Natural Products and Therapeutics

Management of Diabetes Mellitus

Based on Natural Products

Yachana Mishra, PhD
Vijay Mishra, PhD
Editors

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Management of Diabetes Mellitus Based on Natural Products

https://doi.org/10.52305/JCWM1341

Library of Congress Cataloging-in-Publication Data

Names: Mishra, Yachana, editor. | Mishra, Vijay, Dr., editor.
Title: Management of diabetes mellitus based on natural products / Yachana Mishra, PhD (editor), Associate Professor, School of Bioengineering and Biosciences, Lovely Professional University, Phagwara, Punjab, India, Vijay Mishra, PhD (editor), Professor, School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, Punjab, India.
Identifiers: LCCN 2023029998 (print) | LCCN 2023029999 (ebook) |
ISBN 9798886978537 (hardcover) | ISBN 9798886979701 (adobe pdf)
Subjects: LCSH: Diabetes--Alternative treatment | Hypoglycemic agents. | Medicinal plants.
Classification: LCC RC661.A47 M36 2023 (print) | LCC RC661.A47 (ebook) |
DDC 616.4/62--dc23/eng/20230630
LC record available at https://lccn.loc.gov/2023029998
LC ebook record available at https://lccn.loc.gov/2023029999

Published by Nova Science Publishers, Inc. † New York

Dedication

This book is dedicated to our adorable children,
Vidhi Mishra and Jay Mishra.

Contents

Preface

The most prevalent endocrine condition, diabetes mellitus (DM), is characterized by underutilization of glucose, elevated blood sugar levels, and an ineffective or insufficient insulin secretory mechanism. DM is a severe health issue that affects 3% of the global population and 5% of the people in the US. Each year, it accounts for around 5% of all fatalities worldwide. Type 2 diabetes affects more than 90% of diabetic patients, whereas type 1 affects the remaining 10%. Today the management of diabetes without any side effects is still a challenge. Herbal medicines are prescribed widely because of their effectiveness, fewer side effects, and relatively low cost. Numerous active principles produced from plants have proven to have anti-diabetic properties. Herbal treatments for diabetes have been used in patients with insulin-dependent and non-insulin-dependent diabetes, diabetic retinopathy, diabetic peripheral neuropathy, etc. Various plants can lower glucose production, promote glucose utilization, and combat secondary complications.

This book will offer an updated, comprehensive resource of information on diabetes mellitus and its treatment by natural products. The book intends to provide a state-of-the-art collection of reports for primary and clinician investigators interested in treating diabetes mellitus. We believe this book will be of value to clinicians, biochemists, public health authorities, medical laboratory sciences technologists, biotechnologists, pharmaceutical and medical students, and fellows in training. Each chapter begins with a summary of the concepts so that those not actively working in the field can readily understand what follows. We have endeavored to provide this information in a style that is accessible to the broad community of persons who are concerned with the impact of diabetes in our clinics and across wider global communities.

Acknowledgments

We wish to sincerely thank the authors for offering to write comprehensive chapters on a tight schedule. We express our earnest gratitude to the reviewers, who provided their critical views for improving the book chapters. We would like to thank the reviewers of our book proposal for their suggestions in framing the chapters.

Dr. Yachana Mishra and Dr. Vijay Mishra
Editors

Chapter 1

Diabetes Mellitus: Worldwide Statistics and Types

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Abstract

Diabetes mellitus, a metabolic disease, is characterized by persistently elevated blood sugar levels, i.e., hyperglycemia. The present chapter discusses the historical background of diabetes, its symptoms and consequences, different types, and worldwide statistics on diabetes.

Keywords: diabetes mellitus, hyperglycemia, blood sugar

1. Introduction

Diabetes mellitus (DM) is becoming more common, frequently leading to severe metabolic disorders and consequences. Additionally, various therapeutic objectives in diabetes patients affect both quality of life and

