

DIABETES MELLITUS IN CHILDREN: A REVIEW ARTICLE

Jayasuriya Ramakrishnan, Narayanan Chandra Kumar Praveen and Bugubaeva M. M.

Kyrgyzstan India.



*Corresponding Author: Jayasuriya Ramakrishnan

Kyrgyzstan India.

Article Received on 06/10/2023

Article Revised on 26/10/2023

Article Accepted on 16/11/2023

ABSTRACT

Diabetes mellitus (DM) is a syndrome of disturbed energy metabolism, conveniently defined by the degree of hyperglycemia, resulting from an absolute or relative deficiency of insulin action. In this article I gonna explain briefly about that and it's complications as well.

INTRODUCTION

Many different pathogenic processes can lead to the development of diabetes mellitus; however, most children and adolescents have either type 1 or type 2 diabetes. Until recently, children virtually always had type 1 diabetes mellitus (T1DM), caused by absolute deficiency of insulin secretion, whereas type 2 diabetes (T2DM) was predominantly a disease of middle age and the elderly. Over the past 10–20 years, an alarming increase in the prevalence of T2DM has been reported from pediatric diabetes centers in North America and elsewhere in the world. Now, T2DM accounts for a substantial fraction (up to 45%) of new cases of diabetes in children and adolescents at centers in the U.S. that serve large numbers of African-American, Mexican-American, and Native-American youth.^[2-4] A similar increase in the number of young people with T2DM attending pediatric diabetes centers has been observed in many parts of the world, including Japan, India, Australia, and the United Kingdom.^[3,5] Children and adolescents with newly diagnosed T2DM are virtually always overweight or obese. The dramatic increase in the prevalence of pediatric T2DM temporally coincides with the global increase in obesity in children and adolescents. Although T1DM remains the main form of the disease in children worldwide, it is likely that T2DM will be the predominant form within 10 years in many ethnic groups.^[5] This article will focus on T2DM in children and adolescents.

Etiology

- Type 1 diabetes
- Immune mediated
- Idiopathic
- Type 2 diabetes
- Other specific types
- Genetic defects of β -cell function
- Maturity onset diabetes of the young (MODY)
- Mitochondrial diabetes
- Genetic defects in insulin action

- Type A insulin resistance
- Leprechaunism
- Rabson–Mendenhall syndrome
- Lipoatrophic diabetes
- Diseases of the exocrine pancreas
- Cystic fibrosis
- Hemochromatosis
- Pancreatectomy
- Endocrinopathies
- Cushing syndrome
- Pheochromocytoma
- Hyperthyroidism
- Drug or chemical induced
- Glucocorticoids
- Diazoxide
- β -adrenergic agonists
- Pentamidine
- Nicotinic acid
- α -Interferon
- Tacrolimus
- Infections
- Congenital rubella
- Cytomegalovirus
- Uncommon forms of immune-mediated diabetes
- “Stiff-man” syndrome
- Anti-insulin receptor antibodies
- Other genetic syndromes sometimes associated with diabetes
- Down syndrome
- Turner syndrome
- Klinefelter syndrome
- Wolfram syndrome
- Friedreich ataxia
- Alstrom syndrome
- Prader–Willi syndrome
- Bardet–Biedl syndrome
- Myotonic dystrophy
- Hereditary etiology

Table 1. Risk of Developing Type 1 Diabetes for Individuals Who Have an Affected Relative

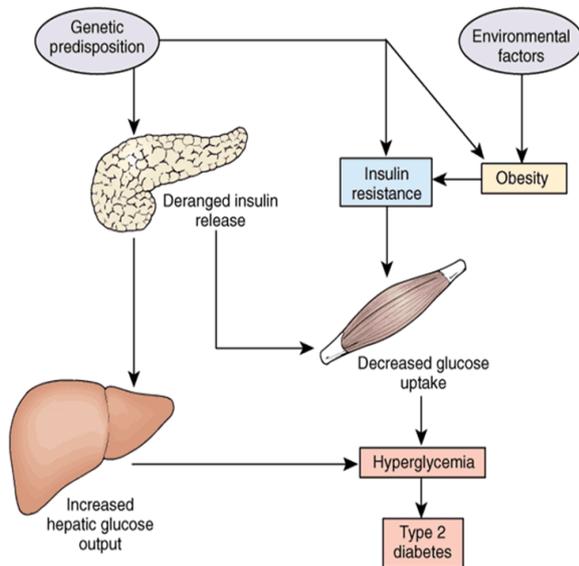
Sibling	Risk
Overall	6%
Identical twin	<50%
HLA identical	15%
HLA haploidentical	6%
HLA nonidentical	1%
Offspring	Risk
Overall	5%
Father who has IDDM	6%
Mother who has IDDM	2%

