# King Khalid University Hospital
# Department of Paediatrics
# Paediatric Diabetic Ketoacidosis Clinical Guidelines

## Introduction

Many patients with diabetes die from diabetic ketoacidosis (DKA) every year. Use of a standard protocol provides consistent results in treating DKA.

These guidelines for the management of Diabetic Ketoacidosis were adopted and adapted from the work originally produced by the International Society for Pediatric and Adolescent Diabetes (ISPAD) that was published in Pediatric Diabetes, 2007: 8: 28–43. These original guidelines were also endorsed by the British Society of Paediatric Endocrinology and Diabetes (2009). Modifications have been made in the light of the ESPE/LWPES consensus statement on diabetic ketoacidosis in children and adolescents (Archives of Disease in Childhood, 2004, 89: 188-194). These original guidelines were also adopted by the British National Institute of Clinical Excellence (2009).

The following key changes included in our guidelines have been recommended recently by the International Society for Pediatric and Adolescent Diabetes (ISPAD), (2009):

1. Reduction in the degree of dehydration to be used to calculate fluids
2. Reduction in maintenance fluid rates
3. More emphasis on safe nursing on general wards
4. Continuation of Normal saline for at least the first 12 hours of rehydration
5. Delay in insulin until fluids have been running for an hour
6. Option to continue insulin glargine during treatment
7. Reminder to stop insulin pump therapy during treatment
8. Option to use hypertonic saline instead of mannitol for the treatment of cerebral oedema

## Scope and Purpose

This clinical pathway was designed to treat children less than 16 years old who presented to King Khalid university Hospital with Diabetic Ketoacidosis.
The aim of this clinical pathway is to treat children with DKA with a safe and evidence based guidelines.

## Stakeholder Involvement

This clinical guidelines were based on the guidelines produced by the International Society for Pediatric and Adolescent Diabetes (ISPAD). It was adapted, amended and reviewed by all parties involved in the management of children with DKA at King Khalid University Hospital. This includes Paediatric Endocrinology Unit, ER and PICU.

This clinical guidelines will be used by medical and nursing team in ER, PICU and paediatrics ward at King Khalid University Hospital.

## Plan of Action

Implementation of these clinical guidelines will be supervised by senior paediatricans (Registrars, Senior Registrars and consultants) in ER, PICU and ward.

An audit will be design to monitor, assess and measure implementation of and deviations from these guidelines.

These clinical guidelines will be reviewed after one year of implementation

## Background

Diabetic Ketoacidosis is an acute and life threatening complication of diabetes. DKA is caused by reduced insulin levels, decreased glucose use, and increased gluconeogenesis from elevated counter regulatory hormones, including catecholamines, glucagon, and cortisol. DKA primarily affects patients with type 1 diabetes, but also may occur in patients with type 2 diabetes, and is most often caused by omission of treatment and infection, Cerebral oedema is the main cause of death in DKA. Proper management of DKA decreases morbidity and mortality.

## Diagnosis of DKA

DKA presents with polyuria, polydypsia, altered level of consciousness, vomiting, dehydration and acidotic breathing.

**Initial Investigations:**

☐ laboratory blood glucose

☐ urea and electrolytes (electrolytes on blood gas machine give a guide until accurate results available)

☐ blood gases (venous blood gives very similar pH and pCO2 to arterial)

☐ urine ketones.

+ other investigations only if indicated e.g. PCV and full blood count (leucocytosis is common in DKA and does not necessarily indicate sepsis), CXR, CSF, throat swab, blood culture, urinalysis, culture and sensitivity etc.

(DKA may rarely be precipitated by sepsis, and fever is not part of DKA.)

## Criteria for the diagnosis of DKA

1. Hyperglycemia (blood sugar > 11 mmol/l
2. Acidosis (venous blood gas <7.3)
3. Bicarbonate < 15 mmol/l
4. Ketonuria

## Inclusion criteria

**Following patients should be included in the pathway:**

• Children less than 16 years of age fulfilling the above diagnostic criteria.

