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Diabetes Epidemic in India-- A Comprehensive Review of Clinical Features, Management and Remedies

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India, the world's second most populous country, now has more people with type 2 diabetes (more than 50 million) than any other nation. With India having the highest number of diabetic patients in the world, the sugar disease is posing an enormous health problem in the country. Calling India the diabetes capital of the world, the International Journal of Diabetes in Developing Countries says that there is alarming rise in. According to a WHO fact sheet on diabetes, 2004 recorded an estimated 3.4 million deaths due to consequences of high blood sugar. WHO also estimates that 80 per cent of diabetes deaths occur in low- and middle-income countries and projects that such deaths will double between 2005 and 2030. A glance at statistics from Global Data proves one point: that the two countries having the highest diabetes prevalence (India and China) score quite low when it comes to the expenditure on the disease. In fact, India's expenditure on diabetes does not figure among the top 10 countries at all. The situation is compounded by the fact that diabetes is one of the most costly health problems in the world. It is points out that healthcare expenditure on diabetes accounted for 11.6 per cent of the total healthcare expenditure worldwide in 2010. Diabetes also imposes large economic burdens in the form of lost productivity and foregone economic growth. It has been estimated that the global burden of type 2 diabetes mellitus (T2DM) for 2010 would be 285million people (2010) which is projected to increase to 438 million in 2030; a 65 % increase . Similarly, for India this increase is estimated to be 58%, from 51 million people in 2010 to 87 million in 2030. The impacts of T2DM are considerable: as a lifelong disease, it increases morbidity and mortality and decreases the quality of life. At the same time, the disease and its complications cause a heavy economic burden for diabetic patients themselves, their families and society. A better understanding about the cause of a predisposition of Indians to get T2DM is necessary for future planning of healthcare, policy and delivery in order to ensure that the burdens of disease are addressed.

Keyword: Diabetes, hyperlipidemia

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INTRODUCTION: Diabetes mellitus is a group of metabolic disorder characterized by hyperglycemia, glycosuria, hyperlipidemia, polyuria, polyphagia, polydipsia, negative

nitrogen balance and sometime ketonemia, Hyperglycemia (high blood glucose level) that result from defects in insulin secretion, or defective response of insulin, or both. Diabetes mellitus, commonly referred to as diabetes (as it will be in this article) was first identified as a disease associated with "sweet urine," and excessive muscle loss in the ancient world. Elevated levels of blood glucose (hyperglycemia) lead to spillage of glucose into the urine, hence the term sweet urine. Normally, blood glucose levels are tightly controlled by insulin, a hormone produced by the pancreas. Insulin lowers the blood glucose level. When the blood glucose elevates (for example, after eating food), insulin is released from the pancreas to normalize the glucose level. In patients with diabetes, the absence or insufficient production of insulin causes hyperglycemia. Diabetes is a chronic medical condition, meaning that although it can be controlled, it lasts a lifetime. The American Diabetes Association estimated that the US economy lost $ 58 billion, approximately half of the direct healthcare expenditure on diabetes in 2007, because of lost earnings due to lost work days, restricted activity days, lower productivity at work, mortality and permanent disability caused by diabetes. Diabetes mellitus is one of the world's major diseases. It currently affects an estimated143 million people worldwide and the number is growing rapidly. In the India, about 1-5% population suffer from diabetes or related complication. So there is need to cure this disease. Anti-diabetic drugs treat diabetes mellitus by lowering glucose levels in the blood. With the exceptions of insulin, exenatide, and pramlintide, all are administered orally and are thus also called oral hypoglycemic agents or oral antihyperglycemic agents. There are different classes of anti-diabetic drugs, and their selection depends on the nature of the diabetes, age and situation of the person, as well as other factors. Diabetes mellitus type 1 is a disease caused by the lack of insulin. Insulin must be used in Type 1,which must be injected or inhaled. Diabetes mellitus type 2 is a disease of insulin resistance by cells. Treatments include agents which increase the amount of insulin secreted by the pancreas, agents which increase the sensitivity of target organs to insulin, and agents which decrease the rate at which glucose is absorbed from the gastrointestinal tract. Researchers around the world mainly focused on insulin, insulin analogues, oral hypoglycemic agents and various other complementary and alternate medicines to control the blood glucose levels in diabetes. Diabetes is a life-long disease marked by elevated levels of sugar in the blood. It is the second leading cause of blindness and renal disease worldwide. Diabetes mellitus is a chronic disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by ineffectiveness of the insulin produced. It is a silent killer disease and affects millions of peoples in the world. This article focuses on the causes, types, factors affecting DM, incidences, preventive measures and treatment of the acute and chronic complications of diabetes with summarizes the accounts of antidiabetic drugs. The emphasis has-been laid in particular on the new potential biological targets and the possible treatment as well as the current ongoing research status on new generation hypoglycemic agents.

SOCIO-ECONOMIC BURDEN OF DIABETES IN INDIA

Diabetes is a chronic illness that requires a combination of pharmacological & non-pharmacological measures for better control. Patient adherence to medication and lifestyle modifications plays an important role in diabetes management. Pharmacists being an important member of the healthcare system have an immense responsibility in counseling these patients. In the last three decades role of pharmacist has changed dramatically. Presently, the pharmacists are becoming more patient oriented than product oriented. Patient counseling by pharmacist deals with providing information to the patients regarding the diseases, medications and lifestyle modifications. In diabetes, self-management and patient adherence to the prescribed medication and lifestyle modifications

is very essential and pharmacist can play an important role in counseling. Patient counseling is an important means for achieving pharmaceutical care. It is defined as providing medication related information orally or in written form to the patients or their representatives, on topics like direction of use, advice on side effects, precautions, and storage, diet and life style modifications. Patient counseling is interactive in nature and involves a one-to-one interaction between a pharmacist and a patient and/or caregiver. The ultimate goal of counseling is to provide information directed at encouraging safe and appropriate use of medications, thereby enhancing therapeutic outcomes. Several guidelines specify the points to be covered by the pharmacist while counseling the patients.

