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Ministry of Health

# Pediatric DKA/HHS Protocol:

## Task Force:

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## Introduction:

Diabetes Mellitus (DM) is the most common endocrine disorder and common chronic disease affecting children and adolescents. It is characterized by persistent hyperglycemia due to relative insulin deficiency or absolute insulin absence in the body.

Prevalence of Diabetes Mellitus worldwide is increasing at an enormous rate. At the start of 21st century, The International Diabetes Federation (IDF) estimated that patients with DM across the world will rise from 171 million in 2000 to 366 million by 2030[1]. But in 2011, it already reached 366 million[1]. Again in 2013, as per IDF, 382 million people of world suffer from DM which is almost 8.3% of adult population, and in less than 25 years these numbers will go above 592 million[2].

The World Health Organization (WHO) report Saudi Arabia ranks 7th in the world and 2nd highest in middle east. Out of total 33.3million population, around 7 million are diabetic and 3 million are having pre diabetes[3].

Diabetes Emergencies like Diabetic KetoAcidosis (DKA), and Hyperosmolar hyperglycemic state is not uncommon acute conditions associated with type 1 diabetes mainly (DKA) and with type 2 diabetes mainly HHS. Despite the lack of extensive and quite good number of studies in Saudi Arabia in regards to the incidence of these complications we can estimate the burden of such problems health and economy wise.

In the ministry of health hospitals, we found different protocols and guidelines followed to manage DKA and HHS which is not a problem per se but to have different protocols in the same hospitals the one in emergency department is different from the one in the ward or in ICU which increase the risk of pitfalls and mistakes in managing the patients in the right way.

Our aim is to unify the protocol of DKA and HHS management in ministry of health hospitals whom is responsible of about 60 % of the population as the first step the second step is implement this protocol and to monitor the implementation by special measures.

## Methodology:

Development of DKA protocol went through 4 phases over a period of 1 year as follows:

**Phase 1:** review the literature of Diabetic Ketoacidosis protocols and guidelines worldwide and impact of implementing these protocol on health conditions as well as on cost.
Then we payed special attention to the studies done in Saudi Arabia in regards to the prevalence and incidence of diabetes emergencies and the impact of these conditions on health and cost.
This phase has been done by panel of experts in the field of Endocrine and Diabetes, where The outcome is a unified DKA management protocol according to the best evidence based practice.

**Phase 2:** the panel of experts has been extended to include pediatric and adult Emergency Medicine and intensive care units whom they reviewed the protocol developed in the first phase and put their input according to their experience in the specialty.

**Phase 3:** the protocol has been reviewed and amended by another panel of experts whom contributing in execution of the protocol as nurses, pharmacists, lab experts as well as quality improvement experts.

**Phase 4:** experts from the different specialties including (pediatric endocrinology and diabetes, pediatric emergency medicine, and pediatric intensive care) from all the regions of kingdom of Saudi Arabia whom they reviewed the protocol and shared their opinion.

## Literature Review:

In children and adolescents, Type 1 DM is on the rise and it varies as per region. The epidemiological data shows overall 3-4% annual increase in type 1 DM[4]. Finland is number 1 in the world for the incidence rates of type 1 DM per 100,000 children per year with 57.2%. Among Top 10 countries with highest incidence of type 1 DM, Saudi Arabia is at number 4 with annual incidence of 33.5%, only 2nd in MENA region after Kuwait. Total number of type 1 DM is Saudi Arabia was recorded at 35000 with annual addition of 3900 new cases per year in 2017[5].

This much high incidence and prevalence of type 1 DM in children in Saudi Arabia may be partially attributed to its young population which as per United Nations is 26% below the age of 14 years[6].
In Saudi Arabia, one of the studies in 2008, showed that prevalence of type 1 DM was highest in

central region with rates as high as 126/100,000 and mostly urban in origin[7]. Which was confirmed in 2015 by another study with urban rates as high as 77.2%[8].

Due to high incidence and prevalence of diabetes in pediatric population, complications of diabetes are seen more frequently in children and adolescents, which include both acute and chronic. Acute Diabetes Complications are hyperglycemic emergencies also called as hyperglycemic crisis, mainly DKA, HHS and hypoglycemic emergency presenting as Hypoglycemia itself[9,10].

About DKA in Saudi Arabia over last 30 years from 1985-2016, epidemiological studies show that Incidence of pediatric DKA is changing over time with highest rates of 77% to around 40.8%[11-20]. Which is still very high as compared to western countries like in USA this rate is around 29-31% , Finland 22% and Sweden 14%[21-22].

