

A REVIEW ON *HETU* OF *PRAMEHA* AND ASSOCIATION BETWEEN ETIOLOGICAL FACTORS OF DIABETES MELLITUS

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ABSTRACT

The Prevalence of obesity and metabolic syndrome is rapidly increasing in India and other south Asian countries, leading to increased mortality and morbidity due to cardiovascular disease and Type 2 Diabetes Mellitus because of rapid nutritional changes, lifestyle and socioeconomic transitions consequent to increasing affluence, urbanization, mechanization and rural-to-urban migration. Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation. Diabetes Mellitus is a metabolic disorder of multiple aetiologies, characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. Life style

changes along with pharmacotherapy is essential for glycaemic control and prevention of complications. Diabetes Mellitus may be correlate with *Prameha* as per Ayurveda. *Prameha* is *Santarpanjanya Vyadhi* and described as *Anushanginam*. This indicates long lasting nature of *Prameha*. *Nidanparivarjan* (~to avoid causative factor) is *Samanya Chikitsa* of *Vyadhi* which prevents the progression of disease. So there is important to know *Nidana* of *Prameha* as per *Ayurvedic texts* as well as etiological factors of Diabetes Mellitus. There is similarity in between *Hetu* of *Prameha* and causative factor of Diabetes Mellitus which described detail in this review.

KEYWORDS: Prameha, Hetu, Anushanginam, Diabetes Mellitus.

INTRODUCTION

The prevalence of obesity and metabolic syndrome is rapidly increasing in India and other South Asian countries, leading to increased mortality and morbidity due to Cardiovascular

disease and Type 2 Diabetes Mellitus.^[1,2] The main drivers are related to rapid nutritional changes, lifestyle and socioeconomic transitions consequent to increasing affluence, urbanization, mechanization, and rural-to-urban migration.^[3,4] The worldwide prevalence of Diabetes Mellitus has raised dramatically over the past two decades, from an estimated 30 million cases in 1985 to 382 million in 2013. Based on current trends, the international Diabetes federation projects that 592 million individuals will have Diabetes by the year 2035. Although the prevalence of both Type 1 & Type 2 Diabetes Mellitus is increasing worldwide, the prevalence of Type 2 Diabetes Mellitus is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialised and the aging of the population.^[5] Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation.^[6] Diabetes Mellitus is a metabolic disorder of multiple aetiologies, characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both.^[7] Park K. stated that Diabetes is an “Iceberg” disease. Diabetic patients, if undiagnosed or inadequately treated, develop multiple chronic complications like diabetic renal disease, diabetic retinopathy and neuropathy are serious health problems resulting in deterioration of the quality of life and premature death.^[8] Diabetes Mellitus may be correlated with *Prameha* as per Ayurveda. *Prameha* is included in *Santarpanjanya Vyadhi*^[9] and also called as *Mahagada* which is difficult to treat.^[10] If *Prameha* is not treated properly for a prolonged period, it will turn into *Madhumeha*.^[11] The peculiarity of Ayurvedic science is the prevention and better control of these diseases. Etiological factors which are responsible for disease formation are called as *Nidana* or *Hetu* as per Ayurvedic texts.^[12] So there is importance to know *Nidana* of *Prameha* as per *Ayurvedic texts* as well as etiological factors of Diabetes Mellitus. There is similarity between *Hetu* of *Prameha* and causative factors of Diabetes Mellitus which are described in detail in this review which helps to glycaemic control and reduce risk for microvascular and macrovascular complications of Diabetes mellitus.

AIM: To study the literature of *Hetu* of *Prameha*, etiological factors of Diabetes Mellitus and association between them.

MATERIALS: References of *Hetu* of *Prameha* from Ayurvedic Texts and etiological factors of Diabetes Mellitus from modern texts were described, compared and interpreted.

METHODS

1. *Hetu* of *Prameha* from all *Samhita* were described.
2. Etiological factors of Diabetes Mellitus were described.
3. Comparison between Ayurvedic *Hetu* and etiological factors of *Prameha* with special reference to Diabetes Mellitus.

