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REVIEW ARTICLE

Study of Retinopathy and Microalbuminuria and Their Relation with Type 2 Diabetes Mellitus

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ABSTRACT

Diabetic retinopathy (DR) is a multifactorial microvascular complication of diabetes mellitus caused by damage to the blood vessels of the retina, the light-sensitive tissue located at the back of the eye. DR has been included by the World Health Organization in the priority list of eye diseases that can be partly prevented but not cured yet. Radiation retinopathy (RR) is a chronic and progressive condition that may result from exposure to any source of radiation, including external beam radiation, plaque brachytherapy, proton beam radiation, helium ion radiotherapy, and gamma knife radiotherapy. RR may be secondary to the treatment of intraocular tumors such as choroidal melanomas, retinoblastomas, and choroidal metastasis or from unavoidable exposure to excessive radiation from the treatment of cephalic, nasopharyngeal, orbital, and paranasal tumors among other malignancies. Microalbuminuria is a condition where a small amount of a protein called albumin is present in the urine. It can be a sign of kidney damage, especially in people with diabetes or high blood pressure. This review article summarizes study of DR, microalbuminuria, and type 2 diabetes mellitus and their correlation with each other.

Keywords: Conventional treatment, Diabetic retinopathy, Microalbuminuria, Type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus refers to a group of diseases that affect the body's blood sugar, i.e., glucose. Glucose plays a vital role in health because it is an important source of energy for the cells that make up the muscles and tissues. Glucose is the main source of fuel for the brain.

Types of diabetes

There are two types of diabetes.

1. Type 1 diabetes
2. Type 2 diabetes.

Type	Characteristic feature	Symptoms
Type I Type I	Less secretion of glucose due to damage of β cells. Due to unknown cause self-antibody damages our body tissues.	Excessive hunger, excessive thirst, blurred vision, fatigue, frequent urination, dramatic weight loss, rapid breathing, flushed face, nausea, vomiting, stomach pain.
Type II	Insulin scantiness due to insulin resistance. Failure of insulin secretion genetically due to impairment of β cell function.	Increased hunger, increased thirst, increased urination, blurred vision, tiredness, and sores those are slow to heal.
Gestational diabetes	Increased thirst, needing to pee more often than usual, a dry mouth, tiredness	Increased, frequent urination. Increased thirst. Fatigue. Nausea and vomiting. Weight loss even with increased appetite. Blurred vision.

Diabetes mellitus is a group of metabolic diseases with high blood sugar levels for prolonged periods. This high blood sugar level produces the symptoms

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of frequent urination, increased thirst, and hunger. This may lead to many complications if not treated timely. Acute complications include diabetic ketoacidosis and non-ketotic hyperosmolar coma. Severe long-term complications include heart disease, stroke, kidney failure, foot ulcers, and damage to the eyes. Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced.

HISTORY OF DIABETES MELLITUS

Evidence of the classification of diabetic comas dates back to 1886, as reported by Professor Julius Dreschfeld when he delivered the Bradshaw lecture on diabetic comas. He described the type of coma, today known as diabetic ketoacidosis, as affecting the largest number of cases, where dyspnea was usually a most marked symptom, followed by coma, and where both the breath and urine of the patients showed characteristic color of acetone, and urine contained a peculiar body giving a deep claret color with perchloride of iron ulceration on the region of the metatarsophalangeal joints, there was impaired sensation on feet, absent knee jerk, and livid and cold legs. At autopsy, degenerative changes were noticed in peripheral nerves.

There was atheromatous disease of the posterior tibial artery and its smallest branches. The hypothesis that microvascular disease underlies some major complications of diabetes (retinopathy, neuropathy, and nephropathy) was put forward in 1941. However, in 1956, Oakley suggested that neuropathy, independent of vascular disease, might cause foot lesions. Oakley's classification of foot lesions is still widely used today. For a long time, autonomic disturbances such as erectile dysfunction and sweating abnormalities were reported. The first scientific and exhaustive review of this subject was published by Jordan in 1936.[36] It was however only in 1945 that the autonomic symptoms were attributed by Rundle to damage to the autonomic nervous system. Since then, and especially in the 1970s, a tremendous amount of knowledge has accumulated. Despite sophisticated investigations, the precise cause and natural history of autonomic neuropathy are not clearly understood. Rundles included the gastrointestinal complications of diabetes as part of the autonomic disturbances. Dilatation of the stomach with retention and atony was first described by Boas in 1925 and by Chaiken and Klein in 1961. However, it was not until the early 1970s that the fundamental importance of diabetic control and in particular the impact of prevailing glucose concentrations on fetal growth and pregnancy outcomes were recognized.

