



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.

Insulin is usually required for treatment i.e patients are insulin dependent. Due to the above features this diabetes is also called as brittle diabetes.

It is sometimes divided into two types

Type IA: It is due to an autoimmune reaction and immunological markers such as antibodies to beta islet cell glutamate decarboxylase and insulin itself are present.

Type IB: Immunological markers of autoimmunity are not seen in this type. It is therefore considered an idiopathic disease.

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

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 severe 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 hyperventilation. 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 glycosylated haemoglobin. Blood glucose levels indicate the recent glycemic status while HbA_{1c}

indicates the glycemic status over the preceding 8 – 10 weeks.

The goals of glycemic control are to maintain

1. Fasting glucose levels
2. 2hrs PP glucose levels– less than 180mg%
3. HbA_{1c} – 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.

HbA_{1c} 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 haemoglobulins. Adults humans have HbA₁, HbA₂ and HbF. HbA₁ has three different fractions separated by chromatography i.e HbA_{1b} and HbA_{1c}.

HbA_{1a1} = Fructose 1-6 bisphosphate

HbA_{1a2} = Glucose 6 –phosphate

HbA_{1b} = pyruvic acid

HbA_{1c} = 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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