A Review Article on Types, Etiology and Complications of Diabetes

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Abstract: Diabetes, characterized by high blood sugar levels, arises from insufficient insulin production or ineffective insulin utilization by the body. It spans various forms, including Type 1, Type 2, and gestational diabetes, each presenting distinct etiological factors and complications. Type 1 diabetes results from autoimmune destruction of pancreatic beta cells, leading to absolute insulin deficiency, while Type 2 diabetes is marked by insulin resistance and progressive beta cell failure, often linked to obesity and sedentary lifestyles. Gestational diabetes emerges during pregnancy due to hormonal changes affecting insulin action, predisposing both mother and child to future health risks. Additionally, monogenic forms of diabetes, influenced by genetic mutations, further contribute to the disease's complexity. Environmental factors, such as hygiene levels, also play a significant role in diabetes prevalence, as evidenced by the hygiene hypothesis. Treatment strategies primarily involve insulin therapy and oral hypoglycemic drugs, while complementary herbal treatments gain attention for their potential benefits. Microvascular complications, including retinopathy, nephropathy, and neuropathy, pose significant health risks, while macrovascular complications such as cerebrovascular events, coronary artery disease, and peripheral vascular disease further exacerbate diabetes-related morbidity and mortality. Additionally, autoimmune disorders like autoimmune thyroid disease and autoimmune gastritis commonly coexist with diabetes, adding to the disease burden. Gestational diabetes presents unique challenges for both mother and child, underscoring the importance of effective management to mitigate associated risks. Understanding the multifaceted nature of diabetes and its complications is crucial for comprehensive care and prevention strategies.

Keywords: Diabetes, Etiology, Diabetes types, Environmental factors, Treatment, Complications.

INTRODUCTION

Diabetes is a condition that happens when your blood sugar (glucose) is too high. It develops when your pancreas doesn't make enough insulin or any at all, or when your body isn't responding to the effects of insulin properly. Diabetes affects people of all ages. Most forms of diabetes are chronic (lifelong), and all forms are manageable with medications and/or lifestyle changes. Glucose (sugar) mainly comes from carbohydrates in your food and drinks. It's your body's go-to source of energy. Your blood carries glucose to all your body's cells to use for energy.

When glucose is in your bloodstream, it needs help — a "key" — to reach its final destination. This key is insulin. If your pancreas isn't making enough insulin or your body isn't using it properly, glucose builds up in your bloodstream, causing high blood sugar.

Over time, having consistently high blood glucose can cause health problems, such as heart disease, nerve damage and eye issues.

There are several types of diabetes. The most common forms include:

*Type 1 diabetes due to beta cell destruction, nearly always insulin deficient);

*Type 2 diabetes (due to a progressive insulin secretory defect on the background of insulin resistance).

* Gestational diabetes: This type develops in some people during pregnancy. Gestational diabetes usually goes away after pregnancy. However, if you have gestational diabetes, you're at a higher risk of developing Type 2 diabetes later in life [1].

Type 1 diabetes

Type 1 diabetes or juvenile diabetes, develops most often in young people; however, type 1 diabetes can also develop in adults. In type 1, the body no longer makes insulin or enough insulin because the body's immune system has attacked and destroyed the cells (pancreatic Beta cells) that make insulin. Don't eat too much sugar, you will become diabetic-this is not true. A person with Type 1 diabetes developed the disease because their immune system destroyed the insulin-producing beta cells

Some rare forms of diabetes result from mutations or

changes in a single gene and are called as monogenic diabetes. Neonatal Diabetes mellitus (NDM) and Maturity-Onset Diabetes of the Young (MODY) are the two main forms of monogenic diabetes [2].

Type 2 diabetes

Type 2 diabetes or adult-onset diabetes, can affect people at any age, even children. However, type 2 diabetes develops most often in middle-aged and older people. People who are overweight and inactive are also more likely to develop type 2 diabetes. It usually begins with insulin resistance—a condition that occurs when fat, muscle, and liver cells do not use insulin to carry glucose into the body's cells to use for energy. As a result, the body needs more insulin to help glucose enter cells. At first, the pancreas keeps up with the added demand by making more insulin. Over time, the pancreas doesn't make enough insulin when blood sugar levels increase, such as after meals. If pancreas scan no longer make enough insulin, it is type 2 diabetes [3].

Gestational diabetes

Gestational diabetes can develop when a woman is pregnant. Pregnant women make hormones that can lead to insulin resistance. All women have insulin resistance later in their pregnancy. If the pancreas doesn't make enough insulin during pregnancy, a woman develops gestational diabetes. Overweight or obese women have a higher chance of gestational diabetes. It most often goes away after the baby is born. However, a woman who has had gestational diabetes is more likely to develop type 2 diabetes later in life. Babies born to mothers who had gestational diabetes are also more likely to develop obesity and type 2 diabetes [4].

