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Pathophysiology and Therapeutic Innovations in Diabetes Mellitus

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ABSTRACT :

Diabetes mellitus (DM) requires accurate diagnosis and treatment as it is a chronic condition. Type 1 diabetes is an autoimmune disease where the body's immune system mistakenly targets and destroys the beta cells in the pancreas that produce insulin. Type 2 diabetes is associated with numerous risk factors, including obesity, physical inactivity, aging, and family history. Monogenic diabetes is primarily caused by abnormal glucose sensing, malfunctioning beta cells, and inadequate insulin synthesis, all leading to hyperglycemia and the development of diabetes. Stopping smoking can improve overall health and reduce risk. Ayurvedic medicine, an ancient Indian medicinal system, offers a wide range of herbal compositions and therapies for the treatment of diabetes (madhumeha).

Keywords: Diabetes, Causes, Treatment

Introduction :

Diabetes is a long-term metabolic disease marked by high blood sugar (or glucose) levels brought on by the body's incapacity to make or utilize the hormone insulin. The hormone insulin, which is generated by the pancreas, helps the body's cells absorb glucose and use it for energy production or storage. This helps to control blood sugar levels.

2. Types of Diabetes:

Type 1 diabetes:

Although there are many varieties of diabetes, these are the specifics:
Affects 5–10% of diabetics, according to the Centers for Disease Control and Prevention (CDC).
Type 1 diabetes is an autoimmune condition in which the body's immune system mistakenly attacks and destroys the insulin-producing beta cells in the pancreas.
Without insulin, glucose cannot enter the cells, leading to high blood sugar levels (hyperglycemia).

Type 1 diabetes typically appears in childhood or adolescence and requires lifelong insulin therapy.
According to the Centres for Disease Control and Prevention (CDC), about 5-10% of people with diabetes have type 1 diabetes.
Type 1 diabetes is an autoimmune condition in which the body's immune system mistakenly attacks and destroys the insulin-producing beta cells in the pancreas [1].

Without insulin, glucose cannot enter the cells, leading to high blood sugar levels (hyperglycemia).
Type 1 diabetes typically appears in childhood or adolescence and requires lifelong insulin therapy.
According to the Centres for Disease Control and Prevention (CDC), about 5-10% of people with diabetes have type 1 diabetes [2].

Pathophysiology:
The immune system of the body unintentionally targets and kills the insulin-producing beta cells in the pancreas, which is the root cause of type 1 diabetes.
The immune system of the body, which is meant to defend against dangerous pathogens, mistakenly views the insulin-producing beta cells in the pancreatic islets as foreign substances in type 1 diabetes and launches an autoimmune reaction to eliminate them.
It is believed that a combination of genetic predisposition and environmental factors, such as viral infections, exposure to particular foods, or other environmental triggers, may have caused this autoimmune attack [3].
Insulin production declines as a result of beta cell loss, and eventually the pancreas is unable to produce enough insulin to properly control blood sugar levels.

Hyperglycemia, or elevated blood sugar, results from the body's inability to absorb glucose from the bloodstream into its cells in the absence of insulin. Consequently, the body starts to break down muscle and fat for energy, which leads to weight loss and the creation of ketones, which can develop into diabetic ketoacidosis (DKA), a potentially fatal illness.
It is thought that a complicated interaction between hereditary and environmental variables causes the autoimmune process associated with type 1 diabetes; however, the precise cause of the autoimmune response is yet unknown [4].
Once the autoimmune process starts, the beta cells are gradually and irreversibly destroyed, making survival entirely dependent on the delivery of exogenous insulin [5].

Type 2 diabetes:

Ninety to ninety-five percent of instances of diabetes are type 2. This kind of diabetes is the most frequent.
Type 2 diabetes is characterized by the body's failure to adequately regulate blood sugar levels due to either insufficient insulin production or resistance to its effects.
Type 2 diabetes is associated with a number of risk factors, such as obesity, physical inactivity, aging, and family history.
Although lifestyle variables are frequently linked to it, genetic susceptibility also plays a part.
Diabetes type 2 may usually be controlled with a mix of dietary and exercise modifications, as well as medication when needed.

Pathophysiology:
Insulin Resistance:
Type 2 diabetes is characterized by insulin resistance, a condition in which the body's cells lose their sensitivity to insulin, which lowers the body's absorption of glucose.
This resistance is frequently linked to sedentary behavior, bad eating habits, and obesity, especially the accumulation of visceral or abdominal fat [6].
In addition, aging, genetics, and other variables including oxidative stress and inflammation can all contribute to insulin resistance.
The body attempts to make up for this by creating more insulin, which results in hyperinsulinemia, or elevated blood levels of insulin [7].