HLA=human leukocyte antigen, IDDM=insulin-dependent diabetes mellitus

*Type 1: Diabetes Mellitus.

Type 1A diabetes results from chronic, progressive T-cell-mediated autoimmune destruction of the β -cells of the pancreas, eventually leading to severe insulin deficiency, manifested by low or undetectable plasma levels of C-peptide.

*Type 2 diabetes mellitus



- Abbreviation - Explanation
- KCL - potassium chloride
- DGpRP - German Society for Paediatric Rehabilitation and Prevention
- BG - blood glucose
- NF - low frequency
- APE - Paediatric Endocrinology Study Group
- C-Peptid - connecting peptide
- ACE - Angiotensin Converting Enzyme
- ABCC8 gene - Gene Localisation for Sulfonylurea Receptor 1

- ACR - albumin creatinine ratio
- ÄZQ - Medical Centre for Quality in Medicine
- AGPD - Paediatric Diabetology Study Group
- AT-1 blocker - angiotensin type 1 receptor blocker
- BAR - German Federal Study Group for Rehabilitation
- BdKJ - German Association of Diabetic Children and Adolescents
- BP - blood pressure
- BMI - body mass index
- Bpm - beats per minute
- CF - Cystic Fibrosis
- CFRD - Cystic Fibrosis Related Diabetes
- CK - creatine kinase
- DAG - German Obesity Association
- DDG - German Diabetes Association
- DELBI - German Instrument for Assessing Guidelines
- DGE - German Nutrition Association
- DGEM - German Association for Nutritional Medicine DiabetesDE Diabetes Germany
- DPV - Diabetes Patient Documentation
- fT4 - free thyroxin
- GAD - glutamate decarboxylase
- HbA1c - glycosylated hemoglobin
- HDL - high density lipoprotein
- IA2 - tyrosine phosphatase IA2 antibody
- IAA - insulin autoantibody
- ICA - islet cell antibodies
- ICT - intensified conventional therapy
- KCNJ11 - potassium inwardly-rectifying channel, subfamily J, member 11
- LDL - low density lipoprotein
- MODY - maturity onset diabetes of the young
- MRT - magnetic resonance tomography
- NaCl - sodium chloride
- NPH -Insulin neutral protamine Hagedorn insulin
- OGTT - oral glucose tolerance test
- PDM - permanent neonatal diabetes mellitus
- pH - potentia hydrogenii (effectiveness of hydrogen) = negative decadic logarithm of hydrogen ion activity
- SGB - German Social Law Book
- STIKO - Standing Committee on Vaccination of the Federal Republic of Germany
- Tg -thyreoglobulin
- TNDM - transient neonatal diabetes mellitus
- TPO-AK - thyroid peroxidase antibody
- TSH - thyroid stimulating hormone/thyrotropin

Symptoms*

- Polyuria
- Polydipsia
- Polyphagia
- Undefined weight loss
- Fatigue
- Malaise
- Obesity
- Restless leg syndrome
- Nocturia

- Enuresis
- Blurred vision

value of 126 mg/dL (7.0 mmol/L) or more also is diagnostic.

