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WILEY ISPAD

ISPAD CLINICAL PRACTICE CONSENSUS GUIDELINES

ISPAD Clinical Practice Consensus Guidelines 2018: Limited Care Guidance Appendix

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DEFINITION, EPIDEMIOLOGY, AND CLASSIFICATION OF DIABETES IN CHILDREN AND ADOLESCENTS

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatr Diabetes 2018: 19 (Suppl. 27): 7–19).

- Diagnostic criteria for all types of diabetes in children and adolescents are based on laboratory measurement of plasma glucose levels (BGL) and the presence or absence of symptoms. If blood glucose testing is unavailable, diabetes can be provisionally diagnosed, in the presence of symptoms, by the finding of high levels of glucose and ketones in the urine.
- In geographical areas where the known incidence of type 1 diabetes is low, health care professionals should be aware that there is a higher rate of diabetic ketoacidosis at presentation due to lack of consideration of the diagnosis.
- The possibility of other types of diabetes should be considered in the child who has:
  - an autosomal dominant family history of diabetes.
  - age less than 12 months and especially in the first 6 months of life.
  - associated conditions such as deafness, optic atrophy, or syndromic features.
  - mild fasting hyperglycemia (5.5-8.5 mmol [100-150 mg/dL]), especially if young, non-obese, and asymptomatic.
  - marked insulin resistance and acanthosis nigricans.
  - a history of exposure to drugs known to be toxic to beta cells or cause insulin resistance.
  - long interruption of insulin therapy without the occurrence of ketoacidosis.
- The differentiation between type 1, type 2, monogenic, and other forms of diabetes has important implications for both treatment and education. Diagnostic tools, which may assist in confirming the diabetes type if the diagnosis is unclear, include:
  - Diabetes-associated autoantibodies: glutamic acid decarboxylase 65 autoantibodies (GAD); Tyrosine phosphatase-like insulinoma antigen 2 (IA2); insulin autoantibodies (IAA), and β-cell-specific zinc transporter 8 autoantibodies (ZnT8). The presence of one of more of these antibodies confirms the diagnosis of type 1 diabetes.
- Molecular genetic testing can help define the diagnosis and treatment of children with suspected monogenic diabetes and should be limited to those who on clinical grounds are likely to be positive.

STAGES OF TYPE 1 DIABETES IN CHILDREN AND ADOLESCENTS

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatric Diabetes 2018: 19 (Suppl. 27): 20–27).

- Individuals with a first-degree relative with type 1 diabetes have an approximately 15-fold increased relative risk of type 1 diabetes.
- The majority of children at risk of type 1 diabetes with multiple islet antibodies progress to diabetes within the next 15 years, compared to ~10% who have a single islet antibody.
- Individuals with islet autoimmunity who are followed regularly until clinical diagnosis present with lower HbA1c and a lower risk of diabetic ketoacidosis.
- Health care professionals should be aware that there are no interventions at present are proven to prevent or delay the onset of type 1 diabetes.
- Diagnostic difficulties that may delay diagnosis include:
  - The hyperventilation of ketoacidosis may be misdiagnosed as pneumonia or asthma (cough and breathlessness distinguish these conditions from diabetic ketoacidosis).
  - Abdominal pain associated with ketoacidosis may simulate an acute abdomen and lead to referral to a surgeon.
  - Polyuria and enuresis may be misdiagnosed as a urinary tract infection.

- Polydipsia may be thought to be psychogenic.
- Vomiting may be misdiagnosed as gastroenteritis or sepsis.

- The child with newly diagnosed type 1 diabetes needs to be cared for in a center with maximal expertise. At diagnosis, insulin treatment may need to be initiated prior to transfer.
- Parents and children with type 1 diabetes should be counseled that the remission phase of diabetes is transient and does not indicate total remission of diabetes.

TYPE 2 DIABETES

The initial treatment of type 2 diabetes mellitus (T2DM) should be tailored to the symptoms and severity of the clinical presentation, including assessment for diabetic ketoacidosis (DKA) and its appropriate care. Metformin is the initial pharmacologic treatment of choice, if insulin is not required for stabilization. Basal insulin, including neutral protamine Hagedorn insulin (NPH), can be used alone or with metformin when acute decompensation is present or if metformin is either not tolerated or ineffective. Both metformin and NPH are relatively inexpensive and widely available. Home glucose testing should be performed as appropriate to the clinical setting and as resources permit but is routinely required in youth with T2DM. Healthy lifestyle change focusing on healthy diet and increased physical activity are a critical component of treatment for T2DM. Care should be taken to implement culturally appropriate therapeutic lifestyle change. Blood pressure should be measured at each visit and other complications, such as albuminuria, retinopathy, dyslipidemia, non-alcoholic fatty liver disease (NAFLD), and polycystic ovary syndrome (PCOS) should be screened for at diagnosis and annually, when possible. Other general guidelines for the care of youth with T2DM should also applicable in areas in which resources and care may be limited.

DIAGNOSIS AND MANAGEMENT OF MONOGENIC DIABETES

Monogenic diabetes is uncommon, accounting for ~1% to 6% of pediatric diabetes cases. However, the diagnosis should be suspected in cases where:

- Diabetes presents in the first year of life, especially before age of 6 months.
- Absence of ketosis at diagnosis or subsequently during intercurrent illnesses.
- Preserved beta-cell function, with low insulin requirements more than 5 years after diagnosis.
- Presence of hearing, visual, or renal impairment. In particular, mitochondrial diabetes should be suspected in patients with diabetes and maternally inherited sensorineural hearing loss.
- Mild stable fasting hyperglycemia which does not progress.
- A family history of diabetes in one parent and first-degree relatives of that affected parent in patients who lack the characteristics of type 1 diabetes (note that monogenic diabetes may present as a spontaneous case due to a de novo mutation [ie, not inherited from parents]).
- Transient neonatal diabetes is usually diagnosed within the first week of life and resolves at around 12 weeks of age.
- Approximately half of neonatal diabetes cases diagnosed during infancy will require lifelong treatment to control hyperglycemia.
- Genetic testing should be considered in all children presenting with diabetes before 6 months of age, as it is available free of charge and its diagnosis may have major effects on treatment.
- Molecular genetic testing can help define the diagnosis and treatment of children with suspected monogenic diabetes. As these tests are expensive, genetic testing should be limited to those who on clinical grounds are likely to be positive.
- *HNF1A*-MODY is the first diagnostic possibility to be considered in familial autosomal dominant diabetes.
- Results of genetic testing should be reported in a clear and unambiguous way to ensure that both clinicians and patients receive adequate and understandable information, since results may have a major effect on clinical management **(E).**
- Some forms of monogenic diabetes are sensitive to sulphonylureas, such as *HNF1A*-MODY and HNF-4α MODY and many cases of permanent neonatal diabetes (Kir6.2 mutations).
- Mild fasting hyperglycemia due to glucokinase deficiency is not usually progressive during childhood but may require insulin during pregnancy (where an affected mother has an unaffected fetus and there is in utero evidence of accelerated growth).

