EVALUATION OF THE EFFECT OF MUSTADI KWATHA IN THE MANAGEMENT OF MADHUMEHA VIS-A-VIS DIABETES MELLITUS (NIDDM)

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Certificate

This is to certify that the thesis entitled "**Evaluation of the effect of Mustadi Kwatha in the Management of Madhumeha vis-a-vis Diabetes Mellitus (NIDDM)"** which is being submitted herewith for the award of the degree of **Doctor of Philosophy (Ayurveda) in Kayachikitsa** of Tilak Maharastra Vidyapeeth, Pune is the result of original research work completed by **Dr . Jayanta Kumar Sarma** under my supervision and guidance. To the best of my knowledge and belief the work incorporated in the thesis has not formed the basis for the award of any degree or similar title of this or any other university or examining body upon him.

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Declaration

I hereby declare that the thesis entitled **"Evaluation of the effect of Mustadi Kwatha in the management of Madhumeha vis-a-vis Diabetes Mellitus (NIDDM)"** completed and written by me has not previously been formed as the basis for the award of any degree or similar title upon me of this or any other Vidyapeeth or examining body.

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Dr. Jayanta Kumar Sarma

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Date: **Dr. Jayanta Kumar Sarma**

Place: Ghataprabha

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ABBREVIATIONS

1.	A.Sa	Ashtanga Sangraham
2.	A.H	Ashtanga Hrudayam
3.	Bhe.S	Bhela Samhita
4.	B.R	Bhaishajya Ratnavali
5.	Bha.Pra	Bhavaprakasam
6.	Cha.Sam	Charaka Samhitha
7.	Chi	Chikitsasthanam
8.	FBS	Fasting blood Sugar
9.	Ha.Sam	Harita Samhitha
10.	Ka.Sam	Kashyapa Samhitha
11.	M.N	Madhava Nidanam
12.	PPBS	Post Prandial Blood Sugar
13.	Su.Sam	Susrutha Samhita
14.	Sha.Sam	Sharangadhara Samhitha
15.	Y.R	Yogaratnakaram
16.	In.	Indriyasthanam
17.	Ni	Nidanasthanam
18.	Sh	Sharirasthanam
19.	Vi.	Vimanasthanam
20.	Uttar.	Utharardham
21.	R.V	Rig-Veda
22.	S.B	Shayana Bhashya
23.	V.S	Vangasena

"Evaluation of the effect of Mustadi Kwatha in the management of Madhumeha vis- a- vis Diabetes mellitus (NIDDM)"

Abstract

Key words: *Madhumeha*, Diabetes Mellitus, *Mustadi Kwatha*, .

Madhumeha is explained as one of the 20 types of *Prameha* described in Ayurveda. In *Madhumeha*, the person voids excessive quantity of urine similar to honey in taste and colour along with sweetness of whole body. *Prameha* has been explained as *anushangi* and *santarpanajanya vyadhi* caused due to overeating. Because of the difficulty in treatment, seriousness and complications, *Madhumeha* has been considered as one of the eight *Maharogas*. The clinical features of *Madhumeha* like *Prabhoota* and *Avila mootrata* are similar to that of Diabetes Mellitus of modern medicine. It is a chronic, life-long state which leads to hyperglycemia as their consequence. It is among the highest prevalent disorders in the world today with the seventh position in the list of the diseases accounting for maximum number of deaths every year in the United States.

Almost 98% of Diabetic population in India constitutes of Type II Diabetes mellitus in which prevalence of it has rose to 12% to 19% in urban areas and 4% to 9% in rural areas as per the published by ICMR in the multi centric study[3]. Hence there is a need of clinical research in getting a control on this disease with a aim to achieve a good glycemic control. *Mustadi kwatha* mentioned in *Bhaishajya Ratnavali* 37thchapter *Prameha Rogadikara* are having *Tikta & Kashaya* are *pradhan rasa* with *pramehagna* property. These properties of *mustadi Kasayam* are potent enough to do the samprapti Vighatana this disease condition.

Objective:

To evaluate the efficacy of *Mustadi Kwatha* in the management of *Madhumeha* vis- a – vis Diabetes mellitus.

Hypothesis:

H_0 = *Mustadi kwatha* is not effective in *Madhumeha* vis-a-vis diabetes mellitus

H_1= *Mustadi kwatha* is effective in *Madhumeha* vis-a-vis diabetes mellitus

Methodology:

This study is a comparative single blind clinical study where 150 patients of both sexes between age group of 30-70 yrs diagnosed as *madhumeha* vis –a- vis Type-II Diabetes Mellitus had been selected based on the classical signs and symptoms. All the patients are selected from the OPD and IPD of *Shri J.G.C.H. S Ayurvedic Medical college & Hospital Ghataprabha*. The patients were divided into Group A & Group B consisting of each 75 patients. In which group A was given *Mustadi Kwatha* 48ml twice daily in *Abhukta kaala* for 90 days along with oral anti diabetic drug and group B were given placebo (Gum acacia) along with regular oral anti diabetic drug. The signs & symptoms has been recorded on the pre designed Proforma and assessed with subjective & objective (FBSL, PPBSL, HbA_1C) parameters before the treatment, after 15 days, 30 days, 45 days, 60 days, 75days and 90 days of the treatment. After 90 days of treatment & after 03 month washout period, the patient were crossed over where, Group A were received placebo along with oral anti diabetic drugs and Group B were received *Mustadi kwatha* along with oral anti diabetic drugs.

Statistical analysis is done by using students'' test and 'z' test.

Findings:

Mustadi Kwatha showed significant relief in both subjective and objective parameters in *Madhumeha* in Group A in comparison to the group B in 90 days of treatment. In cross over study also after 03 month washout period shows similar effect by *Mustadi kwatha*. The *Mustadi Kwatha* has got an added effect in the patients who already in oral ant diabetic medicine.

Conclusion

The present research work was mainly aimed to explore the efficacy of *Mustadi Kwatha* in the management of *Madhumeh*a. The line of treatment was based upon *Tikta, Kasaya Rasa, Usna Virya, Kaphavatahara* and *Pramehaghna* properties of the Polyherbal formulations and *Mustadi Kwatha* and *pathyapathya* are strictly followed.

After the detailed clinical observations, discussion and analysis of results the following conclusions are drawn:

- The clinical trial of both Group A and Group B showed significant relief in both subjective and objective parameters.
- *Mustadi Kwatha* showed significant relief in the objective criteria like FBSL, PPBSL & Glycated hemoglobin -HbA_{1C} after 90 days of treatment in the patients treated along with modern drugs.
- This study also gives clear idea that *Mustadi Kwatha* has got an added effect in all the subjective and objective parameters.
- The serum Cholesterol, Triglyceride, LDL.HDL well controlled during the study treated by Mustadi Kwatha.
- During entire study the serum creatinine and serum urea remains in downward trend towards the normal level, indicates that the indigenous compound does not have any adverse effect in kidney.

