

Diabetes Mellitus

Definition

A chronic multisystem disease of an abnormal metabolic state, characterised by hyperglycaemia due to inadequate insulin action/production.

Causes, Incidence & Risks

- Diabetes mellitus can be a primary or secondary condition
- 95% of cases of DM are primary disorders of insulin production
- DM affects about 30 million people worldwide
- Primary hormone involved is INSULIN, produced by the Beta cells of the Pancreas.
- Secondary DM is due to pancreatic disease e.g Chronic Pancreatitis or hypersecretion of hormones which counter act insulin. (Corticosteroids in patients with Cushing's disease and Growth hormone in patients with Acromegaly.)

- There are two types of Diabetes mellitus:
- **TYPE I** – Insulin Dependent Diabetes Mellitus (IDDM) or Juvenile onset DM
- **TYPE II** – Non-Insulin Dependent Diabetes Mellitus (NIDDM) or late onset

Type I Diabetes Mellitus

- This form of the disease is organ specific i.e. affects the Pancreas.
- It is an autoimmune disorder causing ANTIBODY MEDIATED destruction of the Beta cells of the Pancreas.
- It has a childhood or adolescent onset.
- Usually affects thin people.
- Patients of European extraction are most commonly affected.
- 90% of cases exhibit the antigenic markers HLA-DR3 or HLA-DR4.
- Females = Males in the number of cases.

- It has an acute/subacute onset.
- Ketoacidosis is common (see notes).
- Patients always require INSULIN therapy because insulin levels are absent or very low.
- Peak age of onset 10-13 years old.
- The incidence in Europe has doubled over the past 20-30 years.
- Type I Diabetes mellitus is not totally genetic but the incidence is increased if:
 - Identical twin has DM
 - Parent has DM (Diabetic father 1 in 20-40 chance)
 - (Diabetic mother 1 in 40-80 chance)
 - Sibling has DM 1 in 20 chance

Factors Affecting the Development of Type I Diabetes Mellitus



Second Trigger (Environment, Virus ???)*

Clinical Onset*

Remission (Partial recovery of Beta cell function)

Loss of Insulin Secretion

* The period of time between the initial Beta cell destruction and the onset of clinical symptoms may be months or years.

This time period is called the **DIABETES PRODROME**.

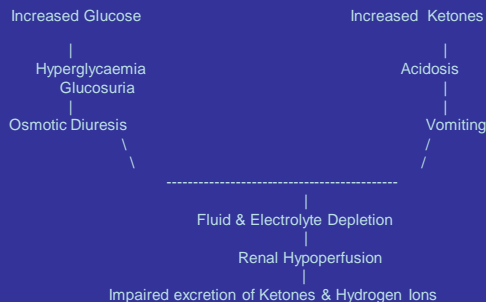
Clinical Presentation

- Acute Presentation
- Young people often present with a 2-4 week history of a TRIAD of symptoms:
 - **POLYURIA** due to osmotic diuresis that occurs when blood glucose levels exceed the renal threshold.
 - **THIRST** due to resulting fluid and electrolyte loss
 - **WEIGHT LOSS** due to fluid loss and increased breakdown of fat & muscle tissue due to insulin deficiency
- Fatigue may also be a common feature

- Ketoacidosis may be the presenting feature if the early signs are not recognised and treated.

Ketoacidosis

- Uncontrolled catabolism associated with insulin deficiency.
- Insulin deficiency is a pre-condition to cause Ketoacidosis, however this is not the sole cause. Other simultaneous causations include:
 - excessive hormonal antagonists to insulin
 - fluid depletion



In absence of insulin:

- Hepatic glucose production increases but peripheral uptake is reduced
- Increased glucose levels causes **OSMOTIC DIURESIS**
 - **LOSS OF FLUIDS & ELECTROLYTES AND DEHYDRATION**
 - **PLASMA OSMOLARITY INCREASES & RENAL PERFUSION DECREASES**
- Simultaneously, rapid **LIPOLYSIS** causes an increase in circulating **FATTY ACIDS** this is converted to **ACETYL CO-ENZYME A** in the liver. Mitochondria converts the Acetyl Co-enzyme A into **KETONE BODIES**.