***Diagnosis**

Plasma glucose concentration greater than 200 mg/dL (11.1 mmol/L) confirms the diagnosis. A fasting glucose

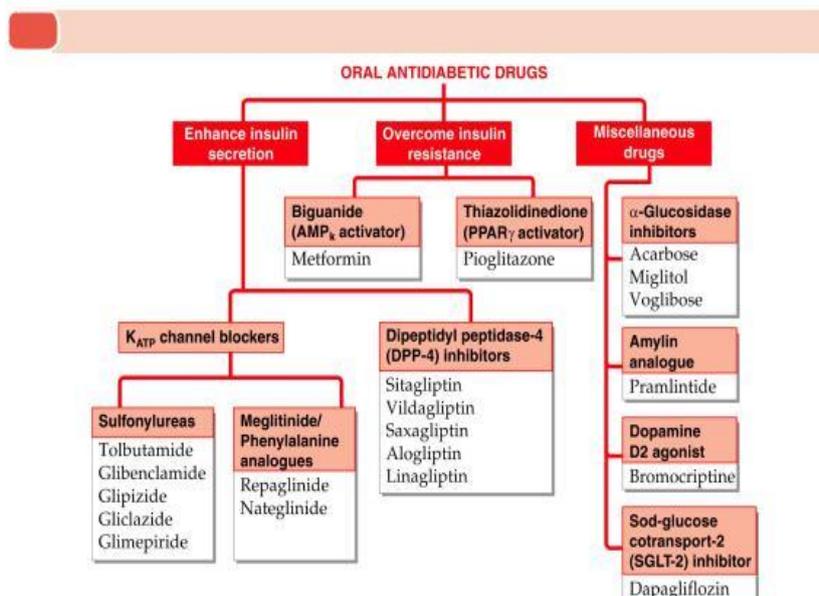
	Normal	Impaired Glucose tolerance	Diabetes Mellitus
Fasting	100 mg	100-125 mg	≥ 126 mg
2-hour value after 75 gm glucose	<140 mg	140-199 mg	≥ 200 mg

➤ **HBA1C**

HbA1c as an indicator of diabetes control.

BLOOD GLUCOSE		STATUS	HbA1c	
mmol/L	mg/dL		%	mmol/mol
5.4	97	Normal	5	31
7.0	126		6	42
8.6	155	Pre-Diabetes	7	53
10.2	184	Diabetes	8	64
11.8	212	Diabetes	9	75
13.4	241		10	86
14.9	268	Diabetes	11	97
16.5	297		12	108

MANAGEMENT
Pharmacotherapy



Insulin dosage

RAPID	Humalog or Lispro	< 15 min	60-90 min	3-5 hrs	<ul style="list-style-type: none"> Inject 10-15 min before mealtime Typically used in conjunction with longer-acting insulin.
	Novolog or Aspart	< 15 min	60-120 min	3-5 hrs	
	Apidra or Glulisine	< 15 min	60-90 min	1-2.5 hrs	
SHORT	Regular (R) Humulin, Actrapid or Novolin	30-60 min	2-5 hrs	6-8 hrs	<ul style="list-style-type: none"> Inject at least 20-30 minutes before mealtime
	Velosulin	30-60 min	2-3 hrs	2-3 hrs	
INTERMEDIATE	NPH (N)	1-2 hrs	4-12 hrs	18-24 hrs	<ul style="list-style-type: none"> Commonly used twice daily Often combined with rapid- or short-acting insulin
	Lente (L)	1-2.5 hrs	3-10 hrs	18-24 hrs	
LONGS	Ultralente (U)	30 min-3 hrs	10-20 hrs	20-36 hrs	<ul style="list-style-type: none"> Covers insulin needs for 24 hrs If needed, often combined with rapid- or short-acting insulin
	Lantus or Glargine	1-1.5 hrs	No Peak	20-24 hrs	
	Levemir or Detemir	1-2 hrs	6-8 hrs	Up to 24 hrs	
PRE-MIXED	Humulin 70/30	30 min	2-4 hrs	14-24 hrs	<ul style="list-style-type: none"> Combination of intermediate- and short-acting insulin Commonly used twice daily before mealtime
	Novolin 70/30	30 min	2-12 hrs	Up to 24 hrs	
	Novolog 70/30	10-20 min	1-4 hrs	Up to 24 hrs	
	Humulin 50/50	30 min	2-5 hrs	18-24 hrs	
	Humalog 75/25	15 min	30 min-2.5 hrs	16-20 hrs	

Insulin pump Complications

Diabetic nephropathy

Diabetic kidney disease (DKD) is kidney disease that is due to diabetes. It is also called diabetic nephropathy. Nephropathy means your kidneys aren't working normally.

