

DIABETES MELLITUS

Diabetes in children is almost invariably type I diabetes mellitus. The incidence of type II diabetes mellitus is on the increasing trend among young people due to obesity.

Table 1. Sign and symptoms of diabetes mellitus

Early	Late
polydipsia	vomiting
polyuria	dehydration
weight loss	abdominal pain
enuresis (secondary)	hyperventilation due to acidosis
	drowsiness
	coma

Table 2. Criteria for diagnosis of diabetes mellitus

- Symptoms of diabetes + casual plasma glucose concentration ≥ 11.1 mmol/L (≥ 200 mg/dL).¹ Casual is defined as any time of day without regard to time since the last meal.

or

- Fasting plasma glucose ≥ 7.0 mmol/L (≥ 126 mg/dL).² Fasting is defined as no caloric intake for at least 8 h.

OR

- 2-h postload glucose ≥ 11.1 mmol/L (≥ 200 mg/dL) during an oral glucose tolerance test (OGTT). Using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water or 1.75 g/kg of body weight to a maximum of 75 g. (WHO).

footnote:

1. Corresponding values (mmol/L) are ≥ 10.0 for venous whole blood and ≥ 11.1 for capillary whole blood.
2. Corresponding values are ≥ 6.3 mmol/L for both venous and capillary whole blood.

Management

Principles of insulin therapy

- daily insulin dosage
 - daily insulin dosage varies greatly between individuals and changes over time
 - the correct dose of insulin for any individual is the dose that achieves the best glycemic control without causing obvious hypoglycemia problems, and achieving normal growth (height and weight)
 - 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) and intercurrent illness.
- guidelines on dosage:
 - during the partial remission phase, total daily insulin dose is usually 0.5 IU/kg/day
 - prepubertal children (outside the partial remission phase) usually require insulin of 0.7–1.0 IU/kg/day
 - during puberty, requirements may rise above 1 and even up to 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.

Table 3. Types of insulin

Types of Insulin	Examples	Onset of Action	Peak	Duration
Rapid-acting insulin	NovoRapid, Humalog	5-15 min	30-60 min	3-5 hours
Short-acting insulin (regular)	Actrapid, Humilin R	30 min	2-3 hours	3-6 hours
Intermediate-acting insulin	Insulatard (NPH) Humulin N	2-4 hours	4-12 hours	12-18 hours
Long-acting insulin	Levemir (Detemir),	<i>Detemir</i> 1-2 hours	<i>Detemir</i> 6-8 hours	<i>Detemir</i> 6-23 hours
	Lantus (Glargine)	<i>Glargine</i> 1 hour	<i>Glargine</i> no peak	<i>Glargine</i> 24 hours

- Frequently used regimens:

Twice Daily Regimens

- 2 daily injections of a mixture of a short or rapid insulin with and intermediate-acting insulins (before breakfast and the main evening meal)
- approximately 1/3 of the total daily insulin dose is short acting insulin and 2/3 intermediate-acting insulin
- about 2/3 of the total daily dose is given in the morning and 1/3 in the evening

Three injections daily

- a mixture of short- or rapid- and intermediate-acting insulins before breakfast;
- a rapid-acting analogue or regular insulin alone before afternoon snack or the main evening meal
- and an intermediate- acting insulin before bed

Basal-bolus Regimen

depending on whether rapid-acting or regular insulin is used:

- Rapid-acting insulin: about 50 % of total daily dose of insulin is given as rapid-acting insulin divided up between 3 – 4 premeal boluses. The rest (about 50%) given as basal nighttime intermediate-acting insulin
- Regular insulin: about 70 % of total daily dose of insulin is given as regular insulin divided up as 3-4 premeal boluses and the rest (about 30%) given as basal night time intermediate-acting insulin. The proportion of basal insulin is less because regular insulin provides some basal effect
- if using regular insulin: inject 20–30 min before each main meal (breakfast, lunch; and main evening meal); if using rapid-acting insulin analogue inject immediately before or after each main meal (e.g. breakfast, lunch; and the main evening meal).
- basal cover is usually given once daily at bedtime. However sometimes it may be needed to be given twice daily (the other dose usually before breakfast)
- insulin pump regimens are regaining popularity with a fixed or a variable basal dose and bolus doses with meals.

