Diabetes Mellitus

By

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**Diabetes Mellitus**

**Definition:**

Diabetes mellitus comprises a heterogeneous group of metabolic diseases that are characterized by chronic hyperglycemia and disturbances in carbohydrate, lipid, and protein metabolism.

Its prevalence is increased worldwide (epidemic) because of obesity and sedentary life in both adults, adolescent and children. These adolescents may present in DKA, and then behave like type 2.

**Presentation:**

- **Type 1:**
  - Classic acute symptoms:
    - Hyperglycemia
    - Polydipsia
    - Polyuria
    - Weight loss
    - Polyphagia
    - Blurred vision
    - Itch
    - 25% present the first time with DKA.

- **Type 2:**
  - The disease is often present for many years before diagnosis:
    - Chronic hyperglycemia
    - Impairment of growth
    - Susceptibility to infections
    - Slow wound healing.

**Classification:**

- Type 1 diabetes (Immune mediated or Idiopathic)
- Type 2 diabetes: (Insulin resistance)
- Gestational diabetes mellitus
- Other specific types:
  - Genetic defects of B-cell function
  - Genetic defects in insulin action
  - Diseases of the exocrine pancreas (chronic pancreatitis)
  - Endocrinopathies (cushing, acromegaly, thyrotoxicosis)
  - Drug- or chemical-induced (steroid)
  - Infections
  - Anti-insulin receptor antibodies
  - Other genetic syndromes sometimes associated with diabetes

**The criteria for diagnosing diabetes:**

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Impaired Glucose Tolerance</th>
<th>DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>&lt;110</td>
<td>110 – 126</td>
<td>≥126</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Impaired Fasting Glucose</td>
<td></td>
</tr>
<tr>
<td>2h post 75 gm glucose</td>
<td>&lt;140</td>
<td>140 – 200</td>
<td>≥200</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Impaired Glucose Tolerance</td>
<td></td>
</tr>
<tr>
<td>Random</td>
<td></td>
<td></td>
<td>≥200</td>
</tr>
</tbody>
</table>

Any of the 3 is diagnostic confirmed by anyone of the 3 on another day.
**IFG & IGT:**
Increases the risk of developing type 2 diabetes (7% per year) and the risk of diabetic complications, particularly cardiovascular.

**OGTT (Oral Glucose Tolerance Test):**
Remains the standard for diagnostic purposes

**FPG:**
is simpler, cheaper, equally accurate, faster, more reproducible, and convenient, and is recommended for routine diagnostic use

**HbA1c:**
is a useful tool for monitoring glycemia and for making therapeutic decisions, it is not for diagnosis of diabetes.

### The difference between type 1 and type 2 DM

<table>
<thead>
<tr>
<th>Age</th>
<th>Type 1 DM</th>
<th>Type 2 DM</th>
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</thead>
<tbody>
<tr>
<td>&lt;30- any age</td>
<td>&gt;40 - any age</td>
<td></td>
</tr>
<tr>
<td>Incidence</td>
<td>5% to 10% of diabetics</td>
<td>90% to 95% of diabetics</td>
</tr>
<tr>
<td>Pathogenesis</td>
<td>In a genetically susceptible individual, environmental insult triggers Autoimmunizedisease.</td>
<td>. Insulin resistance in obese. . B-cell dysfunction in non-obese.</td>
</tr>
<tr>
<td>Genetic predisposition</td>
<td>Moderate Needenvironmental factors</td>
<td>Strong .</td>
</tr>
<tr>
<td>At diagnosis</td>
<td>Auto-antibodies</td>
<td>complications</td>
</tr>
<tr>
<td>Association</td>
<td>Autoimmune diseases</td>
<td>Autoimmune diseases</td>
</tr>
<tr>
<td>Insulin level</td>
<td>no or low</td>
<td>early Increases &amp; late Relatively Decreases</td>
</tr>
<tr>
<td>Stop Insulin</td>
<td>DKA</td>
<td>NKII0 &gt; DKA</td>
</tr>
</tbody>
</table>

### Criteria for screening asymptomatic high risk persons for type 2 DM:

1. Screening all persons at 45 ys, if normal results, repeat at 3-year intervals
2. Screening at a younger age or more frequently in
   - Overweight (↑BMI) or Central obesity with normal BMI
   - First-degree relative with diabetes
   - Members of a high-risk ethnic population
   - Bad Obstetric History (delivering a large baby, perinatal death or GDM)
   - Hypertensive
   - HDL cholesterol <35 mg/dL and/or TG >250 mg/dL
   - IFG or IOT

