase in blood pressure) to insure early intervention.(10)

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