## Exclusion Criteria

**Following patients should *not* be included in the pathway (exclusions):**

1- Children requiring assisted ventilation
2- Children with signs of cerebral edema (headaches, bradycardia, irritability)
3- Glasgow Coma Scale <9

Children with any of the above exclusion criteria need special expertise, involvement of senior medical staff is recommended. However, management of this group of sick patients may follow clinical guidelines in this protocol but not necessarily sticking to it.

**Patients should be considered for removal from the pathway if:**

- No improvement in clinical condition in 48 hours.
- Patient developed cerebral edema
- Patient needed assisted ventilation

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## FULL CLINICAL ASSESSMENT AND OBSERVATIONS :

Assess and record in the notes.

**Conscious Level -**

Institute hourly neurological observations including Glasgow Coma Score whether or not drowsy on admission.

**GLASGOW COMA SCALE (GCS) Maximum score 15, minimum score 3**

| | | | | |
|---|---|---|---|---|
| **Best** | 1 = none | **Best** | 1 = none | *Modification (2-5yrs)* |
| **Motor** | 2 = extensor response to pain | **Verbal** | 2 = incomprehensible sounds | *1 = none* |
| **Response** | 3 = abnormal flexion to pain | **Response** | 3 = inappropriate words | *2 = grunts* |
| | 4 = withdraws from pain | | 4 = appropriate words but confused | *3 = cries or screams* |
| | 5 = localises pain | | 5 = fully orientated | *4 = monosyllables* |
| | 6 = responds to commands | | *Modification (<2yrs)* | *5 = words of any sort* |
| | | | *1 = none* | |
| **Eye** | 1 = none | | *2 = grunts* | |
| **Opening** | 2 = to pain | | *3 = inappropriate crying/unstimulated screaming* | |
| | 3 = to speech | | *4 = cries only* | |
| | 4 = spontaneous | | *5 = appropriate non-verbal responses (coos, smiles, cries)* | |

## Assessment of dehydration:

Over-estimation of degree of dehydration is dangerous.

**Therefore do not use more than 8% dehydration in calculations**

**Mild:** 3% - loss skin turgor, falling urine output, dry mucous membranes

**Moderate:** 5% - as for 3% with sunken eyes, apathy and ill looking

**Severe:** 8 % - poor capillary refill, tachycardia, pulse volume low, drowsy.

# FLUIDS :

## Resuscitation

**If patient very ill (drowsy, shocked, marked hyperventilation), call for senior help immediately**

**A** **Establish airway.** If coma, insert NG tube, free drainage

**B** **Give $O_2$ 100% via face mask with reservoir bag**

**C** **Establish IV access, take initial bloods** (consider 2nd cannula for later samples)
**Cardiac monitoring** (peaked T waves may indicate hyperkalaemia)

► **If prolonged CRT plus other signs of shock, give 10ml/kg IV 0.9% Saline.**
Assess effect. More than one fluid bolus rarely needed.
If hypotensive shock, give initial bolus 20 ml/kg 0.9% Saline
► **If circulation not improved, can give 2nd and (rarely) 3rd bolus (each over 30 mins) ie maximum total 30ml/kg - if shock persists, consult senior paediatrician & inform PICU**

- Overrapid or excessive fluids may increase risk of cerebral oedema
- Aim to rehydrate slowly over 48 hours, not 24 hours

## FLUID VOLUME

### 1. Maintenance fluids in DKA

| | |
|---|---|
| 0 – 12.9 kg | 80 ml/kg/24hrs |
| 13 – 19.9 kg | 65 ml/kg/24hrs |
| 20 – 34.9 kg | 55 ml/kg/24hrs |
| 35 – 59.9 kg | 45 ml/kg/24hrs |
| >60 kg (or adult) | 35 ml/kg/24hrs |

*Note 1: APLS maintenance fluid rates over-estimate requirement. Don't use them in DKA.*

*Note 2: Infant with DKA requires special consideration and larger volumes of fluid may be needed, usually 100-150 ml/kg/24 hours.*

### 2. Dehydration deficit (i.e. 3, 5 or 8%)

% dehydration x weight (kg) x 10 = fluid deficit (ml)
*(e.g. 10 kg child who is 5% dehydrated : 5 x 10 x 10 = 500 mls deficit)*

### 3. Fluid requirement for 48hrs = Maintenance for 48hrs + Deficit - Resus Fluids

Add maintenance for 48 hours (2 x daily maintenance) to calculated deficit; *subtract* volume of resuscitation fluid already given; then infuse over 48 hours. i.e.