Type 1 and type 2 diabetes are the most common causes of kidney disease.

There are 5 stages of DKD. The final stage is kidney failure (end-stage renal disease or ESRD). Going from 1 stage to the next can take many years.

Until DKD is severe, most people with it don't have symptoms. Having your kidney function checked by a simple blood and urine test is the only way to know if there are problems. Normal kidneys don't leak protein. But with diabetic nephropathy, protein shows up in your urine. Albumin is the most common protein in the blood. Albumin leaks into the urine in diabetic nephropathy. Increasing albumin in urine (called albuminuria) is a sign that the kidneys are less able to filter. It also is linked to worsening heart and blood vessels problems in people with diabetes.

A routine urine dipstick test doesn't pick up albuminuria (albumin in the urine) until you are leaking more than 300 to 500 mg a day. This used to be referred to as macroalbuminuria. It's now also called severely increased albuminuria. For amounts less than 300 mg a day, the term is moderately increased albuminuria. This change in wording shows that any amount of protein in the urine is abnormal.

It is rare for kidney failure to happen in the first 10 years of diabetes. Kidney failure often happens 15 to 25 years after the first symptoms of diabetes. If you have had diabetes for more than 25 years without any signs of kidney failure, your risk of having it decreases.

Diabetic Neuropathy

Diabetic neuropathy is a type of nerve damage that can occur if you have diabetes. Diabetic neuropathy is a common complication of both type 1 diabetes and type 2 diabetes.

The best way to prevent or treat diabetic neuropathy is to keep your blood sugar (glucose) and blood pressure well controlled, to attend regular diabetes checks and to avoid smoking. The outcome for early diabetic neuropathy can be good but severe neuropathy is often associated with a poor outcome.

Diabetic neuropathy is a type of nerve damage that can occur if you have type 1 diabetes or type 2 diabetes.

Your peripheral nervous system is a network of nerves called peripheral nerves. These transmit information between your central nervous system (your brain and spinal cord) and all the other parts of your body, including your arms, legs and organs. Your peripheral nervous system is divided into:

Sensory nerves

Electrical impulses transmitted along your sensory nerves allow you to touch and feel sensations such as heat, cold and pain. The information from the sensory nerves passes to your spinal cord and brain.

Motor nerves

Electrical impulses that pass along these nerves pass information from your brain and spinal cord to stimulate your muscles to move.

Autonomic nerves

Your autonomic nervous system controls involuntary actions, such as the beating of your heart and the widening or narrowing of your blood vessels. When something goes wrong in this system, it can cause serious problems which can affect:

- Your blood pressure.

- Your heart.
- Your breathing and swallowing.
- Your digestive system.
- In men, their ability to have/maintain erections during sex - a condition known as erectile dysfunction (impotence).

Diabetic neuropathy can cause problems with the sensory, motor and autonomic nerves. Diabetic neuropathy most often causes damage to the nerves in your legs.

Diabetic Retinopathy

The term retinopathy covers various disorders of the retina, which can affect vision. Retinopathy is usually due to damage to the tiny blood vessels in the retina.

Retinopathy is commonly caused by diabetes but is sometimes caused by other diseases such as very high blood pressure (hypertension).

Over several years, a high blood sugar (glucose) level can weaken and damage the tiny blood vessels in the retina. This can result in various problems which include

- Small blow-out swellings of blood vessels (microaneurysms).
- Small leaks of fluid from damaged blood vessels (exudates).
- Small bleeds from damaged blood vessels (haemorrhages).
- Blood vessels may just become blocked. This can cut off the blood and oxygen supply to small sections of the retina.
- New abnormal blood vessels may grow from damaged blood vessels. This is called proliferative retinopathy. These new vessels are delicate and can bleed easily.

The leaks of fluid, bleeds and blocked blood vessels may damage the cells of the retina. In some severe cases, damaged blood vessels bleed into the jelly-like centre of the eye (the vitreous humour). This can also affect vision by blocking light rays going to the retina.