### Screening for Gestational diabetes mellitus

<table>
<thead>
<tr>
<th></th>
<th>50 gm glucose (Screening)</th>
<th>100 gm glucose (Diagnostic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>1h</td>
<td>140</td>
<td>180</td>
</tr>
<tr>
<td>2h</td>
<td>155</td>
<td></td>
</tr>
<tr>
<td>3h</td>
<td>140</td>
<td></td>
</tr>
</tbody>
</table>
Gestational diabetes mellitus (GDM)
- GDM affects 2% to 5% of all pregnancies (up to 14%)
- Screening between 24 and 28 weeks
- For all women > 25 years old
- For younger women with high risk to develop type 2
- Women at very high risk should be screened at their initial obstetric visit.
- A Positive 50-g glucose screening test indicates 3-hour, 100 gm OGTT
- Follow up after 6 weeks postpartum
- 25% of lean women & 50% of obese women develop diabetes over a 20ys.

Management:

1- Nutrition:
   Balanced, healthy diet:
   - 10% to 20% protein + < 30% fat + 50% to 60% carbohydrate.
   - Soluble fiber delays carbohydrate absorption and improves lipid profiles.

2- Weight management therapy

3- Exercise management therapy:
   - Regular, moderate physical activity for at least 30 minutes/day.
   - No Exercise if FPG >250 mg/dL with ketones, or >300 mg/dL without ketones
   - Self blood glucose monitoring (SBGM) should be performed before and after exercise.

4- Tight control of blood pressure to 130/85

5- Tight control of blood sugar:
   - DCCT Study (type 1 diabetes) showed that intensive treatment prevented or slowed the onset and/or progression of the microvascular complications: retinopathy by 76%, neuropathy by 60%, and proteinuria by 54% with increase in hypoglycemia.
   - UKPDS Study (type 2 diabetes) showed an overall reduction in microvascular complications of 25% with tight control.

Insulin therapy:

Indication
1. Type 1 diabetics
2. Type 2 not responding to oral treatments or surgery.

Insulin regimens
- Starting doses 0.15 to 0.5 U/kg/day up to 1.5 U/kg in severe IR.
- The dose is increased during intercurrent illness, pregnancy & growing child.
- A split or mixed regimen of NPH/regular twice daily (2/3 of the dose before breakfast and 1/3 before dinner; at each time 2/3 NPH and 1/3 regular)
- Bedtime insulin (NPH) and daytime sulfonylurea therapy for type 2 diabetes

Other Antihyperglycemic agents

- Sulfonylureas:
  - insulin secretagogue
  - Glucosamide, Glicilazide, Glipizide & Glimipride
  - They stimulate beta cells to secrete insulin
  - Side effect: Hypoglycemia & Weight gain.

- Biguanides (Metformin)
  - Insulin Sensitizers
  - Increases Hepatic glucose production by inhibiting gluconeogenesis.
  - Increases Glucose uptake and utilization by muscle.
  - Decreases Intestinal glucose absorption.
  - Decreases Weight & Lipids
  - Side effects: Gastrointestinal upsets & Lactic acidosis with advanced hepatic & renal disease

- Alpha-Glucosidase inhibitors
  - Antagonizing pancreatic amylase; so they Decrease Postprandial glucose.
  - It is taken with the first bite of a carbohydrate-containing meal
  - Side effects: Diarrhea and flatulence.
  - No hypoglycemia.

- Thiazolidinediones (Insulin Sensitizers)
  - Decreases Insulin resistance so used in obese patients
  - Pioglitazone & rosiglitazone
  - Decrease lipids
  - No hypoglycemia.
  - Side effects: Liver dysfunction (elevate liver enzymes), edema & weight gain.

- Meglitinides:
  - Insulin secretagogue
  - As sulfonylureas so not combined with sulfonylurea.
  - taken with meals and is omitted in the absence of a meal

Complications of DM:

- Acute complications of DM:
  A- Hypoglycemia.
  B- Diabetic Ketoacidosis: DKA
  C- Hyperosmolar Nonketotic Syndrome: HNKS
## DKA vs HNKS

