

Guidelines and Protocols of **Diabetes Emergencies**



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“Pediatrics”

Guidelines for Diagnosis & Management of Diabetic Ketoacidosis (DKA) in Children under 14 years of Age and/or < 50kg weight

Introduction:

A team from three subspecialties has formulated these guidelines for the diagnosis and management of DKA in children and young people under the age of 14 years: pediatric endocrinology, pediatric emergency care and pediatric intensive care.

It is based on most recent international evidence and guidelines, and structured to be as simple and as safe as possible in the light of evidence based practices.

However, no guidelines can be considered entirely safe and complications may still arise, as the pathophysiology of cerebral edema is still poorly understood. Some patients may need slightly modified approach based on individualized and justified need but these guidelines should be generally implemented at all hospitals.

When to suspect DKA:

You should suspect DKA when having a constellation of the following history and clinical signs

	History	Clinical Features
Suspect DKA	Polyuria Polydipsia Weight loss Tiredness	Dehydration Tachypnea; deep (Kussmaul) respiration Breath that smell like acetone (ketone) Nausea, vomiting, and abdominal pain Confusion, lethargy, drowsiness

Definition of DKA:

By definition, DKA is present when a type I (or sometimes type II) diabetic patient present with hyperglycemia, glycosuria, metabolic acidosis and ketonuria. Please confirm by the following criteria:

	The biochemical criteria	
Confirm DKA	Hyperglycemia (BG >11mmol/L ≈ 200mg/dL) Venous pH <7.3 or bicarbonate <15mmol/L Ketonemia and/or ketonuria	Exclude Hyperosmolar Hyperglycemic State (HHS) (see appendix I) Consider other differential diagnoses (see appendix II)

Caveat 1: Children and adolescents with known diabetes may rarely develop DKA if they did not stop insulin and have normal Blood Glucose levels.

Management in Emergency Room or Urgent Care Area:

The most important aspect of 1st hour management is maintaining the delicate balance between stabilizing the patient and adhering to conservative fluid replacement. The plan can be summarized as follows:

1st Hour Management ER/Urgent Care

For all DKA patients

- Connect to cardiorespiratory monitor & pulse oximeter
 - Analyze ECG to evaluate for signs of hyper or hypokalemia.
 - Support Airway, Breathing, and Circulation as needed (as per PALS recommendations).
 - Airway support (no elective intubation for significant tachypnea, consult expert- see appendix III)
 - Give 100% O₂ by face mask
 - Insert two IV cannulas
 - Insert nasogastric tube if indicated (avoid in obtunded patients if the airway not protected- risk of aspiration)
 - Measure body weight (BW) and estimate for unstable patient (Broselow tape or growth chart)
 - Send urgent labs: Blood glucose, blood gases (capillary or venous), urea & creatinine, electrolytes, serum osmolality, calcium, magnesium, phosphorus, albumin, CBCs with differential.
 - Serum β Hydroxy Butyrate concentrate (if available), urine analysis and urine ketones.
 - Blood culture, urine culture, throat swab, CXR for suspected infection (as clinically indicated).
- **Start fluid replacement as follow:**

Patient could present in shock or only dehydrated but with stable hemodynamics. Table below summarize the management of both scenarios

Fluid Management in 1st hour	Dehydrated, not in shock: Estimate the severity of DKA	If patient is in clinical shock: (weak peripheral pulses, prolonged capillary refill \geq 3 seconds, reduced conscious level)
	<p>Mild: venous pH<7.3 or bicarbonate <15mmol/L</p> <p>Moderate: pH<7.2 or bicarbonate <10mmol/L</p> <p>Severe: pH<7.1 or bicarbonate <5mmol/L</p>	Shock with hypotension (late sign): 10 ml/kg 0.9 Saline bolus over 5-10 minutes. Repeat x3 till normal BP (consult expert)
	Start IV 0.9% Saline at: 5 ml/kg/h for mild/moderate DKA 7 ml/kg/h for severe DKA	Shock, not hypotensive (compensated): 10 ml/kg 0.9 Saline over 1 hour

Caveat 2: Always discuss the management with most senior physician in your area.

Careful with severe cases that can present in obtunded state and consider signs & management of Cerebral Edema upon initial presentation (see details on page 3)

Management Plan after the 1-2 hours

The three fundamental elements of DKA management are rehydration, insulin and electrolytes replacement and close clinical and laboratory monitoring for potential complications and they are summarized as follows:

Management Post 1-2 hours In highly monitored unit	Fluid calculation principles	Insulin	Monitoring (& record)
	<p>IV Maintenance + deficit</p> <p>Maintenance calculation: 100 ml/kg for the first 10 kg + 50 ml/kg for the next 10 kg + 20 ml/kg for the rest BW</p> <p>Deficit calculation: 5% for mild to moderate DKA 10% for severe DKA Correct slowly over 48 hours Start 0.9% Saline (with KCl)</p> <p>Potassium: 40 mEq/L KCl (after 1st void & if K level < 5.5)</p>	<p>Mix 50 unit of soluble insulin (e.g. Regular) in 50 ml 0.9% saline bag (1 ml = 1 unit) (50 units in 500 ml second option, 10 ml = 1 unit)</p> <p>Start after 1-2 hour from fluid initiation</p> <p>Starting dose: 0.05-0.1 unit/kg/hr 0.05 dose for kids: -Younger than 5 years -Newly diagnosed -rapid drop of Blood Glucose >100mg/dl/hr</p>	<p>Hourly: Vital Signs Capillary blood glucose (bed side), Neurological status (pupils & Glasgow Coma Scale (GCS), Fluid intake & output Every 2-4 hours: Blood gases (venous or capillary)</p> <p>Every 4 hours: BG, electrolytes, urea, creatinine, phosphorus, calcium, magnesium</p>

Caveat 3: Fluid volume from insulin bag (when using 500 ml bag for mixing) to be included in the total rehydration fluid. Remove from the total rehydration fluid the fluid boluses that are more than 20ml/kg only. No routine replacement of ongoing losses. Only consider when fluid balance remains negative (check Q 4 hours) Always request fluid early (expect 1hour delay)

To minimize calculation burden, errors, and confusion we recommend the following simplified and slightly more conservative total fluid calculation for first 48 hrs after DKA presentation

Simplified calculated rate by weight	≤15 kg	16 to 40 kg	>40
Maintenance + deficit	5 ml/kg/hr	4 ml/kg/hr	3 ml/kg/hr

NB. All fluids given during resuscitation should be documented carefully, particularly the fluid given in ER.

Special lab consideration In newly diagnosed diabetic:

HbA1C, insulin antibodies, glutamic acid decarboxylase antibodies, thyroid function and thyroid antibodies (if available in your facility laboratory).

The following has been associated with risk of cerebral edema, please avoid them



**DO NOT
DO List**

- DO NOT give insulin bolus
- DO NOT give IV sodium bicarbonate (except in life-threatening hyperkalemia)
- DO NOT give fluid boluses for DKA not in shock
- DO NOT give hypotonic fluid (0.45%, 0.22%) for rehydration
- DO NOT give more than 10 ml/kg fluid bolus each time if in shock
- DO NOT exceed 1.5-2 maintenance/day as a general rule

Goals of Therapy

- ▶ Correct dehydration slowly (over 48 hrs)
- ▶ Correct acidosis and reverse ketosis (don't interrupt insulin if acidosis is not resolving)
- ▶ Restoring blood glucose (BG) to near normal
- ▶ Monitor for DKA complications:
 - Manage the patient in advance care unit (**PICU, High Dependency Unit, ER**)
 - Keep the nurse to patient ratio 1:1 for severe DKA (assign nurse with advanced care skills)
 - **Admission to the ward is not recommended as it carry with it a significant risk of inadequate monitoring and possible life threatening errors (potassium errors, hypoglycemia ...etc)**
- ▶ Identify and treat any precipitating event:
 - Fever could be due to presence of infection, please send cultures and start antibiotics.

Higher risk "patients" who need rigorous monitoring even when managed in PICU are kids with:

- ▶ Severe DKA with pH<7.1
- ▶ Severe dehydration with shock
- ▶ Depressed level of consciousness
- ▶ Those who are at increased risk for cerebral edema
 - <5 years of age (and more risk in <2 years of age)
 - Lower than expected pCO₂ for the degree of metabolic acidosis
 - High urea nitrogen upon presentation

Adjustment and Trouble Shooting

- ▶ When blood glucose (BG) drops to < 14-17 mmol/l (250-300 mg/dl) add Dextrose 5% to 0.9% Saline
- ▶ When BG drop to < 8 mmol/l (≈ 140-150 mg/dl) add D10% to 0.9% Saline
- ▶ With rapid fall of glucose (> 100 mg per hour): Add D10% and can increase to max D12.5% if acidosis is not improving (may decrease insulin to 0.05 u/kg/hr or even down to 0.03 u/kg/hr if acidosis is improving)
- ▶ Hypoglycemic attack < 4 mmol/l (≈ 72mg/dl): Give 2-5 ml/kg D10% bolus, hold insulin for 15-30 min then repeat Blood Glucose.

Potassium Adjustment

Potassium > 5.5 mmol/l	Hold Potassium, repeat level in 2 hrs
Potassium < 3.5 mmol/l	Increase KCl to 60 mmol/l (<i>need good peripheral IV or Central Line</i>)
Potassium <2.5 mmol/l	Monitored administration of extra 1 mmol/kg KCL over 2 hours

Phosphorus Replacement (based on level or symptomatic hypophosphatemia)

Phosphorus < 0.5 mmol/l (1.5 mg/dl): Replace ½ of KCl with Potassium Phosphate

If acidosis is not correcting (assess bicarbonate change more than pH) consider:

- Inadequate fluid resuscitation
- Wrong insulin dose or preparation
- Hyperchloremic metabolic acidosis
- Sepsis (usually with lactic acidosis)
- ▶ Recalculate and assess intake/output every 4h
- ▶ Recheck all preparation
- ▶ Measure chloride and anion gap* (see legend)
- ▶ Look for signs, measure lactate

*Anion Gap calculation: $Na - (Cl + HCO_3) = 12 \pm 2$ (normal).

