Diabetes mellitus

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Objectives of the lecture

Definition of diabetes mellitus (DM)

Magnitude of the problem

Classification of DM

Natural history

Diagnosis of DM

Complications of DM

Prevention and control

Definition of diabetes mellitus

Diabetes , is a syndrome characterized by disordered metabolism and inappropriately high blood sugar (hyperglycemia) resulting from either low levels of the hormone insulin or from abnormal resistance to insulin's effects

Magnitude of the problem

- Diabetes is an “iceberg” disease
- The prevalence of DM in adults is around 4% worldwide
- In 2000, according to the World Health Organization, at least 171 million people worldwide suffer from diabetes.
- Its incidence is increasing rapidly, and it is estimated that by the year 2030, this number will double.
- Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in the more developed countries.

The greatest increase in prevalence is expected to occur in Asia and Africa, where most patients will likely be found by 2030.

The rising prevalence of DM in the developing countries is associated with industrialization and socioeconomic development

The major determinant for the increase in number of diabetics in the developing countries are:

Population growth

Age structure

Urbanization

↑ in Urban\rural population ratio

↑ prevalence of obesity among urban dwellers

lifestyle changes, most importantly a "Western-style" diet.

Classification of DM

- **Type 1 DM: Insulin-dependent diabetes mellitus (IDDM)**
- **Type 2 DM: Non insulin-dependent diabetes mellitus (NIDDM)**
- **Gestational diabetes mellitus (GDM)**
- **Secondary diabetes mellitus**

Type 1 Diabetes Mellitus

It is characterized by loss of the insulin-producing beta cells of the islets of Langerhans in the pancreas, leading to a deficiency of insulin.

The main cause of this beta cell loss is a T-cell mediated autoimmune attack.

Type 1 diabetes can affect children or adults but was traditionally termed "juvenile diabetes" because it represents a majority of cases of diabetes affecting children.

Type 2 Diabetes Mellitus

- It is due to insulin resistance or reduced insulin sensitivity, combined with reduced insulin secretion.
- The defective responsiveness of body tissues to insulin almost certainly involves the insulin receptor in cell membranes.
- In the early stage the predominant abnormality is reduced insulin sensitivity, characterized by elevated levels of insulin in the blood.

Gestational diabetes

Gestational diabetes mellitus (GDM) resembles type 2 diabetes in several respects, involving a combination of relatively inadequate insulin secretion and responsiveness.

It occurs in about 2%–5% of all pregnancies and may improve or disappear after delivery.

Gestational diabetes is fully treatable but requires careful medical supervision throughout the pregnancy.

About 20%–50% of affected women develop type 2 diabetes later in life .

Even though it may be transient, untreated gestational diabetes can damage the health of the fetus or mother.

***Risks to the baby include*:**

- **macrosomia (high birth weight),**
- **congenital cardiac and central nervous system anomalies**
- **skeletal muscle malformations.**
- **Increased fetal insulin may inhibit fetal surfactant production and cause respiratory distress syndrome**

Secondary diabetes mellitus

- **Pancreatic disorders:**

  inflammatory or neoplastic such as chronic pancreatitis and cystic fibrosis

- **Hormonal disorder:**

  Diseases associated with excessive secretion of insulin-antagonistic hormones (Cushing, acromegally)

- **Drug induced:**

  Many drugs impair insulin secretion and some toxins damage pancreatic beta cells ex. Alloxan, rodenticide VALCOR, Corticosteroids, Thiazide diuretics

Natural history

Agent factors

Host factors

Environmental factors

Agent factors

The underlying cause of DM is insulin deficiency which is absolute in IDDM and partial in NIDDM

This is due to:

A. **Pancreatic disorders: inflammatory and neoplastic and cystic fibrosis**
B. **Defects in formation of insulin: synthesis of an abnormal , biologically less active insulin molecule**
C. **Destruction of beta cells e.g viral infection and chemical agents**
D. **Decreased insulin sensitivity: Due to decreased number of adibocyte and momocyte insulin receptors**
E. **Genetic defects: mutation of insulin gene**
F. **Autoimmunity**

Host factors

Age

Genetic markers

Immune mechanism

Obesity

Age

IDDM:

Mainly young people less than 30 years

The peak age of onset is 10-14 years

NIDDM:

Middle age (40 years and ↑ thereafter)

Genetic markers

IDDM is associated with HLA-B8 and B15 and more powerfully HLA-DR3 and DR4

The highest risk of IDDM is carried by individuals with both DR3 and DR4

NIDDM, is not HLA associated

Immune mechanism

Both cell mediated and humeral activity against islet cells

Some people have defective immunological mechanisms and under the influence of environmental triggers, attack their own insulin producing cells

Obesity

Central obesity: fat concentrated around the waist in relation to abdominal organs, predispose individuals for insulin resistance.

