Diabetes Mellitus

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Surat
What is diabetes?

- Group of diseases
- High levels of blood glucose
- Due to defects in insulin production
- Due to defects in insulin action
- Both.

- Metabolic disorder
- Chronic hyperglycaemia
- Disturbances of carbohydrate, fat and protein metabolism
Diabetes – Clinical Features

Common Representation

- Polyuria
- Polyphagia
- Polyuria
- Weight loss.
- Blurring of vision

Severe forms

- Ketoacidosis
- Non-ketotic hyperosmolar state
Later Symptoms

- Fatigue
- Dry skin
- Recurrent infection
- Feet Ulceration
- Sensory loss in lower extremities
- Erectile dysfunction
- Slow Healing of wounds
- Visual disturbance
Types of Diabetes

- Type 1 Diabetes Mellitus
- Type 2 Diabetes Mellitus
- Gestational Diabetes
- Other types:
  - LADA (Latent Autoimmune Diabetes of Adult onset)
  - MODY (Maturity Onset Diabetes of Young)
  - Mutation in Gene
  - Secondary Diabetes Mellitus
Type 1 diabetes

- Insulin-dependent diabetes mellitus (IDDM)
- Juvenile-onset diabetes.
- Immune system destroys pancreatic beta cells
- Children and young adults
- Although disease onset can occur at any age.
- Type 1 diabetes may account for 5% to 10% of all diagnosed cases of diabetes.
Type 2 diabetes

- Non-insulin-dependent diabetes mellitus (NIDDM)
- Adult-onset diabetes.
- 90% to 95% of all diagnosed cases of diabetes.
- Insulin resistance
- As the need for insulin rises
- & Pancreas gradually loses its ability to produce insulin.
- Associated with
  - Older age
  - Obesity & Physical inactivity
  - Family history of diabetes & History of gestational diabetes
  - Impaired glucose metabolism
Type 1 Diabetes: Insufficient Insulin

- Diminished insulin
- Glucose
- Diminished glucose uptake

Type 2 Diabetes: Insulin Resistance

- Insulin
- Glucose
- Defect in signaling to Glut-4
- Diminished glucose uptake
Stimulus: Glucose is absorbed after a meal

**Insulin**
- Stimulus: Glucose is absorbed after a meal
  - Pancreas: β-cells release insulin into blood
  - Liver: Converts glucose to glycogen, fats, and proteins
  - Muscle and other cells use glucose as an energy source, or convert it to glycogen

**Glucagon**
- Pancreas: α-cells release glucagon into blood
- Liver: Converts glycogen to glucose

**Homeostasis**
- Normal blood glucose levels (<110 mg per dl)
  - High blood glucose level
  - Low blood glucose level

**Stimulus**: Cells use or store glucose between meals
Gestational diabetes

- Diagnosed in some women during pregnancy.
- After pregnancy, 5% to 10% of women with gestational diabetes are found to have type 2 diabetes.
Other types of DM

- Maturity Onset Diabetes of Young
  - Surgery
  - Drugs
  - Malnutrition
  - Infections
  - Other illnesses.

- 1% to 5% of all diagnosed cases of diabetes.
LADA

- Latent Autoimmune Diabetes in Adults (LADA)
- Autoimmune type 1 diabetes at older age
- "Slow Onset Type 1" diabetes
MODY – Maturity Onset Diabetes of the Young

- Mutations
  - In enzyme glucokinase
  - In Receptor
- In sufficient insulin release from pancreatic β-cells
Secondary DM

Secondary causes of Diabetes mellitus include:
- Acromegaly
- Cushing syndrome
- Thyrotoxicosis
- Pheochromocytoma
- Chronic pancreatitis
- Cancer
- Drug induced hyperglycemia
# Reference Ranges

<table>
<thead>
<tr>
<th></th>
<th>FBS in mg%</th>
<th>PP2BS in mg %</th>
<th>HbA1C in %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal</strong></td>
<td>70 – 110</td>
<td>&lt; 140</td>
<td>4 – 6.5</td>
</tr>
<tr>
<td><strong>Pre-Diabetic</strong></td>
<td>110 - 126</td>
<td>&lt; 140</td>
<td>4 – 6.5</td>
</tr>
<tr>
<td>(Impaired Fasting Glycemia)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pre-Diabetic</strong></td>
<td>110 - 126</td>
<td>140 – 200</td>
<td>6.5 – 7.0</td>
</tr>
<tr>
<td>(Impaired Glucose Tolerance)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes mellitus</strong></td>
<td>&gt; 126</td>
<td>&gt; 200</td>
<td>&gt; 7.0</td>
</tr>
</tbody>
</table>
Investigation

