

Diabetes Milletus: History, Types, Pathophysiological aspects, Signs and Symptoms, Etymology, Dietary Management, Causes and its associated risk factors.

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ABSTRACT

Diabetes mellitus is a very common disease nowadays. It has mainly two types, type 1 and type 2 both types have different pathophysiology. Type 1 is related to less insulin production or no insulin production by the beta cell in the pancreas, while type 2 is related to the resistance of insulin. For underdeveloped countries, Diabetes mellitus is a considerable socioeconomic problem.

Diabetes mellitus is considered to be a worldwide spread disease. It can occur to all individuals regardless of gender. It is expected that by the end of the year 2049, 629 million people will be infected with diabetes.

Diabetes mellitus is a 3000-year oldest disease and is expressed earlier in Egyptian literature. Scientists proposed different ideas about the pee of diabetic patients, they stated that the sweet taste from the pee of the diabetic patient is due to increased blood glucose level in the body. The global burden of diabetes is increasing day by day; different country has a different percentage of diabetes among them the fewer income countries are on top.

Diabetes mellitus can be managed by different medicinal plant, or daily use herbal, either it is used directly or by making formulation out of it. Some risk factors must be prevented if a person is diabetic, to ensure that diabetes must not induce other diseases.

KeyWords

Beta cells, Type 1 and 2 Diabetes Mellitus, Gestational Diabetes, Wolfram Condition, polycystic ovarian disorder, hyperlipidemia, Hemochromatosis, pancreatitis, Cushing's disease, hyperthyroidism and acromegaly.

1) Introduction

Diabetes mellitus (DM) is considered as the earliest disease that is known to man. It is one of the metabolic disorders in which blood glucose level increases that needs to be checked regularly with proper treatment. Beta-cell found in the Pancreas of a human that secrete a hormone called insulin the main function of insulin is to enhance the absorption of glucose into the cell and gives energy to the cell and is also involved in different other functions. The main cause of DM is the inability to produce insulin and its sensitivity. It is generally categorized into different types, but in all these categories type 1 and type 2 are the most familiar types.

Type 1 is generally related to the inability of the body part called the pancreas which function is to produce insulin which is due to the demolition of pancreatic b-cell by T-cell-mediated autoimmunity [1]. In the case of, type 2 which is the resistance of insulin and lowers the production of insulin. Greater risk of life was found to be in type 1 as in contrast with type 2 because there is a greater chance of having cardiovascular disease and acute metabolic disorders in type 1[2]. To overcome the other problems of diabetes like neuropathy, retinopathy, diabetic foot ulcer, and cardiovascular diseases, it is necessary for every type of diabetes that it must be identified and control at the start of the disease. [3-5].

As it is a significant economic and social problem to many nations [6], advancement in the technological and scientific field has a vigorous part in the innovation of treatment methods [7]. So this leads to the formation of novel therapeutic drugs for example amylin analogs, gastric inhibitory peptide (GIP) analogs, incretin mimetics [8], and drugs targets used for the treatment of diabetes, e.g. dipeptidyl peptidase-4 (DPP4) inhibitors and peroxisome proliferator-activated receptor (PPAR) [9]. Inducing regeneration of b-cell through stem cells or trans-differentiation has an enhancing effect on b-cells' activity and morphology [10]. Clinical studies for the management of diabetes show that the evidence of efficacy and safety for various multifaceted diseases and gene therapy is newly discovered to have great potential. Viral and non-viral gene therapy has shown encouraging outcomes. For instance, Adeno-associated viral (AAV) vector-based gene therapy has shown to increase incessant glycemic control, as well as secondary complications of diabetes, is prevented [11].

2. Epidemiology

Diabetes mellitus is not any more an unfamiliar expression to the worldwide population; it is progressively transcendent in each nation [12], regardless of the pay level. New information assessed that 629 million individuals will experience the ill effects of Diabetes mellitus by the year 2049 [13]. Type 1 Diabetes mellitus is more continuous in youngsters, especially the individuals who range from birth to 14 years of age, however, it

can happen to people of all ages, but the male was more prone to it among adults [14]. While fatty people or adults are generally influenced by type 2 Diabetes mellitus, yet it can show up in kids excessively [15]. Likewise, type 2 diabetes mellitus is assigned as a significant contributor to the absolute diabetes population.

