Clinical Management of Diabetes Mellitus and Diabetic Keto Acidosis in Children

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Table of Contents

List of tables

List of Abbreviations

BG	random blood glucose
FPG	Fasting plasma glucose
DKA	Diabetic Ketoacidosis.
FBC	Full blood count.
HA1c	Hemoglobin A 1C (Glycosylated hemoglobin).
C. Peptide	Connecting peptide.
GAD	Glutamic Acid Decarboxylase.
TSH	Thyroid-stimulating hormone.
GCS	Glasgow Coma Scale
KCL	Potassium Chloride.
TDD	Total daily dose.
SMBG	practice self-monitoring of blood glucose

Calculations

- **Anion gap=Na− (Cl+HCO3): normal is12 ± 2 mmol/L.**
- **Corrected sodium= measured Na+2[(plasma glucose−100)/100] mg/dL.**
- **Effective osmolality (mOsm/kg) =2× (plasma Na) +plasma glucose mmol/L.**
- **Deficit in mL = % dehydration ×body weight (kg) × 10.**
- **0.45% sodium chloride: to prepare 500 ml = 250 ml ,9% Nacl +250 ml distilled water.**

i. Introduction

- Type 1 diabetes mellitus (T1DM) is the most common type of diabetes mellitus in children and adolescents.
- The incidence of type II diabetes mellitus is on the rising trend among young people due to obesity.
- DKA is the result of the metabolic abnormalities resulting from a severe deficiency of insulin or insulin effectiveness. The latter occurs during stress as counter regulatory hormones block insulin action.

ii. Case definitions

- **Diabetic ketoacidosis (DKA):** is a complex disordered metabolic state characterized by hyperglycemia, acidosis, and ketonuria.
- **HbA1c:** shows the average level of blood sugar over the previous 3 months. It shows how control of diabetes is.
- **Connecting (C) peptide:** is a 31 amino acid peptide that bridges the insulin A and B chains in the proinsulin molecule. It is released from pancreas in a 1:1 ratio with insulin as this is secreted.
- **Cerebral edema:** Accumulation of excessive fluid in the substance of the brain.

iii. Symptoms and signs

- Change in school performance
- Thirst
- Weight loss
- Thrush
- Polyuria
- Nocturia (secondary)
- Tiredness
- If obese, no ketonuria or evidence of insulin resistance (e.g., acanthosis nigricans), consider type 2 diabetes
- **DKA** (Vomiting, Dehydration, Abdominal pain, Hyperventilation, Drowsiness, coma)

DKA mostly can be first presentation of T1DM

iv. Investigations

- ***Blood:***
  - glucose
  - electrolytes
  - pH
  - ketones
  - HbA1c
  - FBC
  - TSH and FT4
  - autoantibody screen for thyroid, coeliac, GAD and islet cell antibodies

    - ***Do not arrange glucose tolerance test***

- ***Diagnostic criteria of Diabetes Mellitus:(one of theses)***
  1. Symptoms of diabetes and random blood glucose (BG) ≥200 mg/dL.
  2. Fasting plasma glucose (FPG = no caloric intake for at least 8 hours) ≥126 mg/dL.
  3. Hemoglobin A1c (HbA1c) ≥6.5%

v. Management

A. Principles of insulin therapy

• Daily insulin dosage:

- Dosage depends on many factors such as: age, weight, stage of puberty, duration and phase of diabetes, state of injection sites, nutritional intake and distribution, exercise patterns, daily routine, results of blood glucose monitoring (BGM), glycated hemoglobin (HbA1c) and intercurrent illness.

- **Guidelines on dosage:**

- During the **partial remission phase**, total daily insulin dose is usually **0.5 IU/kg/day**.
- **Pre pubertal children** usually require insulin of **0.7–1.0 IU/kg/day**. (Outside the partial remission phase)
- **During puberty**, requirements may rise to **1 - 2 IU/kg/day**.
- The total daily dose of insulin is distributed across the day depending on the daily pattern of blood glucose and the regimens that are used
- . Insulin may be injected into the subcutaneous tissue of the upper arm, the anterior and lateral aspects of the thigh, the buttocks and the abdomen.
- Rotation of the injection sites is essential to prevent lipohypertrophy or, more rarely, lipoatrophy

➢ **Basal-bolus regimen:**

- The basal-bolus regimen (intermediate-acting insulin/long-acting basal once or twice daily
  {e.g. Glargine or Detemir} and rapid-acting/short-acting boluses {(e.g. Lispro or Insulin Aspart} with meals and snacks) mimics the physiological insulin secretion.
- Basal insulin constitutes about 40 - 60% of the total daily insulin dose (TDD) requirements; the remainder is pre-prandial rapid-acting/short acting insulin.