ROLE OF PHARMACISTS IN DIABETES MANAGEMENT

The pharmacist can Educate The Patients about the proper use of medication, screening for drug interactions, explain monitoring devices, and make recommendations for ancillary products and services. The pharmacist, although not the health care professional to diagnose diabetes, is important in helping The Patient maintain control of their disease. The pharmacists can also Counsel the Patients Regarding Insulin Administration Regularly so that the onset of complications can be postponed by having tight glycemic control. Since the progression and the management pattern of diabetes vary significantly among different populations, the pharmacist should also tailor his counseling pattern according to the population. Some of the special populations with diabetes are mentioned below with the outline of the counseling in these patients. Elderly, Children, Pregnancy, Multiple disorders, Frequent traveling.

Diabetes Mellitus:

Diabetes mellitus is common disease of insulin and glucose metabolism characterized by either destruction of pancreatic islets due to an auto immune process or decreased insulin action combined with inadequate release of insulin from pancreas. Diabetes mellitus is a major health problem in the United States and Europe. In the United States it is estimated that diabetes affect approximately 10 to 15 million people. Due to deficiency of insulin, enough glucose cannot enter into the cells from the blood in circulation and thereby causing higher glucose (or sugar) level in blood, and when this situation persists for longer period of time over days. Months or even years, a complex pathological condition develops and this condition is called as diabetes.

Diabetes mellitus is a chronic complex metabolic disorder resulting from insulin deficiency or insulin resistance primarily characterized by hyperglycemia, altered metabolism of carbohydrate, protein and lipids, and increased risk of vascular complications like cardio-vascular, renal, neural and visual disorders which are related to the duration of the disease.

Classification of diabetes mellitus:

Diabetes mellitus (DM) is broadly divided into two groups.

1. Type I- Insulin dependent diabetes mellitus (IDDM), juvenile onset diabetes mellitus:

Insulin-Dependent Diabetes Mellitus (IDDM) also known as juvenile onset diabetes or diabetes-Type I or Type I DM. This tends to occur in younger individual who are usually thin. These patients are deficient in their production and reserve of insulin. Onset of type I DM is usually very acute and in childhood. Approximately 2% of diabetes in our country belongs to this class.

Type I DM occurs due to idiophatic destruction of insulin producing beta cells in islets of langerhans in the pancreases resulting in inability to produce endogenous insulin which is vital for control of blood sugar and other metabolic functions.

2. Type II- Non-Insulin-dependent diabetes mellitus (NIDDM), maturity onset diabetes mellitus:

This tends to occur in obese persons, although thin persons may also develop NIDDM. NIDDM is much more common than IDDM and accounts for about 85% of patients with diabetes. Type II diabetes is a chronic and multifactorial disease characterized by hyperglycemia as well as insulin resistance in the liver and peripheral tissues and impaired insulin secretion from pancreatic beta-cells. Hyperglycemia in type II diabetes leads to a gradual progression of complications, including neuropathy, retinopathy, arteriosclerosis, and coronary artery disease.

Comparison of two types of diabetes mellitus:

Table No.1:-Contrasting features of two types of primary diabetes:

Features	Type I DM	Type II DM
Frequency	10-20% of diabetic population	80-90% of diabetic population
Age at onset	Early (Below 35 years)	Late (after 40 years)
Body weight	Normal	Obese
Type of onset	Abdrupt	Gradual
Family history	<20%	About 60%
Iselet cell antibodies	Yes	No
Blood insulin level	Decreased Insulin	Increased Insulin
Iselet cell changes	Insulitis, beta cell depletion	No insulitis
Acute complications	Very common ketoacidosis	Hyperosmolar coma
Clinical management	Insulin and diet	Diet, exercise, insulin
Acute complication	Ketoacidosis	Hyperosmolar coma

WHO-CLASSIFICATION OF DIABETES [25]

Diabetes mellitus

- Type 1 diabetes mellitus (IDDM)
- Type 2 diabetes mellitus (NIDDM)
  - (a)Non-obese
  - (b)Obese
- Malnutrition-related diabetes mellitus
- Other types of diabetes mellitus (associated with specific conditions and syndromes)
- Gestational diabetes mellitus

Impaired glucose tolerance

- Non-Obese
- Obese

ETIOLOGY AND PATHOGENESIS[26]

INSULIN METABOLISM

The major stimulus for both synthesis and release of insulin is glucose. The steps involved in biosynthesis and release of insulin from β-cells are as follows

1. Glucose stimulation initiates production of proinsulin in the endoplasmic reticulum. Proinsulin is a single chain of 86 amino acids consisting of A and B chains of insulin, linked together by connecting segment called C-peptide.
2. Proinsulin is transferred to the Golgi complex where the C-peptide is split off by a proteolytic enzyme. Both insulin and C-peptide are then stored in secretory granules in the Golgi complex from where they are released in membranous sacs acquired from the Golgi membranes into the cytoplasm where insulin is converted into zinc insulin crystals.

3. Glucose stimulation of B- cells causes insulin release as a biphasic process. First phase is the immediate release of insulin in response to rise in blood glucose level, followed by slow second phase which continues till the blood glucose level return to normal limits.
4. After glucose stimulation, the membranous sacs containing zinc-insulin crystals and C-peptide in the cytoplasm of B cells are brought to the surface of plasma membrane by microtubule-microfilament system which requires intracellular calcium.
5. The final step is the release of B granules containing insulin and C-peptide by emiocytosis into the extracellular space from where insulin and C-peptide are transported into the capillary system of islets and thence into the systemic circulation.