3. History

Diabetes mellitus (DM) is only of the earliest illnesses and was expressed 3,000 years back in Egyptian literature[16]. Around 1500 B.C the doctors in India noticed the pleasantness of pee of the diabetic individuals and called it "Madhumeha". Ebers papyrus, the most established writing was composed all through a similar time by Egyptians and it was additionally the main archive that clarifies a state of customary purging of urine[17,18]. Around the fifth and sixth century the antiquated Indian doctor Susruta and Sharuka clarified first time about the extraordinary thirst, foul breath, and polyuric state connected with sweet taste substance in the pee. They were the main perceived difference between type I and type II Diabetes mellitus.[19,20] Aretaeus of Cappadocia a Greek doctor, was the principal individual who authored the term diabetes by noticing the clinical circumstance that expanded the recurrence of pee in diabetic people. He was likewise the first to separate diabetes mellitus and diabetes insipidus. Afterward, Thomas Willis in 1670 was incorporated the term Mellitus (nectar sweet) after resuscitating the pleasantness of pee in the patient was because of the high blood glucose level. In 1776, Matthew Dobson, a British physiologist initially checked that the pleasantness of pee is due to the existence of an abundance of glucose in urine and blood.[21] Around 30 BC-50AD, the Aulus Cornelius Celsus has given the total clinical portrayal for diabetes mellitus in Latin and entitled Demedicinal.[22,23] In 1857 Claude Bernard made the idea of that overabundance of glucose creation and the task of the liver in Glycogenesis.[24] In 1889, Oskar Minkowski and Joseph von Mering discovered that the expulsion of the pancreas in the dog produced the improvement of indications of diabetes which significantly credited to the revelation of the function of the pancreas in diabetes mellitus.[25] Later, their disclosure impacts the Banting to accentuation his diabetes examination. In 1921 Banding and Best-segregated insulin from the pancreas and got Nobel Prize in 1923.

4) Global Burden of Diabetes

There is a consistent growth of diabetes were identified all through the world. The population growth, increasing age, way of life changes, urbanization, and minimize physical exercise are the principal factors that cause a worldwide rise in the commonness of diabetes. The main factor for diabetes is decreased physical exercise and increased intake of calories. The worldwide load fluctuates from nation to nation which relies on the financial status of the nations. The extent of the pace of diabetic predominance is converse to the current financial status of the nation. The most elevated ascent was seen in fewer wage nations (92%), trailed by lower-center

wage nations (57%), upper-center pay nations (46%) lastly major league salary nations (25%).[26] A diabetic report distributed by IDF demonstrated that 4 out of 5 individuals live in low and average pay nations. In western nations, the aged individuals are commonly impacted by diabetes yet interestingly, the young and moderately aged adult is for the most part influenced in Asian countries[27,28]. Since the most recent couple of many years, diabetes status has risen from mild disease to one of the chief reasons for morbidity and mortality. Tremendous reports show by the world health organization and the international diabetic federation have given the information that expresses the number of individuals influence by diabetes as of now and later.

The assessment of diabetes frequency is given by the world health organization and the international diabetic federation showed an enormous ascent in the Global load of diabetes. As indicated by IDF diabetes map book the worldwide predominance of diabetes in people between the age of 24 to 79 years was 151 million every 2000, [29] 194 million in 2003,[30] 246million in 2006,[31] 285 million in 2010,[32] 366 million in 2011, 382million in 2013,[33] 413 million in 2015[34] and 425 million in 2017.[35] This level will have been expanded to 642 million in 2040.[36] simultaneously reports additionally recommended that 1 out of 11 adults has diabetes in 2015; this will ascend to 1 out of 10 in 2040. The current international diabetic federation diabetes map book featured that the predominance of diabetes in the adult is 10million more in 2017 than in 2015.

New measurements of diabetic individuals in the individual landmass demonstrated that 37 million out of 2013, 44.3 million individuals in 2015 and 46million in 2017 have diabetes mellitus in North America; 56 million in 2013 and 59.8 million in 2015 in Europe; 20 million in 2013 and 24.2 million in 2015 in Africa; and 138million in 2013 and 153.2 million individuals in 2015 in western Pacific. This indicated that the ratio of diabetic individuals is more prominent than their previous assessment. The assessment of diabetic mortality shows that at regular intervals 1 individual every 6 sec die from diabetes.[37] According to the world health organization 2016[38] reports, 3.7 million individuals have passed on from diabetes in 2012, this was ascended to 5.0 million in 2015. The assessment given in international diabetic federation 2013, among the top 10 nations with more diabetic individuals between the age of 20-79 years, China was in the lead position (98.4 million) trailed by India (65 million), USA(24.4 million), Brazil (11.9 million), Russian Federation (10.9 million), Mexico (8.7 million), Indonesia (8.5 million), Germany (7.5million) and Japan (7.2million).