ETIOLOGIC CLASSIFICATION

Type 1 Diabetes

Type 1 diabetes mellitus (T1DM) comprises several diseases of the pancreatic ß cells which lead to an absolute insulin deficiency. This is usually considered to be the result of an autoimmune destruction of the pancreatic ß cells (type 1A). Some patients with T1DM with no evidence of ß cell autoimmunity have underlying defects in insulin secretion often from inherited defects in pancreatic ß cell glucose sensing and from other genetic or acquired diseases.

Type 2 Diabetes

Type 2 diabetes mellitus (T2DM) is by far the more common type of diabetes and is characterized by insulin resistance resulting from defects in the action of insulin on its target tissues (muscle, liver, and fat), but complicated by varying and usually progressive failure of beta cells' insulin secretary capacity[2]. Most patients with T2DM in the US and Europe are overweight or obese, however in India and China, most T2DM patients have a lean body mass index (BMI), albeit with increased visceral and hepatic fat.

Monogenic Diabetes

Monogenic forms of diabetes are characterized by impaired secretion of insulin from pancreatic β cells caused by a single gene mutation. These forms comprise a genetically heterogenous group of diabetes including, maturity onset diabetes of the young (MODY), permanent or transient neonatal diabetes, and mitochondrial diabetes. MODY is the most common form of monogenic diabetes, with autosomal dominant transmission of one of several genes encoding a primary defect in insulin secretion [5].

Environmental Factors in Diabetes

Besides the familial predispositions, much evidence points to a major role of environmental factors in the disease pathogenesis. More than 60% of identical twins affected by T1DM are discordant for the disease and most of the non- diabetic twins lack islet cell autoantibodies. Over the past 3 decades, the disease frequency is on a steep rise in Western countries that cannot be explained by the accumulation of the susceptible genes. Africans, who dominate the tropics, and Chinese, both have low frequencies of the susceptible genes and low incidence rates of T1DM, except where there has been a high rate of Caucasian genetic admixture.

More persuasively, migrants from countries with low hygiene and low incidence rates of T1DM to countries with high hygiene and high incidence become as susceptible as the natives within a generation. Animals reared in sterile environments have early onsets and increased frequencies of diabetes while those infected with a variety of micro-organisms and parasites become protected [6]. The hygiene hypothesis was proposed. A strong causal relationship between prevailing level of community hygiene, especially

with respect to drinking water and the dramatic increase in the incidence of autoimmune diseases such as T1DM in the modern world, has been referred to as the hygiene hypothesis.

