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Diabetes Mellitus

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Diabetes Mellitus

Introduction

Diabetes mellitus (DM) is a complex metabolic disorder characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Diabetes in children and adolescents typically presents as polyuria, polydipsia, nocturia, and weight loss. This could be associated with polyphagia, behavioral concerns such as poor school performance, and blurred vision. It can also present with ketoacidosis—its most severe form, which can lead to coma and even death if effective treatment is not initiated immediately upon identification.

When above symptoms are seen, bedside glucometer capillary glucose and urine ketone are used for screening for diabetes. Diagnostic criteria for diabetes and prediabetes are defined per the American Diabetes Association (ADA) 2021 guidelines in **Table 1**.

TABLE 1: Diagnostic criteria for diabetes mellitus: Any one to be fulfilled.

	Prediabetes	Diabetes
Fasting plasma glucose	100–125 mg/dL	≥126 mg/dL
*2 hours PG during OGTT	140–199 mg/dL	≥200 mg/dL
Hemoglobin A1C (HbA1C)	5.7–6.4%	≥6.5%
Random plasma glucose		≥200 mg/dL

*Oral glucose tolerance test (OGTT) to measure plasma glucose after 2 hours of 1.75 g/kg glucose load, maximum 75 g

Important points to remember at diagnosis:

- ☑ Clinical symptoms and biochemical abnormality—both should be present while making the diagnosis of DM.
- ☑ Formal plasma glucose measurement is necessary (not capillary blood glucometer value) for confirmation.
- ☑ If urine or blood ketones are positive, urgent referral to higher center essential.

Diagnosis

Types of Diabetes

The most common form in this age-group remains type 1 diabetes which is immune mediated. Type II diabetes, although rare, is on the increasing trend in our country. Type III diabetes includes other forms such as monogenic diabetes/maturity-onset diabetes of the young (MODY), cystic fibrosis-related diabetes (CFRD), fibrocalculous pancreatic diabetes (FCPD), drug-induced diabetes, and lipodystrophic diabetes, which are also being recognized. A detailed classification is described in the International Society of Pediatric and Adolescent Diabetes guidelines.

Factors that favor diagnosis of non-type 1 diabetes mellitus (T1DM) are as follows:

- Overweight/obesity
- Presence of hyperlipidemia at onset
- Absence of ketosis
- Family history of early onset diabetes in preceding two generations
- Medications—steroids and immunosuppressants

Goals of Therapy

- Maintain a good “time in range” (70% and above) defined as percentage of time the blood glucose (BG) values lie in target range of 70–180 mg/dL.
- Prevention of acute complications such as diabetic ketoacidosis (DKA) and hypoglycemia.
- Prevention of long-term complications and achieving good quality of life.
- Achieve normal growth and development.

Management of Diabetes

Pillars of management of diabetes are as follows:

- Medical nutrition therapy
- Physical activity
- Glucose monitoring
- Insulin therapy

Medical Nutrition Therapy

There is no special diet in diabetes. Children should be encouraged to eat a healthy diet with limited intake of snacks, sweeteners, and high glycemic index carbohydrates.

A balanced diet should follow the plate method as below: one-third high-quality high-fiber rich carbohydrates, one-third of fruits and vegetable, and one-third protein. The carbohydrate content of food can be calculated as “carb count” which helps to titrate insulin therapy (as discussed below, **Table 2**). One carbohydrate exchange equals 15 g carbohydrate.

Dietary options become challenging for a patient with a coexistent celiac disease where food should be made gluten free and with a low glycemic index.

TABLE 2: Dietary pattern for diabetes.

