1. Introduction

Diabetes mellitus has in recent times, gained importance as one of the most common, non communicable disease, which contributes to death and disability worldwide. Diabetes affects almost all aspects of intermediary metabolism and is also associated with accelerated aging of the cardiovascular system. Hence diabetes is best de

Inclusion of Prameha among the eight major disorders in Charaka Samhita shows the importance of the disease given by ancient seers. The risk of development of blindness in diabetics increases by 20–25 times as compared to the normal population. High prevalence rate of Diabetic Retinopathy (34.6%), proliferative diabetic retinopathy (7%), diabetic macular edema (6.8%), and Vision threatening Diabetic retinopathy (10.2%) in diabetics was great concerns which led to search and analyze the disease process on the basis of modern pathogenesis and different Timirvyadhi mentioned in Ayurvedic authoritative texts. Thus the present study endeavors to discuss the similarities and differences among the various components of Prameha/Madhumehtajanya Timir with Diabetic retinopathy and its stages. To establish a probable etiopathogenesis of the disease from Ayurveda prospective, all the important literature of both modern medicine and Ayurveda along with online sources were searched and analyzed. All the three dosha along with Rakta dosha and Saptadhatus with four internal Dristipatal of eye are affected in Madhumehajanya timir in different stages of the disease. Avarana and Dhatu kshaya too have important role in development of diabetic retinopathy due to prolonged and uncontrolled hyperglycemia. Agnimandya related Ama formation has a role in pathology of diabetic retinopathy which is quite similar to oxidative theory of diabetic retinopathy explained in modern pathology. Urdhaga raktapitta, Ojas kshaya, Rak- 

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means. Although there are many other causes of vision impairment, VISION 2020 seeks to address the main causes of avoidable blindness, in order to have the greatest possible impact on vision loss worldwide. Diabetic retinopathy is one among the target diseases for VISION 2020 [5].

The prevalence of DR, proliferative diabetic retinopathy (PDR), diabetic macular edema (DME), and VTD (Vision threatening diabetic retinopathy) among individuals with diabetes is 34.6%, 7.0%, 6.8%, and 10.2%, respectively. Estimate shows that the number of people with DR will grow from 126.6 million in 2011 to 191.0 million by 2030, and the number of people with VTD will increase from 37.3 million to 56.3 million, if no urgent action is taken [6]. Innovative alternative therapies and comprehensive approaches are needed to reduce the risk of vision loss by prompt diagnosis and early treatment of Vision Threatening DR (VTDR).

After viewing the magnitude of the problem of the disease, a comprehensive and thorough analysis of all the important literature of both modern and Ayurveda was done and online sources are searched to establish a probable etiopathogenesis of the disease on Ayurvedic prospective. Though there are no direct references are available regarding Madhumeha/Prameha janya Timir, enough evidences are available in all leading treaties of Ayurveda, which substantiate that Timir can be a combination of Madhumeha. In this review study many aspects of basic concepts of Ayurveda were analyzed to find out the probable etiology and pathogenesis of Diabetic retinopathy with probable correlation of different stages of the disease with different types of Timir described in Ayurvedic literature.

2. Samprapti (pathogenesis) of diabetic retinopathy

2.1. Role of Raktapitta in manifestation of diabetic retinopathy

Diabetic retinopathy basically a Dristipatalagata roga is mainly attributed to Sira srotasabhisyandam and raktavaha srotodusti due to a variety of Achakshyushya ahara and vihara karanas especially in Prameha patients. In order to understand the samprapti of diabetic retinopathy in Ayurveda, general samprapti of eye disease must be considered. Nidana of endogenic eye diseases are mainly Achakshyushya factors which vitiates Pitta. The vitiated Pitta in turn vitiates the Pitta vaha srotas. Due to interconnection of Pitta and Raka, which shares Ashyra Ashrayee bhava, the raktavaha srotas is also gets vitiated due to Pitta vitiation. As the nidana factors are Achakshyushya, the vitiated pitta and raka have an affinity towards penetrating the eyes. Hence the vitiated dosha move towards the eyes through jatoordhwa srotas and finally gets confined to the eyes, there is a stage when the Sirasrothas are deeply involved which is known as Sira abhisyanda [7]. The whole pathology of diabetic retinopathy which starts with sroto dusti of Raktavaha srotas manifested as microangiopathy in the form of Attiprapravritti, Sanga and Granthi as haemorrhages, exudates and venous beading in diabetic retinopathy respectively.

