WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 19, 1268-1287. Review Article ISSN 2277–7105

DIABETIC RETINOPATHY: EXPLORING PATHOGENESIS AND *AYURVEDIC* THERAPEUTICS

[1]*Dr. Aman Negi, [2]Prof. (Dr.) Jyoti Gupta and [3]Dr. Amit Kumar Agrawal

[1]PG Scholar, Department of *Shalakya Tantra*, Patanjali Bhartiya Ayurvigyan Evam Anusandhan Sansthan, Haridwar, Uttarakhand, India.

[2]Professor, Department of *Shalakya-Tantra*, Patanjali Bhartiya Ayurvigyan Evam Anusandhan Sansthan, Haridwar, Uttarakhand, India.

[3]Assistant Professor, Department of Shalakya-Tantra, Patanjali Bhartiya Ayurvigyan Evam Anusandhan Sansthan, Haridwar, Uttarakhand, India.

Article Received on
22 August 2024,

Revised on 12 Sept. 2024,
Accepted on 02 Oct. 2024

DOI: 10.20959/wjpr202419-34115

***Corresponding Author**
Dr. Aman Negi
PG Scholar, Department of Shalakya Tantra, Patanjali Bhartiya Ayurvigyan Evam Anusandhan Sansthan, Haridwar, Uttarakhand, India.

ABSTRACT

Eyes serves as a primary sense organ due to its pivotal role in the sensory perception of vision. This sensory capability allows individuals to interpret and interact with their surroundings in profound ways. Ayurveda also mentions about importance of eyes by quoting "*सर्वेन्द्रियाणां नयनं प्रधानम*" that means eyes are the most important sense organ of the body and one should make all necessary efforts to protect the eyes as long as one is alive. The chaotic lifestyle, faulty food habits, reduced physical activity, over exertion at work, subjection to various environmental changes and over exposure to radiations creates a stressful never ending vicious cycle leading to various lifestyle disorders. One of such lifestyle related disorders is Diabetes Mellitus, which if not controlled later on leads to Diabetic Retinopathy (DR). DR is a significant microvascular complication of diabetes, characterised by progressive damage to the retinal blood vessels. Therefore, identifying the risk factors for DR and keeping them under check is of paramount importance in saving the vision, reducing morbidity and thus reducing the economic burden due to blindness in our country. Current treatment modalities include laser therapy, intravitreal injections of anti-VEGF and vitrectomy tailored to the severity of disease. *Acharya Charak* have mentioned *Prameha* among the eight major disorders denoting the importance of the disease. Diabetic retinopathy occurs due to complication of *Prameha.*

To treat the disease it is necessary to understand the pathogenesis/ *Samprapti*. In *Ayuveda classics*, there are various herbal formulations along with *Panchkarma* and *Kriyakalpa* therapies which plays a crucial role in management of diabetes and its complication like DR.

KEYWORDS: Diabetes Mellitus, Diabetic Retinopathy, *Netraroga*, *Kriyakalpa*, Non Proliferative Diabetic Retinopathy (NPDR), Proliferative diabetic retinopathy (PDR).

INTRODUCTION

In our ancient literature, "*Chakshu*" is considered as prime sense organ out of all senses. To emphasize more on the importance of eyes *Acharya Vagbhata* quotes "Sincere efforts should be made by every individual to preserve his/her vision till the last breath of life". Because for an individual who is blind, day and night are the same and this beautiful world is no use of him even if he/she possesses a lot of wealth".[1] Diabetes mellitus (DM) is one of the world's rapidly growing non communicable disease. It is a widely prevalent disease in the current era. More than half of all people in India are at risk of developing diabetes in their lifetime. DM occurs in two forms: Type I or Insulin dependent diabetes mellitus (IDDM) and Type II or Non-insulin dependent diabetes mellitus (NIDDM). This disease results in generalised macro and microvascular complications.[2] Eyes are specially subjected to diabetic disturbances because of their peculiar structure and metabolism. Diabetic Retinopathy (DR) is a specific micro-vascular complication of DM and is one of the leading causes of acquired vision loss mostly in the middle-aged group. Therefore, identifying the risk factors for DR and keeping them under check is of paramount importance in saving the vision, reducing morbidity and thus reducing the economic burden due to blindness in our country.

Nearly all people of Type I and 75% of Type II DM will develop DR after 15 years of duration of DM and 18% will develop retinopathy in less than 15 years of duration of DM. Globally, DR affects about one-third of people with diabetes. It is estimated that there are around 93 million people with DR worldwide, with this number expected to rise as diabetes rates increase. It is estimated to cause up to 2.6% of global blindness cause. About 20 years ago, DR was the 17th leading cause of blindness but now has become the 6th and for working age group (<55 years of age) 2nd in developing countries. Diabetics have a 20-25 times greater risk of blindness as compared to the normal population.[3]

After viewing the magnitude of the problem of the disease, a comprehensive & thorough analysis of all the important *Ayurvedic* and modern literatures was done to establish a

probable mode of aetiopathogenesis of disease on *Ayurvedic* perspective. There is no direct reference about diabetic retinopathy in *Ayurvedic* texts. However, there is indication that vital organs like eye gets affected in *Prameha roga*. *Acharya Pujyapada Mahamuni* in *Netraprakashika* mentioned *Prameha* as *Nidana* of *Netra roga.*[4] *Prameha Poorvaroopa* – "*Hrinnetrajihwashravanopadeha*" gives a direct clue regarding the involvement of vital organs like eye in *Prameha Samprapti.*[5] The symptoms which are mentioned in *Dwitiya Patalagata Timir* can be taken to co-relate the symptoms present in Diabetic Retinopathy. In *Dwitiya Patalagata Timira, Acharya Sushruta* has mentioned "*दृष्टिर्भृशं विह्वलति द्वितीयं पटलं गतै*" i.e., *Drishti* gets *Vihalwa/Vyakula* when *Doshas* are situated in *Dwitiya patala*[6] which means the vision gets impaired in many ways. He further described "*मक्षिका मशकान् केशाञ्जालकानि च पश्यति*" i.e., visualizing false images of fly, mosquito, hairs, webs, circles etc. in front of the eyes which can be taken as floaters probably caused due to haemorrhages in the retina that are micro-vascular complications as mentioned in DR.

