RESEARCH PAPER

IRIS CHANGES IN DIABETIC RETINOPATHY

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ABSTRACT

Diabetic retinopathy (DR) is one of the most common microvascular complications of diabetes mellitus and remains a leading cause of preventable visual impairment and blindness worldwide, particularly among the working-age population. While retinal changes in DR have been extensively studied, increasing evidence suggests that the iris is also significantly affected by diabetes-related vascular and neural damage. Chronic hyperglycaemia, ischemia, and autonomic dysfunction lead to a variety of structural and functional alterations in the iris, including neovascularisation (rubeosis iridis), changes in iris thickness, pupillary abnormalities, pigment epithelial instability, and microvascular leakage.

Iris neovascularisation is a critical indicator of advanced diabetic eye disease and often precedes the development of neovascular glaucoma, a severe and sight-threatening complication. Recent advances in anterior segment imaging techniques, particularly anterior segment optical coherence tomography angiography (AS-OCTA), have enabled non-invasive and quantitative assessment of iris vasculature, allowing earlier detection of subtle vascular changes that may not be clinically visible on routine examination.

This review summarises the anatomical and physiological features of the iris, the pathophysiological mechanisms by which diabetes affects iris structure and function, and the spectrum of iris changes associated with diabetic retinopathy. It also highlights current diagnostic techniques and management strategies, emphasizing the importance of early detection and strict systemic control of diabetes. Improved understanding of iris involvement in diabetic retinopathy may enhance disease assessment, guide timely intervention, and reduce the risk of irreversible vision loss. Future research focusing on iris biomarkers and the integration of anterior segment imaging into routine diabetic eye screening may further improve clinical outcomes.

Keywords: Diabetic retinopathy, Iris, Neovascularisation of iris, Management of diabetic retinopathy, Iris changes in diabetic retinopathy.

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1-INTRODUCTION:

Diabetic retinopathy is an eye condition caused by diabetes. When blood sugar stays high for a long time, it damages the small blood vessels in the eye. This can make vision blurry and, if not treated, can lead to vision loss. Nearly 30-40% of the population has a major eye-related complication of diabetes mellitus [1]. More than 100 million people worldwide suffer from DR, which is a major contributor to blindness and visual impairment, particularly in working-age adults [2]. 45 individuals with advanced diabetic retinopathy were seen on average per month, according to research conducted in Southern India. A small number of these people were referred for assessment, indicating that health care providers and the community need to raise awareness [3].

Diabetic retinopathy (DR) is one of the primary effects of diabetes mellitus (DM), which is still the leading cause of vision loss in individuals of working age []. The International Clinical Disease Severity Scale for DR was used to grade non-proliferative DR in diabetic subjects as either none, mild, moderate, or severe[4].

Clinical signs of vascular anomalies in the retina are used to diagnose DR. Non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) are the two clinical stages of DR. Increased vascular permeability and capillary occlusion are two major findings in the retinal vasculature during NPDR, which is the early stage of DR. Even though the patients may not exhibit any symptoms, fundus photography can identify retinal diseases such as microaneurysms, haemorrhages, and hard exudates during this period. When the new aberrant arteries leak into the vitreous (vitreous haemorrhage) or when tractional retinal detachment occurs, patients may suffer from severe vision impairment during this stage. Diabetic macular oedema (DME) is the most frequent cause of vision loss in DR patients [5]. The duration of exposure and the degree of hyperglycaemia, hypertension, and hyperlipidaemia are the primary risk factors for the development of DR. The primary cause of DM-related morbidity and mortality is cardiovascular and cerebrovascular accidents [6]. Diabetic consequences are generally categorized as microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (heart disease, stroke, and peripheral artery vasculopathy) since diabetes affects both small and large vessels [7]. The iris also has a contributory role in diabetic retinopathy. firstly, we know about what is iris?

