

An Overview of Pramehjanya Upadrava with special reference to Chronic complications of Diabetes Mellitus

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Abstract

According to Ayurveda in the disease Prameha two cardinal features are described i.e. 'Prabhuta mutrata' and 'Avila mutrata' which means excessive and turbid urine. The disease Prameha is said to be kapha dominant, tridoshaja, and chronic in nature involving multiple dushyas predominantly 'Meda'. Upadhravas or complications are the morbid events which develops due to ignorance or inadequate management. Detailed discussion on probable upadhravas is available in classical texts. Modern science has classified the disease diabetes mellitus as type 1 and type 2 on the basis of synthesis and action of the hormone insulin. Various acute and chronic complications leading to morbidity and mortality caused by uncontrolled hyperglycemia are also mentioned. In this article an attempt has been made to overview the complications quoated in Ayurveda literature and modern medical text.

Keywords: Prameha; Upadrava; Diabetes Mellitus; Chronic Complication of Diabetes Mellitus

1. Introduction

As quoted in Charak Chikitsa sthan Upadhravas are manifested only in the later or terminal stage i.e. with the Dushti of all Dhatus. The mild form of Upadrava can be considered as Anu Upadrava and severe form of Upadrava can be termed as Sthoola Upadrava.[1]

The origin of upadrava is either due to improper management of disease or the continuation of vyadhi nidanas. The description of doshaja Upadhravas is not limited only to the respective Pramehas so the Kaphaja, Pittaja and Vataja Upadhravas are the result of the disease according to the predominance of the respective Doshas in the severe form of Prameha. Upadrava manifests upon another disease and also due to same factors which are responsible for the manifestation of the main disease. Hence management of upadrava is having at most importance or significance in Ayurveda. Various Upadhravas quoted in different classical Ayurveda texts can be enlisted as follows [2]

Avipaka, Aruchi, Chhardi, Nidra, Kasa, Pinasa, Pratishyaya, Sharir Shaithilya Makshika Sarpana, Basti Toda, Mehanatoda, Mushkavadaran, Jwara, Daha, Trishna, Amlika, Murccha, Veetbheda, Klama, Pandu, Udvarta, Kampa - Hridgraha - Loulyam, Shula, Anidra, Sosha, Shwasa, Baddhapurish, Putimansa, Pidaka, Alaji, Vidradhi Daurbalya, Stambha.[3]

- Avipaaka (Indigestion): Due to increased Bahudrava Sleshma in Shareera leads to production of Ama and Avipaaka.