Ayurvedic review

Nidan and its significance: A particular factor can be called as *Nidan* only when it will develop a complete disease process (~*Setikartavyata*) in the body.^[12] *Nidanparivarjan* (~to avoid causative factor) is first line of treatment which prevents the progression of disease.^[13]

According to Charaka, the description of *Vikar- vighatkar- Bhava- Abhav* has elaborated. When *Nidan*, *Dosha* and *Dushya* do not combine together or if combined after a long time or in weakened state, disorder will not be there or it will manifest lately or will manifest in a mild form or without all symptoms. While on the contrary the manifestation of the disease will be earlier that too with all symptoms will be produced with more severity.^[14] These three factors *Nidana*, *Dosha* and *Dushya* cause manifestation of *Prameha* due to vitiated *Kapha Dosha* which consisting abundant fluid(*Bahudrava*), *Dushyas* includes *Bahu Abaddha Meda*(~abundant and non-compact fat),*Mansa*(~muscle), *Shariraj Kleda*(~body fluid) and other responsible factors.^[15]

Nidan of Prameha**Table-01: Table showing *Samanya Nidan* of *Prameha*.**

<i>Nidan</i>	Charaka ^[16] (C.C.6/4)	Sushruta ^[17] (S.N.6/3)	Vagbhata ^[18] (A.H.N.10/1,2,3)
Aharaj Nidan			
<i>Madhur</i>	-	+	+
<i>Amla</i>	-	-	+
<i>Lavana</i>	-	-	+
<i>Snigdha</i>	-	+	+
<i>Guru</i>	-	-	+
<i>Picchil</i>	-	-	+
<i>Shita</i>	-	+	+
<i>Navannapan</i>	+	-	+
<i>Sura</i>	-	-	+
<i>Anup Mans</i>	+	-	+
<i>Guda Vaikrut</i>	+	-	+
<i>Ikshu</i>	-	-	+
<i>Pay(Goras)</i>	+	-	+

<i>Dadhi</i>	+	-	-
<i>Medya</i>	-	+	-
<i>Drava Annapan</i>	-	+	-
<i>Gramya Audak Anup Rasa</i>	+	-	-
<i>Meda, Mutra, Kapha vardhak Ahar</i>	+	-	+
<i>Viharaj Nidan</i>			
<i>Asyasukh</i>	+	-	-
<i>Swapnasukh</i>	+	-	-
<i>Diwaswapna</i>	-	+	-
<i>Avyayam</i>	-	+	-
<i>Alasya Prasakta</i>	-	+	-
<i>Eksthan Asan Rati</i>	-	-	+
<i>Shayan Vidhivarjit</i>	-	-	+

Madhavkar(M.N.33/1)^[19], Yogratanakar (Y.R.Prameha Nidan/1)^[20] and Bhavprakash(B.P.38/1)^[21] explained *Prameha Nidan* exactly same as that of Charaka.

Charaka also explained various specific *Hetu* of *Prameha* according to the types of *Prameha* i.e. *Vataj*, *pittaj* and *Kaphaj* which divides as *Aharaj*, *Viharaj* and *Manas Hetu* are as follows.

Kaphaj Prameha Hetu^[22]

Aaharaj Hetu

1. Excessive intake of *Hayanaka*, *Yavaka*, *Chinaka*, *Uddalak* (a type of honey), *Naishadha*, *Itkata*, *Mukundaka*, *Mahavrihi*, *Pramodaka* and *Saugandhaka*.
2. Use of new legumes like *Harenu* i.e. *Vartulkalay* (~greenpea) and *Mashsupya* (~ soup of black gram) with ghee.
3. *Gramya Anup Audak Mans* (~Meat of domesticated, marshy and aquatic animals)
4. *Shak* (vegetables)
5. *Tilpalal* (sesamum paste)
6. *Pisthanna* (~food prepared using flour)
7. *Payas* (~rice cooked with milk)
8. *Krushara* i.e. *Tilpalal Mash Krushara* (~rice cooked with sesamum paste and blackgram).^[23]
9. *Vilepi* (~paste like preparation of rice)
10. *Ikshuvikar* (~Sugarcane products like sugar and jaggery)
11. *Kshir* (milk)
12. *Mandak Dadhi* (~curd)
13. *Navmadya* (~fresh wine)
14. *Drava Madhur Tarun Prayanam* (~excessive intake of liquid and sweet diet)

