

Review Article

Diabetes and the retinal changes in the eye: a threat to the sight

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ABSTRACT

This article discusses the importance of diabetic retinopathy, an eye disease associated with diabetes, which is a systemic disease. The research question addresses the impact of diabetes on the retina of the eye through infection and clinical features. This approach is designed to improve the relationship between early diagnosis and treatment of disease, including laser surgery, corticosteroid injections, and vitrectomy. This article focuses on chronic diabetic retinopathy and eye examination recommendations in the United States and the United Kingdom. To prevent and manage diabetic retinopathy, it is recommended that diabetic patients have regular eye examinations. The results of this study include the importance of good glycaemic control, injections, photocoagulation, and vitrectomy as treatment options. Intravitreal long-acting steroids may also temporarily improve visual acuity by reducing macular oedema. However, long-term use of the drug may cause side effects and may lead to cataracts, steroid glaucoma, and endophthalmitis. It may cause reasons. A recent study of the disease in India shows that the incidence of high blood sugar and its effects on the eye is mainly diabetic retinopathy, including cataracts, neovascular glaucoma and even retinal detachment, which are very dangerous for eye health. Therefore, it is important to inform patients about this disease and perform timely screening because patients need to be informed carefully.

Keywords: Diabetic retinopathy, Glucose level, Vision loss, Laser surgery, Injections, Vitrectomy

INTRODUCTION

Diabetes is a non-infectious, metabolic disease that occurs when insulin secreted by the pancreas (necessary to control blood sugar) is not released or metabolized by blood sugar. Diabetic retinopathy does not cause any symptoms at first, but over time it can develop along with other eye diseases, so you should have your eyes checked at least once a year to protect your eyes as soon as possible. Gestational diabetes during pregnancy can cause diabetic retinopathy. That's why the National Institutes of Health still recommends eye exams. 40-45% of Americans diagnosed with diabetes have some level of diabetic retinopathy, causing them to experience eye problems. Genetics also play an important role in diabetic retinopathy associated with glucose, low lipoprotein, and systolic blood pressure.^{2,3} Diabetic retinopathy screening is part of

standard care for the UK population and is recommended annually.⁴⁻⁶ There are three very effective, effective and important treatments for diabetic retinopathy, including laser surgery, corticosteroid injections or anti-VEGF drugs, and vitrectomy.^{7,8} Kinase and anti-VEGF drugs became available in 2008 and are the best way to prevent diabetic retinopathy.⁹ The key to delaying the onset of diabetic retinopathy is to maintain good blood sugar control.¹⁰

High blood sugar (hyperglycaemia) is the result of persistent blood sugar and, over time, can cause serious damage to many organs in the body, including veins and arteries. Likewise, eyes with diabetic retinopathy should be a concern because unhealthy sugar can accumulate in the blood vessels of the retina over time, causing blindness. There are various types of diabetes.

Gestational diabetes

The placenta produces hormones during pregnancy and birth, increasing the risk of high blood sugar. These mothers and children are more likely to develop type 2 diabetes in the future.¹¹

Type 1 diabetes

It is an autoimmune disease in which the insulin-producing cells in the pancreas are destroyed, so insulin must be injected every day, this type of diabetes is called insulin-dependent diabetes. Additionally, this type of diabetes is more common in children, but teenagers are also affected. Affected individuals experience symptoms such as excessive urination (polyuria), increased thirst (polydipsia), hunger, weight loss, blurred vision, and fatigue.

Prediabetes

This is the early stage of type 2 diabetes, where blood glucose levels become higher than normal but not sufficient to be determined with type 2 diabetes.

Type 2 diabetes

This is known as noninsulin-dependent adult-onset diabetes or insulin-resistant diabetes, due to ineffective use of insulin in the body, either irregular production of insulin or body cells not responding normally to the insulin. Generally, adults are affected with this type of diabetes but it is often found in children too. More than 95% of people have this kind of diabetes. The symptoms are more probably the same as type 1 diabetes and often less marked; therefore, the disorder is determined several years after onset, with the arrived complications.^{12,13}

Another less common kind of diabetes is monogenic diabetes syndrome, a rare condition in young people known as neonatal diabetes and adult-onset diabetes in the young. Cystic fibrosis-associated diabetes and drug or chemical-associated diabetes are associated with steroid use. Type 2 diabetes and risk factors for type 2 diabetes; Age 45 or older, overweight/obesity, high blood pressure, low HDL cholesterol and high triglyceride levels, lack of physical activity, having gestational diabetes, or rebirth. Babies weighing more than 25.9 kilos, polycystic ovary syndrome, history of heart disorder or stroke, smokers. Threats for type 1 diabetes comprise a family history of type 1 diabetes, damage to the pancreas (due to infection, tumours, surgery, or accident), autoantibodies, stress or exercise, and infection.¹¹