In this context of Siraoahbisyandam in eye diseases the Ashraya sthana is Srotas, affected dhata is Raka and vitiated dosha is Pitta. Prameha brings out changes in the dristipatalam which greatly affects vision. In the initial stage, the etiological factors promote utklesa in the vessels which causes changes in the permeability of the vessels especially of head region which is the basic pathologic change for the development of eye diseases. If the stage of Sira abhisyanda continues it spreads to netrasrutas and the same vascular changes takes place in the vessels of eye, because Achakshyushya factors always have affinity towards the opthalmic tissues. In the stage of netraabhisyandam, if there is further vitiation of Pitta dosha, the condition further aggravates and will be confined to Dristipatalam.

Few predisposing factors also influence the development of eye disease associated with prameha. These include— 1. Pittaparakritti of the patient. 2. Hereditary factors. 3. Pitta Kapha predominant season, foods and psychological stress factors like krodha, soka etc., which contribute towards vitiation of Pitta. Vitiated Pitta reaches and amalgamated with Raktu dhatu due to similar properties. All these factors altogether promote prominent changes in the vessels of Dristipatalm. The texture of the vessels is damaged and hence the permeability increases. This results in leakage and hemorrhages from the blood vessels. The blood oozes out like sweat. This again correlates with pathogenesis of Raktapitta, specially quoted by Charaka. Due to lack of circulation there is localized hypoxia which results in development of new vessels. As these vessels are fragile they bleed easily. Exudates formation, neovascularization and proliferation of the tissues which leads to degenerative changes in the retina. In this context Urdhwaga Raktapitta can be correlated with Diabetic Retinopathy, as the seat of Urdhwag Raktapitta are all the seven natural openings of the head. And in eye, as the vessels are minute and due to achakshyushya factors the vessels of dristipatala or retina are affected mostly [Fig. A.1].

2.2. Avaranajanya, Dhatushakshayanya Timir and diabetic retinopathy

According to Vagbhata, Madhumeha is chronic progressive stage of Prameha and of two types: Avaranajanya and Dhatushakshayanya [8]. Madhumeha is Vataja type of prameha and Vata can be aggraved by two ways i.e. Avarana and Kshaya [9]. Avarita vajayajanya madhumeha is krichhrasadhya and dhatushakshayajanya madhumeha is asadhyaa (incurable). As per charak “prameha anussanginam” means diabetes is concomitant in nature. Thus diabetes remains always present with its complications. Due to both avarana and dhatushaya all the ten dushyas goes into state of depletion and produce symptoms according to the seat of that particular dhata. In the case of Diabetic retinopathy main affected dhatu is Raktu dhata, though all the dhatus gets affected and srotas affected are Raktvaha, mam savaha and medovahasrotas mostly. List of doshas, important dushya, dhatu kshaya symptoms, srotas affected and their modern interpretation for pathogenesis of Diabetic retinopathy are mentioned in Table A.1.

2.2.1. Avarana

A. Pranavritta vyana: Pranavayu acts like a controller. It is responsible for Adana karma. Sense organs perceive their objects with the help of Pranavayu. Vyanavayu is responsible for gati or conduction. Hence vyanyayu plays a significance role in Rasa-vikshepana. Conduction is not only related to cardiac cycle but all types of neural conduction should be considered. Whenever the controller Pranavayu will restrict the gati of conducting vyanyayu, the Indriya will not be able to perceive its visaya. It may happen in one Indriya (homonymous) or in all indriyas (heteronomous) together. If it happens in all indriyas it can be compared with the vegetative stage or deep coma. Rasa-Raktu vikshepana (blood circulation) is function of vyanyayu. In case of diabetic retinopathy vascular disorder may arise due to Pranavritta vyana. This initially causes retinal ischemia and followed with successive cascade of retinopathic changes like neovascularisation, cotton wool spots and intra retinal microvascular abnormalities (IRMA). Early break down of blood retinal barrier (BRB), hard exudates formation and macular edema are other symptoms to follow. Symptoms of Pranavrittavyana are Sarva indriya sunyata, smriti kshaya and bala kshaya and the treatment is Urdwa Jatrujagata ciktis (Tripathy Brahmananda, 1999, Caraka Samhita, Chikitsa Sthana, 28:202; P 974). In
this stage Nasya (Trans nasal medication) can be employed to relieve the signs and symptoms of Diabetic Retinopathy.

### B. Rakta vritta vata

The term Rakta vritta vata is associated with the condition Raktaja vyadhi, which is one of the major signs of tapitta. In the context of pathology, Rakta vritta vata involves increased blood flow and circulation, which can lead to haemorrhages and exudative formations. These symptoms are depicted in Fig. A.2.