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- Arochaka (Anorexia): It is a disorder of taste perception where in spite of normal appetite the person is incapacitated to perceive taste and dislikes to eat food. It is mainly due to increased Pichhila and Guru Guna of Kapha and also due to Pitta Dosha vitiation. Rasadhatu Kshaya also causes Arochaka.
- 3) Chardi (Vomiting): It is defined as Bahirgamana (expelling) of Dosha through Mukha due to Utklesha (increase content in stomach) in Amashaya [4]. This Upadrava can also be a symptom of Marma Prappeedana [5], (irritation to vital organs) which occurs in Prameha.
- Nidra (Sleep): It is caused as a result of Kapha Dusti and Tamoguna in Prameha.
- Kasa (Cough): This Upadrava is a result of Pranavaha Srotodusti by Vriddha Kapha and Vata. Kasa results as a consequence of extensive Dhatu Kshaya.
- Pratishyaya (Peenasa): This is caused due to Kapha and Vata, Oja Kshaya and Pranavaha Srotodusti.
- Shaithilya: The Dhatu Kshaya leads to Anibida Samyogata (loss of compactness) leading to shaithilya.
- Makshikopasarpana: This condition is the result of shareer Madhuryata and consequent Madhura Bhava of Sweda [6] (Sweat). This attracts more Makshikas (flies). This condition here should be considered as a symptom indicating Asadhya Avastha, which is likely to be preceded or succeeded by Murchha Adi Upadrasas.
- Bastibheda / Mehana toda (Pain in pubis): This is due to Vata Dusti causing Toda
- Mushkavadarana: (wounds to testicular area) This is defined as Vidarana (break/tear) or Visheerana of Vrushana and may be a result of Kandu or Kusta affecting Vrushana or due to Vranashopha as a result of Pitta and Rakta Dusti causing Avadarana of Vrushana.
- Jwara (Fever): Jwara is mainly due to Pitta dominance [7] among Tridoshas. In Pittaja Prameha relatively there is more involvement of Medas (adipose tissue) and Rakta dhatu Kshaya which further leads to Ojonasha. Due to this there will be decreased Vyadhikshamatva (immunity) leading to Jwara.
- Daha (Burning sensation): Sarvanga Dahanamiva is considered as Daha and it is a Pittaja Nanatmaja Vikara [8]. According to Sushruta Daha is manifested due to Dhatukshaya. In Prameha there is severe Dhatukshaya which is the leading cause for Daha especially in Hasta (palm) and Pada (sole) similar to Agnidagdha Vrana (burnt wound). Mootramarga daha is also seen as a result of ati-pravrutti of mootra.
- Trishna (Thirst): Trishna or pipasa is defined as Paneeya Sevana Iccha i.e. increased desire to drink water (polydipsia), It is one of the important Upadrava of Prameha. This is experienced by most of the patients during the course of the illness. Word Prameha itself denotes that there is excess Sravana of Mootra (polyuria). Due to this Kleda Amsha (fluid) in the Shareera gets depleted. This decreased Kledamsha in turn causes increased Rukhastha which leads to Apdhatu kshaya which leads to Shoshana (dryness) of Gala, Taalu and Osthya leading to Trishna. It is also mentioned that Upasargaja Trishna is one of the complications of Prameha. Here Ushna Guna of Pitta and Ruksha Guna of Vata play a vital role to bring about Trishna. It has been described as Asadhya (incurable) if Trishna develops as a Upadrava of Prameha and Charaka says that it is a Dirgha Roga and results in Marana (death) if neglected or if developed as Upadrava [9].
- Amlika (Sour belching): Means Amlodgara as a result of Shukta paaka of ahar due to Agnimandya caused by Pitta.
- Moorcha (Fainting): This is defined as Chetanachyuti where there is Kasthavatpatana [10] of the patient and he is unable to experience Sukha and Dukha. This is mainly due to Pitta and Rakta Dusti. This phenomenon is a very common Upadrava of Prameha due to Dhatukshaya.
- Vitbheda (constipation): Vata Vriddhi leading to shoshana of dravamsha due to its ruksha guna result into Baddhata of purishata or vidbheda.
- Panduroga (Anaemia): This is a Pittapradhana Vyadhi where due to Dhatvagnimandya leading to asar Rakta Dhatu leading to Panduroga.
- Udavarta: Baddha Pureesha and Vata vitiation causes Udavarta i.e. upward movement of vata.
- Kampa (Tremor): Kampa is called as Ativepanam [11]. Both these lakshanas are due to vata dosha vitiation in different forms or due to variation in gunas
- Hridgraha: A condition where patient experiences as if his heart is being pulled out. This is a symptom of Hridroga that is clinically evident as Upadrava of Prameha. Hridgraha is mainly due to Vata Dusti due to Kshaya or due to Kaphapitta Avarana
- Loulya: A condition where there is an abnormal desire to have all Rasas (Taste) described as Sarvaraseshu Loluptvam due to Vata Vriddhi as a result of Dhatu Kshaya [12]
- Shoola (Pain): It is defined as ruja which is peculiar feature caused by Vata when the disease proceeds to involve Gambira Dhatus like Majja [13]. Apart from this, Shoola occurs in Koshta when there is Baddha Pureeshatva (hard stool) which is also an Upadrava of Prameha.
- Anidra (Disturbed sleep): Due to Pitta and Vata vriddhi.
- Shosha (Depletion): It is due to the Dhatu Kshaya occurring in prameha especially vataja leading to shoshana of shareera.
- Shwasa (Dyspnoea): Shwasa due to Doshaja Marmabhighata like Hridaya, which is Pranavahasrotomoola