Symptoms of diabetes include thirst (dry mouth), weakness, fatigue, blurred vision, numbness and tingling in the arms and legs (less muscle tone), slow wound healing, weight loss, and difficulty urinating. Unexplained infections, such as frequent fungal infections, and dry itchy skin. Other symptoms of type 1 diabetes include nausea,

vomiting or abdominal pain, yeast infection, or urinary tract infection. Symptoms of type 2 diabetes usually begin in adulthood.¹¹

If diabetes continues for a long time, the body's tissues and organs are seriously damaged and this situation becomes life-threatening over time. Some eyes have retinopathy, leading to blindness, while others have cataracts and glaucoma. Other problems include heart disease, chest pain, heart diseases such as heart attack and stroke, high blood pressure including high cholesterol, atherosclerosis (hardening of the arteries), neuropathy, kidney diseases, body diseases and skin diseases, and erectile dysfunction. Hearing loss, depression, dementia and dental problems. Complications of gestational diabetes include preeclampsia (high blood pressure, high protein in the urine, swelling of the legs/feet), risk of gestational diabetes in future pregnancies, and risk of developing diabetes later in life. Gestational diabetes can lead to a higher birth weight and a higher risk of developing type 2 diabetes than a baby with less diabetes, and even death soon after birth.¹¹

Demographics

Diabetes is a disease expected to lead to blindness, kidney failure, heart problems, stroke, and lower extremity deformities. The number of patients affected increased from 108 million in 1980 to 422 million in 2014. Additionally, the disease is estimated to have seriously affected 8.5% of the population in 2014. In the healthcare sector, the criteria for people under 18 years of age, namely income status, are clear. Depending on age. In 2019, diabetes was the 9th leading cause of death. The effects of type 2 diabetes can be controlled by eating a healthy diet, exercising regularly, controlling smoking and drinking, getting regular checkups, and taking medications as needed to treat the problem.¹⁴

DIABETIC RETINOPATHY

Any type of diabetes type 1 and type 2 can develop diabetic retinopathy. Too much glucose level in the retina can choke capillaries, causing decreased vascular flow, so capillaries become abnormal and gaseous exchange hampered (retinal ischemia). The initial stage has few symptoms and is called non proliferative diabetic retinopathy (NPDR), but micro aneurysms require a fundus evaluation, if vision is poor and the image becomes dark or distorted. OCT can confirm the presence of fluid accumulation on the surface of the retina. The second stage is proliferative diabetic retinopathy (PDR), a disease that can lead to many complications without proper treatment and can only be treated with current eye care. Damaged capillaries close and new capillaries form that can enter the vitreous body.¹⁵

PATHOGENESIS

After the diagnosis of diabetes, complications may not occur for 10-15 years. In diabetic retinopathy, retinal artery

stenosis damages the micro vessels and neurons of the retina, subsequently causing microvascular degeneration of the retinal membrane. In this way, blood flows against the capillary wall, creating ischemia and balloon-like microstructures called aneurysms and inflammatory cells are now released by the same degenerate neurons.^{16,17} Depending on the appropriate glucose level, the affected blood vessels and nerves begin to heal; this condition does not affect vision and is known as non-proliferative diabetic retinopathy (NPDR).¹⁸ Diabetic retinopathy does not progress to the proliferative stage. Hypoxia can cause new blood vessels to appear in the retina, leading to further bleeding, increased fibro vascular proliferation, retinal detachment, and neovascular glaucoma if new vessels appear in the anterior-chamber.

SIGN

Retinal haemorrhages deep (dot and blot) are common and superficial (flame shaped) at capillary leakage.

Hard exudates look like yellow white waxy patches at a macular area in a circinate/clump pattern. Cotton wool spots are small whitish, fluffy superficial lesions at nerve fibres.

Vitreous haemorrhage develops due to the proliferation of nonvascularized vessels in the plane of the retina.

A cataract develops due to uncontrolled blood sugar levels which produce enzymes in the lens to convert glucose to a substance called Sorbitol whose presence in the lens leads to cloudy vision.^{19,20}

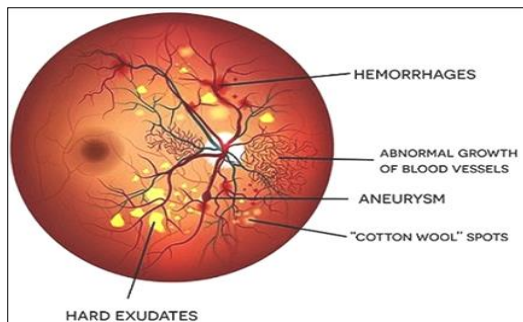


Figure 1: Sign of diabetic retinopathy.