A defect in any one step in the biosynthesis or release may lead to deficiency or defective release of insulin may cause of diabetes.

Insulin is a major anabolic hormone and its main metabolic function is to increase the transmembranous transports of glucose into certain cells of the body. In addition insulin required for glycogen formation in the liver and skeletal muscles, conversion of glucose to triglycerides, and for synthesis of nucleic acids and proteins. Insulin act on its target cells by binding to the insulin receptors present on insulin responsive cells.

ETIOPATOGENISIS OF TYPE-I DIABETES

Type I diabetes, previously called juvenile –onset diabetes or insulin dependent diabetes mellitus (IDDM) comprise about 10-20% cases of diabetes. **Type I** diabetes usually manifests at early age, generally below the age of 40. Characteristically, the plasma insulin levels are low and patient respond to exogenous insulin therapy. The onset of symptoms is generally abrupt with polyuria, polydipsia, and polyphagia. The patients are not obese but have generally progressive loss of weight. These patients are prone to develop metabolic complications such as ketoacidosis and hypoglycemia episode.

Currently, the pathogenesis of type I diabetes is explained on the basis of 3 mutually- interlinked mechanisms, each with sufficient evidences in support. These are genetic susceptibility, autoimmunity, and certain environmental factors.

Genetic susceptibility. Diabetes mellitus runs in families has been known for years

- More recently, however, it has been shown in identical twins that if one twin has type I diabetes, there is a 50% chance of the second twin developing diabetes.
- Secondly, a higher frequency (80%) of type I diabetes has been observed in HLA-DR4 individuals.
- Thirdly, different mutations have been identified with predisposition to the disease.

Autoimmunity. Type I diabetes is believed to be an autoimmune disease that results in specific immunologic destruction of β-Cells of islet of Langerhans. The evidence in support is as follows.

- Presence of islet cell antibodies in patients with type I diabetes.

- Occurrence of lymphocytic infiltration in and around the islets (insulitis).
- Association of type I diabetes with other autoimmune disease.
- Remission of type I diabetes in response to immunosuppressive therapy such as administration of cyclosporine A.
- About 10% cases of type I diabetes have other organ specific autoimmune disease such as Graves' disease, Addison's disease or autoimmune thyroiditis.

Environmental Factors. Epidemiologic studies in type I diabetes have revealed involvement of certain environmental factors in its pathogenesis. These factors are certain viruses, chemicals, and common environmental toxins.

- *Certain viral infections* may precede the onset of type I diabetes e.g. mumps, measles, coxsackie B virus, cytomegalovirus and infectious mononucleosis.
- Experimental induction of type I diabetes with certain chemicals has been possible e.g. alloxan, streptozotocin, and pentamidine.
- Geographic variations in the incidence of type I diabetes suggest some common environmental factors.

It can thus be summarized by interlinking the three mechanisms described above that in type I diabetes some 'environmental factor' initiates the 'autoimmune destruction' of B cells in genetically susceptible individuals.

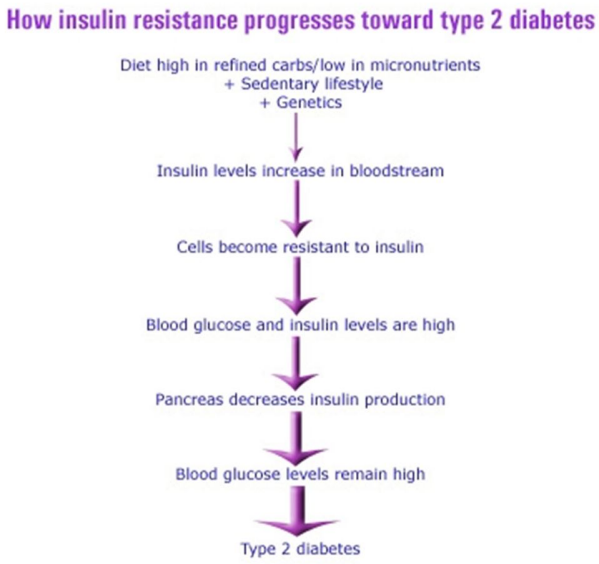


Fig.1.Resistance of insulin towards type II diabetes

IMPACT OF DIABETES

Over time, diabetes can lead to blindness, kidney failure, and nerve damage. These types of damage are the result of damage to small vessels, referred to as microvascular disease. Diabetes is also an important factor in accelerating the hardening and narrowing of the arteries (atherosclerosis), leading to strokes, coronary heart disease, and other large blood vessel diseases. This is referred to as macrovascular disease. Diabetes affects approximately 17 million people (about 8% of the population) in the United States. In addition, an estimated additional 12 million people in the United States have diabetes and don't even know it.

During 1997 year, 13.9 million days of hospital stay were attributed to diabetes, while 30.3 million physician office visits were diabetes related. Remember, these numbers reflect only the population in the United States. Globally, the statistics are staggering.

DIFFERENT TYPES OF DIABETES

There are two major types of diabetes, called **type 1** and **type 2.** Type 1 diabetes was also called insulin dependent diabetes mellitus (IDDM), or juvenile onset diabetes mellitus. In type 1 diabetes, the pancreas undergoes an autoimmune attack by the body itself, and is rendered incapable of making insulin. Abnormal antibodies have been found in the majority of patients with type 1 diabetes. Antibodies are proteins in the blood that are part of the body's immune system. The patient with type 1 diabetes must rely on insulin medication for survival.

In autoimmune diseases, such as type 1 diabetes, the immune system mistakenly manufactures antibodies and inflammatory cells that are directed against and cause damage to patients' own body tissues. In persons with type 1 diabetes, the beta cells of the pancreas, which are responsible for insulin production, are attacked by the misdirected immune system. It is believed that the tendency to develop abnormal antibodies in type 1 diabetes is, in part, genetically inherited, though the details are not fully understood.

