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Eye Problems and Diabetes Management

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Abstract

Diabetes is a complex metabolic condition that requires meticulous management on a global approach. Poor management and control of diabetes often leads to poor disease outcomes. The management of diabetes and its complications presents an increasing challenge to healthcare system throughout the world. New findings regarding chronic eye complications of diabetes (cataract, glaucoma, and retinopathy), their prevalence and incidence, and risk factors involved were discussed in this paper. So, prevention of diabetes will need deeper understanding by the patients and their surroundings before medical advancements throw up a magical cure to it. Pharmacist can play an important role by screening patients at higher risk for diabetes, assessing patient health status and adherence to standards of care, patient education referring patients to other health care professionals as appropriate for other complications monitoring the outcomes build up of awareness and high motivation levels among society as a whole will ensure active co-operation of every individual for a healthy living.

Key-Words: Diabetes, pathogenesis, cataract, glaucoma, retinopathy.

INTRODUCTION

If you have diabetes, regular visits to your ophthalmologists for eye exams are important to avoid eye problems. High blood sugar (glucose) increases the risk of diabetes eye problems. In fact, diabetes is the leading cause of blindness in adults age 20 to 74. If you have eye problems and diabetes, don't buy a new pair of glasses when you notice you have blurred vision. It could just be a temporary eye problem that develops rapidly with diabetes and is caused by high blood sugar levels [1-3]. High blood sugar in diabetes causes the lens of the eye to swell, which changes your ability to see. To correct this kind of eye problem, you need to get your blood sugar

back into target range (90-130 milligrams per deciliter or mg/dL before meals, and less than 180 mg/dL one to two hours after a meal). It may take as long as three months after your blood sugar is well controlled for your vision to fully get back to normal. Blurred vision can also be a symptom of more serious eye problem with diabetes. The three major eye problems that people with diabetes may develop and should be aware of are cataracts, glaucoma, and retinopathy [4].

Pathogenesis of Diabetic Complications

Current research into the pathophysiology of diabetic complications indicates that hyperglycemia is possibly the most important and is definitely central to the development of diabetic complications. The changes that take place in the target organs like the eyes, kidneys, nerves and the heart are medicated through several factors like vascular or endothelial factor, tissue factors, genetic factors and others. The vascular endothelium is not just a passive conduct for passage of blood but a very active and dynamic organ and reacts to several physical and chemical stimuli. The normal endothelial function depends upon adequate supply of nitric oxide necessary vasodilatory signaling and detoxification of reactive oxygen species (ROS) .Chronic hyperglycemia causes a high concentration of glucose within the cells, as the vascular endothelium does not need insulin for the passage of glucose across the cell membrane. Endothelial dysfunction causes ischemia of the target organ and tissue damage. Chronic hyperglycemia also causes glycation of different types of cellular proteins. Glucose gel attached to a terminal amino acid residue to produce a schiff's base that undergoes an Amadori rearrangement and ultimately an irreversible reaction occurs that cross links the proteins. This is called Advanced Glycation End Product (AGE) formation, a very important factor for several diabetic complications including diabetic retinopathy and nephropathy. Several cross-link breakers are undergoing trials at the present moment with hopes of reversing the process.

The Protein kinase (PKC) is a group of enzymes involved in the down regulation of pathways leading to diabetic complications. Chronic hyperglycemia causes a high accumulation of di- acyl glycerol (DAG) in the endothelial cells and activates PKCs. PKC activation leads to increased vascular permeability, extracellular matrix synthesis, contractility, cell growth and angiogenesis. Recent researches have shown that diabetic complications are associated with a preferential activation of beta isoform of PKC. Ruboxistaurin a specific inhibitor of PKCβ-2 isoform has been shown to prevent rise of albumin excretion rate as well as changes in kidney of the db/db mouse. The transforming growth factor-β (TGF-β) is a very important profibrotic growth factor implicated in the development of diabetic neuropathy and over pressed in response of PKC activation. Several other growth factors are similarly over expressed and cause diabetic microvascular complications- platelet derived growth factor (PDGF), insulin like growth factor (IGF-I) and vascular endothelial growth factor (VEGF). Last one is particularly responsible in the angiogenesis diabetic retionopathy. The aldosereductase/ Polyol pathway has also been implicated in the pathogenesis of AGE formation, PKC activation, stimulation of growth factors and diabetic complications. Also reductase is responsible for conversion of glucose into sorbitol that has some osmotic effects. Genetic factors have an important role in the pathogenesis of diabetic complications, particularly diabetic nephropathy. Several genes are under investigation of which angiotensin- converting enzyme (ACE) gene and DD gene have been found to have some modulating effect [5].