➢ **Pump therapy:**

- Insulin pump therapy is gaining popularity with a variable basal rate and bolus doses with meals.
- In young children 1 - 6 years old with T1DM, insulin pump therapy is a safe and efficacious alternative compared with insulin injection.
- Advantages include potential decrease in hypoglycemic episodes and improvement in quality of life

Table (1): Target pre meal and 30-days average blood glucose ranges for each age

Age group(yr.)	Target pre meal BG range (mg/dl)	30-day average BG range (mg/dl)
‹5	100-200	180-250
5-11	80-150	150-200
12-15	80-130	120-180
16-18	70-120	100-150

❖ **Insulin Sensitivity Factor**

- Also referred as **correction bolus**, is the mg/dl drop in blood glucose caused by 1 unit of insulin, used to correct hyperglycemia
- The right correction bolus will return blood glucose to within 30 mg/dl of target blood glucose about 3 hours after given the dose

Sensitivity Factor = Divide: 1700 by Total Daily Insulin (TDD)

1700/TDD

Correction Bolus Formula:

{(Current BG) - (Target BG)}/ (sensitivity Factor)

Example:

Current BG = 200 mg/dl

Target BG = 100 mg/dl

TTD= 34 insulin units

Correction (sensitivity factor) = 1700/34 = 50

So, (200-100)/50= 2.0 units of insulin for a Correction dose

B. Monitoring of glycemic control

- All children and adolescents with type 1 diabetes mellitus should practice self-monitoring of blood glucose (SMBG).
- SMBG should be performed four to six times a day and more frequent in certain conditions such as sick day or during exercise.
- It is a good practice to keep a diary to record glucose levels, insulin dosages and dietary details for treatment adjustments.
- This diary should be reviewed regularly by patients, families and healthcare providers.
- HbA1c every 3 months
- The recommended **HbA1c** target for all patients younger than 16 years is **<7.5%**
- Urine ketones should be checked with persistent hyperglycemia, any illness (regardless of blood glucose level), or with nausea/vomiting.

C. Diet

- A balance and healthy diet for age is required with dietician involvement.
- Diet management: education about how to adjust the timing, size, frequency, and composition of meals

D. Exercise

- Physical activities should be performed regularly and in a safe manner in patients with T1DM.
    - Physical activity that significantly improve glycemic control are:

a. Duration of >60minutes per session.
b. Higher frequency of >3 times in a week.
c. Longer duration program me of >3 months.
d. Avoid strenuous physical activity if pre-exercise BG is high (>250mg/dl) with ketonuria
e. Increase intensity and duration of physical activity in a progressive manner.
f. Do not inject insulin in the site that will be heavily involved in muscular activity e.g. not to inject in the thigh before cycling.
g. Avoid physical activity exercise at peak action of insulin.

h. Monitor BG in evening and night after physical activity to avoid nocturnal hypoglycemia.
i. Carry some sugar and drink more water

E. School

- Patients Should have individualized diabetes management plan in school/day-care center.
- The school teachers should be informed about children having diabetes.

F. Diabetic Education

- Explanation of how the diagnosis has been made and reasons for symptoms.
- Simple explanation of the uncertain cause of diabetes. No cause for blame.
- The need for immediate insulin and how it will work.
- What is glucose? Normal blood glucose (BG) levels and glucose targets
- Practical skills: insulin injections; blood and/or urine testing, reasons for monitoring.
- Basic dietary advice.
- Recognition and treatment of hypoglycemia.
- Diabetes during sick days' illnesses, Advice not to omit insulin to prevent DKA.
- Psychological adjustment to the diagnosis.
- Details of emergency telephone contacts.

G. Fasting during Ramadan with T1DM

- Pre-Ramadan education should address insulin type and action, glucose monitoring, nutrition, physical activity, sick day and hyperglycemia, and recognition and treatment of hypoglycemia
- Optimizing glycemic control before Ramadan is an essential measure to ensure safe fasting
- Frequent blood glucose measurement is necessary during Ramadan to minimize the risk of hypoglycemia and detect periods of hyperglycemia
- Breaking fasting immediately in hypoglycemia is recommended regardless of the timing. This recommendation applies to symptomatic hypoglycemia and asymptomatic hypoglycemia below 70 mg/dl.