DKA Resolution and Shifting to Subcutaneous Insulin

INTRODUCTION OF ORAL FLUID and TRANSITION OF SUBCUTANEOUS INSULIN:

Oral fluids should be introduced when substantial clinical improvement has occurred (mild acidosis/ketosis may still be present) and the patient indicates a desire to eat.

The indication to start subcutaneous insulin

- Patient is fully conscious and willing to eat with no nausea or vomiting
- Ketoacidosis has almost resolved (serum bicarbonate >15 mEq/l twice)
- Venous pH >7.3
- Ketone in urine may still be positive

Fluid management:

- When oral fluid is tolerated, intravenous fluid should be reduced and oral fluid intake should be included in total rehydration fluid calculation
- Start special diabetes diet after stopping insulin infusion (at least 30 minutes after subcutaneous insulin injection)

Insulin Management:

- The most convenient time to change to subcutaneous insulin is just before a mealtime.
- To prevent rebound hyperglycemia, the first subcutaneous injection should be given 15–30 min with rapid-acting insulin (insulin aspart) or 1–2 h with regular insulin, before discontinuing the insulin infusion.

Insulin Dose:

- If patient is known DM1 on appropriate treatment, then to resume patient previous doses
- If new DM1 with DKA start 0.75 unit/Kg /day, as Basal Bolus regime divided to:
 - 30-40 % long acting - Basal (e.g. levemir or Glargine or Degludec)
 - 60- 70 % as rapid acting insulin pre or post meals

(use different arm when the two given in the same time)

Use glargine (lantus) as long acting insulin If age above 3 years and levemir as basal insulin if age < 3 yrs Rapid acting insulin analogue like aspart , lisro , Humalog can be given 15-30 minutes before stopping insulin infusion

- Monitor blood sugar by gluco-check 6 times daily (Before meals and 2 hours post-meals) and adjust the dose of insulin according to blood sugar result.
- Consult pediatric endocrinologist if available.
- Diabetic educator and dietitian should be involved early to educate patient and care giver
- If insulin analogue is not available, you might use two dose insulin regimen as shown in the next table:


Two doses insulin regimens for newly diagnosed diabetes after resolution of DKA

Total daily dose	Pre-pubertal: 0.5-1.0 unit/kg Pubertal: 1.0-1.2 unit/kg
Before breakfast	Two-thirds of total daily dose (TDD) <ul style="list-style-type: none"> ▸ One-third rapid acting insulin ▸ Two third intermediate-acting insulin (e.g. NPH)
Before dinner	One third of TDD <ul style="list-style-type: none"> ▸ One-third rapid acting & Two third intermediate-acting insulin OR ▸ One-half rapid acting & one-half intermediate-acting insulin (e.g. NPH)

Monitor blood sugar by gluco-check 4 times Daily (before meals and at bed time)

DKA Complications & Cerebral Edema Management

Serious DKA Complications & Precautions	Fatal Complications	Other Common Complications		
	Cerebral Edema Hyper/hypokalemia	Inadequate rehydration Hypoglycemia	Aspiration pneumonia Hyperchloremic acidosis	Hypophosphatemia Thrombosis Stroke
	Cerebral Edema Risk Factors			
	Uncontrollable	Controllable		
	<ul style="list-style-type: none"> Younger age (< 5 years) New onset diabetes Longer duration of symptoms Severe hypocapnia (more than expected for acidosis) Increased serum urea nitrogen Severe acidosis 	<ul style="list-style-type: none"> IV Bicarbonate treatment for correction of acidosis Administration of insulin in the first hour of fluid treatment (bolus or infusion) Greater volumes of fluid given in the first 4h A marked early decrease in effective serum osmolality (> 5 mOsm/hr)* Serum sodium (corrected)** dropping or not rising with treatment 		

Cerebral Edema Signs & Symptoms and Management	Highly suspicious	Management
	<ul style="list-style-type: none"> Severe headache Agitation or irritability Unexpected fall in heart rate Increased blood pressure Decreased level of consciousness 	<p>Inform the Most Responsible Physician/consultant Treat immediately with the most readily available of:</p> <ul style="list-style-type: none"> Mannitol 20% (0.5-1 g/kg over 10-15 minutes) or Hypertonic saline 3% (3-5 ml/kg over 10-15 min) Drop fluid rate by one third of total <p>Elevate the head of the bed to 30°</p>
	Life Threatening Signs	
	<ul style="list-style-type: none"> Further deterioration in level of consciousness Abnormalities of breathing pattern (e.g. breathing pauses) Oculomotor palsies Abnormal posturing Pupillary inequality or dilatation 	 <p>Urgent</p>
	Management (Repeat all above steps and consider)	
	<ul style="list-style-type: none"> Mannitol or Hypertonic saline (Repeat in 30 min to 2 hrs if no initial response) Secure Airway (by experienced staff) Do not sedate or suppress patient hyperventilation without control breathing Control ventilation (match patient hyperventilation then increase pCO2 slowly to 35 mmHg) CT when stable (to exclude: hemorrhage, thrombosis) Neurosurgical consultation for other surgical options 	

*Effective Osmolality: $2 \text{ Na} + \text{Glucose}$ (glucose value in mmol/L)

**Corrected Na = measured Na + $2 \left[\frac{\text{plasma glucose} - 100}{100} \right]$ mg/dL

Appendices

Appendix I

Hyperosmolar Hyperglycemic State (HHS) Diagnosis	
HHS	DKA
Usually occurs in Type 2 diabetes	Usually more in Type 1 diabetes
Marked hyperglycaemia (33.3 mmol/L or more) \approx (600 mg/dl)	Hyperglycemia (> 11 mmol/L or more) \approx (200 mg/dl)
No significant hyperketonemia or acidosis (pH >7.3 , bicarbonate >15 mmol/L)	Significant ketonemia and acidosis (pH <7.3 or bicarbonate <15 mmol/L)
Osmolality usually 320 mosmol/kg or more	Osmolality variable but usually < 320 mosmol/kg
High mortality rate	Low mortality rate
More hypovolemia, need faster rehydration	Dehydrated but need slow rehydration
Insulin replacement is second line therapy	Insulin replacement is the mainstay of therapy

Appendix II

Differential Diagnosis of DKA (hyperglycemia, acidosis, and ketosis)	
Diagnosis	Other distinguishing features
Salicylate Intoxication	History, Salicylate level if suspicious
Metabolic Diseases (Inborn Error of Metabolism)	Family history, other features of disease (consult expert)
Severe stress with starvation (?Sepsis)	Examine the patient, features of sepsis, disease progress

Appendix III

Airway considerations Secure the airway in:
Comatose patient (GCS <8)
Abnormal breathing
By expert physician
Hyperventilate (same patient CO ₂ & correct slowly)
NG insertion:
Do not induce vomiting if patient can't protect airway

Initial management of Hyperosmolar Hyperglycemic State (HHS)

Definition:

- Hypovolemia
- Marked hyperglycemia of > 600 mg/dl (33.3 mmol/L) or more
- No significant hyperketonemia or acidosis (pH>7.3, bicarbonate >15 mmol/L)
- Osmolality usually 320 mOsmol/kg or more
- Altered consciousness or seizure

Usually occurs in Type 2 diabetes (improper hydration) and has a high mortality rate.

Goals of treatment: Treat the underlying cause and to gradually and safely:

- Normalize the osmolality
- Replace fluid and electrolyte losses
- Normalize blood glucose
- Prevention of complications:
 - arterial or venous thrombosis
 - cerebral edema
 - central pontine myelinolysis

Fluid therapy: The rate of fluid replacement should be more rapid than is recommended for DKA. The goal is to expand the intra and extravascular volume and restore normal renal perfusion.

- Give an initial bolus should be of 20 mL/kg of isotonic saline (0.9% saline)
- Assume a fluid deficit of approximately 12–15% of body weight.
- Additional fluid boluses should be given, if necessary, to restore peripheral perfusion.
- Thereafter, 0.45–0.9% saline with potassium (like in DKA) should be administered to replace the deficit over 24–48 hours.
- Unlike DKA, replacement of urinary losses is recommended (0.45% or 0.9% saline).

The goal is to promote a gradual decline in serum sodium concentration and osmolality.

- Measure serum sodium concentrations every 2-4 hours
- Adjusted sodium concentration in fluids to promote a gradual decline in corrected serum sodium concentration (0.5 mmol/L per hour).
- Failure of the corrected serum sodium to decline with treatment, consider hemodialysis
- Rapid fall in serum glucose (>5 mmol/l per hour) consider adding 5% glucose to the fluid.