All around the world, there was a significant amount spent on diabetes in 2013 the worldwide use was 548 billion us dollars that raised to 627 billion US dollars in 2015, which comprise 12% of the worldwide health consumption. A large portion of individuals is influenced by type II diabetes. Kids are now also susceptible to it, it was used to occur to adult only.

5) Different types of diabetes and its differences

Various sorts of diabetes are there. Researchers are as yet characterizing and sorting a portion of these varieties and deciding their commonness in the population.

Type 1 diabetes: it is a type of diabetes in which the immune system itself destroys the beta cell of the pancreas. It is called is an autoimmune disease. It ordinarily grows rapidly than various types of diabetes. It is normally recognized in youngsters and children, and some of the time in adults. To live, patients must ensure regular administration of insulin prescription. Type 1 diabetes is also known as juvenile diabetes and insulin-dependent diabetes mellitus (IDDM). But, those conditions are not precise for the reason that different types of diabetes, teenagers can have, adults occasionally have type 1, and insulin treatment can be included in different types of diabetes. A distinction of type 1 that produces at some point at later age, generally after 30 age, is called latent autoimmune diabetes of adulthood (LADA).

In some cases, insulin resistance can be created in patients with immune system diabetes, due to hereditary elements or weight gain. This situation is called double diabetes.

Type 2 diabetes: A metabolic disorder, ordinarily including abundance weight and insulin opposition. At first, the pancreas makes insulin in these patients, then the body has some problem in utilizing this glucose-controlling hormone.

At long last, the pancreas is not able to generate sufficient insulin to fulfill the requirement of the body for it. Type 2 diabetes is by a long shot the very familiar type of diabetes, signifying developed countries having 85 to 95% of cases and a much greater percentage in agricultural nations, as per the IDF. This disease may take years or a very long time to occur. It is typically headed by prediabetes, in which the glucose levels are better than usual however not sufficiently elevated yet for a determination of diabetes. Individuals with prediabetes can regularly postpone or forestall the acceleration to type 2 diabetes by shedding weight through upgrades in diet and exercise, as the Diabetes Prevention Program and other exploration ventures have illustrated.

Type 2 diabetes used to be known as adult diabetes and non-insulin-dependent diabetes mellitus (NIDDM). Those terminologies are not exact as youngsters can also build up this illness, and a few patients need insulin treatment.

Gestational diabetes: An impermanent metabolic issue that usually to the third-trimester nondiabetic pregnant women can occur. Hormonal variations add to this infection, alongside extra weight and family background of diabetes. Gestational diabetes is created in about 4% of pregnant ladies, as per the ADA (American Diabetes Association). Mother and infant can be missed up with Gestational diabetes, containing premature delivery, preeclampsia, macrosomia (larger than an average newborn child), and breathing and jaundice

troubles in the baby. When the pregnancy occurs this infection usually ends, though it raises the risk of type 2 diabetes for the kid and mother.

Secondary diabetes: Diabetes brought about by some other means. The numerous possible outcomes of secondary diabetes vary from infections, for instance, cystic fibrosis, pancreatitis, Down condition, and hemochromatosis to clinical medicines containing corticosteroids, different pancreatectomy, and immunosuppressives diuretics. Maturity-onset diabetes of the young (MODY). An abnormal sickness brought about by a hereditary imperfection acquired from a parent. It is typically analyzed before the age of 25 in individuals of ordinary weight. MODY is in some cases delegated a type of type 2 or auxiliary diabetes (secondary) however is regularly viewed as a different condition.

Wolfram condition: A hereditary issue that includes some complications like insulin-dependent diabetes, deafness, visualization issues, and diabetes insipidus.

Autoimmune polyglandular syndrome (APS): It is a group of immune system endocrine infections. In the total of three two of them highlight type 1 diabetes. Unbalanced diabetes, otherwise called weak or labile diabetes, is a term that might be utilized to portray any instance of ineffectively estimated diabetes paying little mind to the type. These situations include diabetes mellitus ("sugar diabetes"). Diabetes insipidus ("water diabetes") is a discrete endocrine framework issue where the kidneys discharge exorbitantly water [39].

6) Pathophysiological Aspects

Type 2 DM is described by insulin insensitivity due to the resistance of insulin, decrease in the formation of insulin, and ultimate pancreatic b-cell letdown. So as a result it leads to a reduction in the transport of glucose into the liver, fat cells, and muscle cells. So the breaking of fat with hyperglycemia is increased.

