Glycaemic Control and Complications

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Introduction
Diabetes mellitus complications a group of metabolic disorders presenting with hyperglycemia resulting from insulin deficiency or decreased glucose utilization and increased glucose production. The metabolic abnormalities of diabetes mellitus causes secondary pathophysiological changes in multiple organ system resulting in increased morbidity and mortality.

Types of Diabetes Mellitus
Type I DM
It is due to pancreatic beta cell destruction leading to insulin deficiency. It is more common in children, adolescents and young adults usually below 30 years. These subjects are genetically susceptible and are prone to develop ketosis.

Type II DM
It is characterized by variable degree of insulin resistance impaired insulin secretion and increased glucose production. It is preceded by a period of abnormal glucose homeostasis classified as insulin resistance.
impaired fasting glucose or impaired glucose tolerance. Typically it develops with increasing age but again age is no bar and can occur in obese children and adolescents also. The early terminology of insulin dependent and non insulin dependent diabetes mellitus is not used now because type II patients also ultimately require insulin.

**MODY: Maturity Onset Diabetes of Young**
This type is characterized by early onset of hyperglycaemia impaired insulin secretions and autosomal dominant inheritance. Several types of MODY are known depending upon the genetic defects in beta cell functions. They are all characterized by insulin resistance and present like type II DM.

**Gestational Diabetes**
Insulin resistance seen in late pregnancy may lead to IGT and frank diabetes called gestational diabetes mellitus. Most subjects revert to normal glucose tolerance after delivery but have increased risk of developing DM in future.

**Diagnosis of Diabetes Mellitus**
According to WHO guidelines any one of the following is sufficient to diagnose DM.
1) Fasting blood glucose levels > 126 mg%
2) PPBS levels >200 mg%
3) Random blood glucose levels > 200 mg% with symptoms of diabetes mellitus.

**Normal Blood Glucose Levels**
FBS: 100 MG%
PPBS [2hrs]: 140 mg% after 75gm glucose load

**Impaired glucose Tolerance**
FBS : 101 – 126 mg %
PPBS [2hrs]: 140 - 200 mg% after 75gm glucose load

**Insulin Resistance Syndrome**
Also known as metabolic syndrome or the syndrome X, it is characterized by
1) Insulin resistance [increased blood glucose levels inspite of decreased insulin level]
2) Hypertension
3) Dyslipidemia
4) Central Obesity
5) Accelerated cardiovascular disease.

This is probably due to post receptor signaling defect in target tissues e.g skeletal muscle.

**Complications of Diabetes Mellitus**
Hyperglycemia has wide spread effects on different organs and vascular system leading to various complications.

**Acute complications**
1. Diabetic ketoacidosis
2. Hyperglycemic hyperosmolar state

**Chronic complications**

**Micro vascular**
1) Retinopathy and macular odema leading to blindness
2) Neuropathy– Sensory, motor and autonomic
3) Nephropathy – leading to end stage renal disease.

**Macro vascular**
1) Coronary artery disease and MI
2) Cerebrovascular disease stroke etc
3) Peripheral vascular disease.

**Others**
1) Cataract and glaucoma
2) Infections – foot ulcer, osteomyelitis etc
3) Skin infections – Candida and other fungal infections

**Diabetic Ketoacidosis**
It is the most dreaded acute complication resulting from uncontrolled diabetes mellitus leading to serve hyperglycemia. It is characterized by dehydration, hyponatremia, hyperkalemia, acidosis and increased anion gap. common clinical features are nausea, vomiting, pain abdomen, tachycardia, letharginess and CNS depression with hyperventilatin. Patients breath often has a fruity odour of acetone. Ketone body test is strongly positive in urine.

**Assessment of Glycemic control**
It is done by monitoring blood glucose and glucosylated haemoglobin. Blood glucose levels indicate the recent glycemic status while HbA1c.
indicates the glycemic status over the preceding 8–10 weeks. The goals of glycemic controle are to maintain

1. Fasting glucose levels
2. 2hrs PP glucose levels – less than 180mg%
3. HbA1c – less than 7% of total HB.

It is recommended that patients of type I diabetes should monitor blood glucose levels more frequently than type II DM in whom the fluctuation are less and once daily is enough. HbA1c should be monitored twice a year. Normal individuals have glycosylated hemoglobin levels of 6% of the total Hb.

Glycated Hb

Hb molecules in which sugar residues are attached to amino groups of the beta globin chain non enzymatically are called glycated haemoglobinins. Adults humans have HbA1, HbA2 and HbF. HbA1 has three different fractions separated by chromatography i.e HbA1b and HbA1c.

HbA1a1 = Fructose 1-6 bisphospate
HbA1 a2 = Glucose 6 –phosphate
HbA1 b = pyruvic acid
HbA1c = Glucose.

Formation of glycated Hb is irreversible and its blood concentration depends upon the life of RBC and blood glucose levels to which it is directly proportional. Hence its level in the blood gives an estimate of blood glucose over the preceding 6-8 weeks.

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