



Review Article

AYURVEDIC PERSPECTIVE OF DIABETIC PERIPHERAL NEUROPATHY

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ABSTRACT

Diabetic Peripheral Neuropathies (DPN) are chronic debilitating complications following Diabetes mellitus. DPN refers to signs and symptoms of peripheral nerve dysfunction in a patient with Diabetes mellitus (DM) whom other causes of neuropathies have been excluded. The incidence of neuropathy is strongly associated with microvascular comorbidities. In Ayurveda, *Prameha* is one of *Ashtamahagada*, which will finally transform into *Madhumeha* without proper management. As there is no direct reference for diagnosing DPN in Ayurveda, it is essential to understand the causation and association of symptoms based on *Tridoshas* in *Pradhana Vyadhi* (main disease) as well as in *Upadrava* (complications). After analyzing both *Madhumeha* and DPN many similarities were found in respect of *Nidana* (etiology), *Samprapti* (pathology), and *Lakshana* (symptoms). Continuing *Nidana* even after *Prameha Samprapti* leads to its *Upadrava*. The features such as *Kara pada daha* (burning sensation of hand and foot), *Pipeelika sancharamiva* (tingling sensation), *Swapa/ Supthi* (numbness), *Sosha* (wasting), *Angasada* (weakness) are seen in *Prameha* either in the prodromal stage or in actual exhibition stage or complication stage can be correlated as DPN. The prevalence of DPN is also strongly associated with the duration of diabetes and glycemic control. Features of *Avaranajanya and Dhatukshaya Madhumeha* is to be differentiated and correctly diagnosed for the proper selection of treatment. Hence an attempt is made to review the differential diagnosis based on factors like etiopathology and symptoms of DPN in Ayurveda.

INTRODUCTION

Diabetes mellitus (DM) starts as a metabolic disorder with hyperglycemia and continuously progresses to different stages.^[1] The vascular and non-vascular diabetes-related complications are similar for both type 1 and type 2 Diabetes. Microvascular complications include Neuropathy, Retinopathy, and Nephropathy. All blood vessels, both large and small, are affected in patients with diabetes of long duration. Neuropathy is defined as a functional disturbance or pathological change in the nerves.^[2] Peripheral neuropathy is the common neurological problem caused by disordered function and structure of peripheral motor, sensory and autonomic nerves.

Diabetic Peripheral Neuropathy (DPN) refers to symptoms and signs of peripheral nerve dysfunction in a patient with DM, whom other causes of neuropathies (alcoholic, malignancies, nutritional, etc) have been excluded.^[3] Globally an estimated 422 million adults are living with diabetes mellitus according to the latest data from World Health Organization.^[4] The incidences of both type 1 and type 2 diabetes are rising and this is expected to double by 2030. DPN occurs in 50% of individuals with long-standing type 1 and type 2 DM. The prevalence of DPN is strongly associated with the duration of diabetes and glycemic control. The risk of developing neuropathy at the time of initial diagnosis of diabetes is estimated to be 4% to 10% by 5 years and 50% by 25 years. Additional risk factors are Body Mass Index (BMI) and smoking. In type 1 diabetic patients, frequent episodes of hypoglycemia leads to loss of consciousness in old age and in type 2 diabetic patients, worsened metabolic profile along with lower activity level were the major risk factors.^[5] Without proper management, DPN also leads to Diabetic foot ulcers which are the most frequent cause of non-

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traumatic amputation. The Hyperglycemic type of DPN is dominated by sensory symptoms without neurologic signs, that usually reversed by treatment of diabetes. Chronic type (circulatory degenerative) is associated with progressive sensory, motor, and reflex abnormalities.