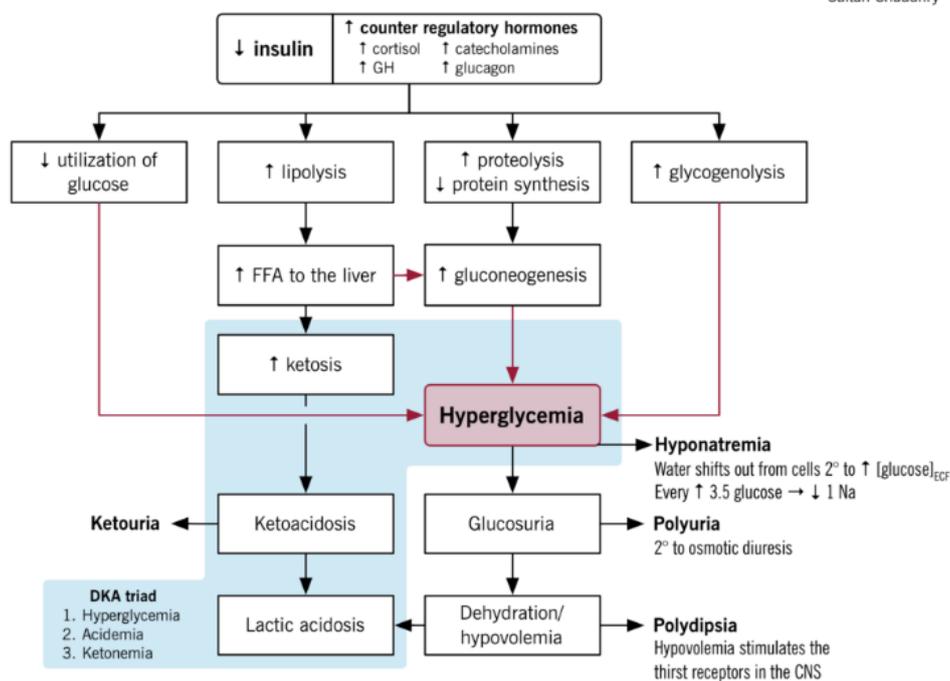
Cataract

Restless leg syndrome

Diabetic Ketoacidosis

Pathogenesis and pathophysiology of diabetic ketoacidosis

Sultan Chaudhry



Diabetic Hyperosmolar syndrome

Metabolic Encephalopathy (dehydration is not too bad on this pt due to pt's creatinine level is only 2.2 but it can be a differential diagnosis). Emphasis more about Metabolic encephalopathy Status/Condition: Critical Code Status: FULL Allergies: NKDA Admit to Unit: ICU Activity Level: bedrest Diet: NPO for now Critical Drips: Insulin

drip per DKA protocol, NS with 150 mEq Sodium Bicarb @150ml/ hr. Respiratory : Room Air Medications :DVT prophylaxis -Heparin SQ, GI Prophylaxis - Protonix IV, Electrolytes protocol to correct levels (Potassium, Magnesium and Phosphorus).

CONCLUSION

So diabetes is a common health issue nowadays not only in youth people but also in children. Commonly due to destruction of pancreatic beta cells, yes that's the type two diabetes mellitus and the main treatment option for this disease is insulin therapy.