2-IRIS: -

The iris, one of the most visually impressive and colourful organs of the human body, It is a thin, contractile disk that sits between the cornea and the lens and controls how much light enters in eye and reaches the retina it plays a role in controlling intraocular pressure because it involves in the circulation of aqueous fluid, it develops from both the optic cup and the periocular mesenchyme during development [8]. The iris has five layers: the anterior border, the stromal layer, the muscle layer, the anterior pigment epithelium layer, and the posterior pigment epithelium layer [9]. The iris stroma is located anteriorly, and the iridial muscles are located above these pigmented cells. As we can see in Table.1(layers of iris)

Table.1 (Layers of iris)

Component	Anatomical Description	Histological / Functional Significance
Anterior Border Layer	Thin, fibro cellular layer on the anterior surface of the iris	Determines iris colour; contains melanocytes and fibroblasts; absence or thinning contributes to crypts
Stroma	Loosely arranged connective tissue containing collagen fibres	Houses blood vessels, nerves, melanocytes, immune cells; provides structural support
Anterior Pigmented Epithelium	Single layer of pigmented cells	Contributes to dilator muscle; blocks light transmission
Posterior Pigmented Epithelium	Heavily pigmented cell layer facing the lens	Prevents light scatter within the eye
Basement Membrane	Thin supporting membrane beneath epithelial layers	Structural support and cell adhesion

By contracting the sphincter pupillae during accommodation, the iris limits peripheral corneal light rays, enhancing the sharpness of the retinal image. The anterior neural plate is the source of the retina, iris, and ciliary body's epithelial layers. There are different parameters of iris as we can see in table.2

Table.2 (Different parameters of iris)

parameters	Description
Position	Between cornea (anteriorly) and lens (posteriorly)
Shape	Circular with a central opening (pupil)
Diameter	~12 mm
Thickness	~0.5 mm
Colour	Depends on melanin pigment (blue, brown, green, etc.)
Central Aperture	Pupil
Periphery	Attached to ciliary body
Anterior Surface	Rough, shows crypts and radial ridges
Posterior Surface	Smooth, deeply pigmented
Zones	Pupillary zone (inner) and Ciliary zone (outer)

Recent developments in ocular surface imaging methods have made it possible to investigate the microstructural impacts of diabetes mellitus on the anterior segment (iris, cornea, conjunctiva, and tear film). Patients with diabetes also have rubeosis iridis, ectropion uvea, and iris atrophy [10]. DM leads to complications such as neuropathy, retinopathy, nephropathy, and cardiovascular disorders, in which hyperglycaemia plays a major role [11].

The iris's posterior face is covered by molecules released by the ciliary non-pigmented epithelium, which then travel to the anterior chamber to cover the anterior face. The lens, cornea endothelium, and outflow route can all be impacted by proteins released by the iris and transported by the aqueous humour. The iris is made up of the dilator and sphincter muscles, a two-cell layer of heavily pigmented epithelium (iris pigment epithelium, or IPE), a stroma of highly vascularized connective tissue that contains melanocytes, melanin granules, and chromatophores, and an anterior cellular border layer that is irregularly shaped and unique to each individual. The iris regulates how much light enters the eye and reacts to light [12]. The eye's surface can also be split into two parts: the ciliary zone and the pupillary zone [13]. These regions are bounded by a ring of tissue known as the collarette, which is a product of the reabsorption of the pupillary membrane during development. Pigment granules in the posterior pigment epithelium, pigment concentration in iris stromal melanocytes, melanin pigment type in iris melanocytes, and the extracellular stromal matrix's light-scattering and absorption capabilities are thought to be the four primary factors that determine iris colour [14].

The purpose of this review is to summarize the changes in the iris seen in diabetic retinopathy, and it highlights diagnostic techniques for detection and know about the clinical implications and managements.

