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Diabetes Mellitus: A Leading Cause of Death Worldwide

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ABSTRACT: Diabetes mellitus, or commonly known as diabetes, is a metabolic disorder characterized by chronic hyperglycemia which results in insulin resistance, impaired insulin synthesis, or sometimes both. Diabetes affects roughly 400 million people worldwide and the majority being those who are from middle to low income countries. With 1.5 million diabetes related deaths worldwide each year, this literature review aims to give information about the 2 types of diabetes and also highlighting the appropriate preventative measures. Type 1 diabetes refers to the lack of insulin production and type 2 diabetes refers to lower production of insulin and increased insulin resistance; both will result in hyperglycemia in diabetic patients. Furthermore, this literature review also aims to explore and describe the pathogenesis and treatments of the 2 types of diabetes.

KEYWORDS: diabetes, prevention, pathogenesis, type 1, type 2.

1. INTRODUCTION

1.1 What is Diabetes

Diabetes is a chronic ailment distinguished by elevated glucose levels in the bloodstream, the body's dominant source of glucose. There are two ways to gain glucose. First, our body produces glucose; however, we can also gain glucose when we consume food. Insulin is a hormone assembled by the pancreas, which helps transport glucose in your cells for energy. If an individual experiences diabetes, their body does not produce adequate quantities of insulin or does not operate insulin properly, which could impact glucose to remain in the blood and not contact cells. This condition can cause long-term harm to other organs in your body and some types of cancer.

1.2 What is Type 1 Diabetes

Type 1 diabetes is called insulin-dependent. It occurs when the pancreas does not produce sufficient amounts of insulin or does not produce insulin at all. Insulin helps to transport blood glucose to enter the cells in your body. Without insulin, blood sugar will not be able to build up in the bloodstream. High blood sugar damages the body, and it also leads to severe symptoms and complications of diabetes. Type 1 diabetes usually develops in children and teens; however, it is less common than Type 2 diabetes which only 5 to 10 percent of people have type 1 diabetes.

1.3 What is Type 2 Diabetes

Type 2 diabetes is a condition that occurs when there are problems in the way that the body controls and uses glucose as a source of energy which can lead to a long-term condition resulting in excessive glucose circulating in the bloodstream; it then leads to disorders in the circulatory, nervous and immune system. There are primarily two problems that cause type 2 diabetes. First, it is when the pancreas cannot produce adequate insulin, and cells respond poorly to insulin and take in less glucose. Type 2 diabetes is common in more senior adults, but there is an increasing number of younger patients with obesity, which leads to more cases of type 2 diabetes in younger people.

2.0 CAUSES

2.1 Causes for type 1 diabetes Genetics

Type 1 diabetes is significantly influenced by genetic predisposition. (*What Is Diabetes?*, 2023)

The chance of developing the illness is enhanced by specific genes. People who have a family history of type 1 diabetes are more prone to the condition. However, not all people with these genetic risk factors will go on to acquire diabetes, indicating that environmental factors also play a crucial role.

Environmental Factors

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Environmental factors are believed to trigger the autoimmune response leading to type 1 diabetes in genetically susceptible individuals.(*What Is Diabetes?*, 2023)

The destruction and the loss of pancreatic beta cells are thought to be linked to viral infections, notably enteroviruses. These viruses might set up an immune response that unintentionally targets the beta cells and kills them.

2.2 Causes for type 2 diabetes

Poor dietary choices

An example of poor dietary choice could be for example a diet that is high in refined carbohydrates and low in fiber can also contribute to the development of type 2 diabetes. (*What Is Diabetes?*, 2023) Refined carbohydrates, such as white bread, white rice, and sugary cereals, are quickly digested and absorbed, causing a rapid rise in blood sugar levels. This repeated spike in blood sugar can strain the pancreas, leading to increased insulin production and, ultimately, insulin resistance.

Overweight, and physical inactivity

Insulin resistance and type 2 diabetes are often seen in individuals who are obese (“Symptoms &Amp;Amp; Causes of Diabetes,” 2023). The distribution of body fat around the body is also a factor to the development of the conditions. Excessive fat accumulation around the abdomen, commonly referred to as visceral fat or belly fat, is linked to insulin resistance, and type 2 diabetes.