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In: Management of Diabetes Mellitus Based on Natural Products
Editors: Yachana Mishra and Vijay Mishra
ISBN: 979-8-88697-853-7

glycemic control. All medical personnel has difficulty when it comes to providing the best treatment for a patient who has diabetes mellitus. Frequently, the diagnosis is made as soon as symptoms appear. Early diagnosis is made possible by screening individuals at high risk, which enables quick therapeutic start-ups and may help avoid long-term consequences. The most helpful diagnostic test is the fasting plasma glucose determination; however, in some cases, the oral glucose tolerance test and random plasma glucose are also used to identify diabetes. The effectiveness of existing treatment options for diabetes mellitus depends on proper individualization. The type and duration of diabetes, the patient's abilities and features, and the individual risk for acute and/or late-stage complications all influence the treatment goals. These complications include macrovascular and microvascular disease, which are defining characteristics of diabetes-related limitations; hypoglycemia, which can be severe and life-threatening; and hyperglycemia, a significant risk factor for the development of cardiovascular disease [1]. For individuals with insulin-dependent diabetes mellitus (IDDM) to achieve satisfactory glucose control, complicated insulin regimens and regular self-blood glucose monitoring are necessary. Several treatments may be used to treat non-insulin-dependent diabetes mellitus (NIDDM), including diet, sulfonylureas, insulin, and combinations. In addition to medicine, nutrition, monitoring, education, and ongoing care are necessary for the therapy to be successful.

2. Diabetes Mellitus and Its Historical Background

A series of metabolic diseases collectively referred to as diabetes, or DM, is characterized by persistently elevated blood sugar levels (hyperglycemia) [1]. The repercussions that DM has caused are social implications, economic, and health illnesses. It is a rapidly spreading global issue. Two major factors contributing to the rise are an aging population and obesity. Furthermore, research has revealed a high risk of increasing diabetes, due to which 50% of the population will not receive the treatment after ten years [2].

Weight loss and polyuria are hallmarks of diabetes, which the Egyptians first described. However, the Greek physician Aertaeus coined the phrase "diabetes mellitus." The words diabetes and mellitus come from the Greek meaning "to pass through." Aretaeus of Cappadocia's treatise is the oldest work (2nd or early 3rd Century CE) containing a specific mention of diabetes. According to his description of the sickness's signs and progression and his

"Pneumatic School" theories, the disease was brought on by dampness and cold. In addition to discussing the snakebite's alternative diagnoses, which also resulted in extreme thirst, he linked diabetes and other disorders hypothesis. His writing was unknown in the West until the first Latin edition was printed in Venice in 1552 [3]. Sushruta and Charaka, two Indian doctors who practiced in the 4th and 5th Centuries CE, distinguished for the first time two distinct forms of diabetes, one of which was linked to youth and the other to obesity. The development of a successful therapy did not occur before the invention of Insulin by Canadians Frederick Banting and Charles Herbert Best in 1921 and 1922, respectively [4]. From this, it has to be learned that the long history of the earliest accounts of diabetes emphasizes how crucial it is to track and observe medical issues as people develop. Early doctors relied on their senses, including smell and taste, to diagnose and gain knowledge. Langerhans produced a thesis pinpointing the cells that would later be recognized as the source of insulin production [5].

3. Prevalence of Diabetes: Worldwide Statistics

Diabetes, which is increasingly prevalent worldwide, is one of the significant and challenging health issues that the human population of the modern world must deal with. The prevalence of diabetes has increased throughout most of the world's regions due to rapid economic growth, urbanization, and the adoption of contemporary lifestyles. Diabetes contributes significantly to long-term sickness and early mortality, with one death occurring approximately every ten seconds. More people die from it annually than from HIV/AIDS. The onset of global industrialization and the incredible growth in obesity has made diabetes a global pandemic. Although it is challenging to determine prevalence due to two primary factors accurately—the vastly disparate criteria and methods of data collection—recent research revealed that the rate of diabetes in adults would increase between 4.4% in 1995 to 6.4% by 2025.

An estimated 463 million adults in the world, or 9.3% of all adults, have diabetes as of the year 2019. These adults range in age from 20 to 79. It is predicted that by 2030, this figure will rise from 578 million, or 10.2%, and by 2045, it will increase to 700 million, or 10.9% of the adult population globally. Estimates for 2019 show that men and women have a high prevalence of diabetes at 9.6% and 9.0% of the global population for each gender, respectively. Additionally, 4.2 million adults aged 20 to 99 died from

diabetes-related problems in 2019. Pregnancy-related diabetes is thought to have affected more than 20 million live births (1 in 6 live births) in 2019. The cost of treating diabetes-related illnesses is estimated at least 760 billion USD, or 10% of all adult expenditures [6].

