### Natural history of diabetes mellitus

#### Definition
- It is a heterogeneous group of disorders characterized by hyperglycemia, and disturbances of carbohydrate, fat and protein metabolism with absolute or relative deficiency of insulin action and or secretion
- Hyperglycemia resulting from defects in insulin secretion, insulin action, or both

#### Epidemiology
- 5% of the general population are diagnosed with diabetes
- Diabetes is a significant co-morbid player in other disease processes
- Majority of diabetics are managed by primary care providers
- Diabetes is the growing heath problem & has risen about six fold since 1950
- DM is the leading cause for, Blindness, ESRF, IHD, CVA, amputation

- Type 1 Diabetes (absolute insulin deficiency, ketosis prone, Immune mediated or Idiopathic)
- Type 2 Diabetes (insulin resistance, relative insulin deficiency, 80% obese)
- Gestational Diabetes (potential prediabetic state during pregnancy)
- Secondary Diabetes
  - Endocrinopathies associated with hyperglycemia
  - Pancreatic disease (Chronic pancreatitis, Cystic fibrosis & Hemochromatosis)
  - Drug or chemical induced
- Genetic defects of beta-cell function or insulin action

#### Type 1
- B-cell destruction usually leading to absolute insulin deficiency (low or undetected c-peptide level)
- Insulin is usually required for survival
- Risk of ketoacidosis
- Autoimmune DM
  - Results from autoimmune destruction of B-cell
  - Destruction could be rapid especially in children or slow especially in adults (Latent Autoimmune Diabetes in Adults LADA)
- Markers of immune destruction
  - Islet cell auto Abs
  - Insulin Auto Abs
  - Auto Abs to glutamic acid decarboxylase (GAD)
- Immunological markers are present in 85-90% of those patients
- Peak incidence in childhood and adolescence
- Environmental factors play a role
- Genetic predisposition
- Patients are usually not obese
- Other autoimmune diseases may be present
- 5-10% of diabetic population

#### Type 2
- They have relative rather than absolute insulin deficiency with resistance to insulin action
- They do not require insulin for survival
- They may remain undetected for long time
- They have increased risk of macro and micro vascular complications
- The autoimmune destruction does not occur
- Ketoacidosis is infrequent
- Obesity is very common
- Insulin level could be normal or elevated
- Insulin sensitivity can be increased by decreasing weight, increasing physical activity and or pharmacologic treatment
- The risk of this type increases with age, obesity, lack of physical activity
- It is more in women with GDM and individuals with HTN or Dyslipidemia
- Genetic predisposition is common
- 85-90% of diabetic population

#### Features of type 1 DM
- 80% occur before age 20 but may occur at any age
- Insulin deficient → autoimmune pathogenesis, HLA linked
- Ketosis prone
- Normal insulin sensitivity

#### Risk factors
1. First degree relative (identical twins)
2. Associated autoimmune disease (vitiligo-goiter-rheumatoid disease )
3. History of non-prolonged breast feeding early — exposure to cows milk
4. Specific high risk genotype HLA DQB1 – 0302 / HLA – DQB1 0201

#### Features of type 2 DM
- Most common after age 40
- Abdominal obesity present in 90%
- Insulin resistance/hyperinsulinemia
- Ketosis resistant
- Hypertension common
- High VLDL, low HDL cholesterol
- Accelerated atherosclerosis
- High in risk in many ethnic groups

#### Risk factors
1. Age > 45
2. Overweight and obesity (abdominal)
3. Family history of diabetes in first-degree relative
4. History of gestational diabetes or Large sizes baby
5. Hypertension, Hyperlipidemia
6. History IGT or IFG
7. Polycystic ovary syndrome
8. History of vascular disease
9. Habitual physical inactivity
10. Family history of diabetes
### 2ry causes of DM

1. **Endocrinopathies:**
   - a) Acromegaly; Cushing’s syndrome
   - b) Glucagonoma; Pheochromocytoma
   - c) Hyperthyroidism; Somatostatinoma
   - d) Aldosteronoma

2. **Drug or chemical-induced** → Vacor; Dilantin; Thiazides; Diazoxide, Pentamidine; α - interferon; Nicotinic acid, Glucocorticoids; Thyroid hormone, β - adrenergic agonists
3. **Hemochromatosis**
4. **Fibrocalculous pancreatopathy**
5. **Infections** → Congenital rubella; Cytomegalovirus

### Main presentation of DM

1. **Symptoms of Hyperglycemia**
   - a. Polyuria, Polydipsia, Polyphagia & Weight loss
2. **Blurred vision**
3. **Infection**
4. **Fatigue and weakness**
5. **Symptoms of complications**
6. **Accidentally discovered during routine lab screening**
7. **Atypical presentation**

### How can you reduce your risk of getting type 2 DM?

1. Weight reduction through improved eating habits
2. Moderate physical activity (30 minutes per day)
3. Regular screening with FBG or OGTT
4. Important to detect and treat early

### Type 1 DM vs Type 2 DM

<table>
<thead>
<tr>
<th></th>
<th>Type 1 DM</th>
<th>Type 2 DM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>&lt;30 – any age</td>
<td>&gt;40 – any age</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>5% - 10% of diabetes</td>
<td>90% - 95% of diabetics</td>
</tr>
<tr>
<td><strong>Pathogenesis</strong></td>
<td>Autoimmune disease</td>
<td>Insulin resistance</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>Usually thin or normal</td>
<td>Usually obese</td>
</tr>
<tr>
<td><strong>Genetic predisposition</strong></td>
<td>Mild to moderate</td>
<td>Strong</td>
</tr>
<tr>
<td><strong>At diagnosis</strong></td>
<td>Auto antibodies</td>
<td>Complications</td>
</tr>
<tr>
<td><strong>Associations</strong></td>
<td>Autoimmune disease</td>
<td>HTN, dyslipidemia</td>
</tr>
<tr>
<td><strong>Presentation</strong></td>
<td>Severe polys</td>
<td>Mild or no symptoms</td>
</tr>
<tr>
<td><strong>Insulin level</strong></td>
<td>No or low</td>
<td>Early high &amp; late relatively low</td>
</tr>
<tr>
<td><strong>Stress; stop insulin</strong></td>
<td>DKA</td>
<td>NKHO &gt;DKA</td>
</tr>
</tbody>
</table>

#### All of the following are diagnostic criteria to diagnose diabetes mellitus (DM) **EXCEPT:**

- a) FPG ≥126 mg/dl.
- b) 2-h post prandial BG ≥200 mg/dl
- c) Symptoms of diabetes alone e.g. polyuria, polydipsia & nocturia
- d) Symptoms of diabetes plus casual plasma glucose concentration ≥200 mg/dl
- e) FPG of (100 – 125 mg%) is called impaired fasting

#### One of the following is not a main element that characterizes the pathophysiology of type 2 diabetes:

- a) Insulin resistance
- b) Autoimmune destruction of pancreatic beta cells
- c) Deregulated hepatic glucose production (HGP),
- d) Hyperinsulinemia

#### Which of the following is true regarding type 1 DM?

- a) The most accepted cause is immune mediated beta cell destruction
- b) It is 90% of cases of DM
- c) There is insulin inefficiency and insulin resistance
- d) Family history of DM in 80% of patient
- e) It is ketosis resistant

#### All of the following statements regarding type 2 diabetes mellitus are true except:

- a) The patient is usually obese
- b) Diabetic ketoacidosis usually common presentation
- c) Hyperlipidemia may be associated
- d) It is the most common type of diabetes
- e) Serum insulin level and C-peptide are normal or elevated