- Pooti Mamsa Pidaka Alaji Vidradhi (Carbunle and similar skin lesions): The vitiated Pitta after vitiating twacha and Rakta leads to Ragayukta Shopha and hence called as Pidaka
- Daurbalya (Debility): Shareera Balahaani may be due to Alpaprana due to Manasika Daurbalya and Mamsopachaya [14] (inadequate nourishment of Muscle) as a result of ati kleda Vahana through Mootra pravrutti. These causes in total lead to Ojonasha causing Daurbalya
- Alasya (Laziness): Alasya is characterized by Karma Abhava due to Mandaguna of Kapha and as a result of Daurbalya. Here there will be crave for desirable touch, displeasure to discomfort and lack of enthusiasm to do work [15].
- Kandu (Pruritis): Kandu as an Upadrava in Prameha is primarily due to Kapha Dosha and also partly by Vata Dosha vitiation.

The classification of the various complications of Diabetes mellitus as per modern texts [16]

1.1. Acute Complications

- Diabetic ketoacidosis
- Hyperosmolar coma
- Hypoglycemia

1.2. Chronic complications

Microvascular

1.2.1. Eye disease

Retinopathy (proliferative/ nonproliferative)

- Macular oedema
- Cataract
- Glaucoma

1.2.2. Neuropathy

- Sensory and motor (mono and polyneuropathy)
- Autonomic

(Gastroparesis, Altered bowel habit, Postural hypotension)

1.2.3. Nephropathy (Renal Failure)

Foot disease (Ulceration, Arthropathy)

1.3. Macrovascular

- CAD-coronary artery disease
- Myocardial ischaemia/infarction
- PVD-Peripheral vascular disease
- Claudication, Ischemia
- CVD-Cerebrovascular disease
- Transient Ischaemic attack, Stroke

1.3.1. Others

- Gastrointestinal
- Genitourinary
- Dermatologic
- Cardiomyopathy

2. A microvascular diabetic complication

Diabetic microvascular complications mainly arise due to uncontrolled, poorly controlled or long-standing Diabetes Mellitus. These are mainly associated with impairment of vascular permeability that affects different tissues and organs of the body including the kidneys, retina and nerves [17]. Chronic, untreated and prolonged Hyperglycemia can further cause increased vascular permeability, disruption of glycocalyx structure, increase in water and protein retention, resulting in generalized edema [18]. Vascular endothelial growth factor (VEGF) is an important element in tissue neogenesis and vascular healing. VEGF-inhibition can also lead to an increase in DM-induced hypertension and glomerular proteinuria, with diminished vascular wound healing [19 a-b].

2.1. Diabetic Nephropathy

Diabetic nephropathy is associated with morphological impairment of the glomerular endothelial cell barrier [20] and the glomerular basement membrane. This, in turn, leads to an elevation of protein filtration in urine, reflecting disturbed protein degradation in the diabetic patient [21]. Oxidative stress progression in DM can induce gene expression of angiotensinogen, leading to renal function impairment [22 a-b].

Approximately one-third of all uncontrolled diabetic patients will suffer from diabetic nephropathy ending with renal dialysis. This can either be due to the previously mentioned genetic susceptibility and/or the reaction of cytokines with reactive oxygen species or advanced glycation end products. The early indicator of diabetic nephropathy is increased urinary albumin excretion [23].

