Diabetes Mellitus

Objectives:

1. To define diabetes mellitus

2. To give an account on hormones affecting glucose metabolism.

3. To give an account on the classification of diabetes mellitus.

4. To give an account on the pathogenesis of T1D.

Definition:

Diabetes mellitus(D.M) **is a metabolic disorder of multiple aetiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.**

Hormones affectiong glucose metabilosm

1. Insulin

2. Glucagon

3. Growth hormone

5. Glucocorticoides (cortisol)

5. Catecholamines (adrenaline)

Effects of Insulin

1. On CHO metabolism:

Insulin ↓ blood glucose level by :-

a. ↑ glucose entry into skeletal muscle and adipose tissue.

b. ↑ glycogen synthesis in the liver and skeletal muscle.

c. ↑ Hepatic glycolysis.

d. ↓ glycogenolysis in the liver and skeletal muscle.

e. ↓ gluconeogenesis in the liver

f. ↓ glucose – 6 – phosphatase activity.

2. On lipid metabolism:-

a. ↑ lipogenesis in the liver and adipose tissue.

b. ↓ lipolysis in the adipose tissue.

c. ↓ ketogeneis in the liver.

3. On protein metabolism:-

a. ↑ protein synthesis in the liver and skeletal muscles.

b. ↓ proteolysis in the skeletal muscles.

Effects of Glucagon

1. On CHO metabolim:

a. ↑ hepatic glycogenolysis

b. ↑ hepatic gluconeogenesis

2. On lipid metabolism:-

a. ↑ lipolysis in the adipose tissue.

b. ↑ ketogenesis in the liver.

Effects of Growth hormone

1. On CHO metabolim:

a. ↑ hepatic gluconeogenesis

c. ↓ peripheral glucose utilization.

2. On lipid metabolism:-

a. ↑ lipolysis in the adipose tissue.

3. On protein metabolism:-

a. GH is protein anabolic hormone

Effects of Cortisol

1. On CHO metabolism:

a. ↑ hepatic glycogenesis.

b. ↑ hepatic gluconeogenesis.

c. ↓ peripheral glucose utilization.

2. On Protein metabolism:-

a. ↑ proteolysis in the skeletal muscles.

Effects of Adrenaline

1. On CHO metabolim:

a. ↑ hepatic and muscle glycogenolysis.

b. ↑ hepatic gluconeogenesis.

2. On Lipid metabolism:-

a. ↑ lipolysis in the adipose tissues.

Aetiological Classification of diabetes mellitus:

Type 1 diabetes:

Usually affect thin younger people, mostly children

It is due to absolute insulin lack

There is slower onset form of T1D:

latent autoimmune diabetes (LADA), occurs in adults

Type 2 diabetes:

Usually affect over weight and obese adults

It is due to insulin resistance and gradual *B* – cell failure

Other specific types:

A. Pancreatic disease:

(pancreatitis, pancreatectomy, neoplastic disease, cystic fibrosis, haemochromatosis)

B. Excessive production of Insulin Anatgonists:

(Acromegaly, Cushing's syndrome, Glucagonoma, phaeochromocytoma, Thyrotoxicosis)

C.Drugs:

(corticosteroids, thiazide diuretics, phenytoin)

D. Viral infections:

(Congenital rubella, Mumps, Coxsackie B virus)

E. Associated with genetic syndromes:

(Down's syndrome, Klinefelter's syndrome , turner's syndrome, DIDMOAD, Friedrich's ataxia, myotonic dystrophy)

Gestationl diabetes:

Hyperglycaemia occurring for the first time during pregnancy

Unclassified diabetes:

Diabetes that cannot be categorized into specific type at the time of diagnosis

Pathogenesis of T1D:

T1D is a T cell-mediated autoimmune disease involving destruction of the insulin-secreting β cells in the pancreatic islets.

Genetic factors account for about one-third of the susceptibility to T1D, the inheritance of which is polygenic.

Over 20 different regions of the human genome show some linkage with T1D but most interest has focused on the human leucocyte antigen (HLA) region within the major histocompatibility complex on the short arm of chromosome 6.

The HLA haplotypes *DR3* and/or *DR4* are associated with increased susceptibility to T1D

Environmental factors have an important role in promoting clinical expression of the disease.

Pathogenesis of T1D

1. Normal pancreatic islets:

Genetic susceptibility to immune dysfunction.

2. Environmental tiggers and regulators leading to:

Insulinitis.

3. Loss of first phase insulin secretion:

Impaired glucose tolerance.

4. Beta-cell dysfunction:

Overt Diabetes.