Diabetes was one of the primary diseases described, with an Egyptian original copy from c. 1500 BCE saying "excessively extraordinary exhausting of the urine." The initially depicted cases are accepted to be type 1 diabetes. Indian doctors around the same time distinguished the sickness and characterized it as madhumeha, or "nectar pee," noticing the pee would pull in ants. The word "diabetes" or "to go through" was initially utilized in 230 BCE by the Greek Apollonius of Memphis. It was viewed as uncommon amid the season of the Roman realm, with Galen remarking he had just seen two cases amid his career. This is perhaps because of the eating regimen and way of life of the people of old, or because the clinical indications were seen during the advanced phase of the illness. Galen named the disease "looseness of the bowels of the pee" (diarrhea urinosa). The soonest surviving work with a point-by-point reference to diabetes is that of Aretaeus of Cappadocia (second or mid-third century CE). He portrayed the manifestations and the course of the illness, which he ascribed to the dampness and coldness, mirroring the convictions of the "Pneumatic School." He conjectured a connection between diabetes and different maladies, and he examined the differential conclusion from the snakebite, which additionally incites exorbitant thirst. His work stayed obscure in the West until 1552 when the main Latin release was distributed in Venice. Type 1 and type 2 diabetes were recognized as independent conditions interestingly by the Indian doctors Sushruta and Charaka in 400–500 CE, with type 1 connected with youth and type 2 with being overweight.

The expression "mellitus" or "from nectar" was included by the Briton John Rolle in the late 1700s to isolate the condition from diabetes insipidus,

which is additionally connected with regular urination. Effective treatment was not created until the early part of the twentieth century when Canadians Frederick Banting and Charles Herbert Best separated and sanitized insulin in 1921 and 1922. This was trailed by the improvement of the long-acting insulin NPH in the 1940s.

PATHOPHYSIOLOGY OF DIABETES

The pathophysiology of diabetes involves plasma concentrations of glucose signaling the central nervous system to mobilize energy reserves. It is based on cerebral blood flow and tissue integrity, arterial plasma glucose, the speed at which plasma glucose concentrations fall, and other available metabolic fuels. Hyperglycemia is a risk for diabetic patients. Because multiple causes can typically contribute to the condition, the pathophysiology of DM might be obscure. Hyperglycemia can affect pancreatic beta-cell activity and lead to insulin secretion problems. As a result, there is a vicious cycle of hyperglycemia that leads to metabolic impairment. In this setting, blood glucose levels exceeding 180 mg/dL are frequently called hyperglycemia, although there is no clear cut-off point due to the multiplicity of processes. At higher blood glucose levels, the glucose transporters in the nephron become saturated, causing osmotic diuresis. Serum glucose levels exceeding 250 mg/dL are likely to elicit polyuria and polydipsia symptoms, but the effect is inconsistent. Excess fatty acids and pro-inflammatory cytokines cause insulin resistance, which impairs glucose transport and increases fat breakdown.

Because the body's response or synthesis of insulin is inadequate, it responds by improperly boosting glucagon, causing hyperglycemia. While insulin resistance is a part of T2DM, the condition is fully manifested when the patient's insulin production is insufficient to compensate for their insulin resistance. The non-enzymatic glycation of proteins and lipids occurs as a result of chronic hyperglycemia. The glycation hemoglobin test can be used to determine the amount of this. Damage to small blood vessels in the retina, kidneys, and peripheral nerves is caused by glycation. The process is accelerated by higher glucose levels. The traditional diabetic consequences of diabetic retinopathy (DR), nephropathy, and neuropathy, as well as the avoidable outcomes of blindness, dialysis, and amputation, are all caused by this damage.