REFERENCES

- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*, 2004; 27(Suppl 1): S5–S10.
- Fagot-Campagna A. Emergence of type 2 diabetes mellitus in children: epidemiological evidence. *J Pediatr Endocrinol Metab*, 2000; 13(Suppl 6): 1395–1402.
- Bloomgarden ZT. Type 2 diabetes in the young: the evolving epidemic. *Diabetes Care*, 2004; 27: 998–1010.
- Gahagan S, Silverstein J. American Academy of Pediatrics Committee on Native American Child Health. American Academy of Pediatrics Section on Endocrinology. Prevention and treatment of type 2 diabetes mellitus in children, with special emphasis on American Indian and Alaska Native children. *Pediatrics*, 2003; 112: e328.
- Atkinson MA, Eisenbarth GS. Type 1 diabetes: new perspectives on disease pathogenesis and treatment. *Lancet*, 2001; 358: 221–229.
- Verge CF, Stenger D, Bonifacio E, Colman PG, Pilcher C, Bingley PJ, Eisenbarth GS. Combined use of autoantibodies (IA-2 autoantibody, GAD autoantibody, insulin autoantibody, cytoplasmic islet cell antibodies) in type 1 diabetes: Combinatorial Islet Autoantibody Workshop. *Diabetes*, 1998; 47: 1857–1866.
- Leslie RD, Atkinson MA, Notkins AL. Autoantigens IA-2 and GAD in Type I (insulin-dependent) diabetes. *Diabetologia*, 1999; 42: 3–14.
- Savola K, Bonifacio E, Sabbah E, Kulmala P, Vahasalo P, Karjalainen J, Tuomilehto-Wolf E, Merilainen J, Akerblom HK, Knip M. IA-2 antibodies—a sensitive marker of IDDM with clinical onset in childhood and adolescence. Childhood Diabetes in Finland Study Group. *Diabetologia*, 1998; 41: 424–429.
- Komulainen J, Kulmala P, Savola K, Lounamaa R, Ilonen J, Reijonen H, Knip M, Akerblom HK. Clinical, autoimmune, and genetic characteristics of very young children with type 1 diabetes. Childhood Diabetes in Finland (DiMe) Study Group. *Diabetes Care*, 1999; 22: 1950–1955.
- The DCCT Research Group. Effects of age, duration and treatment of insulin-dependent diabetes mellitus on residual beta-cell function: observations during eligibility testing for the Diabetes Control and Complications Trial (DCCT). The DCCT Research Group. *J Clin Endocrinol Metab*, 1987; 65: 30–36.
- Hirschhorn JN. Genetic epidemiology of type 1 diabetes. *Paediatric Diabetes*, 2003; 4: 87–100.
- Harrison's principles of medicine 20th edition
- Ghai essentials of paediatrics.
- Dunn CJ, Peters DH. Metformin. A review of its pharmacological properties and therapeutic use in non-insulin-dependent diabetes mellitus. *Drugs*, 1995; 49: 721–749.
- Salpeter SR, Greyber E, Pasternak GA, Salpeter EE. Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus: systematic review and meta-analysis. *Arch Intern Med*, 2003; 163: 2594–2602.
- Yki-Jarvinen H, Dressler A, Ziemer M. Less nocturnal hypoglycemia and better post-dinner glucose control with bedtime insulin glargine compared with bedtime NPH insulin during insulin combination therapy in type 2 diabetes. HOE 901/3002 Study Group. *Diabetes Care*, 2000; 23: 1130–1136.
- Riddle MC, Rosenstock J, Gerich J. The treat-to-target trial: randomized addition of glargine or human NPH insulin to oral therapy of type 2 diabetic patients. *Diabetes Care*, 2003; 26: 3080–3086.
- Golan M, Weizman A, Apter A, Fainaru M. Parents as the exclusive agents of change in the treatment of childhood obesity. *Am J Clin Nutr*, 1998; 67: 1130–1135.
- Brand-Miller J, Hayne S, Petocz P, Colagiuri S. Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. *Diabetes Care*, 2003; 26: 2261–2267.
- CDC Diabetes Cost-Effectiveness Study Group, Centers for Disease Control and Prevention. The cost-effectiveness of screening for type 2 diabetes. *JAMA*, 1998; 280: 1757–1763.
- Fagot-Campagna A, Saaddine JB, Engelgau MM. Is testing children for type 2 diabetes a lost battle? *Diabetes Care*, 2000; 23: 1442–1443.
- DeFronzo RA. Lilly lecture 1987. The triumvirate: beta-cell, muscle, liver. A collusion responsible for NIDDM. *Diabetes*, 1988; 37: 667–687.
- Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, Keinanen-Kiukkaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*, 2001; 344: 1343–1350.
- Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*, 2002; 346: 393–403.
- Schmitz KH, Jacobs DR Jr., Hong CP, Steinberger J, Moran A, Sinaiko AR. Association of physical activity with insulin sensitivity in children. *Int J Obes Relat Metab Disord*, 2002; 26: 1310–1316.