In HHS, the rate of hospitalization is less than 1% of all diabetes related complications[23]. Both DKA and HHS differ in many aspects, which include degree of hyperglycemia, presence of ketonemia, metabolic acidosis and clinical characteristics including degree of dehydration, level of consciousness, presence of co-morbidities and more chances of renal impairment at presentation in HHS. Therefore, it is necessary to address this separately and have separate protocols for management of HHS.

Type 1 DM in itself is associated with reduced life expectancy. One of studies showed that in type 1 DM, the life expectancy is 12 years less than non-diabetics[24]. Similarly, the acute complications of Diabetes like DKA and HHS are associated with high morbidity and mortality if not treated properly. In Children and adolescents with Type 1 DM, DKA is a cause of mortality in almost 50% of patients[25].

Mortality is variable depending on region and the health care facility. Over last 25 years, worldwide mortality had reduced from 8% to less than 1% [26]. In USA, DKA mortality has declined in last 2 decades from 1.1% to 0.4% [27]. In United Kingdom, the mortality has fallen from 1.8% in 2008 to as low as less than 0.16% in 2016 [28-29]. Among European Union countries, it varies from 7.4% in Italy to 4% in Denmark[30-31]. In Australia and New Zealand, the DKA mortality is 1.4%[32]. In China, over period of 20 years, the DKA mortality has decreased from 7.96% to 0.67% [33]. In Pakistan in 2018, one of tertiary care hospitals reported overall inpatient DKA mortality of 5.4%[34]. In India in 2016, a study reported inpatient mortality as high as 30%[35].

In Middle Eastern North African (MENA) Region countries, there are very few studies which have documented mortality from DKA and HHS. In Kenya, one of the studies from Nairobi showed mortality as high as 30%[36]. Available data shows that the DKA mortality is variable in middle eastern countries. For example, in Libya it is 10%, In Jordan it is 4.8% and in Saudi Arabia, the mortality from DKA is 2.9% in one of tertiary care hospital in Jeddah[37-39].

DKA Mortality in children and adolescents is mostly due to cerebral edema which can occur in about 0.5% to 1% of patients with DKA[40,41]. This is preventable in most of cases by implementation of DKA care pathways and protocols of fluid management[42].

Due to more complex and complicated nature of HHS, mortality is very high which ranges from 10-20% and is more than 10 times higher than DKA[43-45].

Another important issue in management of diabetes and diabetes elated complications including acute emergencies, is high cost. In Saudi Arabia, in 2010, out of total health expense of 9.4 billion US$, almost 10% was spent only on diabetes related costs[46]. In USA alone, there occur total of 145,000 DKA cases each year. Cost of management of one DKA patient is around 17500 US$. This amount is so huge that all DKA patient's management cost is of 2.4 billion US$/ year[47,48].

Over last 20 years, with better understanding of pathophysiology and development of evidence based DKA and HHS guidelines and implementation of care pathways, Mortality in DKA /HHS reduced substantially in recent years throughout world[49,50].

Worldwide it has been a standard practice to have national level evidence-based guidelines and hospital protocols for acute diabetes emergencies. The implementation of such standard order set and protocols improve quality of care, reduce morbidity, improve time to DKA resolution, reduce length of stay and improved compliance in shifting to sub cut insulin.

One study from USA in 2017 showed that DKA protocol implementation by computerized orders set in ICU improved time to resolution of DKA and better compliance by physicians in following these guidelines[51]. In February 2017, one of the studies from Saudi Arabia Riyadh, has clearly shown that implementation of clinical practice guidelines at a tertiary care hospital reduced the length of stay in children and adolescents with DKA[52]. The issue of adherence to guidelines is important in DKA and HHS management to improve quality of care[53].

So, keeping in view the high incidence prevalence, high morbidity, high mortality and high cost of Pediatric Hyperglycemic emergencies and importance of acute diabetes emergencies protocol implementation, the aim of our diabetes emergencies management protocols as per vision 2030 is to unify the management throughout the Kingdom of Saudi Arabia, and by reducing the length of stay to reduce the cost of management and reduce morbidity and mortality.