CYSTIC FIBROSIS RELATED DIABETES

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatr Diabetes 2018: 19 (Suppl. 27): 64–74).

When analog insulin is not available, NPH insulin (eg, Humulin N, Protaphane, Novolin N, Insulatard, Isophane, etc) and regular/soluble insulin can be used to treat cystic fibrosis related diabetes (CFRD) but care needs to be taken to avoid late postprandial hypoglycemia. One possible regimen is NPH insulin at bedtime, and regular insulin with breakfast, lunch and supper, in a patient who is eating three meals and three snacks a day.

DIABETES EDUCATION

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatr Diabetes 2018: 19 (Suppl. 27): 75–83). Some particular aspects for countries with limited resources are pointed out below:

All children and adolescents with diabetes and their caregivers should have access to basic education and practical skills training to enable them to survive the onset of diabetes safely and successfully.

Initial learning should be started as soon as possible after diagnosis and should include immediate knowledge-based education and practical survival skills.

This should be followed by graduated levels of education reinforced whenever possible by diagrams, drawings, written guidelines, booklets, and other visual media appropriate to the child's age, maturity, and environmental circumstances.

Diabetes education must be given by someone with experience and expertise in pediatric diabetes management.

Appropriately adapted diabetes education at all ages must be centered on the needs and levels of understanding of both the child and parents/carers.

Diabetes education is most effective when based on self-management and needs to be child and parent-centered. However, peer education will also serve the purpose and can be part of the education program. Diabetes camps might be useful tools for structured diabetes education.

Who should deliver the message:

The education teams should consist of at least three disciplines. These may be a pediatric endocrinologist/diabetologist or a physician trained in the care of children and adolescents with diabetes, a diabetes specialist nurse/diabetes educator/pediatric nurse, and a dietician. However, involvement of a psychologist and a social worker is very important if available.

Since continuing education may not be possible in other setting like domiciliary and community, the education should take place where educational teams are available. If telemedicine is available this might be a tool to establish education despite geographical distances between patients and professional teams.

The topics to be covered at diagnosis and at the continuum of the curriculum, should consider this guideline. A questionnaire handed out to each patient/family might be helpful to make sure all topics were covered. This can be useful since there are always changes of caretakers and scheduled visits.

In case of hospital admissions occur, all of them should be reported and documented whether the admission was due to diabetes-related problems or not. Recurrent admission due to diabetes-related problems may need repetition of diabetes education.

Although carbohydrate counting might be difficult in some areas we would recommend distinguishing between carbohydrate containing food and other foods. Concerning the management of hypoglycemia, we would recommend Nutrition education and how foods effect glucose control (see chapter Nutritional Management).

DELIVERY OF AMBULATORY CARE

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatr Diabetes 2018: 19 (Suppl. 27): 84–104).

Great disparities exist in the level of pediatric diabetes care available to children, resulting from a wide range of factors across the world, from huge imbalances of geographic, economic, and scientific development to gender discrimination. Limited access to insulin, food and supplies, limited access to care, financial burdens, psychosocial instability, and detrimental health beliefs can all contribute to suboptimal care of children with diabetes across the world. For all children with diabetes, the importance of providing a good start with clear, positive messages, support, and advice cannot be overemphasized. In these settings it is imperative to establish, as early as possible, a systematic register of patients, demographics, and treatment records. Such data is vital in defining the problem and needs of this population to effectively advocate for these patients and their families. Programs are underway for this very purpose through organizations such as the Life for a Child and the Changing Diabetes in Children programs (see links to these organizations on www.ispad.org). Champions in the health care arena need to be identified and supported in their advocacy roles.

Access to health care can be a large challenge for poor children, more so in developing countries. Shortages of providers with diabetes expertise are widespread. For example, in Ethiopia, which is densely populated, there is only one pediatric endocrinologist for more than 40 million children.[1] In China, there are only 57 pediatric diabetes specialists and 47 pediatricians for 100 000 children in urban and rural areas, respectively. There are no data about the number of pediatric endocrinologists; multidisciplinary pediatric diabetes clinics are available only in China's leading children's hospitals. Sometimes lack of awareness means death before diagnosis, or soon after diagnosis.[2,3] Increasing awareness and education among health care personnel can help. Additionally, families can be put in touch with each other and can offer peer support and education. While there may not be in person access to the diabetes care team outlined in the core section, health care providers working with children with diabetes and their families need to provide self-management education and have regular follow-up. Communication between visits may rely more heavily on telephone calls. Community health workers may serve as an extension of the specialized diabetes care team, meeting with families and identifying areas that require attention outside of in-person follow-up.

More than half of the world's population is poor or extremely poor, and in large parts of the world, medical care is predominantly an out-of-pocket expense. Diabetes is an expensive condition to manage, and cost of diabetes care may be prohibitive without external support, for example, government support or health insurance. For example, in a study of factors associated with DKA in Ethiopia where the median monthly income was $37, the cost of insulin ($6/vial), blood glucose testing ($2/test), and HbA1c measurement ($13) created great hardship [3]. The treatment prescribed from the onset should be appropriate for the family's economic and educational status. Where costs are borne by the family, options to reduce costs should be explored, for example, conventional rather than analog insulins; syringes rather than pen devices; careful reuse of syringes and lancets; meters with inexpensive strips; families forming groups to enable bulk purchase of diabetes care supplies, obtaining supplies from donor organizations, etc.

