

Type 1 Diabetes in Children (Juvenile Diabetes) — Symptoms and Causes

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Juvenile diabetes is a common chronic disease characterized by hyperglycemia and other metabolic abnormalities. It occurs at any age, but is most common in children and young adolescents. It is a genetic disease with environmental influences that trigger the destruction of pancreatic islet cells. Depletion of insulin levels leads to hyperglycemia, osmotic diuresis, hypovolemia, thirst, and ketoacidosis. Treatment of the disease is by the administration of exogenous insulin and supportive care.



Definition of Type 1 Diabetes in Children

Diabetes is a common chronic disease that is characterized by hyperglycemia and other metabolic abnormalities. In children and adolescents, one variant of the disease is common — type 1 diabetes mellitus or juvenile diabetes.

Epidemiology of Type 1 Diabetes in Children

Type 1 diabetes accounts for **10% of all diabetes cases**. It may present at any age, but the mean **age of presentation is 7-15 years**. More than half of patients with type 1 diabetes are under 20 years of age. However, a quarter of these patients are adults.

The incidence of juvenile diabetes is thought to be rising globally at a rate of 3–10%, with Australia and the Middle East recording the highest rates of increase. The incidence of juvenile diabetes increases as you move away from the equator, with 37–45 cases per 100,000 children being reported in Finland and Sardinia.

Juvenile is a **genetic disease** and children of parents with type 1 diabetes have a 30% chance of developing juvenile diabetes. The disease has a slight male predilection.

Classification of Type 1 Diabetes in Children

The presentation of juvenile diabetes can take various forms which give rise to the various classes of the disease. The **natural stage-wise progress** of the disease is outlined as follows:

- Preclinical β -cell autoimmunity
- Onset of clinical diabetes
- Transient remission — “honeymoon period”
- Established diabetes

Etiology of Type 1 Diabetes in Children

Diabetes type 1 is a genetic disease **influenced by environmental factors** such as viral infections, immunizations, psychological stress, dietary factors such as exposure to allergen-containing cow milk, and perinatal factors that increase the risk of type 1 diabetes. Dizygotic twins have a 5% concordance rate which increases to 50% in monozygotic twins.

Other rare causes of the disease include the congenital **absence of the pancreas** or removal during surgery, in addition to syndromes that occur in association with a **compromised pancreatic function** such as Wolfram syndrome, which is characterized by diabetes, optic atrophy, and deafness.

Pathophysiology of Type 1 Diabetes in Children

The main defect seen in the disease is **pancreatic cell destruction from autoimmune antibodies** which target the islet β -cells that secrete insulin.

The **destruction** of pancreatic β -cells is caused by the following:

1. **Genetic mutations in the MHC genes** (DR4-DQ8 or DR3-DQ2) confer a $\leq 4\%$ susceptibility of developing an autoimmune reaction to the islet cells. With environmental influence, the risk rises to 50%.
2. **Viral infections** such as Coxsackie B3 and B4, CMV, mumps, and rubella trigger an autoimmune reaction due to antigenic mimicry between the PC2 protein of Coxsackie and GAD 65 found in the pancreatic cells.
3. Similarly, weaning infants on **cow milk** triggers a similar reaction due to the molecular mimicry between amino acids in the milk and islet cell antigen 69 in the pancreas.
4. **Cytotoxic drugs** such as pentamidine and Vacor cause direct toxicity to the pancreatic islet cells.

Initially, the damage is minimal and is not clinically evident. The pancreas responds by regenerating new islet cells and there is a reduced need for insulin, a stage

known as the 'honeymoon phase'. However, damage of $\geq 80\%$ manifests with the signs and symptoms of juvenile diabetes. The **destruction could take as little as 3 years in young children or up to 10 years in adolescents.**

Insulin is important in the regulation of plasma glucose levels, and the depletion of insulin triggers the conversion of stored glycogen into glucose, causing hyperglycemia.

Juvenile diabetes is commonly discovered when a child suffers from ketoacidosis. The mechanism of ketoacidosis involves the following:

Loss of glucose in urine and the inability of the cells to utilize glucose due to insulin deficiency cause a state of starvation in the body. When the body detects this depletion in glucose levels, **hormonal compensatory mechanisms** are triggered and increase catabolism by accelerating lipolysis and lipogenesis. There is an increase in the plasma concentration of free fatty acids, lipids, and triglycerides. They are readily converted into ketone bodies such as acetoacetate and β -hydroxybutyrate which cause ketoacidosis and ketonuria.