Exposure to certain viral infections (mumps and Coxsackie viruses) or other environmental toxins may serve to trigger abnormal antibody responses that cause damage to the pancreas cells where insulin is made. Some of the antibodies seen in type 1 diabetes include anti-islet cell antibodies, anti-insulin antibodies and anti-glutamic decarboxylase antibodies. These antibodies can be measured in the majority of patients, and may help determine which individuals are at risk for developing type 1 diabetes.

At present, the American Diabetes Association does not recommend general screening of the population for type 1 diabetes, though screening of high risk individuals, such as those with a first degree relative (sibling or parent) with type 1 diabetes should be encouraged. **Type 1 diabetes** tends to occur in young, lean individuals, usually before 30 years of age, however, older patients do present with this form of diabetes on occasion. This subgroup is referred to as latent autoimmune diabetes in adults (LADA). LADA is a slow, progressive form of type 1 diabetes. Of all the patients with diabetes, only approximately 10% of the patients have type 1 diabetes and the remaining 90% have type 2 diabetes.

Type 2 diabetes was also referred to as non-insulin dependent diabetes mellitus (NIDDM), or adult onset diabetes mellitus (AODM). In type 2 diabetes, patients can still produce insulin, but do so relatively inadequately for their body's needs, particularly in the face of insulin resistance as discussed above. In many cases this actually means the pancreas produces larger than normal quantities of insulin. A major feature of type 2 diabetes is a lack of sensitivity to insulin by the cells of the body (particularly fat and muscle cells).

In addition to the problems with an increase in insulin resistance, the release of insulin by the pancreas may also be defective and suboptimal. In fact, there is a known steady decline in beta cell production of insulin in type 2 diabetes that contributes to worsening glucose control. (This is a major factor for many patients with type 2 diabetes who ultimately require insulin therapy.) Finally, the liver in these patients continues to produce glucose through a process called gluconeogenesis despite elevated glucose levels. The control of gluconeogenesis becomes compromised.

While it is said that type 2 diabetes occurs mostly in individuals over 30 years old

and the incidence increases with age, we are seeing an alarming number patients with type 2 diabetes who are barely in their teen years. In fact, for the first time in the history of humans, type 2 diabetes is now more common than type 1 diabetes in childhood. Most of these cases are a direct result of poor eating habits, higher body weight, and lack of exercise. While there is a strong genetic component to developing this form of diabetes, there are other risk factors - the most significant of which is obesity.

COMPLICATIONS OF DIABETES

Both type 1 and type 2 diabetes ultimately lead to high blood sugar levels, a condition called hyperglycemia. Over a long period of time, hyperglycemia damages the retina of the eye, the blood vessels of the kidneys, the nerves, and other blood vessels.

- Damage to the retina from diabetes (diabetic retinopathy) is a leading cause of blindness.
- Damage to the kidneys from diabetes (diabetic nephropathy) is a leading cause of kidney failure.
- Damage to the nerves from diabetes (diabetic neuropathy) is a leading cause of foot wounds and ulcers, which frequently lead to foot and leg amputations.
- Damage to the nerves in the autonomic nervous system can lead to paralysis of the stomach (gastroparesis), chronic diarrhea, and an inability to control heart rate and blood pressure during postural changes.
- Diabetes accelerates atherosclerosis, (the formation of fatty plaques inside the arteries), which can lead to blockages or a clot (thrombus). Such changes can then lead to heart attack, stroke, and decreased circulation in the arms and legs (peripheral vascular disease).
- Diabetes predisposes people to elevated blood pressure, high levels of cholesterol and triglycerides. These conditions both independently and together with hyperglycemia, increase the risk of heart disease, kidney disease, and other blood vessel complications.

Diabetes can contribute to a number of acute (short-lived) medical problems.

- Many **infections** are associated with diabetes, and infections are frequently more dangerous in someone with diabetes because the body's normal ability to fight infections is impaired. To compound the problem, infections may worsen glucose control, which further delays recovery from infection.
- **Hypoglycemia** or low blood sugar, occurs intermittently in most people with diabetes. It can result from taking too much diabetes medication or insulin (sometimes called an insulin reaction), missing a meal, exercising more than usual, drinking too much alcohol, or taking certain medications for other conditions. It is very important to recognize hypoglycemia and be prepared to treat it at all times. Headache, feeling dizzy, poor concentration, tremor of the hands, and sweating are common symptoms of hypoglycemia. A person can faint or have a seizure if blood sugar level become too low.
- **Diabetic ketoacidosis** (DKA) is a serious condition in which uncontrolled hyperglycemia (usually due to complete lack of insulin or a relative deficiency of insulin) over time creates a buildup of ketones (acidic waste products) in the blood. High levels of ketones can be very harmful. This typically happens to people with type 1 diabetes who do not have good blood glucose control. Diabetic ketoacidosis can be precipitated by infection, stress, trauma, missing medications like insulin, or medical emergencies such as a stroke and heart attack.
- **Hyperosmolar hyperglycemic nonketotic syndrome** is a serious condition in which the blood sugar level gets very high. The body tries to get rid of the excess blood sugar by eliminating it in the urine. This increases the amount of urine significantly, and often leads to dehydration so severe that it can cause

seizures, coma, and even death. This syndrome typically occurs in people with type 2 diabetes who are not controlling their blood sugar levels, who have become dehydrated, or who have stress, injury, stroke, or are taking certain medications, like steroids.

DIABETES CAUSES

Type 1 diabetes: Type 1 diabetes is believed to be an autoimmune disease. The body's immune system specifically attacks the cells in the pancreas that produce insulin.