2.1 Embryology

The tissue that makes up the vertebrate eye comes from different embryonic origins. The anterior neural plate is the source of the retina as well as the iris and ciliary body's epithelial layers. Together with the iris epithelium, the optic cup neuroectoderm gives rise to the sphincter pupillae and dilator pupillae muscles inside the iris stroma. The optic cup is neuroectodermal in origin and gives rise to the epithelial layers of iris and the iris musculature [15]. Fuch's crypts are diamond-shaped lacunae in the anterior-border layer of the iris, which first develop during the reabsorption of the pupillary membrane [16].

2.2 BLOOD SUPPLY AND NERVE SUPPLY

Direct autonomic effects on the vasculature of the iris, choroid, ciliary body, and optic nerve as well as indirect effects on retinal blood flow regulate ocular blood flow. The anterior ciliary arteries, the long posterior ciliary arteries, and anastomotic connections from the anterior choroid supply blood to the iris. The choroid and vortex veins receive the majority of the venous drainage from the anterior portion of the eye [15].

Pupil constriction (miosis) and accommodation result from parasympathetic innervation of the iris sphincter muscle through the short ciliary nerves [17]. Sphincter muscle relaxation, which is essential during times of low light or night vision, is facilitated by the sympathetic fibres. To regulate pupil dilation, sympathetic innervation from the superior cervical ganglion travels via long ciliary nerves to the iris's dilator muscle [15].

3 - Pathophysiology of Diabetes Affecting the Iris

Diabetes mellitus causes pathophysiological changes in ischemia and hypoxia that impact the eye's entire vascular system [18]. Under an electron microscope, Ishikawa saw layered formations, thick masses, and aberrant mitochondria in the peripheral nerves of the iris dilator and sphincter muscles in diabetes individuals [19]. The smooth muscles of the iris may be harmed by the advanced glycosylation end products of diabetic metabolism, which could seriously impair the muscles' ability to contract [20]. There are some structural changes in iris because of diabetes. One of the main causes of avoidable vision impairment and blindness is diabetic retinopathy (DR), a significant microvascular consequence of persistent hyperglycaemia [21]. There are some changes in iris due to diabetic retinopathy as seen figure number.1

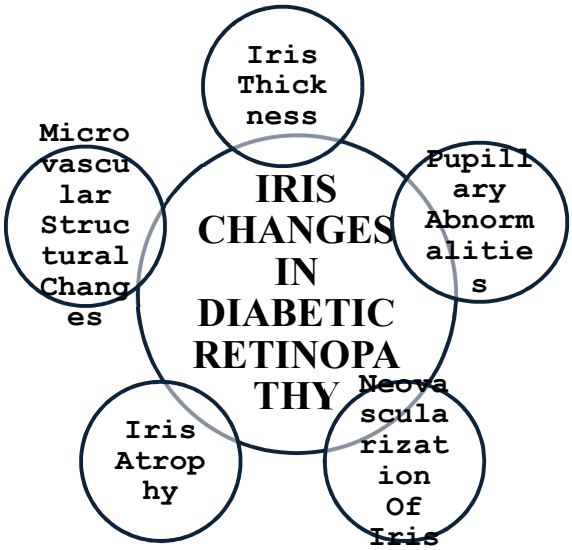

Figure no.1 iris changes in diabetic retinopathy

3.1 Neovascularisation of the iris

Bader first described iris neovascularisation in 1868 [22]. Approximately 66% of patients have neovascularisation of the iris and at the iridocorneal angle, which causes decreased outflow of aqueous humour from the eyeball. Abnormal veins in the iris in a diabetic patient were first recognised by Salus (1928), who termed the disorder rubeosis iridis [23]. Rubeosis iridis is a condition that can occur in both ocular ischaemia and diabetic retinopathy. The distribution of iris neovascularisation can vary - It is most commonly observed around the pupil margin in diabetes mellitus, as well as around the angle and iris root in oculi ischemic syndrome [24]. Rubeosis iridis, a clinical term for iris pathological neo angiogenesis, has been linked to an imbalance in inflammatory and angiogenic factors in both the posterior and anterior ocular chambers of the eye [25]. Retinal hypoxia has been reported in cases of rubeosisiridis and commonly in proliferative retinopathies. It is probable that a portion of the oxygen from the aqueous humour diffuses posteriorly towards the hypoxic retina, resulting in iris hypoxia as a compensatory strategy [26].