The herbal formulation the *Mustadi Kwatha* was significantly effective in the management of *Madhumeha* showing an added effect in patients who are pretreated with oral anti diabetic drug during treatment period.

INTRODUCTION:

Madhumeha is one of the important lifestyle disorder described under *Prameha,* one of the oldest documented disease and its relevance increased now a days. Due to increasing stress and psychological factor, environmental factor, lack of physical activity, the disease *madhumeha* is increasing day by day. *Acharya Charaka* explained that Prameha is of 20 types, where ten caused due to *Slehma,* six due to *pitta,* and four due to *Vata*. *Madhumeha* is included under *Vataja prameha*. The description of *madhumeha* widely available in *Brihattrayrees* and *Laghutrayees*. There are two types of *Prameha* viz *Sthula Prameha* and *Krusha Prameha* according to Charaka. There are another two types of classification has been given in *Astanga Hridaya* viz *Dhatukshayajanya Madhumeha* and *Avaranajanya Madhumeha*. Due toi consumption of food, beverages and activities leading to increase *medas*, mootra and kapha, the ahara dravya which are *madhura* (sweet), *amla* (sour), *lavana* (salt), *snigdha* (fatty), *guru (*foods which are heavy to digest, slimy) and *sheetal* (cold), *navanna* (freshly harvested grains), *Sura* (alcoholic drinks), *anupa mamsa* (flesh of marshy animals), jagery , milk and *ekasthana sanarati* (sedentary lifestyle) and sleeping without proper method causes *Madhumeha (A.H.Ni.*10 verse no.2-3).

The etiological factors which aggravates the *Vata dosa* leads to *Apatarpanajanya Madhumeha (Krusha Prameha)*. The etiological factors which aggravates Sleshma and Pitta leads to *Santarpanajanya Madhumeha (Sthula prameha).* Due to aggravation of *Vata* due to *dhatukshay*a and *margavarodha* with *dosaavarana* the *Madhumeha* produced. *Madhumeha* is produced when all types of *Pramehas* are neglected. And in *madhumeha* the urine is sweet, it resemble like that of honey and the body also become sweet (A.H.Ni.10, verse no. 18-20). In *Madhumeha* where *tridosha* along with involvement of *rasadi dhatus* indicates the difficultness of the disease[1]. On the basis of the dosas and the quality of similar therapy (samakriya), non similar therapy *(asamakriya)* and aspiring great danger involved (*mahatyaya)*; *madhumeha* has been classified in to *sadhya* (curable), *yapya* (palliable) and *parityajya* (rejectable) (A.H.Ni.10 verse no.6)

WHO has designated Diabetes mellitus is a metabolic disorder of multiple etiologies share the phenotype of Hyperglycemia[2]. It is the sweet disorder of antiquity & universality with having higher mortality rate considered as pandemic disease. It the 4th

leading cause of death in worldwide. The prevalence of Diabetes Mellitus increasing day by day and awareness about the disease among the general population makes it is a disease of all groups. Out of total Diabetic population about 98% are belongs to Non insulin dependent diabetes mellitus (NIDDM, Type-II) in India , prevalence rate increased from 12% to 19% in urban & in rural the prevalence is increased from 4% to 9%[3].

The miraculous advancement modern medical science, humanity is passing through a horror of the disease, drug phobia and related complications associated with it, specifically where fast and sedentary life style, stressful work environment account for the man's ignorance towards the principle of health care.

In our Ayurvedic classics enormous treatment modalities have been explained by our acharyas in respect to *Madhumeha* even though it is considered as *mahatyaya* for treatment[4]. Efficacy many of such yoga yet to explore clinically. There is a need of clinical research in hold on the disease not only achieve good glycaemic control but also to treat the root cause of the disease. In *Bruhatrayees* and *Laghutrayees* different formulations are found, among these *Mustadi Kwatha* which is explained in *Bhaisajya Ratnavali* has been selected for the study. *Mustadi Kwatha*[5] comprises the drug like *Musta, Amlaki, Haritki, Bhibhitaki, Haridra, Moorva, Indrayana, Lodhra*, are having the *Tikta, Kasaya rasa pradhana* and *pramehaghna* properties are competent enough to counter the pathogenesis of *Madumeha.*

Hence the study entitled *"*Evaluation of the effect of *Mustadi Kwatha* in the management of *Madhumeha vis-a-vis* Diabetes Mellitus (NIDDM)

Madhumeha is the disease of having merely metabolic derangement and genetic predisposition related with each constituent of the body. So having systemic consideration. Though it is a subtype of *Vataja Prameha* having more prevalence in the society. To understand the iatrogencity, pathophysiology, complications and management first it is merely necessary to emphasize the disease *prameha* whole.

The word '*Prameha'* consists two subwards. i.e. '*pra'* and '*meha'*. The word *Meha* is derived from the root "*mih secane* by adding *'Lue' Pratyaya* to it "*Mehati, Sincati Mutraretansi*" which means to excrete (*Halayudhakosha) Rigveda* mentioned this ward first is *Mehanadthanam Karanallium* (*Rigveda* 10/163.15). The commentator of *Rigveda.*

Syanacarya interpreted the word *mehana* as *medhra,* which denotes to *Shisna* (penis). In *Sanskrit* literature the '*Mih'* is used to denote to make water, to wet, to emit semen.
So this root *'Mih*' is added to prefix 'pra' the word becomes *'prameha'.*

प्रमेह =प्र+मिह –मेहति मुत्रयति इति अर्थ (ड.सुनि.६/१०)

=प्रकर्षेण मेहति यास्मिन रोगे स प्रमेहः

= प्रकर्षेण प्रचुरं वारंवारं वा मेहति यो रोगे स प्रमेहः

In regard to above explanation we can easily postulate that the disease prameha is resulted because of excessive diminution or excretion of something *(Atipravrttija).*

The word *madhumeha* consists of two words: (a*) Madhu* and (b) *Meha*
The word *Madhu* is derived from the root *Manyante visesena Jananti Jana Yas*min. In *Sanskrit* literature *Madhu* word is used in various contests like *Pushparasa, Makarandah, Makshikam, Madhyam, Ksiram, Jalam, Madhurarasa* etc.

मधुमेह= मधु + मेह

= मधु इव मेहति

यस्मत् कारणात मधु इव मेहति मधु सदशं मेहति ॥

अस्मात कारणात् मधुमेह सं ॥

Now the etymology get concise and specific, that the disease in which the excretion is having quality concordant with *madhu* (honey) in its colour, taste, smell and consistency called *madhumeha.*

The *meha* word here mainly related with the excretions through urine. So the definition is the clinical entity in which patient voids the urine having concordance with *Madhu* i.e. of *Kasaya* and *Madhura rasa*, *ruksa* (dry) texture and honey like colour. Body acquires sweetness called *madhumeha* (Ca. Ni. 4/44, A.H.Ni. 10/18). *Susruta* narrated the term in place of Madhumeh is *Ksaudrameh*a. *Ksudrameha* nothing but subtype and synonym of *madhu* (honey). So it is undoubtedly resembles with *Madhumeha*. Further he asserted that when all the *Pramehas* illtreated or neglected get converted into *Madhumeha* and specially he emphasized that the disease *Prameha* along with *Pidaka* should termed as *Madhumeha*.