In addition to providing recommendations for decision-makers, people, members of civil society, and enterprises, the WHO Global Report on Diabetes provides an overview of the diabetes burden and a list of treatments that may be utilized to prevent and treat diabetes [7]. Among persons 18 and older in 2014, 8.5% had diabetes. About 1.5 million deaths in 2019 were directly related to diabetes, and 48% of all diabetes-related deaths occurred in those under 70. Diabetes also contributed to 460000 kidney disease fatalities, and elevated blood glucose is thought to be responsible for 20% of cardiovascular mortality. Age-standardized death rates from diabetes increased by 3% between 2000 and 2019 [8].

The death rate from diabetes climbed 13% in lower-middle-income nations. However, between 2000 and 2019, there was a 22% global decline in the likelihood of dying between the ages of 30 and 70 from any of the four major noncommunicable diseases like cancer, chronic respiratory diseases, diabetes, or cardiovascular disorders. The 219 data sources describing research carried out between 2005 and 2020, covering 215 countries and territories, defined quality requirements. Estimates from nations with comparable economies, ethnicities, geographies, and linguistics were extrapolated for nations whose data did not match quality standards. To produce smoothed age-specific diabetes prevalence estimates, logistic regression was utilized. An attributable fraction technique was used to quantify the costs associated with diabetes-related health care. In order to predict future prevalence, population projections for 2045 were combined with estimates of diabetes prevalence for 2021 [9].

The worldwide prevalence of diabetes among adults aged 20 to 79 was predicted to be 10.5% (536.6 million) in 2021 and 12.2% (783.2 million) in 2045. Diabetes prevalence was comparable between genders and was highest in people aged 75 to 79. In 2021, the prevalence was predicted to be higher in urban (12.1%) than rural (8.3%) locations and in high-income (11.1%) than low-income (5.5%) nations. Between 2021 and 2045, middle-income countries are predicted to experience the most significant relative increase in the prevalence of diabetes (21.1%), followed by high-income (12.2%) and low-income (11.9%) nations. The cost of treating diabetes-related illnesses worldwide was anticipated to be 966 billion USD in 2021 and is expected to rise to 1,054 billion USD by 2045 [10].

About 382 million individuals worldwide had diabetes in 2013, according to statistics, with type 2 diabetes accounting for 90% of cases. With equal rates for men and women, this equates to 8.3% of the adult population. Diabetes was the eighth most significant cause of death worldwide in 2012 and 2013, with a mortality rate of 1.5–5.1 million per year. By the year 2035, it is expected that 592 million people will have died from diabetes. The frequency of newly diagnosed cases of diabetes in the United States declined from 9.3 per 1,000 adults in 2009 to 5.9 per 1,000 adults in 2019, ending nearly two decades of steadily rising rates [11].

The proportion of US people with prediabetes stayed steady between 2005 and 2008, as well as between 2017 and 2020. The notification rate for prediabetes status, however, virtually quadrupled from 6.5% to 17.4%. The rates of diabetes diagnosis are greater among Hispanics than among non-Hispanic Whites, non-Hispanic Blacks, non-Hispanic Asians, and American Indians or Alaska Natives i.e., 14.5%, 12.1%, 11.8%, 9.5%, and 7.4%, respectively.

Globally, there will be 643 million diabetics by 2030 and 783 million by 2045. In low- and middle-income countries, three out of every four adults have diabetes. Adults with diabetes make up almost one in two people (240 million). The disease caused the deaths of nearly 6.7 million individuals. At least USD 966 billion, or 9% of all adult healthcare expenses, were related to diabetes.

Over 1.2 million children and adolescents have type 1 diabetes (T1DM) (0-19 years). Pregnancy-related diabetes affects 21 million live births (about 1 in 6). About 541 million people are at higher risk of developing type 2 diabetes (T2DM). Diabetes prevalence among adults is predicted to increase from 4.0% in 1995 to 5.4% by 2025. The developed world has a greater rate than the developing world. By 2025, there will be 300 million adults worldwide who have diabetes, up from 135 million in 1995. The majority of this numerical growth will take place in developing nations. From 51 to 72 million, there will be a 42% growth in wealthy countries and from 84 to 228 million in developing nations. By 2025, developing countries will host more than 75% of the world's diabetic population [10, 12-16].