**Hourly rate (ml/hour) = $\frac{\text{48 hour maintenance (ml) + deficit (ml) - resuscitation fluid already given (ml)}}{48}$**

**Subtract hourly insulin infusion rate from total hourly rate calculated as above**

Do not include continuing urinary losses in calculations at this stage

It is essential that all fluids given are documented carefully, particularly the fluid which is given in ER and on the way to the ward, as this is where most mistakes occur.

## Fluid calculation

***Example :***

A 20 kg 6 year old boy who is 8% dehydrated, and who has already had 20ml/kg saline, will require

8 % x 20 kg = 1600 mls deficit
**plus** 55ml x 20kg = 1100 mls maintenance each 24 hours
1100 mls
= 3800 mls
**minus** 20kg x 20ml = 400 mls resus fluid
3400 mls over 48 hours = 71 mls/hour

**Insulin infusion 20 ml per hour (0.1 unit/kg/hour) using 50 units of insulin in 500 ml of normal saline**

**So hourly rate of fluid will be**= 71-20= 51 ml per hour

**b) Type of fluid -**

Initially use **0.9% saline with 20 mmol KCl in 500 ml, and continue this sodium concentration for at least 12 hours.**

Once the blood glucose has **fallen to 14 mmol/l** add glucose to the fluid (0.9% saline with 5% glucose and 20 mmol KCl)

**After 12 hours**, continue on 0.9% saline with 5% glucose( or higher if needed) and 20 mmol KCl. If the plasma sodium level is increasing (>145 mmol/L, corrected), change to 500ml bags of 0.45% saline/5% glucose/20 mmol KCl.

Check U & E's 2 hours after resuscitation is begun and then at least 4 hourly
Electrolytes on blood gas machine can be helpful for trends whilst awaiting laboratory results.

## ON-GOING INSULIN & IV FLUID AND ELECTROLYTE MANAGEMENT

Ensure each 500ml fluid bag contains 20mmol KCl (40mmol/litre) unless anuric or peaked T waves.
Alter potassium replacement according to U&Es. More potassium than 40 mmol/L occasionally required.

**Falling Glucose level**

Addition of glucose to IV fluids is required when glucose falls <14mmol/L.

**When glucose falls <14mmols/L, add glucose to IV fluids as follows (don't reduce insulin infusion):**

- **If within first 12 hours**

  Continue 0.9% Saline/KCl as patient still sodium-depleted, but add glucose, use Bags of 500ml 0.9% Saline / 5% glucose (or higher if needed) + 20 mmol KCl

- **If after 12 hours, with plasma Sodium increasing (> 145 mmol/l corrected)**
  Can change to 0.45% Saline / 5% Dextrose (or higher if needed) + KCl 20mmol / 500ml.

- **If after 12 hours, but plasma Sodium is low or falling**

  Corrected sodium level should be rising as blood glucose falls during treatment.
  Do not change to 0.45% Saline/5% Dextrose + KCl 20mmol / 500ml.
  Instead, continue 0.9% Saline/5%glucose + 20mmol KCl / 500ml (see above)

  *Corrected Na = Na + 0.4 ([Glucose] - 5.5)*

**If blood glucose <4mmol/l, give bolus 2 ml/kg 10% glucose and increase glucose in IV fluids:**

Do not stop insulin, although may temporarily be reduced for 1 hour.

0.45% Saline/10% glucose + 20mmolKCl / 500ml can be used

Once pH >7.3 $HCO_3$ >15, consider reducing insulin infusion rate rather than adding glucose to IV fluids if glucose <14mmol/L.

If a massive diuresis continues, fluid input may need to be increased.

## Oral Fluid

Oral fluids should only be offered after substantial clinical improvement and no vomiting

☐ When good clinical improvement occurs before the 48hr rehydration period is completed, oral intake may proceed and the need for IV infusions reduced to take account of the oral intake.