Eye complications

Cataracts and diabetes

A cataract is a clouding of the eye's natural lens, which lies behind the iris and the pupil. These lens works much like a camera lens, focusing light onto the retina at the back of the eye. The lens also adjusts the eye's focus, letting us see things clearly both up close and far away. The lens is mostly made of water and protein. The protein is arranged in a precise way that keeps the lens clear and lets light pass through it. But as we age, some of the protein may clump together and start to cloud a small area of the lens. This is a cataract, and over time, it may grow larger and cloud more of the lens, making it harder to see. Researchers are gaining additional insights about what causes these specific types of proteins (crystallins) to cluster in abnormal ways to cause lens cloudiness and cataracts. One recent finding suggests that fragmented versions of these proteins bind with normal proteins, disrupting normal function [6].

Cataracts are classified as one of three types:

- A **subcapsular cataract** begins at the back of the lens. People with diabetes, high farsightedness or retinitis pigmentosa, or those taking high doses of steroids, may develop a subcapsular cataract.
- A **nuclear cataract** is most commonly seen as it forms. This cataract forms in the nucleus, the center of the lens, and is due to natural aging changes.
- A **cortical cataract**, which forms in the lens cortex, gradually extends its spokes from the outside of the lens to the center. Many diabetics develop cortical cataracts.

Cataract symptoms and signs

A cataract starts out small and at first has little effect on your vision. You may notice that your vision is blurred a little, like looking through a cloudy piece of glass or viewing an impressionist painting. A cataract may make light from the sun or a lamp seems too bright or glaring. Or you may notice when you drive at night that the oncoming headlights cause more glare than before. Colors may not appear as bright as they once did. The type of cataract you have will affect exactly which symptoms you experience and how soon they will occur. When a nuclear cataract first develops, it can bring about a temporary improvement in your near vision, called "second sight." Unfortunately, the improved vision is short-lived and will disappear as the cataract worsens. On the other hand, a subcapsular cataract may not produce any symptoms until it's well-developed. If you think you have a cataract, see an eye doctor for an exam to find out for sure[7].

Causes of cataracts

No one knows for sure why the eye's lens changes as we age, forming cataracts. Researchers are gradually identifying factors that may cause cataracts, and information that may help to prevent them. Many studies suggest that exposure to ultraviolet light is associated with cataract development, so eye care practitioners recommend wearing sunglasses and a wide-brimmed hat to reduce your exposure. Other types of radiation may also be causes. Other studies suggest people with diabetes are at risk for developing a cataract. Hazy or blurred vision may mean you have a cataract. (Fig I)

Fig I

The same goes for users of steroids, diuretics and major tranquilizers, but more studies are needed to distinguish the effect of the disease from the consequences of the drugs themselves. Some eye care practitioners believe that a diet high in antioxidants, such as beta-carotene (vitamin A), selenium and vitamins C and E, may forestall cataract development. Meanwhile, eating a lot of salt may increase your risk.

