Abstract
Diabetes does not spare any section of society, and its prevalence in the paediatric and adolescent age group is rising. This review highlights the etiological and clinical features of childhood diabetes, including secular changes in epidemiology. It discusses the aspects of non pharmacological and pharmacological therapy which are unique to the paediatric age group, and explores current use of novel therapeutic modalities. The article calls for modulation of the psychological environment of the child with diabetes, to help improve his or her quality of life, and sensitizes physicians to take proactive, affirmative action to address the special needs of children with type1 diabetes.

Keywords: Diabetes, Paediatric, Adolescent, Pharmacological therapy.

Classification
Traditionally, diabetes in children was thought to be exclusively type 1 or insulin dependent, in nature. With changing environmental and dietary habits, however, type2 diabetes has begun to occur earlier and earlier, especially in South Asian and in obese children. Paradoxically, malnutrition- related diabetes mellitus (MRDM), a supposedly extinct entity, continues to survive in many paediatric diabetes clinics, under eponyms such as ketosis- resistant diabetes of the youth (KRDY). Another type of diabetes, well documented in adolescents and young adults of African and Punjabi descent, is type 1.5 diabetes (one and a half diabetes). Characterized by an explosive insulin- requiring onset, followed by an indolent course with control on oral hypoglycemics and lifestyle modification, type 1.5 diabetes needs to be recognized in order to plan appropriate management. One famous personality with type 1.5 diabetes is the American actor Halle Berre.

Environmental factors such as cow’s milk, nitrosamines and Vitamin D deficiency are linked with the development of TIDM. Studies suggest a protective role for camel’s milk in the management of type 1 diabetes.

Diagnosis
The diagnostic criteria for paediatric diabetes are the same as for non- pregnant adults. A fasting glucose of ≥126mg% and a postprandial or casual value of ≥200mg is diagnostic of diabetes, if confirmed at least twice, by venous sampling. HbA1c (glycated haemoglobin) is now proposed as a diagnostic test in adults, but has not been validated for diagnostic use in children. Serum C- peptide is a surrogate marker of insulin secretion, and post-glucagon or meal-stimulated C-peptide may be used to differentiate between type 1 and type 2 diabetes. Autoantibody estimation, i.e., islet cell antibodies (ICA), glutamic acid decarboxylase (GAD) antibodies, and insulin auto antibodies (IAA) may help diagnose autoimmune diabetes. Urine ketone and blood ketone estimation are necessary in specific clinical situations, such as sick days, in children with diabetes.

Clinical Difference
The phenotype of children with diabetes helps in differentiating type 1 from type 2 diabetes. Younger, thinner children with classic remote symptoms, weight loss and ketonuria, without a family history of diabetes, are more likely to have type1 diabetes. Older, obese or overweight children, with a positive family history, less explosive onset, and stigmata of insulin resistance (acanthosis nigricans, dyslipidaemia, hyperuricaemia, fatty liver, polycystic ovarian syndrome) are often type2 in nature. Personal experience with a predominantly Punjabi patient pool shows that type 1 patients are usually fairer, more handsome/beautiful, with light coloured eyes and hair, and a glabrous habitus. Type 2 children tend to be darker and more hirsute with black hair and eyes.

Management
Paediatric diabetes is different from adult diabetes, just as children are different from adults. Health care providers should appreciate the subtle, and not so subtle, differences between children with diabetes and their adult counterparts while planning therapy.
Glycaemic Targets
Glycaemic targets for children are less stringent than those for adults. It was earlier recommended that in the age group 0-6 years, one should aim for a pre-meal glucose of 100-180mg% and a bed-time/overnight value of 110-200mg% with HbA1c up to 8.5%. In school children aged 6-12 years, aim for pre-meal glucose of 90-180mg%, bedtime/overnight glucose of 100-180mg% and HbA1c <8.0%. In adolescents and young adults (13-19 years), the targets are less relaxed: aim for 90-130 mg% pre-meal, and 90-150 mg% bedtime glucose, with HbA1c <7.5%. Current guidelines, however, demand an HbA1c <7.5% in all children, irrespective of age.4

Diet
While a calorie-restricted diet is necessary for most adults with type 2 diabetes, children need relatively more calories per unit body weight. This helps them meet the extra requirements for growth and anabolism. It is also imperative that children receive a balanced diet with adequate minerals, vitamins and other nutrients. Therefore, a routine diet chart prepared for an adult clinic will not be appropriate for a child with diabetes.

Physical Activity
We often assume that physical activity and exercise come naturally to children. In today’s world, sadly, this is not always the case. Children should be encouraged to be physically active and take part in outdoor sports, while maintaining a fair balance between calories and exercise. Sportspersons with type 1 diabetes, such as Wasim Akram, can be taken as role models to encourage children to follow a healthy lifestyle.

Psychological Support
Children with type 1 diabetes need extensive psychological care and support, the importance of which is often underestimated. Support is an ongoing process, which is different from, but inclusive of, therapeutic patient education and counselling. Children have to be treated in an age-appropriate manner not as little adults. At the same time, one should avoid “infantilizing” adolescents with diabetes, who dislike “baby talk”.

Support involves a 360° approach to the child’s psychosocio-physical environment, including family, friends, peers, school and community. The child with diabetes must be helped to modulate her or his environment as well as the response to environment stresses, to achieve optimal quality of life.

Psychological support includes structured therapy such as interpersonal therapy, cognitive behavioural therapy (CBT) family therapy and play therapy, which can be used to resolve various psychological conflicts. Non structural interventions, such as empathic listening, catharaxis and creative expression may be of use.