Significance of Prameha and Madhumeha in Ayurveda

Prameha is described among the *Ashtavidha Maharogas* in all authentic Ayurvedic texts.^[6-8] It satisfies all the criteria of *Maharogas* like *Deerghakalanubanditwa* (chronicity), *Prabhootha doshasanchayatwa* (increased accumulation of *Doshas*), *Duschikitsitwa* (difficulty in treatment), *Mahamarmasrithatwa* (involvement of vital parts), *Bahoopadravatwa* (more complications) etc. *Upadrava* (complication) has been defined as the disease which develops after the improper management of *Pradhaana vyadhi*, due to the *Prakopa* of *Rogarambaka Dosh* itself.^[9] The word *Meha* was first found in Rig Veda. The common symptoms for all varieties of *Prameha* are *Prabhuta mutrata* and *Avila Mutrata*. This *Lakshana* along with partial or complete *Poorvaroopa lakshanas* make the diagnosis of *Prameha*. The most prevalent variety of *Prameha* is *Madhumeha*. It is one of the subtypes of *Vataja Prameha*. The term *Madhumeha* denotes excessive flow of sweet urine resembling honey in *Rasa* or *Varna*.^[10] If all other *Pramehas* are left untreated will finally transform into *Madhumeha*.^[11] All *Pramehas* can be generally called *Madhumeha* because in all of them the urine will be sweet and the body also attains a sweet taste.^[12] Thus chronicity and poor glycemic control influence the transformation of *Madhumeha* which is similar to the etiology of DPN. The exact interpretation of symptoms of DPN is not found in the *Samhitas*. But, there are few scattered references for the *Upadrava vyadhis* of *Madhumeha* which bear a close resemblance to the signs and symptoms of diabetic neuropathy. Features such as *Kara pada daha* (burning sensation of hand and foot), *Pipeelika sancharamiva* (tingling sensation), *Supti/Swapa* (numbness), *Sosha* (wasting), *Angasada* (weakness) are seen in *Prameha* either in prodromal stage or in actual exhibition stage or complication stage can be correlated to symptoms of Diabetic peripheral neuropathy. Management of DPN in Ayurveda also differs, according to the type of vitiation of *Tridoshas* in *Madhumeha* ie *Avaranajanya* or *Dhatukshayaja*. Proper diagnosis helps in making better choices of treatment. Hence an attempt has been made to review the differential diagnosis based on factors like etiopathology and symptoms of DPN in Ayurveda.

Avaranajanya and Dhatukshayaja Madhumeha^[13]

All *Pramehas* are said to be *Tridoshaja* in nature. Prognosis shows all the four varieties of *Vatika meha* and *Kapha & Pitta Prameha* which exhibits all the prodromal symptoms are *Asadhya*. By the proper administration of *Bheshaja* and *Pathya* (*Ahara* and *Vihara* including *Ruksha Udvartana*, *Vyayama* etc), it becomes *Yapya* (incurable but manageable disease). *Avaranajanya Madhumeha* occurs due to vitiation of *Vata* caused by *Avarana* of both *Kapha* and *Pitta*. The symptoms are mainly the *Lakshanas* of either *Kapha kopa*, *Pitta kopa*, or both. The normal physiology of *Vata* is hindered due to *Avarana* (occlusion). In *Dhatukshayaja Madhumeha*, due to over indulgence in *Vatakopa Nidan*s, *Saumyadhatu Kshaya* occurs, thereby depletion of *Dhatu*s.

Madhumeha Nidana

Specific *Nidan*s for *Madhumeha* are mentioned as consumption of *Guru*, *Snigdha*, *Amla*, *Lavana Ahara* like freshly harvested rice and fresh wine in excess quantity. This causes vitiation of *Kapha*, *Pitta*, *Medas*, and *Mamsa* that result in *Avarana* of *Vata* by them.^[14] Also those who sleep for prolonged durations and lead a sedentary lifestyle are also affected by *Madhumeha*. Those who have given up physical and mental exercises and also those who are not doing *Samsodhana* (purification therapies) are prone to *Madhumeha*. The excessive indulgence in alcohol is mentioned as *Nidana* in *Basavarajiyam*.^[15] The psychosomatic feature of *Madhumeha* is mentioned as the patient desires to sit down while walking, to lie down while sitting and he sleeps while lying.^[16] Thus patient prefers *Avyayama* (lack of exercise) will further lead to excessive production of defective *Medodhatu*.

Madhumeha Lakshana

The character of *Mutra* at the time of diagnosis of *Madhumeha* is *Madhura* (sweet) and *Pichila* (slimy). The urine voided by the *Madhumehi* resembles honey in attributes. Also it is having *Kashaya rasa* (astringent), *Pandu varna* (pale) and *Ruksha guna*. The natural *Madhura rasa* of *Ojas* (essence of all seven *Dhatu*s) is replaced by *Kashaya rasa* in *Vasti* (urinary bladder). *Vayu*, because of its *Prabhava* acts upon *Ojas* and alters its *Madhura- snigdhadhi guna* and converts *Madhura oja* into *Kashaya rasa*.