Do's	Don'ts
<ul style="list-style-type: none"> ☑ Permit nutritious age-appropriate foods with minimum permissible sugar, if required ☑ Encourage a balanced diet ☑ Promote intake of complex carbohydrates with low glycemic index food (lower risk of postprandial hyperglycemia) ☑ Maintain a log of carbohydrate count, as feasible ☑ Encourage frequent small meals with home-made fluids during acute illness to avoid ketoacidosis ☑ Remember to adjust insulin as per meal plan 	<ul style="list-style-type: none"> ☑ Avoid grazing and irregular meal timings ☑ Avoid prolonged fasting ☑ Avoid skipping meals before exercise or physical activity ☑ Avoid sugar-sweetened beverages/ caffeinated drinks intake ☑ Restrict extra-salt intake in the form of <i>papads</i>, baked and processed food ☑ Avoid diet-free, sugar-free products in excess that have lower sugar but high fat intake ☑ Avoid eating out

A regular fitness and physical activity regime is essential for good metabolic control. Parents should encourage the child to have a simple fitness regime such as walking, running, dancing, using stairs often, and playing in open grounds. Children with diabetes can participate in all sports but should be educated to check BG before exercise and preferably consume a snack if BG is low, to avoid hypoglycemia.

Physical Activity

Glucose Monitoring

Blood glucose monitoring is an essential pillar of management in diabetes. The easiest way to monitor is using a hand-held glucometer which should be used by each patient to check BG daily. An ideal BG log should record premeal and 2-hour postmeal BG values at least thrice a day. Additional testing should be done before a planned physical activity, at bedtime, and if the child develops any uneasiness or discomfort.

The use of continuous glucose monitoring system (CGMS) has simplified the glucose monitoring. This device places a sensor over the skin to measure the glucose level in the interstitial fluid at frequent intervals. The readings from the sensor can be read real time or as records which can show fluctuations (both hypo- and hyperglycemia) that would have gone unnoticed on timed-finger prick checking. The sensors usually last 5–14 days, and may need calibration with finger-prick values of a glucometer.

The CGMS log also helps to calculate the “*time-in-range*” that is defined as the percentage of time when the BG remained between 70 and 180 mg/dL. An optimum value is 70% or more. At present, CGMS of Medtronic, Dexcom, and Abbott are available in India.

The target BG profile that should be maintained is mentioned in **Table 3**.

TABLE 3: Target blood glucose profile in type 1 diabetes.

Time	Normal blood glucose	Goal	Poor control
Fasting	70–100 mg/dL	90–130 mg/dL	>150 mg/dL <90 mg/dL
Postprandial	<140 mg/dL	140–160 mg/dL	>180 mg/dL
Average bed time	<120 mg/dL	110–150 mg/dL	>180 mg/dL <110 mg/dL

Insulin should be started soon after diagnosis of diabetes. Multiple daily injections with the basal-bolus regime are preferred. Poorer metabolic control with premixed twice daily insulin in adolescents makes them unsuitable for use in children.

Regular or rapid/ultra-rapid-acting insulin are administered preprandial timed as per the onset and peak of action. Basal insulin are given once (or twice) a day and timed at a fixed schedule in a day, usually night (**Table 4**). The regime is personalized to suit the child’s meal and activity pattern, and convenience.

Insulin Therapy

TABLE 4: Types of insulin.

Insulin	Onset of action (hours)	Peak of action (hours)	Duration of action (hours)
Ultra-rapid-acting analog [faster-acting insulin aspart (FIAsp)]	0.1–0.2	1–3	3–5
Rapid-acting analog (Lispro, aspart, and glulisine)	0.15–0.35	1–3	3–5
Regular insulin	0.5–1	2–4	5–8
Intermediate acting [neutral protamine Hagedorn (NPH)]	2–4	4–12	12–24
<i>Long acting-analog</i>			
☑ Glargine	☑ 2–4	☑ 8–12	☑ 22–24
☑ Degludec	☑ 0.5–1.5	☑ Minimal peak	☑ >42
☑ Detemir	☑ 1–2	☑ 4–7	☑ 20–24
☑ Glargine-300	☑ 2–6	☑ Minimal peak	☑ 30–36

Insulin Administration

Insulin can be administered using syringes, pens, or advanced technology like insulin pumps.