Insulin therapy

- Blood glucose levels will fall with fluid alone and insulin is NOT required early in treatment.
- Insulin administration should be initiated when serum glucose concentration is no longer declining at a rate of at least 3 mmol/l per hour with fluid administration alone

Order Sheet for Pediatric DKA Patients (< 14 years and/or < 50 kg body weight)

Date:	Time: (military: 24 hour format)	Patient Weight:.....Kg	Length/Height:.....cm	
Admit the patient to: <input type="checkbox"/> PICU		<input type="checkbox"/> HDU Under the care of Dr.		
<input type="checkbox"/> Obtain Patient Weight <input type="checkbox"/> Connect to cardiorespiratory monitor <input type="checkbox"/> Connect to pulse oximeter <input type="checkbox"/> Record vital signs hourly <input type="checkbox"/> Record neurology assessment hourly (pupils size, reactivity, GCS) <input type="checkbox"/> Nothing by mouth (NPO) <input type="checkbox"/> Insert two IV cannulas <input type="checkbox"/> Strict intake and output and record hourly <input type="checkbox"/> Insert Foley's catheter (only if indicated) <input type="checkbox"/> Check Urine for ketones (bedside check) Additional Investigations: <input type="checkbox"/> HbA1C <input type="checkbox"/> Other		Noted by	Laboratory monitoring	Noted by
			Hourly	
			<input type="checkbox"/> capillary blood glucose	
			Every 2 hours	
			<input type="checkbox"/> Capillary or venous blood gases	
			<input type="checkbox"/> Serum electrolytes	
			Every 4 hours	
			<input type="checkbox"/> Serum electrolytes	
			<input type="checkbox"/> Calcium, Phosphorus, Magnesium, Urea, Creatinine	
			Upon Admission	
	<input type="checkbox"/> CBC-differential			
	<input type="checkbox"/> Urine analysis			
	<input type="checkbox"/> Blood culture, Urine culture			
	<input type="checkbox"/> Chest Xray			
Fluid in the first hour:			Noted by	
<input type="checkbox"/> Shock & hypotensive patient: Startml (10 ml/kg) %0.9 Saline IV bolus over 10-5 minutes				
<input type="checkbox"/> Still hypotensive: Repeat bolus ml IV (10 ml/kg) over 10-5 minutes				
Call physician to the bedside if patient is unstable				
<input type="checkbox"/> Shock, not hypotensive: Startml (10 ml/kg) %0.9 Saline IV over one hour.				
<input type="checkbox"/> Not in shock: Startml IV infusion %0.9 saline over 1 hour For severe DKA (bicarbonate <7 : (5 ml/kg and for mild to moderate DKA (bicarbonate >5 :(5ml/kg				
Fluid after 2-1 hours:		Calculation formula	Noted by	
<input type="checkbox"/> Start IV %0.9 saline at.....ml/hour		≤ 15 kg weight: 5 ml/kg/hr,		
<input type="checkbox"/> Potassium Chloride Add 40 mmol/L (20 mmol to 500 normal saline bag)		16 to 40 kg: 4 ml/kg/hr		
<input type="checkbox"/> Add only if patient is passing urine and K level is < 5.5 mmol/L		> 40 kg: 3 ml/kg/hr		
<input type="checkbox"/> Add Dextrose %5 to %0.9 Saline fluid when blood glucose drops to < 250 mg/dl (14 mmol/L)				
<input type="checkbox"/> Add Dextrose %10 to %0.9 Saline fluid when blood glucose drop to < 150-140 mg/dl (8 mmol/L)				
Insulin Infusion: DO NOT GIVE BOLUS and Start after 2-1 hour from fluid initiation			Noted by	
<input type="checkbox"/> Mix 50 unit of Regular insulin in 50 ml %0.9 saline Starting dose:.....ml/hour (= 0.1 unit/kg/hr) (0.1 ml/kg/hr = 0.1 unit/kg/hr)				
<input type="checkbox"/> Or: Mix 50 unit of Regular insulin in 500 ml %0.9 saline Starting dose:ml/hour (= 0.1 unit/kg/hr) (1 ml/kg/hr = 0.1 unit/kg/hr)				
Use 0.05 unit/kg/hr dose for high risk kids Younger than 5 years, Newly diagnosed or with Rapid drop of BG (>100mg/dl/hr)				
Antimicrobials (consider for fever, sepsis):			Noted by	
<input type="checkbox"/>				

Physician Name & Signature:

Nurse Name & signature:

Appendix V:

Glasgow Coma Scale (Maximum score 15, minimum score 3)

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

Appendix VI:

Definition of hypotension in pediatrics (PALS 2015)	
	Systolic BP
Neonate (up to 28 days of age)	<60
Infants (12-1 months)	<70
Children from 1 to 10 years	<+70 (age in years X 2)
Children > 10 years of age	<90

Algorithm for the Management of DKA in Children

Confirm DKA Diagnosis

Hyperglycemia (BG >11mmol/L ≈ 200mg/dL) Venous pH <7.3 and/or bicarbonate <15mmol/L Ketonuria

DKA in Shock	1st Hour Management	DKA not in Shock
<p>Notify PICU, Alert senior primary physician</p> <p>Airway: No elective intubation/ call expert</p> <p>Breathing: %100 O2 by Face Mask, Check O2 Sat</p> <p>Circulation: 2 IV cannulas, cardiac monitor</p> <p>Hypotensive: 10 ml/kg NS bolus over 10-5 min Repeat if hypotensive (x 3) - consider inotropes</p> <p>Shock with normal BP: 10 ml/kg NS over 1 hr</p>	<p>Urgent Labs Blood glucose Blood gases electrolytes Ca, Magnesium Phosphorus Urea, Creatinine</p>	<p>Assess Severity</p> <p>Mild: pH<7.3 or bicarbonate <15mmol/L Moderate: pH<7.2 or bicarbonate <10mmol/L Severe: pH<7.1 or bicarbonate <5mmol/L</p> <p>1st hour fluid: 0.9% saline</p> <p>7 ml/kg/h for severe DKA 5 ml/kg/h for mild/moderate DKA</p>

Always admit high risk patients (e.g. severe DKA, young < 2 years old, newly diagnosed diabetes) to highly monitored area (like PICU, high dependency unit) with nurse to patient ratio of 1:1

Post 1st Hour Management

Insulin (DO NOT GIVE BOLUS)	Simplified calculated rate by weight	Monitoring						
<p>Mix 50 unit of soluble insulin (Regular) in 50 ml %0.9 saline (Alternatively: mix 50 unit in 500 ml %0.9 saline bag, Insulin fluid volume to be included in the total rehydration calculation when using 500 ml bag)</p> <p>Starting dose: 0.1-0.05 unit/kg/hr</p> <p>0.05 dose for kids:</p> <ul style="list-style-type: none"> -Younger than 5 years -Newly diagnosed -Rapid drop of BG (>100mg/dl/hr) -Recently received insulin injection <p>Start after 2-1 hour from starting rehydration fluid</p>	<table border="1"> <tr> <td><15 kg</td> <td>5 ml/kg/hr</td> </tr> <tr> <td>16 to 40</td> <td>4 ml/kg/hr</td> </tr> <tr> <td>>40 kg</td> <td>3 ml/kg/hr</td> </tr> </table>	<15 kg	5 ml/kg/hr	16 to 40	4 ml/kg/hr	>40 kg	3 ml/kg/hr	<p><i>Remove fluid boluses of > 20 ml/kg from the total replacement</i></p> <p>Hourly: Vital Signs Blood glucose, Neurological status (pupils & GCS), Fluid intake & output Every 4-2 hours: Blood gases (venous or capillary)</p> <p>Every 4 hours: Electrolytes, urea & creatinine, phosphorus, calcium, magnesium Other labs: CBC & differential, Blood culture, urine culture (with fever)</p> <p>For new onset diabetes: see guidelines</p>
	<15 kg	5 ml/kg/hr						
	16 to 40	4 ml/kg/hr						
>40 kg	3 ml/kg/hr							
<p>Fluid calculation principles</p> <p>IV Maintenance + deficit Correct deficit slowly over 48 hours Deficit calculation: %10 for severe DKA %5 for mild to moderate DKA Start %0.9 Saline (with KCl) Potassium: 40 mEq/L KCl (add after 1st void & only if K level < 5.5) No routine replacement of ongoing losses but avoid negative balance (reassess every 4 hrs)</p>								

Adjustment and Troubleshooting

- BG < 14-17 mmol/l (250-300 mg/dl) = Add Dextrose 5% to 0.9% Saline
- BG < 8 mmol/l (\approx 140-150 mg/dl) = Change D5% to D10% to 0.9% Saline
- Rapid fall of glucose ($>$ 100 mg/dl per hour): May drop insulin to 0.05 u/kg/hr
 - Or change D5% to D10% if acidosis is not improving
 - Try not to wean insulin dose to $<$ 0.05 u/kg/hr if acidosis still present
- Hypoglycemic attack ($<$ 4 mmol) (72 mg/dl) = 2-5 ml/kg D10% bolus,
 - hold insulin temporarily (15-30 min, repeat BG and restart)
- Potassium $>$ 5.5 mmol/l (not hemolyzed) = Hold Potassium
- Potassium $<$ 3.5 mmol/L = Increase KCl to 60 mmol/l (need good IV)
- Phosphorus $<$ 0.5 mmol/l (1.5 mg/dl) = Replace $\frac{1}{2}$ of KCl with K Phos
- Acidosis not improving = trouble shooting ▸ See attached guidelines
- Always prepare next fluid to be used in advance (expect 1 hour delay)

Monitor for Complications

Cerebral edema: Neuro exam/hourly Hypokalemia: ECG. electrolytes

Aspiration pneumonia: avoid NG if airway protection is questionable

Early Signs of Cerebral Edema

Severe headache Agitation or irritability

Unexpected fall in heart rate

Increased blood pressure Decreased level of consciousness

Mannitol or 3% Saline standby

(see attached guidelines for details)

DKA Resolution

Clinically well, $\text{HCO}_3 \geq 15$

Tolerating oral intake

Switch to oral intake (special diet)

SC insulin as per endocrinologist order or per attached guidelines (appendix III)



DO NOT

- give insulin bolus
- give IV sodium bicarbonate (use only in life-threatening hyperkalemia) give fluid boluses for DKA not in shock
- give hypotonic fluid (0.45%, 0.22%) for rehydration give more than 10 ml/kg of fluid each time if in shock give more than 1.5-2 maintenance per day

Management of Hypoglycemia in Infant and Children below 14 Years

DEFINITION:

- For infants and children: plasma glucose <3.3 mmol/L or 60 mg/dl measured by accurate laboratory method
- For neonate: refer to the neonatal hypoglycemia management protocol.