From above definitions we can easily diagnose the disease and understand its progression.

Acharyacharaka has described *prameha* in detail the description of the etiology, pathogenesis, symptomatology & complications in Cha. Ni 4, where as detailed explanation of treatment is given in Cha.Chi.6, aetiopathogenesis of *madhumeha* along with complications is narrated in Cha. Su 17, Charaka has given *lakshanas* like *Karapadadaha, suptata* in *Karapada, Paridaha* and *Angasuptataas* a *Purvaroopa of* Prameha. And again in Chikitsasthana he has given Daha as an Upadrava of Prameha[5]. Practically Madhumeha is *Vataja Prameha*.

Acharya Sushrata has given *Hastapadatala daha as* a *Purvaroopa* of *Prameha* and *Daha* as an *upadrava* of *Prameha*. He has given elaborate explanations regarding *Nidan Panchaka* in *Su. Ni 6*. He has described *Prameha nivritti Lakshanas* especially, i.e. how to know that the patient is out of the disease. He has described the treatment in three different chapters of chikitsasthana chapter 11th,12th and 13thunder the heading of *Prameha-Chikitsit, Prameha Pidaka Chikitsit*. And exclusive treatment of *Madhumeha Chikitsita*[6].

In *Astanga Hridaya* description of *Prameha Nidan* is found in *Nidansthana* 10th chapter and Treatment aspects are found in *Chikitsasthana* 12th chapter. *Acharya Vagbhtta* has described that *Madhumeha* occurs as a result of *Vataavarana* or *Dhatukshaya*. He has described that all *pramehas* when remain untreated get converted into '*Madhumeha'*. He also explained that *prameha rogi* passes urine similar to the smell & colour of *Madhu,* He also opines that in *Madhumehi* whole body become sweet(Vag. Ni. 10/32). He has enlisted *Karapadadaha, Suptata Changeshu* as a Purvaroopa of *Prameha* and *Daha* as an *Upadrava* of *Pittaja Prameha*. He added some new herbs and herbal compounds as well as for the treatment of the disease and thus the evolution of the drugs for the treatment of *Madhumeha* stated in *Ayurvedic* science[7]. *Vagbhata* categorized the disease under heading *'Mutraatipravrttijja*' and mentioned two types of *Madhumeha i.e. Dhatukshyat* and *avartpathat* and added *sweda* in the *Dusysangraha*. In *Bhela Samhita Nidanasthana*, description of two types of *prameha* is given i.e. *swakritijaprameha* and *prakritija prameha*[8].

In *Harita samhita Acharya Harita* has narrated *prameha* as *Papajanyaroga*. He has enumerated 13 types of *prameha*, with different nomenclature like *Madhuprameha, Puyaprameha, Takraprameha, Rasa prameha, Ghritaprameha* etc[9]. In *Kashyapa* mentioned the symptoms of *pramehi* child in *Vedanadhyana*[10]. In *Madhava Nidana*

Madhavakara has described *prameha* quite vividly in Nidansthana 33, in the form of recollection from the previous sources like *Charaka, Susruta* & *Astanga Hridaya*[11]. He also stated that in *Madhumeha* whole body becomes sweet (Ma. Ni.33/26).

In Gayadasa in *Nyaya Chandrika* narrated that *Avila mutrata* is due to the presence of *dushya* in urine[12]. *Chakrapanidatta* described the treatment of *prameha* in his documentation *Chakradatta.*[13]. *Sharangdhara* has described 20 types of *prameha* in *poorvakhanda*[14]. *Acharya Bhavamishra* added some new herbo-mineral preparations for the treatment of *Madhumeha*[15].

In *Bhaishajya Ratnawali Pramehachikitsa* has been described in 37th chapter. As well as *Ojomeha chikitsa* and *Lasikameha chikitsa* has been described[16].

Diabetes mellitus type II is a metabolic disorder that is characterised by hyperglycaemia in the context of insulin resistance & relative lack of insulin. The classic symptoms are excessive thirst, frequent urination, and constant hunger. Obesity is thought to be primary cause of type II diabetes who are genetically predisposed to the disease. It can initially managed by increasing exercise and dietary changes. If blood sugar level not adequately lowered by these measures then drugs like metformin or insulin may be needed.

Even though miraculous treatment available in the modern medicine for *Madhumeha* i.e. Diabetes, their safety is not well established. Hence there is a great need to evaluate the efficacy of alternate medical treatment described in *Ayurvedic* text is most essential which is safe. Accordingly the Indigenous Compound *Mustadi Yoga* has been taken to evaluate the efficacy in *Madhumeha* which is mentioned in *Bhaisajya Ratnavali*[17].

मुस्ताफलत्रिकनिसासुरदारुमूर्वा
ऐन्द्री च लोध्रसलिलेन क्रतः कषायः I
पाने हितः सकलभेदभवे गदे च
मुत्रग्रहेषु सकलेसु नियोजनीय II (भैषज्यरत्नावली , प्रमेहरोगाधिकार्,३७)

These Hypothesis are as below:

H_0 = *Mustadi kwatha* is not effective in *Madhumeha* vis-a-vis diabetes mellitus

H_1= *Mustadi kwatha* is effective in *Madhumeha* vis-a-vis diabetes mellitus

AIM & OBJECTIVE:

To evaluate the efficacy of the Mustadi Kwatha in the management of Madhumeha (NIDDM)

HISTORICAL REVIEW

Historical Glimpse of *Madhumeha*

Study of consecutive progression of an event is the chief step in any research field. Review of history is a process of collection of development and progress of that particular subject gains importance in unfolding the future plans designing the advanced research. In *Vedic* literature as well as in *Samhita* period having plenty of description of ailments and their remedies signifies the same. *Madhumeha* is a disease explained contextually since from *Daivik Yuga* troubling the human being till date. In this chapter is an attempt has been made to review all the *Ayurveda* and Modern literature providing information related to all ancient background of *Madhumeha*.

Ramayana:

In Ramayana there is an indication where it is mentioned that intake of excessive sweet juices some monkeys passed urine which was sweet in nature[18].

***Kautilya arthashasthra*:**

In *Kautilya arthashastra* it is mentioned that consumsition of burned chameleon, house lizard along with gut of spotted frog and honey leads to *Prameha*[19].

