A Review on Diabetes Mellitus- An Annihilatory Metabolic Disorder

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Abstract:
Diabetes mellitus (DM) is a metabolic disorder characterised by hyperglycaemia due to the impairment of insulin secretion by pancreatic islets. DM is a metabolic disorder which occurs more habitually worldwide. It is indicated by hyperglycaemia with low insulin directed glucose by target cells. Diabetes mellitus is associated with two specific types type and I and type II. Type I diabetes mellitus is due to damage of β cells of pancreatic islets. In type I diabetes mellitus the body fails to produce the insulin and the person requires to administer the insulin. This is also termed as juvenile diabetes. Type II diabetes mellitus is due to the imperfection of β cell function genetically. In type II diabetes mellites the cells fail to use the insulin properly. This is termed as adult onset diabetes. Currently accessible therapy for diabetes mellitus include insulin and oral hypoglycaemics. These drugs act by increasing the insulin secretions in the pancreas or by decreasing plasma glucose concentration by decreasing gluconeogenesis. The present review is to focus on pharmacological and physiological aspects of diabetes, complications and drug therapy.
Key words: Metabolic disorder, Hyperglycaemia, Risk factors, Auto immune disorder, IDDM,NIDDM.

INTRODUCTION:

Diabetes mellitus is the commonest endocrinal metabolic disorder characterised by deficiency of insulin in the body. It is the commonest disorder that affects more than 100 million people worldwide. Metabolic abnormalities in carbohydrates, lipids and proteins results from insulin as an anabolic hormone. Diabetes found to damage the many body systems particularly blood vessels, eyes, kidneys, heart and nerves.

Diabetes mellitus is categorised into two types Type I Insulin Dependent Diabetes Mellitus (IDDM) and type II Non-Insulin Dependent Diabetes Mellitus (NIDDM). Type I diabetes mellitus is characterised by local inflammatory reaction in and around the islets followed by selective destruction of insulin secreting cells whereas Type II diabetes mellitus is characterised by peripheral insulin resistance and it is the condition in which the pancreatic cells fails to use the insulin properly.

People with type I diabetes mellitus, the cells in the pancreas that make the insulin destroyed and the body is unable to make insulin. In type I diabetes mellitus the body is unable to process glucose due to lack of insulin. In type II diabetes mellitus, the pancreas does not produce the enough insulin or insulin does not work properly. This type will occur in people with 40 years old. Type II diabetes mellitus may be controlled with diet, weight management and exercise.

Classification of diabetes mellitus:

Table:1 includes the classification of diabetes mellitus type I and type II with characteristic features and symptoms

Sl.no.	Type of diabetes mellitus	Characteristic features	Symptoms
1.	Type I	Less secretion of glucose due to damage of β cells Due to unknown cause self-antibodies damage our body tissues.	Excessive hunger, excessive thirst, blurred vision, fatigue, frequent urination, dramatic weight loss, rapid breathing, flushed face, nausea, vomiting, stomach pain.
2.	Type II	Insulin scantiness due to insulin resistance. Failure of insulin secretion genetically due to impairment of β cell function.	Increased hunger, increased thirst, increased urination, blurred vision, tiredness, sores that are slow to heal.

Epidemiology:

Type I diabetes mellitus is the common type in low age group people. The prevalence of the type I diabetes is more in both vigorous and scarcity countries. 85-90% of type II diabetes mellitus is prominent in developing countries. It is evaluated that 376 million people had diabetes mellitus in 2011.The people who are living in middle income and low-income countries type II diabetes is more prominent. It is estimated that 439 million people would have type II diabetes mellitus by the year 2030. It is preponderantly noted that the ubiquity of type II diabetes mellitus in adults is more elevated in next two decades and much increased in developing countries. Majority of the people at the age of 45 to 65 may supposed to get the type II diabetes mellitus.

Etiology:

Type I diabetes mellitus: The exact cause of type I diabetes mellitus is not known. It is an auto immune disease. The body's immune system faultily attacks the β cells of pancreas. The scientists don't understand why this happens. Genetic and environmental elements will play the major role in causing type I diabetes mellitus. It is expressed as an autoimmune disease where the beta cells of pancreas are slowly obliterated by the bodys own immune system which reduces insulin production. Researchers commenced that 18 genetic factors are designated as IDDM1-IDDM18 are related to type I diabetes. IDDM1 contains the Human Leukocyte Antigen gene that encodes the proteins called major histocompatibility complexes. This region is attacked by the genes. Environmental factors like stress may affect the beta cells to fall below 5%. Coxsackie viruses are the enteric viruses which attack the intestinal track leads to the destruction of β cells that are helpful for insulin production.