- A predisposition to develop type 1 diabetes may run in families, but genetic causes (a postitive family history) are much more common for type 2 diabetes.
- Environmental factors, including common unavoidable viral infections, may also contribute to type 1 diabetes.
- Type 1 diabetes is most common in people of non-Hispanic, Northern European descent (especially Finland and Sardinia), followed by African Americans, and Hispanic Americans. It is relatively rare in those of Asian descent.
- Type 1 diabetes is slightly more common in men than in women.

Type 2 diabetes: Type 2 diabetes has strong genetic links, meaning that type 2 diabetes tends to run in families. Several genes have been identified, and more are under study which may relate to the causes of type 2 diabetes. Risk factors for developing type 2 diabetes include the following:

- High blood pressure
- High blood triglyceride (fat) levels
- Gestational diabetes or giving birth to a baby weighing more than 9 pounds
- High-fat diet
- High alcohol intake
- Sedentary lifestyle
- Obesity or being overweight
- Ethnicity, particularly when a close relative had type 2 diabetes or gestational diabetes: certain groups, such as African Americans, Native Americans, Hispanic Americans, and Japanese Americans, have a greater risk of developing type 2 diabetes than non-Hispanic whites.
- Aging: Increasing age is a significant risk factor for type 2 diabetes. Risk begins to rise significantly at about age 45 years, and rises considerably after age 65 years.

DIABETES SYMPTOMS

Symptoms of type 1 diabetes are often dramatic and come on very suddenly.

- Type 1 diabetes is usually recognized in childhood or early adolescence, often in association with an illness (such as a virus or urinary tract infection) or injury.
- The extra stress can cause diabetic ketoacidosis.
  - Symptoms of ketoacidosis include nausea and vomiting. Dehydration and often-serious disturbances in blood levels of potassium follow.
  - Without treatment, ketoacidosis can lead to coma and death.

Symptoms of type 2 diabetes are often subtle and may be attributed to aging or obesity.

- A person may have type 2 diabetes for many years without knowing it.
- People with type 2 diabetes can develop hyperglycemic hyperosmolar nonketotic syndrome.
- Type 2 diabetes can be precipitated by steroids and stress.
- If not properly treated, type 2 diabetes can lead to complications such as blindness, kidney failure, heart disease, and nerve damage.

Common symptoms of both type 1 and type 2 diabetes include:

- **Fatigue, constantly tired:** In diabetes, the body is inefficient and sometimes unable to use glucose for fuel. The body switches over to metabolizing fat, partially or completely, as a

fuel source. This process requires the body to use more energy. The end result is feeling fatigued or constantly tired.

- **Unexplained weight loss:** People with diabetes are unable to process many of the calories in the foods they eat. Thus, they may lose weight even though they eat an apparently appropriate or even an excessive amount of food. Losing sugar and water in the urine and the accompanying dehydration also contributes to weight loss.
- **Excessive thirst (polydipsia):** A person with diabetes develops high blood sugar levels, which overwhelms the kidney's ability to reabsorb the sugar as the blood is filtered to make urine. Excessive urine is made as the kidney spills the excess sugar. The body tries to counteract this by sending a signal to the brain to dilute the blood, which translates into thirst. The body encourages more water consumption to dilute the high blood sugar back to normal levels and to compensate for the water lost by excessive urination.
- **Excessive urination (polyuria):** Another way the body tries to rid the body of the extra sugar in the blood is to excrete it in the urine. This can also lead to dehydration because a large amount of water is necessary to excrete the sugar.
- **Excessive eating (polyphagia):** If the body is able, it will secrete more insulin in order to try to manage the excessive blood sugar levels. Moreover, the body is resistant to the action of insulin in type 2 diabetes. One of the functions of insulin is to stimulate hunger. Therefore, higher insulin levels lead to increased hunger. Despite increased caloric intake, the person may gain very little weight and may even lose weight.
- **Poor wound healing:** High blood sugar levels prevent white blood cells, which are important in defending the body against bacteria and also in cleaning up dead tissue and cells, from functioning normally. When these cells do not function properly, wounds take much longer to heal and become infected more frequently. Long-standing diabetes also is associated with thickening of blood vessels, which prevents good circulation, including the delivery of enough oxygen and other nutrients to body tissues.
- **Infections:** Certain infections, such as frequent yeast infections of the genitals, skin infections, and frequent urinary tract infections, may result from suppression of the immune system by diabetes and by the presence of glucose in the tissues, which allows bacteria to grow. These infections can also be an indicator of poor blood sugar control in a person known to have diabetes.
- **Altered mental status:** Agitation, unexplained irritability, inattention, extreme lethargy, or confusion can all be signs of very high blood sugar, ketoacidosis, hyperosmolar hyperglycemia nonketotic syndrome, or hypoglycemia (low sugar). Thus, any of these merit the immediate attention of a medical professional. Call your health care professional or 911.
- **Blurry vision:** Blurry vision is not specific for diabetes but is frequently present with high blood sugar levels.

DIABETES DIAGNOSIS

Doctors use special tests in diagnosing diabetes and also in monitoring blood sugar level control in known diabetics.

The health care professional will take a history including information about the patient's symptoms, risk factors for diabetes, past medical problems, current medications, allergies to medications, family history of diabetes, or other medical problems such as high cholesterol or heart disease, and personal habits and lifestyle.

A number of laboratory tests are available to confirm the diagnosis of diabetes.

Finger stick blood glucose: This is a rapid screening test that may be performed anywhere, including community-based screening programs.

- Although a not as accurate as testing the patient's blood in the hospital laboratory, a

finger stick blood glucose test but is easy to perform, and the result is available right away.