<table>
<thead>
<tr>
<th>Type</th>
<th>DKA</th>
<th>HNKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Type 1 diabetes &gt; type 2 diabetes (only in acute illness)</td>
<td>Type 2 diabetes esp. elderly</td>
</tr>
<tr>
<td></td>
<td>5. Acidosis &amp; hyperosmolarity</td>
<td>More Dehydration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No ketosis, ketonuria or acidosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>More Hyperosmolarity</td>
</tr>
<tr>
<td>Pathogenesis</td>
<td>Decreased Insulin &amp; Increased CR hormones</td>
<td>IR: Increased insulin</td>
</tr>
<tr>
<td></td>
<td>Increased FFA</td>
<td>Decreased FFA</td>
</tr>
<tr>
<td></td>
<td>Increased Ketone bodies</td>
<td>Increased Lactic acid</td>
</tr>
<tr>
<td>Treatment:</td>
<td>1-Fluid replacement</td>
<td>As in DKA, but:</td>
</tr>
<tr>
<td></td>
<td>2-Insulin administration:</td>
<td>1-Greater Fluid replacement</td>
</tr>
<tr>
<td></td>
<td>3-Correct Electrolyte imbalances</td>
<td>&amp; more slowly</td>
</tr>
<tr>
<td></td>
<td>4-Monitor.</td>
<td>2-lower Insulin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-Heparin prophylaxis</td>
</tr>
</tbody>
</table>

### Hypoglycemia

- It is the result of overtreatment of DM, when blood glucose < 50 mg%.
- Causes:
  - Errors in insulin or oral hypoglycemic agent dose,
  - Missed, delayed or inadequate meal
  - Unexpected or unusual exercise

**Hypoglycemic Symptoms**

Profuse sweating, palpitation, hunger, anxiety, confusion, drowsiness, inability to concentrate or coma

**Hypoglycemia Management**

- It depends on the severity and whether the pt. is conscious and able to swallow
- Oral carbohydrates if hypoglycemia is recognized early
- IV glucose (30-50 ml of 50% dextrose) glucagone (1 mg I.M) should be given
- As soon as the pt. is able to swallow, glucose should be given orally

### Chronic Complications of DM

- Diabetes is the sixth leading cause of death
- Diabetes is a cause of 18% of all deaths in people over 25s of age
- Diabetes is the leading cause of ESRD, New cases of blindness and non-traumatic lower limb amputations.
- Cardiovascular disease is the major cause of diabetes-related death
- Cardiovascular disease is 2-4 times in diabetics > normal population
- In diabetics; Increased risk of stroke
- In diabetics; Life expectancy reduced by 5 to 10 years.

**Microvascular Complications**

They are either diabetic neuropathy, diabetic nephropathy or diabetic retinopathy

**Mechanisms:**
- Accumulation of sorbitol
- Advanced glycation end products (AGE)
- Increased oxidative damage
- Hyperinsulinemia, hyperviscosity & platelet dysfunction
- Activation of various growth factors

- **Diabetic Retinopathy (DR)**
  - Either proliferative or non-proliferative DR
  - Comprehensive fundus exam at time of diagnosis as evidence shows some patients may have retinopathy at diagnosis (type 2 and after 5 years in type 1 DM)
  - The frequency of follow-up—consensus is yearly with more frequent follow-up of abnormal findings

- **Diabetic Neuropathy**
  - Peripheral neuropathies either sensory (commonest), motor or autonomic
  - Sensory neuropathy may be presented by pain, paresthesias or loss of sensation
  - Autonomic neuropathy may be presented by postural hypotension, gastroparesis, diarrhea or impotence

- **Diabetic Nephropathy**
  - It may be presented glomerular lesions leading to persistent albuminuria which progress to end stage renal failure
  - Yearly screening for microalbuminuria is essential for early detection

- **Treatment of Microvascular Complications**
  - Prevention is the Key
  - Good Glycemic control
  - Hypertension control < 135/75 mm Hg
  - Smoking cessation
  - Weight reduction
  - Lipid control
  - Aggressive treatment of co-risk factors
  - Regular Exams (fundus, sensory, MIA, ECG, KFT)
  - Low-dose aspirin

**Macrovascular Complications of DM**

They are either cardiovascular disease, cerebrovascular disease or peripheral vascular disease.
Mechanism:

Atherosclerosis & Risk factors:
- Dyslipidemia
- Hypertension
- Obesity
- Hyperglycemia

Management of chronic diabetic Complications:

- Aggressive treatment of hypertension <130/85 mm Hg,
- Use ACEI or ARB for renal protection.
- B-Blockers
- Low-dose aspirin
- Cessation of smoking
- Management of obesity
- Treat Dyslipidemia:
  - goals:
    - LDL cholesterol <100 mg/dL
    - TG <200 mg/dL
    - HDL >45 mg/dL for men & >55 mg/dL for women
- Safe exercise