Availability of insulin and diabetes supplies, such as insulin syringes, glucose meters, and glucose and ketone test strips, may be quite limited, particularly in remote areas. If the family does travel to urban centers for consultation, they can be encouraged to obtain enough quantities of insulin and supplies in the city. It is possible that the individual family may take greater care with transporting and storing insulin at the correct temperatures than vendors for whom this is a niche product with very little profit.

It is also important to address practical issues around home diabetes management. Safe disposal of “sharps” (needles, syringes, lancets)

must consider local conditions. If nothing else is available, parents can be asked to collect all sharps in a thick-walled metal or plastic container (eg, shampoo bottle) and bring them on each visit to the clinic for safe disposal.[4] Insulin cannot be exposed to extreme temperatures, as described in the main chapter.

Food can be in scarce supply, and not all children have food on a daily basis. It is in such situations that multidose modified basal bolus regimens are very useful. The child can take small doses of NPH insulin once or twice a day, and regular insulin only when food is eaten, the dose depending on the amount of food available. Diet in families with low socioeconomic status may be high in fats, trans-fats, salt, and processed (low fiber) carbohydrates. Parents are encouraged to use whole grains, for example, partly polished rather than white rice, home baked bread rather than bread bought from the market, low fat milk and milk products (usually less expensive than full fat), salads instead of oily cooked vegetables, fresh fruit and roasted rather than deep fried snacks; such foods are often less attractive than heavily advertised sweetened (or diet) drinks and crisps. Intensive education and innovation may be necessary to address such situations.

International programs such as Life for a Child, Changing Diabetes in Children (CDiC) and Insulin for Life can alleviate resource shortages to a limited extent, and stability and consistency of providing these resources is essential. It may be more feasible and sustainable to motivate local governments and charitable organizations to help, with greater awareness of the problem. In Bangladesh, it has been shown that public health measures can make a big difference in diabetes care. Unfortunately, low costs options are often ignored by health care providers, corporations, and government.

Diabetes education typically uses written materials and numerical insulin dose calculations. When children and their caregiver(s) have limited literacy and numeracy, different approaches are needed. For example, the majority of Ethiopians have little or no education and females are less educated than males.[5] Females are usually the ones who are giving diabetes care, and because females are less educated this will have a negative impact on the care provided. Even relatively simple tasks such as reading and recording blood glucose values and insulin doses may be difficult. Pictorial educational materials and simple instructions are essential for illiterate families. Innovative measures can be used, such as teaching the mother or child to draw the numbers because they cannot write them, providing premarked syringes (wrapped with colored tape to mark the dose), and using color coding to designate doses of insulin based on proximity of glucose reading to target range. Somewhat similar is the problem of multiple languages or dialects: educational and instructional materials may not be available in the local language. In these circumstances, self-help support groups can be of great value when available.

Poverty significantly increases vulnerability because it tends to be associated with illiteracy or poor education, social deprivation, little or no job security, and inadequate access to health care or institutional support. In many countries families must assume the cost of health care. The expenses incurred with a chronic disease can push a family further into poverty. Such families are then also at higher risk for discrimination. These children tend to have poor glycemic control, and therefore higher rates of acute and chronic complications and mortality. This worsens employability, income, cost of care, and quality of life. In extreme cases, insulin may be stopped due to financial stresses or gender discrimination. In such circumstances, support groups can play a significant role in improving care and even survival. Parents getting even minimal financial support and seeing older well-controlled patients who are successfully educated, working, married, etc. are motivated to look after their own child better.

On the positive side, many developing countries have robust family structures. Support may come from the extended family or community. Compliance may actually be better because of social conditioning to follow instructions, and provision of free or subsidized diabetes care supplies. Availability of "junk foods" may be limited and physical activity levels may be higher. Establishing a trusting relationship with good communication should allow for identification of the child's and family's resources and challenges, so that they can be successful in managing their diabetes.

ASSESSMENT AND MONITORING OF GLYCEMIC CONTROL IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS WITH DIABETES

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatric Diabetes 2018: 19 (Suppl. 27): 105–114).

In situations where care is limited by a lack of resources, including insulin, equipment for self-monitored blood glucose, and HbA1c measurements, targets for assessing and monitoring glycemic control in children with diabetes may need to be adjusted.

- Every effort should be made to continually improve approaches to optimize quality of care.
- Glucose monitoring is very expensive. We recognize that in many countries the cost of these assessments relative to the cost of living may make this technology unavailable.
- All centers caring for young people with diabetes should urge nations, states, and health care providers to ensure that children and adolescents with diabetes have adequate glucose monitoring supplies.
- Testing 3 to 4 times a day several days a week provides more information than a single daily measurement.
- The creative use of self-monitored blood glucoses (BGs) to provide a profile of glucose over a typical day or days will help to adjust doses of insulin; for example, BG checking before and after a standard meal can help to adjust meal-related insulin dose with only two extra tests per day. In this fashion, different meals can be assessed over different weeks. Intermittently scanned continuous glucose monitoring (isCGM) devices may also be available at lower cost than traditional meter-based testing and do not require calibration.
- Urine glucose monitoring is an alternative where there are cost considerations. It provides useful but different information from self-monitored BG. Urinary glucose reflects glycemic levels over the preceding several hours and is affected by the renal threshold for glucose, which in children is approximately 10 to 11 mmol/L (180-200 mg/dL).

  Limitations of urine glucose monitoring include.

- uncertain correlation with BG levels;

- inability to detect hypoglycemia or monitor response to treatment of hypoglycemia;
- less valuable as an educational tool to identify glycemic patterns; and unhelpful in hyperglycemic crises because of the lag phase between recovery and changes in urine glucose.

Target

- As many urine tests as possible should show no glycosuria without the occurrence of frequent or severe hypoglycemia.

Equipment

- Glucose oxidase strips that are relatively inexpensive, convenient, and safe.
- Some non-specific reducing agent methods are used such as Clinitest tablets or Benedict's test. These are less convenient to use and are also potentially dangerous if the chemical reagents come into contact with the skin, esophagus, or gastrointestinal tract.
- Frequency of HbA1c measurement will depend on local facilities and availability; however, every child should have an absolute minimum of one measurement per year.
- Adolescents with stable type 2 diabetes should have at least one HbA1c measurement per year and symptoms of uncontrolled diabetes reinforced frequently since adolescents generally become insulin-requiring more rapidly than adults.