4. Symptoms and Consequences of Diabetes

Unintentional weight loss, increased urination (polyuria), thirst (polydipsia), and hunger (polyphagia) are common indicators of uncontrolled diabetes

(Figure 1). In contrast to T2DM, where symptoms may not even occur, T1DM symptoms may appear suddenly (within weeks or months) [17]. Despite not being diabetes-specific, the onset of the illness might also be signaled by various additional indications and symptoms. They also consist of scratchy skin, impaired vision, lethargy, headaches, and slow wound healing may lead to glucose absorption in the eye's lens, which changes the lens's curvature and impacts vision. Long-term vision loss might also be a side effect of diabetic retinopathy. A range of skin rashes known as diabetic dermadromes can appear in patients with diabetes [18].

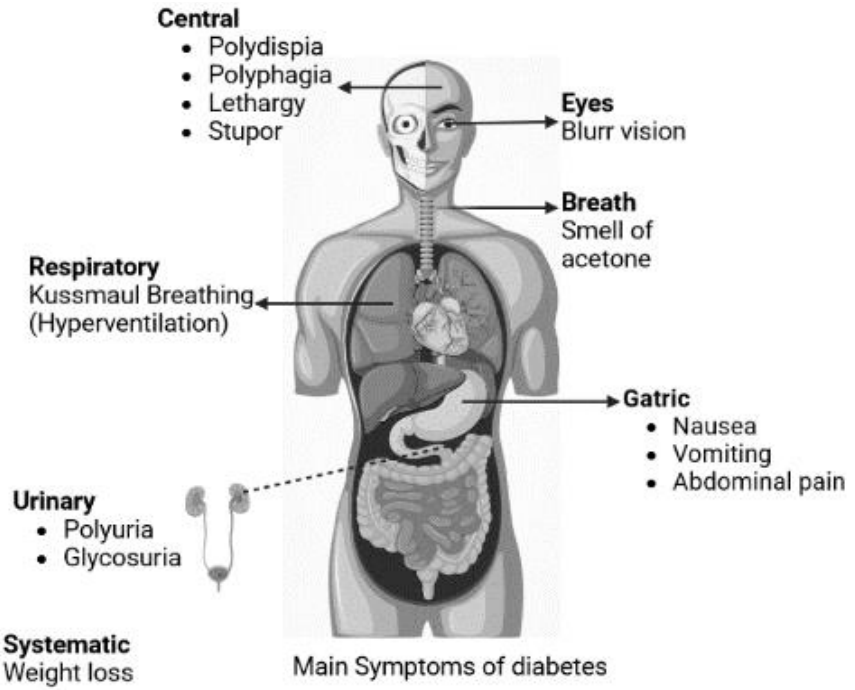

Figure 1. Symptoms of diabetes.

Additionally, diabetes patients may have Diabetic Ketoacidosis (DKA), a metabolic condition characterized by nausea, vomiting, and stomach pain, as well as the acetone odor on the breath, Kussmaul breathing, and in severe cases, a decreased level of consciousness. DKA requires immediate medical attention at a hospital. Dehydration is the primary cause of the hyperosmolar hyperglycemic condition (HHS), which is more common in T2DM. It is a relatively uncommon but severe illness [19].

Depending on the medicine used, hypoglycemia, a low blood sugar caused by treatment, can affect people with T1DM and T2DM. The majority of instances are minor and are not emergencies. In moderate situations, symptoms may include discomfort, shaking, sweating, and an increase in hunger; in severe cases, however, symptoms may include disorientation, violent behavior changes, seizures, unconsciousness, and, very rarely, death or irreversible brain damage [19, 20]. Long-term consequences are more likely in all types of diabetes and often appear after several years (10-20 years); however, they could be the initial symptom in those who haven't previously been diagnosed [21]. One of the primary long-term impacts is damage to blood vessel walls. Cardiovascular disease is two times more likely in those with diabetes, and coronary artery disease accounts for around 75% of those fatalities [22].

Peripheral artery disease and stroke are two examples of other macrovascular disorders [22, 23]. Eye, kidney, and nerve damage are among the most common consequences of diabetes brought on by tiny blood vessel damage. The condition known as diabetic retinopathy, which affects the eyes and can eventually lead to blindness, is brought on by damage to the blood vessels in the eye's retina. Glaucoma, cataracts, and other visual issues are all risk factors for diabetes. It is advised that people with diabetes consult an eye doctor once a year [1, 24].