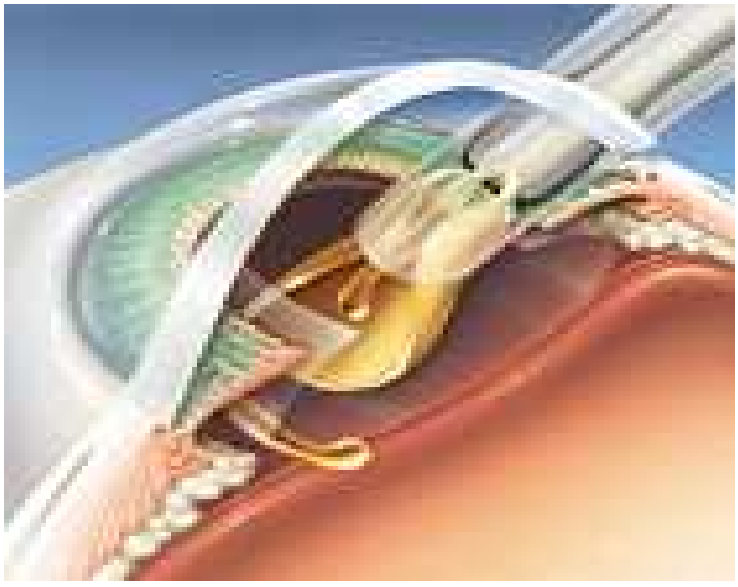

Fig II

Other risk factors include cigarette smoke, air pollution and heavy alcohol consumption. A small study published in 2002 found lead exposure to be a risk factor; another study in December

2004, of 795 men age 60 and older, came to a similar conclusion. But larger studies are needed to confirm whether lead can definitely put you at risk and, if so, whether the risk is from a one-time dose at a particular time in life or from chronic exposure over years.

Researchers say additional studies also are needed to confirm whether hormone replacement therapy (HRT) significantly increases chances that cataracts will form and progress to the point that surgical removal is required. An eight-year study of more than 30,000 postmenopausal Swedish women found a 14 percent increased risk for cataract removal among those who used HRT at any time and an 18 percent increased risk for current HRT users. HRT use combined with regular alcohol consumption appeared to create a 42 percent increased risk of cataract removal, compared with women who had never used HRT or alcohol. (The HRT study was reported in the March 2010 issue of *Ophthalmology)*.

Cataract treatment

When symptoms begin to appear, you may be able to improve your vision for a while using new glasses, strong bifocals, magnification, appropriate lighting or other visual aids.An intraocular lens (IOL) is implanted in the eye in place of the clouded natural lens. Shown is Alcon's AcrySof Natural IOL; it filters out blue light, which may be harmful to eyes. Think about surgery when your cataracts have progressed enough to seriously impair your vision and affect your daily life. Many people consider poor vision an inevitable fact of aging, but cataract surgery is a simple, relatively painless procedure to regain vision. Cataract surgery is very successful in restoring vision. In fact, it is the most frequently performed surgery in the United States, with more than 3 million Americans undergoing cataract surgery each year. Nine out of 10 people who have cataract surgery regain very good vision, somewhere between 20/20 and 20/40. (Fig II)

During surgery, the surgeon will remove your clouded lens and in most cases replace it with a clear, plastic intraocular lens (IOL).New IOLs are being developed all the time to make the surgery less complicated for surgeons and the lenses more helpful to patients. Presbyopia-correcting IOLs potentially help you see at all distances, not just one. Another new type of IOL blocks both ultraviolet and blue light rays, which research indicates may damage the retina. Also, men should be aware that certain prostate drugs can cause intraoperative floppy iris syndrome (IFIS) during a cataract procedure[8]. (Fig III)

Glaucoma and diabetes

Glaucoma refers to a category of eye disorders often associated with a dangerous buildup of internal eye pressure (intraocular pressure or IOP), which can damage the eye's optic nerve that transmits visual information to the brain. With untreated or uncontrolled glaucoma, you might eventually notice decreased ability to see at the edges of your vision (peripheral vision). Progressive eye damage could then lead to blindness. In fact, glaucoma creates at least some vision loss in more than half of the approximately 2.5 million Americans estimated to have the eye disease and is the second leading cause of blindness [9].