## Insulin infusion:

Once rehydration fluids and potassium are running, blood glucose levels will start to fall. There is some evidence that cerebral oedema is more likely if insulin is started early.
**Therefore DO NOT start insulin until intravenous fluids have been running for at least an hour.**
Make up a solution of 1 unit per ml. of human soluble insulin (e.g. Actrapid) by adding 50 units (0.5 ml) insulin to 500 ml 0.9% saline in a syringe pump.
500 ml normal saline + 50 units regular Human insulin
10 ml=1 unit
Standard infusion rate is 0.1 unit/kg/hr= 1 ml/kg/hour
Once the blood glucose level falls to **14mmol/l**, change the fluid to contain 5% glucose or higher if needed in addition to 0.9% saline and potassium. **DO NOT** reduce the insulin. The insulin dose needs to be **maintained** at 0.1 units/kg/hour to switch off ketogenesis.
Consider decreasing insulin infusion to 0.05 unit/kg/hour when pH >7.3.
For **children who are already on long-acting insulin** (especially Glargine (Lantus)), this may be continued at the usual dose and time throughout the DKA treatment, in addition to the IV insulin infusion, in order to shorten length of stay after recovery from DKA.

For children on **continuous subcutaneous insulin infusion (CSII) pump therapy,** stop the pump when starting DKA treatment.

## Potassium:

- K should be given in the initial fluid bags unless anuria is suspected.
- Initially add 20 mmol KCl to every 500 ml bag of fluid.
- Then adjust K supplement according to blood level:
- Use a cardiac monitor and observe frequently for T wave changes.

## Bicarbonate

**Always discuss with the consultant in charge.**
Rarely indicated. Use only if severely acidotic, Ph <6.9, give 0.5 mmol/kg over one hour infusion.

## Observations and continuous management

**Ensure full instructions are given to the senior nursing staff emphasizing the need for:**

- ☐ strict fluid balance
- ☐ measurement of volume of every urine sample
- ☐ hourly **capillary blood glucose** measurements (these may be inaccurate with severe dehydration/acidosis but useful in documenting the trends. Do not rely on any sudden changes but check with a venous laboratory glucose measurement)
- ☐ urine testing for ketones
- ☐ hourly BP and basic observations
- ☐ twice daily weight; can be helpful in assessing fluid balance
- ☐ hourly or more frequent neurological observations initially
- ☐ reporting **immediately** to the medical staff, even at night, symptoms of **headache**, or slowing of pulse rate, or any change in either conscious level or behaviour
- ☐ reporting any changes in the ECG trace, especially T wave changes suggesting hyper- or hypokalaemia

**Start recording all results and clinical signs on a flow chart.**

A doctor should follow the patient closely and ensure that:

- ☐ Urinary catheterisation should be avoided but may be useful in young sick children and children with impaired consciousness.
- ☐ Documentation of fluid balance is of paramount importance. All urine needs to be measured accurately (and tested for ketones ). All fluid input must be recorded (even oral fluids).
- ☐ If a massive diuresis continues fluid input may need to be increased. If large volumes of gastric aspirate continue, these will need to be replaced with 0.45% saline with KCl.
- ☐ Check biochemistry, blood pH, and laboratory blood glucose 2 hours after the start of resuscitation, and then at least 4 hourly. Review the fluid composition and rate according to each set of electrolyte results.

☐ **If acidosis is not correcting**, consider the following

☐ insufficient insulin to switch off ketones

☐ inadequate resuscitation

☐ sepsis

☐ hyperchloraemic acidosis

☐ salicylate or other prescription or recreational drugs

**Subcutaneous Insulin:**

**Consider changing to SC insulin when:**

1- Hydration maintained.
2- Blood glucose <15 mmol/l
3- pH >7.3
4- Bicarbonate >15 mmol/l
5- TCO2 >15 mmol/l

Discontinue the insulin infusion 60 minutes (if using regular insulin) or 30 minutes (if using ultra short analogues such as lispro or aspart) after the first subcutaneous injection to avoid rebound hyperglycaemia.