Some notes on converting from intermediate acting insulin to long acting insulin analogues:

- *Insulin Glargine*
 - usually given once a day. However if needed, it can be given twice a day.
 - when converting from NPH to Glargine, the total dose of basal insulin needs to be reduced by approximately 20% to avoid hypoglycemia. After that, the dose should be individually tailored.
- *Insulin Detemir*
 - is most commonly given twice daily in children
 - when changing to detemir from NPH, the same doses can be used to start with.

Monitoring of glycaemic control

Self-monitoring of blood glucose (SMBG)

The frequency of SMBG is associated with improved HbA1c in patients with type 1 diabetes.

- timing of SMBG.
 - at different times in the day to show levels of BG
 - to confirm hypoglycemia and to monitor recovery; and
 - during intercurrent illness to prevent hyperglycemic crises.
- the number and regularity of SMBG should be individualized depending on
 - availability of equipment;
 - type of insulin regimen; and
 - ability of the child to identify hypoglycemia

Note:

- successful application of intensified diabetes management with multiple injection therapy or insulin infusion therapy requires frequent SMBG (four to six times a day) and regular, frequent review of the results to identify patterns requiring adjustment to the diabetes treatment plan.

Table 4. Target indicators of glycaemic control

Level of control	Ideal (non-diabetic)	Optimal (diabetic)
<i>Clinical assessment</i>		
Raised BG ¹	not raised	no symptoms
Low BG	not low	few mild, no severe hypoglycaemias
<i>Biochemical assessment</i>		
• SBGM values (mmol/L)		
AM fasting or preprandial	3.6 - 5.6	5.0 - 8.0
• PG ² in mmol/L		
Postprandial PG	4.5 - 7.0	5.0 - 10.0
Bedtime PG	4.0 - 5.6	6.7 - 10.0
Nocturnal PG	3.6 - 5.6	4.5 - 9.0
• HbA1c (%) ³	< 6.05	< 7.5

footnote: 1. BG, , blood glucose; 2. PG, plasma glucose; 3. Diabetes Control and Complications Trial Standard

- however, each child should have their targets individually determined with the goal of achieving a value as close to normal as possible while avoiding severe hypoglycemia as well as frequent mild to moderate hypoglycemia

Monitoring of urinary or blood ketones

- urine or blood ketone measurement should be monitored during episodes of uncontrolled hyperglycemia, insulin deficiency, intercurrent illness (sick days), and impending ketoacidosis.

Urine ketone testing

- tablets or urine testing strips (detect increased levels of urinary acetoacetate)

Reading (in mmol/L)	Corresponding
0.5	Trace amounts
1.5	Small amounts
4	Moderate amounts
> 8	Large amounts

Interpretation of urine ketone testing

- moderate or large urinary ketone levels in the presence of hyperglycemia indicate insulin deficiency and risk for metabolic decompensation leading to ketoacidosis.
- the presence of vomiting with hyperglycemia and large urinary ketones must be assumed to be because of systemic acidosis and requires further evaluation.
- urine, in contrast to blood ketone testing, is not helpful in ruling out or diagnosing DKA.

Blood ketone determination.

- because of cost many centres limit the determination of blood ketone to
 - young children (difficult to obtain a urine specimen),
 - and for any individual if the urine ketone measurement is large – i.e., .4–8 mmol/L.
- blood ketone testing is especially important for patients on pumps as they have a much smaller subcutaneous (s.c.) insulin depot
- determination of blood ketone levels can guide management, e.g., if more intensive treatment is required to avert severe ketoacidosis

When should we test for ketones?

- illness with fever and/or vomiting
- persistent blood glucose levels > 14 mmol/L (250 mg/dL), in an unwell child, in a young child, an insulin pump user, or patient with a history of prior episodes of DKA
- persistent polyuria with elevated blood or urine glucose
- episodes of drowsiness
- abdominal pain or rapid breathing

Recommendations for HbA1c measurement

- ideally, in younger children, 4 - 6 times per year. In older children, 3 - 4 times per year
- adolescents with stable type 2 diabetes should have 2 - 4 measurements per year because they can rapidly become insulin requiring (compared to adults).
- HbA1c target range for all age-groups of: < 7.5%
 - if hypoglycemia unawareness is present, glycemic targets must be increased until hypoglycemia awareness is restored
 - in children < 6 yr, be particularly vigilant for unrecognized hypoglycemia.