Insulin
Insulin is the mainstay of management in paediatric diabetes.5 Ideally, a basal-bolus regime should be prescribed to all children with diabetes. Three bolus injections of rapid action insulin, to cover meal-time excursions, along with one (or sometimes two) doses of basal insulin, to manage fasting glycaemia, are administered. The traditional method of calculating dose distribution (2/3 in the morning, 1/3 at night), may not suit all children. In younger patients with type 1 diabetes, there is no endogenous insulin production, and requirements may vary from time to time. Doses can be optimized based on regular blood glucose monitoring. Dose requirements in children are relatively higher than in adults. Daily dose requirement of 1.0U/kg/day is the norm, though it may vary from person to person, from time to time. Adolescents usually need higher doses than this, and requirements may rise during puberty, as well as in the pre-menstrual phase. An average dose distribution would be 50% basal insulin and 50% prandial or regular, with 20%.

Insulin Analogues
Insulin analogues are a preferred mode of therapy in children. Aspart and detemir are approved for use above 2 years of age, lispro above 4 years, while glargine’s use is limited to children >6 years old. Rapid acting analogues have the advantage of flexibility, as they can be injected immediately before or after meal. This allows the parent or child to adjust doses based upon calorie counting. Basal analogues, i.e, detemir and glargine have peakless action, and can be taken once daily to provide control of fasting glycemia. In adults on analogues therapy, the distribution between daytime and night time doses is roughly 55:45, however, this may not necessarily hold true for children.

Novel Regimes
While basal-bolus insulin is the ideal method of managing paediatric diabetes, premixed insulin is sometimes used as a convenient alternative. Premixed insulin is used twice daily, to reduce the number of injections and minimize the need for frequent self-monitoring, while providing
both fasting and postprandial control.

An improvement over this is a three dose regime: premixed insulin, before breakfast and before dinner, along with regular insulin before lunch. This is useful as the intermediate acting component covers the long time period between an early morning breakfast and a delayed lunch in school children. The relatively lower dose of the short-acting component of premixed insulin reduces the risk of hypoglycaemia during school hours. Lunch time regular insulin helps manage evening hyperglycaemia which would have occurred if only premixed insulin were used.

**Insulin Delivery**

Children with diabetes need to be taught appropriate insulin technique as early as possible, though they should inject only under parental supervision. Educational toys such as dolls and paper cut outs can be used to make injections fun. Delivery devices such as syringes with 4mm needles, automatic Injectors, and pens help make injections easier for children. In children, thickness of the skin is slightly less than in adults. After puberty, girls gain subcutaneous mass, while boys experience a decline in subcutaneous fat. This creates a higher risk of intramuscular injection in boys. Currently, the safest needle for children appears to be the 4-mm pen needle. However, when used in children aged 2-6 years, it should be used with a pinched skin fold. With a 6 mm needle, an injection should be given with a skin fold or angled at 45°. Sites for insulin administration are similar in children and adults. The buttocks are often used as site for insulin injection in infants and toddlers.

Insulin pumps are a modern method of insulin delivery, which can be used in children with difficult-to-control diabetes. These pumps provide the advantage of continuous, regulated, insulin delivery. Newer pumps employ the closed loop system, in which insulin dosage is adjusted automatically according to interstitial glucose levels. Dual pumps, which can inject both insulin and glucagon [to avoid hypoglycaemia] are under development.

**Oral Hypoglycaemic Agents**

Oral hypoglycaemic agents (OHAs) were earlier strictly contraindicated in children. A growing body of evidence now supports the use of oral drugs in specific situations in children:

- Type1 children with unexplained escalation of insulin requirement.
- Type1 children with stigma of insulin resistance, eg, obesity, acanthosis nigricians.
- Type1 children with polycystic ovarian syndrome.
- Children with diabetes which cannot definitely be classified as type 1 or type 2.
- Children with type 2 diabetes.

While most experience is with metformin, other drugs such as pioglitazone, acarbose, voglibose, sitagliptin and vildagliptin have also been used in young persons with diabetes. OHAs are absolutely contraindicated in the presence of ketosis.

**Diabetic Ketoacidosis**

Diabetic ketoacidosis (DKA) is a common manifestation of poorly controlled diabetes, and may be the presenting complaint. Ketonuria or ketosis without clinical or biochemical features of acidosis, is even more frequently encountered, and should be taken seriously. Moderate or large ketonuria, as well as ketoacidosis, are indications for indoor management. Using intramuscular rapid acting analogues in patients with ketonuria, without acidosis, may obviate the need for admission.

**The Family with Diabetes**

The child with diabetes does not exist in isolation. Neither can the child with diabetes manage herself or himself alone. Management of paediatric diabetes is incomplete if the parents and normal siblings are not involved in education and counselling. Family involvement is also necessary to allocate responsibilities for health care, based on ability. In our culture, it is the mother who has to do the utmost in managing diabetes. In a child below 12 years age, it is the mother who will either make the health of the child or if neglected lead the way to complications. Meals on time, insulin injections, blood sugar monitoring, play and school and social events have all to be managed by the mother till such time that the child can take care of herself or himself. Conflict between siblings, issues related to confidentiality (as opposed to secrecy), and social stigma also need to be tackled with the help of family members.

**Health Care Provision**

Diabetes care should be provided by a well organized diabetes care team. In our setup, the physician often has to shoulder all responsibility for care. Liaison with a paediatrician, and support of lay educators (non-medical community members) as well as peer educators (other children with diabetes) helps.
patient groups provides a sense of belonging and corrects the feeling of isolation that some children with diabetes face. 8

Conclusion
Paediatric diabetes is a heterogeneous entity, distinct from, and also similar to, adult diabetes. An in-depth understanding of the pathophysiology of childhood diabetes is needed to ensure appropriate management.

References