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Diabetes Mellitus: Review Article

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ABSTRACT:
"Diabetes mellitus", is quite possibly the most widely recognized non-transmittable disease around the world. India faces a few difficulties in diabetes management, remembering a rising phenomenon for rural and urban regions, lack of disease awareness among the general population, limited medical care facilities, significant expense of therapy, imperfect glycaemic control and rising of diabetic complications.Insulin treatment for diabetes is most usually conveyed through subcutaneous infusions, up to four times each day. Long term insulin treatment, compounded by invasive nature of its administration, disapproves of patient consistence, eventually impacting patient results.Although type 1 diabetes is now becoming more common, the main cause of the diabetic epidemic is type 2 diabetes mellitus, which accounts for more than 90% of the diabetes cases.Type 2 diabetes is a severe and frequent chronic disease caused by a complex interaction of genes as well as other risk factors like obesity and a bad diet.

Keyword: Diabetes mellitus, conclusion, cause and treatment.

I. INTRODUCTION:

Diabetes mellitus is a disease that affects the metabolism of carbs, lipids, and proteins. Diabetes mellitus is characterised by a faulty or inadequate insulin secretory response, which leads to impaired carbohydrate (glucose) utilisation and hyperglycemia. Diabetes mellitus (DM) is the most common endocrine disease and is often known as "sugar diabetes. "It's caused by a lack of or inability to manufacture insulin, as well as a decrease in insulin activity," says the author (insulin resistance). According to the International Diabetes Federation (IDF), India currently has 40.9 million diabetics, with that figure expected to climb to 69.9 million by 2025 Insulin and glucagon hormones are secreted by the pancreas. The Langerhans islets contain beta (ß) cells that secrete insulin and alpha cells that secrete glucagon. Insulin reduces blood glucose levels by inhibiting glycogenesis and transporting glucose into the muscles, liver, and adipose tissue. Alpha cells play an important role in controlling blood glucose by producing glucagon and increasing blood glucose levels by accelerating glycogenolysis. Alpha cells play a crucial role in managing blood glucose levels by releasing glucagon and boosting blood glucose levels by speeding glycogenolysis, Despite the fact that brain tissue and erythrocytes do not need insulin to utilise glucose. In addition to a greater risk of obesity, metabolic and cardiovascular problems, and cancer in the fetus's future life after birth. Type 2 diabetes mellitus accounts for 80 percent to 90 percent of all diabete cases.Geographical variation can influence the severity of problems as well as overall morbidity and mortality rates. Furthermore, people with diabetes who engage in modest physical exercise had a marginally decreased risk of death than those who do not. It is now generally understood that for such an occurrence to occur, a precise genetic constitution is required. One of the greatest health concerns confronting WHO African Region governments is the rising burden of diabetes and other noncommunicable illnesses. In diabetes, there is an abnormality in either insulin synthesis or secretion, as shown in Type 1 diabetes mellitus (T1DM) and pancreatic duct stenosis, or the development of insulin resistance or subnormal production, as seen in Type 2 diabetes mellitus (T2DM) and certain secondary diabetes.

Classification:

The World Health Organization (WHO) released the first widely accepted categorization of diabetes mellitus in 1980, and it was updated in 1985. Primary or idiopathic diabetes mellitus is the most prevalent and significant kind of diabetes mellitus, and it is the subject of our discussion. It must be distinguished from secondary diabetes mellitus, which is defined as hyperglycemia caused by specific reasons such as inflammatory pancreatic disorders, surgery, tumours, some medicines, iron overload (hemochromatosis), and certain acquired or congenital endocrinopathies.

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Diabetes mellitus is divided into clinical phases and aetiological forms, as well as additional types of hyperglycemia.

Assigning a type of diabetes to a person is typically based on the circumstances at the time of diagnosis, and many diabetics do not neatly fall into a single category.

Primary diabetes mellitus is most likely a diverse group of disorders with hyperglycemia as a common symptom.

The new diabetes mellitus classification includes stages that indicate various degrees of hyperglycemia in humans who have diabetes mellitus as a result of any of the illness processes that may cause it.