Type II diabetes mellitus: This type of diabetes has powerful genetic predisposition. Type II diabetes is having a risk of child of about 5-10%. There is a inability of insulin production by the beta cells due to insulin resistance. There is a high risk at intra-abdominal region than subcutaneous.

Pathophysiology:

Type I diabetes: This is a long lasting auto immune disorder where there is an annihilation of insulin producing β cells. Type I diabetic patients are adolescents and not obese when they first develop the symptoms. The studies of identical twins shown that genetically predisposed individuals must exposed to additional environmental factors like viral infections. Such viral infections may damage the pancreatic β cells and expose the antigens to initiate the autoimmune process.

Type II diabetes mellitus: It is featured by insulin insensitivity due to insulin resistance which reduces the production of insulin due to pancreatic beta cell failure. This leads to the reduction of glucose transport into the liver, muscle cells and fat cells. Type II diabetes is accompanied by insulin resistance and impaired insulin secretion. Such patients are often obese and usually seen in adults. Insulin resistance leads to plaque formation and hyperphosphorylation. Inactive life style is the strong risk factor for type II diabetes mellitus. So, exercise is useful in the patients.
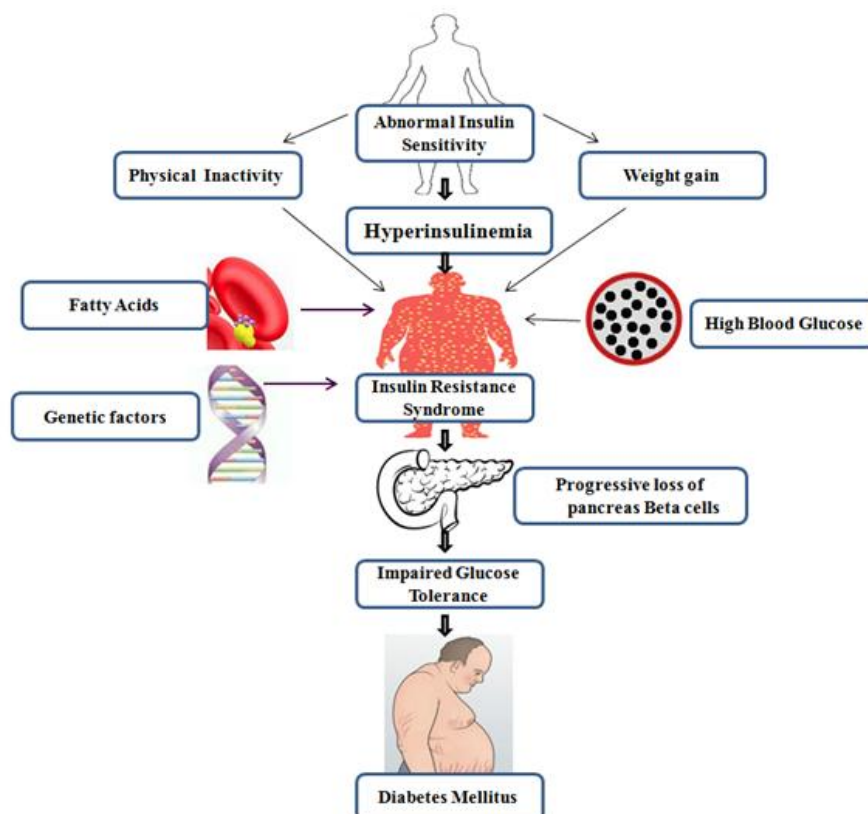
Complications:

As the disease progress tissue damage will occur which leads to severe complications like retinopathy, nephropathy, neuropathy, cardiovascular diseases and ulceration. Type I diabetic patients are more susceptible to coronary artery, heart and peripheral vascular diseases. Type II diabetic patients has a high risk of atherosclerosis associated with hypertension, hyperlipidaemia and obesity and renal diseases.

Diagnosis:

For screening the diabetes, the fasting glucose concentration should be used according to American Diabetes Association. Postprandial blood sugar test, random blood sugar and glucose tolerance tests are used for blood sugar determination. The criteria used for diagnosis of diabetes are

1. Symptoms of diabetes like polyurea, polydipsia and casual blood glucose concentration = 11.1 m.mol/L or 200mg/dL.

2. Fasting plasma glucose= 70-110 mg/dL.

The criteria used for diagnosis of diabetes is shown in table:2

Management:

To eradicate the diabetes in the patients has to take care of their symptoms to slow down the developing risk factor which includes blood pressure, glycaemia, and control of lipids which decreases the macrovascular risks, stoppage of smoking.