PRESENTATION

- In newborn; apnea, cyanosis, poor feeding, sweating tremors, jitteriness, irritability, convulsion, coma.
- Infant and children; Irritability, dizziness, blurred vision, difficulty speech, headache, confusion, feeling faint, personality changes, Palpitations. Hunger, Nausea Sweating, Anxiety Tremulousness Nervousness Ataxia, drowsiness, convulsion, coma.

DIAGNOSIS:

- Reliable blood sugar estimation during symptoms.

ASSESSMENT

History:

- Neonate; prematurity, IUGR, maternal diabetes, perinatal stress e.g. birth asphyxia, sepsis, shock, fasting hypoglycemia or hypoglycemia after meal (hyperinsulinemia)
- Diabetes Mellitus, renal insufficiency/failure, hepatic cirrhosis/failure, other endocrine diseases, or recent surgery
- Drug Hx : Insulin usage or ingestion of an oral hypoglycemic agent, toxic ingestion, new medications
- The social history may include intake and nutritional deficiency
- Review systems for: weight reduction, nausea, vomiting, headache, etc. ..
- Look for other symptoms suggesting infection

Examination:

- Physical findings are nonspecific in hypoglycemia and generally are related to the central and autonomic nervous systems.
- Height, weight (thin stature- ketotic hypoglycemia).
- Assess vital signs for hypothermia, tachypnea, tachycardia, hypertension, and bradycardia (neonates)
- The head, eyes, ears, nose, and throat examination may indicate blurred vision, pupils normal to fixed and dilated, icterus (usually cholestatic due to hepatic disease)
- Cardiovascular disturbances may include tachycardia (bradycardia in neonates), hypertension or hypotension, and dysrhythmias.
- Midline congenital anomalies : Ambiguous genitalia micropenis, facial anomalies, cleft palate, central incisor, nystagmus, etc.
- Respiratory disturbances may include dyspnea, tachypnea,
- GI disturbances may include nausea and vomiting, dyspepsia, and abdominal cramping Hepatomegaly - glycogen storage disease. Any abdominal mas
- Skin may be diaphoretic and warm or show signs of dehydration with decrease in turgor, hyperpigmentations
- Neurologic conditions include coma, confusion, fatigue, loss of coordination, tremors, convulsions, and diplopia and Cataract in case of galactocaemia.

MANAGEMENT PLAN:

Hypoglycemia Blood sugar < 3.3 mmol/l (60 mg/dl)
Collect blood sample for investigations (blood gas, insulin, BOHB, lactate, FFA)

Conscious & Asymptomatic

- Send blood sample for glucose
- Offer feed or sugary drink for older children
- Recheck blood sugar by 15 min

Impair consciousness, convulsion or coma

- Collect sample of blood for investigations.
- IV glucose 10% dextrose normal saline 5 ml/kg over 3-4 minute followed immediately by D10 normal saline in maintenance IVF (6-9 ml/kg/minute) Repeat blood sugar after 15 minute there is No Response Repeat D10 % dextrose bolus if still there is No response
- Increase rate and concentration of glucose infusion. If >12.5% of glucose infusion is needed to maintain normal blood sugar insertion of central line is advisable.
If still there is No response
- Glucagon <20 Kg: 0.5 mg SC/IM/IV; may repeat in 15 minutes if necessary
- >20Kg : 1 mg SC/IM/IV; may repeat in 15 minutes if necessary
- Repeat blood sugar every 15 minutes Once blood sugar is control, oral feeding should be Started glucose infusion should be gradually discontinued.
- Try to find the cause of hypoglycemia.
- Consult pediatric endocrinologist.

Metabolic Clues to Hypoglycemia Diagnosis

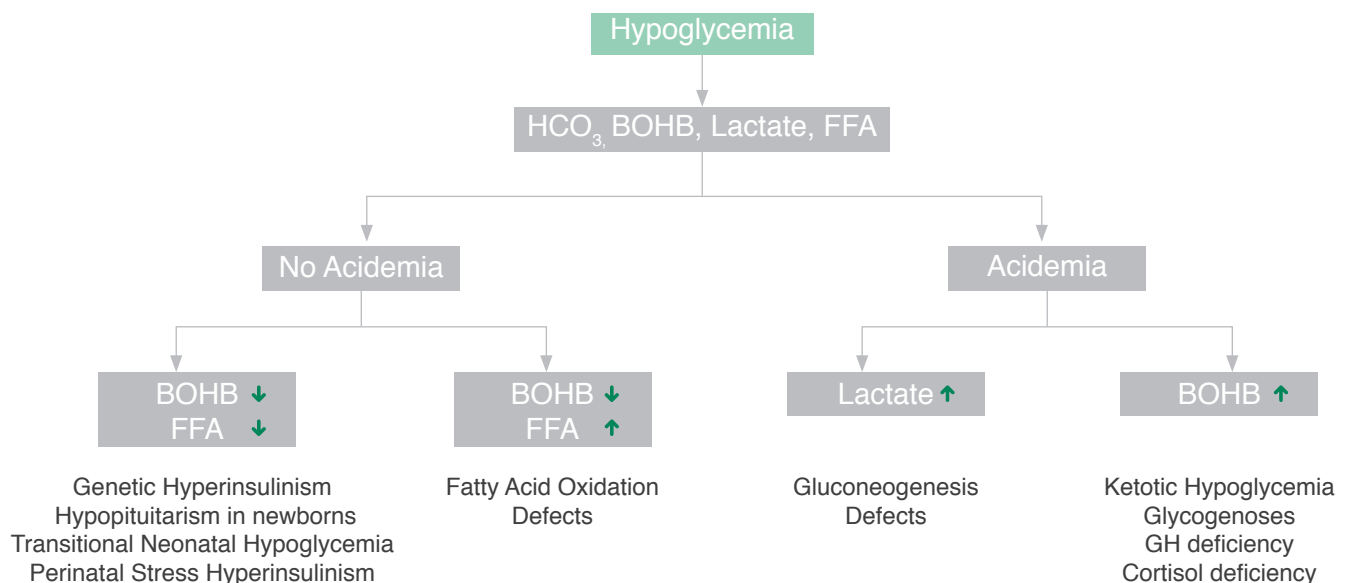


Figure: Algorithm showing how the major categories of hypoglycemia can be determined with information from the critical sample. GH, growth hormone.

INVESTIGATIONS

- Obtain 5-10 ml blood red top and 20 ML urine for further investigation to be safe for 48-72 hr
- Critical Sample: Acute Blood and Urine Tests at time of Hypoglycemia

Blood

- Chemistry panel with bicarbonate
- Insulin, C-peptide
- Cortisol, growth hormone
- Free fatty acids, β -hydroxy butyrate, acetoacetate
- Lactate, ammonia
- Total and free carnitine
- Acyl carnitine profile\ saves serum tube

Urine

Ketotic hypoglycemia

- It is the most common cause of childhood hypoglycemia
- It usually presents between the age of 18 months and 5 years and remits spontaneously by 8 to 9 years of age
- Hypoglycemia usually occurs during illness when food intake is limited
- Diagnosis is confirmed by fasting for several hours under
- close supervision and collecting blood samples for testing At the time of hypoglycemia,
- there is associated ketonemia & ketonuria
- S.alanine levels are reduced
- Treatment consists of frequent feedings of a high-protein, high carbohydrate diet.



Guidelines and Protocols of
Diabetes Emergencies

“Adults”

MANAGEMENT OF HYPOGLYCEMIA IN SUBJECTS WITH DIABETES MELLITUS PATHWAY (ADULTS) (Blood Glucose <4.0 mmol/L - 72mg/dL)

STEP 1

1. Assess ABC, level of consciousness and ability to drink.
2. Send blood sample to the laboratory for verification (but do not wait for result)

STEP 2

Conscious AND able to drink

- Give 15 gram of glucose (sugar) orally (1/2 cup apple or orange juice or one table spoonful sugar dissolved in water or one tablespoon of honey)
- Repeat blood glucose test after 15 minutes
- If blood glucose is still ≤ 4.0 mmol/L (72mg/dl) repeat the process x 3 till glucose is > 4.0 mmol/L (72mg/dl)
- Then give a snack of 15-20 gram of complex carbohydrate such as one toasts

Unconscious OR unable to drink

INTRAVENOUS ACCESS IS SECURED:

- MILD (2.5 – 4.0 mmol/L): \approx (45-72mg/dL)
 - Administer 25 mL 50 % dextrose IV over 1-3 minutes
 - Repeat blood glucose test in 5 minutes
 - If blood glucose is still ≤ 4.0 mmol/L, (72mg/Dl) re-administer the dose and check BG using finger stick in 5 minutes; repeat the process until Blood Glucose level exceed 4.0 mmol/L (72mg/Dl)
- SEVERE (< 2.5 mmol/L) \approx (45 mg/dL)
 - Administer 50 mL of 50 % dextrose IV over 1-3 minutes
 - Repeat blood glucose test in 5 minutes
 - If blood glucose is still ≤ 4.0 mmol/L, readminister the dose (50 mL of 50 % dextrose IV over 1-3 minutes) and check BG using finger stick in 5 minutes; repeat the process until BG level exceed 4.0 mmol/L \approx (72mg/dL)
- NO SECURED INTRAVENOUS ACCESS:
 - Administer 1 mg glucagon subcutaneously or intramuscular
 - Repeat blood glucose test in 15 minutes
 - If blood glucose is still ≤ 4.0 mmol/L \approx (72mg/dL), readminister the dose and check BG using finger stick in 15 minutes; repeat the process until BG level exceed 4.0 mmol/L \approx (72mg/dL)

When the patient is conscious and able to eat give a meal of 30 gram of complex carbohydrate such as 2-3 toasts.