In 1980 and 1985, the World Health Organization (WHO) coined the terms insulin-dependent diabetes mellitus (IDDM) and noninsulin-dependent diabetic mellitus (NIDDM), and the new categorization system defines four forms of diabetes mellitus: Type 1 diabetes (IDDM), type 2 diabetes (NIDDM), "different distinct sorts," and gestational diabetes are the four types of diabetes (WHO Expert Committee 1999). The International Nomenclature of Diseases (IND) in 1991 and the tenth edition of These modifications were reflected in the International Classification of Diseases (ICD-10) in 1992. As a result, diabetes mellitus is categorized into three parts:

1 . (Type1 IDDM) Insulin-Dependent Diabetes Mellitus:

Previously known as juvenile-onset or ketosisprone diabetes, this kind of diabetes is also known as autoimmune diabetes. Other autoimmune conditions that the person may pursue include Graves' disease, Hashimoto's thyroiditis, and Addison's disease. Diabetes mellitus, often called insulin-dependent diabetes mellitus (IDDM), is a form of diabetes which mostly affects adolescents and teenagers. It generally progresses quickly and can be lethal. Antibodies to anti–glutamic acid decarboxylase, islet cell, or insulin are often seen in Type 1 diabetes patients, demonstrating autoimmune processes that contribute to beta-cell death.The American Diabetes Association (ADA) published a report in 2014 that stated: Kind 1 diabetes is a type of diabetes in which the organism (related to b-cell loss, which typically results in absolute insulin shortage) Betacell decomposition occurs at different rates in different persons; in some people, it happens very quickly, while in others, it takes longer.Because the ß-islets cells of the pancreas are destroyed, there is a significant deficit or lack of insulin production. Insulin injections are necessary for treatment. Markers of immunological damage, such as islet cell auto-antibodies and/or auto antibodies to insulin, and auto antibodies to glutamic acid decarboxylase (GAD), are detected in 85-90 percent of persons with Type 1 diabetes when fasting diabetic hyperglycemia is eventually diagnosed. Although there is evidence of an autoimmune process involving auto-antibodies that kill betaislet cells in most persons, the specific aetiology of diabetes mellitus remains uncertain.

2. (Type2 Niddm) Non-Insulin Dependent diabetes mellitus:

Adult-onset diabetes is another name for type 2 diabetes mellitus.On the backdrop of insulin resistance, there occurs a gradual insulin secretary malfunction (American Diabetes Association, 2014)

Insulin deficiency is very frequent in patients with this kind of diabetes. Both kinds of diabetes have long-term problems in the blood vessels, kidneys, eyes, and nerves, which are the leading causes of morbidity and death. Obesity, sedentary lifestyle, rising age (affecting middleaged and older adults), and genetic factor are all predisposing factors (Ross and Wilson 2010). These patients are at an elevated risk of having macro and micro vascular problems.

3. Gestational diabetes mellitus:

GDM, or gestational diabetes mellitus, is a kind of glucose intolerance that develops or is diagnosed during pregnancy. GDM is a syndrome in which women produce Type 1 diabetes mellitus during pregnancy or detect untreated asymptomatic Type 2 diabetes mellitus during pregnancy. GDM (gestational diabetes mellitus) is a kind of diabetes that is diagnosed during pregnancy but does not have a definite cause. Gestational diabetes mellitus (GDM) can occur during pregnancy and go away after delivery; Obesity and type 2 diabetes are more likely to develop in children born to mothers with GDM later in life, a disease connected to genetics.

