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Analysis of *Nidana Panchaka* in Diabetic Retinopathy (*Pramehaja Timira*)

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ABSTRACT

Diabetic retinopathy (DR) is a disease of *dristipatala* (retina) and complication of long-standing uncontrolled diabetes due to defective metabolism and endocrine dysfunction. Prevalence of Diabetes mellitus (DM) has been drastically increased in last few decades. DM is metabolic disease involving inappropriately elevated blood glucose level with disturbance of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both, which lead to micro and macro angiopathy. Diabetic retinopathy refers to retinal changes which is a progressive, degenerative, vision-threatening condition which leads to permanent blindness. Incidence of permanent blindness is 20-25 times higher in diabetics than normal population. It is not possible to compare diabetic retinopathy exactly to any particular disease in *ayurveda*, but there are many references which indirectly point out that *prameha* can cause *netra rogas* as its *upadrava*. Hence analysing the *Nidana Panchaka* of Diabetic Retinopathy (DR) is of prime importance in order to achieve *Samprapti Vighatana.* The aim of this conceptual study is to analyse the *Nidana Panchaka* of diabetic retinopathy which, thereby aid for its effective management.

Key Words *Diabetic retinopathy, Timir, Nidan, Avarana, Raktapitta*

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INTRODUCTION

Diabetes mellitus (DM) is a common disease affecting middle and old aged people and its incidence is increasing day by day due to sedentary life style and stress in routine life. DM has in recent times, gained importance as one of the most common, non-communicable disease, which contributes to death and disability worldwide. Occurance of Diabetes Mellitus has been drastically increased in last few decades. Diabetes affects intermediary metabolism and is also associated with accelerated aging of the cardiovascular system. Hence, DM is metabolic disease involving inappropriately elevated blood glucose level with disturbance of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both, which lead to micro and macroangiopathy[1]. DR is the main cause for vision impairment and blindness among working-age adults, which can be considered as a major vascular complication of DM. Studies showed that, A total of 6218 known

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diabetics were screened. Totally, 5130 data entry forms were considered suitable for further evaluation. About 61.2% were males, 88.6% were between 40 and 80 years of age, almost two-thirds of the patients were from the west and south zones, and over half had diabetes more than 5 years. The data set was predominantly urban 84.7% and 46.1% had no family history. Diabetic retinopathy prevalence in the entire data set was 21.7%. prevalence was more in males(p=0.007), diabetics more than 5 years(p=0.001), those above 40 years(p=0.01), insulin users(p=0.001), and history of vascular accidents(p=0.0014). significantly 22.18% of patients detected with DR had a vision of 6/18 or better in the worse eye[2]. The frequency of the incidence of the DR increases with the length of time the patient has had diabetes, even though the general disease is mild or has been well controlled, and hence it usually occurs in elderly patients and has become much more common since the use of insulin, which has prolonged the life span of Diabetics. Retinopathy is common but not invariable after the disease has lasted 10 years and affects the majority of patients after 20 years. It affects both young and old, for it is the diabetic age and not the chronological age that is important[3].

Symptoms and signs[4]

Opthalmoscopic symptoms of NPDR include:

Microaneurysms-Pericytes, the cells that surround and support retinal capillaries are first to get damaged from high glucose. As a result, wall of the capillary became weakened, little outpouchings, called microaneurysms.

Retinal haemorrhages-Both deep and superficial haemorrhages, occurs from capillary leakage.

Hard exudates-microaneurysms and other damaged blood vessels in the retina allow leakage of fat and fluid within the retina. Accumulation of lipid within the retina is known as hard exudates.

Retinal oedema-This is cause by intraretinal accumulations of fluid from abnormally leaking vessels. Retina appears boggy, thickened or cloudy and greyish white.

Cotton wool spots-As damage progresses, retinal capillaries get occluded, leading to areas of poor circulation in the retina, a process known as “ischemia.” In some areas, ischemic retina appears white and swollen known as “cotton wool spots”

Venous abnormalities

Intraretinal microvascular abnormalities (IRMA)

The hallmark of PDR is the occurrence of neovascularisation seen as fine irregular red lines connecting arterioles with venules, represent AV shunts.