- The test involves sticking the patient's finger for a blood sample, which is then placed on a strip. The strip goes into a machine that reads the blood sugar level. These machines are only accurate to within about 10%-20% of true laboratory values.
- Finger stick blood glucose values tend to be most inaccurate at very high or very low levels, so this test is only a preliminary screening study. Finger stick is the way most people with diabetes monitor their blood sugar levels at home.

Fasting plasma glucose: The patient will be asked to eat or drink nothing for 8 hours before having blood drawn (usually first thing in the morning). If the blood glucose level is greater than or equal to 126 mg/dL (without eating anything), they probably have diabetes.

- If the result is abnormal, the fasting plasma glucose test may be repeated on a different day to confirm the result, or the patient may undergo an oral glucose tolerance test or a glycosylated hemoglobin test (often called "hemoglobin A1c") as a confirmatory test.
- If fasting plasma glucose level is greater than 100 but less than 126 mg/dL, then the patient has what is called impaired fasting glucose, or IFG. This is considered to be prediabetes. These patients do not have diabetes, but they are at high risk of developing diabetes in the near future.

Oral glucose tolerance test: This test involves drawing blood for a fasting plasma glucose test, then drawing blood for a second test at two hours after drinking a very sweet drink containing up to 75 grams of sugar.

- If the blood sugar level after the sugar drink is greater than or equal to 200 mg/dL, the patient has diabetes.
- If the blood glucose level is between 140 and 199, then the patient has impaired glucose tolerance (IGT), which is also a prediabetic condition.

Glycosylated hemoglobin or hemoglobin A1c: This test is a measurement of how high the blood sugar levels have been over approximately the last 120 days (the average life-span of the red blood cells on which the test is based).

- Excess blood glucose hooks itself on to the hemoglobin in red blood cells and stays there for the life of the red blood cell.
- The percentage of hemoglobin that has had excess blood sugar attached to it can be measured in the blood. The test involves having a small amount of blood drawn.
- A hemoglobin A1c test is the best measurement of blood sugar control in people known to have diabetes. A hemoglobin A1c result of 7% or less indicates good glucose control. A result of 8% or greater indicates that blood sugar levels are too high, too much of the time.
- The hemoglobin A1c test is the best test for diabetes follow-up care, than to diagnose diabetes. Still, a hemoglobin A1c result greater than 6.1% is highly suggestive of diabetes. Generally, a confirmatory test would be needed before diagnosing diabetes.
- The hemoglobin A1c test is generally measured about every 3 to 6 months for people with known diabetes, although it may be done more frequently for people who are having difficulty achieving and maintaining good blood sugar control.
- This test is not used for people who do not have diabetes or are not at increased risk of diabetes.
- Normal values may vary from laboratory to laboratory, although an effort is under way to standardize how measurements are performed.

DIAGNOSING COMPLICATIONS OF DIABETES

A person with diabetes should be checked regularly for early signs of diabetic complications. A health care professional can

order some of these tests; for others, the patient should be referred to a specialist.

- The patient should have their eyes checked at least once a year by an eye specialist (ophthalmologist) to screen for diabetic retinopathy, a leading cause of blindness.
- The patient's urine should be checked for protein (microalbumin) on a regular basis, at least one to two times per year. Protein in the urine is an early sign of diabetic nephropathy, a leading cause of kidney failure.
- Sensation in the legs should be checked regularly using a tuning fork or a monofilament device. Diabetic neuropathy is a leading cause of lower extremity ulcers in individuals with diabetes, which frequently lead to amputation of the feet or legs.
- The health care professional should check the feet and lower legs of the patient at every visit for cuts, scrapes, blisters, or other lesions that could become infected. Adults with diabetes should check the soles of their feet and their legs daily with a hand-held mirror, either by themselves or with the assistance of a relative or caretaker.
- The patient should be screened regularly for conditions that may contribute to heart disease, such as high blood pressure and high cholesterol.

DIABETES TREATMENT

Diabetes Self-Care at Home (Lifestyle Changes and Glucose Monitoring)

If a person has diabetes, healthful lifestyle choices in diet, exercise, and other health habits will help to improve glycemic (blood sugar) control and prevent or minimize complications of diabetes.

Diabetes Diet: A healthy diet is key to controlling blood sugar levels and preventing diabetes complications.

- If the patient is obese and has had difficulty losing weight on their own, talk to a health care professional. He or she can recommend a dietitian or a weight modification program to help the patient reach a goal.
- Eat a consistent, well-balanced diet that is high in fiber, low in saturated fat, and low in concentrated sweets.
- A consistent diet that includes roughly the same number of calories at about the same times of day helps the health care professional prescribe the correct dose of medication or insulin.
- A healthy diet also helps to keep blood sugar at a relatively even level and avoids excessively low or high blood sugar levels, which can be dangerous and even life-threatening.

Exercise: Regular exercise, in any form, can help reduce the risk of developing diabetes. Activity can also reduce the risk of developing complications of diabetes such as heart disease, stroke, kidney failure, blindness, and leg ulcers.

- As little as 20 minutes of walking three times a week has a proven beneficial effect. Any exercise is beneficial; no matter how easy or how long, some exercise is better than no exercise.
- If the patient has complications of diabetes (such as eye, kidney, or nerve problems), they may be limited both in type of exercise, and amount of exercise they can safely do without worsening their condition. Consult with your health care professional before starting any exercise program.

Alcohol use: Moderate or eliminate consumption of alcohol. Try to have no more than seven alcoholic drinks in a week, and never more than one or two drinks in an evening. One drink is considered 1.5 ounces of liquor, 6 ounces of wine, or 12 ounces of beer. Excessive alcohol use is a known risk factor for type 2 diabetes. Alcohol consumption can cause low or high blood sugar levels, nerve pain (neuritis), and an increase in triglycerides.

