

CASE STUDY ON DIABETES MELLITUS

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ABSTRACT

Diabetes mellitus¹, is one of the most common non-communicable diseases worldwide. India faces several challenges in diabetes management, including a rising prevalence in urban and rural areas, lack of disease awareness among the public, limited health care facilities, high cost of treatment, suboptimal glycaemic control and rising prevalence of diabetic complications. Insulin therapy for diabetes is most commonly delivered via subcutaneous injections, up to four times a day. Long-term insulin therapy, compounded by the invasive nature of its administration, has caused problems with patient compliance, ultimately influencing patient outcomes. There is an increase in the prevalence of type 1 diabetes also, but main cause of diabetic epidemic is type 2 diabetes mellitus, which accounts for more than 90 percent of all diabetes cases. Type 2 diabetes is a serious and common chronic disease resulting from a complex inheritance- environment interaction along with other risk factors such as obesity and sedentary lifestyle.

Keywords: Diabetes mellitus, diagnosis, cause and treatment.

1. INTRODUCTION

Diabetes mellitus (DM), is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period. Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced. 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 nerves. 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 etc. 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 effects. 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 antidiabetic 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. The World Health Organization (WHO) Global report on diabetes shows that the number of adults living with diabetes has almost quadrupled since 1980 to 422 million adults [3] and is expected to increase to 693 million by 2045. The disease is characterized by high blood sugar levels, due to a deficiency of concentration and/or of activity of insulin, the pancreatic hormone involved in managing glycaemia. There is no cure for diabetes so far, but it can be treated and controlled. Pharmacological therapy and/or insulin may be required in order to maintain the blood glucose level as near as possible to normal and to delay or possibly to prevent the development of diabetes-related health problems. However, disease management can be helped also by healthy eating and physical exercise. Hence, etiology is defined as the science of finding causes and origins in which a disease is arise,

It includes –

1. It is currently believed that the juvenile-onset (insulin dependent) form has an auto immune etiology.
2. Viruses may also play a role in the etiology of diabetes like coxsackie B.
3. Mumps and rubella viruses all have been shown to produce morphologic changes in the islet-cell structure.

4. The genetic role in the etiology of diabetes is controversial. Possibly a genetic trait makes an individual's pancreas more susceptible to one of the above viruses.

2. CLASSIFICATION OF DIABETES MELLITUS

- 1) Type 1 DM
- 2) Type 2 DM
- 3) Gestational diabetes

1. Type I diabetes: is as a result of β -cell destruction which customarily provokes complete insulin insufficiency. It was formerly known as insulin-dependent, juvenile or childhood-onset diabetes and it is occasioned by an autoimmune reaction, in which the immune system invaded against the insulin-producing pancreatic beta cells. Type I diabetes is distinguished by deficient insulin production in the body. In such type of DM the patients require daily administration of insulin so as to normalize the glucose level in the blood. Have not taken the insulin, their life is being threatened and can be fatal. The reason of type IDM is not identified yet being presently not preventable. Albeit, the reasons for type I diabetes are still unclear, changes in environmental risk factors and/or viral infections may have an impact on the appearance of DM. Extreme urination and thirst, continuous hunger, weight loss, vision changes and fatigue are the main symptoms of this type of DM. More often than not, the number of people who diagnosed with type I diabetes is escalated. Result from the pancreas failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "Juvenile diabetes."

2. Type II diabetes: which earlier termed non-insulin-dependent or adult-onset diabetes, assumed to be a result from a continuous insulin secretory defect on the background of insulin resistance on account of the body's inefficient use of insulin. Type II diabetes is the most typical DM. In this type, the body is capable of producing insulin but becomes so resistant that the insulin is ineffective. By the time, insulin levels could subsequently turned out insufficient. The cause of Acta Pharmaceutica Scientia. High blood glucose levels are both the insulin resistance and deficiency. Given that the symptoms (coincidental to type I diabetes symptoms) are generally less noticeable or absent, the illness could be dismissed and be undiagnosed for numerous years, and not until complications have already ascended. For various years, type IIDM was observed only in adults, nowadays it has started to be seen also in children. Until present the exact causes for the development of type II diabetes are unknown, some significant risk factors being pointed out. The most significant ones include: excess body weight, physical inactivity and poor nutrition. Other factors which impacted are ethnicity, family history of DM, past history of gestational diabetes and advancing age.