Viharaj Hetu

1. *Mruja Varjanam* that means *Udvartan* (~abstinence from massage by dry herbal powder which helpful for cleaning of skin).^[23]
2. *Vyayam varjanam* (~lack of physical exercise)
3. *Swapna Shayyasan Prasang* (~Indulgence in sleep, lying down and sitting)

Pittaj Prameha Hetu^[24]**Aharaj Hetu**

1. Excessive intake of diet having dominant in *Amla* (~sour), *Katu* (~pungent), *Lavana* (~salt) *Rasa*
2. *Ushna* (~Hot) *Gunatmak Aahar, Aushadh, Vihar and Kshar*
3. *Ajir nabhojanopsevin* (~intake of food before previous food digested completely)
4. *Visham Aahar sevan*

Viharaj Hetu

1. *Atitikshna Aatap* (~excessive exposure to sunlight)
2. *Agnisantap* (~exposure to heat)
3. *Shrama* (~excessive physical exertion)

Manas Hetu

1. *Krodh* (anger)

These *Aharaj* and *Viharaj Hetu* leads to *Pitta Prakopa* and causes early manifestation of *Pittaj Prameha* as compare to *Kaphaj Prameha*.^[25]

Vataj Prameha Hetu^[26]**Aaharaj Hetu**

1. Excessive intake of diet having dominant in *Kashay* (~Astringent), *Katu* (~pungent), *Tikta* (~bitter), *Rasa* (~taste).
2. *Ruksha* (~dry) and *Sheet* (~cold food) *Gunatmak Aahar, Aushadh* and *vihar*.

Viharaj Hetu

1. *Vyavaya*
2. *Vyayam* (~exercise)
3. *Vaman, Virechan, Asthapan Basti* and *Shirovirechan Atiyog* (~excessive use of *Panchakarma* therapies)

4. *Sandharan* (~supression of natural urges)
5. *Anashan* (~fasting)
6. *Abhighat* (~trauma)
7. *Aatap* (~exposure to sunlight)
8. *Jagaran* (~sleep at late night)
9. *Shonitatisek* (~excessive loss of blood)
10. *Vishamshariranyas* (~sit or lying down in improper position of body)

Manas Hetu

1. *Udweg* (~anxiety)
2. *Shok* (~sadness)

In Madhav Nidan, *Hetu's* are distributed in fourteen types.^[27] *Hetu's* of Prameha may be distributed in following manner in fourteen types.

Table-02: Table Showing Distribution of *Hetu* of *Prameha* according to Fourteen Types of *Hetu*.