SIGNS AND SYMPTOMS OF DIABETES

Diabetes is a chronic metabolic disorder characterized by high blood sugar levels. The signs and symptoms of diabetes can vary depending on the type of diabetes, the severity of the condition, and individual factors. Here is a detailed list of the common signs and symptoms associated with diabetes:

1. Increased thirst (polydipsia): High blood sugar levels can cause dehydration, which in turn triggers excessive thirst. When the kidneys are unable to filter and absorb all of the excess sugar in the blood, the body starts to produce more urine to remove the extra glucose. This increased urination leads to a loss of fluids, causing the body to crave more water to rehydrate.
2. Frequent urination (polyuria): As mentioned above, the kidneys work overtime to remove excess glucose from the blood. This results in increased urine production and frequent trips to the bathroom, especially during the night.
3. Increased hunger (polyphagia): When the body lacks sufficient insulin or cannot use it effectively, the cells are unable to absorb glucose from the bloodstream. As a result, the body's cells are deprived of energy, leading to increased hunger and food cravings.
4. Uned weight loss: Despite consuming more food due to increased hunger, people with diabetes may experience weight loss. This occurs because the body starts to break down muscle and fat stores for energy when it cannot efficiently use glucose from the blood.
5. Fatigue: The inability to utilize glucose as a source of energy can cause persistent tiredness and fatigue. In addition, dehydration and frequent urination can also contribute to feelings of exhaustion.
6. Blurred vision: High blood sugar levels can cause the lens in the eye to swell, affecting its

ability to focus and leading to blurred vision. This symptom is usually temporary and can improve once blood sugar levels are stabilized.

7. Slow-healing wounds or frequent infections: Diabetes can impair the body's ability to heal wounds and fight infections. High blood sugar levels can damage blood vessels, reducing blood flow to affected areas and impairing the immune system's ability to function properly.
8. Tingling, numbness, or pain in the hands or feet (neuropathy): High blood sugar levels can damage nerves over time, especially in the extremities. This can lead to a loss of sensation, tingling, numbness, or burning pain in the hands and feet.
9. Skin problems: Diabetes can cause various skin issues, including bacterial or fungal infections, itching, and dryness. Dark, velvety patches of skin (acanthosis nigricans) can also develop, particularly in areas where skin folds, like the neck or armpits.
10. Sexual dysfunction: Diabetes can lead to erectile dysfunction in men and reduced sexual desire or arousal issues in women. This can be due to nerve damage, blood vessel damage, or hormonal imbalances related to diabetes.
11. Changes in mood: Fluctuations in blood sugar levels can cause irritability, mood swings, and depression in some people with diabetes.

It is essential to recognize the signs and symptoms of diabetes and seek medical help for proper diagnosis and management. Early intervention can help prevent or delay the onset of complications associated with the condition.

DR

DR develops in people with type 1 or type 2 diabetes. It takes years to develop. Two kinds of DR have the potential to diminish vision:

- In non-proliferative retinopathy, the blood vessels in the retina deteriorate. Deteriorating blood vessels can become blocked or deformed. Fluids, fats, and proteins leak out of the abnormal blood vessels. Fluid can collect in the retina. This swelling impairs sharp vision.
- In proliferative retinopathy, new, structurally unstable blood vessels grow on the surface of the retina. These unstable blood vessels cause frequent minor bleeding. The bleeding causes local irritation and scarring.
- Proliferative retinopathy can cause retinal detachment. This is a separation of the layers of the retina. It is one of the most serious consequences of proliferative retinopathy.

HYPERTENSIVE RETINOPATHY

Hypertensive retinopathy occurs in people who have high blood pressure. High blood pressure causes blood vessel abnormalities. Abnormalities may include thickening of the small arteries, blockages of retinal blood vessels, and bleeding from them. Sudden, severe high blood pressure may cause swelling of the optic nerve. People with this disease frequently have no symptoms in their early stages.