4. Other specific type:

Mutations on chromosome 12 in a hepatic transcription factor called hepatocyte nuclear factor (HNF)-1a cause the most frequent kind of monogenic forms of diabetes. They're also known as genetic anomalies of the beta cells. Hyperglycemia usually develops at a young age (typically before the age of 25 years) in several types of diabetes. Persons with diseases of the exocrine pancreas, such as pancreatitis or cystic fibrosis; persons with dysfunction associated with other endocrinopathies (e.g. acromegaly); and persons with pancreatic dysfunction caused by

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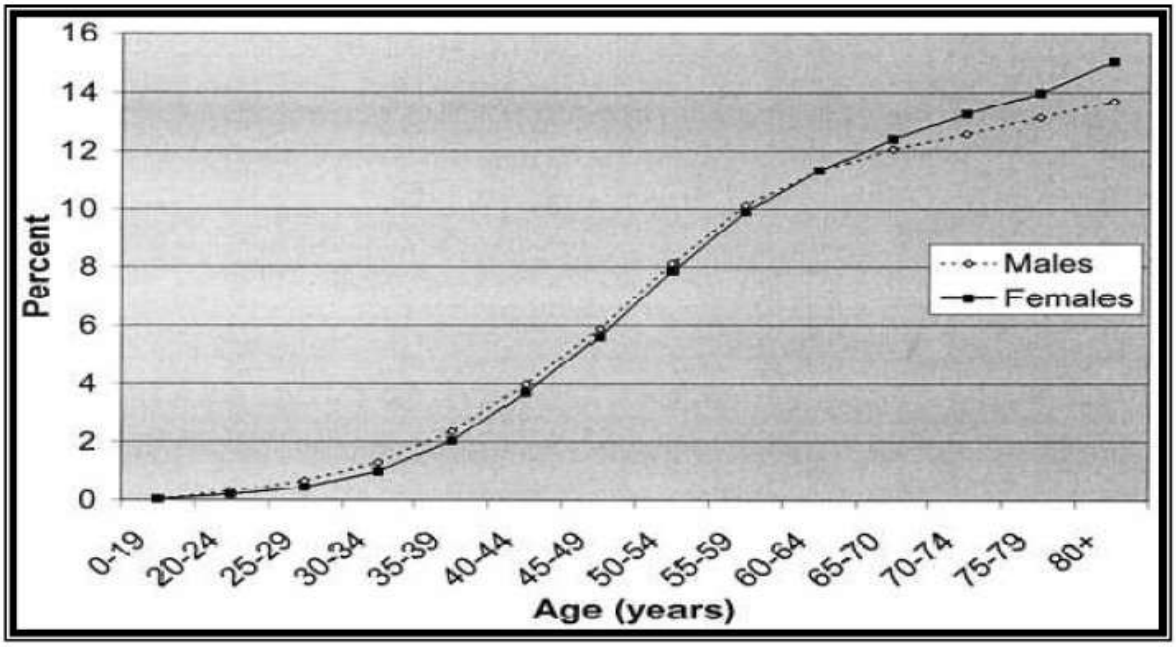
drugs, chemicals, or infections. Some medicines are also used in conjunction with HIV/AIDS therapy or following organ donation.

In a few families, genetic anomalies resulting in the inability to convert proinsulin to insulin have been discovered, and these features are inherited in an autosomal dominant form.

They account for fewer than 10% of all DM cases.

Epidemiology:

In 2011, 366 million individuals were expected to have diabetes; by 2030, that number will have increased to 552 million. Every country is seeing an increase in the number of patients with type 2 diabetes, with 80 percent of those affected living in low- and middle-income countries. In 2011, DM claimed the lives of 4.6 million people[1]. By 2030, it is estimated that 439 million people will have type 2 diabetes because of environmental and lifestyle risk factors[2]. The prevalence of diabetes in adults, particularly type 2 diabetes, is expected to rise over the next two decades, with much of the increase occurring in developing countries, where the majority of patients are between the ages of 45 and 65 years old[3].