Patients type 1 diabetic is typically little youngsters (or teenagers) and not corpulent once they initially create signs. The acquired inclination is there, with a 10-overlap expanded frequency in first-degree family members of a file case, and with some solid histocompatibility antigens (HLA types) relationship. Investigations of indistinguishable twins have demonstrated that hereditarily inclined people should furthermore be presented to a natural factor, for example, viral contamination. Viral contamination may harm pancreatic B cells and uncover antigens that start a self-proliferating immune system measure. When over 90% of the B cell devastated the patient became diabetic. In this sort, insulin inadequacy weakens long haul potentiating and may prompt deficiencies in understanding and memorization. Type 2 diabetes is joined together by insulin obstruction besides hindered insulin discharge, every one of which is significant in its pathogenesis. Patients with these situations are regularly corpulent and generally present in an adult, the frequency rising continuously every passing year as B-cell work decays. This insulin obstruction prompts both A β plaque development and tau hyperphosphory-

lation. During hyperinsulinemia, insulin and A β vie for insulin corrupting catalyst, prompting A β amassing and plaque arrangement. An abatement in insulin receptor flagging prompts hindrance of Akt and dephosphorylation (actuation) of GSK-3 β and brings about tau hyperphosphorylation [40, 41]

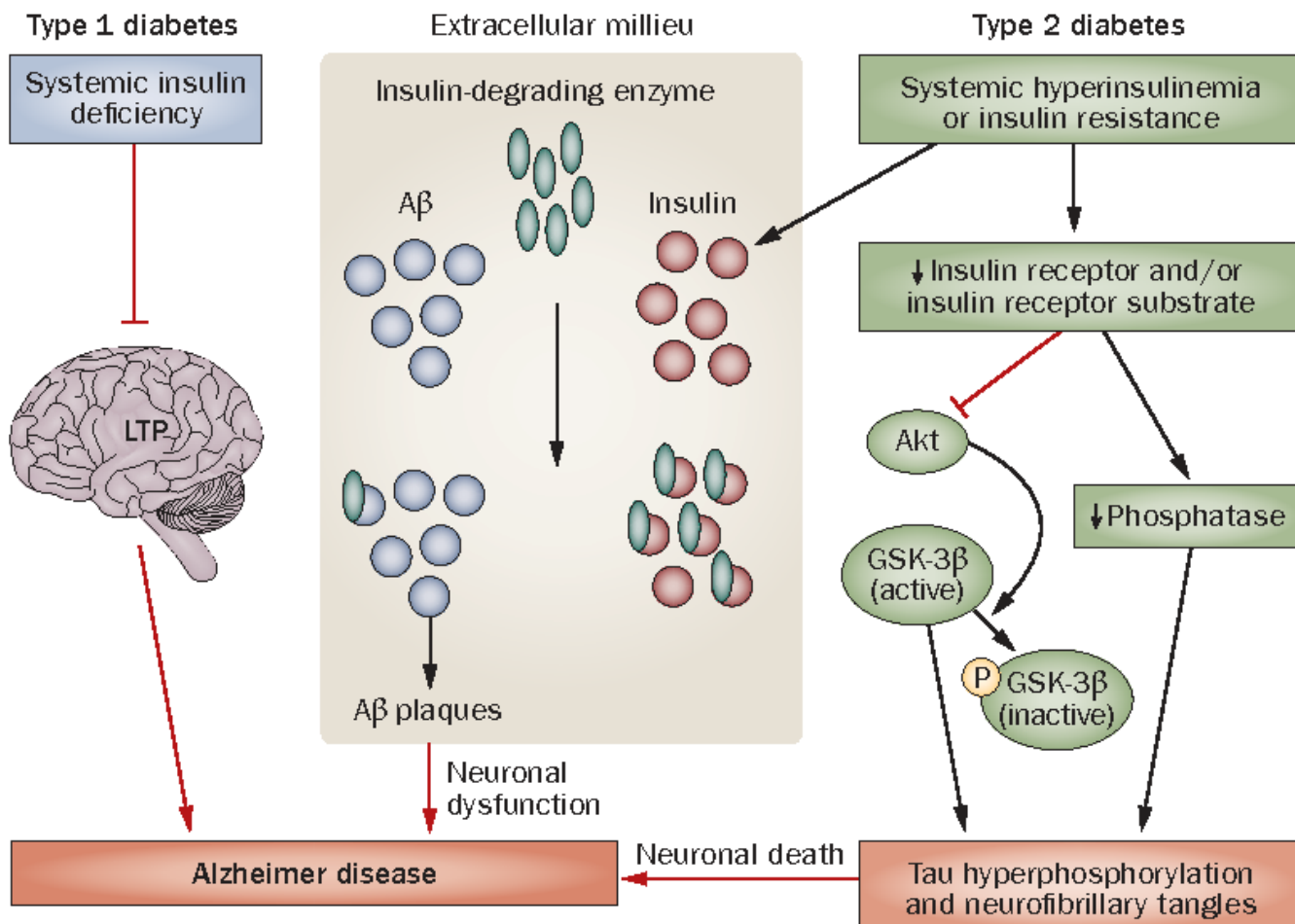


Figure 1: Showing Type I and Type II diabetes Pathophysiology. Abbreviations: A β - Amyloid- β , GSK-3 β -glycogen synthase kinase 3 β , LTP- long term potentiation, P- Phosphate

7. Signs and symptoms of diabetes

Diabetes frequently goes in secret since side effects can be connected to several different origins and a few patients experience no manifestations or carelessness to regard posted warnings.

Comprehensible signs of diabetes contain:

- Extreme thirst (polydipsia)
- Extreme pee (polyuria) and lack of hydration
- Extreme hunger (polyphagia)
- Reduction in weight
- Hazy vision, myopia, or other vision problems
- Slow repairing of wounds

- Skin problems, for example, annoyance or acanthosis nigricans.
- Tiredness, dormancy, or tiredness
- Trembling or shuddering
- Mood swipes or touchiness
- Faintness or fainting
- Coldness, trembling or suffering in the feet, limbs, or hands

Type 1 diabetes often develops rapidly and frequently arises after an ailment, yet indications can be mixed up with seasonal influenza or other normal situations.

Type 2 diabetes can take very long up to years to create and once in a while gets clear simply after long haul inconveniences occur, e.g, sexual brokenness or limb irritation that is because of diabetic neuropathy or claudication (brought about by fringe corridor illness).