Respiratory compensation to combat the metabolic acidosis sets in and the patient begins to take deep rapid breaths. The **breath has a characteristic acetone smell** due to the non-enzymatic conversion of acetoacetate to acetone. With the respiratory compromise, hypovolemia due to osmotic diuresis, and plasmatic hyperglycemia, the brain has compromised perfusion and patients may become comatose or even die.

Clinical Features of Type 1 Diabetes in Children

Juvenile diabetes may present in any of the following forms:

Classical type 1 diabetes mellitus

The body's effort to reverse the hyperglycemia without acidosis causes polyuria, polydipsia, and weight loss despite an increase in appetite (polyphagia).

Polyuria occurs when **serum glucose concentration exceeds the renal threshold for glucose loss via urine**. The body responds by increasing urinary glucose excretion; the body achieves this by increasing both the concentration of urine and frequency of urination. Polyuria may present as nocturia, enuresis, or daytime incontinence in a previous continent child. In children who are not toilet trained, parents may note an increased frequency of wet diapers and/or diapers that are unusually wet.

Increased serum osmolality from hyperglycemia and hypovolemia leads to a **demand for more fluid intake** (polydipsia).

Increased catabolism of stored glucose due to insulin deficiency gives the body an **impression of low glucose supply**; therefore, there is **increased intake**. However, increased fat breakdown and the loss of glucose in urine occur **resulting in weight loss**. This is known as polyphagia.

Some children may also present with diabetic ketoacidosis

If diabetic ketoacidosis is not controlled in its early stages, it could lead to the following:

- **Severe dehydration**
- **Increased catabolism** of fatty acids and lipids into ketone bodies which causes the non-enzymatic conversion of acetoacetate into acetone giving a characteristic acetone breath

- Metabolic acidosis is corrected by **increased respiration**, leading to rapid deep breathing (Kussmaul respiration) that may be confused with respiratory distress
- Respiratory distress coupled with severe hypovolemia and acidosis compromise brain perfusion and children become **comatose**

Silent disease

Some children will be **diagnosed with type 1 diabetes before the onset of clinical symptoms** during routine screening, especially if the clinician has a high index of suspicion; for example, in children who have another close family member with type 1 diabetes.

Other symptoms include:

- **Hyperglycemia:** this lowers the child's immunity and increases susceptibility to infection. The presence of glucose in urine favors the growth of microbes; candidiasis is a common presentation, especially among adolescent girls.
- **Generalized body malaise**
- Alterations in the osmotic milieu of the lens lead to the imbalance of aqueous and vitreous humor flow, with changes in the refractive index and visual disturbances. Children with longstanding hyperglycemia may present with **cataracts** due to the hardening of the lens.

Investigations of Type 1 Diabetes in Children

To make a diagnosis of juvenile diabetes, a patient must fulfill the **general diagnostic criteria** for diabetes, which entail the identification of any 2 of the following findings:

1. Signs and symptoms of diabetes such as **polyuria, polydipsia, and poor weight gain** with a normal or minimally altered feeding pattern
2. **Random blood sugar level** ≥ 200 mg/dL (11.1 mmol/L)
3. **Fasting blood sugar level** ≥ 126 mg/dL (7.0 mmol/L). Fasting blood sugar level is obtained after a period of 8 hours with no caloric intake. A level of 100–125 mg/dL (5.6–6.9 mmol/L) is considered prediabetes and repeat screening is required.
4. Glycated hemoglobin (A1C) $\geq 6.5\%$ indicates a **persistently high level of glucose** for the past 2 or 3 months and may be used to make a diagnosis of diabetes.

Once a diagnosis of diabetes is made, other tests are conducted to **differentiate the various types** of diabetes.

1. Screening for antibodies seen in type I diabetes. Screening should be conducted for islet cell antibodies and glutamate decarboxylase antibodies.
2. Urinalysis for ketones which are more common in type I diabetes.

Investigations to help both in **management and in ruling out differential diagnosis:**

1. Renal function tests to rule out renal failure and to obtain a baseline state prior to the initiation of treatment.
2. Oral glucose tolerance test to differentiate type I diabetes from maturity-onset diabetes of the young (MODY) and hyperglycemia due to other medical conditions.
3. Blood gas analysis to determine and treat metabolic acidosis.

Differential Diagnosis of Type 1 Diabetes in Children

Type II diabetes mellitus	More common in the older and obese population
Diabetes insipidus	Due to the polyuria and thirst Differentiated by the presence of ketones or sustained high glucose level with no other identifiable cause of the thirst
Maturity-onset diabetes of the young (MODY)	Similar presentation and seen in a similar population
Transient hyperglycemia	The disease is ruled out by the identification of another disease that causes hypoglycemia
Congenital abnormalities	Congenital absence of the pancreas, etc

Treatment of Type 1 Diabetes in Children

The most important intervention in the management of juvenile diabetes is **insulin therapy** since there is no endogenous production of insulin.