CLASSIFICATION

Mainly DR is divided in to 2 broad categories

1.Early stage of Non proliferative Diabetic Retinopathy (NPDR)

2.Advanced stage of PDR

ETDRS classification of diabetic retinopathy

1.NPDR (Non proliferative diabetic retinopathy)

A. Very mild NPDR

B. Mild NPDR

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C. Moderate NPDR

D. Severe NPDR

E. Very Severe NPDR

2.PDR (Proliferative Diabetic Retinopathy)

A. Mild-Moderate PDR

B. High-Risk PDR

We find direct reference in "*Netraprakashika*" written by *Poojyapada Mahamuni* clearly mentioning that *netra rogas* are caused due to *Prameha*[5]. *Acharya Charak* mentioned that 'The physician should never feel shy for not knowing the nomenclature of the diseases, and there is no rule that every disease has a name. So, a one should try to understand the causative factors (*Nidan*), manifestation site and pathology of the disease(*samprapti*) and then start the treatment[6]." Hence, analysing the *Nidana Panchaka* of DR is of prime importance in order to achieve *Samprapti Vighatana*. The aim of this conceptual study is to analyse the *Nidana Panchaka* of DR through basic concepts of the *ayurveda* which, thereby aid for its effective management.

MATERIALS AND METHODS

Brihatrayi, laghutrayi with commentaries and other classical texts have been used for this compilation with critical analysis, relevant modern texts, articles from PubMed, google scholar etc were thoroughly searched.

NIDANA(ETIOLOGY)

The exact cause of the DR is unknown. Certain risk factors are known to cause a DR. Poorly controlled DM and progression of previously controlled retinopathy are often associated with an earlier onset of DR.

Hence, we can consider *nidana* of *prameha* as *sannikrishta nidana* for such *timira*. *Achakshushya* factors like excessive use of *Madhura, Amla, Suktaranala, Masha* and *vegavingraha* were mentioned in the *nidana* of *prameha* and these factors can cause *timira* also. Considering the *samprapti ghatakas* of *pramehaja timira*, we can assume that *Raktavaha srotodushti* occurs in DR. Intake of *Vidahianna*(food) and *pana*(drinks), *Snigdha,Ushna* and *Drava* food along with *atapa*(sunlight) and *Anila*(air) are the causative factors for *raktavaha srotodushti*. Therefore, it considered as *viprakrishta nidanas* for *timira* which occurs as a complication of *prameha*.

Some of the *nidanas* of *prameha* are similar with *netra roga nidana* and important is that the *prameha nidana* has many *achakshusya* factors.

1. *Madhur rasa*- in excess use it is responsible for *prameha* as well as *netra rogas*[7].

2. Amla rasa- kleda vriddhi,drava vriddhi,adya dhatu saithilya- ***prameha***[8].

Kapha-pitta *prakopaka,* ***rakta*** *vidaha-****Netra roga***[9].

3. Shuktaaranala- drava-kleda vriddhi- ***prameha***

Amla vipaka, ***kapha-pitta*** *prakopa-* ***Netra roga***[10].

*4. Masha - guru-snigdha,Madhura rasa/ vipaka-****prameha***[11].

Ushna virya- ***Netra roga***[12].

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5. *Vega vinigraha – mutra vega- apana vata dushti-* ***prameha***

Nidra-ashru vega- ***Netra roga***[13]***.***

POORVARUPA

Poorva roopa are *avyakta* because no symptoms are observed before manifestation of the disease.

***RUPA* (Symptoms)**

The *lakshana* of *timira* are comparable with that of DR are as below (Table no. 1).

Table 1 Comparison of symptoms between Timira and DR

TIMIRA	**DR**
Vyavidhamiva pashyati	Hazy, distorted vision
Jalani keshan mashakan rashmischa	Spider web appearance caused due to floaters
Adithya khadyata pashyati	Flashes of light
Pashyeda sookshmani athyartham	Difficulty in seeing minute objects
Dhooma dhoomrani cha ikshate	Blackish and smoky vision

SAMPRAPTI

In *Sushruta Samhita* it is mentioned that when *prameha* is not treated it causes *mamsa* and *shonita dushti*, and further it leads to many *upadravas* of *prameha*. All the *drava dhatus* involved in *prameha* lead to vitiation of *vyana* and *apana vata*. As a result of this, there is ***Rasayani daurbalya*** in whole the body. *Rasayanis* are the microcapillaries responsible for nourishment of tissues. When there is no proper nutrition (ischaemia), many vascular complications may occur like diabetic retinopathy.

According to modern science also the pathology of DR starts with microvascular occlusion due to vascular changes like endothelial cell damage, thickening of basement membrane and loss of capillary pericytes, further leading to formation of microaneurysms, haemorrhages and exudates in the retina.

According to *Astanga Hridaya "Madhumeha"* arises due to below pathology:

1. Due to aggravation of *Vata Dosha* by *Dhatu Kshaya*

2. *Avarana* (Obstruction) of the path of *Vata dosha* by other *Doshas*"[14].