- ☑ **Insulin syringes (Fig. 1):** One should use U-100 syringes with U-100 vials (100 units of insulin/mL) and U-40 syringes with U-40 vials (40 units of insulin/mL). The attached needles are 6 or 8 mm long. Regular and neutral protamine Hagedorn (NPH) insulin are usually available in 40 IU/mL strength, while insulin analogs are usually available as 100 IU/mL. The patient should be instructed to check the strength of insulin vial before use.
- ☑ **Insulin pen:** These are either reusable or disposable (more expensive); typically have 1-unit increments (0.5 unit increments also available). They are easy to carry and convenient. Pen needles are 4, 5 or 6 mm long.



Fig. 1: From left to right—reusable pen with 6 mm needle, pen with 4 mm needle, disposable pen with cartridge, Insulin syringe U-100 (orange caps), and U-40 (red cap). *Source:* Indian Academy of Pediatrics. (2021), Guidelines for Parents: Care of a Child with Diabetes Mellitus. [online] Available from: <https://iapindia.org/pdf/guidlines-for-Care-of-a-child-with-Diabetes-Mellitus.pdf> [Last accessed February, 2022].

- ☑ **Insulin pump:** This delivers short-acting or regular insulin using a battery-operated pump over 24 hours to provide a basal continuous supply. Additional top-up boluses of insulin can be given using the same device for mealtime. The insulin goes through a flexible catheter and a cannula directly into subcutaneous fat over abdomen or gluteal area. These are expensive and require operational expertise.

Insulin Storage

Once in use insulin can be stored at room temperature for 4 weeks or at 4–8°C in the refrigerator for 3 months. Insulin should never be frozen or kept under direct sunlight. Insulin may be stored in clay pots using the double pot method in hot climates if the refrigerator is not available (**Fig. 2**).

Insulin can be self-injected by children >8 years of age⁴ and by the parents in the rest. Insulin is injected subcutaneously in the anterolateral thigh or the anterior abdominal wall (leaving out 2 inches from all sides of the navel). Deltoid region is not ideal for children. Rotation of injection sites to prevent lipohypertrophy is of utmost importance. Proper disposal of lancets and sharps must be taught to all patients and their families.

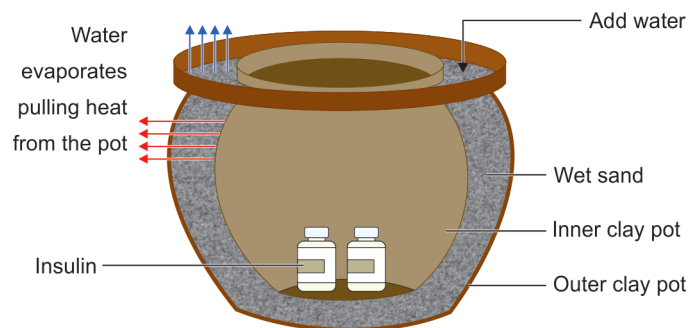


Fig. 2: Storage of insulin in clay pots.

Insulin Dose

If presenting as DKA, a dose of 0.05–0.1 unit/kg/hour of short-acting insulin is given as an intravenous infusion, following which insulin requirement may be as high as 2–3 units/kg/day for the first few days. Typically, as the patient enters the honeymoon phase, the dose comes down to 0.5 units/kg/day or less. Following this, 0.7–1.5 U/kg/day is the usual dose with 40% as basal and 60% as boluses for three meals. The dose and distribution may vary depending on age and puberty.⁴

Insulin sensitivity factor (ISF) is the extent to which the BG is expected to drop (in mg/dL) with 1 unit of regular insulin or rapid-acting analog. This factor can be derived by dividing a constant factor (1,700) by the patient's total daily dose (TDD).