Injuries to the kidneys from diabetes, known as diabetic nephropathy, can result in tissue damage, protein loss in the urine, and eventually, renal failure, which may necessitate dialysis or kidney transplanting. The most frequent side effect of diabetes is diabetic neuropathy, which causes damage to the body's nerves [1]. Numbness, tingling, sudomotor dysfunction, discomfort, and changed pain perception are some of the symptoms that might cause skin injury. It is possible for diabetes-related foot problems, such as diabetic foot ulcers, to develop, are occasionally challenging to treat, and occasionally require amputation. Cognitive decline is associated with diabetes [16, 25].

5. Diabetes and Its Types

Diabetes mellitus (DM) is a metabolic illness that occurs when the body cannot produce or utilize the hormone insulin, which is required to convert foods like sugar, starches, and other carbs into energy. In turn, a lack of insulin or decreased insulin results in persistently elevated blood sugar and tolerance to glucose. It is most likely the oldest sickness that exists for humans. The term

"black death" dates back to the fourteenth century**.** Blood sugar levels continue to be elevated in those who have diabetes. Type 1 diabetes (T1DM), an autoimmune illness, affects 5% of diabetics; Type 2 diabetes (T2DM), which affects 95% of people with the disease, is most frequently brought on by obesity. Other types of diabetes, which are highly uncommon and brought on by a single gene mutation, include gestational diabetes.

4.1. Type 1 Diabetes Mellitus (T1DM)

Juvenile diabetes was previously referred to as type 1 diabetes (T1DM). It is a syndrome that manifests as an autoimmune disease when the immune system targets the beta cells, which are responsible for producing Insulin. Glucose levels in the blood are regulated by the hormone insulin. Frequent urination, increased hunger, thirst, and thirstiness are common signs of this raised blood sugar. Slow wound healing, fatigue, and blurred vision are possible additional symptoms. The fundamental mechanism entails an autoimmune attack on the pancreatic beta cells. Glycated hemoglobin (HbA1C) and blood sugar levels are used to diagnose diabetes. By checking for the presence of autoantibodies, T1DM can be separated from T2DM. T1DM cannot currently be prevented [26].

For survival, insulin therapy is necessary. Insulin is often administered via subcutaneous injection, however, an insulin pump can also be used. Exercise and a diabetic diet are crucial components of management. Diabetes can lead to a wide range of consequences if ignored. Nonketotic hyperosmolar coma and diabetic Ketoacidosis are complications with a reasonably quick onset. Long-term effects include eye damage, heart problems, renal failure, foot ulcers, and foot rashes. Additionally, if more insulin is given than it reduces blood sugar levels, issues from low blood sugar may result. T1DM is thought to account for 5 to 10% of all diabetes cases. The precise number of those afflicted is unknown, despite estimates that 80,000 children worldwide develop the sickness each year [27]. Affected individuals in the US are thought to number between one and three million.

The hallmark symptom of T1DM, which often manifests in children as a few days to weeks of very high blood sugar levels, is increased urination, thirst, and weight loss. Additional symptoms that kids may suffer include poor academic performance, increased appetite, blurry vision, bedwetting, recurrent skin infections, perineal candidiasis, irritability, and increased hunger. Symptoms for T1DM in adults generally last months instead of days

or weeks, and they also encompass a greater spectrum of signs and symptoms. A sustained insulin deficit can also bring on diabetes ketoacidosis. This condition manifests as dry or flushed skin, stomach discomfort, nausea, or vomiting, disorientation, trouble breathing, and a fruity breath odor.

Geographically, in some parts of Europe and North America, the percentage of children whose T1DM is brought on by an episode of diabetic Ketoacidosis can be as low as 15%, whereas it can reach as high as 80% in developing nations. When a person has T1DM, only a small subset of their body's cells, called β-cells, produce Insulin leading to a gradual insulin shortage. Diabetics have continuous hyperglycemia because their bodies lack the hormone insulin, which allows them to respond to blood sugar increases effectively [28].