In some cases, neovascularisation may arise at the angle of the chamber and surface of the iris [27]. The iris, ciliary body, and choroid make up the uvea, which is the part of the eye with the most blood vessels. In the eye, neovascularisation is the source of sight-threatening disorders, such as proliferative diabetic retinopathy (PDR) and neovascular glaucoma (NVG) [28].

The iris vasculature plays a vital role in keeping the anterior chamber of the eye balanced. DR is classified into two types based on clinical findings: early non-proliferative diabetic retinopathy (NPDR) and more advanced proliferative diabetic retinopathy (PDR), which is associated with retinal ischemia and neovascularisation [29]. The development of neovascular glaucoma and iris neovascularisation (INV) are significant outcomes for patients with central retinal vein occlusion, proliferative diabetic retinopathy (PDR), and other diseases [30]. It has been proposed that if iris blood vessels change prior to retinal neovascularization, the retinal disease is in the early stages of DR and RVO [31]. In poorly controlled diabetic patients with widespread posterior segment ischemia that remains unrecognized and untreated, progression from iris neovascularization to NVG (Neovascular glaucoma) is common and can occur after 12-months following the development of iris neovascularization [32].

3.2 Changes in iris thickness

Prior research has demonstrated that diabetic patients' choroidal capillary blood flow is substantially reduced compared to that of healthy individuals [33]. It has been proposed that increased iris thickness and curvature are important factors in the etiology of angle closure [34]. Hyperglycaemia causes the activation of several signal pathways in diabetic patients (Brownlee 1992; Hou et al. 2014; Jain et al. 2018), which may alter the iris's ultrastructure. However, static and dynamic characteristics of the iris volume in individuals with diabetes are yet unknown, though [35].

3.3 Iris atrophy:

Iris atrophy, ectropion uvea, and rubeosis iridis are also seen in diabetic patients [36]. Diabetic iridopathy eventually leads to neovascular glaucoma, a diabetic ocular condition that poses a significant danger to eyesight and potentially blindness [37]. Essential iris atrophy is distinguished by atrophy and weakening of the iris stroma, resulting in holes throughout the iris thickness, as well as the early production of anterior synechia, which causes pupillary abnormalities - In gonioscopy, anterior peripheral synechiae are present in varying degrees, causing angular closure and, as a result, an increase in IOP (intraocular pressure) [38].

3.4 Pupillary abnormalities:

Numerous studies have demonstrated aberrant pupi llary dynamics in diabetes, which may indicate auto nomic dysfunction. However, the relationship betw een these abnormalities and the varied degrees of di abetic retinopathy (DR) has not been well investiga ted [39].

In 28 diabetic patients with proliferative diabetic re tinopathy, Clark examined ocular autonomic dysfun ction[40].

Pupillary abnormalities have been suggested as a p

ossible biomarker for DR since prior studies have s hown a connection between pupillary diameter vari ations and the severity of DR [41]. Researchers investigated the relationship between pupillary responses and the severity of diabetic retinopathy and discovered that individuals with DR had lower values of the amplitude and velocity of pupil contraction and dilation [42].

3.5 Microvascular structural changes:

Diabetic retinopathy (DR), a primary microvascular consequence of persistent hyperglycaemia, is a leading cause of avoidable vision impairment and blindness [21]. Non-proliferative diabetic retinopathy (NPDR) is defined by a variety of retinal microvascular abnormalities, such as microaneurysms, retinal haemorrhages, hard exudates, cotton-wool patches, intraretinal microvascular abnormalities (IRMA), and venous beading or looping [43]. It has been noted that the diabetic iris epithelium is three times more prone to leak pigment and may become depigmented [44]. Pigment deposits on the corneal endothelium and trabecular meshwork are caused by pigment release from the iris [45].