Pathogenesis of diabetic retinopathy (Figure 1)[7]

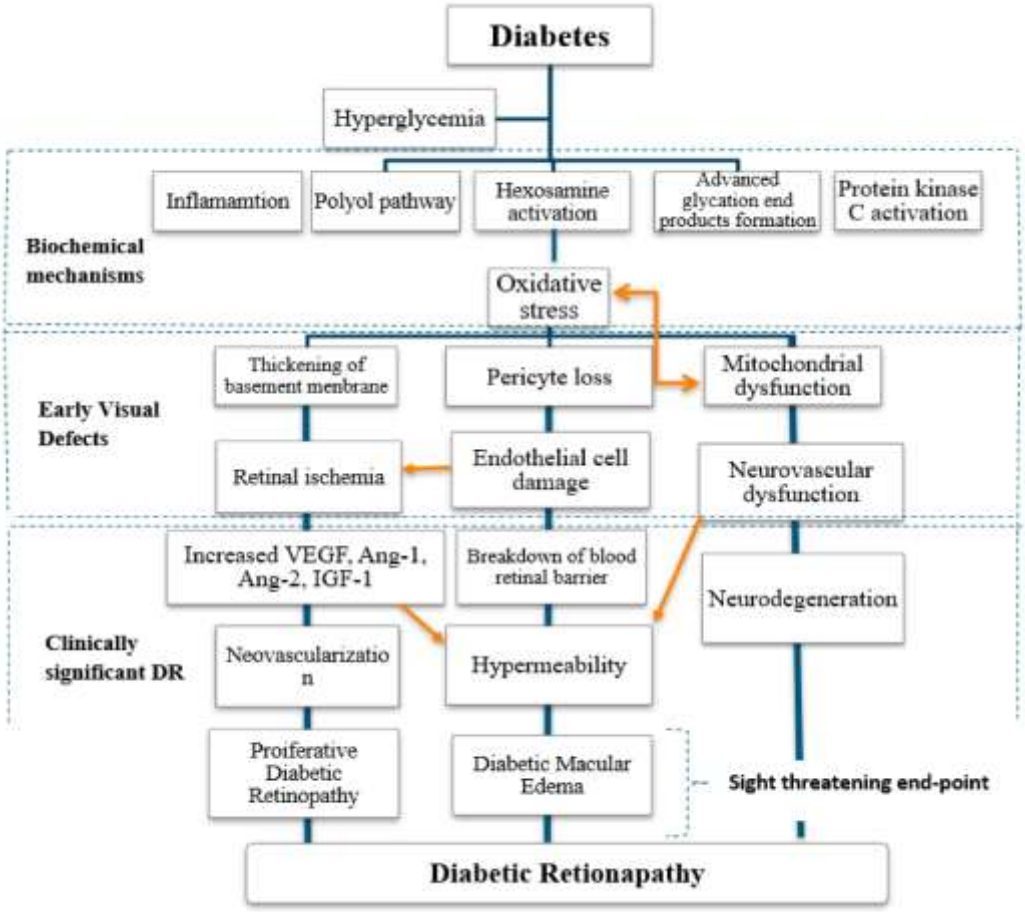

Figure 2: Diagrammatic presentation of the pathogenesis and pathophysiology of DR.

Classification of diabetic retinopathy[8]

It has been classified as follows

1. Non-proliferative diabetic retinopathy (NPDR)
2. Proliferative diabetic retinopathy (PDR)
3. Diabetic maculopathy
4. Advanced diabetic eye disease (ADED)

Symptomatology

Patients are not symptomatic until vitreous haemorrhage takes place or the macula is affected by oedema. Hence, eyes may be harbouring potentially vision-threatening new vessels but may be absolutely asymptomatic. This brings in an additional dimension to the management of the disease since there is a need to convince the patients of the need to undergo treatment even before they are asymptomatic and that they can actually become symptomatic and lose vision after the initiation of the treatment, which can be wrongly attributed to the treatment itself.

Occurrence of vitreous haemorrhage is heralded by symptom of sudden onset of shower of black spots. A large haemorrhage can lead to rapid loss of vision. If the haemorrhage is more pre-retinal in location, it may lead to a visible shadow in field of vision. Macular oedema in contrast, causes less dramatic symptoms. The vision in this case can be variably more and more of retinal destruction will not have any desirable results but effectively destroys peripheral field of vision.

On ophthalmoscopic examination of fundus signs present in NPDR are as follows

- Microaneurysms formed due to focal dilation of capillary wall following loss of pericytes. They are the earliest features of diabetic retinopathy on ophthalmoscopy. Clinically, they are seen as red dots and could be confused with haemorrhages. Fluorescein angiography identifies more of these than are evident clinically, although some of them can be thrombosed and may not be seen on angiography. Microaneurysms can also be seen in other vascular diseases but are characteristic of non-proliferative diabetic retinopathy.
- Retinal haemorrhages occur due to capillary leakage and can either be deep (dot or blot haemorrhages) or flame/ splinter haemorrhages which are superficial in nature.
- Hard exudates- are due to lipid extravasation. They are seen as discrete intraretinal deposits, especially as circinate rings surrounding a cluster of microaneurysms. The lipids

can slowly encroach onto the macular area. Subretinal migration can also take place. In late stages of the disease, subretinal exudates can be replaced by fibrotic plaques.