Increased Ketone Bodies causes
METABOLIC ACIDOSIS

Excess Ketones

Nausea/Vomiting

Fluid Loss & Excreted in Urine

Excreted in Breath
Electrolyte Loss

• **UNTREATED, KETOACIDOSIS IS FATAL**

• **Symptoms of Ketoacidosis**

- Prostration
- Hyperventilation
- Ketone Breath
- Nausea
- Vomiting
- Abdominal Pain
- Confusion
- Stupor
- 5% of patients present in a coma
- Marked dehydration
- Hypothermia

Signs of Ketoacidosis

- Elevated blood glucose levels - Hyperglycemia
- Elevated blood Ketone levels - Ketonaemia
- Elevated urine Ketone levels - Ketonuria

Treatment of Ketoacidosis

- Replace fluids
- Replace electrolytes
- Restore normal acid-base balance – usually achieved by the kidneys once the fluid volume is normal. Occasionally if blood pH is below 7, then isotonic bicarbonate solution is given.

Complication of Ketoacidosis

- Hypotension
- Coma
- Cerebral Oedema
- Hypothermia
- Stasis Pneumonia
- Deep Vein Thrombosis

TYPE II Diabetes Mellitus

- This is a common condition in all populations enjoying an affluent lifestyle.
- Middle aged to elderly onset.
- 2/3 of cases are primary DM. 1/3 of cases are secondary DM.
- Females 4 : 1 Males
- Gradual onset. Usually sub-acute.
- More common in obese people.
- Ketoacidosis is rare.
- Plasma levels of insulin may be normal or raised suggesting end organ resistance.
- Non-autoimmune mechanism.
- The disease may present in a sub-clinical form for several years.
- The incidence of the disease is increased with increasing age and obesity.
- The onset may be accelerated by pregnancy, drugs or con-current illness.
- Prevalence 2% of the UK population.
- Prevalence 2 times more common in Afro-Caribbean's
- Prevalence 5 times more common in S.E. Asians

Genetic Predisposition to Type II Diabetes Mellitus

- Identical twins of a parent with Type II DM have almost 100% chance of developing Diabetes mellitus.
- 25% of patients have a 1st degree relative with Type II Diabetes mellitus.
- The development of this condition is associated with gene abnormalities
- No immune involvement has been identified.
- Patients with Type II DM retain at least 50% of their Beta Pancreatic cells but abnormality develops early in the disease.
- The insulin response in patients with Type II DM to oral glucose is delayed and exaggerated, thereby suggesting end organ insulin resistance.
- Beta cell loss is progressive and amyloid deposition is commonly seen on autopsy.
- Obesity is present in 80% of Type II diabetics.
- Obesity and lack of exercise makes the progression to frank DM more likely.

Sub-Acute Presentation of Diabetes Mellitus

- The onset of the clinical features may occur over several months.
- This form of onset is more common in older patients.
- **Symptoms**
- Thirst (Polydipsia)
- Increased Urination (Polyuria)
- Weight Loss
- Fatigue
- Visual blurring due to glucose induced changes in refraction.

Complications

- (These may be the initial presenting features)
- Staphylococcal skin infections
- Retinopathy
- Polyneuropathy
- Impotence
- Arterial diseases – Myocardial infarctions, peripheral vascular disease

- **Assymptomatic Diabetes mellitus may be discovered due to routine blood or urine analysis.**

Diagnosis

- The diagnosis of Diabetes mellitus, whether it be type I or II, is easy. It is diagnosed with assessment of the blood and urine glucose levels.

Treatment

- The basic guidelines for the treatment of DM is to include dietary control with or without additional medication.
- Good control of blood glucose levels is unlikely to be achieved with insulin or oral medications if the patient's diet is neglected.
- Insulin therapy is always indicated in patients who have ketoacidosis, and is usually indicated in patients under the age of 40 yrs. Insulin is also indicated in older patients where oral therapy has failed.
- In older patients who develop type II DM, dietary changes alone should be used to try and control the disease before embarking on oral medications.
- Thin patients with type II DM are treated with SULPHONYLUREA DRUGS
- Obese patients with type II DM are treated with BIGUANIDE (Metformin)

The Diabetic Diet

- The diabetic diet is no different from that considered to be healthy for the entire population.
- It should contain all of the major food groups with carbohydrates being taken in as complex carbohydrates. Simple sugars and refined carbohydrates should be avoided.
- The calorific intake should be tailored to meet the requirements of the patient. However, the calories should be divided between the major food groups as follows:
 - Carbohydrates should make up 50-55% of the calorific intake
 - Fats should make up 30-35% of the calorific intake
 - Proteins should make up 15% of the calorific intake
- Obese patients should control their calorific intake in order to lose weight.