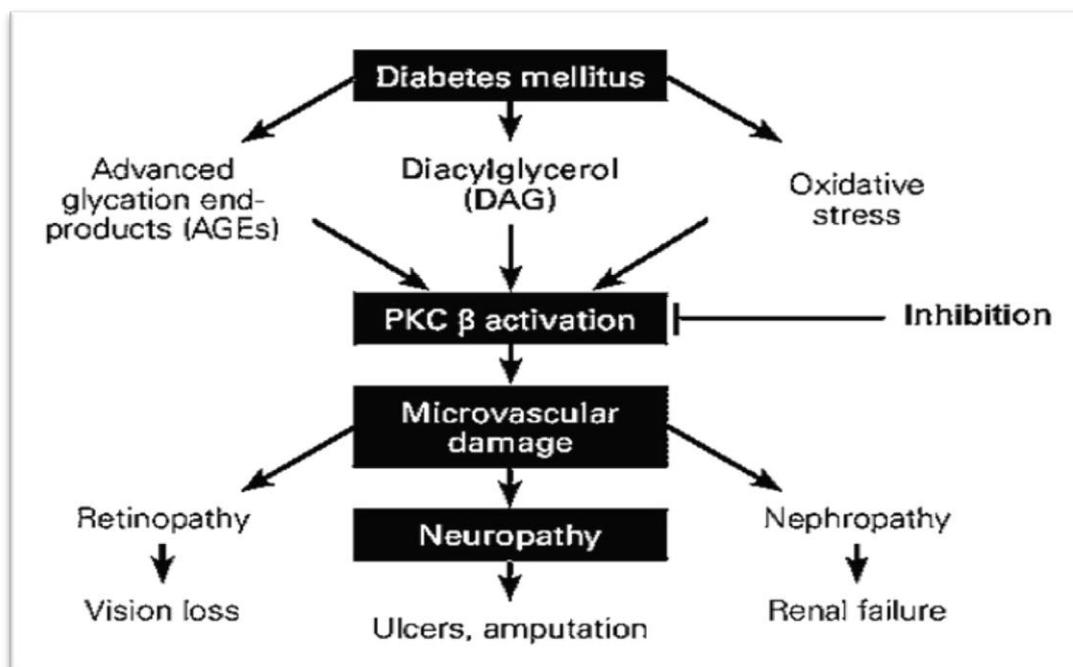


Fig.No.02-Diabetes mellitus

Therapeutic approaches in non-insulin treatment for type 2 diabetes mellitus:-

A number of non-insulin based oral therapies have emerged for the treatment of type 2 DM. These are categorized under the following sub-headings:

- 1) Insulin Secretagogues

- 2) Biguanides
- 3) Insulin Sensitizers
- 4) Alpha Glucosidase Inhibitors
- 5) Incretin mimetics
- 6) Amylin antagonists
- SGLT2 inhibitors

Insulin secretagogues :

These category of drugs (especially sulfonylureas and metiglinides) act by increasing the secretion of insulin from pancreas by binding to sulfonylurea receptor (SUR) of ATP sensitive potassium channel on pancreatic β cells. 1st generation sulfonylurea are Tolbutamide, Chlorpropamide, Tolazamide, Acetohexamide and 2nd generation sulfonylurea includes Glibenclamide, Glipizide, Glimepiride. Development of 2nd generation sulfonylurea was due to increased potency, more rapid onset of action, shorter plasma half-lives and longer duration of action. Common side effects of sulfonylurea includes sign of low blood sugar level such as dizziness, sweating, confusion and nervousness. It may also include hunger, weight gain, skin reaction, stomach upset and dark colored urine

Difference between Type 1 and type 2 diabetes:-

Table no.1:- Diabetes mellitus differance

Feature	Type 1 diabetes	Type 2 diabetes
12	Sudden	Gradual
Age at onset	Mostly in children	Mostly in adults
Body size	Thin or normal	Often obese
Ketoacidosis	Common	Rare
Autoantibodies	Usually present	Absent