A few people, especially youngsters having type 1 diabetes, are undiscovered till they are carried to a clinic with a crisis known as diabetic ketoacidosis. Markers of diabetic ketoacidosis consist of wine-smelling breath or sweet-smelling, hefty perspired relaxing and disarray.

Here and their patients are determined to have diabetes just when enduring different genuine intricacies consist of insulin stun, hyperosmolar hyperglycemic nonketotic disorder, or diabetic trance-like state. To improve evade this type of inconveniences, individuals are prescribed to go through an occasional assessment for diabetes with glucose tests, particularly on the off chance that they have hazard factors [42]

8. Diagnosis

Relating to the American Diabetes Association (ADA), glucose during fasting focus ought to be utilized by and by screening for diabetes; yet postprandial glucose, random glucose, and glucose resistance test are additionally utilized for glucose assurance. For the conclusion of diabetes, anyway, one rule must apply. Indications of diabetes (polyuria, polydipsia, unsolved weight reduction, and so on) as well as the casual concentration of glucose in plasma = 11.1 mmol/L (200 mg/dL).

Plasma glucose during fasting = Its typical reach is 70-110 mg/dl with no caloric administration for 8 h. The WHO arrangement consist of both clinical stages (normoglycemia, impaired glucose tolerance/impaired fasting glucose (IGT/IFG), diabetes) and etiological sorts of diabetes mellitus, indistinguishable from the ADA except for that WHO gathering incorporates the course of action once known as gestational impaired glucose resistance (GIGT) and GDM.

Glucose during fasting = 7.0 mmol/L (126 mg/dL)

And 2-h glucose = 7.8 mmol/L (140 mg/dL) after a 75-g OGTT [43].

9) Etymology of Diabetes Mellitus

The expressions "Diabetes" and "Mellitus" are stated in Greek. "Diabetes" indicates "a passer through; a siphon" even though the "Mellitus" signifies "sweet". It is said that the Greeks give the name Diabetes Mellitus because of the outrageous measures of pee delivered by diabetics pulled in flies and honeybees. The customary method of identifying diabetes mellitus in early age Chinese was by seeing if ants are coming to an individual's pee. In ancient ages, the European specialists tried for diabetes by tasting the pee themselves, an act so often outlined in Gothic convictions [44]

10) Dietary management of diabetes

Dietary administration of diabetes seeks to accomplish most optimistic blood lipid concentrations, proper energy for evenhanded weight, typical development and advancement throughout the prenatal period and breastfeeding, to dodge diabetic confusions, and intended for the development of health by consuming balanced diet [45].