INSULIN THERAPY

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatr Diabetes 2018: 19 (Suppl. 27): 115–135).

- Insulin should be available in sufficient amounts, being consistent in quality and type.
- Use syringes and vials for insulin administration (or pens, if available).
- The principles of insulin use including professional support, are as for Recommended care, but a combination of NPH and Regular insulin may give acceptable blood glucose control.
- Regular and NPH insulin may be mixed in the same syringe, given as premixed insulin or given as separate injections.
- A basal bolus regimen with Regular and NPH is preferred to premixed insulin preparations. NPH insulin should be given twice daily in most cases, in addition, Regular insulin needs to be given 2 to 4 times daily to match carbohydrate intake.
- Premixed insulins may be convenient (ie, few injections), but limit the individual tailoring of the insulin regimen, and can be difficult in cases where regular food supply is not available.
- Insulin storage as for Recommended care.
- In hot climates where refrigeration is not available, cooling jars, earthenware pitcher (matka), or a cool wet cloth around the insulin will help to preserve insulin activity.
- In children on small doses of insulin, 3 mL cartridges instead of 10 mL vials should be chosen for use with syringes to avoid wastage of insulin.

NUTRITIONAL MANAGEMENT

Children and adolescents with diabetes should eat a variety of healthy foods, including fruits, vegetables, dairy, wholegrains, legumes, and lean meat in amounts appropriate for age, stage of growth, and energy requirements.

Growth monitoring is an essential part of diabetes management. Unexpected weight loss or failure to gain weight appropriately may be a sign of: (1) illness (infections, celiac disease), (2) insulin omission, (3) an eating disorder, or (4) issues with food security.

An experienced pediatric dietitian should be available as part of the diabetes team to provide education at diagnosis and at regular review.

Nutritional advice should be adapted to cultural, ethnic, and family traditions as well as the cognitive and psychosocial needs of the individual child. Where possible all relevant family members should be involved in education.

Intensive education should be offered on the need to couple the preprandial insulin dose with carbohydrate amount. Insulin should be given before the meal. Alternatively, for those on fixed insulin doses, a consistent day-to-day intake of carbohydrate should be consumed to match the timing and type of insulin injections. This advice should be regularly reviewed to accommodate changes in appetite, food availability, and physical activity.

Carbohydrate intake is often >50% energy in limited care settings due to food traditions and the cost of high protein foods. Restriction of carbohydrate intake <45% of total energy requirement should be avoided as this may impair growth (For further reading please refer to Nutrition Chapter ISPAD Guidelines 2018).

To enable appropriate matching of carbohydrate intake to the insulin profile, carbohydrate may be measured in grams, portions, or exchanges. A variety of educational tools are available in many countries to assist health professionals and families understand healthy eating concepts, such as the healthy plate model and to enable carbohydrate quantification.

Prevention and management of hypoglycemia, particularly during and after exercise should be discussed.

Drinks high in sugar and foods with high amounts of saturated fat should be generally avoided.

If financial constraints make food scare or erratic, this is an added burden that should be discussed openly, and potential solutions identified.

DIABETIC KETOACIDOSIS AND HYPERGLYCEMIC HYPERSMOLAR STATE

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatr Diabetes 2018: 19 (Suppl. 27): 155–177).

1. Written guidelines should be available for DKA management in children.
2. Weigh the child.
3. Immediately infuse 10 mL/kg of 0.9% saline as an initial bolus, and bolus may need to be repeated until tissue perfusion is adequate. Thereafter, replace fluid deficit over 24 to 48 hours and provide the maintenance fluid requirement. If unable to obtain

intravenous (IV) access in a severely dehydrated patient, consider intraosseous fluid administration.

4. Subsequent fluid management (deficit replacement) can be accomplished with 0.45% to 0.9% saline or a balanced salt solution (Ringer's lactate, Hartmann's solution, or Plasmalyte). The sodium content of the fluid should be increased if measured serum sodium concentration is low and does not rise appropriately as the plasma glucose concentration falls.
5. Potassium: If IV fluids and insulin are available, but potassium is not available, after 1 hour of fluid therapy, give a dose of insulin subcutaneous/intramuscular (IM), 0.1 unit/kg (0.05 unit/kg if child is younger than 5 years), and then arrange urgent transport to a facility that can provide potassium. If serum potassium measurements are not immediately available, an electrogardiogram (ECG) may be helpful to determine whether the child has hyperkalemia or hypokalemia. Prolongation of the PR interval, T-wave flattening and inversion, ST depression, prominent U waves, apparent long QT interval (due to fusion of the T and U waves) indicate hypokalemia. A tall, peaked, and symmetrical T-wave is the first sign of hyperkalemia.
6. Insulin: Do not use IV insulin if BG levels cannot be measured at least every 2 hours. In circumstances where continuous IV administration of insulin is not possible, give IM short-acting insulin (regular) or rapid-acting insulin analogue (insulin lispro, aspart, or glulisine) 0.1 unit/kg (0.05 unit/kg <5 years) every 1 to 2 hours until tissue perfusion has improved. Thereafter, switch to the same dose of SC regular insulin or rapid-acting insulin analogue every 1 to 2 hours, which may be as effective as infusion of IV regular insulin in patients with uncomplicated DKA.
7. When BG is <14 mmol/L (250 mg/dL), give glucose-containing fluids orally and consider reducing the dose of SC insulin from 0.1 to 0.05 unit/kg (or from 0.05 to 0.025 unit per kg) at 1- to 2-hour intervals aiming to maintain BG ~11 mmol/L (200 mg/dL) until complete resolution of DKA.
8. IV fluids: When IV fluids are not available, arrange urgent transport to a facility that can provide IV fluid therapy. Giving insulin before starting IV fluid treatment may precipitate shock and increases the risk of hypokalemia and cerebral edema.
9. Give small sips (or small volumes through a syringe) of oral rehydrating solution (ORS) as frequently as possible without causing the child to vomit. If vomiting does not occur after 1 to 2 hours, give ORS at a rate of 5 mL per kg body weight per hour.
10. In some cases, it may be possible to insert a nasogastric tube and slowly rehydrate with ORS at 5 mL per kg body weight per hour.
11. If ORS is not available, fruit juice and coconut water provide some potassium.
12. Transportation: If the child cannot be transported (eg, roads are blocked), give oral rehydration as above and IM/SC insulin 0.1 to 0.05 unit/kg every 1 to 2 hours. Decreasing urine ketone concentrations indicate resolving acidosis.
13. Laboratory resources: Hourly BG monitoring may not be available. Try to measure BG level at least every 4 hours. If analysis of acid-base status is not available, a bedside blood beta-hydroxybutyrate (ketone) value ≥3 mmol/L together with BG >11.1 mmol/L (200 mg/dL) can be used to confirm the diagnosis of ketoacidosis and monitor the response to treatment.

