

Report On Diabetes Mellitus

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Abstract—Diabetes mellitus is a growing health problem in the world that causes severe morbidity and mortality. The prevalence of diabetes was rising day by day. The facts about the diabetes mellitus, its prevalence, morbidity, and mortality were published in many statistical reports. Diabetes mellitus (DM), or simply diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin, or because cells do not respond to the insulin that is produced. This high blood sugar produces the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger). Conventionally, diabetes has been divided into three types namely: Type 1 DM or insulin-dependent diabetes mellitus (IDDM) in which body fails to produce insulin, and presently requires the person to inject insulin or wear an insulin pump. This is also termed as "juvenile diabetes". Type 2 DM or non-insulin-dependent diabetes mellitus (NIDDM), results from insulin resistance, a condition in which cells fail to use insulin properly, with or without an absolute insulin deficiency.

Diabetes mellitus (DM), or simply diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin, or because cells do not respond to the insulin that is produced. This high blood sugar produces the classical symptoms of polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger). Conventionally, diabetes has been divided into three types namely: Type 1 DM or insulin-dependent diabetes mellitus (IDDM) in which body fails to produce insulin, and presently requires the person to inject insulin or wear an insulin pump. This is also termed as "juvenile diabetes". The third main type is gestational diabetes which occurs when women without a previous history of diabetes develop a high blood glucose level during her pregnancy. It may precede development of type 2 DM.

Currently available pharmacotherapy for the treatment of diabetes mellitus includes insulin and oral hypoglycemic agents. Such drugs acts by either increasing the secretion of insulin from pancreas or reducing plasma glucose concentrations by increasing

glucose uptake and decreasing gluconeogenesis. However, these current drugs do not restore normal glucose homeostasis for longer period and they are not free from side effects such as hypoglycemia, kidney diseases, GIT problems, hepatotoxicity, heart risk problems, insulinoma and they have to take rest of life. Various herbal drugs have been also proved effective due to their beneficial contents in treatment of diabetes.

Index Terms—Diabetes mellitus, Types, Insulin, Diagnosis, autoimmune, Gestational diabetes, Monogenic.

I. INTRODUCTION

1.1 HISTORY OF THE DIABETES

Diabetes mellitus is a growing health problem in the world that causes severe morbidity and mortality. The prevalence of diabetes was rising day by day. The facts about the diabetes mellitus, its prevalence, morbidity, and mortality were published in many statistical reports. Diabetes mellitus (DM) is one of the very oldest diseases and was mentioned three thousand years ago in Egyptian literature. Around 1500 B.C the physicians in India noticed the sweetness of urine of the diabetic people and called it as "Madhumeha". Ebers papyrus, the oldest literature was written around the same time by Egyptians and it was also the first document that describes a condition of frequent emptying of urine. Around 5th and 6th century the ancient Indian physician Susruta and Sharuka described first time about the extreme thirst, foul breath and polyuric state associated with sweet taste substance in the urine. They were the first identified the difference between the type I and type II DM. Aretaeus of cappodocia a Greek physician, he was the first person coined the term diabetes by observing the clinical condition that increased frequency of urine in diabetic individuals. He was also the first to distinguish diabetes mellitus and diabetes insipidus.

Later on, Thomas Willis in 1670 was added the term mellitus (honey sweet) after rediscovering the sweetness of urine in the patient was due to the high blood glucose level. In 1776, Matthew Dobson, a British physiologist first confirmed that the sweetness of urine is due to the presence of excess glucose in blood and urine. Around 30 BC- 50AD, the Aulus Cornelius Celsus has given the complete clinical description for diabetes mellitus in Latin and entitled *De medicina*. Effective treatment was not created until the early part of the twentieth century, when Canadians Frederick Banting and Charles Herbert Best separated and sanitized insulin in 1921 and 1922. This was trailed by the improvement of the long-acting insulin NPH in the 1940s

1.2 GLUCOSE HOMEOSTASIS AND DIABETES MELLITUS

Glucose is a chief fuel in biology. Glucose is metabolized in the mitochondria to release the ATP which provides energy to the cell. This energy is utilized for cell movement, nerve conduction, hormone production and to nourish the genetic machinery of the cell (DNA). Glucose in the body is maintained within the narrow range by two main hormones- Insulin and Glucagon- which acting antagonistically to increase or decrease blood glucose level in the blood. Both these hormones are released by the pancreas. High blood sugar level stimulates the release of insulin which is secreted by Beta cells of Islets of Langerhans in the pancreas that increases the uptake of glucose by cells. Moreover, in the cell, the glucose is used as energy, converted to glycogen and stored mainly in the liver and muscles or used in the synthesis of fats. In some abnormal conditions, the cell resists insulin which leads to considerable reduction in the glucose uptake, glycogen synthase activity, glycogen synthesis and storage in peripheral tissue. While there is a lack of insulin secretion or cell resists insulin, which leads to diabetes mellitus.