2. Decreased Insulin Release:
Impaired insulin secretion results from the pancreatic beta cells' aging inability to continue producing enough insulin to combat insulin resistance.
This can eventually result in beta cell malfunction and apoptosis (cell death), which is partially caused by the beta cells' increased workload in producing more insulin.
Beta cell failure can also be caused by environmental and genetic causes, such as lipotoxicity (high levels of free fatty acids) and glucotoxicity (high blood glucose levels) [8].

3. Hyperglycemia:
Hyperglycemia, or elevated blood sugar, results from the body's decreased ability to control blood glucose levels as a result of insulin resistance and decreased insulin secretion [9].
A vicious cycle of insulin resistance and beta cell failure can be exacerbated by hyperglycemia.

4. Other Factors:
The development of insulin resistance and beta cell dysfunction can also be attributed to chronic inflammation and oxidative stress, which are frequently linked to obesity and a sedentary lifestyle.
The development of type 2 diabetes may also be influenced by genetic predisposition and specific environmental factors, such as exposure to chemicals or viral infections [10].

Type 2 diabetes develops and advances as a result of both insulin resistance and decreased insulin production. Early intervention can help control blood glucose levels and possibly postpone or avoid the onset of problems related to type 2 diabetes through lifestyle changes (diet, exercise, and weight management) and, if necessary, pharmaceutical treatment.

(3). Gestational Diabetes:
Appears in certain pregnant women and normally goes away after giving birth [11].
Raises the likelihood that the mother and the kid may experience type 2 diabetes in the future.

Pathophysiology:
The underlying cause of gestational diabetes mellitus (GDM), also known as the mechanism of action (MOA), is caused by a number of physiological changes and pregnancy-related variables.

1.Insulin resistance:
Progesterone, estrogen, and human placental lactogen (hPL), among other hormones produced by the placenta during pregnancy, are known to increase insulin resistance [12].

These hormones cause the mother's cells to become less sensitive to insulin, but they also aid in transferring nutrients from the mother to the growing foetus.

2. Increased insulin demand:
Increased metabolic demands occur during pregnancy, and the developing foetus needs a constant supply of glucose and other nutrients.
In order to overcome insulin resistance and maintain normal blood glucose levels, the mother's pancreatic beta cells must release more insulin to fulfil this increased demand [13].

3. Beta cell dysfunction:
Impaired insulin production occurs when pregnant women's increased insulin resistance and metabolic needs are not adequately compensated for by their pancreatic beta cells [14].
The hallmark of gestational diabetes is hyperglycemia, or elevated blood glucose levels, which can be brought on by this beta cell dysfunction.

4. Risk factors:
Obesity, advanced maternal age, a family history of diabetes, and some ethnic backgrounds (e.g., Hispanic, African American, Native American, and Pacific Islander) can all raise the chance of developing gestational diabetes [15].
Pre-existing insulin resistance or beta cell dysfunction may be made worse by these risk factors, and the physiological changes associated with pregnancy may make matters worse.

5. Consequences:
Uncontrolled prenatal diabetes can result in issues that affect both the mother and the growing foetus. These complications can include macrosomia, or excessive birth weight, preeclampsia, cesarean delivery, and a higher chance of both the mother and the child having type 2 diabetes later in life [16].

(4). Monogenic Diabetes:

- 1–5% of all cases of diabetes are brought on by a single gene mutation [17].
- Neonatal diabetes and young people with maturity-onset diabetes (MODY) are two examples.

Pathophysiology:
The pathogenesis of monogenic diabetes is mainly defined by aberrant glucose sensing, dysfunctional beta cells, and defective insulin production, which ultimately result in hyperglycemia and the onset of diabetes. To effectively manage monogenic diabetes and avoid complications, early diagnosis and adequate management—which may include lifestyle modifications and, in certain situations, targeted pharmaceutical interventions—are essential.

Symptoms: Depending on the kind of diabetes and how severe it is, different people may experience different symptoms. These are some typical signs of diabetes:

1.Type 1 Diabetes are as follows:

- Increased urination (polyuria) and excessive thirst (polydipsia).
- excessive hunger, or polyphagia.
- Unexpected weight reduction.
- Weakness and exhaustion.
- hazy vision.
- Cuts and bruises heal slowly.