- Breaking fast immediately if glucose level above 300mg/dl.

H. Management of sick days requires:

- Frequent monitoring of BG (2 to 3 hrs.) and urine ketone levels (4hrs).
- Monitoring food and fluid intake.
- Parental involvement and telephone availability of the diabetes clinician
- Never to stop insulin completely

- Elevated blood glucose with absence or only small amount of ketones:

  • Give additional 5% to 10% of the total daily dose (TDD) of insulin (~0.05-0.1 U/kg) as short or rapid-acting insulin subcutaneously and repeat this same dose every 2 to 4 hours according to blood glucose response and clinical condition
- Elevated blood glucose with moderate or large amount of ketones reflects actual or impending DKA with potential for coma or death:

  • Give additional 10% to 20% of the TDD of insulin (~0.1-0.2 U/kg) as short or rapid-acting insulin subcutaneously and repeat this same dose every 2 to 4 hours according to blood glucose response and clinical condition

Management of diabetic ketoacidosis

- DKA is the end result of the metabolic abnormalities resulting from a severe deficiency of insulin or insulin effectiveness.
- Risk is increased in children with:
  - Poor metabolic control.
  - Previous episodes of DKA.
  - Children with unstable family circumstances (e.g., parental abuse).
  - Children with limited access to medical services.
  - Those on insulin pump therapy (interruption of insulin delivery for any reason rapidly leads to insulin deficiency).
- Together with the major complication of cerebral edema, it is the most important cause of mortality in children with diabetes.

- DKA may be classified as mild, moderate, or severe

Table (2): Classification of Diabetic Ketoacidosis.

	Normal	**Mild**	**Moderate**	**Severe**
Hco3(venous)	20-28	< 15 mmol/l	< 10 mmol/l	< 5 mmol/l.
Ph(venous)	7.35-7.45	7.2- 7.29	7.1-7.19	<7.1
Clinical	No change	No change Oriented, alert but fatigued	Kussmaul respirations; oriented but sleepy; arousable	Kussmaul or depressed respirations; sleepy to depressed sensorium to coma

I. Symptoms and signs

- Abdominal pain
- vomiting
- Tachypnoea
- Deep and rapid respiration (Kussmaul breathing)
- Odour of ketones
- Dehydration
- Drowsiness
- Coma

II. Investigations

- Blood glucose
- FBC, Urea and electrolytes and CRP
- Blood gases (venous or capillary)
- Infection screen: blood and urine culture
- If able to obtain sufficient blood, send new diagnosis investigations (HbA1c, TFT, Coeliac screen

III. Management

a. General Resuscitation:

1. ***Airway:*** Secure the airway and consider NG tube placement (to avoid aspiration) in the unconscious patient.
2. ***Breathing:*** Give oxygen to patients with severe circulatory impairment or shock.
3. ***Circulation:*** Insert IV cannula and take blood samples.
    - Cardiac monitor for T waves (peaked in hyperkalemia).
    - Measure blood pressure and heart rate.

b. Fluids:

N.B, it is essential that all fluids given are documented carefully, particularly the fluid which is given in the emergency department and on the way to the ward, as this is where most mistakes occur.

1. Initial fluid bolus:

- **All children** and young people with moderate or severe DKA who are not shocked and are felt to require IV fluids should receive a **10 ml/kg 0.9% saline bolus over 30 minutes**
- Patients with shock require appropriate restoration of their circulation and circulatory volume. **SHOCKED patients** should receive a **10 ml/kg bolus over 15 minutes**.
- Following the initial 10 ml/kg bolus shocked patients should be reassessed and further boluses of 10 ml/kg may be given if required to restore adequate circulation up to a total of 40 ml/kg at which stage inotropes should be considered

2. Ongoing fluid replacement:

- By this stage, the circulating volume should have been restored and the child no longer in shock, calculate fluid requirements as follows,

a) ***Deficit:***

Table (3): Estimation of the fluid deficit should be based on the initial blood ph.