3. Gestational diabetes mellitus (GDM): is a type of DM determined in the second or third trimester of pregnancy that is not clearly overt diabetes. GDM is a provisional disorder that happens in pregnancy and brings enduring danger of type II diabetes. Women with slightly elevated blood glucose levels are diagnosed as having gestational diabetes, whilst women with substantially elevated blood glucose levels are classified as having diabetes mellitus in pregnancy. GDM tends to arise from the 24th week of pregnancy. Screening by means of an oral glucose tolerance test is therefore recommended and must be conducted early in pregnancy for high risk women, and between the 24th and 28th week of pregnancy in all other women. Women with hyperglycemia diagnosed during pregnancy are at greater risk of adverse pregnancy outcomes such as: very high blood pressure and foetal macrosomia, with the vaginal birth being difficult and risky. In some cases, clinicians prescribe insulin or oral medication in order to control the blood glucose levels. Notwithstanding, gestational diabetes normally disappears after delivery but women who have been previously diagnosed are in danger of presenting GDM in subsequent pregnancies and type IIDM later in their life. In addition, infants beared by mothers with GDM also have a higher risk of developing type II diabetes during adolescence or early adulthood Current Status on Medications for Type I and II Diabetes mellitus Howbeit, there is a variety of pharmacological agents for the type II diabetic patients to choose, for type I patients the list is too short. The most significant limitation on antidiabetic treatment is the type of drug administration. Whether insulin formulation was oral then many patients could have a better quality of life. In most cases insulin is the only proposed way in order to reduce the glucose levels. Many researchers now mainly focused on improving the quality of these patients by using novel pharmacological agents. Every patient diagnosed with type I requires lifelong insulin therapy which three main categories are the rapid-acting insulin, long-acting insulin and intermediate options to be chosen. It was 10 years ago when FDA approved an injectable medication known as pramlintide, for people diagnosed with type I diabetes and insulin-treated patients with type II. Amylin is a natural hormone derived from the pancreatic beta cells and is the hormone which synthetic pramlintide was based on. Pramlintide act as follows: "It is administrated after the meal holding it longer in the stomach, promoting weight loss which keeps the blood glucose level low while also suppress the glucagon production". Until today the main approved treatments for type I DM is insulin and Pramnlitide. However some researchers believe that Metformin Acta Pharmaceutica Scientia. Medications of type II DM include several active ingredients and not only insulin. As it was already referred diabetes type II could complicate the health of the patients and affect a huge adult population. The majority of diabetic people are treated with glucose-lowering medication in order to decrease the long-term compromises.

3. PATHOPHYSIOLOGICAL ASPECT

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^{15, 16}. 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 hyperphosphorylation¹. Diabetes mellitus is a chronic disorder of carbohydrates, fats and protein metabolism. A defective or deficient insulin secretory response, which translates into impaired carbohydrates (glucose) use, is a characteristic feature of diabetes mellitus, as is the resulting hyperglycemia.^[1] Diabetes mellitus (DM) is commonly referred to as a “sugar” and it is the most common endocrine disorder and usually occurs when there is deficiency or absence of insulin or rarely, impairment of insulin activity (insulin resistance) ^[2] The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025 ^[3] Insulin and glucagon hormones both are secreted by the pancreas. Insulin is secreted by the beta (β) cells and glucagon is secreted by the alpha (α) cells both are located in the islets of Langerhan’s. Insulin decreases the blood glucose level by the glycogenesis and transport glucose into the muscles, liver and adipose tissue. Neural tissue and erythrocytes do not require insulin for glucose utilization whereas alpha (α) cells play an important role in controlling blood glucose by producing the glucagon and it increases the blood glucose level by accelerating the glycogenolysis. In addition to increased risk of obesity, metabolic and cardiovascular disorders, and malignancy in future life of fetus after delivery. Type II diabetes mellitus comprises 80% to 90% of all cases of diabetes mellitus. Geographical variation can contribute in the magnitude of the problems and to overall morbidity and mortality. Moreover, people with diabetes who undertake moderate amounts of physical activity are at inappreciably lower risk of death than inactive persons. It is now well established that a specific genetic constitution is required for such an event to cause. The growing burden of diabetes and other non-communicable diseases is one of the major health challenges to economic developments bedeviling WHO African Region states Diabetes mellitus is a chronic disorder of carbohydrates, fats and protein metabolism. A defective or deficient insulin secretory response, which translates into impaired carbohydrates (glucose) use, is a characteristic feature of diabetes mellitus, as is the resulting hyperglycemia producing the glucagon and it increases the blood glucose level by accelerating the glycogenolysis. In addition to increased risk of Diabetes mellitus is a chronic disorder of carbohydrates, fats and protein metabolism. A defective or deficient insulin secretory response, which translates into impaired carbohydrates (glucose) use, is a characteristic feature of diabetes mellitus, as is the resulting hyperglycemia.