Insulin resistance

Insulin resistance is a major factor in the development of type 2 diabetes (“Symptoms &Amp;Amp; Causes of Diabetes,” 2023). The resistance of insulin disrupts the normal regulation of blood sugar levels, thus contributing to the onset of type 2 diabetes. In individuals with insulin resistance, the body's cells, particularly those in the liver, muscles, and adipose tissue, become less sensitive to insulin. As a result, glucose uptake by these cells is significantly decreased, leading to hyperglycemia. To counter the effects of decreased sensitivity of cells to insulin, the production of insulin is increased in the pancreas to compensate for its efficiency. The increased insulin production, known as hyperinsulinemia, is an early response to insulin resistance. However overtime, the body struggles to keep up with the elevated level of insulin production, leading to a decline in insulin production after a period of time. As insulin resistance persists and insulin production decreases, the body faces difficulty in regulating blood sugar levels effectively. This imbalance leads to the development of type 2 diabetes, where blood sugar levels become chronically elevated.

Genetics

Genetics play a notable role in the development of type 2 diabetes. Having a family history of the condition can increase an individual's risk, as there are specific genetic variants that can influence susceptibility to the disease. There are several genetic variants that have been identified as associated with increasing the risk of type 2 diabetes. These variants can affect various aspects of glucose and insulin metabolism, including insulin production, insulin action, and the regulation of blood sugar levels.

3.0 HEALTH PROBLEMS

Over an extended period, elevated levels of glucose in the bloodstream can lead to various complications, which may include:

3.1 What are the mechanisms by which diabetes can cause retinopathy?

Diabetic retinopathy is an ocular disorder that can lead to vision impairment and even complete blindness in individuals with diabetes. (*Diabetic Retinopathy | National Eye Institute*, n.d.) This condition primarily affects the blood vessels located in the retina, which is the light-sensitive layer of tissue situated at the back of the eye. Therefore, if you are living with diabetes, it is of utmost importance to undergo a comprehensive dilated eye examination at least once annually. Initially, diabetic retinopathy may exhibit no noticeable symptoms, but early detection plays a crucial role in taking proactive measures to safeguard your eyesight.

In addition to regular eye exams, effectively managing your diabetes through consistent physical activity, a balanced diet, and adherence to prescribed medication can significantly contribute to the prevention or delay of vision loss. By taking these proactive measures, you can actively work towards preserving your visual health and well-being.

What causes diabetic retinopathy?

Diabetic retinopathy arises as a consequence of elevated blood sugar levels resulting from diabetes.(*Diabetic Retinopathy | National Eye Institute*, n.d.) Prolonged exposure to excessive sugar in the bloodstream can inflict damage upon the retina, which

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is the light-sensitive portion of the eye responsible for detecting light and transmitting signals to the brain via the optic nerve situated at the back of the eye.

Diabetes, as a systemic condition, adversely affects blood vessels throughout the body. In the context of the eyes, the detrimental process commences when sugar obstructs the small blood vessels that supply the retina, leading to fluid leakage or bleeding. In response to these obstructed vessels, the eyes attempt to compensate by generating new blood vessels that exhibit impaired functionality. Consequently, these newly formed blood vessels are prone to easy leakage or bleeding, exacerbating the damage to the retinal tissue.

3.2 What are the underlying mechanisms through which diabetes can lead to foot problems?

Individuals with diabetes often experience foot-related complications, which develop gradually as a result of elevated blood sugar levels damaging the nerves and blood vessels in the feet. (National Library of Medicine, n.d.) This condition, known as diabetic neuropathy, manifests as numbness, tingling, pain, or a loss of sensation in the feet.

The absence of pain perception can pose a significant problem since individuals may not be aware of cuts, blisters, or ulcers (open sores) on their feet. Consequently, such wounds are susceptible to infection. The impaired blood vessels associated with diabetes can further hinder proper blood circulation in the feet, leading to poor healing of infections.

Infections coupled with inadequate blood flow can give rise to gangrene, a condition characterized by the progressive death of muscle, skin, and other tissues. In cases where an infection or non-healing foot ulcer persists despite treatment, amputation may be necessary. Amputation involves surgically removing the damaged toe, foot, or a portion of the leg. While this procedure may prevent the spread of a severe infection and potentially save a person's life, it remains a last resort.

3.3 What are the underlying mechanisms through which diabetes can impact the oral cavity?

Diabetes can have an impact on oral health through alterations in saliva, the fluid responsible for maintaining moisture in the mouth. (Ahmad & Haque, 2021) Saliva plays a crucial role in preventing tooth decay by rinsing away food particles, inhibiting bacterial growth, and counteracting the acids produced by bacteria. Moreover, it contains minerals that aid in protecting oral tissues and combating tooth decay.