Dhatu kshayajanya

Ojas is considered as the essence of all *dhatus*[15]. Diminution of *Ojo Dhatu* occur in *Madhumeha*[16]. From this it is obvious that, *Kshaya* of all remaining *dhatus* including *Rakta* and *Mamsa dhatu* happens in *prameha*.

Sira Saithilya is described as a *feature a* of *Rakta Dhatu Kshaya*[17] *Dhamani Saithilya* is mentioned as a *Lakshana* of *Mamsa Dhatu Kshaya*[18]. Loss of pericytes and formation of microaneurysms are earliest sign of Diabetic retinopathy. That can be compared with sirasaithilya as a result of raktakshaya. *Dhamanisaithilya* may compared with endothelial cell damage which causes breakdown of blood retinal barrier leads to retinal oedema, haemorrhages, and leakage of lipids. *Sira* and *Dhamani Saithilya* indicates the dysfunction of the venules and arterioles. Dysfunction of these vessels arise due to Occlusion i.e., Ischemia, leakage etc. Micro Aneurysm, Retinal Haemorrhage, Venous Beading, Intra-Retinal Microvascular Abnormalities (IRMA) and Retinal Oedema are considered as the dysfunction of venules and arterioles[19]. So, it can said that these are the features occurring in DR due to *dhatu kshaya*.

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Dhatukshayajanya samprapti can be corelated more to diabetic retinopathy occurring in IDDM.

Avaranajanya

As per *Charak* "*Prameho Anusanginam*" means diabetes is concurrent in nature. Thus, there is complication present along with diabetes. *Ama* formation due to *agnimandhya* has also important role in *samprapti* of diabetic retinopathy which may compare with oxidative theory of diabetic retinopathy described in modern science. Due to *avarana* and *dhatukshaya* ten *dushyas* goes into state of kshaya and produce symptoms according to that particular dhatu kshaya. In DR main affected *dhatu* is *rakta*, *mamsa,meda dhatu*, though all the *dhatus* gets affected and accordingly affected *srotas* are *raktavaha*, *mamsavaha* and *medovahasrotas* mostly. *Rakta dhatu dushti* can be compared with hematological changes such as increase in platelet adhesiveness, increase in blood viscosity and red blood cells deformation and rouleaux formation in DR. which leads to *sanga* of *raktavaha srotas*. *Mamsa dhatu dusti* can be compared with endothelial cell damage, damage to the cells of retina, pericytes loss and thickening of basement membrane of capillaries. While *medodhatu dusti* can be compared with serum lipids abnormality, leaked lipoproteins and lipid filled macrophages. All these factors lead to *sanga* in *dhamani* and *sira* which can be compared with occlusion of microvessels which leads to hypoxia, thus the wall of the vessels is damaged and permeability increases which results in leakage and haemorrhages from the blood vessels. Due to the breakdown of the blood-retinal barrier, retinal oedema and hard exudates are formed which composed of leaked lipoproteins and lipid filled macrophages. Soft exudates are small whitish superficial lesions, these represent areas of nerve fibre infarcts. IRMA seen as fine irregular red lines connecting arterioles with venules, represent arteriovenular shunts. New vessels formation due to hypoxia and lack of circulation, which is fragile in nature, can bleed easily results in exudate formation and neovascularization. All these factors leads to degenerative changes in retina and lead to haemorrhage and tractional retinal detachment which ultimately result in vision loss[20].

Sunyata, the inability of *indriya* to perceive their *vishaya* is mentioned as a *lakshana* of *Pranavritta Vyana Vayu*. Loss of vision in Diabetic retinopathy can be correlate with *Indriya Sunyata* of *chakshurindriya*. *Prana Vayu*, which controls the function of all other *Vayus* is also responsible for the visual perception. The circulation and visual conduction can be considered as the function of *Vyana Vayu*. So, when the movement of *Vyana Vayu* is obstructed by *Prana vayu*, the circulatory function and the neural conduction is disturbed. There may be ischemia, occlusion, leaking and bleeding of the fundal vessels in retina[21].

RAKTA PITTA JANYA

Achakshyushya factors are main causative factor for *netraroga* which may lead to *dusti* of *pitta dosha*, which leads to vitiation of *pittavaha srotas* and *raktavaha srotas* due to *ashray*

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ashrayee bhava. Due to continuous *nidan sevan pitta* and *rakta dosha* do *urdhvagaman* through *siras* and localised to *netra*, whereas *dosha dusya samurchhana* occurs and disease manifest. When *sirasrotas* are deeply involved it known as *sira abhisyanda*[22]. *Samprapti* of DR start with *sroto dusti* of *raktavaha srotas* manifested as microangiopathy in the form of haemorrhages, exudates and venous beading in DR respectively.in the initial stage, the etiological factors promote changes in the permeability of the vessels specially in *urdhvajatrugata pradesh* and leads to the development of eye diseases. if the stage of *sira abhisyanda* continues it spread to *netrasrotas* and the same vascular changes occurs in the vessels of eye, because *Achaksyushya* factors always have affinity towards the ophthalmic tissues. After *netraabhisyandam*, due to continuous *nidan sevan* there is more vitiation of *pitta dosha*, the condition more aggravates and confined to *dristipatalam*.