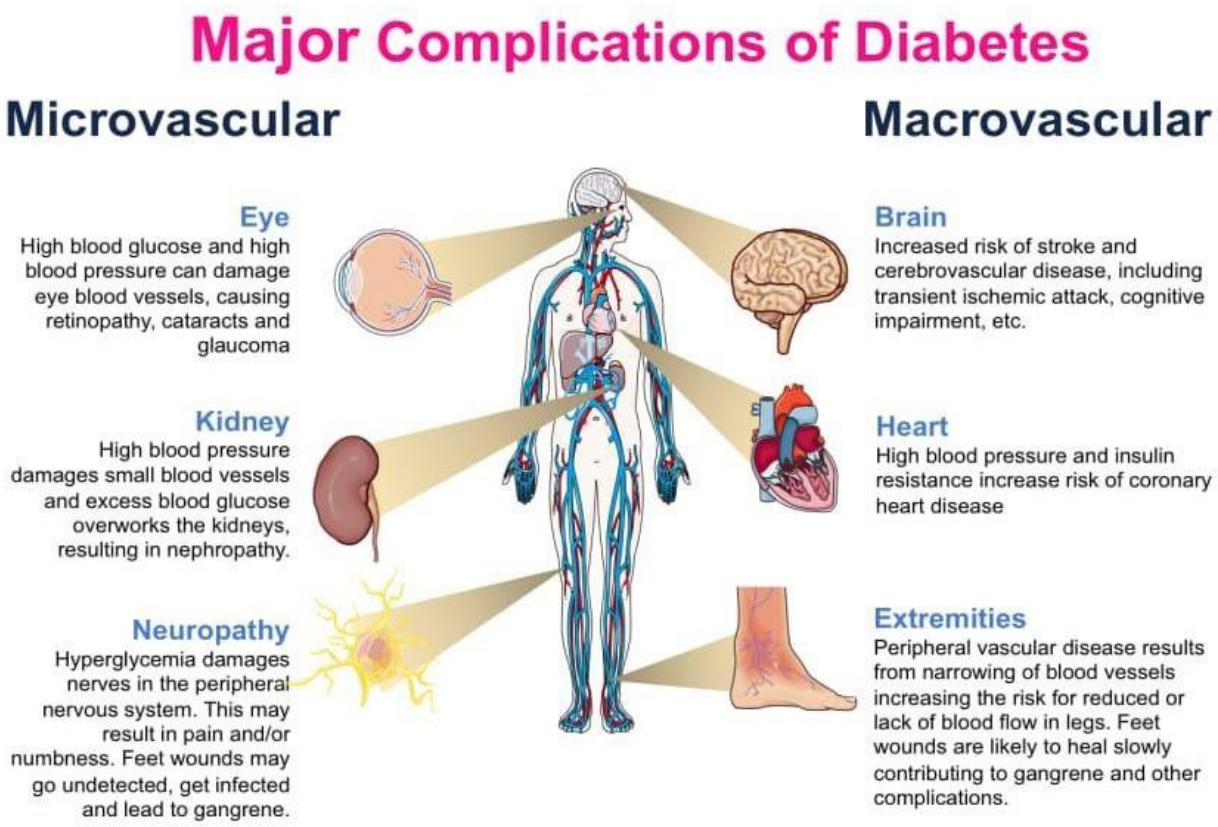
TREATMENT

Insulin and oral hypoglycemic drugs:

Insulin therapy should aim to mimic nature, which is remarkably successful both in limiting postprandial hyperglycemia and preventing hypoglycemia between meals. Site of administration of insulin injection is equally important for better and safe action of insulin and can be given by intramuscular or intravenous route. Different preparations of insulin are available such as human insulin, beef insulin, pork insulin. Insulin therapy is no free from complications and adverse effects. The most important adverse effect are weight gain and hypoglycemia when inappropriate dose of insulin is taken and when there is mismatch between meals and insulin injection. This is also due to reduced energy losses through glycosuria. Sulphonyl ureas such as glibenclamide, glipizide and biguanides such as metformin, phenformin are oral hypoglycemic drugs. Sulfonylureas cause hypoglycemia by stimulating insulin release from pancreatic ß-cells. They bind to sulfonylurea (SUR) receptors on the ß-cell plasma membrane, causing closure of adenosine triphosphate (ATP)- sensitive potassium channels, leading to depolarization of the cell membrane. This in turn opens voltagegated channels, allowing influx of calcium ions and subsequent secretion of preformed insulin granules. Acute administration of sulfonylureas to type 2 DM patient's increases insulin release from the pancreas and also may further increase insulin levels by reducing hepatic clearance of the hormone. Initial studies showed that a functional pancreas was necessary for the hypoglycemic actions of sulfonylureas [7]. Biguanides such as metformin is antihyperglycaemic, not hypoglycemic.

Herbal treatment of diabetes:

In the last few decades eco-friendly, bio-friendly, cost effective and relatively safe, plant-based medicines have moved from the fringe to the main stream with the increased research in the field of traditional medicine. There are several literature reviews by different authors about anti-diabetic herbal agents, but the most informative is the review by Atta-ar-Rahman who has documented more than 300 plant species accepted for their hypoglycaemic properties. This review has classified the plants according to their botanical name, country of origin; parts used and nature of active agents. One such plant is Momordica charantia (Family: Cucurbitaceae), WHO has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called the botanical garden of the world [8].



Microvascular complications Retinopathy:
Diabetic retinopathy (DR) is a well recognized complication occurring both in type 1 and type 2 diabetes mellitus and has been shown that nearly all type 1 and 75% of type 2 diabetes will develop DR after 15 years duration of diabetes.49 Patients with mild NPDR show a 3% incidence of diabetic macular edema (DME) but those with moderate to severe NPDR have a 40% incidence of DME. In the presence of proliferative diabetic retinopathy (PDR) there is a 71% incidence of DME.[9]Visual impairment in diabetic retinopathy is the consequence of diabetic macular edema and PDR.

Nephropathy:
Nephropathy is the leading cause of chronic renal failure, the initial marker being microalbuminurea, which can be screened by measurement of albumin to creatinine ratio in a random spot collection. Even though diabetic nephropathy can be categorized into stages: micro and macro albuminuria based on the values of urinary albumin excretion, yet it has been seen that the risk for developing diabetic nephropathy and cardiovascular disease starts even when urinary albumin excretion values are within the normoalbuminuric range.

Neuropathy:
Diabetic peripheral neuropathy is defined as stocking-glove neuropathy or somatic and/or autonomic neuropathy which affects the longest nerve first before progressing proximally. Distal symmetrical form of diabetic peripheral neuropathy otherwise known as diabetic sensorimotor peripheral neuropathy is the primary risk factor for the development of diabetic foot ulcer, responsible for 85% of lower extremity amputation in diabetes patient[10].

Macrovascular Complications Cerebrovascular events [CVA]:
Cerebrovascular diseases such as stroke, transient ischaemic attack(TIA) are more common in people with diabetes, it is three times more common in those with diabetes. Cerebral vascular disease affects blood flow to the brain, leading to TIA and stroke.