### 2.2.2. Dhatukshaya

- **A. Sirasathilaya** [10] is one of the major signs of rakta shayaas per Sushruta. Loss of pericyes and formation of microaneurysms are earliest signs of Diabetic Retinopathy. These can be correlated with Sirasathilaya due to Rakta shaya. First Patala consists of rasa and rakta dhatu, so manifestation of the disease is in the form of microaneurysms and less severe in nature, which are very similar to background Diabetic retinopathy or mild NPDR and symptoms of 1st Patalagata Timir appears in this stage. If Rakta shaya persists for long time, it may lead to hypoxia related neovascularization in Diabetic retina.

- **B. Dhamanaisathilaya** [10] is one of the features of mamsaksahaya. This can be correlated with endothelial cell loss due to improper apoptosis and loss of capillaries, leads to early break down of blood retinal barriers and signs like dot/blot or flame shape hemorrhages appear in this stage. As 2nd patala consists of sookshma rupi mamma dhatu, symptoms of 2nd patalagata timir are seen in this stage. This stage may be correlated with mild NPDR or moderate NPDR depending upon the extent and severity of affected dhatu.

- **C. Sandhishunyata** [10] is another feature of medakshaya, which may be correlated with junctional cell protein loss or cell adhesion defects and break down of BRB. Appearances of macular edema and exudates formation are prominent signs in this stage. 3rd patala consists of Meda dhatu and when dhatu kshaya reaches the 3rd patala symptoms of 3rd patalagata timir appears. On severity point of view this stage may be correlated with Moderate NPDR based on the extent of dhatu affected. 4th patala of dristipatal is asthishisra in nature and loss of asthi and majja dhatu leads to symptoms of 4th patalagata timir.

### D. Timiradarshana

- **Timiradarshana** is one of the symptoms of majjakshaya (Gupta Atridev, 2008, Ashtanga Hridaya, Sootrasthan, 11:19; P 116) and thus leads to Vata kshaya. Depletion of marrow tissue leads to decrease in blood cells formation and results in hypoxic condition of retinal neurons. Axonal degeneration of retinal nerve fibers 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 in severe NPDR stages of Diabetic retina.

When Avarana samprapti is continued for longer period, it will attain dhatu kshaya avasta and dhatukshaya samprapti will continue in further stages of disease process. Again due to Dhatwagnimandya improperly formed Rasa dhatu in inadequate form is released, which leads to successive Anulomajanya Dhatu kshaya. Here Dhatu kshaya indicates the sookshma/poshak dhatu not the shtoolarupidhatu. Four internal patalas of eye are based on functional part of sookshma and ashthayvedhatu. The manifestations of the diseases depend on the affected dha, dhatu and srotas. These sookshma rupi dhatu of Dristipatala in eyes gets affected easily by the vitiated doshas due to either Avarana or dhatukshayajany samprapti alone or by combination of both. Probable correlation of dhatu kshaya symptoms and pathogenesis of Diabetic Retinopathy is depicted in Fig. A.3.

### 2.3. Ama dha and diabetic retinopathy

Agnimandya at the gastric level (Jatharagni) and at the tissue level is well established in Prameha and Madhumeha in Ayurveda. And in Rakta vyadhi, Agnisada is another feature according to Charak (Tripathy Brahma, 1999, Caraka Samhita, Sootra Sthana, 17:69; P 351). In this stage the disease becomes incurable and this proves the hereditary and genetic predisposition nature of diabetic retinopathy.

In this stage the vitiated dosha obstructed the path of Vata and vata carried the Ojas to the basti.
and causes madhumeha (Tripathy Brahmananda, 1999, Caraka Samhita, Sootra Sthana, 17.78–81; P 355). According to Chakrapani aparā Oja kshaya occurs in madhumeha and the seat of Aparā Oja are ten Mahamula dhamanis. Loss of Oja leads to loss of dhamanis as per ashrayashreyeesambandha. This can be correlated with loss of capillaries and thus due to Ojakshyaya abnormal apoptosis can enhance, leads to loss of capillaries and basement membrane thickening. Among the functions of Oja are bhaya and avâyantara karana (indriya) karma, means motor and sensory functions. Sushruta also mentioned abhīghata, soka (grief), kshaya (dhātukṣhya), kopa (anger) as causes of Ojas kshaya (Trikamji J. Ram N, 2012, Susruta Samhita Dalhana Commentary, Sootra Sthana, 15.23–26; P 72). In case of diabetes along with dhaut kshaya, psychological stress is another factor which plays important role in oja kshaya. Loss or diminution of sensory functions including visual loss which are prominent features oja kshaya.