Epidemiology of diabetes : A global view

Diabetes in India:

According to recent predictions, diabetes would affect around 285 million individuals globally (6.6 percent) in the 20–79 year age group in 2010, and 438 million people by 2030. India has the highest number of diabetic subjects in the world, receiving the dubious title of "diabetes capital of the world. According to the 'International Diabetes Federation's Diabetes Atlas 2006', India's current diabetes population of 40.9 million is likely to climb to 69.9 million by 2025. In the urban population, higher frequency of diabetes mellitus is frequently caused by changes in eating patterns and decreased physical activity[4]. Diabetes is quickly approaching the status of a possible epidemic in India, with more than 62 million diabetic people now diagnosed[5,6]. India (31.7 million people) had the highest number of persons with diabetes mellitus in the world, followed by China (20.8 million) and the United States (17.7 million) in the year 2000. According to Wild et al., the global prevalence of diabetes will increase from 171 million to 366 million in 2030, with India experiencing the greatest growth[3,7].

Pathophysiological aspect:

Insulin sensitivity is a symptom of Type 2 diabetes, which is caused by insulin resistance, decreased insulin production, and eventually loss of the pancreatic beta-cell. As a result, glucose transport into the liver, muscle cells, and fat cells is reduced. With hyperglycaemia, there is an increase in fat breakdown[8,9].When type 1 diabetics first develop the disease symptoms, they are usually young (children or teens) and not obese.Identical twin studies have revealed that people who are genetically prone must also take other precautions

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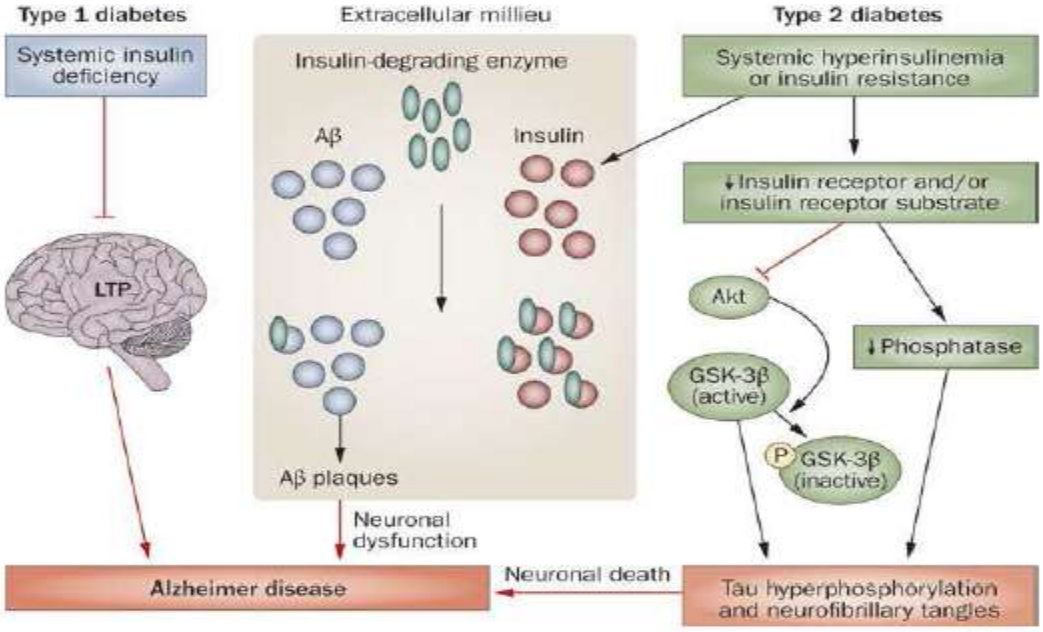
be exposed to a component in the environment, such as a viral infection Pancreatic B cells may be harmed by viral infectionand expose antigens, triggering a self-replicating autoimmune response. The sufferer develops into only when more than 90% of the B cells have been eliminated is a person diagnosed as diabetes.Insulin insufficiency in this case reduces long-term potentiating and may result in learning and memory problems. Insulin resistance and decreased insulin production are both associated with type 2 diabetes, and each plays a role in the disease's development. Obese people are more common, and they usually appear in adulthood, with the frequency increasing with age as B-cell activity declines. Insulin resistance causes both Aβ plaque development and tau hyperphosphorylation in this case. Insulin and Aβ compete for the same insulin-degrading enzyme during hyperinsulinemia, resulting in Aβ buildup and plaque formation. When insulin receptor signalling is reduced, Akt is inhibited and GSK-3 is dephosphorylated (activated), resulting in tau hyperphosphorylation[10,11].