For unknown reasons normally, IA-2, IA-2, and/or ZNT8 proteins will eventually be the target of antibodies after IA-2, IA-2, and/or ZNT8 Insulin or the protein GAD65. People who produce more of these antibodies and who do so earlier in life have a higher chance of developing T1DM symptoms. What led to the development of these antibodies is yet unknown. It has been suggested that the reason might be a diabetogenic trigger, a genetic predisposition, or exposure to an antigen [29].

Idiopathic T1DM, which still has an unknown origin, has cell loss but no indication of autoimmune disease, and it affects the remaining 10–30% of T1DM. Numerous environmental risks have been investigated to understand what triggers cell autoimmunity. The relationship between each risk and diabetes is frequently unclear, although several environmental and life history factors are connected to modest increases in the risk of T1DM. Children whose mothers are overweight, older than 35, or born via cesarean section have a slightly greater risk of developing T1DM.

Small relationships between T1DM risk and dietary fiber or gluten intake have been reported in animal research. Numerous potential environmental factors, such as the length of breastfeeding, have been thoroughly investigated in human research and found to be unrelated to the incidence of T1DM, including the introduction of cow milk to the diet, vitamin D intake, blood levels of active vitamin D, and maternal intake of omega-3 fatty acids [30].

A condition resembling T1DM can be developed when certain drugs decrease the synthesis of insulin or harm β-cells. In 5 to 10% of people who use the antiviral drug didanosine, pancreatic inflammation develops, occasionally leading to long-lasting β-cell destruction. Similarly, diabetes and β-cell damage occur in up to 5% of those taking the anti-protozoal drug pentamidine. Other medications including statins (which may also harm beta

cells), tacrolimus and cyclosporin A used to treat post-transplant immunosuppression, L-asparaginase used to treat leukemia, and gatifloxacin used to treat infection, all induce diabetes by reversibly lowering insulin secretion. T1DM develops as a result of accidental poisoning with the rodenticide Pyrinuron (Vacor). In 1979, the American market for pyrinuron was shut down [28, 29, 31].

T1DM is recognized from other forms of diabetes. Most commercially available tests search for antibodies to glutamic acid decarboxylase, the cytoplasm of beta cells, or Insulin, all of which are the targets of antibodies in roughly 80% of T1DM. IA-2 and ZnT8 are proteins found in beta cells, which are targeted by these antibodies in about 58% and 80% of T1DM, respectively. T1DM may be indicated by extremely low C-peptide levels [32].

The frequent administration of Insulin to control hyperglycemia is the cornerstone of treatment for T1DM. Numerous times each day, subcutaneous insulin injections with a syringe or an insulin pump are necessary, with doses altering to take into account changes in food consumption, blood glucose levels, and physical activity.

Maintaining blood sugar levels between 80 to 130 mg/dL before meals and 180 mg/dL after meals is the goal of therapy.To do this, diabetics frequently check their blood glucose levels at home. The American Diabetes Association (IDA) advises checking blood sugar six to ten times a day, ideally before each meal, before exercise, at sleep, sporadically after meals, and if hypoglycemia symptoms arise [30]. Hemoglobin A1C levels around 7% is the recommended target, according to the ADA [33-39].

4.2. Type 2 Diabetes Mellitus (T2DM)

Ketoacidosis is not common; however, abrupt onset of the hyperosmolar hyperglycemic condition is possible. 90% of diabetes cases are T2DM, while T1DM diabetes, and gestational diabetes make up the majority of the remaining 10%. In T1DM, there is a lower total level of Insulin needed to regulate blood glucose because an autoimmune-induced loss of insulin-producing beta cells in the pancreas. Diabetes is diagnosed using blood tests, such as those for glycated haemoglobin, the oral glucose tolerance test, and fasting plasma glucose (A1C).

The majority of T2DM may be prevented by eating sensibly (high in fruits and vegetables and low in sugar and saturated fats), staying at a healthy weight, and exercising often. The therapy includes dietary changes and

exercise. If blood sugar levels are not appropriately controlled, the medication metformin is frequently suggested. In the future, a lot more people might also need insulin injections. Routine blood sugar monitoring is indicated for those on insulin but may not be necessary for those taking tablets. Diabetes is frequently improved with bariatric surgery in obese patients. Since 1960, both T2DM and obesity rates have sharply grown. Compared to about 30 million in 1985, there were approximately 392 million persons with the condition as of 2015. Although T2DM is increasingly prevalent in young individuals, it often manifests itself in middle or older age. Ten years less life expectancy are related to T2DM. One of the first diseases to be named was diabetes, which was originally mentioned in an Egyptian book from around 1500 BCE. In the 1920s, researchers discovered the significance of insulin in the condition [40].