ASSESSMENT AND MANAGEMENT OF HYPOGLYCEMIA IN CHILDREN AND ADOLESCENTS WITH DIABETES

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatr Diabetes 2018: 19 (Suppl. 27): 178–192).

In many regions of the world, there are several issues which make management of hypoglycemia a daunting process in a child with type 1 diabetes.

Risk factors

A significant risk factor is the lack of a regular or sufficient supply of food. A child who has received a prescribed dose of insulin may suddenly be faced with either no food or a smaller portion which will not be commensurate with the amount of insulin given. Many children, both with and without diabetes, go to bed hungry, therefore nocturnal hypoglycemia is common. For every child with newly diagnosed diabetes, it is mandatory that the child and caregiver are trained in recognizing the signs and symptoms of hypoglycemia before leaving the hospital. However, due to limited availability of resources, in many cases, blood glucose monitoring is performed once or twice a day and may not be readily available to the child when symptoms suggestive of hypoglycemia arise. Severe hypoglycemia is therefore likely to occur at a much higher incidence than that reported in the literature. There may also be a cultural stigma regarding diabetes in children which prevents families advising the school, other family members, or neighbors that their child has diabetes. Therefore, when the parent is not with the child, hypoglycemia can have severe or even fatal consequence. In many regions of limited care, another cause for hypoglycemia is the use of 70/30 premixed insulin which does not allow for flexibility in diet or exercise. A lack of awareness of diabetes in children makes it difficult for a child with hypoglycemia to obtain immediate help.

Management

Management of hypoglycemia is particularly challenging when there is limited access to medical care. Glucagon is not readily available, and the expense may be prohibitive. Empirical treatment is usually given due to unavailability of glucose meters and strips to confirm hypoglycemia as well as the urgency to treat. In countries where neither glucagon nor glucose gel may be available; a powder form (glucose D 25 or anhydrous glucose) is used. Honey is a good alternative but may not be readily available. Another option is products derived from cane sugar to which sucrose may be added. However, if the child is semi/unconscious, sugar or any other powdery substance or thin liquids like a glucose solution or honey should not be given forcibly to the child. The child should be put in a lateral position to prevent aspiration and a thick paste of glucose (glucose powder with a few drops of water or table sugar crushed into powdered sugar with consistency of thick

cake icing) smeared onto the dependent cheek pad; the efficacy of this practice is anecdotal. In situations where there is a danger of aspiration with no IV access available, parenteral glucose solutions may be administered via nasogastric tubes. In most cases, 5% glucose in water or in 0.9% NaCl is available and medical personnel are encouraged to use these infusions. Occasionally only 0.9% NaCl and 50% glucose are available, and practitioners are encouraged to reconstitute instead of giving multiple repeated boluses. Add 100 mL of 50% glucose to 900 mL of 0.9% NaCl to make a 5% glucose solution.

SICK DAY MANAGEMENT

The diabetes care team should prepare brief and easy-to-understand handouts in the local language(s) to ensure families have clear guidance on how to manage diabetes during intercurrent illnesses and how to contact the diabetes team when any management problems or questions arise. With widespread availability of mobile phones, families can receive reminders of key messages during seasons of viral illnesses, with potential to direct messages to those in poor glycemic control or a history of DKA. Seasons with extreme temperatures can also be times of concern. During the summer months, diarrheal illnesses and dehydration are common. As summers become more extreme across the globe, they can be times when glycemic control may deteriorate due to poor storage and transport of insulin in the heat. Families paying out of pocket may be hesitant to discard insulin or to increase doses if it has become less effective. So, families should be reminded to purchase insulin only from reliable sources, to carry a thermos or other cooling device when going to purchase insulin and during travel, and to store it properly at home.

As type 1 diabetes is less common than infections and other diseases, it is often a lower priority for health centers and health care professionals, who may have inadequate knowledge about diabetes management. Therefore, the diabetes care team may need to inform families on how to cope with poorly informed health systems. For example, if the nearest health center provides only primary care, families should be encouraged to carry their sick day instruction handout with them to share the information with the local nurses and other health care workers.

Families should also receive instructions on how to use blood glucose strips for frequent monitoring during illnesses, even if such monitoring is usually not done routinely due to costs. Families should also receive guidance to keep urine ketone strips at home and receive education on how and when to use them (as limited resources prevent use of the more expensive blood monitoring supplies). Although urine ketone strips are inexpensive, they can deteriorate quickly after being opened and especially when exposed to humidity. It may be possible for groups of families to form networks to "share in the expense" of blood ketone strips, if available, in order to use them at times of illness, and to bring them to the health center in case of emergency. As availability of blood ketone strips may be problematic, diabetes care teams may need to be involved in arranging access to families. The costs of blood ketone strips are likely greater than the costs of blood glucose strips and urine strips, but such costs are less than the costs of transport to hospital and inpatient care.

When ketone testing is not available

It is strongly recommended that some form of ketone monitoring be available. However, in some circumstances, no ketone testing may be available or affordable during an intercurrent illness. In these situations, it is critical to emphasize the importance of frequent blood glucose monitoring in order to avoid progression to DKA and need for hospitalization. It can be helpful to provide written recommendations in advance of illness that outline how much additional insulin to give for particular blood glucose levels, based on the child's total daily dose (TDD) or weight. One should also emphasize that the child should be brought to hospital if hyperglycemia persists despite extra insulin and fluids, the child looks ill, or there is persistent vomiting or rapid breathing, as DKA may be developing.