2.Type 2 Diabetes are as follows:

- In the early stages of the disease, many persons with type 2 diabetes have no symptoms.
- more frequent urination and increased thirst.
- heightened appetite.
- Weary.
- hazy vision.
- Heals slowly from cuts and bruises.
- Hand or foot tingling or numbness (caused by neuropathy).

3.Gestational Diabetes:

- Many times, gestational diabetes has no distinct symptoms.
- Some women could feel more thirsty and need to urinate more frequently.
- Tiredness.
- Distorted eyesight.

It's crucial to remember that, particularly in the early stages of type 2 diabetes or gestational diabetes, the symptoms of the disease might occasionally be mild or nonexistent. Timely management and the prevention of consequences depend heavily on routine screening and early diagnosis [18].

Causes:

Diabetes develops because of a number of circumstances, including risk factors. These are diabetes's primary causes:

1.Type1 Diabetes:

An autoimmune condition in which the immune system of the body targets and kills the pancreatic beta cells that produce insulin.
Although the precise origin is unknown, environmental factors, such as viral infections, and genetics are thought to be involved.

2.Type2 Diabetes:

Insulin resistance: When cells in the body grow immune to the effects of insulin, blood sugar levels rise.
Impaired insulin secretion: In order to overcome insulin resistance, the pancreas cannot generate enough insulin.
Physical inactivity and obesity are two key lifestyle variables that increase the risk of insulin resistance and type 2 diabetes.
Genetic predisposition: The risk is increased if type 2 diabetes runs in the family.
Growing older: After the age of 45, in particular, there is an increased risk of type 2 diabetes.
Ethnicity: There is an increased risk for some ethnic groups, including American Indians, African Americans, Hispanic/Latino Americans, and Pacific Islanders.

3.Gestational Diabetes:

Pregnancy-related hormonal changes: elevated amounts of hormones such as human placental lactogen, which may cause insulin resistance.
Age and obesity: The risk increases with older mother age and being overweight or obese prior to pregnancy.
Family history: The risk of gestational diabetes is increased if a first-degree relative has the disease [19].

3. Prevention:

Diabetes is a chronic illness that can be avoided or postponed with a variety of dietary changes and preventative actions. These are a few methods for avoiding diabetes [23]:

1.Sustain a Healthy Weight: Type 2 diabetes risk can be considerably decreased by achieving and maintaining a healthy body weight with a balanced diet and frequent exercise.

2.Take Part in Regular Exercise: By increasing insulin sensitivity and glucose metabolism, participating in at least 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous-intensity aerobic activity each week can reduce the risk of type 2 diabetes.

3.Maintain a Healthful Diet: To lower the risk of type 2 diabetes, adopt a diet high in fruits, vegetables, lean proteins, whole grains, and healthy fats and low in processed carbohydrates, added sugars, and saturated fats.

4.Keep Your Weight in Check During Pregnancy: Reaching and preserving a healthy weight both before and throughout pregnancy.

5.Give Up Smoking: Type 2 diabetes is linked to a higher chance of smoking. In addition to lowering risk, quitting smoking can enhance general health.

6.Control your prediabetes: Modest weight loss and increased physical activity can help lower the risk of developing type 2 diabetes in those with prediabetes, which is defined as raised blood glucose levels but not high enough to be diagnosed as diabetes.

7.Give birth (to infants): Breastfeeding mothers and their offspring may reduce the chance of type 2 diabetes in later life [24].

4. Diagnosis:

1.Testing for fasting plasma glucose (FPG): Diabetes is defined as a fasting blood glucose level of 126 mg/dL (7.0 mmol/L) or above on two different occasions.

2.The OGTT, or oral glucose tolerance test, after consuming a glucose solution, a 2-hour blood glucose level of 200 mg/dL (11.1 mmol/L) or above is indicative of diabetes.

3.Test for Haemoglobin A1C (HbA1c):Diabetes is indicated by a HbA1c reading of 6.5% or above.

4.Test for Random Plasma Glucose :Diabetes may be indicated by a random blood glucose level of 200 mg/dL (11.1 mmol/L) or greater along with hyperglycemia symptoms (increased thirst, frequent urination, etc.)[25].

5. Treatment:

1.Diabetes Type 1:

- Since the body is unable to manufacture insulin, insulin therapy is necessary for the management of type 1 diabetes.
- Insulin pumps or injections are two ways that insulin can be given.
- It is required to test blood glucose levels regularly and modify insulin dosage.

2.Diabetes Type 2:

- The cornerstone of treatment is a change in lifestyle, which includes maintaining a healthy weight, engaging in regular physical activity, and eating a balanced diet.
- Sulfonylureas, DPP-4 inhibitors, and metformin are a few examples of oral drugs that may be administered to assist regulate blood glucose levels.