In addition to these, peripheral neuropathy, itching, recurrent vaginal infections, weariness, and impaired vision are other symptoms frequently present at the time of diagnosis. Taste loss is one of the potential additional symptoms. However, many people get a diagnosis after routine testing since they show no symptoms for the first several years. A tiny percentage of individuals with T2DM may experience hyperosmolar hyperglycemia. A confluence of hereditary and lifestyle factors brings on T2DM. While some of these factors, like food and obesity, are under one's control, others, including advancing age, female sex, and heredity, are not. In many places of Africa, women are more likely than males to be obese. A potential contributing factor to the nutritional state of a woman during fetal development is DNA methylation, which has been hypothesized as one possible mechanism [41, 42].

T1DM and T2DM are defined by the WHO as elevated blood sugar reading along with symptoms. Another way to diagnose diabetes is to have a glycated haemoglobin (HbA1c) level less than 48 mmol/mol (less than 6.5 DCCT%) or a random blood sugar level of greater than 11.1 mmol/L (200 mg/dL) along with typical symptoms. ADA suggested a requirement of 48 mmol/mol (6.5 DCCT%), unless the patient exhibits specific symptoms and has blood sugar levels > 11.1 mmol/L (> 200 mg/dL). The threshold for diabetes diagnosis is based on the relationship between results of glucose tolerance tests, fasting glucose, or HbA1c, and repercussions such retinal problems. Since fasting or arbitrary blood sugar levels are more practical for people, the glucose tolerance test is not advised. HbA1c has the benefits of not requiring fasting and more reliable results, but it also has the drawback of being more expensive than measuring blood glucose. According to estimates, 20% of Americans with diabetes are unaware that they have the condition [43].

In contrast to T1DM, which causes an absolute lack of Insulin due to the destruction of islet cells in the pancreas, and gestational diabetes, which is characterized by a recent onset of high blood sugars associated with pregnancy, T2DM is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency. Antibody testing may be helpful in verifying the diagnosis of T1DM if there is any doubt about it, whereas C-peptide levels could be helpful in confirming T2DM, where C-peptide levels are low in T1DM and normal or high in T2DM [43-48].

4.3. Gestational Diabetes

A woman who does not already have diabetes can acquire gestational diabetes (GD) if she has high blood sugar levels while pregnant. There are typically few symptoms associated with GD, but it raises depression, pre-eclampsia risk, and the need for a Caesarean delivery are all factors. Babies delivered to mothers with GD untreated are more likely to experience macrosomia, postpartum hypoglycemia, and jaundice. Diabetes also increases the risk of stillbirth if left untreated. Children are more likely than adults to become overweight and at the first prenatal appointment for high-risk individuals. Pregnancy exercise and maintaining a healthy weight are preventative measures. Treatment for GD includes a diabetic diet, physical activity, drug (like metformin), and occasionally insulin injections. With diet and exercise, most women can control their blood sugar. Four times a day blood sugar testing is frequently advised for people who are impacted. As soon as possible after birth, breastfeeding is advised. Depending on the demographic examined, GD affects 3-9% of pregnancies. The third trimester is when it is most prevalent. 1% of people under the age of 20, and 13% of it affects persons above the age of 44 [49].

According to the official definition, GD is “any degree of glucose intolerance with onset or first detection during pregnancy.” This concept recognizes the chance that a woman has DM, which may have developed while pregnant or previously undetected. Whether symptoms disappear after delivery has no bearing on the diagnosis; if pregnancy-related glucose intolerance lasts for longer than 24 to 28 weeks, a woman is identified as having GD. The White classification, named after Priscilla White, who initiated investigations on the effect of various kinds of diabetes on perinatal outcome, is commonly used to assess maternal and fetal risk.

According to this classification scheme, gestational diabetes has two subtypes:

Type A1 results on the oral glucose tolerance test (OGTT), but normal blood sugar levels when fasting and two hours after meals; only dietary changes are required to control blood sugar levels. Due to abnormal OGTT findings and abnormal glucose levels after meals or while fasting.