STEP 3

Assess and manage the precipitating factors

STEP 4

Adjust dose of insulin and other hypoglycemic agents.

Call MD if any of the following:

- Patient is put NPO, tube feeding or TPN initiated or stopped
- Persistent nausea/vomiting
- Deterioration of the level of consciousness or seizure
- For patients who presented with hypoglycaemia secondary to long acting sulphonylurea (e.g. Gliclize MR or Glibenclamide) there might be a need for prolonged observation.

Diabetic ketoacidosis management protocol for adults (>14 years)

Diabetic ketoacidosis (DKA) is defined by the biochemical triad of ketosis, hyperglycemia and acidosis. The main treatment of DKA is rehydration, insulin administration and electrolytes balance, mainly potassium, together with identification and treatment of the precipitating factor. Type 1 diabetes mellitus (T1DM) subjects are at risk of developing DKA if they acquire infection, secondary to frequently missed insulin doses or due to marked stress. Furthermore, subjects with newly diagnosed T1DM often present with DKA. Also, subjects with T2DM may present with DKA if they have persistent hyperglycemia for long period of time or they become under the effect of a stressor. Diagnosis of DKA is not difficult and depends on the finding of acidosis, ketosis or significant ketonuria and hyperglycemia. Treatment of DKA mandates good monitoring of fluid status, electrolytes, acidosis and blood sugar. This is a simplified protocol for management of DKA prepared after extensive review of the available evidence based medicine and clinical practice. Most importantly, this protocol provides general guidance; however, it may not suit all patients and will not replace the clinical judgment of the treating physicians.

Clinical presentation

The commonest clinical presentation of DKA and HHS is due to hyperglycemia and include polyuria, polydipsia, weight loss, weakness, and physical signs of dehydration such as dry buccal mucosa, sunken eye balls, poor skin turgor, tachycardia, hypotension and shock in severe cases. Kussmaul respiration, acetone breath, nausea, vomiting and abdominal pain may also occur primarily in DKA. Abdominal pain correlates with the severity of acidosis (3).

Diagnosis

Diagnostic Criteria for DKA:

- Plasma glucose (PG) more than or equal to 200 mg/dl (11.1 mmol/L) or known diabetes;
- Positive serum ketones or significant ketonuria (more than or equal to 2+ urine ketone) and;
- Venous or arterial HCO₃ less than 15 mmol/L and/ or pH less than 7.3. (All 3 biochemical criteria are required for the diagnosis)¹

Investigations

should be directed towards finding the precipitating factors and should be ordered by the treating physician whenever it is appropriate.

N.B-n patients with type 2 diabetes and acidosis check his serum lactate

Markers of severity (Manage in HDU/ICU):

- GCS less than 12
- pH less than 7.1
- Serum ketones more than 6 mmol/L
- HCO₃ less than 5 mmol/L
- K⁺ less than 3.3 or more than 6.0 mmol/L
- Systolic Blood Pressure less than 90 mmHg
- SpO₂ less than 92% in room air and pulse rate more than 100 or less than 60 bpm
- Urine output less than 0.5 ml/kg/hr or evidence of acute kidney injury

Treatment of DKA:

Fluid therapy

Subjects with DKA usually present with variable degrees of dehydration (up to 6 litres) and will require gentle and well monitored fluid replacement. The initial fluid of choice is isotonic saline at the rate of 15–20 ml / kg body weight per hour or 1–1.5 L during the first hour. The choice of fluid for further repletion depends on the hydration status, serum electrolyte levels, and urinary output. In patients who are hypernatremic, 0.45% NaCl infused at 4–14 ml/kg/hour is appropriate, and 0.9% NaCl at a similar rate is preferred in patients with eunatremia or hyponatremia. The goal is to replace half of the estimated water deficit over a period of 12- 24 hours. In patients with hypotension, aggressive fluid therapy with isotonic saline should continue until blood pressure is stabilized (2). The protocol is not designed for subjects who are hemodynamically unstable and those will require management by the ICU team. Quick and over-replacement of fluids is associated with morbidities in DKA subjects e.g. cerebral edema therefore, physicians should always pay attention to the amount of fluids given.

Insulin

Treatment with intravenous insulin should be established once the serum potassium level is more than (3.3 meq/l) and should be continued till the patient is out of DKA and can be shifted to subcutaneous insulin. The only indication to stop insulin is when the K level is less than 3.3 meq/l where replacement with KCL should take be done before insulin is started. The initial insulin dose should be 0.1 unit/kg which should be lowered to 0.05 units /kg if the blood sugar is less than 6 mmol/L. As in the order sheet of the protocol, to avoid hypoglycemia 25 cc of D50% saline can be given as a bolus whenever the Blood Sugar fall below 4 mmol/l. The other option is to add D10%w to the existing fluids to increase and maintain the blood sugar in the target levels.

Potassium Therapy

Most morbidity and mortality in DKA management came from mismanagement of potassium replacement. Although total-body potassium is depleted, mild to moderate hyperkalemia is frequently seen in patients with DKA, due to acidosis, proteolysis and insulinopenia. Insulin therapy, correction of acidosis, and volume expansion decrease serum potassium concentrations. To prevent hypokalemia, potassium replacement is initiated after serum levels fall below the upper limit of normal.

Patients with DKA who had severe vomiting or had been on diuretics may present with significant hypokalemia. In such cases, potassium replacement should begin with fluid therapy, and insulin treatment should be postponed until potassium concentration becomes > 3.3 mEq/L, in order to prevent arrhythmias and respiratory muscle weakness. The order sheet outline few points to take over in case of severe hypokalemia (2). Good monitoring of potassium level is crucial during the management of DKA and the order sheet provides flexibility for the physician to select the timing of repeating the level however aggressive monitoring might be needed especially for those unusually presenting with hypokalemia.

Bicarbonate: (Not routinely needed only in cases of severe Acidosis {pH less than 6.9} not responding to initial treatment).

- If pH is less than 6.9: NaHCO₃ (50 mmol) dilute in 200 ml H₂O infuse at 200 ml/hr, hold if K is below 3.3 mmol/l
- Repeat HCO₃ infusion every 2 hour until pH is more than 6.9.
- Monitor K⁺ level every 2 hours while on Bicarbonate infusion.

Criteria for switching to subcutaneous Insulin:

Venous HCO₃ ≥ 18 mmol/L and/or pH ≥ 7.3, and closed anion gap. The patient is able to take orally. Overlap the first dose of rapid acting insulin for one hour with the insulin infusion before stopping.

Order Sheet for the Management of Adult Patients (more than 14 years old) with DKA

Please admit the patient to: <input type="checkbox"/> General Ward <input type="checkbox"/> ICU, as a case of, secondary to under the care of Dr.		
Vital Signs: <input type="checkbox"/> STAT <input type="checkbox"/> Then every Glasgow coma scale <input type="checkbox"/> STAT <input type="checkbox"/> Then every Diet: <input type="checkbox"/> Diabetic Diet <input type="checkbox"/> NPO Urinary Catheter: <input type="checkbox"/> Yes <input type="checkbox"/> No Nasogastric Tube needed: <input type="checkbox"/> Yes <input type="checkbox"/> No Investigations: VBG: <input type="checkbox"/> STAT <input type="checkbox"/> Then every Urea / Electrolytes: <input type="checkbox"/> STAT <input type="checkbox"/> Then every..... <input type="checkbox"/> CBC <input type="checkbox"/> Urine Analysis <input type="checkbox"/> Urine Ketones <input type="checkbox"/> Urine culture/sensitivity <input type="checkbox"/> Blood Culture <input type="checkbox"/> Random Blood sugar <input type="checkbox"/> Serum Ketones <input type="checkbox"/> Phosphorus <input type="checkbox"/> Ca ²⁺ <input type="checkbox"/> Mg <input type="checkbox"/> CXR <input type="checkbox"/> ECG <input type="checkbox"/> Troponin/CK-MB <input type="checkbox"/> Others Monitoring : Check blood sugar, by glucometer (if hourly blood sugar readings are between 5-10 mmol/L for 3 consecutive hours, then the frequency of blood glucose checking can be reduced to 2 hourly). <input type="checkbox"/> Input/Output Chart <input type="checkbox"/> Daily Weight		
Fluids: (If the patient is hemodynamically unstable, DON'T use this protocol)		
<input type="checkbox"/> If Systolic BP is more than or equal to 90 mmHg , please use the algorithm below: Be cautious with elderly patients, very young patients, and patients with compromised cardiac status due to risk of fluid overload.		
<div style="border: 1px solid black; padding: 5px;"> Weight at presentation more than 50 kg <input type="checkbox"/> 0.9% NaCl 1L over 1st hour(no added potassium chloride) <input type="checkbox"/> 0.9% NaCl 1L over next 2 hours(no added potassium chloride) <input type="checkbox"/> 0.9% NaCl 1L over next 4 hours(with potassium chloride as per potassium replacement algorithm) </div>	<div style="border: 1px solid black; padding: 5px;"> Weight at presentation less than or equal to 50 kg Do not use this protocol </div>	
<input type="checkbox"/> Continue NS fluid at a rate of (100 – 250 ml/hr).....ml/hour with potassium as in potassium algorithm. <input type="checkbox"/> When blood sugar is less than 13 mmol/L ≈ (235mg/dL), change to D5 NS at a rate (100 – 250 ml/hr).....ml/hour. <input type="checkbox"/> If blood sugar is less than 4.0 mmol/L ≈ (72mg/dL), give a bolus of 25 ml of Dextrose 50%.		
Insulin: (Don't start insulin till K level is available) <input type="checkbox"/> Mix 50 units human regular insulin with 50 ml with 0.9% NaCl solution. <input type="checkbox"/> Infuse insulin at a fixed rate (0.1 unit/kg/hr)).....units/hour. (No bolus) <input type="checkbox"/> Check blood sugar hourly by glucometer. <input type="checkbox"/> When the blood sugar is less than 6 mmol/L ≈ (110mg/dL), decrease insulin infusion to (0.05 unit/kg/hr)).....units/hour. <input type="checkbox"/> If the patient is using Levemir/ Glargine continue same dose at the same timeunits atdaily (optional)		
Potassium Chloride Replacement (make sure the patient is passing urine and has a normal renal function) Starting potassium should be:		
<input type="checkbox"/> more than 5.2 mmol/L <input type="checkbox"/> NIL	<input type="checkbox"/> 3.3 to 5.2 mmol/L <input type="checkbox"/> 40 mmol/L To be added to IV fluid, don't exceed the maximum rate of 10 meq/potassium chloride per hour	<input type="checkbox"/> less than 3.3 mmol/L (call the doctor immediately) <ul style="list-style-type: none"> Hold insulin infusion for 2 hours or until serum potassium is more than or equal to 3.3 meq/L Perform ECG Apply cardiac monitor to patient Increase the rate of potassium chloride infusion but don't exceed the maximum rate of 10 meq/potassium chloride per hour. Request a higher potassium chloride concentration infusion from pharmacy. Once ready, give 40 meq of potassium chloride in 500 ml 0.9 % normal saline to run over 4 hours. Resume insulin infusion when serum potassium is more than or equal to 3.3 mmol/L.
Potassium drip concentration should be changed whenever the serum potassium level is checked as per potassium chloride replacement algorithm. Insulin infusion should be resumed after correction of potassium level		
Physician's Name and Stamp: _____		Date: _____
Signature: _____		Time: _____
Nurse's Name: _____		Date: _____
Signature: _____		Time: _____