Factors influencing Samprapthi

1. *Dosha - Tridosha kopa nimitta*

Table 1: Dosha predominance in Madhumeha

Dosha	Avarana janya	Dhatu kshayaja
Kapha	Bahu and Abadha	Kshina
Pitta	Vridha	Kshina
Vata	Avrita	Vridha

2. *Dushya - Rasa, Rakta, Mamsa, Meda, Majja, Shukra, Vasa, Oja, Lasika, Kleda.*
3. *Ama-Medo dhatu gata ama* produced due to *Jadaragnimandya* and *Dhatwagnimandya*.
4. *Srotas- Rasavaha, Raktavaha, Mamsavaha, Medovaha, Majjavaha, Shukravaha, Swedavaha, Mutravaha, Pureeshavaha. Annavaha, Udakavaha.*
5. *Srotodushti- Sanga, Atipravriti*
6. *Adhithana- Vasti*
7. *Vyadhisvabhava- Chirakari*

Pathology of Prameha

Samprapti is a sequence of events manifesting into a disease through *Chaya* (accumulative stage), *Prakopa* (provocative stage), *Prasara* (migration stage), *Sthana-samsraya* (stage of localization), *Vyakti* (manifestation), and *Bheda* (complications). In *Prameha*, *Rogarambhakadosha* is *Kapha* due to *Atisevana* of *Gguru, Snigdha, Picchila* and *Madhura-Amla-Lavana ahara*. This will result in *Agnimandya* (diminution of *Agni*) and formation of *Ama*. *Ama* is the toxic byproduct generated due to improper or incomplete digestion due to *Jadaragni Mandya* and it is not needed for the body. *Jadaragnimandya* follows *Dhatwagnimandya* and by this proper nutrients are not formed for *Dhatu*. The function of digestion by *Pachaka Pitta*^[17] along with *Samana vayu* got vitiated. The derangement of *Avalambaka kapha*^[18] and *Kledaka kapha*^[19] will cause the increased production of *Dravamsa* in *Kapha*. i.e., the production of *Bahudrava sleshma* in excess. This *Bahudravakapha, Ama, Pitta* will cause the overproduction of *Kleda* in the body.^[20] *Kleda* being an *Apya bhava*, causing softening and loosening of solid materials on account of its *Drava, Snigdha, Mridu* properties. Thus the overuse of *Snigdha guna* and *Amla, Lavana rasa* causes an increase of *Shareerakleda*. Continuation of *Nidanas* in *Chaya avastha*, causing severe *Agnimandya* follows *Dhatwagnimandya* and vitiation of *Kapha* leads to *Prakopavastha*. The involvement of *pitta* in the formation of *Kleda* is inevitable as the function of *Pitta* is said to be *Swedana, Kledasruthi, Kotha*, etc. The *Prakupitha Sleshma* propelled by *Vyana vayu* circulated

throughout the body. It will cause blockage to minute channels of circulation. Excess *Dravabhava* of the body is carried in the form of *Kleda* through *Raktha* as *Pitta* have *Asrayasrayibanda* with *Raktha*. In the stage of *Sthana-samsraya*, the possibility of *Kleda* formation in all *Dhatu*s is unavoidable. Defective *Dhatwagni* leads to the formation of *Abadha medodhatu*. The *Prakupita Sleshma* mixes with it because *Medo dhatu* has similar attributes to *Kapha*. Thus the *Dravatha* exceeds a particular limit, increases *Dhatumala* (waste products from *dhatu*s), which is to be eliminated from the body.

Acharya Vagbhata first time includes *Sweda* as *Dushya* of *Prameha*. The excess *Kleda* gets localized in *Mutravaha Srotas* is eliminated out of the *Vasti* by the action of *Apana vayu*. *Prakopa* of *Vyana* which is responsible for the circulation of *Dosha* impairs the systemic functions.

Pathology of Madhumeha

Madhumeha occurs as a sequela to *Kaphaja* or *Pittaja prameha* manifested either into *Avaranajanya* or *Kshayatmaka* type. *Avarana* of *Kapha* and *Pitta* decreases *Chala Guna* of *Vata*, hindering the normal nerve impulse conduction and brings about the deterioration of the myelin sheath. The myelin sheath of neurons consists of a fatty white substance that surrounds the axon of nerve cells, forming the electrically insulating layer. Myelin is about 15-30% proteins; the dry mass is about 70-85% lipids and about 40% water.^[21] Over some time *Samprapthi* of *Dhatu kshaya* occurs leading to *Ojakshaya*. This *Dhatu kshaya* causes *Vata kopa*. *Ojas* is the essence of *Dhatu*s. Among the *Para* and *Apara ojas*, latter is *Ardha anjali pramana* and is *Sleshmika*. *Ojus* is lost through urine in this *Vata kopa* stage of *Madhumeha*. In both stages, proper functioning of *Vyana* doesn't happen correctly leading to signs and symptoms of diabetic neuropathy. Owing to prolonged exposure to the same *Nidana*, continuous vitiation of *Dosha, Dhatu* and *Mala* occurs and the disease progresses to the stage of complication causing various other diseases known as *Upadrava Vyadhi*.

