

Management of T1DM in children and adolescents in primary care

Hong YHJ, Hassan N, Cheah YK, Jalaludin MY, Kasim ZM on behalf of Development Group Clinical Practice Guidelines Management of Type 1 Diabetes Mellitus in Children & Adolescents

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Abstract

The Clinical Practice Guidelines on the Management of Type 1 Diabetes Mellitus in Children & Adolescents was developed by a multidisciplinary development group and approved by the Ministry of Health Malaysia in 2015. A systematic review of 15 clinical questions was conducted using the evidence retrieved mainly from MEDLINE and Cochrane databases. Critical appraisal was done using the Critical Appraisal Skills. Recommendations were formulated on the accepted 136 evidences using the principles of Grading Recommendations, Assessment, Development and Evaluation tailored to the local setting.

Type 1 diabetes mellitus is a chronic disease, which usually occurs at an early age, and is associated with various complications including retinopathy, nephropathy, neuropathy and cardiovascular morbidity. Good glycaemic control early in the disease results in lower frequency of chronic diabetes complications, which in turn reduces the healthcare cost. Accurate classification of diabetes and optimum management with the aim to achieve glycaemic targets is of utmost importance.

Introduction

Type 1 diabetes mellitus (T1DM) is the most common type of diabetes mellitus (DM) in children and adolescents. The incidence of T1DM is low in Asia, which is approximately 2 to 5 per 100,000 person-years. In Malaysia, the incidence of T1DM was not reported by the Malaysian Diabetes in Children and Adolescents Registry 2006–2008 due to several limitations. However, it was found that 71.8% of children with DM under the age of 20 years had T1DM. The median age at diagnosis was 7.6 (interquartile range: 4.6–10.8) years and the majority of patients (58.3%) presented with diabetic ketoacidosis (DKA). Therefore, children with T1DM should be identified early, ideally before the development of DKA as this acute condition is associated with high morbidity and mortality.

Diagnosis

The diagnosis of DM should be made based on the presence or absence of symptoms and biochemical criteria according to the World Health Organization Diagnostic Criteria of 1999.

Diagnostic criteria of DM:

- Classic symptoms of diabetes or hyperglycaemic crisis, with plasma glucose concentration ≥ 11.1 mmol/L
- OR
- Fasting plasma glucose (no caloric intake for at least 8 hours) ≥ 7.0 mmol/L
- OR
- 2-hour post-load glucose ≥ 11.1 mmol/L in oral glucose tolerance test
- OR
- HbA1c $> 6.5\%$ (HbA1c alone in the diagnosis of DM remains unclear and cannot exclude DM when the value is $< 6.5\%$)
- The diagnosis must be confirmed by repeat blood glucose (BG) testing in the absence of unequivocal hyperglycaemia.
- Biochemical features to support the diagnosis of T1DM includes:
 - low or undetectable (fasting) C-peptide levels
 - presence of diabetes-associated autoantibodies (GAD/IAA/ICA512/IA2/ZnT8)

Clinical presentation

Classically, T1DM children and adolescents present with a history of polyuria, polydipsia and weight loss over 2 to 6 weeks. The clinical presentation varies from non-emergency to emergency situations and are shown in **Table 1**.

Table 1. Clinical presentation of T1DM

Non-emergency presentations	Emergency presentations
<ul style="list-style-type: none"> • Recent onset of enuresis in previously toilet-trained children • Vaginal candidiasis especially in pre-pubertal girls • Chronic weight loss or failure to gain weight in growing children • Recurrent skin infections 	<ul style="list-style-type: none"> • Moderate to severe dehydration • Frequent vomiting • Abdominal pain • Continuing polyuria despite the presence of dehydration • Weight loss due to fluid loss, and loss of muscle and fat • Acetone-smelling breath • Hyperventilation • Decreased level of consciousness • Hypotension • Shock

Additional clinical features of T1DM in children and adolescents are shown below (**Table 2**).

Table 2. Additional clinical features of T1DM

Age of onset	Six months to young adulthood
Clinical presentation	Most often acute, rapid onset of symptoms
Autoimmunity	Present
Ketosis	Common
Body habitus	Usually lean but can be overweight following population frequency
Acanthosis nigricans	Typically absent

Symptoms of T1DM may be misinterpreted leading to delayed diagnosis (**Table 3**). Therefore, healthcare providers should have a high index of suspicion of DM/DKA when managing such sick children.

