Diabetic Ketoacidosis (DKA)

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- يعتبر اهم انواع غيبوبات ارتفاع السكر
- **ازاى بتحصل ؟ !**

Marked hyperglycemia

Either in Type 1 or Type 2

Lack of the fuel (glucose) in the Cells as a source of energy

(↓ Glycolysis)

The body uses another source of energy (Fat)

Lipids catabolism

Acute marked lipolysis

Production of ketone bodies in the body & blood (acids)

Acetoacetate (acetone) blood/urine

Beta hydroxybutyrate (blood only)

High anion gap Metabolic Acidosis

(Ketoacidosis: DKA)

- **ازاى تعرف الغيبوبه من أعراضها ؟ !**

- Marked Polyuria
- Dehydration (hypovolemia due to Massive osmotic diuresis)
- **Signs of dehydration**
  - Dry tongue /lips
  - Absence of axillary sweats
  - Dry skin (loss of skin turgor) -->elicit only in young patients
  - Orthostatic hypotension
  - In severe cases --> hypovolemic shock
- Rapid breathing (kussmaul breathing)
- Acetone odour
- Abdominal pain & vomiting

  Thought to be due to ileus related to metabolic acidosis and electrolytes disturbances
- Variable degrees of confusion/coma related to severity
- The patient is Known Diabetic esp. T1DM, particularly young patient
- **Predisposing factors** (infection, fever, MI, stroke, missed insulin).
- In T2DM, it is less common than Type 1

  --> occurs with severe infection e.g pneumonia, MI, stroke etc.

- **ايه الخطوة اللى بعد كده ؟!!**

- **Next step**

Random blood glucose ≥ 250

+ Acetone in urine (≥ 2+ acetone in urine)

+ ABG

متوقع تلاقى ايه فى ال ABG ؟

- Low PH < 7.3
- Low HCO3 < 15
- Low PaCO2
- High anion gap [Na - { Cl + HCO3}] ≥ 12

Other labs & imaging according to case

- ECG in ACS/MI
- CT brain in strokes
- Blood culture, procalcitonin, CRP in sepsis

❖ DKA DIAGNOSTIC CRITERIA:

Establish the diagnosis of DKA by The international diagnostic criteria (ADA & JBDS)

ADA: American Diabetes Association

JBDS: Joint British Diabetes Societies

DKA diagnostic criteria:

♦ ADA diagnostic criteria

- Random blood glucose > 250 mg/dl.
- Arterial pH < 7.3.
- Bicarbonate < 15 mEq/l.
- Moderate ketonuria or ketonemia.

♦ JBDS diagnostic criteria:

All of these must be present to make the diagnosis

#The 'D'	blood glucose concentration of >11.0 mmol/L (> 200 mg/dl) or known to have diabetes mellitus
#The 'K'	capillary or blood ketone concentration of >3.0 mmol/L or Significant ketonuria (2+ or more on standard urine sticks)
#The 'A'	bicarbonate concentration of <15.0 mmol/L and/or venous pH <7.3

هل الغيبوبه درجات ؟ ايوه طبعا

	Mild DKA	Moderate DKA	Severe DKA
PH	7.25 - 7.3	7 - 7.25	< 7
HCO3	15 - 18	10 - 15	< 10
Sensorium	Patient : alert	Patient : alert/drowsy	Patient : stupor/coma

❖ Treatment protocol (JBDS guidelines 2021)

✪ Pillars of Treatment goal

• Restoration of circulatory volumes

• Suppression of ketogenesis

• Reduction of blood glucose

• Correction of electrolyte disturbance

0 - 60 Minutes (Immediate Management upon Diagnosis)

✪ Aims

• Commence IV 0.9% sodium chloride solution

• Establish monitoring regime appropriate for the person with diabetes; generally

- ✓ hourly blood glucose (BG) كل ساعه
- ✓ and hourly ketone measurementكل ساعه,
- ✓ with at least 2 hourly serum/blood potassium كل ساعتين
- ✓ and bicarbonate for the first six hours

• Clinical and biochemical assessment of the individual

• Involve the diabetes specialist team at the earliest possible stage

• Consider referral to HDU environment (ICU) if criteria for severity are met or if facilities for intensive monitoring are unavailable.