Diabetes mellitus (DM) is commonest endocrine disorder that affects more than 100 million people worldwide (6% population). It is caused by deficiency or ineffective production of insulin by pancreas which results in increase or decrease in concentrations of glucose in the blood. It is found to damage many of body systems particularly blood vessels, eyes, kidney, heart and nerves¹. Diabetes mellitus has been classified into two types i.e. insulin dependent diabetes

mellitus (IDDM, Type I) and non-insulin dependent diabetes mellitus (NIDDM, Type II). Type I diabetes is an autoimmune disease characterized by a local inflammatory reaction in and around islets that is followed by selective destruction of insulin secreting cells whereas Type II diabetes is characterized by peripheral insulin resistance and impaired insulin secretion. The presence of DM shows increased risk of many complications such as cardiovascular diseases, peripheral vascular diseases, stroke, neuropathy, renal failure, retinopathy, blindness, amputations etc³. Drugs are used primarily to save life and alleviate symptoms. Secondary aims are to prevent long-term diabetic complications and, by eliminating various risk factors, to increase longevity. Insulin replacement therapy is the mainstay for patients with type 1 DM while diet and lifestyle modifications are considered the cornerstone for the treatment and management of type 2 DM. various types of hypoglycemic agents such as biguanides and sulfonylureas are also available for treatment of diabetes. However none of these medications is ideal due to their toxic side effects and diminution of responses is observed sometimes in their prolonged use. The main disadvantage of currently available drugs is that they have to be given throughout the life and produce side effects⁶. Medicinal plants and their bioactive constituents can be used for treatment of DM throughout the world especially in countries where access to the conventional anti-DM agents is inadequate. Various experimental models are also available to screen anti diabetic activity of plant. The present review therefore is an attempt to know more precisely about diabetes mellitus, its clinical presentation, epidemiological data, complications and current available treatment of diabetes.

1.3 EPIDEMIOLOGY

It is estimated that 366 million people had DM in 2011; by 2030 this would have risen to 552 million. The number of people with type 2 DM is increasing in every country with 80% of people with DM living in low- and middle-income countries. DM caused 4.6 million deaths in 2011. It is estimated that 439 million people would have type 2 DM by the year 2030. The incidence of type 2 DM varies substantially from one geographical region to the other as a result of environmental and lifestyle risk factors. It is predicted that the prevalence of DM in adults of which type 2 DM

is becoming prominent will increase in the next two decades and much of the increase will occur in

developing countries where the majority of patients are aged between 45 and 64 years.