- Cotton wool spots are soft exudates are discrete areas of retinal infarction and are seen as opalescent areas of retina.
- Venous beading - Segments of retinal veins can be dilated, seen as beading.
- Intraretinal Microvascular Abnormalities (IRMA) - Adjacent to areas of capillary closure, vascular abnormalities can be seen which could signify intra-retinal neovascularization or dilated pre-existing capillaries (**Figure 2**)

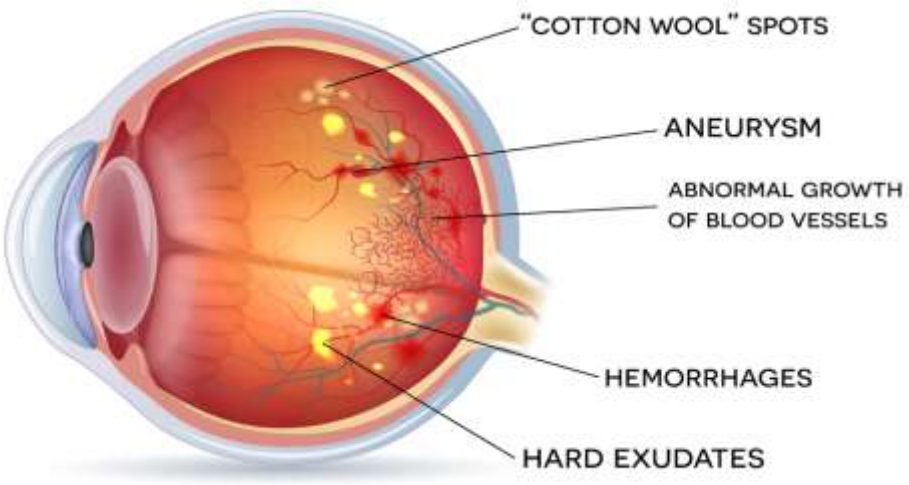

Figure 2: Showing Illustration of the signs present in diabetic retinopathy.

Signs present in Proliferative diabetic retinopathy

- The most important sequel of diabetic retinopathy is the occurrence of capillary closure. Although the extent and location of the capillary closure is best seen on fluorescein angiography, extensive areas of capillary closure may be clinically seen as relatively featureless retina. Shimuzu's studies on angiography have shown the clear connection between the extent of capillary closure and the severity of neovascularization in a four step scale:

(i) None
(ii) New vessels on retina alone
(iii) New vessels involving disk
(iv) New vessels in anterior chamber

- Neovascularisation-Proliferation of new vessels from capillaries, in form of NVD (neovascularisation at optic disc) or NVE (neovascularisation elsewhere).

- Fibrovascular epiretinal membrane formed due to condensation of connective tissue around the new vessels.
- Vitreous detachment

Abbreviated Early Treatment of Diabetic Retinopathy Scale (ETDRS)

Severity	Definition
Non Proliferative Diabetic Retinopathy (NPDR)	
No DR	No retinal lesions
Very Mild NPDR	Microaneurysm only
Mild NPDR	Any or all of; microaneurysms, retinal haemorrhages, exudates, cotton wool spots. No IRMA (Intraretinal Microvascular Abnormalities) or significant beading
Moderate NPDR	• Severe retinal haemorrhages in 1-3 quadrants or mild IRMA • Significant venous beading can be present in no more than 1 quadrant. • Cotton wool spots commonly present
Severe NPDR	The 4-2-1 rule; one or more of: • Severe haemorrhages in all 4 quadrants • Significant venous beading in 2 or more quadrants • Moderate IRMA in 1 or more quadrants
Very severe NPDR	Two or more of the criteria for severe NPDR
Proliferative Diabetic Retinopathy (PDR)	
Mild- Moderate PDR	New vessels on the disc (NVD) or new vessels elsewhere (NVE), but extent insufficient to meet the high risk criteria.
High risk PDR	• New vessels on the disc (NVD) in about ½ disc area • Any NVD with vitreous haemorrhage • NVE greater than ½ disc area with vitreous haemorrhage.

Signs of Diabetic maculopathy

- Macular oedema due to increased permeability of retinal capillaries.
- Central hard exudates
- Ischaemic changes in macula

Classification of Macular oedema

The early treatment for diabetic retinopathy study (ETDRS) classified the macular oedema into:

(i) Thickening of the retina at or within 500 microns of the centre of macula

(ii) Hard exudates at or within 500 microns of the macula, if associated with thickening of the retina

(iii) A zone of retinal thickening one disk area or more in size, a part of which is within one disk diameter of the centre of the macula.

More recently the classification has been simplified as:

(i) Mild: Some retinal thickening or hard exudates in posterior pole but distant from the centre of the macula

(ii) Moderate: Retinal thickening or hard exudates in posterior pole approaching the centre of the macula but not actually involving the centre

(iii) Severe—Retina thickening or hard exudates involving the centre of macula.