1) Intravenous access and initial investigations

- Rapid ABC (Airway, Breathing, Circulation)
- Large bore IV cannula, and commence IV fluid replacement
- Clinical assessment
  - Respiratory rate
  - temperature;
  - blood pressure;
  - pulse;
  - oxygen saturation

- Glasgow Coma Scale.

N.B.:

A drowsy individual in the context of DKA is seriously concerning and the person requires critical care assessment. Consider an NG tube with airway protection to prevent aspiration

- Full clinical examination
- Initial investigations should include:
    - Blood ketones
    - Capillary blood glucose
    - Venous plasma glucose
    - Urea and electrolytes (including phosphate if necessary)
    - Venous blood gases
    - Full blood count
    - Blood cultures
    - ECG
    - Chest radiograph if clinically indicated
    - Urinalysis and culture
    - Continuous cardiac monitoring
    - Continuous pulse oximetry
- Consider precipitating causes and treat appropriately
- Establish usual medication for diabetes
- Pregnancy test in women of child bearing age
- COVID-19 testing - particularly in those not known to have a prior diagnosis of diabetes

2) Restoration of circulating volume

- Assess the severity of dehydration using pulse and blood pressure.
- As a guide 90 mmHg may be used as a measure of hydration but take age, gender and concomitant medication into account.

I. Systolic BP (SBP) on admission below 90 mmHg

- Hypotension is likely to be due to low circulating volume, but consider other causes such as heart failure, sepsis, etc.
- Give 500 ml of 0.9% sodium chloride solution over 10-15 minutes.
- If SBP remains below 90 mmHg this may be repeated.

N.B: most individuals require between 500 to 1000 ml given rapidly

- If there has been no clinical improvement reconsider other causes of hypotension and seek an immediate senior assessment. Consider involving the ITU/critical care team
- Once SBP above 90 mmHg follow fluid replacement as shown below ↓

II. Systolic BP on admission > 90 mmHg

- Below is a table outlining a typical fluid replacement regimen for a previously well 70 kg adult
- This is an illustrative guide only. A slower infusion rate should be considered in young adults

✪ FLUID VOLUME

✅ 0.9% sodium chloride 1 L	without potassium chloride	over 1st hour
✅ 0.9% sodium chloride 1 L	with potassium chloride	over next 2 hours
✅ 0.9% sodium chloride 1 L	with potassium chloride	over next 2 hours
✅ 0.9% sodium chloride 1 L	with potassium chloride	over next 4 hour
✅ 0.9% sodium chloride 1 L	with potassium chloride	over next 4 hour
✅ 0.9% sodium chloride 1 L	with potassium chloride	over next 6 hours

- Re-assessment of cardiovascular status at 12 hours is mandatory, further fluid may be required

3) Potassium replacement

- Hypokalaemia and hyperkalaemia are life threatening conditions and are common in DKA.
- Serum potassium is often high on admission (although total body potassium is low) but falls precipitously upon treatment with insulin. Regular monitoring is mandatory.
- Potassium replacement in mmol/L of infusion solution
  - Over 5.5 ➔ Nil
  - 3.5-5.5 ➔ 40 mmol
  - Below 3.5 ➔ Senior review as additional K needed to be given

4) Commence a Fixed Rate Intravenous Insulin Infusion(Insulin protocol)

- Start a continuous insulin infusion via an infusion pump. This is made of 50 units of human soluble insulin (Actrapid®, Humulin S®) made up to 50 ml with 0.9% sodium chloride solution. Ideally this should be provided as a ready-made solution
- Infuse at a fixed rate of 0.1 unit/kg/hr (i.e. 7 ml/hr if weight is 70 kg)
- Only give a bolus (stat) dose of intramuscular insulin (0.1 unit/kg) if there is a delay in setting up insulin infusion pump

✪ Aims:

- Clear the blood of ketones and suppress ketogenesis
- In the absence of ketone measurement, bicarbonate should rise by 3.0 mmol/L/hr and blood glucose should fall by 3.0 mmol/L/hr (50 mg/dl)
- Maintain serum potassium in the normal range
- Avoid hypoglycaemia