In most developed nations, the fourth or fifth driving reason for morbidity is DM which can impact epidemic extents in recently industrialized nations. Because of the customary way of life, not many rural individuals are influenced by type 2 diabetes mellitus [46]. To acquire great blood glucose control, low admission of calories and weight reduction is significant. The extent of starches, proteins, and fats that should be praised stay hazy [47]. To stop, oversee, or bring down the pace of improvement of diabetes, clinical nourishment treatment is significant [48].

If there should be an occurrence of type 1 DM the part of nutrition is multiplied, it aids in glycemic control practically consistent just as lessens long haul complications. At the point where we are concerned with overseeing diabetes with nutrition, the standards are the same for type 2 just as type 1 DM [49].

a) *Momordica charantia*

Momordica charantia is the botanical name of melon which is bitter, it is commonly used in the treatment of DM. Insulin resistance is the most fundamental problem at the cellular level in non-insulin-dependent diabetes mellitus (NIDDM) patients. This resistance leads to hypertriglycerolaemia, increased secretion of very-low-density lipoprotein (VLDL), and hyperinsulinemia [50]

The bitter melon shows its effect by increasing the tolerance of glucose and help in declining the blood glucose level. If a person is diabetic he might be facing obesity, bitter melon also helps in overcoming obesity. Furthermore, it increases insulin sensitivity and improves insulin secretion by refining the condition of damaged B-cells by shielding and safeguarding. [51]

b) Cinnamon

Cinnamon has a place with the Lauraceae family. Its botanical name is *Cinnamomum zeylanicum*. Cinnamon has been utilized as a flavor in ordinary daily schedule just as therapeutically since antiquated occasions [52]. It is used as an anti-inflammatory and has the properties to lower the disease, decrease the lipid level, used as an antioxidant, against microbial infection, used for diabetes and cancer, as well as can be used to overcome diseases related to neurological functions like Parkinson and Alzheimer [53].

c) Cloves

It has a place with the Myrtaceae family. Its botanical name is *Eugenia Caryophyllata* or *Syzygium aromaticum*. It has blood glucose controlling properties. It can likewise be utilized to stop blood clumps because of the existence of eugenol in it [54]. The significant phenolic constituents present are isoquercitrin, kaempferol, gallic acid, ellagic acid, and caffeic acid. Experimental usage of powder of cloves in rodents, it is demonstrated that this powder displays numerous helpful activities like hypoglycemic, cancer prevention, against hyperlipidemia, and hostile to hepatotoxic. It lessens the processing of sugars and checks oxidative pressure [55].

d) Capsicum annum

It has a place with a family called Solanaceae. *Capsicum* has antihyperglycemic and antihypercholesterolemic properties because it contains different varieties such as Serrano and Fresno. Therefore for a diabetic patient, it is suggested to use it often. It is generally used as red chili powders [56]. The lowering of blood glucose level by *Capsicum* may be due to the inhibition of reabsorption of intestinal glucose. With the regular usage of *Capsicum* Postprandial hyperinsulinemia could be the possible result [57].

e) Coccinia indica

Coccinia indica has a place with the family Cucurbitaceae, it is found mostly in India and is commonly used for the treatment of diabetes. An experimental result shows its hypoglycemic and hypolipidemic properties, which was performed on alloxan diabetic rodent [58]. Various clinical trials proved its safety and efficacy of various parts of the plant and their derived formulation having anti-diabetic properties. *Coccinia indica* additionally has mitigating, antipyretic, hepatoprotective, hypolipidemic, and pain-relieving activities [59].

f) Vaccinium myrtillus

It is commonly known as blueberry and belongs to the family Ericaceae, it has hypoglycemic properties and is a natural source for lowering blood glucose level. Wild berries help in different other functions as it can be used against microbe, inflammation, aging, cancer, and used for management of diabetes. A greater amount of phy-

tochemicals can be found in its e.g flavonols, Anthocyanins, proanthocyanidins, and phenolic acids [60].