Diet

- a balance and healthy diet for age is required with dietician involvement

Exercise

- no restriction.
- eat fast-acting carbohydrates frequently during strenuous exercise
- plan injection sites according to activity e.g. inject insulin in the arm if cycling

Diabetic Education

At diagnosis: survival skills

- 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 dietetic advice
- simple explanation of hypoglycemia
- diabetes during illnesses. Advice not to omit insulin – prevent diabetic ketoacidosis
- diabetes at home or at school including the effects of exercise
- psychological adjustment to the diagnosis
- details of emergency telephone contacts

Medic alert

- wear the medic alert at all times as this may be life saving in an emergency situation.
A form to request for a medic alert can be obtained from the local diabetes educator.

Diabetes support group

- Persatuan Diabetes Malaysia (PDM) or Malaysian Diabetes Association, Diabetes Resource Centre at the regional centre or the respective hospital
- encourage patient and family members to enroll as members of diabetes associations and participate in their activities

School

- the school teachers should be informed about children having diabetes so that some flexibility can be allowed for insulin injections and mealtimes
- symptoms and treatment of hypoglycaemia should be informed so that some emergency measures can be commenced at school

Other complications and associated conditions

- monitoring of growth and physical development.
- screening of thyroid function at diagnosis of diabetes. Then every second year if asymptomatic, no goitre or thyroid autoantibodies negative. More frequent assessment is indicated otherwise.
- in areas of high prevalence for coeliac disease, screening for coeliac disease should be carried out at the time of diagnosis and every second year thereafter. More frequent assessment if there is clinical suspicion of coeliac disease or coeliac disease in first-degree relative.
- routine clinical examination for skin and joint changes. Regular laboratory or radiological screening is not recommended. There is no established therapeutic intervention for lipodystrophy, necrobiosis lipoidica or limited joint movement.

Table 7. Screening, risk factors, and interventions for vascular complications: the levels of evidence for risk factors and interventions pertaining to adult studies, except for improved glycemic control.

Retinopathy	Nephropathy	Neuropathy	Macrovascular disease
When to commence screening?			
annually from age 11 yr if 2 yrs diabetes duration and from age 9 yrs with 5 yr of duration (E)	annually from age 11 yr if 2 yrs diabetes duration and from age 9 yrs with 5 yr of duration (E)	unclear	after age 12 yrs (E)
Screening methods			
fundal microphotograph or mydriatic ophthalmoscopy (less sensitive) (E)	urine albumin:creatinine ratio or first morning albumin concentration (E)	history and physical examination	lipid profile every 5 yr blood pressure annually (E)
Risk factors			
hyperglycaemia (A) high blood pressure (B) lipid abnormalities (B) higher BMI (C)	high blood pressure (B) lipid abnormalities (B) smoking (B)	hyperglycaemia (A) higher BMI (C)	hyperglycaemia (A) high blood pressure (A) lipid abnormalities (B) smoking (B) higher BMI (B)
Potential intervention			
improved glycemic control (A) laser therapy (A)	improved glycemic control (A) ACEI and AIIIRA (A) blood pressure lowering (B)	improved glycemic control (A)	improved glycemic control (A) blood pressure control (B) statins (A)

Abbreviations. BMI, body mass index; ACEI, angiotensin converting enzyme inhibitor; AIIIRA, angiotensin II receptor antagonists

Table 6. Target levels for different parameters to reduce the risk of microvascular and cardiovascular diseases in children and adolescents with type 1 diabetes; the level of evidence are from adult studies.

Parameter	Target level	Evidence grade
haemoglobin A1c (<i>Diabetes Control and Complication Trials Standard</i>)	< 7.5 % without severe hypoglycaemia	A
low density lipoprotein cholesterol	<2.6 mmol/l	A
high density lipoprotein cholesterol	>1.1 mmol/l	C
triglycerides	<1.7 mmol/l	C
blood pressure	<90th percentile by age, sex, height	C/B
body mass index	<95th percentile (non obese)	E
smoking	none	A
physical activity	>1 h of moderate physical activity daily	B
sedentary activities	<2 h daily	B
healthy diet	caloric intake appropriate for age and normal growth fat < 30% of caloric intake and saturated fat < 10 % caloric intake fiber intake 25-35 g daily increased intake of fresh fruit and vegetables	E