- For subjects who presented with unexplained hypoglycemia (either on using insulin or oral hypoglycemic agents) a reduction in the insulin dose and/or Oral Hypoglycemic Agents (10-25%) should be considered
- For individuals who presented with explained hypoglycemia, consider lowering the dose.
- Enhance DM related education

Order Sheet for the Management of Adult Patients (more than 14 years old) with DKA

Confirm DKA Diagnosis (All 3 biochemical criteria are required for the diagnosis)¹:

- Plasma glucose (PG) more than or equal to 200 mg/dl (11.1 mmol/L) or known diabetes;
- Positive serum ketones or significant ketonuria (more than or equal to 2+ urine ketone) and;
- Venous or arterial HCO₃ less than 15 mmol/L and/ or pH less than

Bicarbonate: (Not routinely needed only in cases of severe Acidosis {pH less than 6.9} not responding to initial treatment).

- If pH is less than 6.9: NaHCO₃ (50 mmol) dilute in 200 ml H₂O infuse at 200 ml/hr, hold if K is below 3.3 mmol/l
- Repeat HCO₃ infusion every 2 hour until pH is more than 6.9.
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- Venous HCO₃ more than 18 mmol/L and/or pH more than 7.3, and closed anion gap.
- The patient is able to take orally.

Overlap the first dose of rapid acting insulin for one hour with the insulin infusion before stopping.

Markers of severity (Manage in HDU/ICU):

- GCS less than 12
- pH less than 7.1
- Serum ketones more than 6 mmol/L
- HCO₃ less than 5 mmol/L
- K⁺ less than 3.3 or more than 6.0 mmol/L
- SBP less than 90 mmHg
- SpO₂ less than 92% in room air and pulse rate more than 100 or less than 60 bpm
- Urine output less than 0.5 ml/kg/hr or evidence of acute kidney injury

Definition: Diabetic ketoacidosis is defined by the biochemical triad of ketonemia, hyperglycemia and acidemia. The main treatment of DKA is rehydration, insulin administration and electrolytes balance, mainly potassium, together with identification and treatment of the precipitating factor.

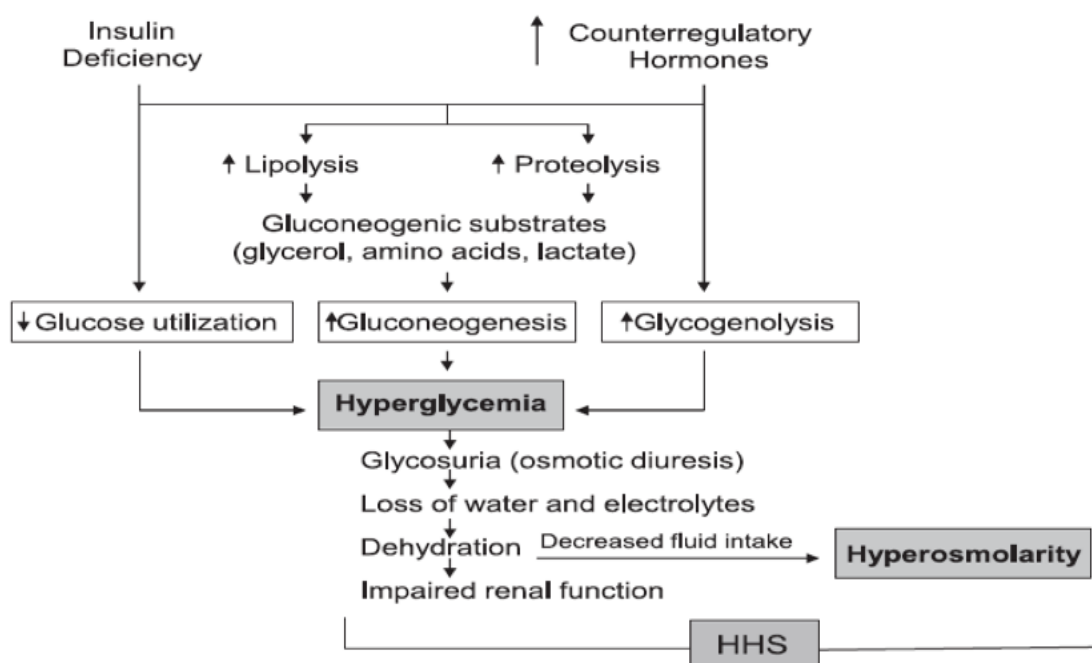
Protocol for diagnosis and management of adults with hyperglycemic, hyperosmolar state

Introduction:

The hyperosmolar hyperglycemic state (HHS) is a syndrome characterized by severe hyperglycemia, hyperosmolality, and dehydration in the absence of ketoacidosis. The estimated incidence account for <1% of hospital admissions in patients with diabetes. Most cases of HHS are seen in elderly patients with type 2 diabetes; however, it has also been reported in children and young adults. The overall mortality rate is estimated to be as high as 20%, which is about 10 times higher than the mortality in patients with diabetic ketoacidosis (DKA). The prognosis is determined by the severity of dehydration, presence of comorbidities, and advanced age. Treatment of HHS is directed at replacing volume deficit and correcting hyperosmolality, hyperglycemia, and electrolyte disturbances, as well as management of the underlying illness that precipitated the metabolic decompensation. Low-dose insulin infusion protocols designed for treating DKA appear to be effective; however, no prospective randomized studies have determined best treatment strategies for the management of patients with HHS.

Pathophysiology:

HHS is characterized by extreme elevations in serum glucose concentrations and hyperosmolality without significant ketosis. These metabolic derangements result from synergistic factors including insulin deficiency and increased levels of counter regulatory hormones (glucagon, catecholamines, cortisol, and growth hormone) . Hyperglycemia develops because of an increased gluconeogenesis and accelerated conversion of glycogen to glucose (glycogenolysis) and by inadequate use of glucose by peripheral tissues, primarily muscle. From the quantitative standpoint, increased hepatic glucose production represents the major pathogenic disturbance responsible for hyperglycemia in DKA. As the glucose concentration and osmolality of extracellular fluid increase, an osmolar gradient is created that draws water out of the cells. Glomerular filtration is initially increased, which leads to glycosuria and osmotic diuresis. The initial glycosuria prevents the development of severe hyperglycemia as long as the glomerular filtration rate is normal. However, with continued osmotic diuresis, hypovolemia eventually occurs, which leads to a progressive decline in glomerular filtration rate and worsening hyperglycemia.



Diagnostic Criteria of HHS :

- Marked Hyperglycemia ($>$ plasma glucose $>$ 30 mmol/L \approx (540mg/dL), without significant hyperketonemia(negative urine ketones or trace) or acidosis (PH $>$ 7.3, serum Bicarbonate $>$ 15)

plus

- Serum Osmolality $>$ 320 mOsmol/kg) β .

Precipitating factors:

- New diagnosis of T2DM
- Infection
- High dose steroids
- Myocardial infarction
- Vomiting
- Stroke
- Thromboembolism
- Poor treatment compliance
- Impaired sense of thirst

Presentation:

- Patients with HHS may present with :
- Confusion
- Coma
- Seizures
- Vomiting
- Features of the precipitating factor

Physical examination findings:

- Dehydration
- Hypotension
- Coma
- Confusion
- Focal neurology
- Features of the precipitating factor

Investigations:

- Laboratory glucose
- Urea & electrolytes
- Venous blood gas (VBG) to rule out DKA (unless hypoxic, then do arterial blood gas or ABG)
- Urine analysis
- Serum osmolality (if difficult to obtain, then use calculated osmolality).
- Further tests:
- Chest X Ray
- ECG, CBC, CRP, Troponin, CK-MB, Amylase
- Consider CT Brain if obtunded.

