Type 2 Diabetes Mellitus in Children — Screening and Treatment

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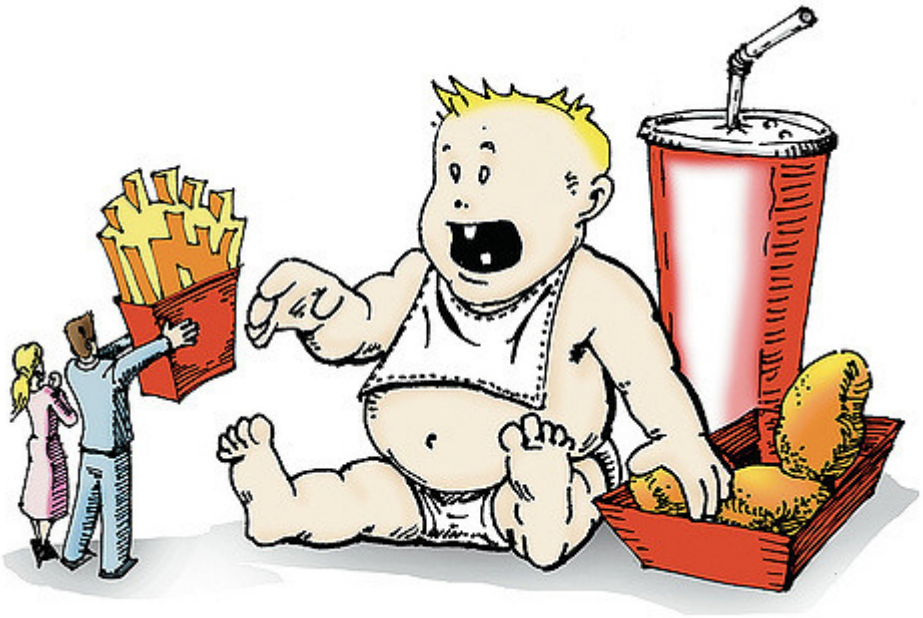
Type 2 diabetes mellitus is becoming more recognized in children, especially African American, American Indian and Asian children. Obesity is another very important risk factor for type 2 diabetes mellitus in children. Children with type 2 diabetes usually have a family history of the disease, are obese, have signs suggestive of insulin resistance, and have the typical symptoms of diabetes, such as polyuria and polydipsia. The symptoms, however, are usually of a more insidious onset compared to type 1 diabetes mellitus. Diet, lifestyle modifications and monotherapy with metformin are the main treatment options for type 2 diabetes mellitus in children.



Overview

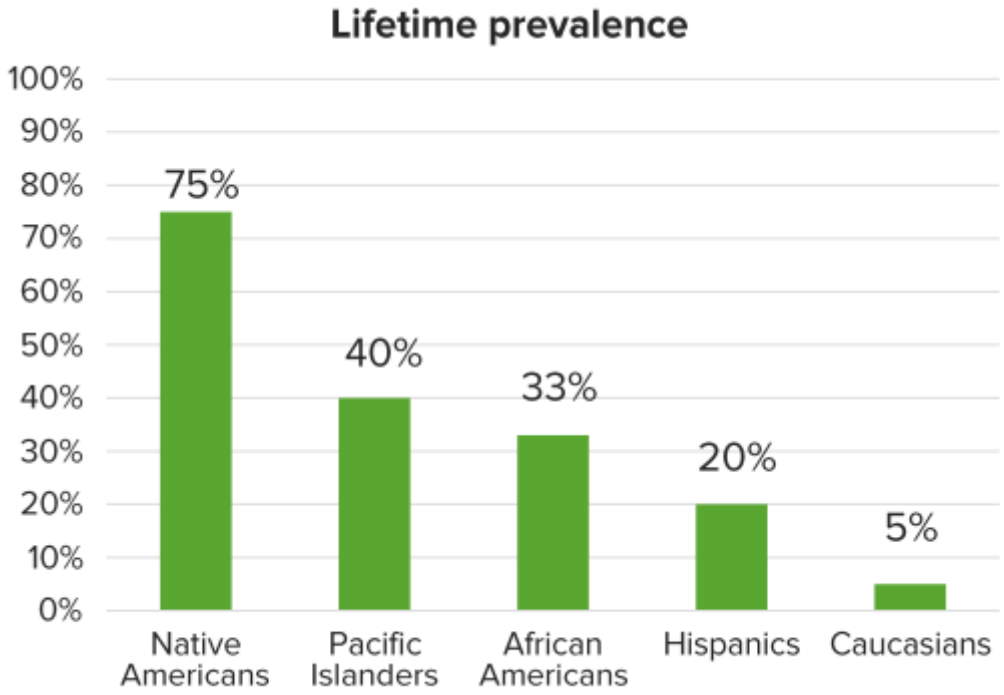
Type 2 diabetes mellitus is a **metabolic condition that is characterized by various metabolic derangements such as peripheral insulin resistance and hyperglycemia**. The condition affects multiple system organs including the cardiovascular system, the cerebrovascular system, the kidneys, liver, and the eyes. These complications are responsible for an increase in morbidity and mortality of patients.