In *Urdhvaga Raktapitta* there will be bleeding from the *Jatrurdhwa* structures like *Mukha, Nasa* and *Chakshu*. Here *Rakta* and *Pitta* which are already in a vitiated form, the sites where the vessels are already dilated, due to *Atipravrutti* of *doshas*, *Rakta Srava* (hemorrhage) from the dialated vessels and causes retinal haemorrhages.

SROTO DUSHTI

After analysing the pathogenesis of NPDR and PDR it is clear that all four type of *Sroto Dusti* ie, *Atipravruthi, Sanga, Siragranthi, Vimarga Gamanam* are occurs in manifestation of DR. Retinal vessel occlusion can be considered as *Sanga* whereas, development of micro aneurysms can be correlated to *Siragranthi*, retinal haemorrhage (dot or blot haemorrhages) to *Ati Pravruti* and neovascularization, Vitreous haemorrhage, exudates etc. to *Vimarga Gamana*. *Viddha lakshana* of *Raktavaha srotas* includes *sonitagamana* and *rakta netrata*[23].

SAMPRAPTIGHATAKA

DOSHA - Pitta rakta pradhana tridosha

DUSHYA- Rasa,Rakta,Mamsa,meda

ADHISHTANA -Netra Patala

SROTAS - Rasavaha srotas, Raktavaha srotas, mamsavaha srotas, Medovaha srotas

SROTO DUSHTI - Atipravruthi, Sanga, sira granthi, Vimarga gamana

AGNI - Dhatwagni mandhya

AMA – Sama

SADHYASADHYATA- Kashta sadhya/Asadhya

UPASAYA-ANUPASAYA

Pathya Ahara includes grains such as *yava* (barley), *godhooma* (wheat), *lohitsali* (red rice), *shastika*, *mudaga* (green gram) etc. which are puran(old) and which do shaman of *kapha* and *pitta dosha* mixed with more *ghrit* (butter fat), vegetables, meat of animals of *jangala desha* (meat of animals lives in forests), *dadima* (pomegranate), *sita*(sugar), *saindhava* (rock salt), *Triphala* (Terminalia chebula, Terminalia belerica, Emblica officanalis), *draksha* (grapes), rain water (i.e.pure cold water) for drinking etc

Apathya Ahara: *Masha, aranala, matsya, dadhi, phanita, vesavara, pinyaka(*oil cake*),sura,* food

and drinks which are *amla, lavana, vidahi, teekshna, katu, and guru*[24].

Pathya Vihara includes Use of *anjana,tarpan,aschyotan,Nasya*,proper sleep,*Padabhyanga, Netra seka* using *triphala* and *yastimadhu* etc

Shaman and *Sodhan chikitsa both* are important in *ayurvedic* therapies. There is impurities occurs at the srotas/ capillary level due to dhatwagnimandhya. For this *virechana* can be done, along with *'kriya kalpa'* / ocular therapeutics procedures stops the bleeding in retina and reducing the chances of recurrence.

Apathya vihara: *Krodha, shoka, maithuna, vata, vinmutra, vegavarodha, sukshmekshana*(looking at minute objects), *snana, atapa, prajalpana* (excessive talking), *chardana*[25].

CONCLUSION

The probable *nidana panchaka* and *samprapti ghataka* of the DR are discussed. *Achakshushya* factors are common *nidana* for *prameha* and *timira*. Purva roopa is *avyakta* in the DR. *Lakshna* of DR can be corelated to different *lakshana* explained in the *timira*. Treatment is nothing but correcting of *samprapti ghataka*. *Ayurveda* focuses on providing strength to the blood vessels of the retina and optic nerves due to which the further haemorrhages are prevented and vision is improved. *Ayurvedic* medicine act on micro-angiopathies and correct the health of capillaries. They also help in establishing blood retinal barrier reducing the oedema. Treating the *madhumeha* is the foremost care of DR. Treatment of *Urdhaga raktapitta,Sroto shodhana chikitsa,Dhatwagni mandya chikitsa,Avarana chikitsa* and *timira chikitsa* are also used in the different stage of DR.

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