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## The protocol:

# 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 MOH 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<br>Polydipsia<br>Weight loss<br>Tiredness | Dehydration<br>Tachypnea; deep (Kussmaul) respiration<br>Breath that smell like acetone (ketone)<br>Nausea, vomiting, and abdominal pain<br>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)<br>Venous pH <7.3 or bicarbonate <15mmol/L<br>Ketonemia and/or ketonuria | **Exclude Hyperosmolar Hyperglycemic State (HHS) (see appendix I)**<br>**Consider other differential diagnoses (see appendix II)** |

**Caveat 1:** Children and adolescents with known diabetes may rarely develop DKA with normal BG levels

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**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 if the airway not protected- ?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 ß 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:**

**Fluid Management in 1st hour**

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

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

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

**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 hrs)

Always request fluid early (expect 1 hr 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).*

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| The following has been associated with risk of cerebral edema, please avoid them | |
|---|---|
| DO NOT DO List | DO NOT give insulin bolus<br>DO NOT give IV sodium bicarbonate (except in life-threatening hyperkalemia)<br>DO NOT give fluid boluses for DKA not in shock<br>DO NOT give hypotonic fluid (0.45%, 0.22%) for rehydration<br>DO NOT give more than 10 ml/kg fluid bolus each time if in shock<br>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.
  - Psychosocial assessment is crucial to identify correctable causes and prevent recurrences

**Higher risk patient 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<br>➢ When BG drop to < 8 mmol/l (≈ 140-150 mg/dl) add D10% to 0.9% Saline<br>➢ 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)<br>➢ Hypoglycemic attack (< 4 mmol): Give 2-5 ml/kg D10% bolus, hold insulin for 15-30 min then repeat BG | |
| **Potassium Adjustment** | |
| Potassium > 5.5 mmol/l (not hemolyzed) | Hold Potassium, repeat level in 2 hrs |

| | |
|---|---|
| Potassium < 3.5 mmol/l | Increase KCl to 60 mmol/l *(need good peripheral IV or Central Line)* |
| 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 | ➢ Recalculate and assess intake/output every 4h |
| • Wrong insulin dose or preparation | ➢ Recheck all preparation |
| • Hyperchloremic metabolic acidosis | ➢ Measure chloride and anion gap* (see legend) |
| • Sepsis (usually with lactic acidosis) | ➢ Look for signs, measure lactate |

**Anion Gap calculation: Na – (Cl + HCO3) = 12 ± 2 (normal).*

**DKA Resolution and Shifting to Subcutaneous Insulin**

**INTRODUCTION OF ORAL FLUID and TRANSITION OF SUBCUTENEOUS 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 diabetic 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, divided to:
  - 30-40 % long acting (e.g. levemir or Glargine)
  - 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 4 times daily (Before meals and at bed time ) 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<br>Pubertal: 1.0-1.2 unit/kg |
| **Before breakfast** | Two-thirds of total daily dose (TDD)<br>➢ One-third rapid acting insulin<br>➢ Two third intermediate-acting insulin (e.g. NPH) |
| **Before dinner** | One third of TDD<br>➢ One-third rapid acting & Two third intermediate-acting insulin OR<br>➢ One-half rapid acting & one-half intermediate-acting insulin (e.g. NPH) |

**Serious DKA Complications & Precautions**

**DKA Complications & Cerebral Edema Management**

| Fatal Complications | Other Common Complications | | |
|---|---|---|---|
| Cerebral Edema<br>Hyper/hypokalemia | Inadequate rehydration<br>Hypoglycemia | Aspiration pneumonia<br>Hyperchloremic acidosis | Hypophosphatemia<br>Thrombosis<br>Stroke |

**Cerebral Edema Risk Factors**

| Uncontrollable | Controllable |
|---|---|
| ➢ Younger age (< 5 years)<br>➢ New onset diabetes<br>➢ Longer duration of symptoms<br>➢ Severe hypocapnia (more than expected for acidosis)<br>➢ Increased serum urea nitrogen<br>➢ Severe acidosis | ➢ IV Bicarbonate treatment for correction of acidosis<br>➢ Administration of insulin in the first hour of fluid treatment (bolus or infusion)<br>➢ Greater volumes of fluid given in the first 4h<br>➢ A marked early decrease in effective serum osmolality (> 5 mOsm/hr)*<br>➢ Serum sodium (corrected)** dropping or not rising with treatment |