Abdominal fat is especially active hormonally, secreting a group of hormones called adipokines that may possibly impair glucose tolerance.

Obesity is found in approximately 55% of patients diagnosed with type 2 diabetes .

Environmental factors

- Sedentary life style (↓ interaction between insulin and receptors)
- Diet (Quantity)
- Viral infections (rubella, mumps)
- Chemical agents
- Stress
- Other factors: economic status, education, urbanization

diabetes risk factors

Non-Modifiable risk Factors – Risk factors that cannot be changed.

Age

Family History

Ethnicity:

Modifiable Risk Factors – Risk factors that you have control of or can be changed.

- **Weight**
- **Activity Level**
- **High Blood Pressure**
- **High Blood Lipids**
- **Fasting Blood Glucose: A fasting blood glucose over 100 mg/dL may indicate that you have impaired glucose tolerance (IGT)**
- **Smoking: Smoking is a health hazard. Active smokers have a 44 percent increased risk of developing type 2 diabetes.**

Diagnosis of DM

- **Clinical picture:**

  Symptoms

  Signs

- **Investigations**

Clinical picture

- **The classical triad of diabetes symptoms is polyuria , polydipsia and polyphagia.**
- **In type 2 diabetes the symptoms develop much more slowly and may be subtle or completely absent.**
- **Type 1 diabetes may also cause a rapid significant weight loss (despite normal or even increased eating) and irreducible fatigue.**

Investigations

Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the following:

fasting plasma glucose level at or above 126 mg/dL (7.0 mmol/l)

plasma glucose at or above 200 mg/dL (11 mmol/l) two hours after a 75 g oral glucose load as in a glucose tolerance test .

random plasma glucose at or above 200 mg/dL (11 mmol/l)

Patients with fasting glucose levels between 100 and 125 mg/dL (6.1 and 7.0 mmol/l) are considered to have impaired fasting glycemia .

Patients with plasma glucose at or above 140 mg/dL or 7.8 mmol/l two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance .

Of these two pre-diabetic states, the latter in particular is a major risk factor for progression to full-blown diabetes mellitus as well as cardiovascular disease

An elevated level of glucose irreversibly bound to hemoglobin termed glycosylated hemoglobin or *HbA1c* (of 6.0% or higher is considered abnormal)

HbA1c is primarily used as a treatment-tracking test reflecting average blood glucose levels over the preceding 90 days

Complications of DM

Acute complications

Chronic complications

Acute complications

- **Diabetic ketoacidosis**
- **Hypoglycemia**

Chronic complications

Macrovascular disease due to damage to the arteries leads to:

- Atherosclerosis
- Coronary artery disease, leading to angina or myocardial infarction ("heart attack")
- Stroke (mainly the ischemic type)
- Peripheral vascular disease, which contributes to intermittent claudication as well as diabetic foot.
- Diabetic myonecrosis ('muscle wasting')

Microangiopathy : **cause one or more of the following :**

Diabetic retinopathy

growth of friable and poor-quality new blood vessels in the retina as well as macular edema) swelling of the macula ,(which can lead to severe vision loss or blindness. Retinal damage (from microangiopathy) makes it the most common cause of blindness among non-elderly adults .

Diabetic neuropathy,

abnormal and decreased sensation, usually in a 'glove and stocking' distribution starting with the feet but potentially in other nerves, later often fingers and hands. When combined with damaged blood vessels this can lead to *diabetic foot*

Diabetic nephropathy **,damage to the kidney which can lead to chronic renal failure, eventually requiring dialysis**

Diabetes mellitus is the most common cause of adult kidney failure worldwide in the developed world .

Prevention and control

- Type 1 diabetes risk is known to depend upon a genetic predisposition based on HLA types (particularly types DR3 and DR4), an environmental trigger and an uncontrolled autoimmune response that attacks the insulin producing beta cells
- Some research has suggested that breastfeeding decreased the risk
- Giving children 2000 IU of Vitamin D during their first year of life is associated with reduced risk of type 1 diabetes .

Type 2 diabetes risk can be reduced by making changes in diet and increasing physical activity

The American Diabetes Association(ADA) recommends maintaining a healthy weight, getting at least 2½ hours of exercise per week

having a modest fat intake, and eating a good amount of fiber and whole grains