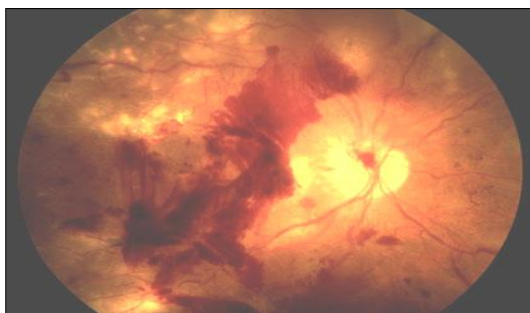


Figure 2: Vitreous haemorrhage.

SYMPTOMS

Floater/dark strings, due to high blood sugar levels in bloodstream vessels get leaked, and the blood spots in the retina create a shadow of tiny particles called floater/dark strings.

Central blindness: leakage from damaged blood vessels in the macula is responsible for central blindness.^{21,22}



Figure 3: Microanurism on OCT.



Figure 4: Floaters.

A distorted vision may lead oedematous macula due to leaky capillaries with visual distortion and discomfort in night vision take place.

Complete blindness occurs due to high blood sugar, further damage to the retina, and even total blindness.



Figure 5: Comparison of distortion in vision.



Figure 6: Blurr off of central vision.

CLASSIFICATION OF DIABETIC RETINOPATHY

The original diabetic retinopathy classification system was the Airlie House classification (1968) of early treatment diabetic retinopathy study (ETDRS).^{23,24} It comprised of stereo photographs in 7 standard photographic fields and its improved version counted as the gold standard for many years.²⁵ Although ETDRS estimates the benefits of macular photocoagulation surgery in reducing the vision loss of clinically significant macular oedema (CSME), first reported by ETDRS, it is considered an excellent tool for research studies but has little clinical value.

These three are determined by light bio microscopy: central macular thickness (about 500 µm or within), hard exudates (at or near 500 µm of central macular thickness), and areas of retinal thickening around the macula (1-disc space or larger).²⁶

Diabetic macular edema (DME) is sometimes classified as focal DME (caused by local drainage from micro aneurysms surrounded by rings of hard exudate) and Diffuse DME is defined as internal blood vessel/edema and hard exudates resulting from disruption of the retinal barrier are not frequently seen even in diffuse DME.²⁷ Later in the UK, the National Research Council, the Scottish Diabetic Retinopathy Grading Scheme and the Royal College of Ophthalmologists introduced another two-element classification system based on visual impairment: retinopathy (risk of new blood vessels appearing) and macular degeneration (risk of damage to the central area of the fovea). Additionally, the International College of Ophthalmology (ICO) classification is associated with retinal micro aneurysms, hemorrhages, venous blebs, intra-retinal microvascular abnormalities, hard exudates (lipid deposits), cottony spots, and signs of retinal neovascularization.

Fluorescein angiography can also reveal some features of diabetes and contrast with clinical imaging, including foveal avascular zone (FAZ), capillary loss, and telangiectasia. While arteriolar and RPE abnormalities are seen in the early and middle stages, dye leakage and its manifestation with cystoid degeneration are isolated in

the late stage of FA.²⁸

The well-known, non-invasive, non-contact transpupillary imaging called optical coherence tomography (OCT) provides cross-sectional images of the macula, estimation of macular thickness, and assessment of the vitreomacular interface.²⁹ Various macular morphological changes are associated with DME, alone or in combination with decreased visual acuity, cystoid macular oedema, posterior vitreous traction, and sometimes serous retinal detachment and traction retinal detachment.³⁰

Based on scientific evidence, a simple classification of DR, the International Clinical Disease Severity Scale, was developed in collaboration with the Wisconsin Epidemiology Study of Diabetic Retinopathy (WESDR) and ETDRS.³¹

Types of diabetic retinopathy comparison of five recommended stages as specified below.

TYPES OF DIABETIC RETINOPATHIES

No apparent diabetic retinopathy

There are no symptoms in this stage, but the risk of infection and blindness may require regular monitoring and appropriate treatment. It includes all abnormalities and requires periodic evaluation of the retina.

Mild non-proliferative diabetic retinopathy

Micro aneurysm is a sign with a latency period of 6 to 12 months and needs to be financially controlled.