However, diabetes and certain medications used for its treatment can diminish the production of saliva by the salivary glands. Reduced saliva flow increases the risk of dental cavities, gum disease, and other oral health problems.(Ahmad & Haque, 2021)

Furthermore, diabetes can elevate the levels of glucose (blood sugar) in saliva. Elevated blood glucose levels can lead to an accumulation of glucose in saliva. This glucose serves as a nutrient for harmful bacteria, which, in combination with food, forms a soft, adhesive film known as plaque. If plaque is not effectively removed, it can harden near the gum line, forming a substance called tartar. Tartar buildup can contribute to gum disease.

If left untreated, these oral health issues can result in tooth loss. Research indicates that nearly 25% of adults aged 50 and above with diabetes in the United States experience severe tooth loss, compared to approximately 16% of those without diabetes.

3.4 What are the underlying mechanisms through which diabetes can lead to stroke

Hypertension, diabetes, smoking, and dyslipidemia are major risk factors for stroke that can be modified through lifestyle changes and medical interventions.(Chen et al., 2016b) Among these, diabetes is a well-established risk factor for stroke. It can induce pathological changes in blood vessels at various locations, and if the cerebral vessels are directly affected, it can lead to a stroke.

Furthermore, individuals with stroke and uncontrolled glucose levels tend to experience higher mortality rates and poorer outcomes post-stroke. However, the association between tight control of hyperglycemia and improved outcomes during the acute phase of stroke requires further investigation through Phase III clinical trials.

Taking measures to control diabetes, along with addressing other associated risk factors, is an effective approach for preventing both initial strokes and recurring strokes.(Chen et al., 2016b) By managing these modifiable risk factors, individuals can significantly reduce their risk of stroke occurrence and improve their overall health outcomes.

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3.5 What are the mechanisms by which diabetes can lead to chronic kidney disease?

The kidneys are composed of numerous tiny filters called nephrons. In the case of diabetes, high blood sugar levels can gradually cause damage to the blood vessels in the kidneys and impair the function of nephrons. (*Diabetes and Kidney Disease (Stages 1-4)*, 2022) Additionally, individuals with diabetes often develop high blood pressure, which further contributes to kidney damage. (*Make the Connection*, 2021)

Chronic Kidney Disease typically progresses slowly and does not exhibit noticeable signs or symptoms in its early stages. As a result, individuals may remain unaware of the condition unless their doctor specifically tests for it.

Diabetic nephropathy is a common complication of both type 1 and type 2 diabetes.(*Make the Connection*, 2021) Poorly controlled diabetes can lead to damage in the clusters of blood vessels responsible for filtering waste from the blood in the kidneys. This, in turn, can result in kidney damage and the onset of high blood pressure.

High blood pressure can exacerbate kidney damage by increasing pressure within the delicate filtration system of the kidneys.

Diabetes can harm the kidneys through the following mechanisms:

1. Blood vessels inside the kidneys: Elevated blood sugar levels can narrow and obstruct the small blood vessels within the kidney's filtering units. Consequently, the kidneys suffer damage, and a protein called albumin, which should remain in the blood, leaks into the urine.
2. Nerves in the body: Diabetes can also inflict damage on the nerves throughout the body. These nerves play a vital role in transmitting messages between the brain and various body parts, including the bladder. When the nerves controlling the bladder are damaged, individuals may lose the sensation of a full bladder. The pressure exerted by a full bladder can harm the kidneys.
3. Urinary tract: Prolonged retention of urine in the bladder increases the risk of urinary tract infections. Bacteria thrive in urine with high sugar levels, leading to infections. While such infections typically affect the bladder, they can potentially spread to the kidneys. (*Make the Connection*, 2021)

3.6 What are the underlying mechanisms by which diabetes can be associated with nerve problems?

Diabetic neuropathy is a condition characterized by nerve damage that occurs as a result of diabetes. (Feldman, 2019) This complication is commonly observed in individuals with both type 1 and type 2 diabetes. The underlying mechanism involves the prolonged presence of high blood sugar levels, which can initiate a cascade of events leading to nerve damage.

Elevated blood sugar levels associated with diabetes can trigger the production of excessive reactive oxygen species (ROS) within the body. ROS are highly reactive molecules that can cause damage to cells and tissues, including nerves. The increased oxidative stress generated by ROS can impair the structure and function of nerve cells, resulting in nerve damage.

Additionally, persistent hyperglycemia can disrupt the energy metabolism of nerve cells, leading to an imbalance in cellular processes. This disruption can lead to the accumulation of toxic substances within the cells, further contributing to nerve dysfunction and damage.