Managing at a temporary facility

If a sick child is referred to a temporary facility or primary care center without IV access prior to transfer to a full medical facility, slow fluid administration can be given carefully through a nasogastric tube until IV access is available. Subcutaneous regular insulin given every 4 hours has been shown to effectively and safely manage children with pH >7.0.[6] If blood gas testing is not available, serum bicarbonate concentration can be used in lieu of venous pH as an accurate predictor of the severity of DKA.[7]

EXERCISE

Ideally, the child or adolescent should know his/her blood glucose values before and after participating in physical activity. If blood glucose monitoring is not possible, the advice is to participate in lower intensity activity at same time every day. All activities should include eating a snack, for example, a fruit, biscuits (10-15 g of carbohydrates), or a sandwich every 30 minutes during activity.

Physical activity should be limited/ avoided if:

- There is an acute illness.
- Blood glucose is too low, <5 mmol/L (90 mg/dL) or too high, >14 mmol/L (252 mg/dL) before the activity.
- There is inadequate food for compensation of low blood sugars and the duration of activity.
- Ketones are present at a level >0.6 mmol/L (blood) or presence of urine-ketones which first would require actions with extra insulin and/or added carbohydrates depending on the reason for the ketosis.
- Patient is dehydrated.

Practical recommendation to the child with diabetes:

- Talk with your doctor or diabetes educator before starting any new exercise regimen or changing the time of your activity.
- Your doctor will let you know about any changes in testing schedule, medication, or other things you might need to pay attention about for exercise and sports.
- You may need to test more frequently for first few days and adjust your insulin accordingly. So, make sure you have enough supply of glucose test strips and strips for urine ketones.

- Make sure you are wearing an ID bracelet or similar that says you have diabetes and have an emergency contact number.
- Avoid taking injections in the part of the body most used in that sport (like injecting in the thigh right before playing cricket). The abdominal site is probably preferable for injection, for absorption of insulin during exercise.
- Moderate exercise in (enough to make you puff) uses an extra 10 to 15 g of carbohydrate each hour. Vigorous exercise may use 2 to 3 times this amount. Do check blood glucose after 30-60 minutes after moderate-vigorous exercise. The usual signs of hypoglycemia are often not easy to discern during exercise.
- It is always advised to tell the coaches and playmates about your diabetes and give them written instructions so that they can respond to your hyperglycemia on the ground.

Always carry a bag pack with you having the following:

- Glucose tablets or similar or a juice box.
- A sandwich or some other healthy snack.
- Your glucose meter and supplies.
- A big bottle of water.

MANAGEMENT OF CHILDREN WITH DIABETES REQUIRING SURGERY

Management of children and adolescents with diabetes requiring surgery in resource limited countries.

1. Whenever possible follow the guidelines described in the full chapter for recommended care.
2. Children with type 1 diabetes requiring major surgery should be referred to a center with sufficient resources to provide safe care (including but not limited to: infusion pumps, insulin analogues, blood gases, urea and electrolytes, and bedside glucometers).
3. Elective surgery should be scheduled as the first case of the day, preferably in the morning.
4. Children with type 1 diabetes requiring surgery need insulin, even if fasting, to prevent ketoacidosis. At least half of the usual basal insulin dose should be given before surgery.
5. Insulin can be infused using burettes connected to IV fluids bags and adding 50 to 100 units of regular insulin to 50 to 100 mL of 0.9% sodium chloride (1 mL = 1 unit) and given on a separate line or with a Y-connection, that should be changed every 6 hours.
6. Alternatively, insulin can be given subQ hourly in the same dose as the infusion. NPH insulin given once or twice can give a good basal dose.
7. Children undergoing major surgery (expected to last at least 2 hours) or who have received NPH insulin should receive dextrose in their IV infusion to prevent hypoglycemia. Children undergoing minor surgery or procedures (lasting for less than 2 hours) may initially receive an IV infusion without dextrose if treated with basal/bolus insulin regimen or continuous subcutaneous insulin infusion.
8. Blood glucose monitoring should be performed before, during and immediately after general anesthesia to detect hypo- and hyperglycemia. Aim for blood glucose in the range 5 to 10 mmol/L (90-180 mg/dL) during and for 7.8-10 mmol/L (140-180 mg/dL) after surgery.
9. In absence of blood gases use urine ketone in freshly voided urine and in case of general anesthesia a temporary urinary catheter can be used.
10. Where there are no facilities for urea and electrolytes, use clinical signs of hydration status and urine output and avoid adding potassium if patient is oliguria. If no glucometer available use (fresh) urine glucose to monitor the patient. If no facilities for IV fluids use oral rehydration solution.
11. The usual recommendation is no solid food for at least 6 hours before surgery. Clear fluids and breast milk may be allowed up to 4 hours before surgery (check with the anesthetist).
12. Emergency surgery:

a. If ketoacidosis is present, follow an established treatment protocol for diabetic ketoacidosis and delay surgery, if possible, until circulating volume and electrolyte deficits are corrected.
b. If there is no ketoacidosis, start IV fluids and insulin management as for elective surgery.

PSYCHOLOGICAL CARE OF CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatr Diabetes 2018: 19 (Suppl. 27): 237–249).

The principles and recommendations in the full chapter are largely generic and therefore should apply to all health care settings irrespective of the resources available.

- Diabetes care for young people should include the recognition of the potentially serious impact of diabetes on both psychosocial functioning in the child, adolescent, and the family and also the adverse effects on metabolic control.
- Professionals caring for young people with diabetes should be prepared to discuss the psychological difficulties associated with diabetes (including depression, acting out, rebellion) and have access to other professionals with more specialist expertise in this field.

ADOLESCENCE

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatr Diabetes 2018: 19 (Suppl. 27): 250–261).