2.5. Prameha and diabetic retinopathy

Among 20 pramehas, 19 pramehas except Madhumeha are almost having renal and urinary pathoogy. Main pathological features of prameha are: Pravuta avilamutrata means increase in quantity of turbid urine in patients with prameha. Proteinuria can be correlated with pravuta avilamutrata [11]. As in long run; prameha is converted to madhumeha stage, this nephropathy signs are mostly associated with chronic cases of diabetes. Proteinuria leads to hypoalbuminemia and this decreases serum osmolarity [12], which again leads to salt and water retention in extracellular space of retina. This may be another cause of diabetic macular edema and retinal edema in general.

3. Visual symptoms of timir and diabetic retinopathy

Diabetic Retinopathy can be compared to Timira involving all the four patalas. Patalas are described on the basis of functional composition of dhaṭus of dṛṣṭi. The symptoms of vision are manifested when the vitiated dōsha afflicting the concerned dhatu in dṛṣṭi patalas. All the three dōsā in single or in combination can affect one or more patalas of dṛṣṭi patalas (Retina). On the basis of different symptoms of Timira and stages of Diabetic Retinopathy, a probable differentiation and classification of Diabetic retinopathy is depicted in Table A.2.

4. Management of diabetic retinopathy in Ayurveda

Treatment is all about correcting and preventing the etiopathological mechanism (Samprapti vighatana). So as per etiopathological mechanisms described above, the first and foremost care should be given to prevent madhumeha. The treatment of diabetic retinopathy revolves around treating the causes of madhumeha, management of Urdwaga Raktapitta, treatment of Avarana, prevention of dhaut kshaya including oja kshaya and prevention of Agnimandya in general.

4.1. Agni chikitsa

Eye is not different from the body. So when we treat eye ailments it’s necessary to treat the body at cellular level. Agnimandya at tissue level is called Dhatwagnimandya. With proper dipana pachana drugs, like Trikatu churna, Jatharagni as well as Dhatwagni can be corrected as per individual requirement.

4.2. Srotas sodhan chikitsa

Sodhan chikitsa are important part of all the Ayurvedic therapies. Due to dhatwagnimandya, accumulation of impurities occurs at the srotas/capillary level. For this Virechan can be advocated. Nasya with oil prepared from chakshyusya drugs should be used for urdhwa-jatrugata srotas sodhan.

4.3. Raktapitta Samak Chikitsa

Treatment of Raktapitta and Raktaja vyadhi are similar as per charak. These are Raktapittahari kriya, virechan, upavasa (fasting) and Raktamoksha (Tripathy Brahmananda, 1999, Caraka Samhita, Sootra Sthana, 24:18; P 431). As Bloodletting is contraindicated in case of Timir, except Raktamoksha, all the procedures should be advised in case of different stages of Madhumehajanya timir. Even Yogratnakar and Chakradutta have mentioned Langhana (fasting) as Sadpachanan for treatment of eye diseases in general. As in diabetic retinopathy main dōsha involved are Vata and Pitta along with Kapha anubandha, the Pitta should be treated first, as the aggravated dōsha becomes more powerful in its own functional place (Tripathy Brahmananda, 1999, Caraka Samhita, Chikitsa Sthana, 28:188; P 971).

4.4. Avarana chikitsa

The Avarana should be treated by measures which are Anabhisyandi (non obstructive), Snigda (unctuous) and Srotosudhikar (purifier of channels). Depending on the strength of the patient, Yanana Basti and mrudu samsodhan therapy can be given. All the palliative and preventive Rasayan drugs are useful for the prevention and treatment of Avrīttta induced disorders. Especially Shilajatu, Guggulu, Chyavanaprash and Brahma rasayan are mostly helpful (Tripathy Brahmananda, 1999, Caraka Samhita, Chikitsa Sthana, 28:240–242; P 981). These Rasayan drugs are also useful in diabetic retinopathy cases, as oxidative stress theory is well established in pathology of Diabetic Retinopathy and Ama theory in madhumeha too has role in development of Diabetic Retinopathy. Eranda Taila is beneficial in almost all the Avarana and works as Sramidsana. Yanana Basti, Yasthidamadu Ksheera Basti, Panchatikata Pancha Prasristika Basti and Guduchyadi Ksheera Basti may be administered in Pitta and Rakta Avarana [13].