Coronary artery disease [CAD]:
A study conducted on diabetic population revealed

that more than 3 out of 4 diabetic patient die of causes related to atherosclerosis and in most cases (75%) because of CAD. Type 2 DM increases the risk of CAD by 2-4 times in the overall population.64CAD is caused by atherosclerosis characterized by the formation of plaques. With increase in size of the plaques there occurs angina; sudden rupture of the plaque leads to the acute coronary syndrome (ACS), which is a medical immergency.

Peripheral vascular disease [PVD]:
PVD also known as peripheral arterial disease (PAD) is an occlusive disease of the large peripheral arteries (especially of the legs) excluding the coronary and intracranial vessels, primarily caused by atherosclerosis. Traditional risk factors of PAD include age, diabetes, smoking, obesity and hypertension, whereas non-traditional risk factors include race, chronic kidney disease and hypercoagulable states [10,11] .

Some other complications are:
Diabetic foot:
By this, we refer to the lesions observed on the diabetics at the region by the knees and below and are related to pain, sensory disorder, skin dryness, development of calluses, wounds and ulcers, often complicated by severe local infections and leading to the development of gangrene with amputation of the fingers.
Autoimmune thyroid disease [ATD]: Autoimmune thyroiditis is a group of inflammatory thyroid disorders with either hypothyroid, euthyroid or hyperthyroid state. Type-1 Diabetes is often accompanied by autoimmune diseases. Autoimmune thyroid diseases are amongst the most common. Recent studies confirm an increased incidence of autoimmune thyroid diseases even in type-2 Diabetes. The occurrence of common features of autoimmune diseases and the co association of multiple autoimmune diseases in the same individual or family supports the suggestion that there may be common genetic factors [12].
Autoimmune gastritis [AIG]: Autoimmune gastritis is an autoimmune disease in which the stomach deteriorates because the immune system attacks the healthy cells of the stomach lining. It affects the upper two-thirds of the stomach because the antibody that the body is mistakenly producing binds to a specific cell in that area of the stomach's inner lining. These cells, the parietal cells, loose their ability to effectively produce the hydrochloric acid that they are supposed to. This means that people with gastritis are unable to efficiently absorb the vitamin B12 and iron, which results in iron-deficiency anemia and vitamin B12 deficiency and can ultimately lead to pernicious anemia [11].
Pernicious anemia: Pernicious anemia can be considered an end stage of autoimmune gastritis. Approximately 10- 15% of PCA-positive patients and up to 25% of those with autoimmune gastritis present with pernicious anemia.
Two mechanisms are responsible for vitamin B12 malabsorption in patients with pernicious anemia. First, the progressive loss of parietal cells leads to failure of intrinsic factor production and a reduction in vitamin B12 absorption. Second, intrinsic factor autoantibodies prevent the formation of the vitamin B12-intrinsic factor complex [13].
Complications of Gestational diabetes:
Most women who have gestational diabetes deliver healthy babies. However, uncontrolled blood sugar levels can cause problems for you and your baby.
Complications in your baby can be caused by gestational diabetes, including:

- Excess growth. Extra glucose can cross the placenta. Extra glucose triggers the baby's pancreas to make extra insulin. This can cause your baby to grow too large. It can lead to a difficult birth and sometimes the need for a C-section.
- Low blood sugar. Sometimes babies of mothers with gestational diabetes develop low blood sugar (hypoglycemia) shortly after birth. This is because their own insulin production is high.
- Type 2 diabetes later in life .Babies of mothers who have gestational diabetes have a higher risk of developing obesity and type 2 diabetes later in life.
- Death. Untreated gestational diabetes can lead to a baby's death either before or shortly after birth.

Complications in the mother also can be caused by gestational diabetes, including:

- Preeclampsia. Symptoms of this condition include high blood pressure, too much protein in the urine, and swelling in the legs and feet.
- Gestational diabetes. If you had gestational diabetes in one pregnancy, you're more likely to have it again with the next pregnancy [14,15].

CONCLUSION

To overcome diabetic complications requires a comprehensive approach that includes managing blood sugar levels, adopting a healthy lifestyle, regular medical check-ups, medication adherence, and seeking education and support. Firstly, controlling blood sugar levels through medication, dietary modifications, and regular monitoring is paramount. Additionally, adopting a healthy lifestyle, including regular exercise and a balanced diet, plays a pivotal role in preventing and managing complications. Moreover, attending regular medical check-ups enables healthcare professionals to assess overall health status, detect any emerging issues early, and adjust treatment plans accordingly. Adhering to prescribed medications is essential for maintaining optimal blood sugar control and preventing further complications. By taking proactive steps to control diabetes and prevent complications, individuals can lead healthier lives and reduce the risk of long-term health issues associated with the condition.

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