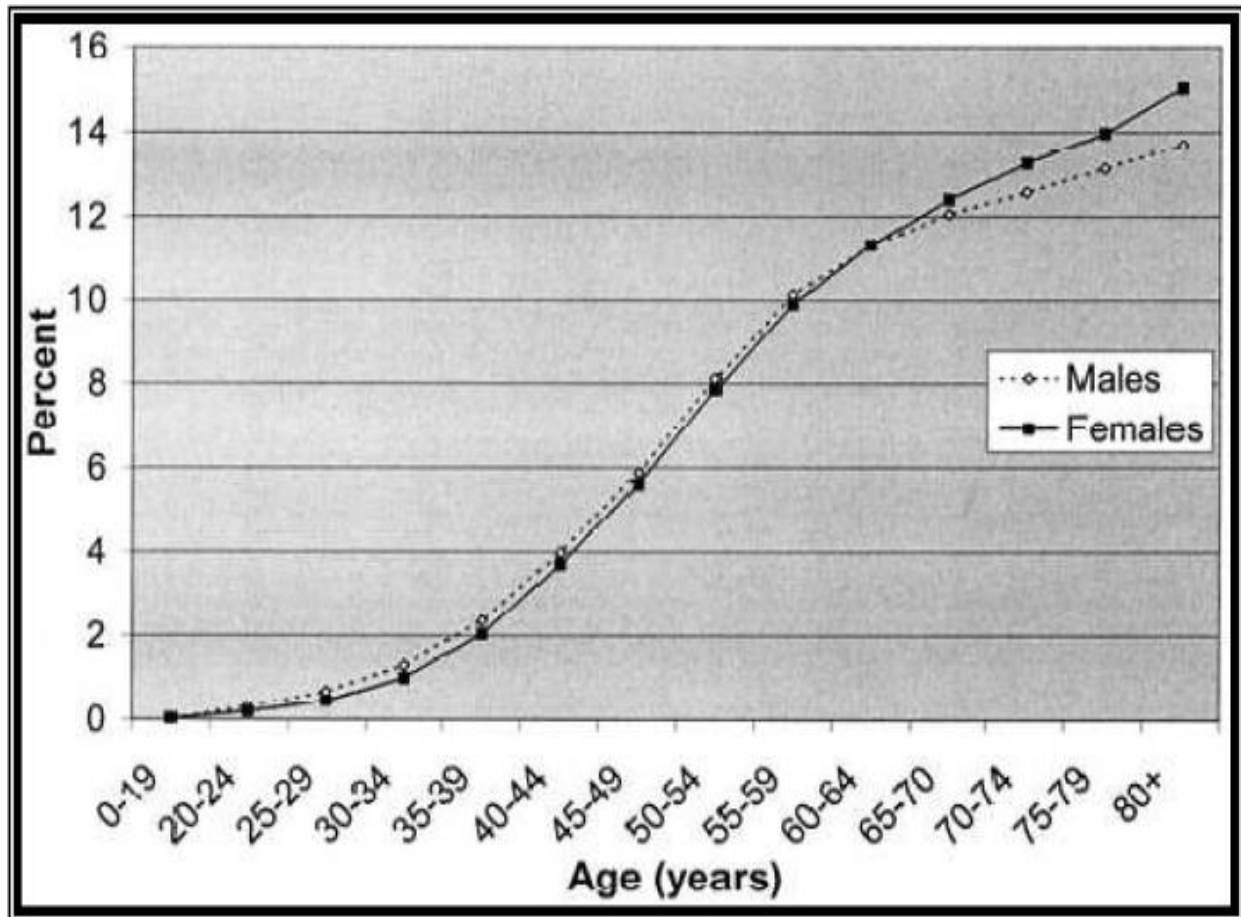


Fig. No. 1: Epidemiology of diabetes: A global view

1.4 DIABETES IN INDIA

According to recent estimates, approximately 285 million people worldwide (6.6%) in the 20–79 year age group will have diabetes in 2010 and by 2030, 438 million people (7.8%) of the adult population, is expected to have diabetes. India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the “diabetes capital of the world”. According to the Diabetes Atlas 2006 published by the International Diabetes Federation, the number of people with diabetes in India currently around 40.9 million is expected to rise to 69.9 million by 2025 unless urgent preventive steps are taken. The “Asian Indian Phenotype” refers to certain unique clinical and biochemical abnormalities in Indians which include increased insulin resistance, greater abdominal adiposity i.e., higher waist

circumference despite lower body mass index, lower adiponectin and higher high sensitive C-reactive protein levels. Higher prevalence of diabetes mellitus often results from in changes in dietary patterns and decreased physical activity in the urban population. Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease. In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India, while China (42.3 million) and the United States (30.3 million) will also see significant increases in those affected by the disease.

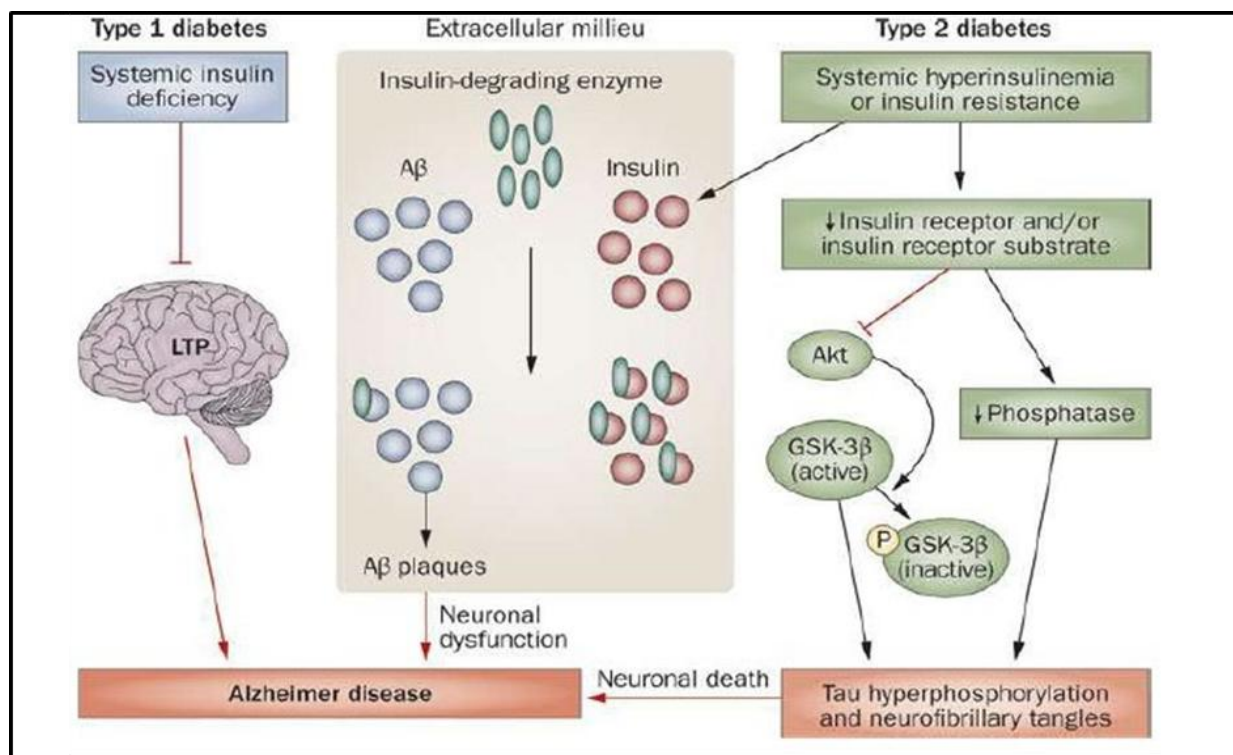


Fig. No. 2: Pathophysiology of Type I and Type II diabetes. Abbreviations: Aβ- Amyloid- β, GSK-3β-glycogen synthase kinase 3β, LTP- long term potentiation, P- Phosphate