Ce reb ral

| Highly suspicious | Management |
|---|---|
| ➢ Severe headache | Inform the Most Responsible Physician/consultant |

| | |
|---|---|
| ➢ Agitation or irritability<br>➢ Unexpected fall in heart rate<br>➢ Increased blood pressure<br>➢ Decreased level of consciousness | Treat immediately with the most readily available of:<br>➢ **Mannitol** 20% (0.5-1 g/kg over 10-15 minutes) or<br>➢ **Hypertonic saline** 3% (3-5 ml/kg over 10-15 min)<br>Drop fluid rate by one third of total<br>Elevate the head of the bed to 30° |

| Life Threatening Signs |
|---|
| ➢ Further deterioration in level of consciousness<br>➢ Abnormalities of breathing pattern (e.g. breathing pauses)<br>➢ Oculomotor palsies<br>➢ Abnormal posturing<br>➢ Pupillary inequality or dilatation<br>**Urgent** |
| **Management**<br>**(Repeat all above steps and consider)** |
| ➢ **Mannitol** or **Hypertonic saline** (Repeat in 30 min to 2 hrs if no initial response)<br>➢ Secure Airway (by experienced staff)<br>➢ **Do not sedate or suppress patient hyperventilation without control breathing**<br>➢ Control ventilation (match patient hyperventilation then increase pCO2 slowly to 35 mmHg)<br>➢ CT when stable (to exclude: hemorrhage, thrombosis)<br>➢ Neurosurgical consultation for other surgical options |

***Effective Osmolality: 2 Na + Glucose (glucose value in mmol/L)**
****Corrected Na = measured Na + 2 [(plasma glucose-100/100)] 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) | Hyperglycemia (> 11 mmol/L or more) |
| No significant hyperketonemia or acidosis (pH>7.3, bicarbonate >15 mmol/L) | Significant ketonemia and acidosis (pH <7.3 or bicarbonate <15mmol/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 CO2 & 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: _____ | Patient Weight:_____ Kg | Length/Height:_____ cm |

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| | | | |
|---|---|---|---|
| | (military: 24 hour format) | | |

Admit the patient to: ☐ PICU ☐ HDU Under the care of Dr._____

| | Noted by | | Noted by |
|---|---|---|---|
| ☐ Obtain Patient Weight | | **Laboratory monitoring** | |
| ☐ Connect to cardiorespiratory monitor | | Hourly | |
| ☐ Connect to pulse oximeter | | ☐ capillary blood glucose | |
| ☐ Record vital signs hourly | | Every 2 hours | |
| ☐ Record neurology assessment hourly (pupils size, reactivity, GCS) | | ☐ Capillary or venous blood gases<br>☐ Serum electrolytes | |
| ☐ Nothing by mouth (NPO) | | Every 4 hours | |
| ☐ Insert two IV cannulas | | ☐ Serum electrolytes | |
| ☐ Strict intake and output and record hourly | | ☐ Calcium, Phosphorus, Magnesium, Urea, Creatinine | |
| ☐ Insert Foley's catheter (only if indicated) | | Upon Admission | |
| ☐ Check Urine for ketones (bedside check) | | ☐ CBC-differential | |
| Additional Investigations: | | ☐ Urine analysis | |
| ☐ HbA1C | | ☐ Blood culture, Urine culture | |
| ☐ Other ..... | | ☐ Chest Xray | |

| **Fluid in the first hour:** | Noted by |
|---|---|
| ☐ Shock & hypotensive patient: Start _____ml (10 ml/kg) 0.9% Saline IV bolus over 5-10 minutes. | |
| ☐ Still hypotensive: Repeat bolus_____ml IV (10 ml/kg) over 5-10 minutes<br>Call physician to the bedside if patient is unstable | |
| ☐ Shock, not hypotensive: Start _____ml (10 ml/kg) 0.9% Saline IV **over one hour**. | |
| ☐ Not in shock: Start _____ml IV infusion 0.9% saline over 1 hour | |
| For severe DKA (bicarbonate <5): 7 ml/kg and for mild to moderate DKA (bicarbonate >5): 5ml/kg | |

| **Fluid after 1-2 hours:** | **Calculation formula** | **Noted by** |
|---|---|---|
| ☐ Start IV 0.9% saline at _____ ml/hour | ≤ 15 kg weight: 5 ml/kg/hr, | |
| ☐ **Potassium Chloride** Add 40 mmol/L (20 mmol to 500 normal saline bag) | 16 to 40 kg: 4 ml/kg/hr | |
| ☐ Add only if patient is passing urine and K level is < 5.5 mmol/L | > 40 kg: 3 ml/kg/hr | |
| ☐ Add Dextrose 5% to 0.9% Saline fluid when blood glucose drops to < 250 mg/dl (14 mmol/L) | | |
| ☐ Add Dextrose 10% to 0.9% Saline fluid when blood glucose drop to < 140-150 mg/dl (8 mmol/L) | | |