Sr. No	Hetu	Samnikrushta	Viprakrushta	Pradhanik	Vyabhichari	Nij	Agantuj	Dosh	Vyadhi	Ubhay	Asamyandriyarth Sanyog	Pradnyaparadh	Parinam	Vyanjak	Utpadak
1	<i>Aasyasukha</i>		+			+		+				+			+
2	<i>Swapnasukha</i>		+			+		+				+			+
3	<i>Divasvapna</i>		+			+		+				+			+
4	<i>Avyayam</i>		+			+		+				+			+
5	<i>Alasya</i>		+			+		+				+			+
6	<i>Atitikshna Aatap Agni(p)</i>		+			+		+					+	+	
7	<i>Hayanak</i>		+			+		+				+			+
8	<i>Yavak</i>		+			+		+				+			+
9	<i>Chinak</i>		+			+		+				+			+
10	<i>Uddalak</i>		+			+		+				+			+
11	<i>Naishadh</i>		+			+		+				+			+
12	<i>Itkat</i>		+			+		+				+			+
13	<i>Mukundak</i>		+			+		+				+			+
14	<i>Mahabrihi</i>		+			+		+				+			+
15	<i>Pramodak</i>		+			+		+				+			+
16	<i>Saugandhaknavanam</i>		+			+		+				+			+
17	<i>Sarpishmata nav Harenu</i>		+			+		+				+			+
18	<i>Mash</i>		+			+		+				+			+
19	<i>Gramya Anupa Audak Mans</i>		+			+		+				+			+
20	<i>Shak</i>		+			+		+				+			+
21	<i>Tilpalal</i>		+			+		+				+			+
22	<i>Pishtanna</i>		+			+		+				+			+
23	<i>Payas</i>		+			+		+				+			+
24	<i>Krushara</i>		+			+		+				+			+

25	Vilepi		+			+		+				+			+
26	Ikshuvikar		+			+		+				+			+
27	Kshir		+			+		+				+			+
28	Navmadya		+			+		+				+			+
29	Mandak Dadhi		+			+		+				+			+
30	DravMadhurTarun Prayanam		+			+		+				+			+
31	Mruja Vyayam varjan		+			+		+				+		+	
32	Swapna Shayyasan Prasang		+			+		+				+		+	
33	Ushna, Amla, Lavan (P)		+			+		+				+			+
34	Kshar (P)		+			+		+				+			+
35	Ajirna Bhojanopsevin (P)		+			+		+				+		+	+
36	Santap (P)		+			+		+				+			+
37	Shram (P)		+			+		+				+			+
38	Krodha (P)		+			+		+				+			+
39	Visham Aahar(P)		+			+		+				+			+
40	Kashay, Katu, tikta(V)		+			+		+				+			+
41	Ruksha,Laghu(V)		+			+		+				+			+
42	Sheet(V)		+			+		+				+			+
43	Vyavyaya(V)		+			+		+				+			+
44	Vyayam(V)		+			+		+				+			+
45	SanshodhanKarma Atiyog(V)		+			+		+				+		+	+
46	Sandharan(V)		+			+		+				+		+	+
47	Anashan(V)		+			+		+				+			+
48	Abhighat(V)		+					+	+			+		+	+
49	Aatap(V)		+					+	+			+	+	+	+
50	Udveg(V)		+			+		+				+		+	+
51	Shok(V)		+			+		+				+		+	+
52	Shonit Atisek(V)		+			+		+				+			+
53	Jagaran(V)		+			+		+				+			+
54	VishamShariranyas(V)		+			+		+				+			+
55	Kulaj(Beej dosha)	+		+		+				+			+		+

Where P-Pittaj Prameha Hetu, V-Vataj Prameha Hetu

Adi-Bala-Pravritta or Kulaja Vikara

Sushruta stated that *Adi- Bala- Pravritta- Vyadhi* are caused by *Dushita-Shukra* or *Dushita-Shonita*, which include *Kushtha*, *Arsha Prabhritataya*.^[28] Where ‘*Prabhritayaha*’ word indicates that *Grahani*, *Prameha* and *Yakshma* are also to be included in *Adi-Bala-Pravritta-Vyadhi* explained by *Dalhana*.^[29] Sushruta explained while describing *Prameha*, classified into two groups that is *Sahaja* (genetic factors) which is caused due to *Matru Pitru Bija Dosh*.^[30] Charaka already stated *Kulaj Prameha* which is cause due to *Beejdosha Asadhya* to treatment.^[31] Charaka explained that *Garbha Vikriti* is due to defect in *Beeja*, *Beejabhaga* and *Beejabhagavayav*.^[32] This can be correlate with Sperm or Ovum, Chromosomes and genes respectively that means Diabetes Mellitus due to genetic defects.