II. CLASSIFICATION OF DIABETES

Classification is based on the production of insulin by the pancreas or the cells of the body response properly towards the insulin production. There are three main types of diabetes mellitus:

2.1. INSULIN DEPENDENT DIABETES MELLITUS (TYPE1 IDDM)

It is also called as Type 1 diabetes mellitus. This type of diabetes mellitus is also called autoimmune diabetes and previously known as juvenile-onset or ketosisprone diabetes. The individual may also seek with other autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis, and Addison's disease. In this type of diabetes pancreas does not produce insulin properly or no insulin is produced by pancreas. It is also known as insulin dependent diabetes mellitus (IDDM) or juvenile diabetes or early onset diabetes. The causes for type 1 diabetes are unknown. It is less common than type 2, generally only 10% of all diabetes cases are type 1. Patients suffering from type 1 diabetes should take insulin injections for the rest of their life. They should likewise guarantee appropriate blood-glucose levels via doing consistent blood tests and

taking after an uncommon eating routine.

The main cause of type I or Juvenile diabetes is due to autoimmune insulinitis, where the insulin-producing beta cells in the pancreas are destroyed by the body's defense system. As a result, the body is unable to produce sufficient insulin that it needs. Hence type I diabetes requires exogenous insulin therapy to survive. The other causes of type 1 diabetes are genetic and environmental factors such as viral infection and certain chemicals. Despite the fact that this disease usually occurs in children or young adults, it can also affect people irrespective of age. Type I diabetes is less common and accounts for only about 10% of the diabetic people.

2.2. NON-INSULIN DEPENDENT DIABETES MELLITUS (TYPE2 NIDDM)

It is also called as Type 2 diabetes mellitus. Type 2 diabetes mellitus is also known as adult-onset diabetes. The progressive insulin secretory defect on the background of insulin resistance (American Diabetes Association, 2014). People with this type of diabetes frequently are resistant to the action of insulin. The long-term complications in blood vessels, kidneys, eyes and nerves occur in both types and are the major

causes of morbidity and death from diabetes. The causes are multifunctional and predisposing factor includes: Obesity, Sedentary lifestyle, increasing age (affecting middle aged and older people), Genetic factor (Ross and Wilson 2010), such patients are at increased risk of developing macro vascular and micro vascular complications.

In type 2 diabetes the body does not create enough insulin to address its own particular issues or cell does not respond properly against the insulin. This is known as insulin resistance. Type 2 diabetes is also known as "Non-Insulin- Dependent Diabetes Mellitus" (NIDDM) or "adult-onset diabetes". It happens in 75 to 90% of all instances of diabetes in UK. Type 2 diabetes as a rule grows steadily after some time. Most

people with the condition might be ignorant of their ailment particularly at early stages as there might be no particular side effects. Type 2 diabetes is frequently connected with weight. Corpulence related diabetes is now and then alluded to as development onset diabetes since it is more normal in more seasoned individuals. In numerous early instances of type 2 diabetes treatment might be conceivable by simply eating a solid eating regimen and checking blood glucose levels routinely. In any case, as type 2 diabetes is a dynamic condition in the long run medicines might be required. There are a few gatherings of oral pills that can be taken to control the glucose. In some serious type 2 diabetics insulin infusions might be vital Figure 1.

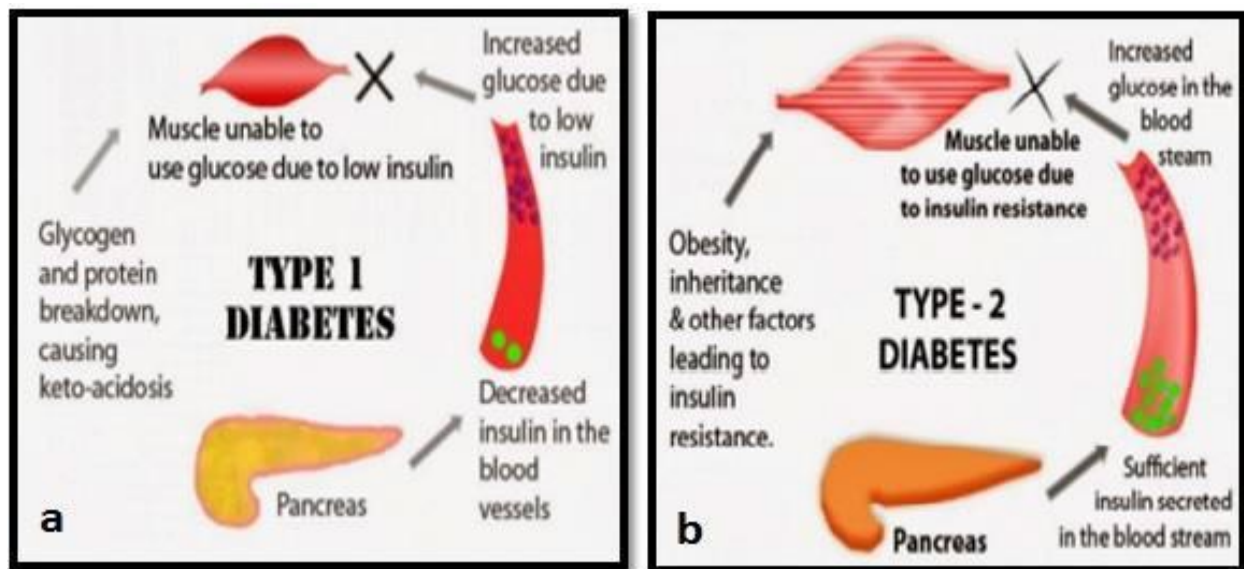


Figure No.3. (a) Type 1 diabetes mellitus and (b) Type 2 diabetes mellitus.