Advanced diabetic eye disease- It is the end result of uncontrolled PDR. It marked by complications such as-

- Persistent vitreous haemorrhage.
- Retinal detachment: The retina can be pulled by the pre-retinal traction. It may be seen as distortion of the posterior pole without actual detachment. However, shallow retinal detachment is best picked up on optical coherence tomography rather than clinically. The traction retinal detachment can have different configuration depending on the location and extent of the vitreoretinal attachments. Focal traction leads to conical retinal detachment while broad-based attachments lead to more extensive detachments. Sometimes the whole posterior pole can be detached like a table-top with adherence of the fibro-vascular tissue to the entire area. On top of a basic traction induced retinal detachment, a retinal break can form, especially at the base of the proliferation leading to a combined rhegmatogenous-tractional retinal detachment.
- Neovascular glaucoma

Risk factors

- Dyslipidaemia, a high BMI, puberty, pregnancy, cataract surgery.[9]
- Duration of DR, presence of diabetic neuropathy, nephropathy.[9]
- Duration of DM: is an important determining non-modifiable factor. It has a definite bearing on the incidence of retinopathy. After 20 years of suffering from diabetes, nearly 100 percent of juvenile diabetics develop retinopathy while only 50 percent of them develop proliferative disease. This incidence is much lower in the older onset diabetics.
- Poor metabolic control is less important, nut is nevertheless relevant to the development and progression of DR.
- Age at diagnosis: In a 10-years incidence study of proliferative diabetic retinopathy (WESDRS, Klein *et al.*, 1994) it was found that proliferative diabetic retinopathy was less

likely to have developed in patients who were under 10 years of age at diagnosis, suggesting that pre-pubertal years might have a neutral effect on progression.

- Hypertension: A 34 percent reduction in risk of deterioration of retinopathy was achieved by a tight control of blood pressure in the UKPD study.
- Pregnancy: Significant worsening of retinopathy has been demonstrated with pregnancy.
- Anaemia: Diabetic patients with Haemoglobin level less than 12 mg/dl are having twice the risk for retinopathy.
- Addictions like smoking, alcohol etc.
- In accordance with various studies, DR is classified as a polygenic disorder that is genetically inherited, with researchers having discovered an obvious familial clustering. DR and PDR are found to be 27% and 52% heritable respectively.[10] Studies have shown that a family history of DR increased the risk of DR among individuals by almost two to three- fold.[11]

Ancillary Investigations

- Urine examination
- Fasting and post-prandial blood sugar levels
- HbA1C (Glycosylated haemoglobin)
- Lipid profile
- Funduscopic examination – Direct and indirect
- Fundus fluorescein angiography
- OCT (Optical coherence tomography)

Other investigations

- Ultrasonography (USG)
- Ultrasound Bio microscopy (UBM).

Management

Interventions fall into three following categories to minimize the risk of vision loss due to DR: the primary prevention of microvascular problems, the early identification of retinopathy and the effective treatment of existing disease.[12]

- Prevention- By periodic screening of diabetic retinopathy through fundoscopy, OCT, FFA.
- Strict regulation of blood sugar level (glycaemia), hypertension, dyslipidemia.

- Lifestyle modification which includes proper balanced diet, regular exercise and exempting from any kind of smoking, alcohol or drug abuse.
- Intravitreal Anti-VEGF like Bevacizumab (1.25 mg), Ranibizumab (0.5 mg)
- Intravitreal steroids like Fluocinolone Acetonide intravitreal implant.
- Intravitreal injection of Triamcinolone.
- Laser therapy

➢ Macular photocoagulation-It is of 2 types: Focal photocoagulation and Grid photocoagulation. This is an efficient therapy in treating the clinically prominent macular oedema.[13]

➢ Panretinal Photocoagulation (PRP) by Argon or YAG laser. It is used in treating severe NPDR & PDR cases.[14]

➢ Sub-threshold laser using the diode laser has been reported to result in similar efficacy in PDR, while minimizing the retinal damage.

➢ PASCAL (Pattern scan laser) laser:

a) Laser exposure duration is much less, 10 ms for macular laser and 20 ms for peripheral laser.

b) Semi-automated laser delivery of present patterns

c) There is improved comfort, advanced precision and less choroidal inflammation, less burn spread and in general less collateral damage.

- Vitreoretinal surgery like PPV (Pars plana virectomy) to deal with vitreous haemorrhage and detachment.
- Other medications: Aspirin, anti-platelet treatment and use of aldose reductase inhibitors have not been found to be useful in the treatment of diabetic retinopathy. Lowering the serum lipids has been found to be an important step in the management of diabetic macular oedema when associated with raised serum lipids.
- The limitations and drawbacks of different procedures are shown in **Figure 3.**