The principles and recommendations in the full chapter are generic and therefore should apply to all health care settings irrespective of the resources available. Understanding the physiological and psychological changes of adolescence and developing a specific

approach to the communication, education, and support of the adolescent patient and their family, which is sensitivity to their needs, cultural and religious background, is essential. It is acknowledged that many patients and families with diabetes come from a low-income background and are cared for in health care systems that are significantly resource limited. Nevertheless, the approach to managing the adolescent with diabetes in terms of developing trusting and motivating relationships with them, encouraging self-reliance and self-efficacy, and engendering the trust and support from their family are general ones that should be applicable to all settings.

MICROVASCULAR AND MACROVASCULAR COMPLICATIONS IN CHILDREN AND ADOLESCENTS

Prevention

- Intensive education and treatment should be used in children and adolescents to prevent or delay the onset and progression of vascular complications.
- Screening for complications should be performed preconception and each trimester of pregnancy.

Albuminuria

- Screening for albuminuria should start from age 11 years with 2 to 5 years diabetes duration using a first morning urine samples for urinary albumin/creatinine ratio (ACR).
- Because of biological variability, two of three urine samples should be used as evidence of albuminuria. Confounders are exercise, menstrual bleeding, infections, fever, kidney diseases, and marked hyperglycemia. Abnormal screening tests should be repeated, as albuminuria may be transient.
- Angiotensin converting enzyme inhibitors or angiotensin receptor blockers agents should be used in adolescents with persistent albuminuria to prevent progression to proteinuria

Retinopathy and other ocular conditions

- Screening for diabetic retinopathy should start from age 11 years with 2 to 5 years diabetes duration and should be performed by an ophthalmologist, optometrist, or a trained experienced observer through dilated pupils via bio-microscopy examination or fundal photography.
- A comprehensive initial eye examination should also be considered to detect cataracts, major refractive errors, or other ocular disorders.

Neuropathy

- Screening for peripheral neuropathy should start from age 11 years with 2 to 5 years diabetes duration and annually thereafter.
- Specific and simple tests to evaluate diabetic neuropathy include assessment of sensation, vibration, and reflexes in the feet for peripheral neuropathy.

Blood pressure

- Blood pressure (BP) should be measured at least annually. angiotensin-converting-enzyme inhibitor (ACEI) are recommended for use in children with diabetes and hypertension, which is defined in children as BP equal to or above the 95th percentile for age, sex, and height, and in adolescents (age ≥13 years) as systolic blood pressure (SBP) ≥130 and/or diastolic blood pressure (DBP) ≥80 mm Hg.

Lipids

- Screening for dyslipidemia should be performed soon after diagnosis (when diabetes stabilized) in all children with type 1 diabetes from age 11.

Lifestyle

- Prevention or cessation of smoking will reduce progression of albuminuria and cardiovascular disease.

Type 2 diabetes

- Complications screening should commence at diagnosis. Attention to risk factors should be escalated because of the increased risk of complications and mortality.

OTHER COMPLICATIONS AND DIABETES-ASSOCIATED CONDITIONS IN CHILDREN AND ADOLESCENTS

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatr Diabetes 2018: 19 (Suppl. 27): 275–286).

- Regular monitoring of anthropometric measurements and physical development, using growth standards, are essential in the continuous care of children and adolescents with type 1 diabetes.
- Screening of thyroid function by measurement of thyroid stimulating hormone (TSH) and antithyroid peroxidase antibodies is recommended at the diagnosis of diabetes and, thereafter, every second year in asymptomatic individuals. More frequent assessment may be indicated in the presence of symptoms, goiter or positive thyroid autoantibodies.
- The diagnosis of hypothyroidism is confirmed by demonstrating a low free thyroxine (T4) level (or if not available, total T4) and a raised TSH concentration.
- Screening for celiac disease should be performed at the time of diabetes diagnosis, and at 2 and 5 years thereafter, as it is frequently asymptomatic. More frequent assessment is indicated if the clinical situation suggests the possibility of celiac disease or the child has a first-degree relative with celiac disease. Screening for IgA deficiency should be performed at diabetes diagnosis.

- Children with type 1 diabetes detected to have positive celiac antibodies on routine screening, should be referred to a pediatric gastroenterologist. If small bowel biopsy is not possible in a child with positive screening tests, then a trial of a gluten-free diet is recommended if celiac disease is suspected. Response should be determined from improvement in growth, bowel habit and reduction in titer of screening antibodies.
- Upon confirmation of the diagnosis of celiac disease, patients should receive educational support from an experienced pediatric dietitian. Educational materials (translated into local language) for patients and families should be made available.
- Diabetes care providers should be alert for the symptoms and signs of adrenal insufficiency (due to Addison disease) in children and adolescents with type 1 diabetes although the occurrence is rare.
- Routine clinical examination should be undertaken for skin (eg, lipodystrophy) and joint changes (eg, limited joint mobility).
- Patient education regarding proper injection techniques, rotating injection sites with each injection and non-reuse of needles remain the best strategies to prevent lipohypertrophy/lipoatrophy.
- Injection sites should be regularly assessed at each clinic visit for lipohypertrophy and lipoatrophy as they are potential causes of glucose variability.
- Screening for vitamin D deficiency, particularly in high risk groups (eg, darker skin pigmentation, covered clothing, celiac disease) should be considered in young people with type 1 diabetes and treated using appropriate guidelines.