Daivika Yuga

Since from the prehistoric age the information of *Madhumeha* i.e. Diabetes Mellitus, existed with the Indians. The primitive reference (1000 BC in the Ayurvedic literature) is found in mythological form where it is mentioned that by eating *Havisha*, a special food which is used to be offered at the times of Yagna conducted by *Dakshaprajapat*i. It is also found the reference that the *adya deva lord Ganesha* is crazy of cosuming sweet and likes inactivity. He is also said to have the habit of eating *jambu phala* and *kapittha*. It is to be noted that, the voracious eating habit and physical inactivity is the cause of *Madhumeha*. The *jambu phala* and *kapittha majja* is known as important medications of the *Madhumeha.* The origine *Shivagutika*[20] is mythologically related to *Madhumeha* in the same story of *Lord Ganesha* which is popularly used in this ailment.

PURANA KALA:

VEDAS –

- In *Rig-Veda* mentioned the word *mehanadtanam karanallium*. The word *mehana* is interpreted as *medhra*, which denotes to *shishna* (penis) by the commentator of *Rig-Veda, Sayana*.
- In *Atharva Veda* - there is a reference related to the disease '*Asrava*' along with its treatment. According to Sayanacharya the Asrava means *'Mutraatisara*' the English translator Whitney (1962) interpreted it as flux and Griffith (1962) as morbid flow. Leman has translated the meaning of *Asarv*a as Diabetes Mellitus. The *Vatic* nature of this ailment was highlighted Sayanacharya [21].
- In *Puranas* i.e. in *Agnipurana*, treatment of *Kshoudra* and *Akshoudra meha* are described[22] and in Garudapurana the depiction of nidana, prakara, *upadravas* and *Chikitsa* of *Prameha* is found[23].

YAGNAVALKA SMRITI*:*

Madhumeha is depicted as *Badhyaruk* i.e.; chronic and painful disease[24] in *yagnavalka smriti*.

BRAHMA SAMHITA:

Prameha was proclaimed by the words ***'Prasrava' Asrava' Momutrate*** *Vinaya pitaka & Pacittiya:* (6BC - 2 AD) – by this way Madhumeha was indicated [25].

SAMHITA KALA:

The detailed description of the disease *Madhumeha vis-a-vis Prameha* is found in all Samhitas.

***CHARAKA SAMHITA*:**

In *Charaka samhita* there is detailed description *nidana, samprapti, bheda, lakshanas,* and *upadravas* of *Prameha* in *Nidanasthana* 4th Chapter[26]. Importance of Ojus in context of *samprapti* of *Madhumeha* and relation of *avrita Vayu* is cited in *Sutrasthana* 17th Chapter[27]. *Prameha Pidakas*, *Sadhyasadhyata*, two types of *prameha, Krisha* and *Sthoola pramehi Chikitsa* is cited in *Chikitsasthana* 6th Chapter[28]. It is described as one among the *Astamahagada's* in *Indriya Sthana* 9th chapter[29]. As a whole detailed description of *Prameha* vis-à-vis found in *Charaka Samhita*.

***SUSHRUTA SAMHITA*:**

Acharya Sushruta has specifically mentioned that the *Prameha* when not treated at appropriate time leads to *Madhumeha* in the 6th chapter[30] of *Nidan Sthana*. The complete disease and its therapeutic aspect of *Prameha, Pramehapidaka, Madhumeha* in *Chikitsa Sthana* chapters namely 11th, 12th, 13th successively[31]. He had used the terminology like *Kshaudra Meha'* instead of *Madhu Meha* in vatic variety in *Nidana Sthana* 6th chapter. There is a specific description decoctions for specific type of *Prameha* and the Specific dietary Pattern which should not be used and to be used cited in *Chikitsa Sthana*.

***Astanga Hridaya*:**

In *Astanga Hridaya* there is similar description of *Prameha* as found in *Charaka* and *Susruta Samhita*. Enumeration of twenty types of *Prameha* with symptomatology with s*amanya* and *doshik* treatment explained in detail. While expounding the *chikitsa,* new drugs like *Rodhrasava, Ayaskriti,* and *Shilajatu Rasayana* etc were described[31]. If the *Pramehas* if left untreated for long term it will progress to vatika type. *Vagbhata* opines that the *Sweda* is one of the *Dushya* in causation of *Madhumeha*[32].

Bhela Samhita:

Contemporary of *Charaka* i.e. in *Bhela Samhita* also described two types of prameha. There in an indication of congenital and acquired factor of *Madhumeha* i.e. Diabetes mellitus found in *Bhela* as *prakrita* (congenital) and *swakritaja* (aquired) in *nidanasthan*a 6th Chapter and also citation of involvement of fat metabolism as *medopradhoshaja and in shukra vyapattija rogas*[33].

Harita samhita:

There is a different description found in relation to the cause of *Madhumeha* as *Papajanya* and enumerated 13 types of *Prameha* with different nomenclature in comparison to other samhita like *Jala Prameha, Rudhira Prameha, Puya prameha, Lavana prameha, Takra Prameha, Khatikameha, Sukrameha,* etc[34]. There is specific description of *Aushadhiyoga* for specific type of Prameha and mentioned *Arista lakshnas* and *Madhumeha.*

Kashyapa Samhita:

The description of 20 subtypes of *prameha*, its signs and symptoms related to *Balapramehi* (Juvenile Diabetes) is described in *Vedanadhyaya* of *Sutrasthana*[35].

MEDIEVIAL PERIOD (800 AD – 1900 AD)

This Medieval period of Indian medicine is nothing but the period of commentators. Most of them described the content in in a mixing form of all samhitas.

***Madhava nidana*:** *Madhavakara* compilled the description found in *brihatrayees*[36].

***Sarangadhara Samhita*:** Mentioned the 20 types of *Prameha* along with treatment some yogas for the treatment of *prameh*a[37].

***Bhavaprakash*:** In *Bhavamishra* described the Madhumeha along with its upadravas and *aristha lakshanas* of *prameha*. There are description of herbomineral compound preparations[38].

Yogaratnakara:

In *Yogaratnakar* the description *Prameha* and *Madhumeha* along with some *vati kalpana, churna* preparations and *Rasoushadhis* like *Vanga bhasma* etc. are found. It is stated that *Prameha* is not seen in female, because of the purification of the body by the *Rutusrava*[39].

Bhaishajya Ratnavali:

Bhaishajya Ratnavali explained *Madhumeha* with detail description regarding the *Pathyapathya, Yogas, Prameha Pitikas* & their treatment[40].

Vangasena:

Explained, *nidana, bheda, lakshana*, and *chikitsa*, also in similar way as in other samhita where there are mention of the 21 types of *pramehas*[41]

Rasaratna samucchaya*:*

In *Rasaratna samucchaya* there is mention of the *pancha nidanas* of *prameha* vis-à-vis *madhumeha* and *pramehagna kalpas* in 17th chapter[42].

HISTORICAL MILESTONES OF DIABETES MELLITUS[43]

The term “Diabetes” of to pass through was first used in 250 BC by Greek Allonius Momphis.

1552 B.C. - Earliest known record of Diabetes mentioned on 3rd Dynasty Egyptian papyrus by physician Hesy-Ra; mentions Polyuria (frequent urination) as a symptom.