4.5. Dhaut kshaya Chikitsa

As dha tukshaya leads to all vascular changes in diabetic retinopathy. Madhumeha is vata dōsha prevalent and is considered as asadhya (incurable) because of maha atyayatwat (due to chronic depletion of successive dhatu). Thus Charak has mentioned Paritarpam (nourishing therapy) after purification therapy for diabetic patients. Even Timir is included under Vataja nanattmaja vyadhi, so Timir can be treated with Santarpan chikitsa after proper purification therapy. So Basti treatment may be administered for madhumehajanya timir, as Basti therapy does both sodhana and shaman.

4.6. Vatamuloman chikitsa

Virechan and Basti with chakshyushya drugs should be advocated to control Vata. Soothar (anti-inflammatory) treatment can be instituted with Basti treatment to reduce retinal/macular edema in general. In this context Madutalikaa Chakshyusya Basti (Gupta Atridev, 2008, Ashtanga Hridaya, Kalpathan, 4:27–28; P 600) may be administered in Diabetic macular edema (DME) cases, as this Basti is beneficial in Rakapitta as well as chakshyusya in nature.
4.7. Urdwa jatruta chikitsa

Nasya, Shirodhara, Shirolepa and Shiropichi treatments can be given in different stages of diabetic retinopathy on the principle of “Vata shaman treatment for head and body, and pitta Shama treatment for eyes” (Santhakumari P.K, 2009, P 231).

4.8. Kriya kalpa and management of diabetic retinopathy

Kriya kalpa is an integral part of ayurvedic ocular therapeutics. Pariserka, Aschyotan, Tarpan and Putapaka can be given after proper evaluation of indications and contraindications.

4.8.1. Tarpana

Tarpan procedure in posterior segment diseases of eye like DR is of great importance as most of the drug permeation to intraocular tissues occurs through the cornea to the aqueous humor and ciliary vessels. As retinal pigment epithelium is continued as the non pigment epithelium of ciliary body, the drugs get absorbed through cornea may reach to the inner 3/4th retinal layers and outer 1/4th layers of retina gets from choroidal vessels from systemic route. Pre corneal drug retention, tissue contact time, molecular weight and size of the drug, lipophilicity of medicine affects the amount of drug permeation through the cornea. In Tarpan procedure the medicated Ghritas are administered and kept in eyes for 15–20 min. Drug availability in intraocular tissues increases due to longer duration of drug contact and, lipophilic and hydrophilic nature of drugs in medicated ghritas in Tarpana procedure. Lipophilic drugs are better permeated through epithelium and endothelium and hydrophilic drugs are better penetrated through the stromal layer of cornea. In case of different stages of DR the medicines like Patoladi ghrita, Jivantyadi ghrita, Drakshyadi ghrita can be used in Tarpan procedure to alleviate hemorrhagic signs due to raktipita samak, ropaka and rasayana properties of these drugs. Doorvadya ghrita Tarpana is effective in mild to severe NPDR and PDR (Raktapitta janya) cases [14]. Mahatriphala Ghrita (Gupta Atridev, 2008, Ashtanga Hridaya, Uttarasthana, 13:13–15; P 671) can be used for Tarpana in PDR cases as neovascularisation is a pathological feature in PDR (Pranavritta vyana janya) and Triphala has anti VEGF properties [15] in eyes owes to reduce symptoms in PDR cases. In retinal ischemic conditions of DR due to Dhatukshyajanya pathology Jivantyadi Ghritta Tarpana (Gupta Atridev, 2008, Asthanga Hridaya, Uttarakrutha, 13:7–9; P 671) can be advised.

4.8.2. Putapaka

Putapaka is similar to Tarpana in procedure of administration but methods of preparation of drug differ. This preparation contains herbomineral drugs processed with ghee, meat and fats of animal origin and subjected to heating in a furnace. This liberates nanoparticles of drug in ionized form which easily penetrates into cornea due to ionized and lipophilic nature of the drug and reaches the posterior segment tissues of the eye in a similar pathway like Tarpana procedure. As the drugs are in minute form and due to vyayavi and vilkashi guna of drugs owes to addition of agni during preparation, the drug reaches the inner retinal layers. Ropana type of putapaka is indicated in Pitta, Rakta, Vrana conditions of eye and thereby Ropana Putapaka can be used in different stages of DR. Breast milk, meat of animals of Jangala origin, honey, ghee and Tikta rasa herbal drugs are used for Ropana Putapaka [16]. Putapaka prepared from Tikta dravya like Vasa can be used after Tarpana karma for optimum therapeutic effect in different stages of DR cases.