- FBS
- PP2BS
- Oral Glucose Tolerance Test
- I.V. Glucose Tolerance Test
- HbA1C
- Urinary Sugar - Protein
- Lipid Profile
- Renal Function Test
- Fundus Examination
- Nerve Conduction Study
Complications

- Acute complications
- Chronic complications
Acute complications

- Diabetic Ketoacidosis
- Hyperosmolar Non-ketosis Coma
- Hypoglycemia
Diabetic ketoacidosis (DKA)

- Acute and dangerous
- On presentation at hospital,
  - Dehydrated
  - Hypotension & shock
  - Abdominal pain is common and may be severe.
  - Breathing = Rapid and Deep.
  - Kussmull’s breathing
  - Fruity smell from breath
  - May progress to coma.
Investigation in DKA

- Electrolyte
- Blood Glucose
- Blood Ketone body
- ABG
  - pH
  - pO2
  - pCO2
  - HCO₃⁻
Hyperosmolar Nonketotic Coma

- Symptoms are similar to DKA
- Due to osmotic effect of high glucose levels
- Water loss increases and eventually lead to dehydration.
- Progressively dehydrated
- Electrolyte imbalance.
- Lethargy
- Ultimately progress to a coma
Hypoglycemia

- Due to several diabetes treatments.
- Sweaty & Weak.
- Altered Consciousness
- Coma, Seizures

**Caused by**
- Too much dose of insulin or oral hypoglycemic drugs.
- Incorrectly timed insulin
- Too much or incorrectly timed exercise
- Not enough food
Chronic complications

- Microvascular diseases
- Macrovascular diseases
  - Coronary artery disease
  - Peripheral vascular disease
  - Intermittent claudication
  - Stroke
  - Diabetic foot
Microvascular diseases

- Diabetic cardiomyopathy,
- Diabetic nephropathy
- Diabetic neuropathy
- Diabetic retinopathy
Management of Diabetes Mellitus
The major components of the treatment of diabetes are:

- Diet and Exercise
- Oral hypoglycaemic therapy
- Insulin Therapy
Diet & Exercise

- **Dietary treatment should aim at:**
  - Ensuring weight control
  - Providing nutritional requirements
  - Allowing good glycemic control
  - Correcting any associated blood lipid abnormalities

- **Exercise**
  - Reduce abdominal obesity
  - Minimum 30 – 40 minutes brisk walking
  - Aerobic exercise
Nutritional Requirement

- Carbohydrate
  - 60-70% calories from carbohydrates & monounsaturated fats

- Protein
  - 10-20% total calories

- Fat
  - <10% calories from saturated fat
  - 10% calories from PUFA
  - <300 mg cholesterol

- Fiber
  - 20-35 grams/day

- Alcohol
  - Type I – limit to 2 drinks/day, with meals
  - Type II – substitute for fat calories
B. Oral Anti-Diabetic Agents

- **Classes of Oral anti-diabetic agents:**
  1. Sulfonylureas
  2. Biguanides
  3. Thiazolidinediones
  4. Alpha-glycosidase inhibitors
  5. Meglitinides
  6. Dipeptidyl peptidase-4 inhibitor
Sulfonylureas

Mechanism: Stimulation of insulin secretion

1st generation:
- Tolbutamide
- Chlorpropamide

2nd generation:
- Glybenclamide
- Glipizide

3rd generation:
- Glymepiride
Biguanides

- Phenformin
- Metformin

**Mechanism**
- Decrease glucose production from Liver by mild inhibiting ETC complex –I
- Decrease intestinal absorption of Glucose
Thiazolidinediones (TZDs)

- Representative Drugs
  Rosiglitazone
  Pioglitazone
- Pharmacological effects
  - Improving function of insulin sensitivity
  - Decrease insulin resistance
α-glucosidase inhibitors

- **Representative Drugs**
  - Acarbose
  - Voglibose

- **Mechanism**
  - Competitively inhibiting alpha amylase
  - To inhibit digestion of starch & disaccharides

- Main adverse reaction
  - Flatulence, diarrhea.
Meglitinides

- **Representative Drugs**
  - Repaglinide

- **Key point**
  - Increase insulin release by inhibiting ATP-sensitive K$^+$-channel
  - No direct effect on insulin release
  - Used alone or together with biguanides
  - Carefully used for patients with kidney or liver impaired.
Dipeptidyl Peptidase-4 (DPP) Inhibitor