The second type of *Prameha* is *Apathyanimittaj* is acquired form of *Prameha* can correlate with Type 2 Diabetes Mellitus.

Table-3: Table Showing types of Prameha according to Sushruta.

Types	<i>Sahaja</i>	<i>Apathyanimittaj</i>
Causes	<i>Beejdoshat</i>	<i>Ahit Aahar, Apathya</i>
Sign and symptoms	1) <i>Ruksha</i> (~dry skin_) 2) <i>Krish</i> (~lean) 3) <i>Alpashi</i> (~less eater) 4) <i>Pipasabhrish</i> (~polydypsia) 5) <i>Parisaranshila</i> (~restless,always desire to wander)	1) <i>Sthula</i> (~obese) 2) <i>Bahuaashi</i> (~eats more) 3) <i>Snigdha</i> (~smooth skin) 4) <i>Shayyasan, Swapnashil</i> (~like to sit down and sleep always)

Pre disposing factors

Charaka has described three predisposing factors of *Prameha* and said that as birds attracted towards their nests, similarly *Prameha* affects people who are-voracious eater, have aversion to bath and avoid walking.^[33]

Risk Group: The person who is *Mandostahi* (~dull in activities), *Atisthul* (~over obese), *Atisnigdha* (~over unctuousness/oily) and *Mahashan* (~voracious eater) will die early due to *Prameha*.^[34]

If a woman eat excessive sweet things at the time of pregnancy the offspring will be suffering from *Madhumeha*, *Mukata* or *Sthaulya*.^[35]

Modern View

According to modern science etiological factors of Diabetes Mellitus includes.

1. Type 1 Diabetes Mellitus^[36]

A) Genetic

Table-4: Table Showing Genes responsible for Type 1 Diabetes Mellitus.

Genes
HLA on chromosome 6
HLA DR3 and DR4haplotype
HLA-DQA1*0301, DQB1*0302, and DQB1*0201
the CTLA-4 gene, interleukin 2 receptor, CTLA4, and PTPN22

Table-5: Table Showing Risk of type 1 Diabetes among first-degree relatives of patients with Type 1 Diabetes.^[37]

Relative with Type 1 DM	Percentage overall risk
Identical twin	35%
Non identical twin	20%
HLA-identical sibling	16%
Non-HLA-identical sibling	3%
Father	9%
Mother	3%
Both parents	Upto 30

B) Immune mediated- Autoimmune process is thought to be triggered by an infectious or environmental stimulus and to be sustained by a beta cell-specific molecule.

Table-6: Table showing Autoantibodies among Newly diagnosed Type 1 Diabetes Mellitus.^[38]

Name of Autoantibody	Prevalence among newly diagnosed Type 1 Diabetes Mellitus
Insulin Autoantibodies(IAA)	70%
Glutamic acid decarboxylase autoantibody(GADA)	74-79%
Insulinoma-associated autoantigen 2autoantibody(IA-2A)	75-78%
Zinc transporter and autoantibody(ZnTBA)	71%
Islet cell autoantibodies (ICAs)	85%

C) Environmental factors: Putative environmental triggers include viruses (coxsackie, rubella, enteroviruses most prominently), bovine milk proteins, and nitrosourea compounds.

2. Type 2 Diabetes Mellitus-may range from predominantly insulin resistance with relative insulin deficiency

A) Genetic: The concordance of type 2 DM in identical twins is between 70 and 90%. Individuals both parents have type 2 DM, the risk approaches 40%. Genetic polymorphisms have also been found in the genes encoding the peroxisome proliferator-activated receptor γ , inward rectifying potassium channel, zinc transporter, IRS, and calpain 10.

B) Metabolic Abnormalities: Abnormal muscle and fat metabolism Insulin resistance, the decreased ability of insulin to act effectively on target tissues (especially muscle, liver and fat) is a prominent feature of type 2 DM and results from a combination of genetic susceptibility and obesity.