In the past, type 2 diabetes was rarely seen in children and was known as adult-onset diabetes. Today, however, type 2 diabetes mellitus is becoming more recognized in

children. Increasing incidences are occurring worldwide with each nation having its own demographics on prevalence.

Epidemiology of Type 2 Diabetes Mellitus in Children

Type 2 diabetes mellitus in children is becoming **more common since the last century with most** cases being diagnosed amongst the minority communities. The estimated incidence of type 2 diabetes mellitus in American Indian children is around 49 cases per 100,000 persons. The incidence of type 2 diabetes mellitus in other minority groups such as Asian and African American children is also high and range from 19 to 22.7 cases per 100,000. Up to 45% of newly diagnosed cases of diabetes mellitus in children are attributed to type 2 diabetes mellitus.



Lifetime prevalence in Diabetes Mellitus Type 2 in Children. Image created by Lecturio

Risk Factors

The most important risk factor for type 2 diabetes mellitus in children is **obesity**. This finding was confirmed by several local and international studies that were performed in the United States, Japan, Australia, Britain, and India. Pediatric type 2 diabetes mellitus is more common in girls. Type 2 diabetes mellitus in children usually starts at puberty.

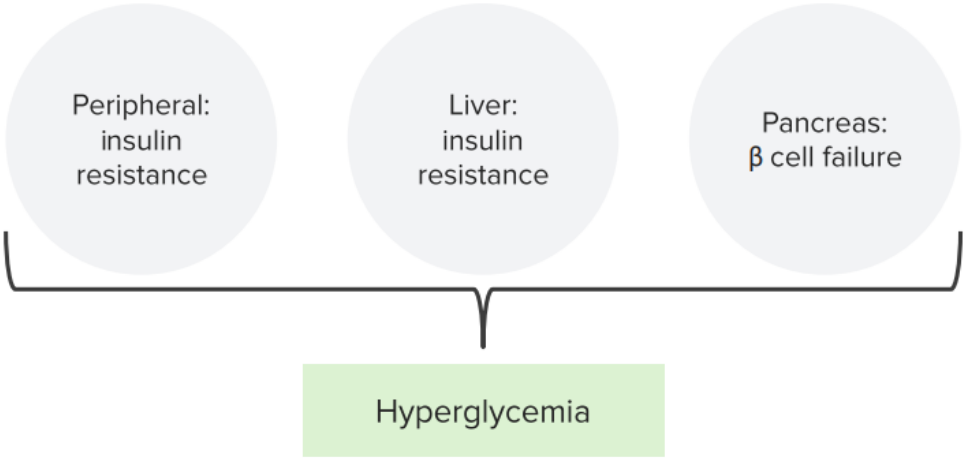
It is attributed to the physiological development of a state in which insulin resistance develops; thus, a child with other risk factors has a high chance of their beta cell functioning inadequately leading to the development of type 2 diabetes mellitus.

Other risk factors for type 2 diabetes mellitus in children include **a family history of type 2 diabetes, high birth weight, maternal gestational diabetes or maternal type 2 diabetes mellitus, and are not breastfed during infancy**. Additionally,

conditions with marked insulin resistance, such as polycystic ovarian syndrome, predispose the child to an increased risk of developing type 2 diabetes mellitus. Studies have also shown that antipsychotic drugs increase the chance of individuals developing type 2 diabetes mellitus with a high significance for children.