1 – Re-Assess and Monitor Vital Signs

- During this time, individuals should be reviewed hourly initially to ensure that adequate progress is being made in reducing the ketone and/or glucose concentrations
- Consider urinary catheterisation if the person is incontinent or anuric (i.e. not passed urine by 60 minutes)
- Consider naso-gastric tube insertion if the person is obtunded or persistently vomiting
- If the oxygen saturation falls, then perform an arterial blood gas measurement and request a repeat chest radiograph
- Regular assessment of Glasgow Coma Scale score, if this drops then urgent brain imaging should be considered
- Maintain an accurate fluid balance chart; the minimum urine output should be no less than 0.5 ml/kg/hr
- Continuous cardiac monitoring in those with severe DKA
- Give prophylactic low molecular weight heparin as per NICE guidance

2 – Review Metabolic Parameters

- Measure blood ketones and capillary glucose hourly
- The hourly glucose readings should be recorded
- Review the response to insulin infusion hourly by calculating the rate of change of ketone level fall (or rise in bicarbonate or fall in glucose)
- Assess the resolution of ketoacidosis
- If the bicarbonate is not rising by at least 3.0 mmol/L/hr call a prescribing clinician to increase the insulin infusion rate by 1 unit/hr increments hourly until the bicarbonate is rising at this rate
- Alternatively use plasma glucose. If the glucose is not falling by at least 50 mg/dl --> increase the insulin infusion rate by 1.0 unit/hr increments hourly until glucose falls at this rate.

N.B: Glucose level is not an accurate indicator of resolution of acidosis in ketoacidosis, so the acidosis resolution should be verified by venous gas analysis

- Measure venous blood gas for pH, bicarbonate and potassium at 60 minutes, 2 hours and 2 hourly thereafter
- Continue the insulin infusion until the pH over 7.3 and/or venous bicarbonate over 18 mmol/L
- Do not rely on urinary ketone clearance to indicate resolution of DKA, because these will still be present when the DKA has resolved
- If the glucose falls below (< 250 mg/dl) commence 10% glucose given at 125 ml/hour alongside the 0.9% sodium chloride solution. In addition consider reducing the rate of intravenous insulin infusion to 0.05 units/kg/hr. نص المعدل المحسوب فى الاول
- Monitor and replace potassium because it may fall rapidly

3- Identify and treat precipitating factors

6 To 12 Hours Management

✪ Aim:

The aim within this time period is to:

- Ensure that clinical and biochemical parameters are improving at the correct rates
- Continue IV fluid replacement
- Continue insulin administration
- Assess for complications of treatment e.g. fluid overload, cerebral oedema
- Continue to treat precipitating factors as necessary
- Avoid hypoglycaemia

1- Re-assess the individual and monitor vital signs

- Regular assessment of Glasgow Coma Scale score, if this drops then urgent brain imaging should be considered

2 – Review biochemical and metabolic parameters

- At 6 hours check the venous pH, bicarbonate, potassium, as well as blood ketones and glucose
- Resolution of DKA is defined as ketones : negative and venous pH over 7.3 (do not use bicarbonate as a surrogate at this stage because the hyper-chloraemic acidosis associated with large volumes of 0.9% sodium chloride will lower bicarbonate levels)

12 - 24 Hours Management

✪ Expectation:

By 24 hours the ketonaemia and acidosis should have resolved in most people.

✪ Aim:

- Ensure that the clinical and biochemical parameters are improving or have normalised
- Continue IV fluids if the person is not eating and drinking

- Re-assess for complications of treatment e.g. fluid overload
- Regular assessment of Glasgow Coma Scale score, if this drops then urgent brain imaging should be considered
- Continue to treat any precipitating factors as necessary
- Transfer to subcutaneous insulin if the individual is eating and drinking normally.
  - Ensure that the subcutaneous insulin is started before the IV insulin is discontinued.
  - Ideally give the subcutaneous fast acting insulin at a meal and discontinue IV insulin 30-60 minutes later

1 – Re-assess the individual and monitor vital sign

2 – Review the biochemical and metabolic parameters

- At 12 hours check venous pH, bicarbonate, potassium, as well as blood ketones and glucose
- Resolution of DKA is defined as
  - ketones: negative
  - PH over 7.3

✪ **Expectation:**

☞ People who have had DKA should be eating and drinking and back on normal insulin after 24 hours treatment

☞ Conversion to subcutaneous insulin

The person with diabetes should be converted to an appropriate subcutaneous regime when biochemically stable (blood ketones less than 0.6 mmol/L, pH over 7.3) and they are ready and able to eat.