For known diabetic patient go back to previous insulin regimen. For newly diagnosed diabetic, consider starting sc insulin with 0.5 –0.7 unit/kg/day. Use of Glargine and ultra short acting insulin analogue is encouraged especially for newly diagnosed diabetics. Young children (< 5 years old) may be given 30% of the total daily dose of insulin as Glargine while children 6 to 10 years require 40% of total daily dose of insulin as Glargine. Old children >10 years old can be given 50% of the total daily dose of insulin as Glargine. The rest of the total daily dose of insulin is devided into 3 doses and given 5 to 10 minutes before meals in form of aspart or lispro. Extra doses of ultra short insulin (lispro or aspart) may be needed according to glucose profile. This sc insulin regimen is just a guide. Deviation from this insulin regimen may be justified for some patients according to general condition of patients, glucose profile and preference of attending consultant.

**Discharge criteria for inpatients:**

- Clinically improved with resolution of hyperglycemia, ketonuria and acidosis
- Stable blood sugar on subcutaneous insulin
- Feeding well
- Family understands and agrees to prescribed therapies and follow-up plans

- **Cerebral Oedema**

  Always discuss cerebral oedema with the consultant on call.
  Remove patient from clinical pathway if cerebral oedema occurs.
  Cerebral oedema is the most common cause of death in DKA. It should be considered if there are any changes in the neurological status.

| **Consider CEREBRAL OEDEMA (at presentation, or may develop in first 12 hours)**<br>If drowsy/coma, nurse in PICU | |
|---|---|
| Headaches? | Irritability/drowsiness? |
| Convulsions? | Focal neurological signs? |
| Abnormal posturing? | Falling GCS? |
| Rising BP, falling pulse? | Papilloedema? |
| Poor respiratory effort? | Falling $O_2$ saturations? |

- More dramatic changes such as convulsions, papilloedema, respiratory arrest are late signs associated with extremely poor prognosis

## Management :

If cerebral oedema is suspected **inform consultant on call immediately.**

The following measures should be taken **immediately** while arranging transfer to PICU–

- ☐ exclude hypoglycaemia as a possible cause of any behaviour change.
- ☐ give **hypertonic (3%) saline** (5mls/kg over 5-10 mins) **or Mannitol** 0.5 – 1.0 g/kg stat (= 2.5 - 5 ml/kg Mannitol 20% over 20 minutes). This needs to be given as soon as possible if warning signs occur (eg headache or pulse slowing).
- ☐ restrict IV fluids to 1/2 maintenance and replace deficit over 72 rather than 48 hours
- ☐ the child will need to be moved to PICU (if not there already)
- ☐ discuss with PICU consultant. Do not intubate and ventilate until an experienced doctor is available
- ☐ once the child is stable, exclude other diagnoses by CT scan - other intracerebral events may occur (thrombosis, haemorrhage or infarction) and present similarly
- ☐ a repeated dose of Mannitol may be required after 2 hours if no response
- ☐ document all events (with dates and times) very carefully in medical records

## OTHER COMPLICATIONS :

- ☐ **Hypoglycaemia and hypokalaemia** – avoid by careful monitoring and adjustment of infusion rates. Consideration should be given to adding more glucose if BG falling quickly even if still above 4 mmol/l.

- ☐ **Systemic Infections** – Antibiotics are not given as a routine unless a severe bacterial infection is suspected.

- ☐ **Aspiration pneumonia** – avoid by nasogastric tube in vomiting child with impaired consciousness.

**Other associations** with DKA require specific management:

Continuing abdominal pain is common and may be due to liver swelling, gastritis, bladder retention, ileus. However, beware of appendicitis and ask for a surgical opinion once DKA is stable. A raised amylase is common in DKA.

Other problems are pneumothorax ± pneumo-mediastinum, interstitial pulmonary oedema, unusual infections (eg TB, fungal infections), hyperosmolar hyperglycaemic non–ketotic coma, ketosis in type 2 diabetes.

## References:

1) British Society of Paediatric Endocrinology and Diabetes DKA guidelines. Updated by Julie Edge Oxford , Feb 2004. based on ESPE/ LWPES consensus statement on DKA. Arch. Dis Child. 2004; 89: 188-194.

2) International Society for Pediatric and Adolescent Diabetes (Pediatric Diabetes, 2007: 8: 28–43).

3) British Society of Paediatric Endocrinology and Diabetes. DKA guidelines (2009).