2.3. GESTATIONAL DIABETES

It is the third type of diabetes. This type affects female during pregnancy. A few ladies have large amounts of glucose in their blood, and their bodies can't create enough insulin to transport the greater part of the glucose into their cells, bringing about dynamically rising levels of glucose. Pregnant ladies with gestational diabetes could conceivably have prior type 1 or type 2 diabetes. Much of the time, gestational diabetes creates amid the second trimester of pregnancy (weeks 14- 26) and vanishes after the child is conceived. Gestational diabetes can build the danger of wellbeing issues creating in an unborn infant. Consequently it is imperative to identify it early and

treat it suitably. Analysis of gestational diabetes is made amid pregnancy. The dominant part of gestational diabetes patients can control their diabetes with activity and eating routine. Between 10% to 20% of them should take some type of blood-glucose-controlling solutions. Undiscovered or uncontrolled gestational diabetes can raise the danger of entanglements amid labour.



Figure No. 4. Gestational diabetes.

2.4. OTHER SPECIFIC TYPE (MONOGENIC TYPES)

Developed with mutations on chromosome 12 in a hepatic transcription factor referred to as hepatocyte nuclear factor (HNF)-1a. They also referred to as genetic defects of beta cells. These forms of diabetes are frequently characterized by onset of hyperglycemia at an early age (generally before age of 25 years). They are also referred to as maturity onset diabetes of the young (MODY) or maturity-onset diabetes in youth or with defects of insulin action; persons with diseases of the exocrine pancreas, such as pancreatitis or cystic fibrosis; persons with dysfunction associated with other endocrinopathies (e.g. acromegaly); and persons with pancreatic dysfunction caused by drugs, chemicals or infections. Some drugs also used in the combination with the treatment of HIV/ AIDS or after organ transplantation.

III. PATHOGENESIS

3.1. PATHOGENESIS OF TYPE 1 DIABETES MELLITUS

Type 1 diabetes mellitus is an autoimmune disorder connected with specific annihilation of insulin producing pancreatic β -cells. The onset of diseases shows the end phase of β -cell annihilation proceeding type 1 diabetes mellitus. There are a number of features represent that type 1 diabetes mellitus is an autoimmune disorder:

1. Nearness of immuno-equipped and adornment cells in invaded pancreatic islets.
2. Nearness of islet cell particular autoantibodies.
3. Adjustments of T cell immunoregulation, in specific in CD4+ T cell compartment.
4. Reaction to immunotherapy.
5. Successive event of other organ particular immune system illnesses in influenced people or in their family individuals.

The pathogenesis of specific β -cell pulverization inside the islet in type 1 diabetes mellitus is hard to take after because of checked heterogeneity of the pancreatic sores. At the onset of plain hyperglycemia, a blend of pseudoatrophic islets with cells creating glycogen (a cells), somatostatin (d cells) and pancreatic poly-peptide (PP cells), typical islets, and islets containing both b-cells and penetrating lymphocytes and monocytes might be seen. Lymphocytic invasion is discovered just in the islet containing leftover β -cells and is likely that the chronicity with which type 1 diabetes mellitus creates mirrors this heterogeneity of islet injuries. As opposed to this chronicity in the normal history of the sickness, β -cells are quickly devastated when pancreas is transplanted from indistinguishable twin givers into their long term diabetic twin mates without immunosuppression. In these cases, gigantic insulinitis grows quickly with invading T lymphocytes showing an anamnestic immune system response. Likewise, this perception additionally demonstrates that the incessant time course in type 1 diabetes mellitus (however not in a transplanted pancreas) is an outcome of down administrative phenomena part taking in immune opathogenesis of the disorder. Actuation of islet antigen - particular CD4+ T cells show up to be outright essential for the advancement of diabetes in every single creature model of type 1 diabetes mellitus .CD4+ islet particular T-cell clones produced from diabetic NOD mice, when infused into pre diabetic or non-diabetes inclined F1 mice, affect insulinitis and diabetes. It was additionally reported that CD4+ T cells are adequate to actuate insulinitis while CD8+ T cells add to the seriousness of the harm. These discoveries together with the proof that insulinitis in endless joining versus host infection may happen without CD8+ T cells recommend that CD4+ T cells might be the main immune competent cells required in the disease procedure. In any case, it appears that one and only subset of CD4+ T cells are in charge of illness

incitement.