3.GestationalDiabetes:

- Changes in lifestyle are advised, such as eating a balanced diet and doing frequent exercise.
- Insulin or oral medicines may be administered to regulate blood glucose if lifestyle modifications prove ineffective.

4.Observation and Administration:

- using continuous glucose monitoring (CGM) devices or self-testing on a regular basis to monitor blood glucose levels.
- visits with medical professionals on a regular basis to monitor diabetes management and modify treatment as necessary.
- management of probable side effects, such as renal, heart, and eye problems, by routine testing and suitable intervention [26].

6. Drugs used in diabetes treatment:

Diabetes is treated with a variety of medications, most commonly type 2 diabetes. These are a few of the frequently utilized drug classes:

1.Metformin:

- One biguanide drug that is frequently used as the first line of treatment for type 2 diabetes is metformin.
- It aids in lowering the amount of glucose produced by the liver, raising insulin sensitivity, and encouraging the uptake of glucose by peripheral tissues.

2.Sulfonylureas:

- Glipizide and glyburide are examples of sulfonylureas that induce the pancreas to generate more insulin.
- When monotherapy is insufficient for glycemic control, they are frequently used in conjunction with metformin or other medicine [27].

3.Meglitinides:

- The pancreas releases insulin in response to meals when meglitinides, such as nateglinide and repaglinide, are taken.
- They are taken prior to meals and have a shorter half-life than sulfonylureas.

4.TZDs, or thiazolidinediones:

- TZDs, such as pioglitazone and rosiglitazone, improve the sensitivity of liver, fat, and muscle tissues to insulin.
- They frequently accompany metformin in usage.

5.Inhibitors of Dipeptidyl Peptidase-4 (DPP-4):

- DPP-4 inhibitors, such as linagliptin and sitagliptin, extend the effects of incretin hormones, which increase the release of insulin and decrease the synthesis of glucagon.
- They have a low chance of hypoglycemia and are usually well tolerated.

6.Agonists of glucagon-like Peptide-1 (GLP-1):

- GLP-1 agonists, such as semaglutide and liraglutide, imitate the activities of the incretin hormone GLP-1, which inhibits the release of glucagon and increases insulin secretion.
- These are injectable drugs that have the potential to aid in weight loss.

7.Inhibitors of Sodium-Glucose Cotransporter-2 (SGLT2):

- SGLT2 inhibitors, such as empagliflozin and dapagliflozin, decrease blood glucose levels by preventing the kidneys from reabsorbing glucose, which increases the excretion of glucose in the urine.
- Additionally, they might improve renal and cardiovascular outcomes.

8.Insulin:

- The hormone insulin controls blood glucose levels. It is crucial for treating type 1 diabetes and may also be necessary for certain people with type 2 diabetes.
- Insulin pumps can be used to continuously infuse insulin or administer injections of different types of insulin, including short-acting, intermediate-acting, long-acting, and rapid-acting [28].

7. Ayurvedic medicine used in diabetes:

Ayurvedic medicine, an age-old Indian medical system, provides a range of herbal formulations and therapies for the treatment of diabetes mellitus (madhumeha). The following are a few popular Ayurvedic treatments for diabetes:

1. Bitter melon (Momordica charantia): Bitter melon, sometimes called karela, is one of the most popular Ayurvedic herbs for diabetes treatment. It has ingredients such polypeptide-p, vicine, and charantin that may have hypoglycemic (blood sugar-lowering) properties [29].
2. Fenugreek (Trigonella foenum-graecum): In addition to being high in fiber, fenugreek seeds also contain substances like 4-hydroxyisoleucine that may improve glucose metabolism and insulin sensitivity.
3. Turmeric (Curcuma longa): Curcumin, found in turmeric, a popular spice in Indian cooking, has been demonstrated to offer possible antidiabetic benefits via enhancing insulin sensitivity and lowering inflammation [30].
4. Ashwagandha (Withania somnifera): Indian ginseng, or ashwagandha, is an adaptogenic herb used in Ayurveda medicine to treat a variety of ailments, including diabetes. It is thought to possess antioxidant and hypoglycemic qualities.
5. Shilajit (Asphaltum punjabinum): Ayurveda uses shilajit, a blackish-brown fluid that is exuded from rocks in the Himalayan region, to treat a variety of illnesses, including diabetes. It is thought to possess hypoglycemic and antioxidant qualities.

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