Management

Treatment Goals:

The goals of treatment of HHS are to treat the underlying cause and to gradually and safely Normalise the plasma osmolality

Replace fluid and electrolyte losses Normalize blood glucose

Other goals include prevention of arterial or venous thrombosis, cerebral edema, central pontine myelinolysis and foot ulceration.

Immediate Management:

Make sure the patient has intact airway, breathing and circulation and support as indicated Cardiac monitor
Urinary catheter (if indicated)

Consider central venous pressure and nasogastric tube if there is a necessity.

Intravenous fluid

If the patient is hemodynamically unstable, aggressive resuscitation should be done initially to stabilize the patient first until Systolic BP is > 90 then follow this fluid replacement policy). Be cautious with elderly patients, and patients with compromised cardiac and renal status due to risk of fluid overload.

- Patients with HHS often have fluid deficit of over 8 liters (10-22 ml/kg). Fluid resuscitation is the main stay of treatment together with a small dose of insulin, however, it's important not to correct the fluid and electrolytes abnormalities too quickly as this could precipitate cerebral edema and heart failure.
- Aim to replace 4 liters of the fluid losses in the first 12 hours starting with 0.9 % N.S
- Start a liter of 0.9 % N.S over one hour with no added potassium while waiting for the lab result of serum potassium.
- Give 3 more liters of 0.9 % NS over the next 11 hours with added potassium as detailed in gthe potassium section.
- If the blood glucose is < 13 mmol/L, change to D5 0.9% NS at the same rate.
- Monitor therapy by measuring/calculating serum osmolality($\text{Osmolality} = \{ 2X (\text{Na}) + \text{Glucose}(\text{mmol/L}) + \text{Urea} (\text{mmol/L}) \}$ at time : 0 hours, 3 hours, 6 hours, 12 hours and then 12 hourly untill resolution of metabolic abnormalities. If serum osmolality is falling too quickly (i.e. > 5 mOsmol/kg/hr) , reduce the rate of intravenous fluids.
- Aim to reduce serum osmolality by about 5 mOsmol/kg per hour.
- Expect an initial rise in serum sodium after initiation of treatment, however, as far as serum osmolality is falling, continues with 0.9 % N.S. However, if serum osmolality is not declining by > 5 mOsmol/kg per hour despite adequate positive fluid balance and /or serum Na > 150) , then change fluid to 0.45 % N.S.
- The rate of fall in serum sodium should not exceed 10 mmol/L over 24 hours.

Potassium

Aim to keep serum potassium levels in the normal range. Make sure the patient has good urine output and has normal renal function. Be cautious as most patients with HHS may have a degree of renal impairment due to severe dehydration.

<input type="checkbox"/> more than 5.2 mmol/L	<input type="checkbox"/> 3.3 to 5.2 mmol/L	<input type="checkbox"/> less than 3.3 mmol/L
<input type="checkbox"/> NIL	<input type="checkbox"/> 40 mmol/L	<input type="checkbox"/> Hold insulin for 2 hours or until potassium more than or equal to 3.3 mmol/L <input type="checkbox"/> Increase the rate of the fluid replacement not more than or equal to 10 meq/ potassium chloride per hour or <input type="checkbox"/> Give potassium chloride 40 meq in 500 ml normal saline to run over 4 hours
		<input type="checkbox"/> Apply cardiac monitor to patient
		<input type="checkbox"/> Perform ECG

Insulin

Mix 50 units of regular insulin in 50 ml of 0.9 % N.S In a syringe. Use intravenous route for insulin infusion as per the following sliding scale. Patients with HHS need half the dose of insulin that is used to Treat DKA. Make sure the patient has received reasonable amount of fluid (at least 1 Liter of I.V fluid) before insulin is started due to the risk of circulatory collapse in case of sudden reduction of plasma glucose without enough intravascular volume repletion. Please do not exceed a maximum of 0.05 units/kg/ hour (e.g. 4 units in an 80 kg patient).

Capillary Blood Glucose mmol/L	Intravenous Insulin Infusion Rate (ml/hr)
If blood sugar \geq 13 mol/ \approx (540mg/dL)	IV insulin (0.05/kg/hr).....Units/hr
If blood sugar <13 mmol/l \approx (540mg/dL)	IV insulin 0.025/kg/hr.....Units/hr
If blood sugar is < 5mmol/l \approx (90mg/dL)	Start D10 as in the fluid algorithm

Time line for interventions :

First Hour:

Start 1 Liter of 0.9% N.S over one hour

Only commence i.v insulin infusion (0.05 units/kg/hour) if there is significant ketonemia or ketonuria 2+ (Mixed DKA and HHS). Remember, i.v fluid alone can result in significant drop in plasma glucose in patients with HHS. The earliest start of i.v insulin infusion should be after the patient has received at least one liter of i.v fluid.

Clinical assessment including foot exam Investigations:

(VBG, U&E, Lactate, CBC, CRP, Measured/calculated plasma osmolality, ECG, CXR, urine analysis and culture, blood cultures).

Monitoring:

Hourly blood sugars

Serum osmolality, serum sodium, serum potassium at time zero and then 3 hourly (or more frequent if needed)

Hourly Urine out put

Pulse oximetry, cardiac monitor (if available) Prophylactic Low molecular weight heparin. Decide about antibiotic need.

60 minutes-6 hours:

Aims:

To achieve gradual decline in osmolality (by \sim 5 mosmol/kg/hour)

- Use 0.9 % N.S and target 2-3 liters positive fluid balance by 6 hours (be careful with cardiac patients)
- Observe goals regarding osmolality, and glucose fall
- Aim for target plasma glucose between 10-15 mmol/L \approx (180-270mg/dL)

If the glucose is not falling less than 5 mmol/L \approx (90mg/dL)

- If fluid balance is inadequate, increase fluid rate
- If already in positive fluid balance, commence low dose i.v insulin (0.05 units/kg/hour).

Aim to maintain potassium in the normal reference rate.

6 hours -12 hours

Aim to achieve a fluid balance of 3-6 liters by 12 hours Make sure clinical an biochemical paramerts are met

Assess for occurrence of complications

Continue to treat the precipitating factor

Avoid hypoglycemia (change fluid to D5 0.9 % NS if glucose falls below 13 mmol/L)

12-24 hours:

Ensure continuous improvement in clinical and biochemical parameters

Continue i.v fluid to replace the remaining balance of fluid loss within the next 12 hours. Continue insulin as per sliding scale in the insulin algorithm

Assess for complications.

Further management

Full anticoagulation with low molecular weight heparin and TED stockings should be considered in all patients unless contraindicated

Broad spectrum antibiotics should be started if there is evidence of infection. Treat precipitating factor as appropriate.

Foot protection:

These patients are at very high risk of developing foot ulceration, therefore, an initial foot examination and assessment must be done, together with application of heel protectors for those at risk of ulceration such as patients with neuropathic feet, foot deformities and peripheral vascular disease.

Anti-infective agents:

An infective source should be sought on clinical history and physical examination and CRP may be helpful. Antibiotics should be given when there are clinical signs or imaging and /or laboratory evidence of its presence.

Recovery phase

Complete correction of electrolytes and osmolality abnormalities may take more than 24 hours (unlike DKA). Therefore, too aggressive correction could prove harmful. Recovery in most of these patients, who are usually elderly, will be determined by their previous functional status.

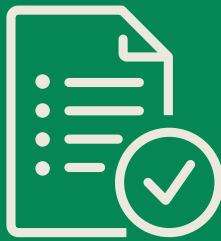
I.V insulin can be discontinued once they are eating and drinking normally but i.v fluids may be required for longer if oral intake is poor.

Most patients should be transferred to subcutaneous insulin (regime should be individualized). Newly diagnosed patients with diabetes or well controlled patients on oral agents could be considered for oral agents after their condition becomes stable. All patients need to be seen by diabetes educators for more education.

Order Sheet for the Management of Adults with Hyperosmolar Hyperglycemic State

(Please remember: Clinical Judgment always supersedes pathway recommendations and protocols)