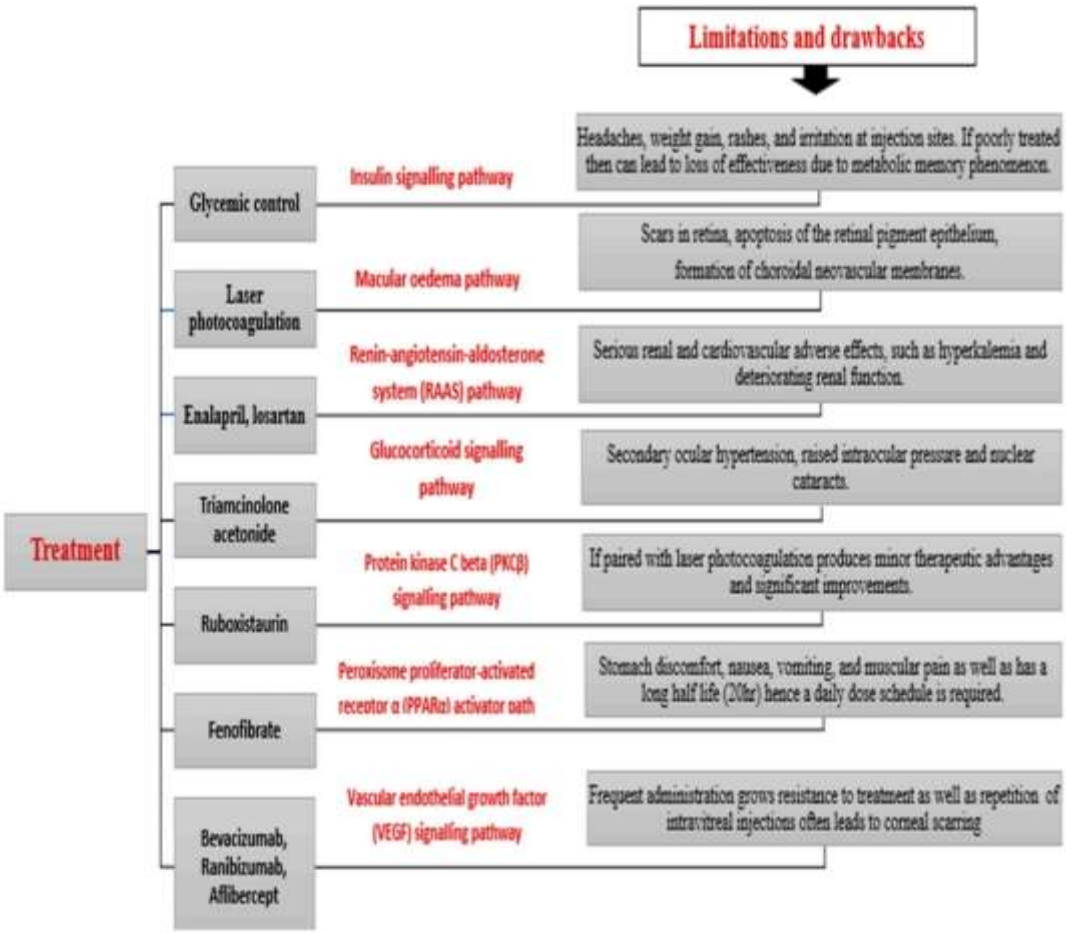

Figure 3: List of the current therapeutic techniques for diabetic retinopathy (DR) management, including their limitations and drawbacks.

Samprapti* (Pathogenesis) of diabetic retinopathy according to *Ayurveda

Ayurveda is built on the notion of *Dosha-Dhatu* equilibrium. *Samprapti Vighatana* facilitates treatment planning.

Madhumeha is primarily characterized by a predominance of *Vata Dosha* and an associated *Kapha* imbalance. *Vata* can be aggravated by two main mechanisms: ***Avarana*** and ***Dhatu kshaya.***[15] According to *Vagbhata, Madhumeha* is seen as a chronic, progressive condition of *Prameha* and is classified into two types:

1. *Avaranajanya Madhumeha*
2. *Dhatukshyajanya Madhumeha*

In *Charaka's* perspective, *Madhumeha* is seen as a concomitant condition, meaning that it frequently accompanies other complications. The chronic nature of this disease can lead to a

depletion of the ten *Dushyas*, manifesting symptoms depending on the affected *Dhatus*. *Avaranajanya Madhumeha* is difficult to manage (*Krichhrasadhya*), while *Dhatukshyajanya* is often deemed incurable (*Asadhya*). Effective management of *Madhumeha* necessitates a holistic approach, addressing both the root causes of *Vata* imbalance and the resulting tissue depletion to mitigate complications.

Pranavayu functions as a vital controller within the body, overseeing processes known as *Adana karma*. It plays a crucial role in how the sense organs perceive their respective objects, relying on *Pranavayu* for guidance. In contrast, *Vyanavayu* is responsible for conduction, significantly impacting processes like *Rasavikshepana,* which pertains to the movement and circulation of bodily fluids. If *Pranavayu* restricts the movement of *Vyanavayu*, the sense organs (*Indriyas*) may fail to perceive their objects. This dysfunction can affect one sense organ (homonymous) or multiple organs simultaneously (heteronymous). In the context of blood circulation, *Vyanavayu* plays a key role in *Rasa-Rakta vikshepana* (Blood circulation). Conditions such as diabetic retinopathy may emerge when *Pranavayu* interferes with *Vyanavayu* function. This can trigger a series of changes, including decreased retinal blood flow leading to retinal ischemia and increased VEGF activity. Early breakdown of the blood-retinal barrier, facilitates increased fluid accumulation leads to swelling of the retina (Macular oedema), which can impair vision and leakage of lipoproteins (Hard exudates). Manifestations of *Pranavritta Vyana* includes "*Sarvindriyanam sunyatvam*". In *Madhumeha*, *Avarana* can lead to an eye disorder. Since the eye is also considered an *Indriya* and *Avarana* leads to its *Sunyatvam* hence this can be correlated to *Avaranajanya Madhumehaja Timir.*

In the *Vidhisonitiya Adhyaya* of the *Charak Sutrasthan*, various aetiologies are outlined that contribute to an increase in the quantity of *Rakta Dhatu*. This increase can hinder the movement of *Vata dosha*, disrupting normal circulation and causing stagnation, particularly in the *Raktavaha srotas*. The symptoms associated with *Raktavritavata* include *Raktayukta shotha mandala*, which can be compared to symptomatology such as dot and blot haemorrhages which is a peculiar and one of the important feature of DR. In the context of DR, the disease often begins with a phase of *Raktakshya* (Retinal hypoxia). However, as the condition progresses, there is an increase in blood circulation, which can lead to haemorrhagic and exudative changes in the retina. This progression highlights the complex interplay between vascular changes and the manifestations of diabetic retinopathy.