Moderate non-proliferative diabetic retinopathy

Symptoms include micro aneurysms, pinpoint haemorrhages (intraretinal haemorrhages or venous bead haemorrhages), hard exudates, and cottony spots. The presence of IRMA indicates ischemia and is a precursor to neovascularization.²⁶

Severe non-proliferative diabetic retinopathy

Intraretinal hemorrhages with microvascular abnormalities are the sign and It is the key level and the ETDRS data indicates a 50% chance of high risk for DM type 2 patients and its diagnosis is based on the 4:2:1 rule of the ETDRS i.e. bleeding in all 4 quadrants (Figure 7a), venous beading (VB) in 2 or more quadrants (Figure 7b), or intraretinal microvascular abnormality (IRMA) in 1 or more quadrants (Figure 7c). The vacancy period is 3 months and financial control is required.^{32,33}

Proliferative diabetic retinopathy (PDR)

The most common type of diabetic retinopathy and is characterized by neovascularization of the optic disc, retina, iris, and angle alone or tractional retinal detachment

with vitreous/preretinal hemorrhages or blurred vision. Diabetic macular oedema (DME) is an additional complication of PDR and is divided into central and central involvement. One of the specific symptoms of macular oedema is the presence of hard exudates and retinal thickening, although the treatment at this stage can preserve vision and not improve it.

Non-central DME involves retinal thickening that does not affect the central macular region. A financial review is required every 3 months. Central DME is affected by retinal thickening in the central region of the macula and requires monthly evaluation.

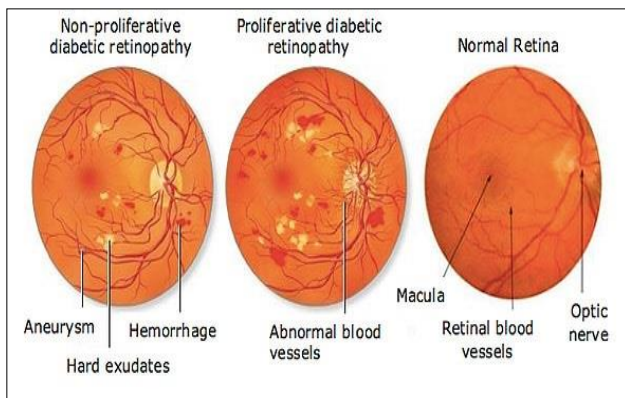


Figure 7: Stages of diabetic retinopathy.

DIAGNOSIS

Various eye exam required for the diagnosis of diabetic retinopathy comprises of visual acuity examination; dilated retinoscopy and fundus examination; Fundus photography will be used in the future to identify debris and exudates in the direction of retinal vessels; Fundus fluorescein angiography (FFA) is used to examine the leakage, direction, and condition of the arteries and choroidal vessels; and optical coherence tomography produces coherent retinal images (B-scan) that can help treat macular oedema.^{34,35}

Treatment

If diabetic retinopathy is very severe and needs to be treated specifically, the risk is calculated at the higher end. Therefore, diabetic eye examination is important in determining the development of retinopathy. If a person can control their blood sugar well, they can prevent vision loss from retinopathy.³⁶

Early diabetic retinopathy

At the stage where the patient has a mild to moderate non proliferative type of diabetic retinopathy, no management is required but it is important to always go on regular checkups, because mild diabetic retinopathy can slow the progression of the disease as long as sugar is controlled.

Advanced diabetic retinopathy

If the patient has diabetic retinopathy or macular edema, treatment is required according to the type of retina-related disease. Eye injections provide the following treatments:

Injectible medication into the eye

These medications, called vascular endothelial growth factor (VEGF) inhibitors, are injected into the vitreous body of the eye. This medication eliminates the expansion of new blood vessels. The two drugs approved by the United States (FDA) to treat diabetic macular edema are ranibizumab (Lucentis) and aflibercept (Eylea). A third drug, bevacizumab, is also used to treat diabetic macular edema. A study published in 2017 found that Aflibercept (Eylea) was more effective than Ranibizumab (Lucentis) and Bevacizumab.³⁷ Side effects of this medication will include mild pain, burning, itching, and even eye floaters and soreness with symptoms of glaucoma for 24 hours. Some serious side effects include blood clots, heart attack, or stroke.³⁶

Triamcinolone acetonide, a type of steroid used as an intravitreal injection and effective for about 3 months, is also related to improving vision by reducing macular oedema. Side effects of the drug include cataracts, steroid-induced glaucoma, and endophthalmitis.³⁸

Photocoagulation

It is also known as focal laser treatment which helps slow down the leakage of blood and fluid in the vitreous of the eye patients who are blind due to macular oedema will not get better if they receive this treatment, but it may reduce the pain of macular oedema.