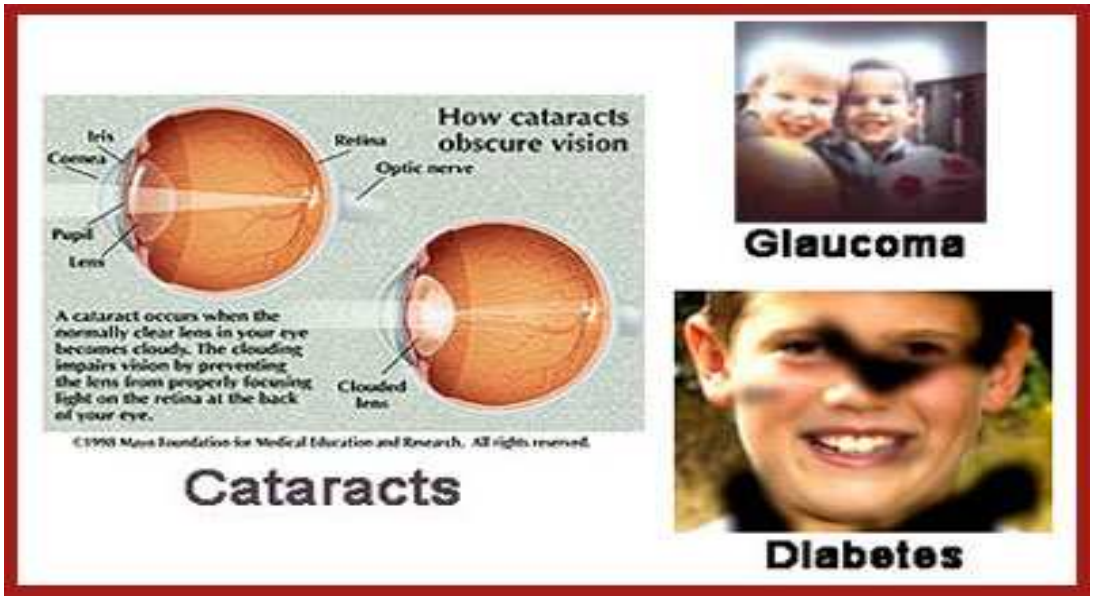

Figure III: How cataract obscure vision

Glucoma symptoms

Glaucoma often is called the "silent thief of sight," because most types typically cause no pain and produce no symptoms until noticeable vision loss occurs. For this reason, glaucoma often progresses undetected until the optic nerve already has been irreversibly damaged, with varying degrees of permanent vision loss. But with acute angle-closure glaucoma, symptoms that occur suddenly can include blurry vision, halos around lights, intense eye pain, nausea and vomiting. If you have these symptoms, make sure you see an eye care practitioner or visit the emergency room immediately so steps can be taken to prevent permanent vision loss.

Diagnosis, screening and test for glaucoma

During routine eye exams, a **tonometer** is used to measure your intraocular pressure, or IOP. Your eye typically is numbed with eye drops, and a small probe gently rests against your eye's surface. Other tonometers send a puff of air onto your eye's surface.An abnormally high IOP reading indicates a problem with the amount of fluid (aqueous humor) in the eye. Either the eye is producing too much fluid, or it's not draining properly.Normally, IOP should be below 21 mmHg (millimeters of mercury) — a unit of measurement based on how much force is exerted within a certain defined area.If your IOP is higher than 30 mmHg, your risk of glaucoma damage is 40 times greater than someone with an IOP of 15 mmHG or lower. This is why glaucoma treatments such as eye drops are designed to keep IOP low.

Other methods of monitoring glaucoma involve imaging of the eye's optic nerve and internal structures (**scanning laser polarimetry** or SLP, **optical coherence tomography** or OCT, **confocal scanning laser ophthalmoscopy**, etc.) to establish a baseline and make sure no obvious changes have occurred over a period of time, which might indicate progressive glaucoma damage.