Table 2: Upadras of Prameha according to Sushruta Samhitha

Kapha prameha	Pitta prameha	Vata prameha
<i>Makshikopasarpana</i>	<i>Vrishanayoravadarana</i>	<i>Hridgraha</i>
<i>Alasya</i>	<i>Vasti bheda</i>	<i>Loulya</i>
<i>Mamsopachaya</i>	<i>Medra toda</i>	<i>Anidra</i>
<i>Pratisyaya</i>	<i>Hrit soola</i>	<i>Stambha</i>
<i>Saithilya</i>	<i>Amleeka</i>	<i>Kampa</i>
<i>Arochaka</i>	<i>Jwara, Peeta vitmootranetrata</i>	<i>Soola</i>
<i>Avipaka</i>	<i>Atisara, Nidranasa</i>	<i>Badha pureeshatwa</i>
<i>Kapha praseka</i>	<i>Arochaka</i>	

<i>Chardi</i>	<i>Vamadu, Panduroga</i>	
<i>Nidra</i>	<i>Paridhoopana</i>	
<i>Kasa</i>	<i>Daha, Pipasa</i>	
<i>Swasa</i>	<i>Moorcha</i>	

Analysis of symptoms of Diabetic Peripheral Neuropathy

Predominantly sensory or sensorimotor distal polyneuropathy is the most common of the diabetic neuropathies and it constitutes three-fourths of all diabetic neuropathy cases. Distal portions of longer nerves are affected first, the lower legs and the feet are involved before the hands, producing the typical “glove and stocking pattern” of sensory deficit.^[22] Large fiber variant have features of painless paresthesias beginning at the toe and feet, impairment of vibration, joint position sense and diminished muscle stretch reflexes. In advanced cases, significant ataxia may develop. Patients with disproportionate large fiber involvement may manifest muscle weakness, atrophy of intrinsic foot muscles, and weakness of extensors and flexors of the toes and ankles with foot drop. Small fiber variant presents with the dissociated pattern of pain (deep, burning, stinging, an aching character often associated with spontaneous shooting pains) and allodynia to light touch and temperature deficit with preserved vibration and position sense, preserved tendon reflexes and strength, painless foot ulcers and neuropathic joint degeneration. Autonomic neuropathy follows the small fiber variant type. Diabetic Autonomic Neuropathy (DAN) impairs the functions of cardiac, gastric and genito urinary system.^[23] The various symptoms related to *Madhumeha* mentioned in Ayurvedic classics are concordant with sensory, motor and autonomic symptoms of diabetic neuropathy analyzed as follows.

Table 3: Sensory Symptoms of Neuropathy

S.No.	Symptoms	Lakshana	References
1.	Numbness	<i>Swapa/ Supti</i>	<i>Medakaphavrita vata</i> ^[24] <i>Prameha purvarupa</i> ^[25]
2.	Burning sensation	<i>Daha</i>	<i>Raktavrita vata</i> ^[26] <i>Prameha purvarupa</i> <i>Prameha upadrava</i> ^[27]
3.	Pricking sensation	<i>Suchibhirivanistoda</i>	<i>Raktavrita vata</i>
4.	Heaviness of limbs	<i>Guruta</i>	<i>Kaphavrita vata</i>
5.	Tingling sensation	<i>Pipeelika sancharamiva</i>	<i>Mamsavrita vata</i> ^[28]
6.	Abnormal pain perceptions	<i>Toda, Shula, Sparsavaigunya, twak sosham</i>	<i>Swedakshaya</i> ^[29] <i>Prameha upadrava</i> ^[30] <i>Pitta avritavata</i> ^[31]

Table 4: Motor symptoms of neuropathy

S. No.	Symptoms	Lakshana	Reference
1.	Wasting	<i>Mamsopachaya Sosha</i>	<i>Prameha upadrava</i> ^[32]
2.	Weakness	<i>Dourbalya, Angasada</i>	<i>Prameha upadrava</i> ^[33]
3.	Involuntary movements	<i>Kampa</i>	<i>Prameha upadrava</i> ^[34]