| **Insulin Infusion:** DO NOT GIVE BOLUS and Start after 1-2 hour from fluid initiation | **Noted by** |
|---|---|
| ☐ Mix 50 unit of Regular insulin in 50 ml 0.9% saline **Starting dose:** _____ ml/hour (= 0.1 unit/kg/hr)<br>(0.1 ml/kg/hr = 0.1 unit/kg/hr) | |
| ☐ Or: Mix 50 unit of Regular insulin in 500 ml 0.9% saline **Starting dose:** _____ml/hour (= 0.1 unit/kg/hr)<br>(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** |
|---|---|
| ☐ | |

**Physician Name & Signature:**_____ **Nurse Name & signature:** _____

**Appendix V:**

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

| | |
|---|---|
| **Best Motor Response** | 1 = none<br>2 = extensor response to pain<br>3 = abnormal flexion to pain<br>4 = withdraws from pain<br>5 = localizes pain<br>6 = responds to commands |
| **Eye Opening** | 1 = none<br>2 = to pain<br>3 = to speech<br>4 = spontaneous |
| **Best Verbal Response** | 1 = none<br>2 = incomprehensible sounds<br>3 = inappropriate words<br>4 = appropriate words but confused<br>5 = fully orientated |

| Modification of verbal response score for children | |
|---|---|
| **2-5 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 (1-12 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

وزارة الصحة
Ministry of Health

# Confirm DKA Diagnosis

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

## DKA in Shock

Notify PICU, Alert senior primary physician
**Airway**: No elective intubation/call expert
**Breathing**: 100% O2 by Face Mask, Check O2 Sat
**Circulation**: 2 IV cannulas, cardiac monitor
**Hypotensive**: 10 ml/kg NS bolus over 5-10 min
Repeat if hypotensive (x 3) - consider inotropes
**Shock with normal BP**: 10 ml/kg NS over 1 hr

## 1· Hour Management

**Urgent Labs**
Blood glucose
Blood gases
electrolytes
Ca, Magnesium
Phosphorus
Urea, Creatinine

## DKA not in Shock

**Assess Severity**
**Mild**: pH<7.3 or bicarbonate <15mmol/L
**Moderate**: pH<7.2 or bicarbonate <10mmol/L
**Severe**: pH<7.1 or bicarbonate <5mmol/L

**1· hour fluid: 0.9% saline**
7 ml/kg/h for severe DKA
5 ml/kg/h for mild/moderate DKA

**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 1· Hour Management

### Insulin (DO NOT GIVE BOLUS)

**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)*
**Starting dose: 0.05-0.1 unit/kg/hr**
0.05 dose for kids:
*-Younger than 5 years*
*-Newly diagnosed*
*-Rapid drop of BG (>100mg/dl/hr)*
*-Recently received insulin injection*
**Start after 1-2 hour** from starting rehydration fluid

### Simplified calculated rate by weight

| | | |
|---|---|---|
| <15 kg | 5 ml/kg/hr | *Remove fluid boluses of > 20 ml/kg from the total replacement* |
| 16 to 40 | 4 ml/kg/hr | |
| >40 kg | 3 ml/kg/hr | |

### Fluid calculation principles

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)**

### Monitoring

**Hourly:** Vital Signs
Blood glucose, Neurological status (pupils & GCS),
Fluid intake & output
**Every 2-4 hours:**
Blood gases (venous or capillary)
**Every 4 hours:**
Electrolytes, urea & creatinine, phosphorus, calcium, magnesium
**Other labs:**
CBC & differential, Blood culture, urine culture (with fever)
**For new onset diabetes:**
see guidelines

### Adjustment &Trouble Shooting

- BG < 14-17 mmol/l (250-300 mg/dl) = Add Dextrose 5% to 0.9% Saline
- BG < 8 mmol/l (≈ 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) = 2-5 ml/kg D10% bolus,
  - hold insulin temporarily (30-60 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 ½ 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)**

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

| DKA Resolution |
|---|
| Clinically well, HCO3 ≥ 15<br><br>Tolerating oral intake |
| Switch to oral intake (special diet) |
| SC insulin as per endocrinologist order<br>or per attached guidelines (appendix III) |