Visual field testing is a way for your eye doctor to determine if you are experiencing vision loss from glaucoma. Visual field testing involves staring straight ahead into a machine and clicking a

button when you notice a blinking light in your peripheral vision. The visual field test may be repeated at regular intervals to make sure you are not developing blind spots from damage to the optic nerve or to determine the extent or progression of vision loss from glaucoma.

Gonioscopy also may be performed to make sure the aqueous humor (or "aqueous") can drain freely from the eye. In gonioscopy, special lenses are used with a biomicroscope to enable your eye doctor to see the structure inside the eye (called the drainage angle) that controls the outflow of aqueous and thereby affects intraocular pressure. Ultrasound biomicroscopy is another technique that may be used to evaluate the drainage angle [9].

Types of glaucoma

The two major types of glaucoma are *chronic or primary open-angle glaucoma* (POAG) and *acute angle-closure glaucoma*. The "angle" in both cases refers to the drainage angle inside the eye that controls aqueous outflow. Other variations include *normal-tension glaucoma, pigmentary glaucoma, secondary glaucoma and congenital glaucoma*.(Fig,IV)

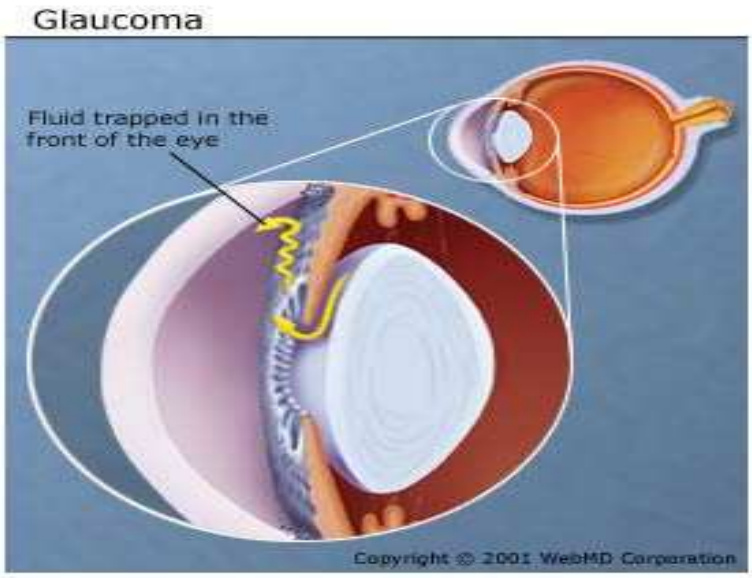

Fig IV

Your eye pressure (intraocular pressure) will be measured with a tonometer. Some tonometers blow a puff of air onto your eye's surface. Others rest gently against the surface of your eye, which will be numbed with eye drops. Glaucoma can be very destructive to your vision; in fact, it's the second-leading cause of blindness in the United States.(Fig V)

Primary open-angle glaucoma **(POAG).** About half of Americans with chronic glaucoma don't know they have it. This common type of glaucoma gradually reduces your peripheral vision without other symptoms. But by the time you notice it, permanent damage has already occurred.If your IOP remains high, the destruction caused by POAG can progress until tunnel vision develops, and you will be able to see only objects that are straight ahead.

Angle-closure glaucoma. Angle-closure or narrow angle glaucoma produces sudden symptoms such as eye pain, headaches, halos around lights, dilated pupils, vision loss, red eyes, nausea and vomiting.These signs may last for a few hours, then return again for another round. Each attack takes with it part of your field of vision.

Normal-tension glaucoma. Like POAG, normal-tension glaucoma (also termed normal-pressure glaucoma, low-tension glaucoma or low-pressure glaucoma) is an open-angle type of glaucoma that can cause visual field loss due to optic nerve damage. But in normal-tension glaucoma, the eye's IOP remains in the normal range.Also, pain is unlikely and permanent damage to the eye's optic nerve may not be noticed until symptoms such as tunnel vision occur. The cause of normal-tension glaucoma is not known. But many doctors believe it is related to poor blood flow to the optic nerve. Normal-tension glaucoma is more common in those who are Japanese, are female and/or have a history of vascular disease.