g) *Trigonella foenum graecum*

It has a place with the family Fabaceae. Its common name is fenugreek, it is used for both type 1 and type 2 DM. Diosgenin and saponins found in fenugreek have antihyperlipidemic and anti-diabetic therapeutic activity. It can be used in the laboratory as a hypoglycemic herb [61]. Galactomannan-rich soluble fiber found in fenugreek might be the reason for its anti-diabetic activity. Amino acid stimulates β -cells in the pancreas so amino acid 4-hydroxy isoleucine may be the reason for insulinotropic properties and its use against diabetes. Deferred stomachic voidance and hindrance of aldohexose transport have been proposed as possible mechanisms [62]

h) *Prunus dulcis*

Its common name is almond. Almonds can bring down postprandial blood glucose levels and oxidative harm in typical sound people [63]. As almond has different variety it may be sweet or bitter and has very vital dietary values. They can be used for different purpose differently, it can be used as a flour for cake and biscuits because it contains no starch. Patients with DM can use biscuits and cakes in which the flour of almond is used. [64]

i) *Ficus religiosa*

Peepal tree is the common name used for it. It has a place with the Moraceae family which consists of a β -sitosterol-D-glucoside active constituent having a hypoglycemic effect in rabbits that are made diabetic by Alloxan and in pituitary diabetic rats [65]. Practically all the parts of these plants have some curative values however we are only concerned with the glucose-lowering effect of this plant. For the treatment of diabetes bark of the plant is used. FREE also indicated imperative growth in polyose and serum insulin content in skeletal muscles and liver of STZ-evoked diabetic rats though a fundamental exhaustion inside serum fatty oil level and whole cholesterolin was seen [66]

j) *Emblica Officinalis*

Its common name is Amla. Amla fruit contains medicinal values that are used for heart problems, cancer, hepatic disorders, and diabetes also it can be used as an agent against inflammation. Amla has also some benefits of memory effects [67]. Amla fruit is used for both whether a person has diabetes or not it can be used in both conditions. Oxidative stress and neuropathic pain were reduced in rats having diabetes. In rats having NIDD it can enhance the glycemic status and oxidative stress. Its mechanism of glucose-lowering properties is not explained well yet [68].

Amla natural product has different medical advantages. It tends to be utilized in complications like problems,

malignancy, ulcer prevention, and hepatotoxicity also for a diabetic patient [69]

k) Onion

Its botanical name is *Allium cepa*, which have its place in the family Amaryllidaceae. It is cultivated in the United States, India, and China. It is commonly used as a flavoring agent in food, contains many active constituents that are medically important for cholera, stomach disease, asthma, and hepatitis [70]. Allyl propyl disulfide is the most important constituent used for diabetes. Onion extract e.g glibenclamide enhance insulin release and its action also enhances the utilization of glucose and its cellular uptake rate. [71]

Onion has many medicinal values, it is helpful in high blood pressure and use as hypocholesterolemic, cardiovascular problems, blood glucose-lowering agent, and anti-cancer. Due to its glucose-lowering effect and antihyperlipidemic effect NIDD patient can use onions [72].

l) Areca catechu

It contains many active constituents but Arecoline is the most important one that has a blood glucose-lowering effect. Most often subcutaneous administration of alkaloidal contents of areca catechu shows its blood glucose-lowering effect for 4 to 6 hours [73]. It has effective hypoglycemic activity in rats having streptozotocin-induced in them [74].

Areca catechu blossoms produced a hyperglycemic effect in fasting [75].

m) Camellia Sinensis

Green tea displays different medical advantages as it is antibacterial, against inflammation, against mutagenic, against diabetes, antiviral also against the cancer-causing agent. Its watery concentrate fundamentally comprises catechins like ECG, EGC, EC, EGCG [76]. Through its utilization, the hypoglycemic effect was shown in mice having diabetes, but the level of insulin was not affected. Whenever utilized for a long time, it upgrades insulin affectability, yet it may likewise prevent resistance of insulin issues, anti-hypoglycemia and other metabolic imperfections in rodents are due to fructose [77] *Camellia sinensis* improved insulin movement in STZ diabetic rats. Trials demonstrated that its lower dosages effects the production and activity of insulin. [78].

n) Phaseolus vulgaris

It is used for the treatment of diabetes, seeds have important medicinal values. But the exact mechanism is still unclear yet different authors propose that it works by enhancing β -cells and thus result in increased secretion of insulin. Different mechanisms was proposed but two most probable mechanisms center around the function of phytohaemagglutinin inhibitors and α -amylase inhibitors [79].

o) Syzygium cumini

The seed of *Syzygium cumini* shows an anti-diabetic effect in those rats in which streptozotocin (STZ) was initiated. The hypoglycemic effect was shown by 'Mycaminose' and it was found that ethyl acetate extract and methanol has also hypoglycemic action [80].