Smoking: If the patient has diabetes, and smokes cigarettes or use any other form of tobacco, they are raising the risks markedly for nearly all of the complications of diabetes. Smoking damages blood vessels and contributes to heart disease, stroke, and poor circulation in the limbs. If a person needs help to quit tobacco use, talk to a health care professional.

Self-monitored blood glucose: Check blood sugar levels frequently, at least before meals and at bedtime, then record the results in a logbook.

- This log should also include insulin or oral medication doses and times, when and what the patient ate, when and for how long they exercised, and any significant events of the day such as high or low blood sugar levels and how they treated the problem.
- Better equipment now available makes testing blood sugar levels less painful and less complicated than ever. A daily blood sugar diary is invaluable to the health care professional in evaluating how the patient is responding to medications, diet, and exercise in the treatment of diabetes.
- Medicare now pays for diabetic testing supplies, as do many private insurers and Medicaid.

DIABETES MEDICAL TREATMENT

The treatment of diabetes is highly individualized, depending on the type of diabetes, whether the patient has other active medical problems, whether the patient has complications of diabetes, and age and general health of the patient at time of diagnosis.

- A health care professional will set goals for lifestyle changes, blood sugar control, and treatment.
- Together, the patient and the health care professional will formulate a plan to help meet those goals.

Education about diabetes and its treatment is essential in all types of diabetes.

- When the patient is first diagnosed with diabetes, the diabetes care team will spend a lot of time with the patient, teaching them about their condition, treatment, and everything they need to know to care for themselves on a daily basis.
- The diabetes care team includes the health care professional and his or her staff. It may include specialists in foot care, neurology, kidney diseases, and eye diseases. A professional dietitian and a diabetes educator also may be part of the team.

The health care team will see the patient at appropriate intervals to monitor their progress and evaluate goals.

Type 1 diabetes

Treatment of diabetes almost always involves the daily injection of insulin, usually a combination of short-acting insulin (for example, lispro [Humalog] or aspart [NovoLog]) and a longer acting insulin (for example, NPH, Lente, glargine [Lantus], detemir [Levemir]).

- Insulin must be given as an injection just under the skin. If taken by mouth, insulin would be destroyed in the stomach before it could get into the blood where it is needed.
- Most people with type 1 diabetes give these injections to themselves. Even if someone else usually gives the patient injections, it is important that the patient knows how to do it in case the other person is unavailable.
- A trained professional will show the patient how to store and inject the insulin. Usually this is a nurse who works with the health care professional or a diabetes educator.
- Insulin is usually given in two or three injections per day, generally around mealtimes. Dosage is individualized and is tailored to the patient's specific needs by the health care professional. Longer acting

insulins are typically administered one or two times per day.
- Some people have their insulin administered by continuous infusion pumps to provide adequate blood glucose control. Supplemental mealtime insulin is programmed into the pump by the individual as recommended by his or her health care professionals.
- It is very important to eat after the taking insulin, as the insulin will lower blood sugar regardless of whether the person has eaten. If insulin is taken without eating, the result may be hypoglycemia. This is called an insulin reaction.
- There is an adjustment period while the patient learns how insulin affects them, and how to time meals and exercise with insulin injections to keep blood sugar levels as even as possible.
- Keeping accurate records of blood sugar levels and insulin dosages is crucial for the patient's diabetes management.
- Eating a consistent, healthy diet appropriate for the patient's size and weight is essential in controlling blood sugar level.

Type 2 diabetes

Depending on how elevated the patient's blood sugar and glycosylated hemoglobin (HbA1c) are at the time of diagnosis, they may be given a chance to lower blood sugar levels through lifestyle changes, without medication.

- The best way to do this is to lose weight if the patient is obese, and begin an exercise program.
- This will generally be tried for 3 to 6 months, then blood sugar and glycosylated hemoglobin will be rechecked. If they remain high, the patient will be started on an oral medication, usually a sulfonylurea or biguanide (metformin [Glucophage]), to help control blood sugar levels.
- Even if the patient is on medication, it is still important to eat a healthy diet, lose weight if they are overweight, and engage in moderate physical activity as often as possible.
- The health care professional will initially monitor the patient's progress on medication very carefully. It is important to receive just the right dose of the right medication, to regulate blood sugar levels in the recommended range with the fewest side effects.
- The doctor may decide to combine two types of medications to achieve blood sugar levels control.
- Gradually, even people with type 2 diabetes may require insulin injections to control their blood sugar levels.
- It is becoming more common for people with type 2 diabetes to take a combination of oral medication and insulin injections to control blood sugar levels.

Diabetes treatment: Lowering blood sugar

Several classes of type 2 diabetes medicines exist. Each works in different ways to lower blood sugar. A drug may work by:

- Stimulating the pancreas to produce and release more insulin
- Inhibiting the production and release of glucose from the liver
- Blocking the action of stomach enzymes that break down carbohydrates
- Improving the sensitivity of cells to insulin

Each class of medicine has one or more drugs. Some of these drugs are taken orally, while others must be injected. And some type 2 diabetes pills contain a combination of two classes of drugs.

Compare diabetes medications

Here's an at-a-glance comparison of common diabetes medications. More medications are available depending on your needs and situation. Ask your doctor about your options and the pros and cons of each.

