Diabetes mellitus

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Definition

- Diabetes mellitus is a complex metabolic disorder characterized by chronic hyperglycaemia due to insulin deficiency, resistance or both.

types

- Diabetes may be primary or secondary .
- Gestational diabetes refers to glucose intolerance appearing for the first time in pregnancy
- ***Primary diabetes is classified into***:
- *Type 1 diabetes, which usually has an immune pathogenesis and is characterized by severe insulin deficiency.*
- *Type 2 diabetes, which results from a combination of insulin resistance and less severe insulin deficiency.*
- ***Secondary diabetes can be subdivided into:***
- diabetes secondary to exocrine pancreatic disease
- diabetes secondary to endocrine disease
- diabetes secondary to drugs and chemicals
- diabetes secondary to infection
- genetic mutation.

Type I DM

- Type 1 diabetes is a disease of insulin deficiency and accounts for 5–10% of all cases of diabetes.

- It is immune-mediated in the vast majority of cases.

- **Typically presents in childhood and young adulthood**, reaching a peak incidence around the time of puberty, but can present at any age.

- The onset of type 1 diabetes is typically **abrupt and severe,** with marked hyperglycemia developing over several days to weeks, and may be associated with a precipitating event, such as infection, pregnancy, or MI. Look for fatigue, polyuria, polydipsia, blurring of vision, weight loss, and dehydration.

- MOA : autoimmune destruction of the insulin producing cells of a genetically predisposed individual By auto antibodies directed against pancreatic islet constituents → followed by a phase of asymptomatic loss of β cell Secretory capacity (Insulitis) → Eventually, when the remaining β cells are no longer able to produce enough insulin to meet the body's needs, diabetes symptoms start to develop.

Type I DM

- **Approximately 20% of patients with type 1 diabetes develop other organ-specific autoimmune diseases, such as vitiligo, celiac disease, Graves disease, hypothyroidism, Addison disease and pernicious anemia.**

Type II DM

- Type 2 diabetes is characterized by a combination of insulin resistance and a β-cell secretory defect. With time, progressive β-cell dysfunction can develop, leading to absolute insulin deficiency.

- In general, type 2 diabetes **presents less dramatically** than type 1 diabetes.

- DKA is rare because patients maintain some degree of insulin secretion allowing for suppression of lipolysis.

- Because symptoms may be subtle, the time to diagnosis may be delayed. Consequently, **approximately 20% of patients with type 2 diabetes have microvascular complications of the disease at presentation; an even higher percentage may have CAD or peripheral vascular disease.**

- Most patients with type 2 diabetes are obese or at least have abdominal obesity

Clinical presentation of DM

Presentation may be acute, subacute or asymptomatic, or an individual may present with a complication of diabetes.

- *Acute presentation :* Children and young adults often present with a 2–6-week history of the classic triad of symptoms:

• *polyuria due to the osmotic diuresis that results when blood* glucose levels exceed the renal threshold

• *thirst and polydipsia due to the resulting loss of fluid and electrolytes*

• *weight loss due to fluid depletion and accelerated breakdown* of fat and muscle secondary to insulin deficiency.

→ Ketonuria is often present in young people and may progress to ketoacidosis if these early symptoms are not recognized and treated.

- *Subacute presentation :* The clinical onset may be prolonged over several months or years, particularly in older people.
Thirst, polyuria and weight loss are usually present, but the individual may complain of other symptoms such as lack of energy, visual blurring (owing to glucose-induced hanges in refraction), or pruritus vulvae or balanitis due to *Candida i*nfection.

- *Complications as the presenting feature ,* incuding micro and macrovascular complications , staphelococcus infections and gangrene.

- *Asymptomatic diabetes* approximately half of people with diabetes are unaware of their condition. are made as an incidental finding and several countries have introduced screening programmes to identify those with asymptomatic undiagnosed diabetes.

General observation
Does patient look well/
 unwell?
Weight loss (T1DM)
Weight gain (T2DM)
Dehydrated?
Breathing (air hunger,
 Kussmaul breathing)

Face
Cranial nerve palsy,
 particularly CNIII
Eye movements
Ptosis

Neck
Carotid pulses/bruits
Check thyroid gland for
 goitre (autoimmune)

Hands
Carpal tunnel
Dupuytren's contracture
Muscle wasting
Limited joint movement

Dupuytren's contracture

(From Palastanga N. Anatomy and
Human Movement, 6th edn, with
permission.)

Abdomen
Hepatomegaly (fatty liver)

Skin
Vitiligo (autoimmune)
Pigmentation (e.g. axillary
 acanthosis nigricans in
 insulin resistance)
Granuloma annulare
Bullosis

Vitiligo

Eyes
Fundoscopy
 - Cataracts, against red
  reflex
 - Retinopathy (p. 726)
 - Visual acuity
Eyelids – xanthelasma

Cataracts

Retinopathy

Mouth
Candidiasis

Insulin injection sites
Bruising
Lipohypertrophy
Lipoatrophy (rare)

Legs
Muscle wasting
Hair loss
Sensory neuropathy (glove
 and stocking)
Reflexes (lost in
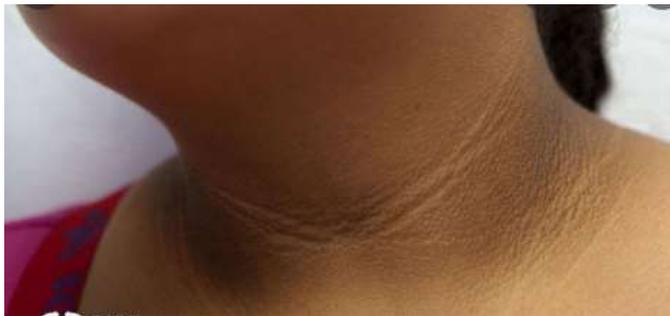 sensorimotor neuropathy)
Necrobiosis lipoidica