Alloantigen RT6 in CD4⁺ cell are not present in diabetes inclined BB rats and seem to ensure AO rats from MLD-STZ incited diabetes. Down-direction of diabetogenic immune system reaction by the spleen cells got from creatures treated with adjuvants could likewise be clarified by CD4⁺ T cell subsets transaction. Abnormal state of TH1 type cytokines IL-2 and interferon γ are found to connect on the other hand/and to upgrade prompting of immune system diabetes in trial models. The TH-1 type cells, and specifically their item IFN- γ , initiate macrophages. In creature, models of type 1 DM electron minuscule investigations of pancreata appeared that macrophages

are the main cell type attacking the islets. In vitro contemplates and contemplates on perfused pancreas recommend that Interleukin 1 (IL-1) and tumor corruption variable (TNF α), two cytokines fundamentally created by macrophages, affect basic changes of β -cells and concealment of their insulin discharging limit.

In any case, it appears that IL-1 and TNF don't contribute apparently to the cytotoxic action of macrophages. Interferon γ is likewise an effective activator of macrophages for nitric oxide blend. As of late, confirmation has been given demonstrating, that no synapse movement is included in diabetes advancement Figure 3.1.

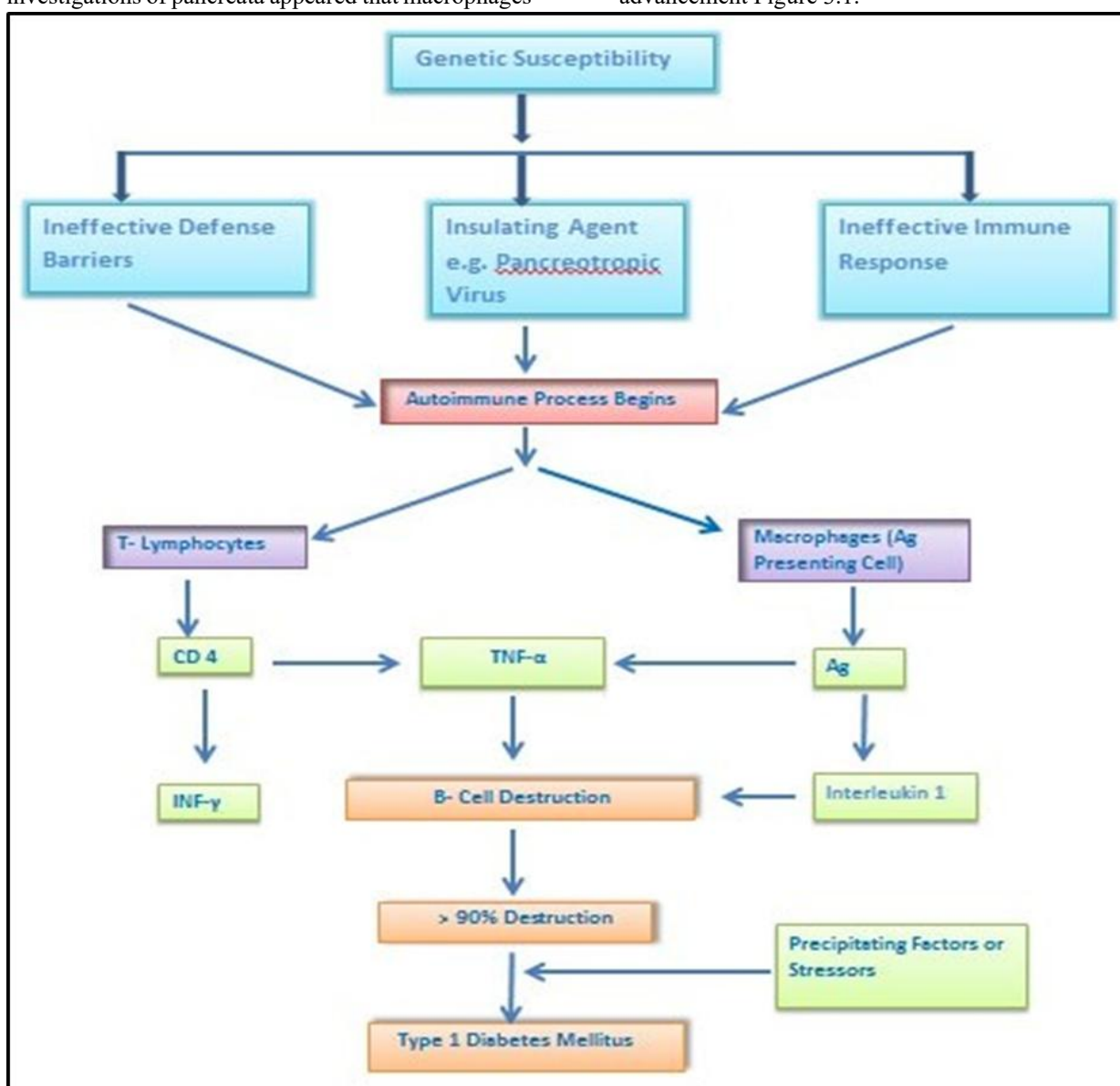


Figure No. 5. Synapse movement

3.2. PATHOPHYSIOLOGICAL ASPECTS

Type 2 DM is characterized by insulin insensitivity as a result of insulin resistance, declining insulin production, and eventual pancreatic beta-cell failure. This leads to a decrease in glucose transport into the liver, muscle cells and fat cells. There is an increase in the breakdown of fat with hyperglycemia. Type 1 diabetic patients are usually young (children or adolescents) and not obese when they first develop symptoms. There is an inherited predisposition, with a 10-fold increased incidence in first-degree relatives of an index case, and strong associations with particular histocompatibility antigens (HLA types). Studies of identical twins have shown that genetically predisposed individuals must additionally be exposed to an environmental factor such as viral infection. Viral infection may damage pancreatic B cells and expose antigens that initiate a self-perpetuating autoimmune process. The patient becomes overtly diabetic only when more than 90% of the B cells have been destroyed. In this type, insulin deficiency attenuates long term potentiating and might lead to deficits in learning and memory.