1st Century A.D. - Diabetes described by Arateus as the melting down of flesh and limbs into the urine.

164 A.D. - Greek physician Galen of Pergamum mistakenly diagnoses Diabetes as an ailment of the kidneys.

Up to 11th Century -Diabetes commonly diagnosed by 'water tasters,' who drank the urine of those suspected of having diabetes; the urine of people with Diabetes was thought to be sweet-tasting. The Latin word for honey (referring to its sweetness), 'mellitus', is added to the term Diabetes as a result.

16th Century - Paracelsus identifies Diabetes as a serious general disorder.

Late 1850 - French physician, Priorry, advises Diabetes patients to eat extra large quantities of sugar as a treatment.

1869 - Paul Langerhans, a German medical student, announces in a dissertation that the pancreas contains two systems of cells. One set secretes the normal pancreatic juice; the function of the other was unknown. Several years later, these cells are identified as the islets of Langerhans.

1870 - French physician, Bouchardat, notices the disappearance of glycosuria in his Diabetes patients during the rationing of food in Paris while under siege by Germany during the Franco-Russian War; formulates idea of individualized diets for his Diabetes patients.

1889 - Oskar Minkowski and Joseph von Mering at the University of Strasbourg, France, first remove the pancreas from a dog to determine the effect of an absent pancreas on digestion.

Early 19th Century -First chemical tests developed to indicate and measure the presence of sugar in the urine.

19th Century - French researcher, Claude Bernard, studies the workings of the pancreas and the glycogen metabolism of the liver. Czech researcher, I.V. Pavlov, discovers the

links between the nervous system and gastric secretion, making an important contribution to science's knowledge of the physiology of the digestive system.

Late 19th Century - Italian Diabetes specialist, Catoni, isolates his patients under lock and key in order to get them to follow their diets.

1900-1915 - 'Fad' Diabetes diets include: the 'oat-cure' (in which the majority of diet was made up of oatmeal), the milk diet, the rice cure, 'potato therapy' and even the use of opium.

1908 - German scientist, Georg Zuelzer develops the first injectable pancreatic extract to suppress glycosuria; however, there are extreme side effects to the treatment.

1910 - Sharpey-Schafer Coined the Term Insulin English physiologist Sir Edward Albert Sharpey-Schafer's study of the pancreas led him to the discovery of a substance that would normally be produced in people without diabetes: insulin. He derived the name from the Latin *insula*, meaning island, referencing the insulin-producing islets of Langerhans in the pancreas (identified in 1869 by German scientist Paul Langerhans).

1910-1920 - Frederick Madison Allen and Elliot P. Joslin emerge as the two leading Diabetes specialists in the United States. Joslin believes Diabetes to be 'the best of the chronic diseases' because it was 'clean, seldom unsightly, not contagious, often painless and susceptible to treatment.'

1913 - Allen, after three years of Diabetes study, publishes Studies Concerning Glycosuria and Diabetes, a book which is significant for the revolution in diabetestherapy that developed from it.

1919 - Frederick Allen publishes Total Dietary Regulation in the Treatment of Diabetes, citing exhaustive case records of 76 of the 100 Diabetes patients he observed, becomes the director of Diabetes research at the Rockefeller Institute.

October 31, 1920 - Dr. Banting conceives of the idea of insulin after reading

Moses Barron's 'The Relation of the Islets of Langerhans to Diabetes with Special Reference to Cases of Pancreatic Lithiasis' in the November issue of Surgery, Gynecology and Obstetrics. For the next year, with the assistance of Best, Collip and Macleod, Dr. Banting continues his research using a variety of different extracts on de-pancreatized dogs.

Summer 1921 - Insulin is 'discovered'. A de-pancreatized dog is successfully treated with insulin.

December 30, 1921 - Dr. Banting presents a paper entitled 'The Beneficial Influences of Certain Pancreatic Extracts on Pancreatic Diabetes' summarize his work to this point at a session of the American Physiological Society at Yale University. Among the attendees are Allen and Joslin. Little praise or congratulation is received.

1940s - Link is made between Diabetes and long-term complications (kidney and eye disease).

1944 - Standard insulin syringe is developed, helping to make Diabetes management more uniform.

1955 - Oral drugs are introduced to help lower blood glucose levels.

1959 -Two major types of Diabetes are recognized: type 1 (insulin-dependent) Diabetes and type II (Non-insulin-dependent) diabetes.

1960 - The purity of insulin is improved. Home testing for sugar levels in urine increases level of control for people with diabetes.

1970 - Blood glucose meters and insulin pumps are developed. Laser therapy is used to help slow or prevent blindness in some people with diabetes.

1983 - First biosynthetic human insulin is introduced.

1986 - Insulin pen delivery system is introduced.

1993 - Diabetes Control and Complications Trial (DCCT) report is published. The DCCT results clearly demonstrate that intensive therapy (more frequent doses and self-adjustment according to individual activity and eating patterns) delays the onset and progression of long-term complications in individuals with type 1 diabetes.

1995- Metformin, a biguanide which prevents glucose production in the liver becomes available in the U.S

1996- The drug acarbose becomes available in the U.S Lispro is introduced by Eli Lily and Company as the world's fastest acting insulin.

1997- Troglitazone of a class thiazolidinediones which improves insulin sensitivity in musle cells eventually removed from market due to liver toxicity. Later Rosiglitazone and Pioglitazone brought into market.

1998 –Repaglinide belonging to a class of drugs known as meglitinides stimulate insulin secretion in the presence of glucose.

The United Kingdom Prospective Diabetes Study (UKPDS) is published.

UKPDS results clearly identify the importance of good glucose control and good blood pressure control in the delay and/or prevention of complications in type II diabetes.

2002- Treatment with the anti-CD3 monoclonal antibody slows the deterioration of insulin production and improves metabolic control during the first year of Type 1 Diabetes in majority of patients.

The American Diabetes Association defines preDiabetes as impaired fasting glucose or impaired glucose tolerance.

2005- Exenatide is approved as first in class incretin mimetic.

2006- FDA approves JANUVIA (sitagliptin phosphate), the first in a new class of drugs known as DPP-4 inhibitors that enhance the body's ability to lower elevated blood sugar.

2013-FDA approves Invokana (Canagliflozin), first in a new class of drugs known as the SGLT-2 inhibitors, for lowering elevated blood sugar in patients with type 2 Diabetes.

2014-Albiglutide is a new long lasting GLP-receptor agonist for use as monotherapy or in combination with other agents for the treatment of adults with Type 2 Diabetes Mellitus.

2014-There was no effect by long-term intensive therapy of glycemic control on macro vascular outcomes.

2015-Intensive insulin therapy for 6.5 years during the DCCT reduced the risk of all types of mortality in patients with Type 1 Diabetes Mellitus compared with conventional therapy.