4 - Techniques of evaluating iris changes

Every patient has iris changes in diabetic retinopathy which include measurement of best corrected visual acuity.

We can do intraocular pressure measurement via slit-lamp biomicroscopy, Goldmann applanation tonometry, or non-contact tonometry.

Slit-lamp bio microscopy was used to evaluate the anterior segment of the eye, which included the conjunctiva, cornea, sclera, anterior chamber, iris, pupil, and lens.

A noncontact air puff tonometer (TX-F, Canon, Tokyo, Japan) was used to measure intraocular pressure (IOP) [46].

In recent years, a variety of devices, including optical coherence tomography, ultrasonic biomicroscope, Scheimpflug imaging, scanning slit tomography, and interferometry, have been frequently employed to evaluate the anterior region [47]. Although AS-OCT has long been used to provide high-resolution cross-sectional imaging of the anterior segment, it has long been challenging to implement anterior segment optical coherence tomography angiography (AS-OCTA) to visualise the iris's blood vessels. Although studies have occasionally been published to examine the dynamic information of blood flow in the iris, none have been found for the detection of glaucoma [48].

Following pharmacologic mydriasis, all participants underwent indirect ophthalmoscopy, optical coherence tomography (OCT) of the peripapillary RNFL and macular GCC (Cirrus HD-OCT 4000; Carl Zeiss Meditec AG, Jena, Germany), and 45° colour fundus photography of the Early Treatment of Diabetic Retinopathy Study (ETDRS) standard fields 1 (optic disc-centred) and 2 (macula-centred) (Nonmyd WX3D; Kowa Company Ltd., Aichi, Japan) [49].

Reports indicate that iris neovascularisation was detected by AS-OCTA imaging [50]. In recent years, AS-OCTA has been used to see the blood vessels in the iris so that researchers can learn more about different disorders [51]. Optical coherence tomography angiography (OCTA) of the anterior region allows for the visualisation and quantitative analysis of iris blood vessels [52].

Anterior segment optical coherence tomography angiography (AS-OCTA) offers a non-invasive, fast, and quantitative picture of the iris vasculature [46]. It may provide thorough iris vasculature imaging with fast scanning speeds that allow 360° imaging of the iris, which delivers extensive information about the iris vasculature [53]. As a result, AS-OCTA looks to be a promising new technique for researching the iris vascular system in diabetes patients. CASIA2 anterior segment optical coherence tomography was used to pick a high-quality image that clearly showed the iris, angle, and scleral spur [54]. In comparison to iris fluorescein angiography, AS-OCTA is more effective at examining the iris vasculature, providing more comprehensive information about blood vessels.

Using diabetic eye illness as an example, standard t reatments such as laser photocoagulation, antivascu lar endothelial growth factor injections, and vitrect omy minimise the risk of vision loss, but they only address late disease stages such as proliferative DR and diabetic macular oedema [55].

5 - Management consideration: -

Firstly, Hyperglycaemia and high blood pressure are risk factors for the development and progression of diabetic retinopathy. It can also affect the iris surface.

Hyperglycaemia must be strictly controlled in order to reduce the risk of diabetic retinopathy formation or progression. Strict blood glucose management also reduced the frequency of progression in clinically significant macular oedema, proliferative diabetic retinopathy, and severe NPDR, according to long-term follow-up [56]. The duration of diabetes and the intensity of hyperglycaemia are widely accepted as the most important risk factors for developing retinopathy [57].

Laser treatment, anti-VEGF medications, and intravitreal corticosteroids are all cost-effective ways to manage diabetic retinopathy to varying degrees [58].

Anti-VEGF injections are the standard treatment for diabetic retinopathy, and they are available off-label or through the US Food and Drug Administration for all stages of the disease [59].