Oral medications			
Medications	**Action**	**Advantages**	**Possible side effects**
Meglitinides Repaglinide (Prandin) Nateglinide (Starlix)	Stimulate the release of insulin	Work quickly	Severely low blood sugar (hypoglycemia); weight gain; nausea; back pain; headache
Sulfonylureas Glipizide (Glucotrol) Glimepiride (Amaryl) Glyburide (DiaBeta, Glynase)	Stimulate the release of insulin	Work quickly	Hypoglycemia; weight gain; nausea; skin rash
Dipeptidy peptidase-4 (DPP-4) inhibitors Saxagliptin (Onglyza) Sitagliptin (Januvia) Linagliptin (Tradjenta)	Stimulate the release of insulin; inhibit the release of glucose from the liver	Don't cause weight gain	Upper respiratory tract infection; sore throat; headache; inflammation of the pancreas (sitagliptin)
Biguanides Metformin (Fortamet, Glucophage, others)	Inhibit the release of glucose from the liver; improve sensitivity to insulin	May promote modest weight loss and modest decline in low-density lipoprotein (LDL), or "bad," cholesterol	Nausea; diarrhea; rarely, the harmful buildup of lactic acid (lactic acidosis)
Thiazolidinediones Rosiglitazone (Avandia) Pioglitazone (Actos)	Improve sensitivity to insulin; inhibit the release of glucose from the liver	May slightly increase high-density lipoprotein (HDL), or "good," cholesterol	Heart failure; heart attack; stroke; liver disease
Alpha-glucosidase inhibitors Acarbose (Precose) Miglitol (Glyset)	Slow the breakdown of starches and some sugars	Don't cause weight gain	Stomach pain; gas; diarrhea
Injectable medications			
Medications	**Action**	**Advantages**	**Possible side effects**
Amylin mimetics Pramlintide (Symlin)	Stimulate the release of insulin; used with insulin injections	May suppress hunger; may promote modest weight loss	Hypoglycemia; nausea or vomiting; headache; redness and irritation at injection site
Incretin mimetics Exenatide (Byetta) Liraglutide (Victoza)	Stimulate the release of insulin; used with metformin and sulfonylurea	May suppress hunger; may promote modest weight loss	Nausea or vomiting; headache; dizziness; kidney damage or failure

Aim of therapy of diabetes mellitus:

- To control symptoms with diet, exercise and drugs.
- To maintain the optimum body weight.
- To correct the metabolic disturbances.
- To prevent the degenerative vascular complications.

Indication for insulin therapy:

- Insulin dependent diabetes mellitus.
- Non-insulin dependent diabetes mellitus patients who are underweight those who have history of onset before 30-35 years and those in whom diabetes is of very long standing.
- During surgical procedure.
- Diabetic pre-coma and coma.
- Pregnant diabetics.

Insulin therapy:

Insulin therapy, included in this group are all the type I diabetics and all diabetics who are ketosis prone, with or without the stress due to trauma, surgery or infection. Insulin is also required by type II diabetics who cannot be maintained adequately on oral hypoglycemic agents or dietary regulation and exercise.

Oral Anti-diabetic agents:

The main chemical groups of oral hypoglycemic agents used in therapy are

sulfonylureas, biguanides, and thiazolidinediones and related compounds.

1) Sulfonylureas:

These compounds are chemically related to sulphonamides. The sulfonylurea group of drugs was developed as a result of the chance observation that a sulphonamide derivative (used to treat typhoid) resulted in a marked lowering of blood glucose.

Mechanism of Action:

Sulfonylureas stimulate the release of insulin by the beta cells of the iseletes langerhans. They act by increasing the beta cell seneitivity to glucose Infact

Sulfonylurea increases insulin release at substimulatory concentration of blood glucose.

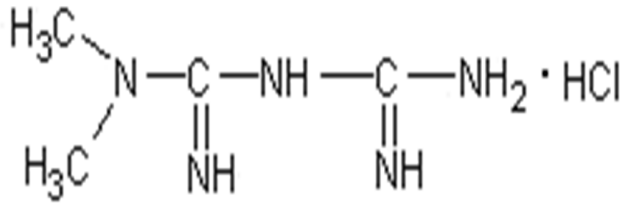
The principal mechanism of action of sulfonylurea is to release of insulin from the functionating beta cells of pancreas, they have no significant effect on the blood sugar. The sulfonylureas may have other actions, such as inhibition of secretion of glucagon, and action at post receptor intracellular sites to increase insulin activity.

1) Biguanides:

A second group of oral hypoglycemic agents that are chemically distint from the sulfonylureas are the biguanides. The food and drug administration has banned sale the only biguanided. The biguanides differ markedly from sulfonylureas: cause little or no hypoglycemia in non-diabetic subjects and do not stimulate pancreatic beta-cells.

Biguanides lower blood glucose. They increase glucose uptake and utilization in skeletal muscle (thereby reducing insulin resistance) and reduce hepatic glucose production (gluconeogenisis). Metformin, apart from lowering blood glucose, additionally reduces low density lipoprotein, and very low density lipoproteins (LDL and VLDL) respectively.

The structure of metformin is given below;



1) Thiazolidinediones:

The introduction of thiazolidinediones in the treatment of adults onset diabetes mellitus was a major breakthrough since the introduction of sulfonylureas in 1950's. Thiazolidinediones (TZDs) a recent class of oralhypoglycemic agents. Currently, two member of this class namely pioglitazone and rosiglitazone are widely prescribed oral blood glucose lowering drugs for the treatment of type II diabetes mellitus both singly or in combination.

CONCLUSION

Diabetes mellitus is not completely curable but, it is controllable to a great extent. So, you need to have thorough diabetes information to manage this it successfully. The control of diabetes mostly depends on the patient and it is his/her responsibility to take care of their diet, exercise and medication. Advances in diabetes research have led to better ways of controlling diabetes and treating its complications. Hence they include:-New improved Insulin and its therapy, (external and implantable insulin pumps) have advanced well to manage elevated blood sugars without any allergic reactions. Oral hypoglycemic drug, controls diabetes type 2.New improved blood glucose monitor (new device for self-blood glucose monitoring), and hemoglobin A1c laboratory test to measure blood glucose control during previous 3 months. Effective availability of the treatments for affected body organs due to diabetes. Better ways to manage mother and its fetus health during the gestational diabetes phase.

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