SIGNS AND SYMPTOMS OF RETINOPATHY

The signs and symptoms of retinopathy may vary depending on the type and severity of the condition. Some people may not experience any symptoms in the early stages, while others may have noticeable changes in their vision. Here are some common signs and symptoms of retinopathy:

1. Blurred vision: One of the earliest and most common symptoms of retinopathy is blurry vision, which may gradually worsen over time. This can make it difficult to read, drive, or recognize faces.
2. Floaters: Floaters are small, dark spots, or lines that appear to float in your field of vision. They are often caused by blood or other substances leaking into the vitreous gel that fills the eye. Floaters may be more noticeable when looking at a bright, plain background, such as a white wall or clear sky.
3. Difficulty seeing in low light conditions: Retinopathy can make it challenging to see clearly in dimly lit environments, such as during nighttime or in poorly lit rooms.
4. Sudden vision loss: In some cases, retinopathy

may lead to sudden vision loss, which can be partial or complete. This may occur due to a retinal detachment, hemorrhage, or other complications.

5. Distorted vision: Some people with retinopathy may experience distorted vision, where straight lines appear wavy or objects seem to change shape or size.
6. Dark or empty areas in the field of vision: Retinopathy can cause dark or empty spots in your field of vision, which can make it difficult to see certain areas clearly.
7. Changes in color perception: Retinopathy can sometimes affect the way colors are perceived, making them appear dull or washed out.
8. Flashes of light: Some individuals with retinopathy may see occasional flashes of light, which are usually brief and may be more noticeable in the dark.

If you experience any of these symptoms, it is important to consult an eye care professional promptly for a comprehensive eye examination. Early detection and treatment of retinopathy can help prevent or slow down the progression of vision loss.

MICROALBUMINURIA

Microalbuminuria is considered an early sign of kidney damage and is often seen in people with diabetes, hypertension, or other conditions that affect the kidneys. It is also an indicator of increased risk for cardiovascular disease. Detecting microalbuminuria can help identify individuals at risk for progressive kidney disease and prompt early intervention to prevent or slow down further damage.

The diagnosis of microalbuminuria typically involves measuring the albumin-to-creatinine ratio (ACR) in a urine sample. This ratio provides an estimate of the amount of albumin in the urine, adjusted for variations in urine concentration. An ACR of 30–300 mg/g is considered to be in the microalbuminuria range.

Treatment and management of microalbuminuria often focus on addressing the underlying cause, such as controlling blood sugar levels in diabetic patients or managing blood pressure in hypertensive patients. Lifestyle changes, including maintaining a healthy diet, regular exercise, and smoking cessation, can also help improve kidney function and reduce the risk of developing more severe kidney problems. In some cases, medications such as angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) may be prescribed to help protect the kidneys and reduce albuminuria.

CAUSES OF MICROALBUMINURIA

Microalbuminuria, the presence of small amounts of albumin in the urine, can be caused by several factors, often related to conditions that damage the kidneys or affect their function. Below is a detailed explanation of the primary causes of microalbuminuria:

1. Diabetes: Diabetes is one of the most common causes of microalbuminuria. High blood sugar levels can damage the blood vessels in the kidneys, leading to a condition called diabetic nephropathy. Over time, this damage impairs the kidneys' ability to filter waste products from the blood properly, causing albumin and other proteins to leak into the urine. Both type 1 and type 2 diabetes can lead to microalbuminuria, with a higher risk in individuals who have poor blood sugar control, long-standing diabetes, or additional risk factors like high blood pressure or smoking.
2. Hypertension: High blood pressure is another leading cause of microalbuminuria. Elevated blood pressure can cause damage to the glomeruli, the tiny blood vessels responsible for filtering waste products in the kidneys. This damage can reduce the effectiveness of the filtration process, leading to albumin leakage into the urine. Microalbuminuria is not only a sign of kidney damage but also a risk factor for cardiovascular disease in hypertensive patients.
3. Glomerulonephritis: Glomerulonephritis is an inflammation of the glomeruli, the small blood vessels in the kidneys responsible for filtering waste products from the blood. Various factors can cause glomerulonephritis, including

infections, autoimmune diseases, and certain medications. The inflammation and subsequent damage to the glomeruli can impair the kidneys' filtering ability, leading to microalbuminuria.