Type 2 diabetes is accompanied both by insulin resistance and by impaired insulin secretion, each of which are important in its pathogenesis. Such patients are often obese and usually present in adult life, the incidence rising progressively with age as B-cell function declines. In this insulin resistance leads to both A β plaque formation and tau hyperphosphorylation. During hyperinsulinemia, insulin and A β competes for insulin degrading enzyme, leading to A β accumulation and plaque formation. A decrease in insulin receptor signaling leads to inhibition of Akt and dephosphorylation (activation) of GSK-3 β and results in tau hyperphosphorylation. Type 2 DM is characterized by insulin insensitivity as a result of insulin resistance, declining insulin production, and eventual pancreatic beta-cell failure.

IV. DIAGNOSIS

4.1. SCREENING AND DIAGNOSIS

According to the American Diabetes Association (ADA), the fasting glucose concentration should be used in routine screening for diabetes; but postprandial blood sugar, random blood sugar and glucose tolerance test are also used for blood sugar determination. For the diagnosis of diabetes, at least

one criterion must apply:

- Symptoms of diabetes (polyuria, polydipsia, unexplained weight loss, etc) as well as casual plasma glucose concentration = 11.1 mmol/L (200 mg/dL).
- Fasting plasma glucose = Its normal range is 70-110 mg/dl with no caloric intake for at least 8 h.

The World Health Organization (WHO) classification includes both clinical stages (normoglycaemia, impaired glucose tolerance/impaired fasting glucose (IGT/IFG), diabetes) and etiological types of diabetes mellitus, identical to the ADA except that WHO group includes classification formerly known as gestational impaired glucose tolerance (GIGT) and GDM: fasting glucose = 7.0 mmol/L (126 mg/dL) and/or 2-h glucose = 7.8 mmol/L (140 mg/dL) after a 75-g OGTT.

Tests for screening and diagnosis of DM are readily available. The test recommended for screening is the same as that for making diagnosis, with the result that a positive screen is equivalent to a diagnosis of pre-diabetes or DM.³² Although about 25% of patients with type 2 DM already have micro vascular complications at the time of diagnosis suggesting that they have had the disease for more than 5 years at the time of diagnosis.³³ It is still based on the American Diabetic Association (ADA) guidelines of 1997 or World Health Organization (WHO) National diabetic group criteria of 2006, which is for a single raised glucose reading with symptoms (polyuria, polydipsia, polyphagia and weight loss), otherwise raised values on two occasions, of either fasting plasma glucose (FPG) ≥ 7.0 mmol/L (126 mg/dL) or with an oral glucose tolerance test (OGTT), two hours after the oral dose a plasma glucose ≥ 11.1 mmol/L (200 mg/dL).³² The 1997 ADA recommendations for diagnosis of DM focus on the FPG, while WHO focuses on the OGTT.³² The glycated hemoglobin (HbA1c) and fructosamine is also still useful for determining blood sugar control over time. However, practicing physicians frequently employ other measures in addition to those recommended.

4.2. COMPLICATIONS

As the disease progresses tissue or vascular damage ensues leading to severe diabetic complications such as retinopathy, neuropathy, nephropathy, cardiovascular complications and ulceration. Long standing type 1 DM patients are susceptible to micro vascular complications; and macro vascular disease (coronary artery, heart and peripheral vascular

diseases). Type 2 DM carries a high risk of large vessel atherosclerosis commonly associated with hypertension, hyper lipidaemia and obesity. Most patients with type 2 diabetes die from cardiovascular complications and end stage renal disease.

The increased blood glucose in diabetes mellitus leads to many complications such as metabolic changes, increased oxidative stress, cardiovascular and renal diseases. The complications of diabetes are increasing in the poor urban slum dwellers, the middle-class people and even in the rural areas. This is due to increased physical inactivity and dietary changes and increased stress among the people of the society. Unfortunately increased risk of complications in the underprivileged diabetic subjects might be due to delay treatment. A research study mentioned that people with less physical activity are more prone to metabolic syndrome and hypertension.

4.3. MANAGEMENT

Through lifestyle and diet modification. Studies have shown that there was significant reduction in the incidence of type 2 DM with a combination of maintenance of body mass index of 25 kg/m², eating high fibre and unsaturated fat and diet low in saturated and trans-fats and glycemic index, regular exercise, abstinence from smoking and moderate consumption of alcohol. Suggesting that majority of type 2 DM can be prevented by lifestyle modification. Patients with type 2 DM should receive a medical nutrition evaluation; lifestyle recommendations should be tailored according to physical and functional ability.