❖ **ملحوظه هاامه :**

✓ Don't discontinue IV insulin infusion immediately after resolution of DKA biochemically , you have to start basal bolus regimen 1 hour before discontinuation of IV insulin

ADA PROTOCOL FOR DKA MANAGEMENT

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❖ البروتوكول الأمريكى لعلاج الDKA

Emergent diabetic ketoacidosis (DKA) management in adults:

✪ Rapid overview

- DKA is characterized by hyperglycemia, an elevated anion gap metabolic acidosis, and ketonemia.
- Dehydration and potassium deficits are often severe.
- Serum glucose is usually greater than 250 mg/dL (13.9 mmol/L) and less than 800 mg/dL (44.4 mmol/L).

✪ Clinical features

- DKA usually evolves rapidly over a 24-hour period.
- Common, early signs of ketoacidosis include nausea, vomiting, abdominal pain, and hyperventilation.
- The earliest symptoms of marked hyperglycemia are polyuria, polydipsia, and weight loss.
- As hyperglycemia worsens, neurologic symptoms appear and may progress to include lethargy, focal deficits, obtundation, seizure, and coma.

✪ Common causes of DKA include:

- Infection
- Noncompliance
- inappropriate adjustment
- cessation of insulin
- new-onset diabetes mellitus
- myocardial infarction and stroke

✪ Evaluation and laboratory findings

- Assess vital signs, cardio-respiratory status, and mental status (GCS)
- **Assess volume status:**
  - vital signs,
  - skin turgor,oral mucosa,
  - Urine output.
- **Obtain the following studies:**
  - serum glucose
  - urinalysis and urine ketones
  - serum electrolytes,
  - BUN and creatinine
  - plasma osmolality
  - mixed venous blood gas
  - electrocardiogram
  - Serum ketones if urine ketones present.
- **Additional testing** is obtained based on clinical circumstances and may include: blood or urine cultures, lipase, chest x-ray

✪ Management

- Stabilize the patient's airway, breathing, and circulation.
- Obtain large bore IV (≥16 gauge) access; monitor using a cardiac monitor, and pulse oximetry.
- Monitor serum glucose hourly, and basic electrolytes and venous pH or bicarbonate every two to four hours until the patient is stable.
- Determine and treat any underlying cause of DKA (e.g., pneumonia or urinary infection, myocardial infarction).

❖ FLUID MANAGEMENT

➲ Replete ECF volume and free water deficits:

- Typical water deficit (6 - 8 L)
- Give several liters of IV isotonic (0.9%) saline as rapidly as possible to patients with signs of shock.
- Give IV isotonic (0.9%) saline at 15 to 20 mL/kg per hour (i.e., 1 to 1.5 L per hour for an average-sized adult), in the absence of cardiac compromise, for the first few hours to hypovolemic patients without shock
- After intravascular volume is restored, i.e. [the patient is clinically Euvolemic] give one-half isotonic (0.45%) saline at 4 to 14 mL/kg per hour if the corrected serum Na+ is normal or elevated; isotonic saline is continued if the corrected serum Na+ is reduced.

ملحوظه :

لابد من حساب ال
Corrected Na for glucose ،،
ممكن تحسبه من App أو من على النت ،،

ولابد من توفير ال half normal Saline ،، إذا كان ال corrected Na عالى أو طبيعى لتطبيق البروتوكول بشكل دقيق ،،
اما اذا كان أقل من معدله الطبيعى ،، ال normal saline هو المناسب فى هذه الحاله

➲ Add dextrose {Glucose 10% rate 125 ml/hrs to the saline solution when the serum glucose reaches ~200 mg/dL (11.1 mmol/L).