C) Environmental factors: Obesity, nutrition, and physical activity modulate the phenotype.^[39] Life style changes due to urbanization and modernisation have caused unhealthy diet habits, lack of physical activity and increased stress leading to overweight or obesity with higher level of insulin resistance.^[40]

D) Polycystic ovary syndrome (PCOS): Insulin resistance is seen in a significant subset of women with PCOS, and the disorder substantially increases the risk for type 2 DM, independent of the effects of obesity.^[39]

Insulin Resistance Syndromes : The metabolic syndrome, the insulin resistance syndrome and syndrome X are terms used to describe a constellation of metabolic derangements that includes insulin resistance, hypertension, dyslipidaemia (decreased HDL and elevated triglycerides), central or visceral obesity, type 2 DM or IGT/IFG, and accelerated cardiovascular disease.^[41]

3) Other types of Diabetes Mellitus^[42]

A) Genetic defects of Beta cell development or function characterised by mutations in

1. MODY1 (Maturity onset Diabetes of Young): Hepatocyte nuclear transcription factor (HNF) 4 α
2. MODY2: Glucokinase
3. MODY3: HNF-1 α
4. MODY4: Insulin promotor factor-1(IPF-1)
5. MODY5: HNF-1 β
6. MODY6: NeuroD1
7. Mitochondrial DNA

8. Subunits of ATP sensitive potassium channel
9. Proinsulin or Insulin
10. Other pancreatic islets

B) Genetic defects in Insulin action

1. Type A insulin resistance
2. Leprechaunism
3. Rabson Mendenhall syndrome
4. Lipodystrophy syndrome

C) Disease of exocrine pancreas-Pancreatitis, Pancreatotomy, Neoplasia, Cystic Fibrosis, Haemochromatosis, fibrocalculous pancreatopathy, mutations in carboxyl ester lipase.

D) Endocrinopathies

1. Acromegaly
2. Cushing's syndrome
3. Glucagonoma
4. Pheochromocytoma
5. Hyperthyroidism
6. Somatostatinoma
7. Aldosteroma

E) Drugs or chemical induced: Glucocorticoids, vacor (a rodenticide), Pentamidine, Nicotinic acid, Diazoxide, B-Adrenergic agonists, Thiazides, Calcineurine and mTOR inhibitors, hydantoins, asperginase, alpha interferon, protease inhibitors, antipsychotics(atypical and others), epinephrine

F) Infections: Congenital rubella, cytomegalovirus, coxsackievirus. Infections increases the production of stress hormones such as cortisol, growth hormone precipitate an acute exacerbation of insulin resistance and insulin deficiency.^[43]

G) Uncommon forms of immune-mediated Diabetes-“Stiff person” syndrome, anti-insulin receptor antibodies.

H) Other genetic syndromes sometimes associated with diabetes-Wolfram's syndrome, Down's syndrome, Klinefelter's syndrome, Turner's syndrome, Friedreich's ataxia, Huntington's chorea, Laurence-Moon-Biedl syndrome, porphyria, Prader-Wili syndrome.^[41]

4) Gestational Diabetes Mellitus: Glucose intolerance developing during pregnancy is classified as gestational diabetes mellitus (GDM). Insulin resistance is related to the metabolic changes of late pregnancy, and the increased insulin requirements may lead to IGT or Diabetes.^[5]

DISCUSSION

While comparing the *Hetu* of *Prameha* with Causative factors of Diabetes Mellitus four types of *Hetu* was considered that are *Aharaj*, *Viharaj*, *Manas* and *kulaj Hetu*.

Table-7: Table Showing Association between *Hetu* of *Prameha* and Etiological factors of Diabetes Mellitus.