1. Assume **a 5%** fluid deficit in children and young people in **mild DKA** (Indicated by **a blood pH 7.2-7.29 &/or bicarbonate <15**)
2. Assume **a 5%** fluid deficit in children and young people in **moderate DKA** (Indicated by **a blood pH of 7.1- 7.19 &/or bicarbonate <10**)
3. Assume **a 10%** fluid deficit in children and young people in **severe DKA** (Indicated by **a blood pH <7.1 &/or bicarbonate <5**)

- **Resuscitation fluid**: The volume of any fluid boluses given for resuscitation in children with **shock should NOT be subtracted** from the estimated fluid deficit.
- **The initial 10ml/kg bolus** given to all **non-shocked** patients requiring IV **fluids SHOULD be subtracted** from total calculated fluid deficit.
- The deficit should be replaced over 48 hours alongside appropriate maintenance fluids

b) ***Maintenance:***

- Maintenance (24 hr) = **100 mL/kg** (for the first 10 kg) **+**
  50 mL/kg (for the second 10 kg) **+**
  20 mL/kg (for all remaining kg).

c) ***Fluid Calculation:***

- Calculate the fluid deficit (either 5% or 10% dehydration depending on whether the patient has mild, moderate or severe DKA), subtract the initial 10ml/kg bolus (unless given for Shock) then divide this over 48 hours and add to the hourly rate of maintenance fluid volume, giving the total volume evenly over the next 48 hours.

Hourly rate = ({Deficit – initial bolus} / 48hr) + Maintenance per hour

- To avoid excessive amounts of fluid in overweight and obese children it is recommended that consideration be given to using **a maximum weight of 75kg or 97th centile weight for age.**

d) ***Type of fluid***

- Use 0.9% or 0,45% saline with 20 mmol potassium chloride in 500 ml (40 mmol per liter) until blood glucose levels are less than 250mg/dl
- If the patient is hypokalemic, start potassium replacement immediately after initial volume expansion and before starting insulin therapy.
- If the patient is hyperkalemic, defer potassium replacement therapy until urine output is documented

Table (4): Potassium chloride dose in infusion fluids.

Serum/Plasma K+(mEq/L)	Potassium Chloride (KCL) Dose in Infusion Fluids
< 2.5 mEq/L	Carefully monitored administration of potassium chloride 0.2-0.5 mmol/kg in sodium chloride 0.9% by separate infusion over 1 hour
2.5-3.5 mEq/L	80 mmol/L via **central line**
3.5-5.5 mEq/L	40 mmol/L
K+ >5.5 mEq/L	Only Sodium chloride 0.45%

- Corrected sodium levels should rise as blood glucose levels fall during treatment. Some have suggested that Corrected Sodium levels give an indication of the risk of cerebral edema.
- Do not give intravenous sodium bicarbonate to children with DKA.

- Plasma glucose concentration typically decreases at a rate of 50-90 mg/dl/ h, depending on the timing and amount of glucose administration.
- When blood glucose falls below 250 mg/dl use a glucose containing fluid.

Table (5): Glucose dose in infusion fluids.

Blood glucose	**Fluid: sodium chloride 0.45% with potassium chloride**
<110mg/dl	Glucose 10%
<250-110 mg/dl	Glucose 5%
>250 mg/dl	No glucose

- Once glucose goes below 180 mg/dL, the osmotic diuresis stops and rehydration accelerates without further increase in the infusion rate.
- If the blood glucose falls below70 mg/dl, give a bolus of 2 ml/kg of 10% glucose and increase the glucose concentration of the infusion. Insulin can temporarily be reduced for 1 hour.

4. ***Fluid losses***
    - Do not give additional intravenous fluid to replace urinary losses.
    - Urinary catheterization should be avoided but may be useful in the child with impaired consciousness.
    - If a massive diuresis continues for several hours' fluid input may need to be increased.
    - If large volumes of gastric aspirate continue, these will need to be replaced with sodium chloride 0.9% with potassium chloride.

5. ***Oral fluids***
    - If receiving intravenous fluids for DKA do not give oral fluids until ketosis is resolving and there is no nausea and vomiting.
    - In the case of gastric paresis, a nasogastric tube may be necessary.

c. Insulin infusion

1. Do not give insulin as bolus.
2. Start insulin infusion 1–2 hr after IV fluid bolus.
3. Add 50 units regular (soluble) insulin in 50mL normal saline, (1 unit=1mL), via IV syringe pump at 0.05–0.1 units/kg/hr.
4. If no fall in glucose after 2 hr (very unusual, check pump and patency of IV cannula), increase insulin by 20%.
5. If no fall after 4 hr, increase to 0.1 unit/kg/hr and re-evaluate (e.g. sepsis, insulin errors).
6. If blood glucose falls exceeds 90 mg/dl /hr, reduce insulin infusion rate to0.05 unit/kg/hr initially then adjust if necessary.
7. DO not reduce insulin below 0.02 units/kg/hr till DKA resolved.
8. Do not stop insulin infusion.
9. Check capillary glucose in 1 hr.
10. Do not add insulin directly to fluid bags.
11. For children on continuous subcutaneous insulin infusion (CSII) pump therapy, stop the pump when starting intravenous insulin.