The complex interplay of these factors, including increased oxidative stress and metabolic disturbances, contributes to the development of diabetic neuropathy.(Feldman, 2019)

Managing blood sugar levels and implementing lifestyle modifications to control diabetes are crucial in preventing or slowing down the progression of this condition. Additionally, early detection and treatment of diabetic neuropathy can help mitigate symptoms and improve overall quality of life for individuals affected by this complication.

3.6 What are the underlying mechanisms by which diabetes can be linked to skin conditions?

When diabetes affects the skin, it often indicates that blood sugar levels have been consistently high. Certain skin changes may even manifest before a diabetes diagnosis, while others could indicate the need for adjustments in diabetes treatment.

Hyperglycemia, or high blood sugar, can have detrimental effects on blood vessels, including those supplying the skin. Impaired blood flow restricts the delivery of oxygen and vital nutrients to the skin cells, rendering them more susceptible to infections, delayed healing, and various skin issues. Moreover, elevated blood sugar levels provide an abundant food source for bacteria, creating an ideal environment for their growth. Consequently, individuals with diabetes face an increased risk of developing skin infections. (*Diabetes and your skin* 2022)

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4.0 TREATMENTS

4.1 Treatments for Type 1 Diabetes

For individuals with Type 1 diabetes, there are two potential options for managing the condition:

1. Insulin pumps: Insulin pumps offer an alternative to insulin injections using a pen. They provide more flexibility in diabetes management. Further information on insulin pumps, including the eligibility criteria outlined by the National Institute for Health and Care Excellence (NICE) to qualify for a free pump, can be obtained. (Uk, n.d.-b)
2. Islet cell transplant: People with Type 1 diabetes may have the opportunity to undergo an islet cell transplant. This procedure can help prevent severe episodes of low blood sugar (hypoglycemia). More information regarding islet cell transplants, including their nature and the steps to access this treatment, is available. (Uk, n.d.-b)

4.2 Treatments for Type 2 Diabetes

For individuals with Type 2 diabetes, various treatment options are available to manage blood sugar levels:

1. Medications: Metformin is the most common tablet prescribed, but there are multiple types available. Some medications stimulate insulin production by the pancreas (e.g., sulphonylureas), while others aid weight loss if needed. The choice of medication depends on individual circumstances and is determined through consultation with a doctor. (Uk, n.d.-b)
2. Weight loss surgery: Different surgical procedures targeting the stomach or intestine can help individuals with obesity lose weight. Studies have shown that weight loss surgeries can lead to remission of Type 2 diabetes.
3. Diet and exercise: Many people with Type 2 diabetes manage their condition through lifestyle modifications, including a healthy diet and increased physical activity. Research, such as the DiRECT study, has demonstrated that weight loss can effectively induce remission of Type 2 diabetes. Information and guidance on adopting a healthy lifestyle are available to support individuals.
4. Insulin: While not always necessary immediately, insulin may be used as a short-term treatment to rapidly lower high blood sugar levels in some individuals with Type 2 diabetes. Certain circumstances, such as pregnancy, severe illness, or surgery, may also require insulin. If other medications have not effectively managed blood sugar levels or are unsuitable, insulin treatment may be initiated. It is important to attend medical appointments and continue healthy lifestyle practices, such as staying active and maintaining a nutritious diet, to reduce the risk of diabetes complications. Weight gain may be observed when initiating insulin therapy, but it is essential to remember that this is not the individual's fault. (Uk, n.d.-b)

5.0 PREVENTIONS

Achieving and maintaining weight loss is crucial for diabetes prevention. By aiming to lose 5 to 10% of current body weight, such as 5 to 10 kilograms if you weigh 100 kilograms, you can significantly reduce the risk of developing diabetes or delay its onset. Sustaining this weight loss is equally important to prevent regaining the lost weight. (*What Is Diabetes?*, 2023)

It is essential to follow a healthy dietary plan, which involves reducing overall calorie intake and making wise food choices. This includes eating smaller portions, limiting the consumption of fats and sugars, and focusing on a diverse array of foods from all food groups, with an emphasis on whole grains, fruits, and vegetables. It is recommended to moderate the intake of red meat and avoid processed meats to promote better health outcomes.

Regular exercise provides numerous advantages, including weight management and improved blood sugar control, thereby lowering the risk of developing type 2 diabetes. Aiming for at least 30 minutes of physical activity most days of the week is advised. If you have been physically inactive, seeking guidance from a healthcare professional can help determine suitable types of exercise and gradually progress towards your desired goals.