Primary prevention is the main aim at preventing diabetes from occurring in susceptible individuals or in general population. Regular physical activity is an important component of the prevention and management of type 2 diabetes mellitus. Prospective cohort studies have shown that increased physical activity, independently of other risk factors, has a protective effect against the development of type 2 diabetes. Dietary and lifestyle modifications are the main goals of treatment and management for type 2 diabetes. The majority of people with type 2 diabetes is overweight and usually has other metabolic disorders of the insulin resistance syndrome, so the major aims of dietary and lifestyle changes are to reduce weight, improve glycemic control and reduce the risk of coronary heart disease (CHD), which accounts for 70% to 80% of deaths among those with

diabetes. Insulin replacement therapy is the mainstay for patients with type 1 DM while diet and lifestyle modifications are considered the cornerstone for the treatment and management of type 2 DM. Insulin is also important in type 2 DM when blood glucose levels cannot be controlled by diet, weight loss, exercise and oral medications.

Oral hypoglycemic agents are also useful in the treatment of type 2 DM. Oral hypoglycemic agents include sulphonylureas, biguanides, alpha glucosidase inhibitors and thiazolidinediones. Their main goal is to restore normal metabolic

disorder such as insulin resistance and inadequate insulin secretion from pancreas. Diet and lifestyle strategies are to reduce weight, improve glycemic control and reduce the risk of cardiovascular complications, which account for 70% to 80% of deaths among those with diabetes.

V. TREATMENT

5.1. INSULIN AND ORAL HYPOGLYCEMIC DRUGS

Insulin therapy should aim to mimic nature, which is remarkably successful both in limiting postprandial hyperglycemia and preventing hypoglycemia between meals²⁶. Site of administration of insulin injection is equally important for better and safe action of insulin and can be given by intramuscular or intravenous route. Different preparations of insulin are available such as human insulin, beef insulin, pork insulin.

Insulin therapy is no free from complications and adverse effects. The most important adverse effect are weight gain and hypoglycemia when inappropriate dose of insulin is taken and when there is mismatch between meals and insulin injection. Weight gain after starting insulin therapy for uncontrolled diabetes is an inevitable consequence and is the result of increased truncal fat and muscle bulk. This is also due to reduced energy losses through glycosuria. Sulphonyl ureas such as glibenclamide, glipizide and biguanides such as metformin, phenformin are oral hypoglycemic drugs. Sulphonylureas cause hypoglycemia by stimulating insulin release from pancreatic β -cells. They bind to sulphonylurea (SUR) receptors on the β -cell plasma membrane, causing closure of adenosine triphosphate (ATP)-sensitive potassium channels, leading to depolarization of the cell membrane. This in turn opens voltagegated channels, allowing influx of

calcium ions and subsequent secretion of preformed insulin granules.

Acute administration of sulfonylureas to type 2 DM patient's increases insulin release from the pancreas and also may further increase insulin levels by reducing hepatic clearance of the hormone. Initial studies showed that a functional pancreas was necessary for the hypoglycemic actions of sulfonylureas.

Biguanides such as metformin is anti-hyper glycaemic, not hypoglycemic³². It does not cause insulin release from the pancreas and does not cause hypoglycemia, even in large doses³³. It has been shown to increase peripheral uptake of glucose, and to reduce hepatic glucose output by approximately 20-30% when given orally but not intravenously. Impaired absorption of glucose from the gut has also been suggested as a mechanism of action.

5.2. HERBAL TREATMENT OF DIABETES

In the last few decades eco-friendly, bio-friendly, cost effective and relatively safe, plant-based medicines have moved from the fringe to the main stream with the increased research in the field of traditional medicine. There are several literature reviews by different authors about anti-diabetic herbal agents, but the most informative is the review by Atta-ar-Rahman who has documented more than 300 plant species accepted for their hypoglycaemic properties. This review has classified the plants according to their botanical name, country of origin; parts used and nature of active agents. One such plant is *Momordica charantia* (Family: Cucurbitaceae). WHO has listed 21,000 plants, which are used for medicinal purposes around the world? Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called the botanical garden of the world.

VI. CONCLUSION

The term diabetes mellitus includes several different metabolic disorders that all, if left untreated, result in abnormally high concentration of a sugar called glucose in the blood. Diabetes mellitus type 1 results when the pancreas no longer produces significant amounts of the hormone insulin, usually owing to the autoimmune destruction of the insulin-producing beta cells of the pancreas. Diabetes mellitus type 2, in

contrast, is now thought to result from autoimmune attacks on the pancreas and/or insulin resistance. The pancreas of a person with type 2 diabetes may be producing normal or even abnormally large amounts of insulin.

The main goal of diabetes management is, as far as possible, to restore carbohydrate metabolism to a normal state. To achieve this goal, individuals with an absolute deficiency of insulin require insulin replacement therapy, which is given through injections or tablets. Insulin resistance, in contrast, can be corrected by dietary modifications and exercise. Other goals of diabetes management are to prevent or treat the many complications that can result from the disease itself and from its treatment. By keeping the blood sugar level under control, diabetes can become patient's companion and he/she can enjoy life joyfully.

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