2015- A Mendelian randomization study found that decreased genetic HMG CoA reductase activity is associated with a higher risk of type 2 Diabetes.

2015-Trial studies have evaluated that blood pressure lowering is associated with long-term benefits on mortality and cardiovascular disease in Diabetic patients.

DISEASE REVIEW

The involvement of srotas in Madhumeha can be understood by following depiction found in samhita are as follows:-

(1) *Prabhuta Avila Mutrata* - implies *Mutravaha srotodushti* (urinary tract involvement)

(2) *Purvarupa* of *Prameha, Snigdhagatrata* etc. - implies *Medovaha srotodushti* (involvement of adipose tissue)

(3) *Putimamsapidaka (Prameha Pidaka)* – implies *Mamsavaha Srotodushti* (involvement of muscular tissue)

(4) *Pipasa, Mukha-Talu-Kantha Shosha* - Indicates *Udakavaha Srotodushti*

There is a major role of the organs of **mootravaha samsthana like** as vrikka and basti. The pradhana dooshyas in *Madhumeha* i.e. *medas* (fat), nothing but *medavaha Srota* whose the *moola sthana* is *vrikka* and *vapavahana*. The *Pippasa* is also an important clinical feature of *Madhumeha* which also indicates the involvement of *Udakavaha Srota* and *Talu & kloma are moolas* for ***udakavaha srotas***.

In all *dhatu parinama Yakrita* (Liver) plays important role. In *Madhumeha* there is are alteration of *dhatu Parinama*. Hence the liver is responsible in the *samprapti* of *Madhumeha.*

After discussion of above points, the inclusion of following organs can be justified:-

BASTI

Embryological origin: *Acharya Shusruta* explained that the basti is a considered as *matruja avayava* in *garbha Sharira*. As per the A*charyas* it is derived from the *prasada bhaga* of *raktha* & *kapha pachita* by *pitta* where *vayu* also enters & *ashayas*[**44**].

Anatomical site: While describing the *Sthana* of *basti Charaka* has stated that it's situated in between the *sthoola guda, sevani, sukravaha naadies & mootravaha naadies*[45]. *Sushruta* mentioned that *basti, vrushana & guda* are all interrelated and situated in *shroni guha*[**46**]. According to *Vagbhatta* the *Vasti* is situated in *kati pradesha*[**47**].

Shape & structure: *Acharya Sushruta* stated that the shape of Basti is looks like that of alabu & full of sira snayus all around and having tanu twak. Its one exit which lies in its mouth downwards[48]. According to *Vagbhatta* its shape as dhanurvakra i.e. bent like bow having one downward opening & made of *mamsa & rakta dhatu*.

Marma*:* The basti is the location of one of the *sadhyopranahara marmas* asccording to *Acharyas.*

Srotas: According to *Charaka Basti* is the moola of mootravaha srotas. Sushruta stated that the diseses like *mootaraghata, asmari, prameha, sukra dosha* are developed from *basti.*

VRIKKA

Embryological origin: It is also a *matruja avayava* metioned in *Garbha Sharira*. It is developed from the *prasada bhaga* of *rakta* and *medha*. According to *Adamallas* statement that the *vrikka'*s are two in number and round shaped organ which are derived from essence of *Rakta & meda*[49].

Anatomical site & Number : According to Ayurveda the *Vrikka* are two in number; one is present in *dakshina parshva* & other is in *vama parshva*[50] & are situated in *koshta*[51] pradesha. There is a statement regarding its location by *Charaka, Chakrapani & Dalhana* that the *vrikka* is two in number & situated below the chest[52].

Shape: *Dalhana* in his commentary stated that *Vrikka* are two fleshy bodies each situated on either side of spine & their shape as being like rounded bodies (*kukshi golaka pinda)*[53].

Srotas: *Vrikka* is also medovaha sroto mooola[51].

VAPAVAHANA

Embryological origin: it is a *matruja bavayava*.

Anatomical site: It is one of the *koshtanga*[51].

Shape: Its is *vartivath/tailavartivath* and *snigdha*[54].

Srotas: It's *medovaha srotomoola*.

KLOMA

Embryological origin: It is *matruja bhava avayava*.

Anatomical site: According to all *Acharyas* mentioned that it is one of the *koshtangas*[55]. There are different opinion regarding its anatomical position. *Chakrapani*

has said that it is the *hridayastha pippasa sthana*[54]. *Sushruta* had said that *kloma* is explained with yakrit which is located in the right side of the body. *Dalhana* while commenting on *kloma* said that it's in right side of body and lies below *Yakrit* and it is called as *tilakam*[50]. *Vagbhatta* also has the same opinion. According to Sharangadhara it is formed by the combination with pitta and is Agni roopi.

Srotas: The *Kloma* is the *moola* for *udaka vaha srotas*[56]. *Charaka* says that talu *moola* and *kloma* is the seat of *udakavaha srotas*. If these srotas are afflicted the pathological changes i.e. *shosha* of *talu & kloma & trishna* are clinical symptoms develops. *Sushruta* also has the same opinion & said that an injury to this srotas can lead to *sadhyo marana*.

TALU

Embryological origin: It is a *pitruja avayava. Charaka* and *Kashyapa* states that the union of two bones forms talu.

Anatomical site: It is located above *kanta* & becomes the base of *Shiras.*

Srotas: It is the *moola* of *udaka vaha srotas*[57]. *Charaka* mentioned talu shosha & *pippasa* will exist if *udakavaha srotas* is vitiated[54].

YAKRIT

The *Vedik* commentrator *Sayanacharya* while commenting on the word *Yakan* coined in *Atharva Veda* described that *Yakan* is situated near the heart. The word *yakan* in his view means *yakrit*. It is a *matruja avayava* & is included under the *koshtanga*[58]. The *Yakrita* embryologically is formed from *rakta*. *Yakrita* is situated on the right side of the body below the *hridaya*[57] & is the moola for *rakthavaha srota*. According to *Sushruta* the *raktha dhara kala* is present in the *yakrita*[59].

ANATOMICAL COSIDERATION

Diabetes Mellitus is a syndrome and a metabolic disorder of impaired carbohydrate, fat, and protein, caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin secreted by the ß-cells of Islets of langerhans of pancreas, but other hormones of pituitary and adrenal glands are also intimately related to the development of Diabetic State. The Liver plays an important role in the metabolism for carbohydrate. It stores glucose in the form of glycogen under the influence of Insulin.

Any alteration in this function leads to diabetes. In this context the anatomy of these organs involved will be described in brief.

Pancreas[60]

The Pancrease is having both exocrine and endocrine secretion. The Exocrine part secretes the digestive pancreatic juice like amylase,lipase and trypsin ; and the endocrine part secretes insulin hormone from beta cells of pancease where as alpha cell secrets glucagon etc. It arises as a larger dorsal bud forms part of the head, whole neck, body and tail of pancreas. And a smaller ventral bud forms uncinate process and an inferior part of head of pancreas. Ventral bud duct fuses with dorsal bud duct to become main pancreatic duct. Location: lies transversely across the posterior abdominal wall, at the level of 1st and 2nd lumbar vertebrae. Size and shape: It is J- shaped set obliquely, about15-20cm long, 2.5-3.8cm broad and 1.2-1.8cm thick and weighs about 90gm. It is divided into head, neck, body and tail.