IV. Monitoring treatment

1. Hourly capillary blood gas and glucose.
2. Complete DKA summary sheets.
3. ***Medical reviews***

a. At 2 hr after starting treatment, and then ≥4-hrly, carry out and record results of:
   1. Glucose (laboratory measurement).
   2. Blood pH and HCO3.
   3. Plasma sodium, potassium and urea.

b. Doctor to carry out face-to-face review at start of treatment, and then 4-hrly, and more frequently if:
   1. Aged < 2 yr.
   2. Severe DKA (blood pH < 7.1).
   3. Any other reasons for special concern

c. At each face-to-face review assess following:

1. Clinical status (including vital signs and neurological status).
2. Blood investigation results, ECG trace.
3. Cumulative fluid balance record.

d. Transition to Ssubcutaneous. insulin injections

1. The change to subcutaneous insulin should occur when ketoacidosis has resolved (**serum bicarbonate ≥15 mEq/l and venous pH >7.3)**, and **oral intake is tolerated**.
2. The most convenient time to change to subcutaneous insulin is just before a meal.
3. Use regular in insulin in this transitional stage.
4. To prevent rebound hyperglycemia, the first subcutaneous injection should be given 1 hr before stopping the insulin infusion, to allow sufficient time for the injected insulin to be absorbed.

5. If using ***insulin pump therapy:***

a) Restart pump ≥60 min before stopping intravenous insulin.

b) Change insulin cartridge and infusions set

c) Insert cannula into new subcutaneous site.

6. In patients with established diabetes, the patient's usual insulin regimen may be resumed.
7. Newly diagnosed diabetes after resolution of DKA**.**
8. Total daily dose to be divided and given every 6 hrs and measuring blood sugar direct before dose and 2hrs after dose.
9. Usually, this transitional stage continues for1 to 2 days then shift usual insulin regimen (Aspart and Glargine).
10. The basal insulin glargine should be 25-30% of TDD in toddlers and 40-50% in older children. The remaining portion of the TDD is provided as bolus insulin as Lispro or aspart, insulin analogs 3 times a day.

Table (6): Insulin regimens for newly diagnosed diabetes after resolution of DKA.

Age	Insulin (units/kg/day)
Prepubertal	0.75-1.0
Pubertal	1.0-2.0
Post pubertal	0.8-1.0

V. Complications

1. Cerebral edema

a) Immediately assess a child or young person with DKA for **suspected** cerebral edema if they have any of these early manifestations:

- Headache.
- Agitation or irritability.
- Unexpected fall in heart rate.
- Increased blood pressure.

b) If a child or young person develops any of these signs:

- Deterioration in level of consciousness.
- Abnormalities of breathing pattern, for example respiratory pauses.
- oculomotor palsies.
- Abnormal posturing.
- pupillary inequality or dilatation.

c) Treat them Immediately for cerebral oedema using the most readily available of

- Mannitol 20% (0.5-1 g/kg over 10-15 minutes) or
- Hypertonic saline 3% (2.5-5 ml/kg over 10-15 minutes).
- In addition, fluids should be restricted to ½-maintenance rates and discuss further care with referral center**.**
- Once the child is stable, exclude other diagnoses by CT scan - other intracerebral events may occur (thrombosis, haemorrhage or infarction).

- A repeated dose of Mannitol may be required after 2 hours if no response.
- Document all events (with dates and times) very carefully in medical records.

2. ***Hypoglycaemia and hypokalaemia:*** avoid by careful monitoring and adjustment of infusion rates. Consideration should be given to adding more glucose if BG falling quickly even if still above 70 mg/dl**.**
3. ***Systemic Infections***: Antibiotics are not given as a routine unless a severe bacterial infection is suspected.
4. ***Aspiration pneumonia:*** avoid by nasogastric tube in vomiting child with impaired consciousness.