Pigmentary glaucoma. This rare form of glaucoma is caused by pigment deposited from the iris that clogs the draining angles, preventing aqueous humor from leaving the eye. Over time, the inflammatory response to the blocked angle damages the drainage system. You are unlikely to notice any symptoms with pigmentary glaucoma, though some pain and blurry vision may occur after exercise. Pigmentary glaucoma affects mostly white males in their mid-30s to mid-40s.

Secondary glaucoma. Symptoms of chronic glaucoma following an eye injury could indicate secondary glaucoma, which also may develop with presence of eye infection, inflammation, a tumor or an enlarged cataract.

Congenital glaucoma. This inherited form of glaucoma is present at birth; with 80 percent of cases diagnosed by age one. These children are born with narrow angles or some other defect in the drainage system of the eye. It’s difficult to spot signs of congenital glaucoma, because children are too young to understand what is happening to them. If you notice a cloudy, white, hazy, enlarged or protruding eye in your child, consult your eye doctor. Congenital glaucoma typically occurs more in boys than in girls [10].

Glaucoma treatments

Treatment can involve glaucoma surgery, lasers or medication, depending on the severity. Eye drops with medication aimed at lowering IOP usually are tried first to control glaucoma. Because glaucoma often is painless, people may become careless about strict use of eye drops that can control eye pressure and help prevent permanent eye damage. In fact, non-compliance with a program of prescribed glaucoma medication is a major reason for blindness caused by glaucoma. If you find that the eye drops you are using for glaucoma are uncomfortable or inconvenient, never discontinue them without first consulting your eye doctor about a possible alternative therapy. (Fig.V)

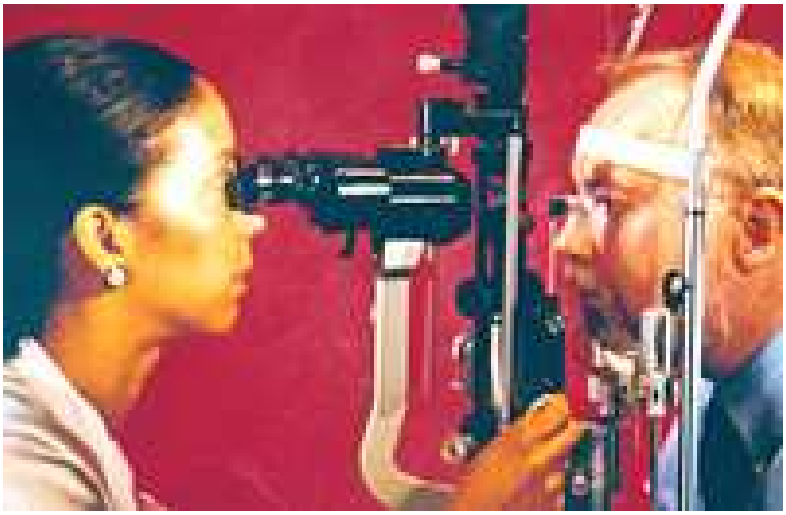

Figure V: Glaucoma infected eye

Diabetic retinopathy

The retina is a group of specialized cells that convert light as it enters through the lens into images. The eye nerve or optic nerve transmits visual information to the brain. Diabetic retinopathy is one of the vascular (blood-vessel related) complications related to diabetes. The diabetes eye problem is due to damage of small vessels and is called a "microvascular complications." Kidney disease and nerve damage due to diabetes are also microvascular complications. Large blood vessel damage (also called macrovascular complications) includes complications like heart disease and stroke.

Diabetic retinopathy is the leading cause of irreversible blindness in industrialized nations. The duration of diabetes is the single most important risk for developing retinopathy. So the longer you have diabetes, the greater the risk of this very serious eye problem. If retinopathy is not found early or is not treated, it can lead to blindness [9].