4.8.3. Pariseka/Seka

Seka is done as Poorvakarma before Tarpana. This helps in vasodilatation of superficial vessels and some amount of medicines get absorbed through the medial canthus which is highly vascularised. Ropana type of Seka is indicated in Rakta and Pitta diseases of eye. Thus Ropana type of Seka advised in DR helps in improving texture of blood vessels, endothelial repair and thereby prevents loss of the pericytes, which is an initial factor in DR development. Pariseka with drugs having Tikta Kashaya Rasa and Chakshyusya properties helps in healing intra retinal blood vessels and arrests bleeding due to Shambhana properties. This might prevent vascular endothelial growth factor (VEGF) activation, which is primarily responsible for retinal neovascularisation in PDR cases. Triphaladi Pariseka [17] Manjisthadi Pariseka (Gupta Atridev, 2008, Ashtanga Hridaya, Uttarakrutha, 16:13; P 686), Chandanadi Pariseka and Vasakadi kwatha Pariseka (Sastri Lakshmi, 2013, Yogaratnakara, Netraroga Chiktisa, P 388) will helpful in reducing Raktripita pathology in different stages of DR pathology.

4.8.4. Aschyotana

Aschyotana is the technique of introducing small volume of drug in open eye repeatedly. The medicines introduced in the form of medicated decoction are absorbed through the blood vessels of fornices of conjunctiva, sclera and highly vascularized part of inner canthus. Therapeutic actions of Aschyotana are like Seka procedure. The drops which are lipid base in the form of medicated Ghee preparations permeates through the cornea due to both lipophilic and hydrophilic drug molecules in the medicated ghee preparations. Medicines like Triphaladi ghrita, Doorvadi ghrita and Patoladi ghrita can be used as Aschyotananain the dose of 3–4 drops in mild to moderate DR cases. Triphaladi [17], Prapoundarikadi (Sastri Lakshmi, 2013, Yogaratnakara, Netraroga Chiktisa, P 391) and Manjisthadi (Gupta Atridev, 2008, Ashtanga Hridaya, Uttarakrutha, 16:13; P 686) Aschyotana can be used in initial stages of NPDR cases.

4.8.5. Anjana

Anjana is a medicinal preparation which is applied on the lower palpebral conjunctiva or the cul-de-sac. Drug permeability to intraocular tissue depends on their hydrophilicity and lipophilicity mainly occurs through the conjunctiva and cornea by paracellular and transcellular pathways respectively. pH, viscosity, tonicity, molecular size and molecular weight of the active ingredients are factors responsible for the therapeutic effect of Anjana. According to its form Anjana is of 3 types i.e. Gutika, Rasurikriya and Churna. Gutika and Churna types of Anjana can be correlated with ophthalmic suspensions and Rasurikriya type is with aqueous solutions/eye drops. Gutika and Churna Anjana have micro particles which may be deposited in the cul-de-sac and increases the pre corneal retention time and thereby increases the drug bioavailability to intraocular tissues. Due to large molecular size both the trans-sclera and trans-corneal drug absorption may occur in Anjana procedure. Ropana and Dristiprasadana type of Anjanas might be helpful in treating and preventing DR pathogenesis in pakwavastha. Sarivadyanjana (Gupta Atridev, 2008, Asstanga Hridaya, Uttarakrutha, 13:65; P 676) and Drakshyadi varti anjana (Gupta Atridev, 2008, Asthanga Hridaya, Uttarakrutha, 13:74; P 677) described by Vagbhatta in Pittaja and Raktaja Timir chiktisa respectively may help in hemorrhagic
4.9. Chakshyusya/Netrya Basti