Pan retinal photocoagulation (PRP) has been the primary treatment for PDR since over 40 years ago when the Diabetic Retinopathy Study established its efficacy [60]. Many individuals have no proliferative diabetic retinopathy, but others develop

proliferative diabetic retinopathy (PDR), which can cause blindness due to traction retinal detachment, vitreous haemorrhage, or neovascular glaucoma - Pan retinal photocoagulation (PRP) has been the conventional treatment for most eyes with PDR for decades, but it kills retinal tissue, which can lead to iatrogenic peripheral vision loss or worsening of diabetic macular edema (DME), leading in central vision loss [58].

Neovascular Glaucoma (NVG) is most commonly a subsequent consequence of proliferative diabetic retinopathy (PDR), central retinal vein occlusion (CRVO), or ocular ischemia syndrome [26]. It is very important to monitor neovascular glaucoma, it can be monitor by tonometer (air puff tonometer, applanation tonometer) as by neovascularisation of iris there is chances of raised IOP.

The treatment of NVG is based on two main principles: inhibiting neovascularization and controlling IOP [59]. Topical β-blockers, carbonic anhydrase inhibitors, and α-agonists may help lower IOP. Prostaglandin analogues are frequently used to improve uveoscleral outflow, but they may have less than the typical IOP-lowering effect in NVG [60].

A balanced diet and lifestyle, including exercise and weight control, may minimize the risk of getting diabetes in some patients [61].

Conclusion:

Diabetic retinopathy remains one of the leading causes of preventable vision loss worldwide, and growing evidence highlights the iris as an important yet often overlooked structure affected by this disease. Diabetes-induced microvascular dysfunction, chronic hyperglycaemia, ischemia, and autonomic neuropathy result in significant structural and functional alterations of the iris, including neovascularization, changes in iris thickness, pupillary abnormalities, pigment epithelial instability, and microvascular leakage.

Iris neovascularization, particularly rubeosis iridis, represents a critical marker of advanced disease and frequently precedes the development of neovascular glaucoma, a sight-threatening complication. Advances in anterior segment imaging, especially anterior segment optical coherence tomography angiography (AS-OCTA), have improved the non-invasive visualization and quantitative assessment of iris vasculature, allowing earlier detection of subtle vascular changes. Understanding iris involvement in diabetic retinopathy enhances insight into disease severity, progression, and prognosis. Early identification of iris changes, combined with strict systemic control of hyperglycaemia and timely ocular interventions such as anti-VEGF therapy and laser photocoagulation, may reduce irreversible visual impairment. Future research should focus on longitudinal assessment of iris biomarkers and the integration of anterior segment imaging into routine diabetic eye screening to improve clinical outcomes.

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Table 1 (Layers of iris)

Component	Anatomical Description	Histological / Functional Significance
Anterior Border Layer	Thin, fibro cellular layer on the anterior surface of the iris	Determines iris colour; contains melanocytes and fibroblasts; absence or thinning contributes to crypts
Stroma	Loosely arranged connective tissue containing	Houses blood vessels, nerves, melanocytes,

Component	Anatomical Description	Histological / Functional Significance
	collagen fibres	immune cells; provides structural support
Anterior Pigmented Epithelium	Single layer of pigmented cells	Contributes to dilator muscle; blocks light transmission
Posterior Pigmented Epithelium	Heavily pigmented cell layer facing the lens	Prevents light scatter within the eye
Basement Membrane	Thin supporting membrane beneath epithelial layers	Structural support and cell adhesion

Table 2 (Different parameters of iris)

parameters	Description
Position	Between cornea (anteriorly) and lens (posteriorly)
Shape	Circular with a central opening (pupil)
Diameter	~12 mm
Thickness	~0.5 mm
Colour	Depends on melanin pigment (blue, brown, green, etc.)
Central Aperture	Pupil
Periphery	Attached to ciliary body
Anterior Surface	Rough, shows crypts and radial ridges
Posterior Surface	Smooth, deeply pigmented
Zones	Pupillary zone (inner) and Ciliary zone (outer)