Histology[61]

- Exocrine component portion of the pancreas is a compound tubular gland
- Terminal secretory portion of this gland is known as acini or alveoli.
- They constitute 80% to 90% of the pancreatic mass
- The main excretory duct of the gland is the **duct of Wirsung**, giving out several intralobular or intercalated ducts.
- Acinus small> intercalated ducts >interlobular duct >pancreatic duct

Endocrine Pancreas[62]

- Accounts for only 2% of the pancreatic mass
- The endocrine cells are islet of Langerhans is group of epithelioid cells situated between the pancreatic alveoli.
- Four major cell types: Alpha (A) cells secrete glucagon, Beta (B) cells secrete insulin, Delta (D) cells secrete somatostatin, and F cells secrete pancreatic polypeptide.

LIVER[63]

- It is a large, solid, gland situated in the right upper quadrant of the abdominal cavity.

- It is derived from the caudal end of foregut; an endodermal hepatic bud arises during 3rd week of development.
- Kupffer's cells and blood cells are formed from mesoderm of septum transversum.
- It is reddish brown in colour, soft in consistency, and very friable.
- It weighs about 1600g in males and 1300g in females.
- It has 5 surfaces: Anerior, posterior, superior, inferior, and right. One prominent inferior border separates the anterior surface from the inferior surface.
- Two lobes: Right and left.

PITUITARY GLAND[64]

- It is a reddish-grey, small oval-shaped structure, situated at the base of the brain, in the sella turcica of the sphenoid bone.
- It is attached to the floor of the third ventricle by a stalk.
- Average weight in adults 0.5 to 0.6g.
- Average dimensions are 10mm anteroposteriorly, 6mm dorsoventrally, 13mm laterally.
- Anatomically consist of 2 parts: anterior lobe secretes Growth hormone, STH, Prolactin, ACTH, TSH, FSH, LH and MSH, where as posterior lobe secretes vasopressin (ADH) and oxytocin.
- The gland has two main parts adenohypophysis and neurohypophysis which differ from each other embryologically, morphologically and functionally.

ADRENAL GLAND[65]

- These are a pair of important endocrine glands situated on the posterior abdominal wall over the upper pole of the kidneys behind the peritoneum, opposite the vertebral end of the 11th intercostals space and the 12th rib.
- Each gland measures 50mm in height, 30mm in breadth, 10mm in thickness, weighs about 5gm.
- They are made up of two parts: Outer cortex of mesodermal origin, and an inner medulla of neural crest origin.
- **Cortex** consists of three zones.

- **Zona glomerulosa**: Is outer zone contains groups of columnar cells with spherical nuclei secretes mainly aldosterone, small amount of glucocorticoids and sex hormones.
- **Zona fasciculata**: Is middle widest zone has cells arranged in radiating columns, also contain lipid droplets(liposomes) so sometimes these cells are called as spongiocytes secretes predominantly glucocorticoids.
- **Zona reticularis**: Is inner zone made up of an irregular network of rows of cells secretes sex hormones, and small amount of glucocorticoids but no aldosterone.
- The **adrenal medulla** consist of chromaffin cells which either secrete adrenaline or noradrenaline. The medulla produces mainly catecholamines.

PHYSIOLOGY

Exocrine Pancreas[66]

- The pancreatic digestive enzymes are secreted by pancreatic acini, and large volumes of sodium bicarbonate solution are secreted by the small ductules and larger ducts leading from the acini.
- Pancreatic secretion contains multiple enzymes for digesting all of the three major types of food: proteins, carbohydrates, and fats. It also contains large quantities of bicarbonate ions, which play an important role in neutralizing the acidity of the chyme emptied from the stomach into the duodenum.
- The most important of the pancreatic enzymes for digesting proteins are trypsin, chymotrypsin, and carboxypolypeptidase.
- The pancreatic enzyme for digesting carbohydrates is pancreatic amylase.
- The main enzymes for fat digestion are pancreatic lipase, cholesterol esterase, and phospholipase.
- Basic Stimuli That Cause Pancreatic Secretion

  1. Acetylcholine,
  2. Cholecystokinin,
  3. Secretin,
- Phases of Pancreatic Secretion

Pancreatic secretion occurs in three phases, the same as for gastric secretion: the cephalic phase, the gastric phase, and the intestinal phase.

Endocrine Pancreas[67]

The pancreas, in addition to its digestive functions, secretes two important hormones, insulin and glucagon, that are crucial for normal regulation of glucose, lipid, and protein metabolism. The islets of endocrine pancreas contain three major types of cells, alpha, beta, and delta cells. The beta cells, constituting about 60 per cent of all the cells of the islets, lie mainly in the middle of each islet and secrete insulin and amylin, a hormone that is often secreted in parallel with insulin, although its function is unclear. The alpha cells, about 25 per cent of the total, secrete glucagon. And the delta cells, about 10 percent of the total, secrete somatostatin. In addition, at least one other type of cell, the PP cell, is present in small numbers in the islets and secretes a hormone of uncertain function called pancreatic polypeptide.

Historically, insulin has been associated with "blood sugar," and true enough, insulin has profound effects on carbohydrate metabolism. Yet it is abnormalities of fat metabolism, causing such conditions as acidosis and arteriosclerosis that are the usual causes of death in diabetic patients. Also, in patients with prolonged diabetes, diminished ability to synthesize proteins leads to wasting of the tissues as well as many cellular functional disorders.

Insulin Chemistry and Synthesis

Insulin is a small protein; human insulin has a molecular weight of 5808. Insulin is synthesized in the beta cells by the usual cell machinery for protein synthesis, beginning with translation of the insulin RNA by ribosomes attached to the endoplasmic reticulum to form an insulin preprohormone. But it is then cleaved in the endoplasmic reticulum to form a proinsulin most of this is further cleaved in the Golgi apparatus to form insulin and peptide fragments before being packaged in the secretory granules. However, about one sixth of the final secreted product is still in the form of proinsulin. The proinsulin has virtually no insulin activity. To initiate its effects on target cells, insulin first binds with and activates a membrane receptor protein. It is the activated receptor, not the insulin that causes the subsequent effects.

The insulin receptor is an example of an enzyme-linked receptor. Autophosphorylation of the beta subunits of the receptor activates a local tyrosine kinase, which in turn causes phosphorylation of multiple other intracellular enzymes including a group called insulin-receptor substrates (IRS). The net effect is to activate some of these enzymes while inactivating others. In this way, insulin directs the intracellular metabolic machinery to produce the desired effects on carbohydrate, fat, and protein metabolism.