Though Basti is considered as the best treatment for Vata Dosha it is advised even for the treatment of Pitta Dosha, Kapha Dosha and Sarvadhatu AshritaVaydhi (Trikamji J, Ram N, 2012, Susruta Samhita Dalhana Commentary, Chikitsa sthana, 35:6; P 525). Sushruta described both Timir and Adhimantha are among eye diseases which can be treated with Basti Chikitsa (Trikamji J, Ram N, 2012, Susruta Samhita Dalhana Commentary, Chikitsa tasma, 35:5; P 525). While describing the importance of Basti Chikitsa, Acharya Sushruta has mentioned “Chakshyuhu Prinayati”, which means improves vision. While describing treatment of Timir, Vagghata mentioned Basti as one of the treatment procedure along with Murdhabasti, Tarpana, Alepana etc. Again he had mentioned Niruha and Anuvasana Basti procedure for VatajaTimir (Gupta Atridev, 2008, Ashhtag Hridaya, Uttar-arthana, 13:47, 62; P 674–675). Chakshushya Basti [18] is especially mentioned by Vagghata for its Chakshusya, Pramehahara and Raktapittahara properties. This is a type of Siddhahasti and contains ingredients of MadhutaIkika Basti (Erandaooloo Kwath, Madhu, Taila, ShatpushapKalka and Saindhavavanna) with Yastimadhu Kalka. Yogvahi, Raktapittahar and Sandhan properties of Madhu helps in better absorption of the drugs and healing effect on intra retinal blood vessels. Sukshma and Tiknna Guna of Saindhav helps in reaching up to micro channels and break down of morbod Dosh. Chakshushya effect of Saindhava lavender attributed to temporary osmotic BRB disruption for better enhancement of drug absorption in Basti procedure. Taila is best drug for Vata dosha alleviation. Vyavayi, Ushna, Guru and Snighda properties of Taila pacifies Vata dosha and improves drug permeability of cell chitkaya. Rasayana, chakshushya and ropana properties of Yasthimadhu help in repair and regeneration of intra retinal blood capillaries. Shatpushpa increases the retention time of Basti and has Akshiqahara properties. Vrisya and Vatahar properties of Erandamooola Kashaya help in pacifying Vata, regeneration of retinal capillaries and provide nutrition to retinal ganglion cells. Other Chakshusya Basti formulations like Sthiradi Niruha Basti (Tripathy Brahmananda, 1999, Caraka Samhita, Siddhi Sthana, 3:36–37; P 1204) and Mustadi Yapan Basti can be advised in different stages of DR. Panchatikta Pancha prasritika Basti (Tripathy Brahmananda, 1999, Caraka Samhita, Chikitsa Sthana, 8:8; P 1261) can be advised in initial stages of active Sirabhisyand and diabetic retinopathy patients having predominant in kleda and kapha vitiation i.e., NPDR due to retinal ischaemia. In case of Dhutakshya stages of DR, Sthiradi Niruha Basti can be administered, which has nutritive effect on retinal neuronal layers. The rationale behind use of Basti in posterior segment diseases of eye including DR is to introduce large volume of drugs through systemic route. Drug ionization through proper emulsification, lipophilicity, and molecular weight, pH and transit time of drugs are the factors which influences drug absorption and bioavailability to the ocular tissues. Basti treatment meets all these properties along with unique anatomical characteristic of a large surface area which can deliver enormous drug to posterior segment of eye for effective therapeutic effect in the ocular conditions. Pathogenesis of major diseases of posterior segment of eye is caused by Sir Srotas Abhisyand due to doshaavarna, dhaukayya with resultant reduction of supply of nutrients to the ocular tissues. Basti does both Sodhana and Shamana along with the enhancement of nutritional status of dhatu in the body which also applies to the dhatus or Patalas in Eye. Stimulation of autonomic nervous system could be the possible mechanism behind action of Basti. There is a close resemblance in the functioning of Vata Dosha and nervous system and Basti is prescribed as the best remedy for Vata. It again validates the efficacy of Basti karma on nervous system as well as in ocular disorders. There is a close resemblance between pharmacological actions of Basti, with colon specific drug delivery system (CSDDS) [19] and strategies required for CNS drug delivery [20]. Methods such as produrg, carrier mediated drug delivery, drug manipulation by lipophilic analogs and osmotic brain barrier disruption or blood retinal barrier disruption strategies described by modern pharmacologists, completely compliments with classical methods of Basti procedure. The rectal columns have a rich vascular bed and have their own arteries and veins. While the superior rectal vein drains via the inferior mesenteric vein into the portal vein, the inferior and middle rectal veins drain directly into the inferior vena cava via the internal pudendal vein and the internal iliac vein. This type of vascular supply of rectum helps in achievement of systemic drug effect.

4.10. Oral systemic drugs

Triphaladi churna, Triphaladi kwatha, Mahavasadi kwatha [14], Vasakadi kwatha and Amrutadiguggulu [21] can be advised in mild to severe NPDR and PDR cases.

5. Conclusion

Diabetic retinopathy is a disease of Dristipatala (retina) and complication of long standing uncontrolled diabetes due to defective metabolism and endocrine dysfunction. All the three doshas are affected with rakta (as both dosha and dushya), mainly vata, pitta, raka and kapha anubandha. All the dhatus are affected with rakta, meda and mansa predominant, sira srotas of rakta vaha srotas and Ojavya dhamani gets affected in successive stages. If the DR pathology is analyzed properly, it possesses all the four features of srotogaunyata i.e., Atipuravritti, Sanga, Siragranthi and Vimarga gamana. Sanga is manifested by the retinal vessels occlusion leading to hypoxic related ischaemia. Siragranthi is nothing other than development of microaneurysms, Vimarga gamana is the retinal haemorrhages and Atipuravritti can be correlated to the Neovascularization where new vessels are formed. Agnimandya and Ama formation, raktipitta, avarana and dhatu kshaya are few aspects of pathogenesis and development of Diabetic retinopathy and this may provide inputs for development of treatment protocol for the disease in Ayurveda in future.