Pathophysiology of Type I and Type II diabetes. Abbreviations: Aβ- Amyloid- β, GSK-3β-glycogen synthase kinase 3β, LTP- long term potentiation, P- Phosphate

Some common sign and symptoms:

In diabetes mellitus, cell does not have the ability to metabolize in the normal form and due to this the cells does not get enough nutrition[12]. The chronic effect of diabetes mellitus includes the blindness, neuropathy, nephropathy which may leads to kidney failure and foot ulcer it may also lead to sexual dysfunction[13].

There are many other symptoms which may occur due to

- Gluconeogenesis from amino acids and body protein, which results in muscle atrophy, tissue disintegration, and an increase in blood glucose levels.
- Catabolism of body fat results in the release of some of its energy as well as an increase in the creation of ketone bodies[12]

Etiology of Diabetes Mellitus:

1. Juvenile-onset (insulin dependent) form has an auto immune etiology.
2. Virus may also play a role in diabetes like coxsackieB.
3. Mumps and rubella viruses shows a morphologic changes in the islet-cell structure.
4. Controversial is the genetic role in the etiology of diabetes a genetic trait makes an individual's pancreas more susceptible to one of the above viruses.

Causes of Diabetes Mellitus:

ß cell gluco-receptor disturbances or abnormalities that cause them to respond to greater glucose concentrations or relative ß cell insufficiency. Insulin secretion is hampered in

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either case, and this can lead to ß cell failure[14]. The principle in micro vascular disease leads to neural hypoxia and the effect of hyperglycaemia on neuronal metabolism[15]

1. Insulin sensitivity in peripheral tissues is reduced due to a decrease in the number of insulin receptors and insulin receptor 'down regulation.' Many people are hypersensitive and hyperinsulinaemic, but their blood sugar levels are normal; they also have dyslipidemia, hyperuriaemia, and abdominal obesity. As a result, there is some insulin resistance. Particularly at the liver, muscle, and fat levels. Hyperinsulinemia has been linked to the development of diabetes[13]. Angiopathy is a condition in which the blood vessels get clogged.
2. Hyperglycemia hormone (glucagon) excess, etc. Obesity results in a relative insulin deficit, as the ß cells lag behind. Two ideas has been establish. Nitric oxide metabolism, leading in changes in the perineural environment Nerve injury and blood flow[14].
3. There are a few more types of diabetes mellitus that aren't as common. particular (type 3) genetic abnormalities, such as "maturity onset diabetes of the young" (MODY) Other endocrine abnormalities, such as gestational diabetes mellitus and pancreatectomy (GDM)[13].
4. Diabetes mellitus can be caused by a receptor imbalance. The Glucagon-like peptide-1 (GLP-1) receptor and the peroxisomes proliferator-activated receptor are two examples of specialised receptors.Glycosidase and dipeptidyl peptidase IV are examples of enzymes[13].
5. Diabetic neuropathy research is now focused on advanced glycation-end products, oxidative stress, The polyol pathway and protein kinase C[15].

Diabetes Mellitus Diagnosis:

A single abnormal blood glucose measurement should never be used to diagnose diabetes in an asymptomatic individual.If diabetes is diagnosed, the practitioner must be convinced that the diagnosis is correct because the implications for the patient are severe and long-lasting[16] Urine sugar, blood sugar, glucose tolerance test, renal glucose threshold, diminished glucose tolerance, increased glucose tolerance, renal glycosuria, extended glucose tolerance curve, cortisone stressed glucose tolerance test, intravenous glucose tolerance test, and oral glucose tolerance test are all used to diagnose diabetes mellitus.