Pan retinal photocoagulation

Scattered laser treatment, the second name of this procedure, shrinks the abnormal capillaries and allows the area far from the macula to be treated with a scattering laser. Complications after laser treatment can lead to blurred vision during the day as well as blurred vision and night vision. During this procedure, the retina is burned many times, 1,600 to 2,000 times in a single location or in bilateral patterns such as squares, rings, or arcs, to reduce oxygen.³⁹⁻⁴¹

The outcome of laser treatment includes headache, blurred vision, sensitivity against the light, reduced night or peripheral vision, slight vitreous haemorrhage, and the feel of a permanent black spot against the centre of the visual field.³⁶

Vitrectomy

Vitrectomy is used to make a small incision in the affected eye to remove blood from the vitreous and scar tissue from the retina. The procedure is done under general

anaesthesia. Even if the treatment is completed it is possible to experience blurry vision and future retinal damage, so it is important to get regular eye exams even after treatment for diabetic retinopathy.⁴²

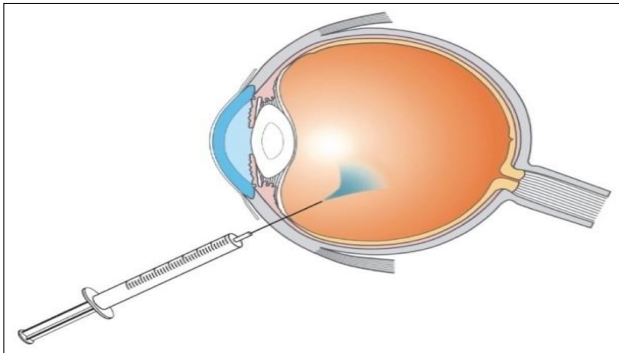


Figure 8: Procedure of intra vitreal injection.

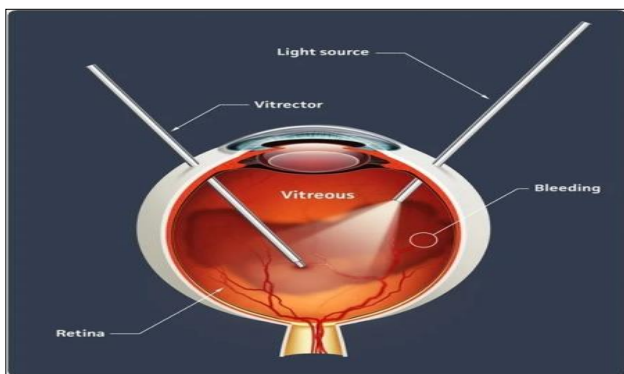


Figure 9: Vitrectomy.

Risks of vitrectomy include cataracts, bleeding, retinal detachment, fluid accumulation, and moderate to severe eye pain.³⁶ Some advanced treatments are also available for diabetic retinopathy. Peptide products such as creative peptides, Eli Lilly and Cebix have been used to treat vascular degeneration with remarkable results.⁴⁴⁻⁴⁶ This is followed by stem cell therapy, where the idea is to inject bone marrow-derived stem cells into the affected area of the eye to regenerate it. The vascular system has been studied in clinics in Brazil, Iran and the USA.⁴⁷

The mask (medical device), tested since 2016, eliminates green light from the eyelids of sleeping people which limits the activity of rods in the retina and dark modification is expected to decrease.^{48,49} As of 2016, large clinical trials are still being conducted.⁴⁸ However, clinical studies conducted in 2018 have not yet shown long-term clinical results.⁵⁰

Non-steroidal anti-inflammatory drugs should be considered in the treatment of macular edema.⁵² Long-term intravitreal injections of steroids can temporarily improve vision by reducing macular edema.⁵¹ Chronic side effects include cataracts, steroid-induced glaucoma, and endophthalmitis.⁵¹

CONCLUSION

The incidence of diabetes is increasing in India, its main impact is on the eyes, manifesting as diabetic retinopathy, which can lead to cataracts, neovascular glaucoma and even retinal detachment, which is very dangerous for eye health. Cataracts can be treated with surgery, but diabetic retinopathy cannot. To ensure that patients with diabetic retinopathy do not suffer serious injury, patient education and review time are crucial as having problems/symptoms can be life-threatening. Patients who experience blurred vision while running should be counselled about visual impairment.

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