4. CAUSES OF DIABETES MELLITUS

1) causes Of type 1 diabetes:-

Type 1 diabetes occurs when your immune system, the body’s system for fighting infection, attacks and destroys the insulin -producing beta cells of the pancreas. Scientists think type 1 diabetes is caused by genes and environmental factors, such as viruses, that might trigger the disease. Studies such as Trial Net are working to pinpoint causes of type 1 diabetes and possible ways to prevent or slow the disease.

2) causes type 2 diabetes:-

Type 2 diabetes—the most common form of diabetes—is caused by several factors, including lifestyle factors and genes. Overweight, obesity, and physical inactivity You are more likely to develop type 2 diabetes if you are not physically active and are overweight or have obesity. Extra weight sometimes causes insulin resistance and is common in people with type 2 diabetes. The location of body fat also makes a difference. Extra belly fat is linked to insulin

resistance, type 2 diabetes, and heart and blood vessel disease. To see if your weight puts you at risk for type 2 diabetes, check out these Body Mass Index (BMI) charts.

Insulin resistance:

Type 2 diabetes usually begins with insulin resistance, a condition in which muscle, liver, and fat cells do not use insulin well. As a result, your body needs more insulin to help glucose enter cells. At first, the pancreas makes more insulin to keep up with the added demand. Over time, the pancreas can't make enough insulin, and blood glucose levels rise.

Genes and family history

As in type 1 diabetes, certain genes may make you more likely to develop type 2 diabetes. The disease tends to run in families and occurs more often in these racial/ethnic groups: Genes also can increase the risk of type 2 diabetes by increasing a person's tendency to become overweight or have obesity.

3) causes of gestational diabetes:-

Scientists believe gestational diabetes, a type of diabetes that develops during pregnancy, is caused by the hormonal changes of pregnancy along with genetic and lifestyle factors.

Insulin resistance: Hormones produced by the placenta *NIH external link* contribute to insulin resistance, which occurs in all women during late pregnancy. Most pregnant women can produce enough insulin to overcome insulin resistance, but some cannot. Gestational diabetes occurs when the pancreas can't make enough insulin. As with type 2 diabetes, extra weight is linked to gestational diabetes. Women who are overweight or have obesity may already have insulin resistance when they become pregnant. Gaining too much weight during pregnancy may also be a factor. Hormonal changes, extra weight, and family history can contribute to gestational diabetes.

Genes and family history:- Having a family history of diabetes makes it more likely that a woman will develop gestational diabetes, which suggests that genes play a role. Genes may also explain why the disorder occurs more often in African Americans, American Indians, Asians, and Hispanics/Latinas.

Some else cause diabetes:-

Genetic mutations:- *NIH external link*, other diseases, damage to the pancreas, and certain medicines may also cause diabetes.

Cystic fibrosis *NIH external link* produces thick mucus that causes scarring in the pancreas. This scarring can prevent the pancreas from making enough insulin.

Hemochromatosis causes the body to store too much iron. If the disease is not treated, iron can build up in and damage the pancreas and other organs.

Hormonal diseases:- Some hormonal diseases cause the body to produce too much of certain hormones, which sometimes cause insulin resistance and diabetes.

-Cushing's syndrome occurs when the body produces too much cortisol—often called the “stress hormone.”

-Acromegaly occurs when the body produces too much growth hormone.

-Hyperthyroidism occurs when the thyroid gland produces too much thyroid hormone.

Damage to or removal of the pancreas:- Pancreatitis, pancreatic cancer, and trauma can all harm the beta cells or make them less able to produce insulin, resulting in diabetes. If the damaged pancreas is removed, diabetes will occur due to the loss of the beta cells.

5. 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 microvascular complications; and macrovascular disease (coronary artery, heart and peripheral vascular diseases). Type 2 DM carries a high risk of large vessel atherosclerosis commonly associated with hypertension, hyperlipidaemia and obesity. Most patients with type 2 diabetes die from cardiovascular complications and end stage renal disease. Complications of Diabetes mellitus DM may induce several complications or can co-exist with other diseases. In everyday clinical management of diabetic patients, doctors battle with diabetic complications which are very common and come in broad spectrum of manifestations. The complications are divided in microvascular and macrovascular. The macrovascular, which are more severe, are coronary disease, stroke and peripheral neuropathy. The microvascular are sneakier and in long-term may lead on macrovascular complications are diabetic retinopathy, diabetic nephropathy and diabetic foot. In this part several case reports are present among the numerous found in the literature. Neonatal diabetes is a rare form of diabetes mellitus (DM) which might occur during the first six months of infant's life. The two forms permanent and transient have been associated with