Table 3. Misinterpretation of T1DM symptoms

Symptoms	Misdiagnoses
Hyperventilation during DKA	Pneumonia or asthma
Abdominal pain associated with DKA	Acute abdomen
Polyuria and enuresis	Urinary tract infection
Polydipsia	Psychogenic polydipsia
Vomiting	Acute gastroenteritis or sepsis
Impaired level of consciousness	Meningitis/encephalitis

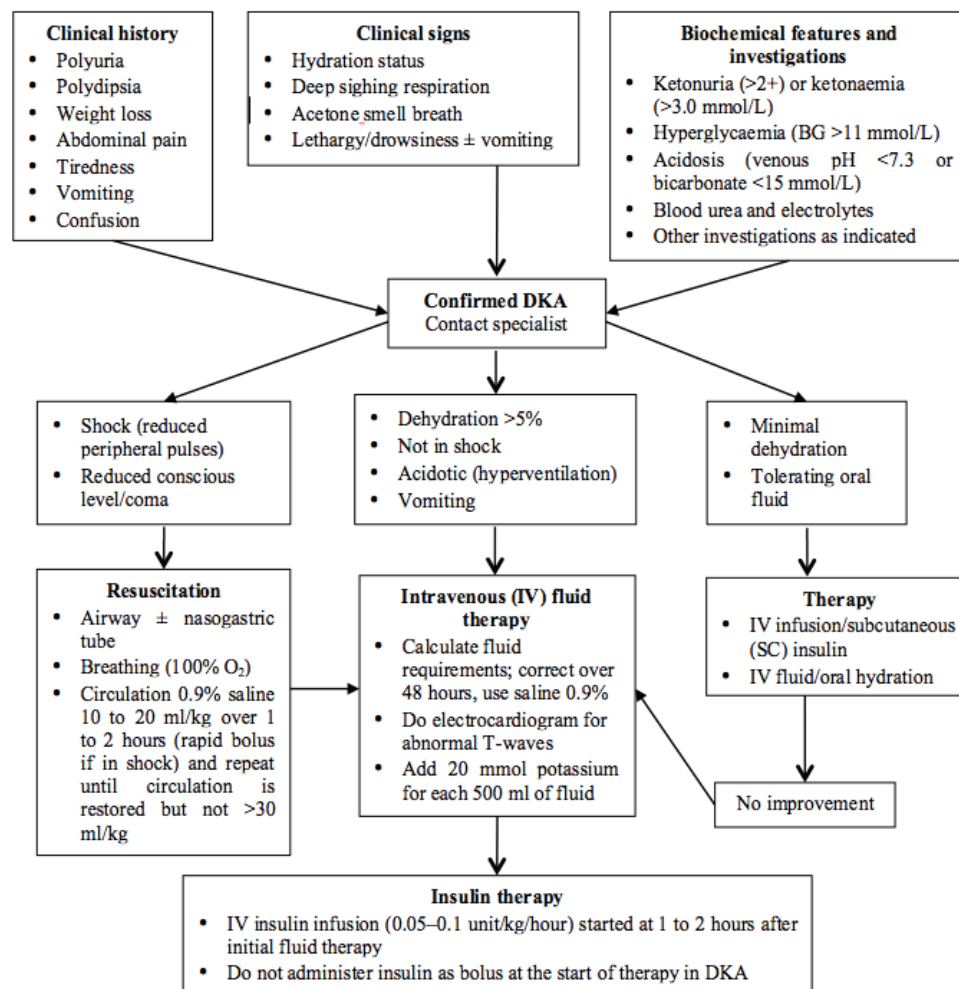
DKA

Risk factors for DKA in newly diagnosed diabetes include:

- young patient (<2 years old)
- delayed diagnosis
- low socio-economic status
- children in countries with low prevalence of T1DM

The immediate assessment and management of DKA are illustrated in the algorithm below.

Immediate assessment and management of DKA



Co-morbidities

Patients with T1DM have a higher prevalence of autoimmune diseases compared with patients without diabetes. At diagnosis of T1DM, screening of thyroid function and measurement of antithyroid peroxidase antibody should be done. If thyroid function is normal and antibody is absent, thyroid screening should be repeated every 2 years. However, screening should be more frequent in patients with goitre or positive thyroid antibody.

Treatment

All patients with T1DM should aim to achieve glycaemic targets to maintain normal growth and pubertal development, while avoiding severe hypoglycaemia. The recommended HbA1c targets for all patients younger than 18 years is <7.5% (58 mmol/L).

Treatment of T1DM consists of:

- Insulin therapy

Intensive insulin therapy is the preferred regimen. The basal-bolus regimen (intermediate-acting insulin/long-acting basal once or twice daily and rapid-acting/short-acting boluses with meals and snacks) mimics the physiological insulin secretion. Basal insulin constitutes about 40% to 60% of the total daily insulin dose (TDD) requirements; the remainder is pre-prandial rapid-acting/short-acting insulin.

The guidelines for TDD are as below:

- partial remission phase: <0.5 IU/kg/day
- pre-pubertal period: 0.7 to 1.0 IU/kg/day
- pubertal period: 1.2 to 2 IU/kg/day

- **Medical nutrition therapies**

Appropriate nutritional strategies should be tailored to the age, insulin regimen and physical activities.

- **Physical activity**

Physical activities should be performed regularly and in a safe manner (insulin therapy and dietary adjustment).