The *Dushyas* involved in *Prameha roga* include ***Rasa, Rakta, Mamsa, Medas, Majja, Shukra, Lasika, Oja,*** and *Vasa*. According to the principle of *Kedari Kulya Nyaay*, the depletion of *Rasa Dhatu* results in the depletion of various other *Dhatus*. This interconnectedness highlights how an imbalance in one tissue can affect the overall health of the body.

1. *Sirasaithilya*[18] is recognized as a significant indicator of *Raktakshaya* according to *Sushruta*. This condition refers to the loosening or weakening of the blood vessels, which can manifest as various symptoms. In the early stages of retinopathy, a generalized dilation of retinal veins can be recognized, assumed to be related to retinal hyperperfusion. In the later stages also focal venous changes may develop indicating that the retinopathy has progressed to a pre-proliferative stage. These focal changes include beading, loops, and reduplications of the larger retinal venules.
2. *Dhamanisaithilya*[18] is identified as a significant characteristic of *Mamsakshaya*. It gives us an idea about the loss of sclerosis of the vascular wall in diabetic patients which is due to stiffening of the collagen caused by advanced glycosylated products with collagen cross-linking and elastin degeneration. Also, the lumen of the retinal arteries have been reported to become narrower due to the growth of smooth muscle cells and vascular fibrosis.
3. *Sandhishunyata*[18] is a characteristic of *Medakshaya*, which can be associated with the loss of junctional cell proteins or defects in cell adhesion. This disruption contributes to the breakdown of the blood-retinal barrier (BRB). As a result, prominent signs such as macular oedema, dot/blot haemorrhages, and the formation of exudates may appear, indicating significant retinal damage and fluid accumulation.
4. *Majjakshaya* accounts for the depletion of marrow tissue leads to decrease in blood cells formation and results in hypoxic condition of retinal neurons. Axonal degeneration of retinal nerve fibres occur due to *Vata kshaya*, which may be correlated with hypoxia and this hypoxic axonal degeneration leads to formation of cotton wool spots or soft exudates.
5. *Oja* signifies the very essence of all *Dhatus.*[16] According to *Chakrapani, Apara Oja kshaya* occurs in *Madhumeha*[17], and its location is in the ten *Mahamula dhamanis*. The loss of *Oja* results in the deterioration of *Dhamanis* due to the principle of *Ashraya-ashrayeesambandha*, which emphasizes the interdependence between the support (*Ashraya*) and the supported (*Ashrayee*). This can be correlated with the sclerosis of the retinal vessels which is a constant finding in adults who have had diabetes over a period of years.

According to *Ayurveda, Mandagni* is the root cause of all the diseases. *Mandagni* results in generation of *Ama* along with improper production of the successive *Dhatu* and imbalance of *Dosha*. In *Ayurveda*, the concepts of *Agnimandya* at both the gastric level (*Jatharagni*) and the tissue level (*Dhatwagni*) are closely linked to conditions like *Prameha*. Additionally, in the context of blood disorders (*Raktaja vyadhi*), *Agnisada* is a significant feature, as noted by Charak. Since, *Rakta* is one of the *Dushyas* in *Madhumeha*, issues related to *Dhatwagnimandya* can lead to the accumulation of *Ama* at the tissue level. This accumulation can be likened to the Hexosamine flux, Reactive Oxygen Species (ROS), polyol pathway flux, formation of Advanced Glycation End products (AGEs) and PKC activation due to the increased oxidative stress in the retina (**Figure 4**). These all of which are critical in the development of vascular changes and neurodegenerative changes in retina leading to DR.

Capillary endothelial cell damage and loss of capillary pericytes are one of the foremost factors in pathogenesis of Diabetic Retinopathy. Vessels are composed of tissue, elastin fibres, and smooth muscle cells.[18] *Kapha dosha* has distinctive property of *Sandhibandhan* which ensures the compactness of these fibres and tissues.[19] *Kapha dosha* vitiation can disrupt its usual function causing *Sandhibandhan Vikriti*[20, 21] and damaging endotheial cells and capillary pericytes. All types of *Sroto dusti*, including *Atipravruthi, Sanga, Siragranthi*, and *Vimarga gamana*, have a role in the pathophysiology of NPDR and PDR. According to *Acharya Charaka and Vagbhata*, the eye dread from the *Kapha dosha*.[22] Any organ of *Pitta* origin that becomes *Avrudha* by *Kapha dosha* will undoubtedly lead to *Srotoavarodha*. This further causes ischemia or compromised blood flow due to occlusion in arterioles and venules leading to development of cotton wool spots.

- Formation of venous beading can be linked to *Siragranthi*.
- Occurrence of retinal haemorrhages and exudate can be considered as *Vimarga gaman*.
- Neovascularization can be compared to *Atipravruthi*.