People with type I diabetes rarely develop retinopathy before puberty. In adults with type I diabetes, it is rare to see retinopathy before five years' duration of diabetes. The risk of retinal damage increases with progressive duration of diabetes. Intensive control of blood sugar levels will reduce your risks of developing retinopathy. The DCCT, a large study of people with type I diabetes showed that people with who achieved tight control of their blood sugars with either an insulin pump or multiple daily injections were 50%-75% less likely to develop retinopathy, nephropathy (kidney disease), or nerve damage (all microvascular complications)[10]. People with type 2 diabetes usually have signs of eye problems when diabetes is diagnosed. In this case, control of blood sugar, blood pressure, and blood cholesterol with diabetes have an important role in slowing the progression of retinopathy and other eye problems [5, 11].

Classification of diabetic retinopathy

1. *Non-proliferative diabetic retinopathy* (NPDR) or, background diabetic retinopathy (BDR) is the first stage of the disease. The earliest change is the thickening of vascular basement membrane and loss of capillary pericytes. Pericytes function as contractile smooth muscles-like

cells that control capillary tone and probably act as blood-retinal barrier. Examination by ophthalmoscope reveals sac-like dilation of the retinal capillaries, which appear as small red dots on the retina and are called micro aneurysms. With further increase in capillary permeability, hemorrhages appear in different layers of the retina. Dot hemorrhages are small, round superficial hemorrhages and are frequently indistinguishable from microaneurysms. Blot hemorrhages have fuzzier borders and are situated in deeper layer of the retina. Flame-shaped hemorrhages are elongated and situated in the superficial neurosensory layer of the retina. Treatment with LASER prevents visual loss in at least 50 percent of such patients.

2. *Severe NPDR (pre-proliferative retinopathy):* This stage is more advanced with further ischemia of the retina. Blot hemorrhages are larger and cotton-wool spots are more in number. In areas of retinal ischemia, venous segments are beaded or. Sometimes looped. Retinal capillaries are, at places, show irregular margins and dilations- called IRMA (intra retinal microvascular abnormality)

3. *Proliferative diabetic retinopathy* (PDR): The hallmark of this stage is the new vessel formation in retina and into the vitreous (neovascularization). Prolonged retinal ischemia causes liberation of different growth factors (described above), which, in turn, result in proliferation of new vessels. These vessels are fragile and bleed easily and cause fibrosis and traction of retina. Bleeding is quite common in the vitreous chamber (vitreous hemorrhage), causing sudden loss of vision. Furthermore, these growth factors increase retinal permeability. New vessel formation may take place in the iris (rubeosis iridis) and may increase intraocular pressure and produce glaucoma[1,5,12].(fig VI)

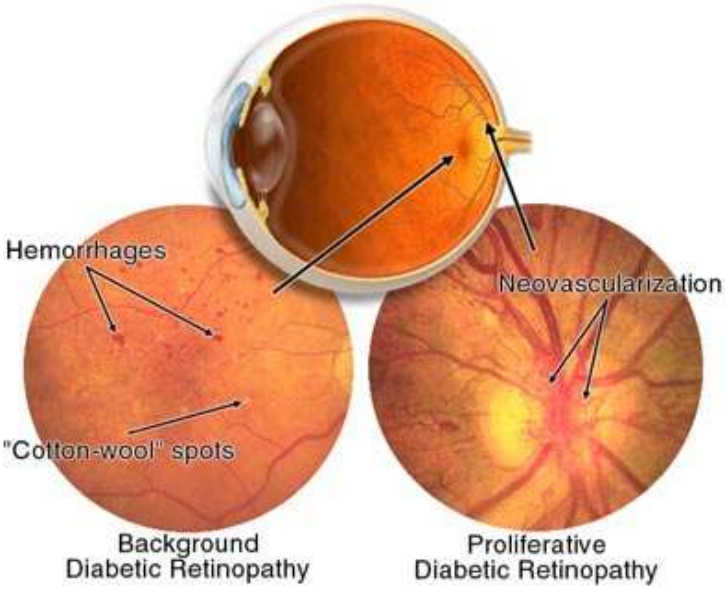

Figure VI: diabetic retinopathy

Diagnosis

- Direct ophthalmoscopy with dilated pupils (approximately ½ hour after 1 percent tropicamide given to each eye) is a useful examination for an experienced physician but has several

limitations. Firstly, the field of viewing is narrow and two dimensional. Secondly, macular edema and neovascularization cannot be properly evaluated [13].