2.2. Diabetic Retinopathy

DM is indirectly diagnosed via an eye test for impaired vision. The risk of blindness in diabetic subjects is associated with prolonged incidence of renovascular changes' [24]

Hyperglycemia induced activation of PKC can result in elevation of many metabolic pathways, stimulation of cell growth and apoptosis, and increase in cellular permeability. Hyperglycemia and states of oxidative stress associated with diabetic retinopathy also stimulate certain apoptotic growth factors that may contribute to diabetic cataract formation [25]. Furthermore, the elevated glucose level in retinal cells of diabetic individuals may lead to increased risk of retinopathy and accompanying blindness [26].

2.3. Diabetic Neuropathy

Chronic Hyperglycemia may lead to either sensory or motor neuropathic problems or autonomic nervous system dysfunction, including arrhythmias, gastroparesis, incontinence and sexual dysfunction [27]. Patients with long-term diabetes may have one or more types of neuropathies.

2.3.1. Peripheral Neuropathy

Diabetic peripheral neuropathy is one of the major complications affecting patients with DM. This can lead to either sensory or sensorimotor neuropathies that increase the risk of foot ulceration and amputation in some cases of uncontrolled diabetic patients [28]. Chronically elevated blood glucose levels and the resulting activated polyol pathway, with reduced blood supply to endoneurial tissues, are all associated with reduced protective nitric oxide formation and Na^+/K^+ ATPase dysfunction [29]. It leads to worsening of oxidative stress and acceleration of neurodegradation. Moreover, elevation of intraneural sorbitol can induce nerve cell necrosis and subsequently, cellular degradation [30]. Glycation of proteins within nerves in patients with DM accelerates nerve degeneration [31].

2.4. Autonomic neuropathy

2.4.1. Diabetes and Gastrointestinal Dysfunction

Autonomic neuropathy may cause dysfunction of the digestive system producing symptoms such as early satiety, bloating, nausea, vomiting, abdominal pain and heartburn. Slowed stomach emptying, or gastroparesis, is usually detected in diabetic patients with prolonged HG. Diabetic enteropathy also leads to acid reflux disease, delayed bowel movement, constipation, diarrhoea, and increased rate of bacterial, viral and fungal gastrointestinal tract infections.

Furthermore, diabetes-induced HG is associated with salivary and exocrine pancreatic insufficiencies due to a reduction in the synthesis and secretion of amylase, an important digestive enzyme responsible for the breakdown of carbohydrates [32].

2.4.2. Diabetes and Erectile Dysfunction

Erectile dysfunction is a common complication of DM, and is mainly related to disturbed communication between vascular and neuronal systems due to either weakened blood circulation in penile tissue or impairment of neuronal stimulation [33]. Impotence related to DM is much more frequent in diabetic than in non-diabetic men. Increased free radicals, such as malondialdehyde, are believed to disrupt the neuronal and vascular activities controlling penile erection. Impaired ejaculation and diminished satisfaction are other symptoms that diabetic patients may encounter [34].

3. Diabetic Foot and Wound Healing

Diabetic foot occurs as an interplay of abnormal structure and function of blood vessels and nerves leading to reduced angiogenesis, loss of sensation, unhealed secondary wound infections, ulceration and subsequently foot amputation. Diabetic foot ulceration is mainly due to neuropathy and ischemia occurring together. Diabetic foot is associated with increased incidence of foot trauma due to decreased proprioception. The underlying ischemia results in impaired wound-healing in the injured area(s), and superimposed infections lead to ulceration [35].

All stages of the complex wound-healing cascade are impaired in DM and compounded by many factors including inflammation, proliferation, angiogenesis, apoptosis, reduced chemotaxis and matrix formation, diminished bacterial resistance, and deterioration of the antioxidant protective system.

4. Non-classical chronic complications of diabetes mellitus

4.1. Periodontal Disease

Impairment of the immune system in diabetic patients enhances the development of periodontal disease due to increased bacterial accumulation between teeth and gingiva, accelerating gum infection and promoting bone demolition. Chronic periodontitis can lead to gum retraction, swelling, bleeding, and tooth loss. Diabetic patients also experience salivary insufficiency, which is associated with a reduction in salivary amylase and fluid secretion [36].