<i>Hetu</i> of <i>Prameha</i>	Causative factor of Diabetes Mellitus
<i>Sahaj Prameha-Beejdosha</i>	Genetic defects-Type 1 DM
<i>Apatthyanimittaj- Ahitkar and Apathya Ahar Vihar</i>	Physical Inactivity and Obesity due to unhealthy dietetic habits-Type 2 DM
<i>Navannapan in excess quantity, Kapha Medovardhak Ahar</i>	Overeating and High calorie diet
<i>Ushna Gunatmak Ahar and Aushadh</i>	Drug or chemical induced
<i>Navamadya</i>	Alcohol induced Pancreatitis
<i>Kshir</i>	Bovine milk protein
<i>Ajirna Bhojanopsevinam, Visham Ahar</i>	Unhealthy Diet habits
<i>Vyayam Varjanam</i>	lack of physical exercise
<i>Asyasukham</i>	Sitting job or sedentary life style
<i>Swapnasukham, Divasvap</i>	Improper sleeping habits, Sleep at Day time
<i>Krodh, Udveg, Shok</i>	Stress factor
<i>Abhighataj</i>	Traumatic Pancreatitis

Aharaj Hetu

1. While going through above *Hetu* of *Kaphaj Prameha* includes *Madhur*, *Amla*, *Lavan Rasatmak Ahar*; *Guru*, *Snigdha Guna dominant Ahar* which leads to increase *Vikrit Kapha* and *Meda Dhatu* and *Kleda Utpatti* turns into *Prameha* Which can be correlate with causes of Type 2 Diabetes mellitus includes overeating and high calorie diet leads to obesity and insulin resistance.

2. *Ushna Gunatmak Ahar* and *Aushadh* cause for *Pittaj Prameha* which can correlate the drug induced Diabetes Mellitus.

3. *Navamadya* is cause for *Prameha* which can be correlate with Diabetes Mellitus due to alcohol induced Pancreatitis.

4. Excessive intake of *Kshir* is cause for *Prameha* while bovine milk proteins is environmental factor responsible for Type 1 Diabetes Mellitus.

5. *Ajirna Bhojanopsevinam* and *Visham Ahar Sevinam* means taking meal without judgement of *Agni Status* causes of *Pittaj Prameha* while unhealthy dietic habits are etiological factor for Diabetes Mellitus.

Viharaj Hetu: *Vyayam Varjanam*, *Asyasukham* and *Swapnasukham* can be compare with lack of physical exercise, sedentary life style cause of Type 2 Diabetes Mellitus.

Manas Hetu: *Krodh*, *Udveg* and *Shok* are causative factor for *Prameha* while Stress factor is the major cause of Diabetes Mellitus.

Kulaj Hetu

1. If a woman eat excessive sweet things at the time of pregnancy the offspring will be suffering from *Madhumeha*, *Mukata* or *Sthaulya*. Permanent neonatal diabetes may be caused by several genetic mutations, usually requires treatment with insulin, and phenotypically is similar to type 1 DM.^[44] The in utero environment also contributes, and either increased or reduced birth weight increases the risk of type 2 DM in adult life.^[39]

2. *Kulaj Prameha* caused due to *Matru Pitru Dosha* can be correlate with the genetic defect in Diabetes Mellitus.

Other Hetu

Abhigat cause for *Vataj Prameha* which can correlate with Pancreatitis caused due to trauma results in Diabetes Mellitus.

CONCLUSION

The prevalence of Diabetes is rising day by day. WHO projects that Diabetes will be the 7th leading cause of death in 2030.^[45] Therefore medical therapy along with prevention is necessary for control of such type of disease. As prevention is better than cure there is important to know etiological factor of disease. Avoid etiological factors of *Prameha* and Diabetes mellitus play major role for prevention of disease from Pre diabetes condition to Diabetes and reduce risk of complication. Although the genetic factor cannot be modified, its interaction with the environmental factors can be prevented by modifying obesity, diet and physical activity.

Kapha Dosha is plays a major role in *Prameha Samprapti* though *Vata* and *Pitta* are associated *Dosha*. Excess *Kapha* and *Kleda* may be associate to receptor insensitivity and cellular signal failure because of *Strotorodh* therefore if all the *Nidan* of *Prameha* will avoid then it will be better prevention to turn *Kaphaj Prameha* to *Madhumeha*.

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