alterations in the KCNJ11 and ABCC8 genes most frequently and in the GATA6 gene less frequently. These mutations coexist with gastrointestinal and heart abnormalities. Such is a report of a Caucasian male infant with a GATA6 mutation that developed DM due to pancreatic hypoplasia, ventricular and atrial septal defect, an absent gallbladder and a right inguinal hernia²³. DM was also correlated with Friedreich's ataxia (FA). A 14-year-old male adolescent had insulin-dependent DM on a FA background, while being under treatment with insulin. Studies have shown that islet pancreatic cells reduction that happen in FA is the cause of DM²⁴. There are cases that pancreatic neuroendocrine tumor (PNET) was connected with DM developing. Such is a case of a patient with a pancreatic somatostatin tumor. ABCC8 mutation in a homozygous state was also connected with DM. The insulin-dependent DM that occurs due to this mutation can be misinterpreted with neonatal DM, although its beginning is later. In those patients sulfonylurea treatment was chosen as primary medication. Despite diabetic striatopathy is a common complication on adults was only reported twice in children. In those cases along with weight loss, polyuria, and polydipsia was reported hemichorea–hemiballism that was receded after glucose control. Among others taking right clinical history of a patient and not only the lean on the lab results for diabetic patients is quite important. A 40-year-old man with many diabetic complications and trouble in glucose regulation was misdiagnosed as DM type I while he was suffering from Neonatal DM as long as two weeks old. The proper taking of the family history revealed that his mother and his brother was also suffering from the same problem. This will help the patient now on his family making options. In another report, a Caucasian woman, 55 years of age without medical history and not ever under any medication, presented with signs of diabetic retinopathy and high blood glucose. Patient's lab tests were found normal. The clinical history revealed recent appearance of polyuria and polydipsia. That set the diagnosis of DM type I which should always be in the front line of a medical doctor's thinking. However, in this case did not conformed with the patient's age. Another category of DM complications is the infections. This category includes bone infections such as patellar osteomyelitis. Two reports of patellar osteomyelitis were revealed, both in adult diabetic women with uncontrolled blood glucose and no formerly medical history. The two patients presented with knee pain and after lab and screening tests were found that they suffered from patellar osteomyelitis. Both were treated with surgery and oral antibiotics with good prognosis. It is believed that diabetic neuropathy which causes dwindling or absence of pain is one factor of the late doctor's consultation. It remains to be found the reasons of the increased frequency of bone and other systemic infections in patients with DM. A rare complication that was recorded on a DM patient was Cryptococcosis. This is a common fungal infection on patients that are under chronic immunosuppressant therapy. A 48-year-old man with a lung mass suspected to be cancer had that infection. Cryptococcosis can appear on immunocompetent patients only with a predisposing background and DM is one of them. Another uncommon fungal infection is mucormycosis which has been proven to present more often to DM patients.

6. SYMPTOMS

Diabetes symptoms depend on how high your blood sugar is. Some people, especially if they have prediabetes, gestational diabetes or type 2 diabetes, may not have symptoms. In type 1 diabetes, symptoms tend to come on quickly and be more severe.

Some of the symptoms of type 1 diabetes and type 2 diabetes are:

- Feeling more thirsty than usual.
- Urinating often.
- Losing weight without trying.
- Presence of ketones in the urine. Ketones are a byproduct of the breakdown of muscle and fat that happens when there's not enough available insulin.
- Feeling tired and weak.
- Feeling irritable or having other mood changes.
- Having blurry vision.
- Having slow-healing sores.
- Getting a lot of infections, such as gum, skin and vaginal infections.
- Polydipsia (increased thirst)
- Polyphagia (increased hunger)
- Lethargy
- Blurred vision
- Smell of acetone
- Nausea
- Vomiting

- Abdominal pain

Type 1 diabetes can start at any age. But it often starts during childhood or teen years. Type 2 diabetes, the more common type, can develop at any age. Type 2 diabetes is more common in people older than 40. But type 2 diabetes in children is increasing.