4) Beherman et al. Diabetic Ketoacidosis. Nelson Textbook of Pediatrics, 2004.

5) Diabetes Protocol. Department of Diabetes, Endocrinology, and Growth. National Children's Hospital, Dublin.

6) Consensus Guidelines 2009. International Society for Pediatric and Adolescent Diabetes.

7) Brook C, Hindermarsh P. Diabetes. Clinical Pediatric Endocrinology, 2001.

8) DKA Clinical Pathway. Vanderbilt University Medical Center, 2002.

9) Hocaniuk A, Pope M. Pediatric Diabetic Ketoacidosis. Isle of Wight Healthcare, NHS, UK.

10) Algorithm for Management of DKA. European Society of Pediatric Endocrinology, 2006.

11) Management of Acute Gasteroenteritis, Clinical Pathway. Department of Pediatrics, Saad Specialist Hospital, 2006.

12) DKA Clinical Pathway. Kaiser Permanente University Center, 2002.

13) Pediatric Diabetic Ketoacidosis Clinical Pathway. Department of Pediatrics, Saad Specialist Hospital, 2006.

Any information related to the use of these guidelines would be very valuable. Please address any comments to:

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# Algorithm for DKA

**History**
- polyuria
- polydipsia
- weight loss
- abdominal pain
- lethargy
- vomiting
- confusion

**Signs**
- assess % dehydration
- deep sighing respiration (Kussmaul)
- smell of ketones
- lethargy, drowsiness

**Biochemistry**
- elevated blood glucose >11mmol/l
- acidaemia: pH<7.3, Bicarbonate <15
- ketones in urine
- check U + Es, Creatinine
- other tests as indicated

**Confirm Diagnosis**

*Diabetic Ketoacidosis*

**Shock**
**Reduced conscious level**

**Dehydration > 3%**
**Clinically acidotic**
**Vomiting**

**Dehydration < 3%**
**Clinically well**
**Tolerating fluid orally**

**Resuscitation**
- Airway ± NG tube
- Breathing (100% $0_2$)
- Circulation (slow bolus 10ml/kg IV 0.9% saline,if hypotensive give 20 ml/kg saline, repeat 10 ml/kg until circulation restored. Total boluses>30ml/kg rarely needed

**Intravenous therapy**
- calculate fluid requirements
- correct over 48 hours
- 0.9% saline for at least first 12 hours
- add KCl 20mmol per 500ml bag
- 1 hour after IV fluids commenced, start Insulin infusion 0.1U/kg/hour

**Subcutaneous Therapy**
- start with subcut insulin
- give oral fluids

**No improvement**

Ketones rising
Looks unwell
Starts vomiting

**Observations**
- hourly blood glucose
- neurological status at least hourly
- hourly fluid input:output chart
- U+Es & blood gas 2 hours after start of IV therapy, then 4-hourly
- dip test every urine for ketones

**No improvement**

**Re-evaluate:**
- fluid balance & IV therapy
- if continued acidosis, may require further resuscitation fluid
- check insulin dose correct

**Neurological deterioration**
**Warning signs:**
Headache, irritability, slowing heart rate, reduced conscious level, specific signs raised intra-cranial pressure

**Exclude hypoglycaemia**
**Is it cerebral oedema?**

**Blood glucose falls <14 mmol/L**

**Intravenous therapy**
- During initial at least 12 hours: use 0.9% saline 5% glucose or higher if needed
- After 12 hours: continue same fluid, if sodium rising (>145 corrected) change to 0.45% saline/ 5% glucose. ensure KCl 20mmol/500ml bag
- consider reducing Insulin 0.05U/kg/hour, only when pH>7.30 and/or Bicarbonate >15

**Management**
- secure airway, 100% $0_2$
- head-up tilt to bed
- 3% Saline 3 ml/kg IV **or** Mannitol 0.5 -1.0 g/kg IV
- call senior staff
- restrict IV fluids by 50%

**Subcutaneous Insulin**
Start regular s/c Insulin **then** stop IV Insulin infusion 1 hour later (or after 30 minutes if starting rapid acting analogs

**Resolution of DKA**
Clinically well, drinking well, tolerating food
pH or bicarb normal
Urine ketones falling (but may still be positive)