Type A2 requires further therapy with insulin or other medications. Reduced health issues for both mother and child due to GD treatment with diet and insulin. More labor inductions are also done in conjunction with GD treatment. The diabetes should be confirmed to be gone 6 weeks after delivery by performing another OGTT. After then, it is suggested to regularly screen for T2DM.

After giving delivery, women with GD who get lifestyle interventions seem to have less postpartum depressive symptoms and are more likely to reach their weight reduction objectives, who receive no therapies. Additionally, they have lower birthweight percentages and a lower likelihood of having kids who are large for gestational age. Which lifestyle modifications work best will require more investigation, though. Probiotics are used by certain GD patients, but it's unclear whether they have any advantages over conventional medicine for lowering blood sugar, treating hypertension, or starting labor early. Insulin therapy may be required if oral medications, exercise or diabetic diet are insufficient to regulate blood glucose levels [49-54].

Detecting GD is done with the O'Sullivan test. A patient who is fasting is given 50 g of glucose. A blood sample is taken every hour. Plasma values over 1500 mg/L suggest GD [55].

Treatment options include insulin therapy, medication, food, exercise, stopping cigarette smoking, weight reduction, dietary recommendations, a diabetic diet, and dietary fibre are all examples of self-care. Anti-diabetic drugs, blood thinners, statins, and insulin are some examples of medications [55, 56].

4.4. Miscellaneous Types of Diabetes

4.4.1. Latent Diabetes

It is becoming clear that certain individuals may have T1DM that develops slowly and is marked because of the existence of autoantibodies. T2DM who have been diagnosed quickly become insulin-dependent; Latent diabetes

(LADA), a T1DM variant that progresses gradually, may occur in these persons. Adult-onset autoimmune diabetes is distinguished from other types of autoimmune diabetes by the lack of a diabetes-related autoantibody and the presence of a need for insulin therapy for a certain amount of time following diagnosis [57].

4.4.2. Mature Onset Diabetes of the Young (MODY)

Mature onset diabetes of the young, often known as MODY, is an autosomal dominantly inherited variant of the condition brought on by heterozygous mutations in many transcription factors involved in the development and maturation of pancreatic beta-cells. Double diabetes is defined as the incidence of hyperglycemia in children and young adults with the concomitant presence of indicators common to both T1DM and T2DM.

4.4.3. Brittle Diabetes

T1DM is intrinsically unstable, which makes the disease fragile. A small percentage of T1DM, primarily young women, have persistently poor metabolic control, which is characterized by significant instability of glycemia readings and frequent, irregular hypoglycemia or diabetic ketoacidosis episodes that cannot be ascribed to other causes. These patients' quality of life is severely diminished, especially how frequently they experience acute episodes, hospital stays, and the rapid onset of chronic problems [58].

4.4.4. Diabetes Insipidus

Increased diluted urine output due to vasopressin deficiency, AVP resistance, or excessive water consumption characterizes diabetes insipidus. When the urine volume is greater than $21/m^2/24$ hours, which is around 150 mL/Kg/24 hours at birth, 100–110 mL/Kg/24 hours till the age of 2, and 40–50 mL/Kg/24 hours in older children and adults, polyuria is present. Neonatal DM is a single gene abnormality that manifests in the first six months of life. Not producing enough insulin, not gaining weight as soon as anticipated, and misdiagnosing T1DM with high plasma glucose [59]. Among the variables that cause diabetes are excessive growth hormone, polycystic ovarian disorders, insulin receptor abnormalities, lipodystrophy, obesity, and excessive glucocorticoids.

Conclusion

The prevalence of diabetes mellitus is rising globally, and females are more likely to develop it than males. Diabetes also has an impact on youngsters. Children with diabetes often exhibit symptoms of dehydration, chronic vomiting, metabolic disturbances, or major concurrent illnesses that call for appropriate therapy and intravenous rehydration. For the treatment of diabetes, there are many well-known treatments in the market, including Metformin, Insulin injection, and other medicines. The causes of diabetes mellitus include poor lifestyle choices, smoking, drunkenness, and other issues. For people with diabetes, blood sugar levels must be under control. The vast scope of the diabetes epidemic is highlighted in the WHO global report, as well as the opportunity to halt the current course of events. The UN Political Declaration on NCDs, the WHO NCD Global Action Plan, and the Sustainable Development Goals all provide the political framework for coordinated action to combat diabetes.

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