- Indirect ophthalmoscopy provides a three dimensional, panoramic view of the retina and is very useful for evaluation of the changes in retina.
- Indirect biomicroscopy with a slit lamp provides 3-D viewing of the optic disk and the macula with excellent evaluation of macular edema and neovascularization.
- Fundus fluorescein angiography (FFA) is the photographic picture of the retina, after intravenous injection of sodium-flourescein, taken with a fundus camera13. This provides record of the patient as well as detects areas of capillary closure and leaking of microaneurysms [14]

Management:

1. Glycemic control is effective in prevention (both primary and secondary) of diabetic retinopathy in both type 1 and type 2 diabetic patients. In poorly controlled patient with pre-existing diabetic retinopathy, the management of diabetes may be done in close association on handling diabetic retinopathy.
2. Control of hypertension (preferably with ACEI or ARB) and dyslipidemia.
3. Cessation of smoking.
4. Laser treatment has revolutionized the outcome of diabetic retinopathy in terms of loss of vision. The mechanism by which laser prevents further visual loss is rather hypothetical (reduction of retinal hypoxia and thereby reducing neovascularization and vascular 'steal' phenomenon). The indication of laser is CSME, widespread lesions and neovascularization [5,15].

Clinical Practice Recommendations:

- Annual detailed eye examination by an ophthalmologist for all type 2 diabetes patients.
- Annual detailed eye examination by an ophthalmologist for all types 1 diabetic patients, 5 years after first diagnosis.
- Screening for retinopathy for diabetic women when pregnancy is diagnosed and the same for all GDM patients at diagnosis of GDM.
- Six-monthly follow-up for patients with BDR
- Frequent follow-up is advised for patients with poor glycemic control and those with CSME, PPDR or PDR [5, 16].

American Diabetes Association guidelines for people with diabetes to help prevent eye problems:

- People with type 1 diabetes should have a dilated eye exam by an ophthalmologists or optometrist within three to five years after diagnosis.
- People with type 2 diabetes should have a dilated eye exam by an ophthalmologist or optometrist shortly after diagnosis.
- Annual eye exams should be done with both eye type 1 and type 2 diabetes by an ophthalmologist or optometrist; more frequently if necessary.
- When considering pregnancy, women with a history of diabetes should have an eye exam prior and during pregnancy. This does not pertain to women with gestational diabetes [19].

Summary
Diabetes is a disorder that slowly degrades vital functions of the body and creates disability affecting sense of well-being among diabetics. Management of glycaemia in diabetes is crucially important for prevention of both acute and chronic complications. Regular SMBG needs to be encouraged. To prevent diabetic eye complications have your doctor screen your eye annually. Also control high blood pressure, cessation of smoking, also laser treatment has revolutionized the outcome of diabetic retinopathy in terms of loss of vision [2, 4,19]. Women with diabetes who later become pregnant should have a comprehensive eye exam during the first trimester and close follow-up with an eye doctor during the rest of their pregnancy to avoid serious eye problems with diabetes. Pharmacist can play an important role in diabetes care by screening patients at high risk for diabetes, assessing patient health status and adherence to standards of care, educating patient to empower them to care for themselves, referring patients to other health care professionals and monitoring the outcomes. Self-monitoring of blood glucose should form an integral part of overall diabetes care management program. A buildup of awareness and high motivation levels among society as a whole will ensure active co-operation of every individual for a healthy living [21].

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