Insulin-to-carbohydrate ratio (ICR) (or the grams of carbohydrate for which 1 unit of rapid- or short-acting insulin is needed) is calculated by dividing the constant 500 by the TDD. The amount of carbohydrate being consumed can be titrated for premeal insulin dose as per the ICR, i.e., to calculate the amount of insulin needed for the amount of carbohydrate,

The BG logs can be analyzed with ICR and ISF to optimize insulin dosage and meal patterns. Intelligent use of these ratios helps with better glycemic control.

- ☑ Monitor growth (anthropometry)—3–6 monthly
- ☑ Check insulin dose prescribed and *compliance* to same
- ☑ *Examine*—site of injection, method, and complications at local site
- ☑ Check record book which should contain date and time of:
 - Glucose levels—*crosscheck with glucometer*
 - Carbohydrate intake—diet plan being followed to be reviewed for balanced diet, carb counts if available to titrate premeal short-acting insulin
 - Insulin dosage—whether doses adjusted as per self-monitoring of blood glucose (SMBG)/carbohydrate intake
 - Note of special events affecting glycemic control (e.g., illness and exercise)
 - Hypoglycemic episodes, describing of severity and potential alterations in the usual routine to help explain the cause for the event
- ☑ Blood glucose logs for “Time-in-Range”—to be reviewed at each visit
- ☑ Hemoglobin A1C (HbA1C) monitoring every 3 months
- ☑ Explain symptoms of hypoglycemia such as lethargy, increased irritability, excessive sweating, tremors, and its prevention and treatment
- ☑ Inform *SICK DAY* management:
 - Do not omit insulin
 - When unwell frequent random BG and ketone (urine or blood) monitoring is needed, usually 2–3 hourly. Top-up insulin is often needed.
 - Calculate TDD (**Table 5**). This is the sum of all insulin being given in a day. To give extra dose of rapid-acting or regular insulin subcutaneous. This helps to prevent DKA.

TABLE 5: Calculation of total daily dose (TDD).

Blood glucose value	Urine ketone	Blood ketone	Extra insulin
180–400 mg/dL	Moderate	0.6–1.5 mmol/L	10–15% of TDD
180–400 mg/dL	Large	>3 mmol/L	20% of TDD
>400 mg/dL	Moderate	0.6–1.5 mmol/L	15–20% of TDD
>400 mg/dL	Large	>3 mmol/L	20% of TDD

- *If BG < 80 mg/dL:* Regular insulin should be omitted. Frequent feeds in small quantities should be given with 2–3 hourly BG monitoring. Basal insulin should be given. If urine ketones are positive, basal insulin can be reduced by 30%.
- *Hospitalize:* If child is drowsy, vomiting more than three times, not tolerating oral feeds, develops fast breathing, and has significant abdominal pain.

- ☑ Ensure screening for long-term complications (**Table 6**).

TABLE 6: Screening guidelines.

Complications	Initial testing	Frequency	Test
Thyroid disease	At diagnosis	Every 1–2 years or sooner if symptoms	TSH and antithyroid antibodies
Celiac	At diagnosis	Within 2 years and again at 5 years or sooner if symptoms	IgA and anti-tissue transglutaminase
Hypertension	At diagnosis	Each visit	Elevated BP based on ≥ 90 th% for age, sex, and height on three separate occasions
Dyslipidemia	≥ 10 years of age at diagnosis once glucose control established	If abnormal annually; every 5 years if initially normal	Goal LDL—cholesterol < 100 mg/dL
Nephropathy	At puberty or age ≥ 10 years whichever comes first, if T1DM ≥ 5 years	Annually	Albuminuria; urine albumin-to-creatinine ratio
Retinopathy	T1DM ≥ 3 –5 years when ≥ 10 years or puberty, whichever comes first	Annually	Dilated eye examination
Neuropathy	At puberty or ≥ 10 years, whichever earlier if T1DM > 5 years	Annually	Foot examination

(BP: blood pressure; IgA: immunoglobulin A; LDL: low-density lipoprotein; T1DM: type 1 diabetes mellitus; TSH: thyroid-stimulating hormone)

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