Prognosis and Complications of Type 2 Diabetes Mellitus in Children

The exact frequency of long-term complications of type 2 diabetes mellitus in children is unknown, but preliminary results show that children are as likely as adults in developing the long-term complications of the disease. The long-term complications of type 2 diabetes mellitus in children **include nephropathy, neuropathy, retinopathy and coronary artery disease**. These complications are due to microvascular disease and the direct toxic effects of hyperglycemia.



“Hyperglycemia” Image created by Lecturio

Additionally, hypoglycemia due to aggressive diabetic control is known to be associated with **cognitive and intellectual deficits in the future** and should be avoided. In fact, some studies have claimed that recurrent and severe hypoglycemic episodes in children are potentially more hazardous to brain development than the natural history of the disease.

Acute complications of type 2 diabetes mellitus are more commonly seen in adolescents and teenagers. **Diabetic ketoacidosis and hyperglycemic-hyperosmolar states** are being more commonly recognized in children. Children with type 2 diabetes are also at an increased risk of developing dyslipidemia and hypertension.

Despite recent advances in treatment plans for type 2 diabetes mellitus in adults and children, the risk of nephropathy is still not obliterated. Mortality remains higher in children with type 2 diabetes mellitus compared to healthy children or to children with type 1 diabetes mellitus.

Etiology and Pathophysiology of Type 2 Diabetes

Mellitus

Type 2 diabetes mellitus has a heterogeneous etiology; thus, the genetical susceptibility can be in social, environmental, as well as behavioral factors. Patients with type 2 diabetes mellitus have **impaired basal insulin secretion, peripheral insulin resistance, and impaired hepatic glucose production**.

Type 2 diabetes mellitus occurs when both insulin secretion and insulin inaction are present. Impaired insulin secretion and relative hypoinsulinemia are usually mild at the onset of the disease, but clinically relevant as these patients show impaired glucose tolerance but not frank diabetes. Eventually, peripheral insulin action is impaired by insulin resistance which is also worsened by dyslipidemia. Dyslipidemia is also becoming more severe as the disease progresses; hence, a vicious cycle develops.

The liver is also sensitive to insulin in normal conditions and this sensitivity is decreased in type 2 diabetes mellitus. This is associated with increased glucose production by the liver and worsening of the hyperglycemia. At a certain point, the pancreatic beta-cells are no longer able to keep up with the demand for insulin due to severe insulin resistance. With insulin resistance coupled with diminished beta cells functioning, frank type 2 diabetes develops.

The main difference in the pathophysiology of type 2 diabetes between children and adults comes from a recent study that showed up to 15% of female adolescents do not have any form of insulin resistance! This finding might point towards a different pathology of type 2 diabetes mellitus in children.

Clinical Presentation of Type 2 Diabetes Mellitus in Children

The distinction between type 2 and type 1 diabetes mellitus in children is challenging. Type 2 diabetes mellitus usually has a **slow and gradual onset**. The family history of type 2 diabetes is usually positive. Additionally, children with type 2 diabetes mellitus are more likely to be obese compared to those with type 1 diabetes mellitus. Asymptomatic children may be checked for hyperglycemia and glycosuria.

The race of the child is a very important clue towards the type of diabetes mellitus. African Americans, Asians, and American Indians are more likely to have type 2 diabetes compared to the general population. Studies have shown that, generally, children from minority groups have higher levels of insulin compared to same-aged white children. It suggests that race predisposes people to develop diabetes due to higher chances of insulin resistance.

The body mass index in children with type 2 diabetes mellitus is usually above the 85^{th} percentile. Insulin resistance plays a key role in the pathology of type 2 diabetes mellitus, despite some conflicting pathology studies, and acanthosis nigricans is seen in up to 90% of the children with type 2 diabetes. The patches that are mostly located in intertriginous areas can easily be identified in obese and darker skinned people.

Females with type 2 diabetes mellitus, acanthosis nigricans, hirsutism, and menstrual abnormalities should be evaluated for the possibility of polycystic ovarian syndrome. Chronic anovulation and hyperandrogenism are strong characteristics of the polycystic ovarian syndrome. Hypertension is also commonly seen in children with type 2 diabetes mellitus.