Treatment of Diabetes Mellitus:

The treatment consists of eliminating the causing factor and administering high doses of daily insulin. Once the condition is under control, the insulin need returns to normal. The goals of diabetes mellitus management can be met by:

1. To halt or slow the progression of the disease's short and long-term risks.
2. To return the diabetic's disrupted metabolism as close to normal as possible while maintaining comfort and safety.
3. To empower the patient with the information, motivation, and resources necessary to carry out this self-administered enlightened care.

A] Types of Therapy Involved In Diabetes Mellitus:

1. Stem cell treatment

Researchers have discovered that monocytes/macrophages may play a key role in chronic inflammation and insulin resistance in T2DM patients[17]. A revolutionary method called stem cell educator treatment aims to manage or reverse immunological dysfunctions[18]. The procedure usually involves collecting blood from patients in a closed-loop system, purifying lymphocytes from whole blood, co-cultivating them in vitro with adherent cord blood-derived multi-potent stem cells (CB-SCs), and administering the educated lymphocytes (but not the CB-SCs) to the patient's circulation[18].

2. The use of antioxidants

For oxidative stress treatment in T2DM patients, a number of antioxidants such as vitamins, supplements, plant-derived active substances, and medicines having antioxidant activities have been employed. Vitamin C, vitamin E, and carotene are all excellent supplements for preventing oxidative stress and its consequences[19]. Antioxidants are powerful antioxidants that help to reduce the risk of diabetes and its complications.

3. Anti-inflammation therapy

The changes suggest that inflammation is important in the development of T2DM and associated consequences[20,21]. These include changed levels of certain cytokines and chemokines, the number and activation state of different leukocyte populations[22], increased apoptosis, and tissue fibrosis in T2DM, particularly in adipose tissue, pancreatic islets, the vasculature, circulating leukocytes and liver[22,23]. Immunosuppressive medications are available.

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B] Dietary Control:

a sufficient calorie value Both diabetic and non-diabetic patients should follow adequate dietary control, which includes:

1. All foods are balanced in terms of protein, carbohydrate, and fats. In some circumstances, carbohydrate intake must be limited.
2. Should be as close to normal as feasible.
3. Food intake should be divided into meals which are of similar size.
4. Reduce overall calorie intake by lowering fat and carbohydrate intake.
5. The patient must be counselled to maintain a consistent food diet.

C] Newer Insulin Delivery Devices:

A number of modifications have been developed to increase the effectiveness and convenience of the process of Insulin administration precision as well as achieving Glycaemic. Pen devices, insulin pumps, inhaled insulin, implantable pumps, syringes and various types of insulin delivery routes.

D] Anti-diabetic or oral hypoglycaemic agents:

In 1957, phenformin, a clinically useful biguanide, was developed in parallel with sulfonylureas.α-glucosidase inhibitors,meglitinide analogues,thiazolidinediones,dipeptidyl peptidase-4(DPP-4) inhibitorshave been developed in recent years[13].

Herbal treatment of diabetes:

With growing study in the field of traditional medicine, eco-friendly, bio-friendly, cost-effective, and reasonably safe plant-based medications have moved from the margins to the mainstream in the last few decades. There are multiple literature reviews on anti-diabetic herbal compounds by various authors, but the most useful is the review of Atta-ar-Rahman, who has recorded over 300 plant species recognised for their hypoglycaemic activities. The plants in this review were categorised based on their botanical name, country of origin, parts used, and active agent nature. Momordica charantia (Cucurbitaceae) is one of these plants[24]. The World Health Organization (WHO) has compiled a list of 21,000 plants used for therapeutic purposes around the world. India has 2500 species, with 150 of them being used economically on a considerable basis. India is the world's largest producer of medicinal herbs and is known as the world's botanical garden[25].

Alternative therapies of Diabetes Mellitus

Many efficient alternative remedies for treating diabetes mellitus have been developed, mainly in India. These treatments are highly effective and have no negative side effects. Yoga, acupuncture, hydrotherapy, and medicinal plants are examples of alternative therapies that are growing increasingly popular.