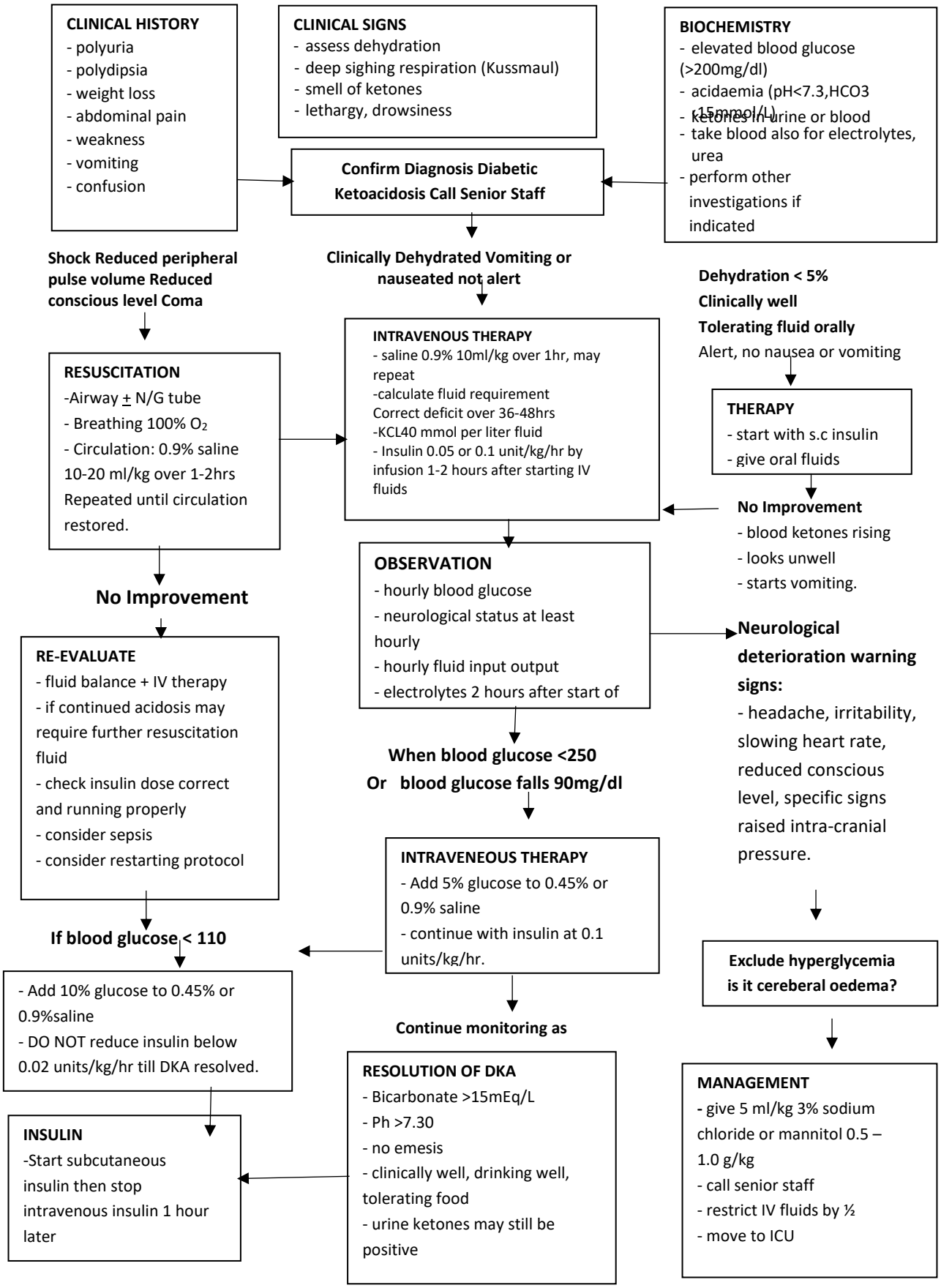
a. Education and follow up

1. After a child has recovered from an episode of DKA, discuss with him and his family members or careers (if appropriate) the factors that may have led to the episode.
2. Ensuring that patient or and family can give correct dose with proper way.
3. Parents and patients should learn how to recognize and treat impending DKA with additional rapid- or short acting insulin and oral fluids.
4. Parents and patients should have access to a 24-h telephone helpline for emergency advice and treatment.

Table (7): DKA flow sheet.

Date/ time	GCS	BP	HR	RR	glucose	Na	K	ca	PH	Hco3	pco2	Ketones Urine	urea	Iv fluid	Insulin dose IU/h	UOP

Algorithm for the Management of Diabetic Ketoacidosis



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