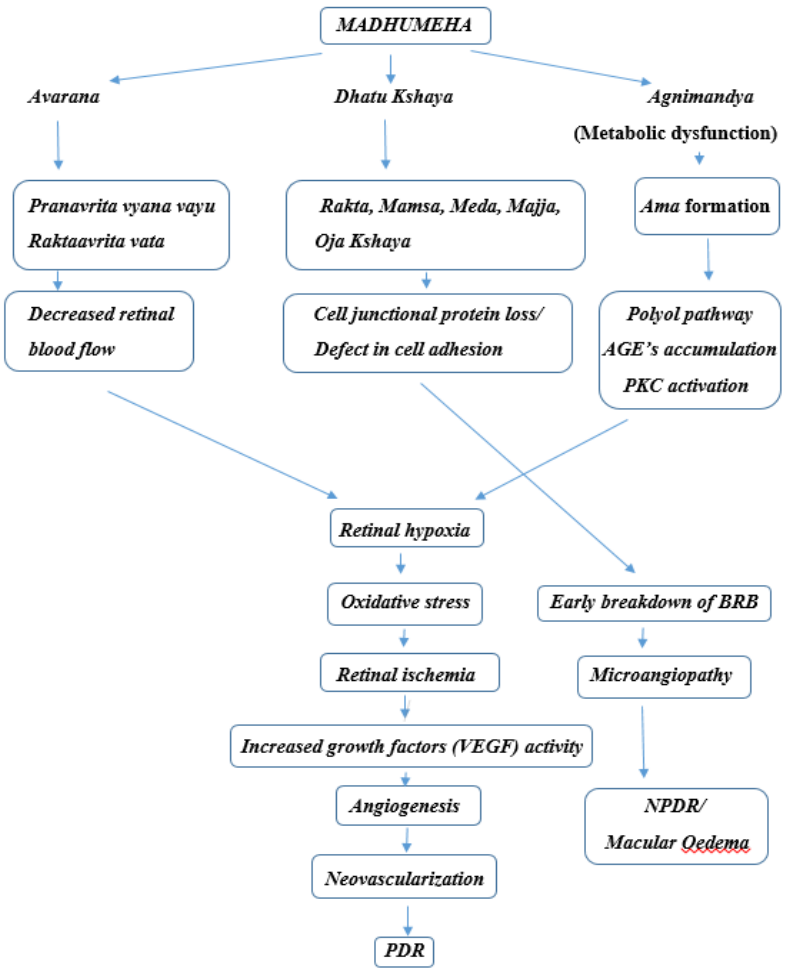

Figure 4: Showing pathogenesis of diabetic retinopathy through the lens of *Ayurveda.*

Management of diabetic retinopathy in *Ayurveda*

The fundamental treatment principle of *Ayurveda* is *Nidan parivarjan* which means restraining from unhealthy food habits (*Apathya ahara*) and lifestyle (*Apathya Vihar*).

The treatment protocol in DR should involve drugs which have *Madhumehahar*, *Shothagna*, *Raktaprasadana*, *Chakshushya* and *Balya* properties.

Chikitsa* of *Agnimandya

The eye is an integral part of the body, and thus, when addressing eye conditions, it is essential to consider treatment at the cellular level of the entire body. *Agnimandya* at the tissue level is referred to as *Dhatwagnimandya*. To restore balance, appropriate *Deepana* and *Pachana* therapies, such as *Trikatu churna*, *Shunthi-Dhanya-Musta churna* etc. can be utilized to correct both *Jatharagni* and *Dhatwagni* according to individual needs. This holistic approach ensures that both the digestive and tissue metabolism are optimized for effective healing.

Avarana Chikitsa

Avarana should be addressed with treatments that are *Anabhisyandi***,** *Snigdha*, and *Srotosudhikar* (purifying for the channels). Depending on the patient's condition, *Mridu samsodhan* therapy may be appropriate. Additionally, all palliative and preventive *Rasayana* medicines are beneficial for both the prevention and management of disorders induced by obstruction. These *Rasayana* therapies are particularly valuable in cases of diabetic retinopathy, as the role of oxidative stress is well recognized in the pathology of this condition.

***Shodhana chikitsa, Kriyakalpas* and other therapeutic management strategies**

Virechan **-**According to *Pratimargharan chikitsa sidhanta*, *Virechan* is the best way of *Kaya shodana* in case of haemorrhages from *Urdhwanga* route. It is also useful in the disorders in which *Pitta* is associated with *Vata* or *Kapha*. *Eranda Taila* mixed with milk is given to treat almost all the *Avarana.*[23] *Triphala, Trivrita* is also indicated for *Virechan*.

Nasya- *Nasya* with *Chakshushya* drugs infused oils can be administered to expel out the morbid *Doshas* in *Urdhawjatrugat srotas. Nasya* with *Durva ghrita* can also be administered in resolving the retinal haemorrhages as it has *Rakta-sthambak* property.

Basti*[24] –** While *Basti* is primarily regarded as the most effective treatment for *Vata Dosha*, it is also recommended for conditions related to *Pitta Dosha,** *Kapha Dosha*, and *Sarvadhatu Ashrita Vyadhi*. In emphasizing the significance of this treatment, *Acharya Sushruta* noted that it "*Chakshyuhu Prinayati*," indicating its potential to enhance vision. *Basti* with *Chakshushya* drugs should be advocated in alleviating the *Vata dosha* and reducing retinal oedema. *Madutailika Chakshushya Basti* can be used in treating diabetic macular edema (DME) since this *Basti* is effective in *Rakta & Pitta Dushti* also. *Yapana Basti, Yasthimadhu Ksheera Basti, Panchatikta Pancha Prasritika Basti* and *Guduchyadi Ksheera Basti* can also be used.