7. PREVENTIONS

1) Type 1 diabetes can't be prevented. But the healthy lifestyle choices that help treat prediabetes, type 2 diabetes and gestational diabetes can also help prevent them: Eat healthy foods. Choose foods lower in fat and calories and higher in fiber. Focus on fruits, vegetables and whole grains. Eat a variety to keep from feeling bored.

2) Get more physical activity. Try to get about 30 minutes of moderate aerobic activity on most days of the week. Or aim to get at least 150 minutes of moderate aerobic activity a week. For example, take a brisk daily walk. If you can't fit in a long workout, break it up into smaller sessions throughout the day.

3) Lose excess pounds. If you're overweight, losing even 7% of your body weight can lower the risk of diabetes. For example, if you weigh 200 pounds (90.7 kilograms), losing 14 pounds (6.4 kilograms) can lower the risk of diabetes. But don't try to lose weight during pregnancy. Talk to your provider about how much weight is healthy for you to gain during pregnancy.

4) To keep your weight in a healthy range, work on long-term changes to your eating and exercise habits. Remember the benefits of losing weight, such as a healthier heart, more energy and higher self-esteem.

8. 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 4.

Diagnosis And Treatment

Many people are unaware that they have diabetes. In 2012, for example, it was estimated that 8.1 million of 29.1 million American cases were undiagnosed. The disease is usually discovered when there are typical symptoms of increased thirst and urination and a clearly elevated blood sugar level. The diagnosis of diabetes is based on the presence of blood glucose concentrations equal to or greater than 126 mg per 100 ml (7.0 mmol per litre) after an overnight fast or on the presence of blood glucose concentrations greater than 200 mg per 100 ml (11.1 mmol per litre) in general. People with fasting blood glucose values between 100 and 125 mg per 100 ml (6.1 to 6.9 mmol per litre) are diagnosed with a condition called impaired fasting glucose (prediabetes). Normal fasting blood glucose concentrations are less than 100 mg per 100 ml (6.1 mmol per litre). While the blood glucose concentrations used to define diabetes and impaired fasting glucose are somewhat arbitrary, they do correlate with the risk of macrovascular and microvascular disease. Patients with impaired fasting glucose are likely to have diabetes later in life. Oral glucose tolerance tests, in which blood glucose is measured hourly for several hours after ingestion of a large quantity of glucose (usually 75 or 100 grams), are used in pregnant women to test for gestational diabetes. The criteria for diagnosing gestational diabetes are more stringent than the criteria for diagnosing other types of diabetes, which is a reflection of the presence of decreased blood glucose concentrations in healthy pregnant women as compared with nonpregnant women and with men. The duration and severity of hyperglycemia can be assessed by measuring levels of advanced glycosylation end products (AGEs). AGEs are formed when hemoglobin molecules in red blood cells undergo glycosylation (binding to glucose), and the bound substances remain together until the red blood cell dies (red blood cells live approximately 120 days). AGEs are believed to inflict the majority of vascular damage that occurs in people with diabetes. A glycosylated hemoglobin called hemoglobin subtype A1c (HbA1c) is particularly useful in monitoring hyperglycemia and the efficacy of diabetes treatments. Before the isolation of insulin in the 1920s, most patients died within a short time after onset. Untreated diabetes leads to ketoacidosis, the accumulation of ketones (products of fat breakdown) and acid in the blood. Continued buildup of these products of disordered carbohydrate and fat metabolism result in nausea and vomiting, and eventually the patient goes into a diabetic coma. Treatment for diabetes mellitus is aimed at reducing blood glucose concentrations to normal levels. Achieving this is important in

promoting well-being and in minimizing the development and progression of the long-term complications of diabetes. Measurements of HbA1c can be used to assess whether an individual's treatment for diabetes is effective. Target values of HbA1c levels should be close to normal.

1) DIET AND EXERCISE:

All diabetes patients are put on diets designed to help them reach and maintain normal body weight, and they often are encouraged to exercise regularly, which enhances the movement of glucose into muscle cells and blunts the rise in blood glucose that follows carbohydrate ingestion. Patients are encouraged to follow a diet that is relatively low in fat and contains adequate amounts of protein. In practice about 30 percent of calories should come from fat, 20 percent from protein, and the remainder from carbohydrates, preferably from complex carbohydrates rather than simple sugars. The total caloric content should be based on the patient's nutritional requirements for growth or for weight loss if the patient is obese. In overweight or obese patients with type 2 diabetes, caloric restriction for even just a few days may result in considerable improvement in hyperglycemia. In addition, weight loss, preferably combined with exercise, can lead to improved insulin sensitivity and even restoration of normal glucose metabolism.