Yoga:

Yoga comes from the Sanskrit term 'Yuj,' which means 'union of the body, breath, and mind.' Through an enzymatic process, stretching the abdomen during yoga exercise stimulates pancreatic cell regeneration and increases glucose utilisation and metabolism in peripheral tissues, liver, and adipose tissues[26,27]. During yoga, the blood supply to the muscles is improved, and the muscles are relaxed, resulting in higher glucose uptake and a reduction in blood glucose levels[28].Yoga enhances the activity of hepatic lipase and lipoprotein lipase, which alters lipid metabolism and also increases triglyceride storage in adipose tissue while lowering blood triglyceride levels[29].The sensitivity of the pancreatic beta cells to glucose has improved as a result of the various Yoga poses, resulting in increased insulin secretion [28].

Acupuncture:

Acupuncture is well known for its use as an alternative therapy for chronic pain. It has, however, been employed in the treatment of diabetes and its consequences in recent years. Acupuncture stimulates the pancreas, causing it to produce more insulin, increase the number of receptors on target cells, and speed up the use of glucose, reducing blood glucose levels[30]. Although acupuncture has shown to be useful in the treatment of diabetes, its mechanism of action is yet uncertain.

Medicinal plants:

Ayurveda claims that various medicinal plants have been recognised as having anti-diabetic properties. The majority of herbal remedies made from these therapeutic plants are said to have few or no negative effects[33].Acacia arabica (Babul), Aegle marmelose (Bael), Agrimonia eupatoria (Church steeples), Allium cepa (Onion), Allium sativum (Garlic), Ghrita kumara (Aloe vera), Azadirachta indica (Neem), Caesalpinia bonducella (Fever Nut), Caesalpinia bonducella (Bitter Apple)Mangifera indica (Mango), Momordica charantia (Karela), Morus alba (Mulberry), Mucuna pruriens (Kiwach), O (Methi) [34]. Evidence suggests that the active compounds of medicinal plants are also used in the development of modern

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allopathic drugs used to treat diabetes mellitus. For example, Metformin, the first-line conventional medication, was created from the guanidine-rich medicinal herb Galega officinalis. Herbal medicine is inexpensive and has few or no negative effects in poor nations, 70-95 percent of the population considers it for primary health care. The World Health Organization's (WHO, 2013) estimates that 80 percent of the world's population still uses herbs and other conventional medicines to meet their major health care needs. Many diabetics in India rely on natural medications to manage their condition.

Hydrotherapy:

Some people with type 2 diabetes mellitus are unable to exercise due to diabetic problems, hot-tub therapy is indicated to improve blood supply to skeletal muscles. In diabetic persons, 30 minutes of hot tub therapy reduced body weight, mean plasma glucose level, and mean glycosylated haemoglobin level, according to a study. When recommending hot tub therapy for diabetic patients, extra caution should be taken to guarantee optimum water sanitation and temperature[32].

Important Features of Oral Hypoglycaemic Agents:

Diabetes mellitus is a modern-day disease that has a significant impact on the quality of life of those affected.Diabetes mellitus is a common complication of Cushing syndrome, which is caused by chronic glucocorticoid exposure and manifests as central obesity, proximal muscle weakness, hirsutism, neurophysiological disturbance, macro-vascular complication autonomic neuropathy, digestive problems, and dental problems[13], among other symptoms.

II. CONCLUSION:

Diabetes mellitus refers to a group of metabolic abnormalities that cause an abnormally high level of a sugar called glucose in the blood. Type 1 diabetes develops when the pancreas stops producing large amounts of the hormone insulin, mainly due to autoimmune damage of the pancreas' insulin-producing beta cells. Diabetes mellitus type 2 is caused by autoimmune pancreatitis and/or insulin resistance. A person with type 2 diabetes may have a pancreas that produces normal or even abnormally excessive levels of insulin. The basic goal of diabetic treatment is to restore normal glucose metabolism. Individuals with an extreme insulin deficit require insulin replacement therapy, which is administered via injections or pills. Insulin resistance, on the other hand, can be treated with dietary changes and exercise. Thus the information regarding diabetes, its prevalence, complications, current management, and alternative remedies has been provided in this review.

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