Tarpan **-**Various *Ghritas* can be utilized according on the stage of DR. *Ghrita*, known for its *Raktpitta shamak* and *Ropan* qualities, can help reduce haemorrhagic symptoms and can be administered in *Tarpan*. *Durvadya ghrita* tarpan is effective in mild to severe NPDR and PDR (i.e., *Rakta pittaja*).[25] *Triphala* has anti VEGF properties hence, *Mahatriphaladi ghrita* can be given in all stages of DR.[26] In case of different stages of DR, medicines like *Patoladi ghrita*[27], *Jeevantyadi ghrita*[28], *Drakshyadi ghrita* can be used in *Tarpan* procedure to

alleviate haemorrhagic signs due to *Raktapitta samak*, *Ropaka* and *Rasayana* properties of these drugs.

Aschyotana- is a method of repeatedly administering a small volume of medication directly into the open eye. The medicines, usually in the form of medicated decoctions, are absorbed through the blood vessels located in the conjunctival fornixes', sclera, and the highly vascularized inner canthus. The therapeutic effects of *Aschyotana* are similar to those of the *Seka* procedure. *Prapoundarikadi*[29] *and Manjisthadi Ashchyotana*[30] can be used in NPDR cases.

***Putpaka*[31] –** It refers to the topical application of plant extracts and lipids in the eyes for a set duration. This method is identical to *Tarpan* however it is prepared differently. For the various stages of DR, administration of *Ropana Putpaka* can be done.

Seka- *Seka* is done as a *Poorva karma* before *Tarpan.* This helps in vasodilatation of superficial vessels and some amount of medicines gets absorbed through medial canthus. Drugs like *Vasa, Amalaki, Lodhra, Yashti, Triphala* etc can be used in *Seka.*

Takradhara- The process of *Takradhara* might accelerate the function of *Tarpaka kapha*, and may also bring in the specific action as demanded by the disease condition like blockage of channels by *Kapha* which can be taken as micro vascular occlusion which is the basic pathological process seen in Diabetic Retinopathy.

Along with the *Kriyakalpa* procedures, following key principles outlined in *Dincharya, Ritucharya, Sadvritta* and *Swasthvritta* may help in minimizing the risk & severity of diabetic retinopathy and restoring the vision.

Samshamana Chikitsa

Triphaladi choorna, Triphaladi Kwatha, Mahavasadi Kwatha[25]*, Vasakadi Kwatha*[32] *and Amrutadi Guggulu.*[33]*, Phalatrikadi Kwatha*[34] *(equal quantity of-Haritaki, Vibahtaki, Amalaki, Daruharidra, Haridra, Indrayava, Mustha*) and *Ayurvedic* formulations having antioxidant properties are very helpful in mitigating the damage done to endothelial cells and pericytes in diabetic retinopathy such as *Sitopaladi choorna, Nisha-amalaki. Triphala, Manjistha choorna, Punarnavasatak Kwatha, Giloy Satva, Chandraprabha vati, Mahayograj guggulu.*[35]

CONCLUSION

Diabetic retinopathy is a significant complication of diabetes, characterized by damage to the blood vessels in the retina. Tremendous advancement made in the science of ophthalmology in recent years like FFA, OCT, Fluorescein angiography has paved a way for better diagnosis & timely management of various stages of DR. Modern science provides various procedures like laser therapy, Anti-VEGF intravitreal injections and vitreoretinal surgery. These procedures have several drawbacks such as they are invasive in nature, may only provide temporary relief or stabilization. Patients often need repeated sessions which are expensive thus proves to be economic burden. While there are various effective treatments for diabetic retinopathy, these drawbacks highlight the importance of a comprehensive management plan that can be achieved by incorporating *Ayurvedic* protocol, monitoring blood sugar level, regular eye examinations.

Diabetic retinopathy is a condition affecting the *r*etina and is a complication of long-term uncontrolled diabetes, resulting from metabolic defects and endocrine dysfunction. All three *Doshas* - *Vata*, *Pitta*, and *Kapha* are involved, with *Rakta* acting as both *Dosha* and *Dushya*. The predominant *Dhatus* affected include *Rakta*, *Meda*, and *Mamsa*, with involvement of the *Sira srotas* of the *Raktavaha srotas* and *Ojavaha dhamani* at various stages.

When analysing the pathology of diabetic retinopathy, it exhibits all four features of *Srotovaigunya: Atipravritti*, *Sanga*, *Siragranthi*, and *Vimarga gamana*. *Sanga* is indicated by the occlusion of retinal vessels, leading to hypoxia and ischemia. *Siragranthi* refers to the formation of venous beading, while *Vimarga gamana* corresponds to retinal hemorrhages and exudates and *Atipravritti* can be related to neovascularization, where new blood vessels are formed. Key aspects of the pathogenesis include *Agnimandya*, formation of *Ama*, *Avarana*, and *Dhatu Kshaya. Ayurvedic* protocols involves drugs which have *Chakushya*, *Shothahara* properties like *Triphla*, *Lodhra*, *Vasa*, *Panchkarma* modalities like *Virechan* and *Basti* facilities the elimination of all the aggravated *Doshas* and simultaneously balancing the mitigated *Doshas*, *Dhatu*, deranged *Agni. Kriyakalpa* procedures like *Tarpan*, *Aschyotana*, *Seka*, *Putpaka* along with antioxidant drugs can effectively control DR by restoring endothelial cells in the retina vessels, alleviating oedema and any further haemorrhages. By focusing on individualized treatments that incorporate dietary modifications, herbal formulations, detoxification modalities and lifestyle changes. *Ayurveda* aims to address the root causes of the condition. This integrative method may help to improve overall eye health

and support metabolic balance, potentially mitigating the progression of diabetic retinopathy. However, it is essential to complement these practices with conventional medical care and regular monitoring, ensuring a comprehensive strategy for managing diabetes and its complications.

Source of funding: None.

Conflict of interest: None.

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