General management of diabetic patients' education must need

1. Process of treatment of disease
2. Planning of food
3. Planning of physical activity
4. Proper awareness of medication
5. Blood sugar level monitoring
6. Awareness in acute and chronic issues
7. Nutrition therapy
8. Promoting health strategies.

Type I Diabetes mellitus: First drug of choice for type I diabetes is insulin in the form of injections and pumps. Various types of insulins like long acting, intermediate acting and short acting are used. Long acting insulins are insulin glargine (LANTUS), insulin detemir (LEVIMIR). Intermediate acting insulins are NPH (HUMULIN N, NOVOLIN N). Some angiotensin receptor blockers, ACE inhibitors, aspirin and cholesterol lowering drugs are used. Islet grafting is used as a therapy for type I DM. Types of insulins, dose, onset of action, peak plasma concentration is as shown in table: 3

Type II diabetes mellitus:

Oral hypoglycaemic agents are useful for the treatment of type II DM and also the insulin. Alpha glycosidase inhibitors, biguanides, thalizodediones are normally used. The aim of these drugs is to correct the resistance of insulin and insufficient insulin secretion. These drugs are given in combinations with suitable diet and change in life style. Oral hypoglycaemic agents' classification with brand names is included in table no.4

Table.2: Diagnosis of diabetes mellitus.

Type	Diagnosis	Plasma glucose concentration
Normal	Fasting and 2hr Post prandial	< 6.0mmol/m, <7.8mmol/m
Diabetes	Fasting and 2hr post prandial	>7.0mmol/m, >11.1mmol/m
Impaired glucose tolerance	Fasting and post prandial	<7.0mmol/m,7.8-11.0mmol/m
Impaired Fasting Glycemia	Fasting	6.0-6.8mmol/m

Table: 3 Types of insulin preparations.

Type	Onset	Peak	Duration	Comments
Rapid acting insulins	5-15 min	30-60 min	2-5 hr	Can be injected at the start of meal
Short acting insulins	30 min	1-3hr	4-8hr	Usually injected 15-30 min before a meal.
Intermediate acting insulin	1-2hr	4-8hr	8-12hr	Used to control glucose levels between meals. May becombined with short acting insulin
Long acting insulin	30-60min	-	16-24hrs	once daily

Table: 4 Classification of oral hypoglycaemic agents.

Sl no.	Drug	Generic name	Brand name
1.	Biguanides	Metformin	GLUCOPHAGE
2	Sulphonyl ureas	Glibenclamide	DAONIL, EUGLUCON
		Glimperide	DIABETA
		Glipizide	GLYNASE
3	Meglitinide	Repaglinide	PRANDIN
		Natoglinide	STARLIX
4	Thiazolidinediones	Rosiglitazone	AVANDAMET
		Pioglitazone	ACTOS, AVANDIA
5	Alpha glycosidase inhibitors	Acarbose	PRECOSE, GLYCET

Diet and exercise:

People with type I and type II DM should eat regular meals and snacks to keep the sugar levels stable. Exercise also helps to regulate the blood sugar levels.

Diabetics and genetics:

A diabetic is a complex metabolic disorder which depends on genetic factors and environmental factors. Genes play a major role in molecular mechanism of diabetes. Identification of gene mutations and gene polymorphisms of many genes involved in metabolic pathways may increase the blood glucose levels. It is evidently shown that a gene mutation or polymorphism may not show the same effect among different individuals within a population.

Molecular genetics of Type II Diabetes mellitus:

The collective and broad genomic variations are involved in the development of diabetes mellitus. The characterisation and identification of many genes are associated with the type II DM. Genome wide association studies in various populations are identified as 70 loci associated to Type II DM. United Nations population studies resulted the identification of similar nucleotides are linked to the risk of type II DM. It is associated with the level of triglycerides.

Molecular genetics of Type I Diabetes mellitus:

Type I DM is described as an autoimmune disorder that results in destruction of pancreatic islets, single gene mutations and SNP are found to be associated with type I DM. Type I DM includes the Auto immune regulator gene which effects the tolerance to self-antigens and laeds to immunity. In addition mutations in the histone deacetylase SIRTI gene is expressed in beta cells which involved in the regulation of insulin.

CONCLUSION:

This review explains the introduction for diabetes which is a growing health care problem affecting individual's health care system New drugs are emerging to treat the diabetes and they have good impact on prevention and management of disease.

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