2) INSULIN THERAPIES:

Diabetics who are unable to produce insulin in their bodies require insulin therapy. Traditional insulin therapy entails regular injections of the hormone, which are often customized according to individual and variable requirements. Beef or pork insulin, made from the pancreatic extracts of cattle or pigs, can be used to treat humans with diabetes. However, in the United States, beef and pork forms of insulin are no longer manufactured, having been discontinued in favour of human insulin production. Modern human insulin treatments are based on recombinant DNA technology. Human insulin may be given as a form that is identical to the natural form found in the body, which acts quickly but transiently (short-acting insulin), or as a form that has been biochemically modified so as to prolong its action for up to 24 hours (long-acting insulin). Another type of insulin acts rapidly, with the hormone beginning to lower blood glucose within 10 to 30 minutes of administration; such rapid-acting insulin was made available in an inhalable form in 2014. The optimal regimen is one that most closely mimics the normal pattern of insulin secretion, which is a constant low level of insulin secretion plus a pulse of secretion after each meal. This can be achieved by administration of a long-acting insulin preparation once daily plus administration of a rapid-acting insulin preparation with or just before each meal. Patients also have the option of using an insulin pump, which allows them to control variations in the rate of insulin administration. A satisfactory compromise for some patients is twice-daily administration of mixtures of intermediate-acting and short-acting insulin. Patients taking insulin also may need to vary food intake from meal to meal, according to their level of activity; as exercise frequency and intensity increase, less insulin and more food intake may be necessary. Research into other areas of insulin therapy include pancreas transplantation, beta cell transplantation, implantable mechanical insulin infusion systems, and the generation of beta cells from existing exocrine cells in the pancreas. Patients with type 1 diabetes have been treated by transplantation of the pancreas or of the islets of Langerhans. However, limited quantities of pancreatic tissue are available for transplantation, prolonged immunosuppressive therapy is needed, and there is a high likelihood that the transplanted tissue will be rejected even when the patient is receiving immunosuppressive therapy. Attempts to improve the outcome of transplantation and to develop mechanical islets are ongoing.

4) DRUG USED TO CONTROL BLOOD GLUCOSE LEVELS:-

There are several classes of oral drugs used to control blood glucose levels, including sulfonylureas, biguanides, and thiazolidinediones. Sulfonylureas, such as glipizide and glimepiride, are considered hypoglycemic agents because they stimulate the release of insulin from beta cells in the pancreas, thus reducing blood glucose levels. The most common side effect associated with sulfonylureas is hypoglycemia (abnormally low blood glucose levels), which occurs most often in elderly patients who have impaired liver or kidney function.

9. GOALS OF MANAGEMENT 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 thiazolidenediones. 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.

10. TREATMENT

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 meals. 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. Sulfonylureas cause hypoglycemia by stimulating insulin release from pancreatic β -cells. They bind to sulfonylurea (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 antihyperglycaemic, not hypoglycemic. It does not cause insulin release from the pancreas and does not cause hypoglycemia, even in large doses. 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.

Current Status on Medications for Type I and II Diabetes mellitus:

Howbeit, there is a variety of pharmacological agents for the type II diabetic patients to choose, for type I patients the list is too short. The most significant limitation on antidiabetic treatment is the type of drug administration. Whether insulin formulation was oral then many patients could have a better quality of life. In most cases insulin is the only proposed way in order to reduce the glucose levels. Many researchers now mainly focused on improving the quality of these patients by using novel pharmacological agents. Every patient diagnosed with type I requires lifelong insulin therapy which three main categories are the rapid-acting insulin, long-acting insulin and intermediate options to be chosen. It was 10 years ago when FDA approved an injectable medication known as pramlintide, for people diagnosed with type I diabetes and insulin-treated patients with type II. Amylin is a natural hormone derived from the pancreatic beta cells and is the hormone which synthetic pramlintide was based on. Pramlintide act as follows: "It is administrated after the meal holding it longer in the stomach, promoting weight loss which keeps the blood glucose level low while also suppress the glucagon production". Until today the main approved treatments for type I DM is insulin and Pramlnitide. However some researchers believe that Metformin Acta Pharmaceutica Scientia and Sodium Glucose Co-Transporter 2 Inhibitors approved for type II DM could also be involved for type I DM Medications of type II DM include several active ingredients only insulin. As it was already referred diabetes type II could complicate the health of the patients and affect a huge adult population. The majority of diabetic people are treated with glucose-lowering medication in order to decrease the long-term compromises. The main classes of diabetes therapeutics are seven with the main differentiations of such medications include safety, glucose-lowering, type of delivery (oral or injectable) and so on. The history of type II diabetic formulations is long since the first use of synthetic guanidine to take place on 19185 . After almost one century, new drugs against type II diabetes based on peptides have been approved from FDA. A brief history of diabetes type II medications is presented in Table 3. It is widely known between clinicians and patients that insulin is the primary choice for the treatment of type I diabetes. Nonetheless, insulin use is not only limited for type I but can also be applied for type 2 diabetic patients. This is fact when the other antidiabetic formulation does not fulfill the criteria to low blood glucose. The main categories as already reported in literature are also demonstrated in Table 3. Moreover, what researchers should evaluate is the limitation on oral medications and this is why many pharmaceutical technologists and companies target on oral administration of antidiabetic drugs.