4. Kidney infections: Infections such as pyelonephritis, which affects the kidney's tubules and interstitial tissue, can cause temporary or permanent damage to the kidney's filtering system, resulting in microalbuminuria.
5. Heart disease: Microalbuminuria can be a result of heart disease, as it reflects increased pressure in the blood vessels that may damage the blood vessels in the kidneys. This damage can impair the kidneys' ability to retain albumin, causing it to leak into the urine.
6. Obesity: Obesity is a risk factor for microalbuminuria, as it can contribute to the development of insulin resistance, diabetes, and hypertension, all of which can damage the kidneys and result in albumin leakage.
7. Family history: A family history of kidney disease, diabetes, or hypertension may increase the risk of developing microalbuminuria. Genetic factors may play a role in the predisposition to these conditions and their complications, including kidney damage.
8. Smoking: Smoking is a significant risk factor for microalbuminuria, as it can contribute to the development of diabetes, hypertension, and atherosclerosis, which can damage the blood vessels, including those in the kidneys.
9. Age: Older adults are at a higher risk of developing microalbuminuria, as kidney function naturally declines with age. In addition, the prevalence of conditions such as diabetes and hypertension increases with age, contributing to a higher risk of kidney damage.
10. Ethnicity: Certain ethnic groups, such as African Americans, Hispanics, and Native Americans, are at a higher risk of developing microalbuminuria due to a higher prevalence of diabetes and hypertension in these populations.
11. Other causes: Some medications, such as non-steroidal anti-inflammatory drugs, can cause microalbuminuria by affecting the blood flow to the kidneys. In addition, systemic lupus erythematosus, an autoimmune disease, and other rare genetic disorders can cause kidney damage, leading to microalbuminuria.

RELATION BETWEEN DIABETES WITH RETINOPATHY AND MICROALBUMINURIA

Retinopathy (R) is a multifactorial microvascular complication of diabetes mellitus caused by damage to the blood vessels of the retina, the light-sensitive tissue located at the back of the eye. R has been included by the World Health Organization in the priority list of eye diseases which can be partly prevented but not cured yet. In its early stages, R may cause only mild vision problems, but, over time, persistently high blood sugar levels can lead to the obstruction of the tiny blood vessels that nourish the retina, cutting off its blood supply. As a result, the eye reacts by triggering an abnormal growth of new retinal vessels, causing micro-hemorrhages and edemas in the macular region, thus leading to severe visual impairment and eventually blindness. These intra-retinal microvascular changes are used to classify R into non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). NPDR is characterized by a complex array of vasodegenerative lesions within the retinal microvascular bed, such as thickening of capillary basement membranes, loss of pericytes and vascular smooth muscle cells, capillary occlusion, and microaneurysms. PDR is caused by an abnormal growth of new blood vessels (retinal neovascularization) in response to inflammation and/or ischemic damage and hypoxia, eventually giving rise to vitreous hemorrhages and tractional retinal detachment. A direct consequence of inner blood-retinal barrier breakdown is the development of macular edema. Retinal neovascularization and macular edema are the result of increasing secretion of pro-inflammatory cytokines, and pro-angiogenic growth factors, among which predominate the vascular endothelial growth factor. The retina is a highly metabolically active tissue, and high glucose concentrations are particularly detrimental to its functioning.

TREATMENT

The treatment of microalbuminuria aims to address the underlying cause and reduce the risk of further kidney damage. The following are the common interventions and management strategies:

1. Blood sugar control: For individuals with diabetes, maintaining good blood sugar control is crucial in preventing or slowing the progression of kidney damage. This involves monitoring blood glucose levels regularly, adhering to prescribed medications, and following a diabetes friendly diet and exercise plan
2. Blood pressure management: In patients with hypertension, maintaining optimal blood pressure is essential in preventing further kidney damage. This may involve lifestyle changes, such as weight loss, regular exercise, a low-sodium diet, and stress reduction, as well as medications such as ACE inhibitors or ARBs that can help protect the kidneys
3. Medications: In addition to ACE inhibitors and ARBs, other medications may be prescribed to manage microalbuminuria or the underlying cause. These may include diuretics, calcium channel blockers, or beta-blockers, depending on the specific patient's needs
4. Lifestyle modifications: Adopting a healthy lifestyle is essential in managing microalbuminuria and reducing it.

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