Ophthalmoscopy is indicated in all children newly diagnosed with type 2 diabetes mellitus to establish a baseline and detect early diabetic retinopathy. This is very important as the most commonly-feared complication of type 2 diabetes mellitus in children and adults remains vision loss.

Screening for Type 2 Diabetes Mellitus in Children

Children who are overweight, i.e. body mass index above the 85^{th} percentile for age and sex, and have two of the following should be screened for type 2 diabetes mellitus:

1. The family history of type 2 diabetes mellitus in a first or second-degree relative,
2. Belong to one of the high-risk race or ethnicities mentioned previously,
3. Have acanthosis nigricans, hypertension, dyslipidemia or polycystic ovarian syndrome.
4. Polyuria is absent or mild and has glycosuria without ketonuria.
5. Disorders with insulin resistance.

Screening of the children who meet the previously-mentioned criteria should commence by the age of 10 years, performed every two years, and be based upon a fasting plasma glucose test.

Diagnostic Workup for Type 2 Diabetes Mellitus in Children

Children with polyuria, polydipsia, or unexplained weight loss, who have a random plasma glucose concentration of 200 mg/dl or more, are diagnosed with diabetes. Additionally, children who undergo a fasting plasma glucose test and have a concentration of 126 mg/dl or more or a 2-hour plasma glucose value of 200 mg/dl or more are also diagnosed with diabetes.

These tests do not help in differentiating between type 2 and type 1 diabetes mellitus. Fasting C-peptide and insulin levels are usually increased in type 2 diabetes, but not in type 1 diabetes. Glutamic acid decarboxylase and islet cell antibodies are negative in type 2 diabetes mellitus.

The risk of nephropathy in type 2 diabetes mellitus in children is higher compared to that associated with type 1 diabetes mellitus; therefore, microalbuminuria should be excluded. Dyslipidemia is also commonly seen in children with type 2 diabetes mellitus and should be excluded.

Treatment of Type 2 Diabetes Mellitus in Children

The goals of treatment of type 2 diabetes mellitus in children are to **maintain a fasting plasma glucose concentration less than 126 mg/dl**, resolution of polyuria, Nocturia, and polydipsia, maintaining a healthy body weight, correcting dyslipidemia and improving the adaptation of the child to the chronicity of the condition. Improving adaptation is better achieved through the participation of the whole family in the management plan.

Image: “The pyramid for the five major food groups. The recommended amounts for school-age children are listed in black letters, while our findings for the obese group are written in red and those for the non-obese group in blue characters.” by Garipağaoğlu M, Sahip Y, Budak N, Akdikmen O, Altan T, Baban M – J Clin Res Pediatr Endocrinol (2008). License: CC BY 2.5

The three main aspects of the treatment of type 2 diabetes mellitus are **diet, lifestyle modifications, and pharmacotherapy**. A healthier diet that is rich in fiber and protein and the incorporation of daily exercise, if possible, is recommended. Metformin should be started as soon as possible. The aim should be to lower HbA1C to a level below 9%.

Statins and angiotensin-converting enzyme inhibitors are indicated in children who do not achieve normotensive blood pressure and who still have elevated LDL and low HDL cholesterol levels despite lifestyle modifications.

Low-density-lipoprotein cholesterol, Statins combined with a low intake of fat, and plant sterols that have been found to consistently reduce LDL-C levels up to 15% are also effective management practices. There has been little research on what

Insulin therapy should be initiated if metformin alone was not sufficient to correct hyperglycemia in a child with type 2 diabetes mellitus. To consider metformin monotherapy as inefficient, the treatment course should be lasting for at least three months.

Overall, children who develop type 2 diabetes mellitus are at a much higher risk compared to adults who develop the disease in the long-term. They have increased risks of developing hypertension, dyslipidemia, and cardiovascular disease, as well as stroke.

References

Reinehr T. Type 2 diabetes mellitus in children and adolescents. *World Journal of Diabetes*. 2013;4(6):270-281. doi:10.4239/wjd.v4.i6.270.

Notes