Feet
• Feel for peripheral pulses
• Skin – colour, ulcers,
 gangrene
• Look between toes for
 infection
• Sensory loss
 - Neuropathic foot ulcer
 - Charcot neuroarthropathy

Neuropathic ulcer

Charcot joints

Diagnosis of Diabetes and prediabetes

STUDY TABLE: Diagnosis and Classification of Type 2 Diabetes Mellitus				
Diagnosis	Fasting Glucose	Random Glucose	2-Hour Glucose During OGTT	Hemoglobin A_{1c}
Increased risk for diabetes (prediabetes)	100-125 mg/dL	140-199 mg/dL	140-199 mg/dL	5.7%-6.4%
Diabetes	≥126 mg/dL	≥200 mg/dL with symptoms	≥200 mg/dL	≥6.5%

❑ Prediabetes :
➢ Impaired fasting glucose : fasting glucose bwtween 100-125
➢ Impaired glucose tolerance , 2 hour blood glucose reading between 140-200mg/dl

❑ Regarding diagnosis of diabetes One abnormal laboratory value is diagnostic in symptomatic individuals; two values are needed in asymptomatic people.
The glucose tolerance test is only required where there is diagnostic uncertainty and for diagnosis of cystic fibrosis-related diabetes and gestational diabetes.

management

- Intensive lifestyle modification ;exercise, weight loss , Diet) is appropriate for all patients with prediabetes or type 2 diabetes.
- Insulin
- Non-insulin oral medications (for Type II DM)
- Non-insulin injectable medications , (for Type II DM)

Treatment of Type I diabetes

- Patients with type 1 diabetes are treated with **intensive insulin therapy, which includes intermediate-acting or long-acting** insulin for basal coverage and preprandial analog or regular insulin injections throughout the day.

- Intensive insulin therapy can also include **Insulin pumps: in which Subcutaneous infusion of rapid-acting insulin is delivered continuously for basal insulin requirements and** given in intermittent boluses for prandial needs.

- Insulin requirements can also be given in the form of premixed formulation, also less advisable to reduce the frequency of injections.

DM II treatment

- **Biguanides (Metformin)**
- **Sufonylurea** **(_eg. Glimipirde, Glibenclamide, Glybride)**
- **Meglitinides** **(eg. Nateglinide)**
- **Thiazolidinediones** **(eg. Pioglitazone, rosiglitazone)**
- **GLP1 receptor agonist** **(eg. Exenatide, liraglutide**
- **α-glucosidase inhibitors** **(Acarbose)**
- **DPP4-inhibitor** **(Saxagliptin, Sitagliptin, Linagliptin):**
- **SGLT2 inhibitors** **(Empagliflozin, dapagliflozin, canagliflozin):**
- **Amylin mimetic** **(Pramlintide**
- **Insulin**

- Metformin is the recommended first-line oral agent for newly diagnosed type 2 diabetes due to known effectiveness and low hypoglycemia risk. → Metformin is contraindicated at eGFR less than 30 mL/min/1.73 m².
- Dual therapy should be initiated If the hemoglobin A_{1c} level is 9% or higher at the time of diagnosis.
- Insulin Therapy should be started at the time of diagnosis if HbA1C >=10
- If therapy didn't meat the goal after 3 months , advancement from monotherapy >> dual therapy >> triple therapy >> combination injectable therapy is recommended .

Choosing the oral anti-diabetic agent depends on the patient's profile including comorbidities and BMI and characteristics of each medication (advantages and disadvantages)

- Antidiabetes agents that cause :
- Hypoglycemia : Sulphonylurea , Meglitinides , Insulin

- weight gain : Sulphonylurea , Meglitinides , Thiazolidiediones , Insulin
- Weight loss : GLP-I , pramlintide ,SGLT2 inhibitors
- Weight neutral : Metformin (with some possible weight loss , DPP-4 inhibitors

- Decrease CVD risk : GLP-1, SGLT2 inhibitors ,Metformin , Thiazolidiedione (Possible)
- Aggravate HF : DPP-4 inhibitors, Thiazolidiedione

Goal of therapy

- HbA1C < 7.0 % , Preprandial glucose level 80-130 postprandial glucose level 1-2hours after a meal < 180 .

Complications of DM

- Diabetic Ketoacidosis
- Hyperglycemic Hyperosmolar State
- Hypoglycemia

-Diabetic Foot Ulcer
-Infections

- **Microvascular**
  - Retinopathy
  - Nephropathy
  - Neuropathy

- **Macrovascular**
  - Accelerated arteriosclerosis
  - Myocardial infarction
  - Stroke
  - Lower extremity ischemia (PVD)

Screening for complications of dm

- **Patients with type 1 and type 2 diabetes should be screened regularly for diabetic complications,** including **retinopathy** (comprehensive eye examination**),** **nephropathy** (albumin-to creatinine ratio), **neuropathy** (10 g monofilament, 128-Hz tuning fork, pedal pulses, and ankle reflex), and **cardiovascular disease** (BP and fasting lipid profile measurements).

- Screening for complications in patients with type 1 diabetes should begin at 5 years after diagnosis and should be performed **annually thereafter.**

- Screening for complications in patients with type 2 diabetes should begin **at the time of diagnosis** and be performed **annually thereafter.**

Recommended vaccinations

- Persons with diabetes should receive age-appropriate vaccinations as recommended by the Advisory Committee on Immunization Practices guidelines.

- Additionally, patients with diabetes should receive **influenza vaccinations annually**, the **pneumococcal polysaccharide vaccine (PPVS23**), and **the series of hepatitis B vaccinations.**

Thank you