4.2. Diabetes and Skin Disorders

Manifestations of diabetes can also involve the skin. Chronic dermal infections are due to increased blood glucose supply to the skin. The HG in turn increases the occurrence of bacterial and fungal infections, leading to pruritus and

other symptoms of skin disease. In addition to HG, increased accumulation of subcutaneous adipose tissue related to obesity stimulates colonization and growth of *Candida albicans*. Also, skin dehydration may lead to changes in the normal dermal flora, and give way to colonization by pathogenic bacteria. Furthermore, DM is associated with delayed wound-healing [37]

5. Other conditions that may be associated with diabetes mellitus

5.1. Hypertension

It is now known that DM is a major risk factor in the development of hypertension. Moreover, diabetes-induced hypertension is one of the influencing causes of cardiovascular disease, including heart failure and other long-term complications, such as retinopathy, nephropathy and cerebrovascular accidents [38]. There is extensive evidence showing that controlling hypertension in DM can significantly diminish these diabetic complications [39]. End-stage renal disease is mainly associated with increased hypertension in DM, HG and glycated haemoglobin, all of which can lead to microalbuminuria due to reduced glomerular filtration [40].

5.2. Obesity and dyslipidemias

Obesity is a leading risk factor for many chronic diseases including insulin-resistance, type 2 DM, gastroesophageal reflux, hypertension, dyslipidemia, cardiovascular diseases and certain types of cancers [41]. Obesity can develop due to modern lifestyle habits such as excessive food intake, reduced physical activity, environmental factors, psychological effects and genetic susceptibility, which all have an effect on general health and mortality [42]. In addition to the harmful effect of HG on the progression of cardiovascular diseases, increased levels of cholesterol, LDL, total cholesterol, triglycerides and low level of HDL cholesterol may contribute to the development of heart disease in diabetic patients [43].

6. Conclusion

In Ayurveda classics the term prameha clearly refers typically to 'Prabhuta' i.e. excessive and 'avil' i.e. turbid urination. Excessive urination eventually leading to variable degree of dehydration and hypovolemia which gives rise to Trishna dourbalya, Bhrama, aalasya, vitbheda, shosha etc. The term 'Avil' i.e. increase turbidity refers to abnormal content present in the urine which are evacuated

inadvertently from the body leading to obvious loss of dhaatuposhakansh like phosphates, proteins glucose etc. leading to depletion of them and contributing in upadravas like dourabalya, shosha, Balahani, anidra, Pandu and various kinds of pain indicating dhaatu shaithliya. The upadravas like arochak, avipak, chhardi, kapha praseka, pratishaaya, amlika, Pandu, jwara are due to derangements produced in kapha attributes leading to aamashay dushti and agnimandya. Daha is particularly observed as kara pada daha or mootramarga daha and on the contrary sometimes suptata indicates vyan dushti. Prameha nidanas causing rasa – rakta dhatu dushti leads to twak dushti produces symptoms like puti mamsa, various prameha pidakas. alaji and vidradhi which explain the frequent manifestation.

Aacharya charak mentioned madhumeha as ojomeha indicating ojovisramsas i.e. loss of the supreme dhaatu 'Oja' leading to updrawas like with hrid-graha, moorchha, klama. Shosha, pandu daurbalya etc. Thus, it can be concluded that long-term complications of DM co-related with prameha upadravas may lead to severe morbidity or death.

Modern advanced in the laboratory investigations have drastically changed the approach towards the disease now before the complications arises the manifestations of the disease can be managed well in time and morbidity and mortality can be prevented or delayed.

This overview provides precise information about chronic complications of diabetes mellitus and a probable co relation with Ayurved aspect.

Compliance with ethical standards

Disclosure of conflict of interest

The authors confirm that this article content has no conflict of interest.

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