Table 5: Autonomic symptoms of neuropathy

S. No.	Symptoms	Lakshana	Reference
1	Constipation	<i>Badhapurishata</i>	<i>Prameha upadrava</i>
2	Indigestion	<i>Avipaka</i>	<i>Prameha upadrava</i>
3	Diarrhoea	<i>Atisara</i>	<i>Prameha upadrava</i>
4	Thirst	<i>Pipasa</i>	<i>Prameha upadrava</i>
5	Anorexia	<i>Arochaka</i>	<i>Prameha upadrava</i>
6	Impotency	<i>Klaibya</i>	<i>Rasavaha srotovikara</i>
7.	Fainting	<i>Moorcha</i>	<i>Rasavaha srotovikara</i>

DISCUSSION

Neuropathy in a patient suffering from diabetes mellitus is usually diagnosed based on symptoms, medical history, and a physical examination. Continuation of *Nidanas* even after disease manifestation cause irreversible changes in *Samprapthi*. Decision of type of treatment is based on the proper diagnosis of the disease. Along with *Nidana parivarjana* and *Pathya*, *Sodhana* and *Samana* is needed. If the patients are obese and having good strength *Samsodhana* is needed according to vitiated *Dosha bala*. If the patients are weak, their strength should be increased by giving *Santharpana*. Food which will reduce *Meda*, *Kapha* and that pacify *Vata* is advisable. Foods that have low glycemic index should be used and they should have predominantly *Tikta* rasa. Due to the excessive intake of *Guru*, *Snighdha*, *Picchila* and *Madhura-Amla-Lavana Ahara*, *Kapha dosha dushti* occurs. *Rasa Medo Dhatu Dushti* happens due to *Agnimandya* and *Ama*. According to Sushruta samhitha, the vitiated *Kapha* gets associated with deranged *Pitta*, *Vata* and *Medas* gives rise to ten types of *Kaphaja prameha*. The vitiated *Pitta* in conjunction with vitiated *Vata*, *Kapha*, *Rakta* and *Medas* causes six varieties of *Paittika Prameha*. The vitiated *Vata* in conjugation with deranged *Kapha*, *Pitta*, *Medas*, *Majja* and *Vasa* causes *Vataja Prameha*. When a patient attains *Madhumeha*, *Vatakopa* occurs either due to *Avarana* or *Dhatukshaya*. In DPN also hypothesis regarding the etiology and pathogenesis of nerve dysfunction were related to the high concentration of glucose in blood which results in metabolic disturbances to increase the endoneurial vascular resistance. Later structural damage of nerves (demyelinating process) occurs in prolonged duration of diabetes. In the ischemic pathogenesis of DPN, a patchy multifocal pattern of fiber loss is seen. Under conditions of hyperglycemia of prolonged duration, the accumulation of AGE's (advanced glycosylation end products) with collagen and basement membrane, leads to thickening of the basement membrane.^[35] AGE's also block the effect of nitric oxide known to cause vasodilatation or relaxation of contractile vessels, therefore, resulting in loss of relaxation phase in the vasculature. In the Polyol pathway, glucose is converted to sorbitol and the slow degradation of sorbitol results in its accumulation may cause osmotic changes that damage the cell. Also the elevated level of sorbitol causes a reduction in uptake of myoinositol into neuronal tissues, which in turn results in an inhibition of tissue $\text{Na}^+/\text{K}^+-\text{ATPase}$ activity.^[36] Here the formation of AGE and increased sorbitol can be considered similar to the formation of *Ama*. The most common form of diabetic neuropathy is distal sensory polyneuropathy has similar symptoms of the *Avarana* type while majority cases of motor involvement shows the features of the *Dhatukshaya* type. Treatment of

each type differs as *Srotosodhana* is needed for *Avarana* while *Dhatukshaya* requires *Brumhanam* (restorative measures). Symptoms of DPN can be relieved by strict glycemic control and proper treatment in the initial stage. Progression of disease occurs due to improper management. *Avarana* stage of *Madhumeha* can be managed well than the *Dhatukshaya* stage with respect to the prognosis.

CONCLUSION

Etiology, symptoms of DPN and correlating it with Ayurvedic counterparts, had drawn the following conclusions about DPN. It shows different clinical symptoms according to the affected nerve fiber populations. *Nidana parivarjana* and *Samprapthi vighattana* are essential in treating diseases of Ayurveda. In DPN, Pathogenesis continues as a never-ending cycle. So, it is very difficult to attain *Dhatu samyata*. Hence irrespective of correlating the symptoms of DPN in to a single disease, the role of *Tridoshas*, nature of *Avarana*, and the type of *Madhumeha* is to be considered for a better choice of management to prevent further progression towards complication.

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