❖ K^+ MANAGENENT

➲ Replete potassium (K^+) deficits:

- Regardless of the initial measured serum K^+, patients with DKA have a large total body K^+ deficit.
- If initial serum K^+ is below 3.3 mEq/L, hold insulin and give potassium chloride 20 to 40 mEq/hour IV until K^+ concentration is above 3.3 mEq/L; rarely, additional potassium supplementation may be necessary to avoid life-threatening muscle weakness and cardiac arrhythmias.

- If initial serum K^+ is between 3.3 and 5.3 mEq/L, give potassium chloride 20 to 30 mEq per liter IV fluid; maintain serum K^+ between 4 to 5 mEq/L.
- If initial serum K+ is above 5.3 mEq/L, do not give potassium; check serum K+ every 2 hours; delay administration of potassium chloride until serum K+ has fallen to 5 to 5.2 mEq/L.

❖ INSULIN MANAGEMENT

- Do not give insulin if initial serum K+ is below 3.3 mEq/L; replete K^+ and fluid deficit first.
- Insulin infusion should be given to all patients as soon as possible unless serum K^+ below 3.3 mEq/L
- Insulin regimen : 0.1 units/kg IV bolus, then start a continuous IV infusion 0.1 units/kg per hour;
- If serum glucose does not fall by at least 50 to 70 mg/dL (2.8 to 3.9 mmol/L) in the first hour, double the rate of insulin infusion.
- When the serum glucose reaches 200 mg/dL (11.1 mmol/L), it may be possible to decrease the infusion rate to 0.02 to 0.05 units/kg per hour.
- Continue insulin infusion until ketoacidosis is resolved, serum glucose is below 200 mg/dL (11.1 mmol/L), and subcutaneous insulin is begun.

❖ BICARBONATE MANAGEMENT

➲ Give sodium bicarbonate to patients with pH below 6.90:

- If the arterial pH is below 6.90, give 100 mEq of sodium bicarbonate plus 20 mEq of potassium chloride in 400 mL sterile water over two hours; may be repeated if venous pH remains below 7.00.

Criteria of DKA resolution and conversion to S.C insulin protocol

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The American Diabetes Association (ADA) guidelines for DKA recommend that IV insulin infusion be tapered and a multiple-dose, subcutaneous insulin schedule be started when the blood glucose is <200 mg/dL (11.1 mmol/L) and at least two of the following goals are met

- Serum anion gap <12 mEq/L (or at the upper limit of normal for the local laboratory)
- Serum bicarbonate ≥15 mEq/L
- Venous pH >7.30

✔ The IV insulin infusion should be continued for one to two hours after initiating the subcutaneous insulin because abrupt discontinuation of IV insulin acutely reduces insulin levels and may result in recurrence of hyperglycemia and/or ketoacidosis.

If the patient is unable to eat, it is preferable to continue the IV insulin infusion

✅ For patients with known diabetes who were previously being treated with insulin, their pre-DKA insulin regimen may be restarted.

✔ In insulin-naive patients, a multidose insulin regimen should be started at a dose of 0.5 to 0.8 units/kg per day, including bolus and basal insulin until an optimal dose is established

✪ Complications

Cerebral edema

- Cerebral edema in DKA is primarily a disease of children, and almost all affected patients are younger than 20 years old
- Headache is the earliest clinical manifestation, followed by lethargy and decreased arousal.
- Neurologic deterioration may be rapid. Seizures, incontinence, pupillary changes, bradycardia, and respiratory arrest can develop.
- Symptoms progress if brainstem herniation occurs, and the rate of progression may be so rapid that clinically recognizable papilledema does not develop

Treatment

- Case reports suggest benefit from prompt administration of mannitol (0.25 to 1.0 g/kg) and perhaps from hypertonic (3 percent) saline (5 to 10 mL/kg over 30 min)
- These interventions raise the plasma osmolality (Posm) and generate an osmotic movement of water out of brain cells and a reduction in cerebral edema.