TODDLERS

Whenever possible, the guidelines described above in the preceding sections should be followed. It is important to remember that building a good rapport with the family and providing comprehensive diabetes education are inexpensive and remain the most effective strategies to improve diabetes management by the family. Knowledge about the effects of insulin, food, and physical activity on glucose levels are essential to protect the child from acute and chronic complications of diabetes under all circumstances. The first few visits of the family are the most crucial in this regard. Initial approach to diagnosis and treatment is based upon staffing and facilities at specialized centers for the care of young children with diabetes, with many centers recommending hospitalization. Parents should be counseled and educated in detail. The challenges in managing type 1 diabetes in the preschool child are several-fold higher in resource-limited settings. Awareness, health infrastructure, and number of medical professionals trained in the management of childhood diabetes are inadequate for a significant proportion of the population in many countries in South East Asia and sub-Saharan Africa. The diagnosis is often delayed, and may even be missed in some cases, resulting in death before diagnosis. Common misdiagnoses are gastroenteritis, pneumonia, asthma, urinary tract infection, genital tract infection (candidiasis), enuresis, and malaria. Parents may take longer to come to terms with the diagnosis and the need for lifelong insulin therapy. The financial implications of the condition add to the psychological distress brought about by the diagnosis. Risk of acute and chronic complications, as well as mortality, is higher in these children due to suboptimal management. In the United States, young people of African descent have increased risk of short-term complications (ketoacidosis and severe hypoglycemia) when adjusted for socioeconomic status, and higher HbA1c even when adjusted for mean glucose levels. HbA1c was higher even when fasting glucose is insulin dosing, and to use self-monitoring of blood glucose (SMBG) at least on sick days if available. With limited number of strips, the family can, for example, measure before and 2 hours after lunch 1 week, and before and after dinner the next to get a more stringent picture of the day compared with random checks. Urine strips should be available for ketone monitoring during sick days. Another issue that may compound the challenge in resource-limited settings is that some parents may have low levels of literacy and health literacy, meaning thereby that they cannot read the numbers on the insulin syringe and on the glucometer. For example, in India, literacy rate is 74.04% according to the 15th official census in 2011 (http://www.census2011.co.in/literacy.php). In such cases, it is helpful to identify a suitably literate relative, friend or neighbor who can undergo diabetes education along with the parents and assist them in the domiciliary management. The parents should also be encouraged to learn the basics of reading and writing. In the case of low literacy, a simpler insulin regime such as twice daily dosing with premixed insulin can be given. Hearing the number of clicks from an insulin pen can obviate the need to read the number of units. Teaching the parents to recognize “Hi” and “Lo” on glucometer, to treat hypoglycemia based on symptoms alone, and to recognize hyperglycemia and ketonuria by urinary strips is also useful to prevent life-threatening episodes. Vomiting in a child with diabetes should always be regarded as imminent ketoacidosis, and appropriate treatment should be sought immediately in the absence of knowledge and diagnostic measurements. If the child is not feeling well with other symptoms, the first line of treatment should be something containing sugar to treat impending hypoglycemia. This should be well known by all the older children and adults who are close to the child with diabetes, and they should know where to readily find a source of sugar. To conclude, the goals of management of type 1 diabetes in resource-limited settings must be situated in the context of the resource-limited environment and based on the family's educational and financial status. Avoidance of acute life-threatening complications and continuation of regular treatment and follow-up are the immediate goals.

MANAGEMENT AND SUPPORT OF CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES IN SCHOOL

T1D is both challenging and demanding and, wherever children live in the world, sending their child to school is a very anxious and daunting time for parents, carers and also for the child with diabetes.

In less-resourced settings this can be compounded by other issues such as lack of insulin and diabetes supplies, food insecurity, transport challenges, and even local conflict and war.

School is a time of learning, making friends, having fun, and finding peer groups. However, for children with diabetes, this can instead be a time when they are excluded or isolated or stigmatized.

As health professionals caring for these vulnerable young people, we must ensure as best we can that they receive the same educational opportunities as other children in their community, providing the potential for fruitful employment and the chance for further education.

Key messages for teachers in less-resourced countries:

- Children with diabetes, wherever they live, should not be limited in what they can do, and should be able to attend school, receive an education and live happy, fulfilled lives.
- Most schools are very supportive; however, a child's nurse or doctor can visit the school to explain diabetes and its management in a clear and concise manner, or a parent or carer might feel confident enough to do this themselves with support from the local team. Such visits and contact with the school and the health professional can be extremely encouraging to parents and children.
- A simple individualized management plan for the child with diabetes is a good guide for the teacher to follow day-to-day at school. This should include step by step instructions for management of emergencies and contact details of parents/carers.
- Many children may be on a twice daily insulin regimen; however, if they are on multiple daily injections which entails a lunch-time injection at school, a safe, private place is required for them to give their injection.
- A refrigerator or cool place/container (eg, clay pot) is required for storage of insulin particularly in hot climates.
- Children with diabetes should be allowed to test their BG level as necessary depending on availability of test strips.
- School personnel should be educated on the management of hypoglycaemia, and parents should ensure that appropriate treatment and re-treatment is available at the school.
- Emergency assistance should be called if the child is unable to eat or drink to treat the hypoglycemia.
- School personnel need to be aware that prior to and during physical activity the child with diabetes may need to eat or drink to avoid hypoglycemia.
- When blood glucose levels are high (hyperglycemia), children should be allowed to drink water, and use the toilet as necessary.
- Teachers should be aware that other children may tease the child with diabetes. Simple explanation to classmates is encouraged.
- Teachers should also understand the classic symptoms of T1D, so they can identify undiagnosed children in the future. It is not at all uncommon for T1D to be mistaken for malaria, appendicitis, and pneumonia in countries with less resources. Posters have been developed in local languages highlighting the symptoms of T1D, and the signs of diabetic ketoacidosis.

The International Diabetes Federation (IDF) "Life for a Child" initiative has developed an education website that includes resources for schools. Also, the IDF "Kids and Diabetes in School" (KiDS) project tackles diabetes (including types 1 and 2 diabetes, and healthy food choices and lifestyle advice) management in school by the development of visual materials, coupled with an education program for school personnel, parents, and children. This project was successfully trialed in Brazil and India and is now available in multiple languages.

DIABETES TECHNOLOGY

Whenever possible, follow the guidance described in the full chapter for recommended care (Pediatr Diabetes 2018: 19 (Suppl. 27): 302–325).

- In resource limited areas, cell phones may allow patients to utilize diabetes applications to assist with their care.
- Integration of bolus calculators that are available through commercial blood glucose meters or accessed on a cell phone may assist with more precise insulin dosing, which may assist patients in achievement of targeted glycemic control.
- Use of CGM, where available, may serve as a replacement for SMBG and provide retrospective data review to allow for more fine-tuned insulin doses adjustment recommendations.
- Automated decision support systems may help patients optimize their insulin regimens, regardless of whether the insulin delivery modality is via injection or pump therapy.
- As provider availability is critical to improve health care accessibility, use of telemedicine may allow patients in rural areas to have consultations with subspecialists.
- Local clinicians can also be assisted with management of complex conditions through tele-mentoring through consultation with a specialist.

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