Please admit the patient to: <input type="checkbox"/> General Ward <input type="checkbox"/> ICU, as a case of, secondary to, under the care of Dr.		
Vital Signs: <input type="checkbox"/> STAT <input type="checkbox"/> Then every Glasgow coma scale <input type="checkbox"/> STAT <input type="checkbox"/> Then every Investigations: VBG (to rule out DKA) : <input type="checkbox"/> STAT <input type="checkbox"/> Serum Urea, Electrolytes and serum Osmolality : <input type="checkbox"/> STAT <input type="checkbox"/> 3 hours <input type="checkbox"/> 6 hours <input type="checkbox"/> 12 hours <input type="checkbox"/> Then every <input type="checkbox"/> CBC <input type="checkbox"/> Blood Culture <input type="checkbox"/> Urine Culture & Microscopy <input type="checkbox"/> Random Blood sugar <input type="checkbox"/> Serum Ketones <input type="checkbox"/> Urine Ketones <input type="checkbox"/> CXR <input type="checkbox"/> ECG <input type="checkbox"/> Troponins/CK-MB <input type="checkbox"/> Amylase <input type="checkbox"/> serum Lactate <input type="checkbox"/> HbA1c <input type="checkbox"/> Check blood sugar, by glucometer, every hour (if hourly readings are very stable (i.e. Between 5-10 mmol/L for 3 consecutive hours) then the frequency of blood glucose checking can be reduced to 2 hourly).		
Diet: <input type="checkbox"/> Diabetic Diet <input type="checkbox"/> NPO <input type="checkbox"/> Input/output Chart Urinary Catheter: <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Daily Weight Thrombophylaxis Given <input type="checkbox"/> Yes <input type="checkbox"/> NO (explain why not given, is it contraindicated? <input type="checkbox"/> Yes <input type="checkbox"/> No		
Fluids: (If the patient is hemodynamically unstable, DON'T use this protocol and resuscitate the patient first as per local ER protocols) <input type="checkbox"/> In hemodynamically stable patients (e.g. BP > 90/60 mmHg, O2 Saturation > 92 %), please use the algorithm below: Be cautious with elderly patients, and patients with compromised cardiac and renal status due to risk of fluid overload		
Order	Instruction	
<input type="checkbox"/> Give one liter of 0.9 % N.S (without KCl) over one hour. <input type="checkbox"/> Give 3 liters of 0.9 % N.S over the next 12 hours, typically at rate of 250 ml/hour (N.B rate may be individualized) (with KCl as indicated in the potassium algorithm). <input type="checkbox"/> Then, decrease the rate of I.V 0.9%NS to (100-250 ml /hour).....ml/hour(individualized) (with KCl as indicated in the potassium algorithm) <input type="checkbox"/> Whenever blood sugar is less than 13mmol/L ≈ (540mg/dL) please change the I.V fluid to D5 0.9 NS and adjust insulin infusion (if already started) as indicated in the insulin algorithm. <input type="checkbox"/> When the blood sugar drops to ≤ 5 mmol/L ≈ (90mg/dL), add D10% W to run at a rate of (50-100 ml/Hr), however, this should be stopped if blood sugar reaches 10 mmol/ ≈ (180mg/dL)	<ul style="list-style-type: none"> • Monitor therapy by measuring/calculating serum osmolality (Osmolality = { 2X (Na) + Glucose (mmol/L) + Urea (mmol/L) } at time : 0 hours, 3 hours, 6 hours, 12 hours and then 12 hourly until resolution of metabolic abnormalities. • Aim to reduce serum osmolality by 5 mOsmol/kg per hour. If serum osmolality is falling by > 5 mOsmol/kg/hour, reduce the rate of intravenous fluids by 25-50 %. • If serum osmolality is not declining by > 5 mOsmol/kg per hour despite adequate positive fluid balance and /or corrected serum Na > 150) , then change fluid to 0.45 % N.S at the same rate. • The rate of fall in corrected serum sodium should not exceed 10 mmol/L over 24 hours. • The total fluid infusion rate shouldn't exceed 250 cc/hr except for the • first liter of 0.9 % N.S. 	
Potassium: Aim to keep serum potassium levels in the normal range. Make sure the patient has good urine output and has normal renal function. Be cautious as most patients with HHS may have a degree of renal impairment due to severe dehydration.		
<input type="checkbox"/> more than 5.2 mmol/L	<input type="checkbox"/> 3.3 to 5.2 mmol/L	<input type="checkbox"/> less than 3.3 mmol/L (call the doctor immediately)
<input type="checkbox"/> NIL	<input type="checkbox"/> 20 mmol/L <input type="checkbox"/> 30 mmol/L <input type="checkbox"/> 40 mmol/L	<ul style="list-style-type: none"> • Hold insulin infusion for 2 hours or until serum potassium is ≥ 3.3 mmol/L. • Perform ECG & Apply cardiac monitor • Treatment options : Option 1 • Give higher concentration of potassium chloride infusion but don't exceed the maximum rate of 10 mEq KCL per hour by peripheral line (or 20 mEq KCL per hour by central line). Option 2 • Give 40 mEq of potassium chloride in 500 ml 0.9 % normal saline to run over 4 hours. Option 3 • Use your local hospital policy to treat hypokalemia • Monitor serum potassium q 2 hourly and resume insulin infusion when serum potassium is ≥ 3.3 mmol/L.
Insulin (Do not start i.v insulin infusion if serum potassium is < 3.3 mmol/L). Mix 50 units of regular insulin in 50 ml of 0.9 % N.S (1 ml=1 unit). Use intravenous route for insulin infusion as per the following sliding scale Make sure the patient has received reasonable amount of fluid before insulin is started due to risk of circulatory collapse and cerebral edema.		
Capillary Blood Glucose mmol/L	Intravenous Insulin Infusion Rate (Unit/hr)	
If blood sugar ≥ 13 mmol/l ≈ (540mg/dL)	IV insulin (0.05/kg/hr).....Units/hr	
If blood sugar <13 mmol/l ≈ (540mg/dL)	IV insulin 0.025/kg/hr.....Units/hr	
If blood sugar is < 5mmol/l ≈ (90mg/dL)	Add D10% W as in the fluid algorithm (rate: 50-100 ml/hour)	
If blood sugar < 4 mmol/L ≈ (72mg/dL)	Stop insulin infusion, treat hypoglycemia with a bolus of 25 ml of Dextrose 50%.	
N.B: if the patient is already taking long acting insulin, please continue the same. Physician's Name and Stamp: _____ Date: _____ Signature: _____ Time: _____ Nurse's Name: _____ Date: _____ Signature: _____ Time: _____		



Reference for Guidelines and Protocols of Emergency Diabetes

Reference for Guidelines and Protocols of Emergency Diabetes Adults:

1. Management of hyperosmolar hyperglycaemic state in adults with diabetes. Scott AR1; Joint British Diabetes Societies (JBDS) for Inpatient Care; JBDS hyperosmolar hyperglycaemic guidelines groupCollaborators (26) Allan B, et al Diabet Med. 2015 Jun;32(6):714-24. doi: 10.1111/dme.12757.
2. Pasquel FJ1, Umpierrez GE2. . Hyperosmolar hyperglycemic state: a historic review of the clinical presentation, diagnosis, and treatment. Diabetes Care. 2014 Nov;37(11):3124-31. doi: 10.2337/dc14-0984.
3. Fishbein HA, Palumbo PJ. Acute metabolic complications in diabetes. In Diabetes in America. National Diabetes Data Group, National Institutes of Health, 1995, p. 283–291 (NIH publ. no. 95-1468)
4. RosenbloomA. Hyperglycemic hyperosmolar state: an emerging pediatric problem. J Pediatr 2010;156:180–184 pmid:20105637 CrossRef PubMed Web of Science Google Scholar
5. Milionis HJ, Elisaf MS. Therapeutic management of hyperglycaemic hyperosmolar syndrome. Expert Opin Pharmacother 2005;6:1841–1849 pmid:16144505 CrossRef PubMed Google Scholar
6. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. Diabetes Care 2009;32:1335–1343 pmid:19564476 FREE Full Text Google Scholar
7. Fadini GP, de Kreutzenberg SV, Rigato M, et al. Characteristics and outcomes of the hyperglycemic hyperosmolar non-ketotic syndrome in a cohort of 51 consecutive cases at a single center. Diabetes Res Clin Pract 2011;94:172–179 pmid:21752485 CrossRef PubMed Google Scholar
8. Wachtel TJ, Silliman RA, Lamberton P. Prognostic factors in the diabetic hyperosmolar state. J Am Geriatr Soc 1987;35:737–741 pmid:3611564 PubMed Web of Science Google Scholar
9. Umpierrez GE, Kelly JP, Navarrete JE, Casals MM, Kitabchi AE. Hyperglycemic crises in urban blacks. Arch Intern Med 1997;157:669–675 pmid:9080921 CrossRef PubMed Web of Science Google Scholar.
10. Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis
11. M. W. Savage, K. K. Dhatariya, A. Kilvert, G. Rayman, J. A. E. Rees, C. H. Courtney, L. Hilton,
12. P. H. Dyer and M. S. Hamersley, for the Joint British Diabetes Societies. Diabetic Medicine 2011. DOI: 10.1111/j.1464-5491.2011.03246.
13. Hyperglycemic Crises: Diabetic Ketoacidosis (DKA), And Hyperglycemic Hyperosmolar State (HHS) Adair R Gosmanov, M.D., Ph.D., F.A.C.E., Elvira O Gosmanova, M.D., F.A.S.N., and Abbas E Kitabchi, M.D., Ph.D., M.A.C.E. Endo textbook
14. Umpierrez G, Freire AX. Abdominal pain in patients with hyperglycemic crises. Journal of critical care 2002; 17:63-67

Reference for Guidelines and Protocols of Emergency Diabetes pediatrics

1. BSPED Recommended Guideline for the Management of Children and Young People under the age of 18 years with Diabetic Ketoacidosis 2015. Julie A Edge, Oxford: Approved by BSPED Clinical Committee 2015
2. Wolfsdorf JI, Allgrove J, Craig ME, et al. Diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Pediatr Diabetes*. 2014;15(Suppl. 20):154-179.
3. British Columbia's Children's Hospital (October, 2015). British Columbia Children's Hospital Diabetic Ketoacidosis protocol.
4. Diabetes (type 1 and type 2) in children and young people: diagnosis and management (NG18). Evidence-based recommendations on the diagnosis and management of type 1 and type 2 diabetes in children and young people NICE guideline Published August 2015 Last updated November 2016
5. Wolfsdorf JI, Allgrove J, Craig ME, Edge J, Glaser N, Jain V, Lee WWR, Mungai LNW, Rosenbloom AL, Sperling MA, Hanas R. A. Published in *Pediatric Diabetes* 2014: 15(Suppl. 20): 154-179. Uploaded: 2. Sept 2014
6. BSPED Recommended Guideline for the Management of Children and Young People under the age of 18 years with Diabetic Ketoacidosis 2015