Case study:

Patient demography:

Age: 40

Gender: Male

Height 5'7

Weight 75 kg

Present/Past surgical history: there is no significant.

Sr.No	Vital sing	Patientvalue	Normal value
1	Temperature	101 F	98.6F
2	Pulse	130 b/min	72-80 B/min
3	Blood pressure	120/70 mm/Hg	120/80 mm/Hg

Table.no 2:- Tablets used in diabetes mellitus

Tablet name	Contain	Manufacturer	Uses
metsmall 500 Tablet	Metformin Hydrochlorideng Sustained Release Tablets IP 500mg	Dr.Reddy's Laboratories Ltd	Metsmall 500 Tablet SR is used in the treatment of type 2 diabetes mellitus. It is used in addition to diet and exercise to improve blood sugar control in adults with type 2 diabetes.
Glyree 1 Tablet	Glimepiride Tablets IP	Ipca Laboratories Ltd	Glyree 1 Tablet is used to lower the blood sugar levels in type 2 diabetes mellitus when diet, physical exercise and weight reduction alone are not adequate.. It is used along with diet and exercise to improve blood sugar control in adults with type 2 diabetes.
Vogli 0.3 Tablet	Vogibose Mouth Dissolving Tablets	Medley Pharmaceuticals	Vogli 0.3 Tablet MD is used in the treatment of type 2 diabetes mellitus. It is used along with diet and exercise to improve blood sugar control in adults with type 2 diabetes.
Lantus 100 IU/ml	Insulin Glargine Injection I.P. (Monocomponent Insulin Glargine r-DNA Origin)	Sanofi India Ltd	Lantus 100IU/ml Solution for Injection is used in the treatment of diabetes mellitus (Type 1 & Type 2).
Human Mixtard 70/30 Suspension for Injection 401U/ml	Insulin Isophane/NPH (70%) + Human Insulin/Soluble Insulin (30%)	TORRENT PHARMACEUTICALS LTD. Under licence from: Novo Nordisk India Private Ltd.	Human Mixtard 70/30 Suspension for Injection 401U/ml is used in the treatment of diabetes mellitus (Type 1 & Type 2).
Human Actrapid 401U/ml Solution for Injection	Human insulin (40IU)	TORRENT PHARMACEUTICALS LTD. Under licence from: Novo Nordisk India Private Ltd.	Human Actrapid 401U/ml Solution for Injection is used in the treatment of diabetes mellitus (Type 1& Type 2)

11. CONCLUSION

Diabetes mellitus (DM), is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period. There is no cure for diabetes so far, but it can be treated and controlled. Pharmacological therapy and/or insulin may be required in order to maintain the blood glucose level as near as possible to normal and to delay or possibly to prevent the development of diabetes-related health problems. However, disease management can be helped also by healthy eating and physical exercise. Diabetes mellitus having 2 types diabetes. i.e. Type 1 and Type 2 diabetes. It can be treated with some treatments like insulin therapies. Diabetes mellitus having some symptoms such as Feeling tired and weak, Feeling irritable or having other mood changes, Having blurry vision, Having slow-healing sores, Getting a lot of infections, such as gum, skin and vaginal infections, Polydipsia (increased thirst), Polyphagia (increased hunger), Lethargy, Blurred vision, Nausea, Vomiting, Abdominal pain

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