11) Causes of diabetes and risk factors

There are a lot of causes for diabetes that are very complex and not completely understood. It can be caused by many factors, including various inclining conditions and risk factors. In most of the cases, it was observed that it can be caused due to environmental factors, genetics, and a person's habits.

There may be the opposite risk factors, for example in western people the autoimmune Diabetes (LADA) is more usual, while metabolic diabetes in other ethnicities. There are more chances of T1D in kids, while with increasing age there are more chances of T2D diabetes and gestational diabetes. Metabolic syndrome, prediabetes, and resistance to insulin are a greater risk factor for type 2.

Some other factors are;

1) Genetics and Family ancestry: Genes might be the cause of diabetes as some sort of diabetes is caused due to gene passing through offspring, some defective genes may cause MODY (Maturity onset diabetes of the young) while some cause Wolfram syndrome and it can lead to cause other diabetic forms as well e.g. type 1 and type 2 DM.

2) Family clinical record is also powerful to differing degrees: American Diabetes Association (ADA) state that, if a person who's both parents are type 1 diabetes have 10 to 15% chances of getting type 1 diabetes, while the person who's both parents have type 2 has a 50% chances of getting type 2 diabetes.

3) Body type and weight and: Fatness and increased weight are the main issues in gestational and T2D. Metabolic syndrome and resistance to insulin are promoted by excessive fat around the abdomen.

Excessive weight is not related to type 1 and LADA, people with autoimmune diabetes have normal weight. But recent studies show that fatness may lead to T1D and the reason for the rise in rate of T1D may be obesity in childhood. Moreover, some patient who has autoimmune diabetes may be prone to insulin resistance due to weight gain so-called as double diabetes.

4) Level of physical activity: Physical exercise play a vital role in a person's health, lack of exercise is answerable for diabetes and obesity worldwide.

5) Diet: Forgetting diabetes, diet is mostly debated cause. Research shows that carbohydrates and other soft drinks containing an excessive amount of sugar may be the risk factor for metabolic diabetes, and food having low sugar content like whole-grain minimize the risk. The ADA state that the main reason for diabetes is over-

weight which is due to overeating, it is not the sugar that causes diabetes. And some researcher state that feeding cow's milk in childhood is related to it, while some researcher is on it.

6) Other sicknesses: Some other diseases may induce diabetes-like Hypertension, polycystic ovarian disorder, hyperlipidemia, and asthma lead to type 2. And immune system diseases like celiac infection lead to type 1 diabetes. Hemochromatosis, pancreatitis, Cushing's disease, hyperthyroidism and acromegaly, and other genetic conditions may lead to secondary diabetes [81, 82].

7) Hormones: Hormones are found in the human body that mainly passes messages throughout the body. It can also be the cause of diabetes in different aspects. Like, the hormone for stress such as cortisol may lead to altering the level of glucose in T2D, and during pregnancy in women lead to T1D in the kids. The growth and sex hormones are also responsible to make teenage people more prone to diabetes. Also, the hormones used for treatment may induce secondary diabetes such as injected contraceptives, growth hormones, anabolic steroids, and corticosteroids.

8) Medical therapies: As discussed earlier in hormonal treatment same case is here in medical treatment. As we use medicine for the treatment of one disease it can also have the side effect of inducing other diseases, like beta-blockers, antipsychotics, antiretrovirals, antidepressants, and some immunosuppressive are associated with secondary diabetes. Radiation therapy and pancreatectomy may induce secondary diabetes

9) Other environmental aspects: The study suggests that a lot of chemical reactions occur in our body as a result free radicals are produced, which can lead to the development of diabetes. Furthermore, free radicals can be generated as a result of smoke, air pollution, and genetic problem, when free radicals are produced it can damage cells, also those cells that responsible for the production of insulin. T1D is more prone to occur in winter as compared to summer because of the cold environment

10) Viruses: After developing a viral disease in most people, they are diagnosed with type1 diabetes. The virus that is linked with diabetes is rubella, coxsackievirus, and mumps.

11) Smoking: Smoking is considered a causative agent for diabetes, but it is more susceptible to type 2 diabetes.

12) Alcohol: Extreme utilization of liquor is a dangerous aspect of diabetes. For instance, it can produce pancreatitis. But several researchers have discovered that light drinking might diminish the opportunity of getting diabetic. A large part of these dangerous elements can be clarified as unmanageable, for example, hereditary qualities and age, or helpful, for example, exercise and diet.

Conclusion

In sum, we must say that Diabetes Mellitus whether it be type 1 or 2 is one of the disease that has been most prevalent in today's world and we must fight it out by exercising, taking good food and good life style.

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