However, this form of therapy must be administered **in conjunction with other supportive measures** to maximize the benefits of exogenous insulin with minimum doses. These measures include:

1. **Diabetic education and counseling** of the adolescent and parents/caregivers to ensure adherence to insulin and to avoid the psychological effects of any behavioral changes.
2. **Dietary modifications** and intake of low-fat high-fiber food.
3. **Regular exercises** to trigger weight loss and avoid the development of insulin resistance.
4. **Regular glucose monitoring** to detect the onset of complications and enhance early intervention.

Emerging methods of treatment

1. **Pancreatic transplantation:** replacement of the dysfunctional pancreas restores the endogenous source of insulin.
2. **Islet cell transplantation:** a group of islet cells is taken from a functional pancreas and transplanted into the dysfunctional one.
3. **Stem cell transplantation:** early diagnosis of juvenile diabetes prior to the destruction of the pancreatic cells can be treated with stem cell transplantation from one's own stem cells, which halts the autoimmune reaction to the pancreatic cells.
4. **Vaccination** against the development of antibodies such as glutamate decarboxylase antibodies.

Complications of Type 1 Diabetes in Children

Complications of diabetes can be divided into short-term and long-term complications.

Short-term complications

Hypoglycemia

This occurs when **blood sugar falls below the lower limit of normal**; thus, the body lacks the energy to perform various functions. Hypoglycemia manifests as increased sympathetic activity due to hormone secretion with sweating, light-headedness, fatigue, blurred vision, rapid heartbeat, irritability, and irregular heartbeat.

Common causes of hypoglycemia include the erratic use of higher doses of insulin, poor oral intake, or other processes that reduce the body's glucose or its demand for insulin. Intake of a fast-acting carbohydrate such as glucose, fruit juice, or candy (15 g) treats hypoglycemia.

Hyperosmolar hyperglycemic state

This occurs when **blood sugar rises to extreme levels** but ketoacidosis has not yet set in. A hyperosmolar hyperglycemic state arises because of the administration of low doses of insulin or infection which could raise the demand for insulin within the body. Common manifestations include increased urination, thirst, fatigue, and difficulty concentrating. A revision of insulin dose is needed in most cases. A hyperosmolar hyperglycemic state is more common in adults and the elderly.

Diabetic ketoacidosis

Cellular starvation of energy leads to lipolysis and conversion into ketone bodies which causes nausea, vomiting, abdominal pain, and the fruity smell of acetone. Inpatient management with vigorous fluid infusion and insulin administration is required. The condition is associated with high mortality due to cerebral edema especially if sodium bicarbonate was used in treatment.

Long-term complications

Diabetic retinopathy

This is a **late complication** of juvenile diabetes after long periods of the disease. Consistently elevated blood sugar levels lead to the glycation of lens proteins. Other changes that impair vision are the damage to the small vessels that supply the retina and revascularization with new weaker vessels that rupture easily.

Diabetic nephropathy

This occurs due to **damage to the kidney** microvasculature by elevated blood glucose levels. There is glycation of proteins leading to glomerular basement membrane thickening which results in hypertension and further damage to the kidneys.

Diabetic neuropathy

Damage to the small arteries that supply the peripheral nerves leads to **reduced sensation and damage to these nerves**. The loss of sensation predisposes the patients to skin injuries that rarely heal due to high blood sugar levels that support microbial growth.

The recent literature has shown that peripheral neuropathy in type 1 diabetes might also result from toxic end-products of glycation due to hyperglycemia.

The effects of hyperglycemia on the central nervous system include impaired blood-brain-barrier permeability and impaired function of the visual cortical pathways. These can result in impairments in color vision and contrast-detection long before the development of the first signs of diabetic retinopathy.

Hypoglycemic episodes, which are more common in type 1 diabetes, also have an adverse effect on higher cortical functions. Recent studies show a correlation between the rate and severity of hypoglycemic episodes and the onset of mild cognitive impairment.

Course and Prognosis of Type 1 Diabetes in Children

Type I diabetes is a chronic disease that is well managed by the **lifelong administration of insulin**. The disease, however, if not properly managed, increases the body's demand for insulin to a very high level. This predisposes the body to the development of complications, shortening a person's life by about 10 years compared to a normal person.

Children diagnosed with the disease have an **altered growth pattern**, although they eventually attain the recommended height and weight for age.

References

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