Diabetic Drug Therapy

- **Sulphonylurea Drugs** – These have 2 actions; they increase insulin secretion and reduce end organ resistance to insulin
- They are contra-indicated in pregnant patients and should be avoided in young ketotic patients.
- All sulphonylurea drugs increase weight and should not be used with obese patients.
- Drug names include:
 - Tolbutamide – Orinase
 - Glipizide – Glucotrol
 - Tolazamide – Tolinase
 - Glyburide – Micronase, Diabeta

- **Biguanide (Metformin)** – this acts by reducing glucose absorption from the gut and increases insulin sensitivity.
- It does not promote weight gain.
- Usually used in middle aged and older patients.
- Side effects include:
 - Anorexia
 - Epigastric Pain
 - Diarrhoea

- **Insulin** – Insulin is administered as a subcutaneous injection. The administration of insulin can be via a hypodermic needle and syringe or by 'pen' administration.
- New types of administering devices are becoming available which use high pressure to force the insulin through the skin without the use of a needle.
- Pen administration has the disadvantage that it cannot be used to administer insulin that is suspended in a zinc and protamine solution.
- Zinc & Protamine insulin has the added benefit of having a long lasting effect due to the retarding action of the zinc and protamine.
- Insulin in clear solution only has short lived effects and should only be used in the treatment of Ketoacidosis or prior to surgery.

- Insulin therapy tries to reproduce our normal pattern of insulin secretion.
- To try and achieve this, intermediate insulin is given to control afternoon and night blood glucose levels and short lived glucose is given in the morning and evening to match meal times.
- Ideal control of insulin levels is difficult due to:
 - Insulin is normally secreted directly into the portal system and passes directly to the liver at high levels. The insulin injected by diabetic patients passes into the systemic circulation before reaching the liver at lower levels.
 - Subcutaneous insulin takes 60-90 minutes to reach peak plasma levels.
 - The absorption of insulin into the systemic circulation of diabetic patients is variable.
 - Basal insulin levels are usually constant but vary in diabetics.

Complications of Insulin Therapy

- include:
 - Scarring at injection sites
 - Injection site abscess (rare)
 - Local allergic response
 - Insulin resistance
 - Hypoglycaemia – Tremor, palpitations, sweating, pallor.

Hypoglycaemia

- This is a common side effect.
- Early symptoms may include drowsiness, the patient becomes detached from their surroundings & pallor.
- The patient's behaviour becomes clumsy, inappropriate or irritable and aggressive.
- Some patients will slip into a coma.
- Virtually all diabetic patients experience episodes of hypoglycaemia and 1 in 3 will go into a coma at some point during their life.
- Irregular eating habits and alcohol excess may precipitate hypoglycaemic states.
- Diagnosis is made upon the clinical features and treatment revolves around the administration of rapidly absorbed carbohydrates i.e. glucose sweets. Unconscious patients are given I.V. glucose solution.

Measuring Control

- Urine tests and blood tests are used to monitor the glucose levels within each and to measure the effectiveness of the disease control.
- Effective control is important – retrospective studies have shown that patients with poor disease control have the highest levels of complications

Diabetic Emergencies

- Ketoacidosis – see earlier notes
- Non-Ketotic Hyperosmolar States
- This condition is caused by severe hyperglycaemia without ketosis – IT IS A MEDICAL EMERGENCY
- Patients with non-ketotic hyperosmolar states are usually in middle to older age and often have undiagnosed Diabetes mellitus.
- It is commonly precipitated by the consumption of glucose rich foods, concurrent medication e.g. diuretics or steroids or by concurrent illness.
- *Clinical Presentation* - Dehydration
- Stupor or coma
- Periph. Vas. Disease May predispose to a stroke, M.I. or