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Conflict of interest

None declared.

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Raktapitta and Diabetic Retinopathy Pathogenesis

Madhumeha aetiological factors  |  Raktaja Vyadhi aetiological factors

Vitiation of Rakta Dhatu

Akshi raga  |  Rakttapitta
Tamah darshana

Bleeding in eyes

Splinter hemorrhage, dot/blot haemorrhages & exudation

Retinal/ Macular oedema, NPDR & PDR

Fig. A.1. Raktapitta and diabetic retinopathy pathogenesis.

Madhumeha

(Vata predominant Pitta and Kapha anubandha)

Avarana Janya  |  Dhatu Kshya Janya  |  Agni Manda

Avarana Janya Madhumeha

Pramavrita Vyana Vayu  |  Raktavrita Vata

Blood flow to eye

Decreased retinal blood flow

Retinal ischemia

Increased VEGF activity

Increased angiogenesis factor

Neovascularization

PDR

Blood viscosity↑
Leucocytes activation↑
RBC aggregation↑

Early breakdown of BRB

NPDR

Fig. A.2. Avaranajanya Madhumeha Samprapti and pathogenesis of diabetic retinopathy.
Fig. A.3. Dhatu kshaya symptoms and pathogenesis of diabetic retinopathy.
**Madhumeha**

**Agni Mandya**

- Metabolic derangement
- Increased Ama Formation
- Increase *Mala* formation
- Endocrine dysfunction

**Polyol pathway**

- Increased Prostaglandin
- Increased sorbitol synthesis
- Inflammation
- Osmotic stress

**AGEs accumulation**

- Increased VEGF up regulation
- Increased leukocyte adhesion
- Increased vascular permeability
- Increased thrombogenicity

**PKC activation**

- ROS
- Increased super oxide ions

**Oxidative stress**

- Lipid peroxidation

**Microangiopathy in diabetic retinopathy**

 in all the stages of NPDR & PDR

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*Fig. A.4.* Agnimandya, Amadosha and oxidative stress pathogenesis of diabetic retinopathy.
Probable correlation of Dhātu Kṣhaya symptoms and vis-à-vis diabetic retinopathy symptoms.

**Table A.1**

| Doshya                        | Kṣhaya ṭokṣhaya | Interpretation of diabetic retinopathy symptoms |
|-------------------------------|----------------|-----------------------------------------------|
| Meda (Surplus and unutilized fat or adipose tissue) | Sandhisunyata | Cell junction or adhesion defect/Break down of blood retinal barrier. Macular edema and Exudates formation. |
| Mamsa (Muscular tissue/muscle protein) | Dhāmanisaiṭhīya | Loss of junctional adhesion molecule/endothelial cell loss. |
| Raktā (Blood) | Sirasaṭhīya | Loss of pericytes, weakening of capillary walls and formation of microaneurysms. |
| Majā (Marrow tissue) | Timiraradārṣa | I; blood cell formation — anemia — hypoxia — breakdown of BRB — loss of nerve fibers — cotton wool spots. |
| Sukra (Semem) | Panduta | Proves hereditary and genetic predisposition of Diabetic retinopathy. |
| Ojas (Resistance factor/Immunity) | Vyāthītendrīya | Diminish in function of sense organs including blurred in vision. |

**Table A.2**

| Patalas | Doshaja Timir | Visual symptoms | Modern correlation/classification of DR |
|---------|---------------|-----------------|----------------------------------------|
| 1st (Teja Jalashrita) | Vataja | Blurring of vision, Erythropsia, Micropsia | Mild NPDR |
| 2nd (Mamsaśhrīrā) | Pittaja | Color vision defects | Moderate NPDR |
| | Raktaṭa | Smoky vision | Severe NPDR |
| | Sannipataja | Polyopia, Diplopia | PDR |
| | Photopsis | Visual field defects | Vitreos hemorrhages |
| | Parīmālaye Kachā | Phosphenes | Retinal detachment |
| | | | Diabetic Cataract |
| | | | |
| 4th (Ashtyaśhrīrā) | Sannipatika Linganāsha | Snowflake cataract | High Risk PDR |
| | | Loss of vision | Florid PDR |

NPDR—Non proliferative Diabetic Retinopathy, PDR—Proliferative Diabetic Retinopathy.

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