Consulting with your healthcare provider is essential to explore additional preventive measures specific to your situation. Depending on your level of risk, your provider might suggest diabetes medications or other interventions to further delay or prevent type 2 diabetes. Regular communication with your healthcare team is essential for personalized guidance and support in managing your health. (*What Is Diabetes?*, 2023)

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6.0 PATHANOGENESIS

6.1 Type 1 Diabetes

Certain genes, specifically variations in human leukocyte antigen (HLA) genes, such as HLA-DR and HLA-DQ, increase the risk of developing type 1 diabetes. These genes are involved in regulating the immune response, and their variants can contribute to the immune system mistakenly attacking beta cells. Type 1 diabetes is characterized by an autoimmune response, where the immune system mistakenly identifies beta cells as foreign and attacks them. (DiMeglio et al., 2018d) Environmental triggers, such as viral infections or dietary factors, may initiate the autoimmune response in susceptible individuals. The triggering event leads to the activation of specific immune cells, particularly T cells, which play a central role in the autoimmune process. Cytotoxic T cells and helper T cells are involved in the destruction of beta cells. Cytotoxic T cells directly attack and destroy beta cells, while helper T cells contribute to the inflammatory response and amplify the autoimmune reaction. Once inside the pancreatic islets, the activated immune cells release cytokines and other inflammatory mediators that further promote the destruction of beta cells. This inflammatory response leads to the disruption and loss of beta cell function. As the autoimmune response progresses, the destruction of beta cells results in a decline in insulin production. Insulin is crucial for regulating blood sugar levels, so the loss of insulin production leads to elevated blood glucose levels. As beta cell destruction reaches a critical threshold, individuals begin experiencing symptoms associated with high blood sugar levels, such as excessive thirst, frequent urination, unexplained weight loss, fatigue, and blurred vision. (DiMeglio et al., 2018d)

6.2 Type 2 Diabetes

There is a strong genetic component to type 2 diabetes, with certain genes being associated with an increased risk. These genes influence factors such as insulin production, insulin action, and glucose metabolism. Insulin resistance: Insulin resistance occurs when the body's cells become less responsive to the effects of insulin, leading to decreased glucose uptake from the bloodstream. This condition is influenced by obesity, physical inactivity, and certain hormonal factors. Adipose tissue (fat cells) releases inflammatory substances and hormones that can interfere with insulin signaling, contributing to insulin resistance. Beta cell dysfunction: In type 2 diabetes, the beta cells in the pancreas that produce insulin may become dysfunctional over time. Initially, the beta cells compensate for insulin resistance by producing more insulin. However, as insulin resistance persists, the beta cells may gradually lose their ability to secrete sufficient insulin, leading to relative insulin deficiency. Glucose intolerance and hyperglycemia: Insulin resistance and beta cell dysfunction result in impaired glucose regulation. The body's ability to control blood sugar levels becomes compromised, leading to hyperglycemia. Initially, this manifests as impaired glucose tolerance, where blood sugar levels rise after meals but return to normal over time. However, as the disease progresses, the body struggles to maintain normal blood sugar levels, resulting in persistent hyperglycemia. Metabolic abnormalities: Chronic hyperglycemia can lead to various metabolic abnormalities, such as increased liver glucose production, impaired suppression of glucagon (a hormone that raises blood sugar levels), and altered lipid metabolism. These abnormalities further contribute to elevated blood sugar levels and the development of other metabolic complications often associated with type 2 diabetes, such as dyslipidemia (abnormal blood lipid levels) and cardiovascular disease. (Galicia-Garcia et al., 2020)

7.0 CONCLUSION

Diabetes is a chronic metabolic illness that causes high blood sugar levels. Based on its underlying causes and mechanisms, there are many forms of diabetes. Type 1 diabetes and type 2 diabetes are the two main kinds of the disease. An autoimmune disease known as type 1 diabetes occurs when the body's immune system mistakenly targets and kills the insulin-producing cells in the pancreas. Lack of insulin synthesis as a result causes unchecked high blood sugar levels. Contrarily, type 2 diabetes is mostly characterized by insulin resistance, which means that the body's cells stop responding to insulin. The pancreas first responds by manufacturing more insulin, but eventually it might not be able to keep up with the increased demand. Diabetes is a severe disease that affects a wide range of patients and should not be overlooked; therefore, precautions should be taken to prevent the illness.

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