- **Psychosocial support**

Young patients with T1DM have higher prevalence of affective disorders (anxiety

and depression) compared to non-diabetics. Regular assessment should be performed in all patients for the early recognition of psychosocial problems with referral to appropriate expertise.

Hypoglycaemia

Hypoglycaemia is defined as low BG level that predisposes patients to potential harm and the threshold for initiation of the treatment is 3.9 mmol/L. Patients can be symptomatic or asymptomatic. Signs and symptoms of hypoglycaemia are due to adrenergic activation and neuroglycopenia as shown **Table 4** below.

Table 4. Signs and symptoms of hypoglycaemia

Autonomic symptoms and signs	Neuroglycopenic signs and symptoms	Behavioural signs and symptoms	Non-specific symptoms
<ul style="list-style-type: none"> • Shakiness • Sweatiness • Tremors • Palpitations • Pallor 	<ul style="list-style-type: none"> • Poor concentration • Blurred or double vision • Disturbed colour vision • Difficulty in hearing • Slurred speech • Poor judgment and confusion • Problems with short-term memory • Dizziness and unsteady gait • Loss of consciousness • Seizure • Death 	<ul style="list-style-type: none"> • Irritability • Erratic behaviour • Agitation • Nightmares • Inconsolable crying 	<ul style="list-style-type: none"> • Hunger • Headache • Nausea • Tiredness

The goal of hypoglycaemia treatment is to increase BG by approximately 3 to 4 mmol/L or restore the BG to a target level of 5.6 mmol/L. Refer to **Table 5** on the treatment.

Table 5. Treatment of hypoglycaemia

Severity	Mild/moderate hypoglycaemia	Severe hypoglycaemia
Definition	Low BG of 3.3 to 3.9 mmol/L	Severe neuroglycopenia that results in coma or seizure and requires parenteral therapy
Treatment	<ul style="list-style-type: none"> • Give oral glucose of 0.3 g/kg (1 teaspoon ≈ 5 g) • Check BG after 10 to 15 minutes, repeat oral glucose administration if there is no improvement. • Thereafter, consume complex carbohydrates (e.g., fruit, bread, cereal or milk) to prevent recurrent hypoglycaemia. 	<ul style="list-style-type: none"> • Rapid treatment with IV dextrose 10% (2–3 ml/kg) • If IV access is not available, SC/ intramuscular glucagon can be given (0.5 mg for patients <12 years old and 1.0 mg for those >12 years old).

Special situations

The healthcare providers need to provide clear guidance to patients and their caregivers on how to manage special situations in T1DM such as:

- sick days
 - do not omit insulin
 - more frequently monitoring of BG and blood/urine ketone
 - adjust insulin dose accordingly
- eating out
 - adjust the dose and timing of meal time insulin accordingly
 - check pre- and post-meal BG

- fasting during Ramadan
 - provide Ramadan-focused patient education and follow individualised management plan
- schooling
 - provide individualised diabetes medical management plan in school/day-care centre

Screening for complications

It is important to maintain good glycaemic control in patients with T1DM to prevent long-term complications. The suggested screening schedule is shown in the **Table 6** below.

Table 6. Screening schedule for complications

Complications	Screening schedule	Screening method
Retinopathy	<ul style="list-style-type: none"> • Start at age 10 or at onset of puberty if this is earlier, after 2 to 5 years' diabetes duration • Annually thereafter 	<ul style="list-style-type: none"> • Fundal photography or • Mydriatic ophthalmoscopy (less sensitive)
Nephropathy	<ul style="list-style-type: none"> • Start at age 10 or at onset of puberty if this is earlier, after 2 to 5 years' diabetes duration • Annually thereafter 	<ul style="list-style-type: none"> • Urinary albumin:creatinine ratio or • First morning urinary albumin concentration or • Timed urine collections for albumin excretion rates
Neuropathy	<ul style="list-style-type: none"> • Unclear 	<ul style="list-style-type: none"> • History and physical examination
Macrovascular disease	<ul style="list-style-type: none"> • After age 10 years 	<ul style="list-style-type: none"> • Lipid profile every 5 years • Blood pressure annually

Referral

Referral of children and adolescents with T1DM to paediatricians/paediatric endocrinologists should be made in the following conditions:

- uncertainty with classification of diabetes
- difficult metabolic control
- concomitant co-morbidities and other management issues
- inadequate resources and expertise in management

Acknowledgement

Details of the evidence supporting the above statements can be found in Clinical Practice Guidelines on the Management of Type I in Children & Adolescents 2015, available on the following website: Ministry of Health Malaysia: <http://www.moh.gov.my> and Academy of Medicine: <http://www.acadmed.org.my>. Corresponding organisation: CPG Secretariat, Health Technology Assessment Section, Medical Development Division, Ministry of Health Malaysia and contactable at htamalaysia@moh.gov.my.