- Sitagliptin
- Saxaliptin

**Mechanism of Action**
- DPP-4 inactivate Incretins
- So DPP-4 inhibitor increase incretins
- Inhibit insulin degradation
- Decrease Glucagon
Indication of Insulin Therapy

**Short-term use:**
- Acute illness, surgery, stress and emergencies
- Pregnancy
- Insulin may be used as initial therapy in type 2 diabetes
- in marked hyperglycaemia
- Diabetic ketoacidosis
- Hyperosmolar nonketotic coma

**Long-term use:**
- If targets have not been reached after optimal dose of combination therapy
<table>
<thead>
<tr>
<th>Insulin type/action</th>
<th>Brand names (generic name in brackets)</th>
<th>Basal/bolus</th>
<th>Dosing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-acting analogue (clear)</td>
<td>Humalog® (insulin lispro) NovoRapid® (insulin aspart)</td>
<td>Bolus</td>
<td>Usually taken right before eating or to lower high blood glucose</td>
</tr>
<tr>
<td>Onset: 10–15 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak: 60–90 minutes</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Duration: 4–5 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-acting (clear)</td>
<td>Humulin®-R Novolin®ge Toronto</td>
<td>Bolus</td>
<td>Taken about 30 minutes before eating, or to lower high blood glucose</td>
</tr>
<tr>
<td>Onset: 0.5–1 hour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak: 2–4 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration: 5–8 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate-acting (cloudy)</td>
<td>Humulin®-N Novolin®ge NPH</td>
<td>Basal</td>
<td>Often taken at bedtime, or twice a day (morning and bedtime)</td>
</tr>
<tr>
<td>Onset: 1–3 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak: 5–8 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration: up to 18 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extended long-acting analogue</td>
<td>Lantus® (insulin glargine) Levemir® (insulin detemir)</td>
<td>Basal</td>
<td>Usually taken once or twice a day</td>
</tr>
<tr>
<td>(Clear and colourless)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset: 90 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak: none</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration: 24 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premixed (cloudy)</td>
<td>Humalog® Mix 25™ Humulin® (20/80, 30/70) Novolin®ge (10/90, 20/80, 30/70, 40/60, 50/50)</td>
<td>Combination of basal and bolus insulins</td>
<td>Depends on the combination</td>
</tr>
<tr>
<td>A single vial contains a fixed ratio of insulins (the numbers refer to the ratio of rapid- or fast-acting to intermediate-acting insulin in the vial)</td>
<td></td>
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</tbody>
</table>
Treatment of DKA

1. Improve circulatory volume
2. Decrease Serum glucose
3. Clear serum of ketonebodys
4. Correct electrolyte imbalances
Treatment of DKA

Principles of Treatment:

• Replacement of fluid deficits.
• Correction of acidosis & hyperglycemia via Insulin administration.
• Correction of electrolytes imbalance.
• Treatment of underlying cause.
Fluids replacement

Intravenous solutions

- Replace extravascular and intravascular fluids
- Replace electrolyte losses
- Dilute both the glucose level

Insulin is needed to help

- switch from a catabolic state to an anabolic state
- uptake of glucose in tissues
- reduction of gluconeogenesis
- reduce ketone production.
Fluid Correction

- Initial correction of fluid loss is either
  - by isotonic NaCl solution
  - by lactated Ringer solution.
- The recommended schedule:
  - Administer 1 -3 L during the first hour.
  - Administer 1 L during the second hour.
  - Administer 1 L during the following 2 hours
  - Administer 1 L every 4 hours
- When blood sugar < 180 mg/dL
  - 5-10% dextrose with half isotonic NaCl solution.
- In maintenance, half-normal saline at 200-1000 mL/h
Insulin Therapy

- Regular insulin infusion = 0.1 U/kg/hour
- Serum Glucose should not decrease more than 100mg%/hour
- If Glucose falls < 200 prior to correction of acidosis,
  - change IV fluid from 5% Dextrose or 10% dextrose
  - But don’t decrease the rate of insulin infusion.
- Use initial bolus of insulin (IV/IM) is controversial.
Correction of Acidosis

- Insulin therapy
  - Stops Lipolysis
  - Decrease production of ketone bodies.
- Normal saline
  - Correction of dehydration
  - Normalize the blood PH.
- Bicarbonate therapy
  - should not be used unless severe acidosis (pH<7.0)
Correction of Electrolyte Imbalance

- If K+ is low.
  - As soon as the urine output is restored, potassium supplementation
- If K+ is high
  - Potassium should be corrected
    - Furosemide
    - Insulin
    - Salbutamol
    - Bicarbonate
Thank You