Mechanisms of Insulin Secretion

The beta cells have a large number of glucose transporters (GLUT- 2) that permits a rate of glucose influx that is proportional to the blood concentration in the physiologic range. Once inside the cells, glucose is phosphorylated to glucose-6-phosphate by glucokinase. This step appears to be the rate limiting for glucose metabolism in the beta cell and is considered the major mechanism for glucose sensing and adjustment of the amount of secreted insulin to the blood glucose levels. The glucose-6-phosphate is subsequently oxidized to form adenosine triphosphate (ATP), which inhibits the ATP-sensitive potassium channels of the cell. Closure of the potassium channels depolarizes the cell membrane, thereby opening voltage-gated calcium channels, which are sensitive to changes in membrane voltage. This produces an influx of calcium that stimulates fusion of the docked insulin-containing vesicles with the cell membrane and secretion of insulin into the extracellular fluid by exocytosis. Other nutrients, such as certain amino acids, can also be metabolized by the beta cells to increase intracellular ATP levels and stimulate insulin secretion. Some hormones, such as glucagon and gastric inhibitory peptide, as well as acetylcholine increase intracellular calcium levels through other signaling pathways and enhance the effect of glucose, although they do not have major effects on insulin secretion in the absence of glucose. Other hormones, including somatostatin and norepinephrine (by activating a-adrenergic receptors), inhibit exocytosis of insulin. Sulfonylurea drugs stimulate insulin secretion by binding to the ATP-sensitive potassium channels and blocking their activity. This results in a depolarizing effect that triggers insulin secretion, making these drugs very useful in stimulating insulin secretion in patients with type II diabetes.

Effect of Insulin on Carbohydrate Metabolism

Immediately after a high-carbohydrate meal, the glucose that is absorbed into the blood causes rapid secretion of insulin. The insulin in turn causes rapid uptake, storage, and use of glucose by almost all tissues of the body, but especially by the muscles, adipose tissue, and liver. Insulin promotes conversion of excess glucose into fatty acids and Inhibits gluconeogenesis in the Liver.

The brain is quite different from most other tissues of the body in that insulin has little effect on uptake or use of glucose. Instead, the brain cells are permeable to glucose and can use glucose without the intermediation of insulin.

Effect of Insulin on Fat Metabolism

Insulin promotes fat synthesis and storage. Insulin has several effects that lead to fat storage in adipose tissue. First, insulin increases the utilization of glucose by most of the body's tissues, which automatically decreases the utilization of fat, thus functioning as a fat sparer. However, insulin also promotes fatty acid synthesis. This is especially true when more carbohydrates are ingested than can be used for immediate energy, thus providing the substrate for fat synthesis. Almost all this synthesis occurs in the liver cells, and the fatty acids are then transported from the liver by way of the blood lipoproteins to the adipose cells to be stored.

Insulin deficiency increases use of fat for energy, causes lipolysis of storage fat and release of free fatty acids, increases plasma cholesterol and phospholipid concentrations. Excess usage of fats during insulin lack causes ketosis and acidosis.

Effect of Insulin on Protein Metabolism

Insulin promotes protein synthesis and storage**.** During the few hours after a meal when excess quantities of nutrients are available in the circulating blood, not only carbohydrates and fats but proteins as well are stored in the tissues; insulin is required for this to occur. The manner in which insulin causes protein storage is not as well understood as the mechanisms for both glucose and fat storage. Insulin lack causes protein depletion and increased plasma amino acids.

Factors and Conditions that Increase or Decrease Insulin Secretion:

Increase Insulin Secretion	Decrease Insulin Secretion
• Increased blood glucose	• Decreased blood glucose
• Increased blood free fatty acids	• Fasting
• Increased blood amino acids	• Somatostatin
• Gastrointestinal hormones (Gastrin, cholecystokinin, secretin Gastric inhibitory peptide)	• a-Adrenergic activity
	• Leptin
• Glucagon, growth hormone, Cortisol	
• Parasympathetic stimulation; Acetylcholine	
• b-Adrenergic stimulation	
• Insulin resistance; obesity	
• Sulfonylurea drugs (glyburide, Tolbutamide)	

Relation between insulin and other hormones[68]

1. Anterior pituitary
   - Growth hormone inhibits the uptake of glucose into muscle and adipose tissue and enhances the release of fatty acids from depot lipids and increase the release of glucose from liver resulting in hyperglycemia which in turn stimulates b-cells to synthesize more insulin. It also has lipolytic action.
   - ACTH through adrenal cortex, TSH through thyroid, increases blood sugar level.
2. Posterior pituitary

   A large dose of vasopressin and oxytocin raise the blood sugar level temporarily.
3. Blood sugar level

   High blood sugar stimulates and low blood sugar depresses the secretion of insulin by direct acting on the pancreatic islets and through the right vegus.
4. Adrenal cortex

   Glucocorticoids prevent the utilization of glucose in the muscle and adipose tissue and stimulate gluconeogenesis in the liver and thus oppose the

action of insulin, but these corticoids and insulin have got some similar function that both promote glycogenesis.

5. Glucagon

   It has got antagonistic effect against insulin. It produces hyperglycemia. But at time it helps insulin in the uptake of glucose by the peripheral tissue.

6. Somatostatin inhibits both insulin and glucagon secretion.
7. Thyroxine

   It has got hyperglycemic effect and thus opposes the effect of insulin and stimulates the secretion of it.

8. Epinephrine, norepinephrine cause glycogenolysis and hyperglycemia.
9. Gastro-intestinal harmones like secretin, pancreozymin and gastrin stimulate insulin secretion.
10. Other factors

    Factors that stimulate secretion of insulin are fatty acids, ketone bodies, insulin antibodies, calcium, magnesium, potassium; ATP, cyclic AMP and which inhibit are insulin itself, starvation, hypoxia, bigunide, etc.

LIVER[69]

- **Metabolic function**

a) Carbohydrate metabolism: It is especially important in maintaining a normal blood glucose level. During fasting, glucose derived from glycogen (glycogenolysis) or form newly synthesized glucose (gluconeogesis) is added to the blood.

b) Fat metabolism: Dietary fat is largely triglycerides, and it enters the body in chylomicrons. Triglycerides taken up by liver and are broken down to 2-carbon fragments that are used in many metabolic processes. Hepatocytes use cholesterol to make bile salts that are useful in emulsification and absorption of fats.

c) Protein metabolism: Dietary proteins enter into portal vein and most of the amino acids are taken up by the liver. The liver utilizes them for endogenous hepatic protein, plasma protein synthesis and for production of urea. Indeed all plasma albumin and most of its globulins other than gamma globulins are produced here.

- **Excretory function:**

Drugs, toxins, poisons, cholesterol, bile pigments and heavy metals are detoxified in the liver. Liver converts fat-soluble metabolized drugs into water-soluble substances and makes them suitable for excretion along with urine. Liver metabolizes 90% of ingested alcohol.

- **Protective function**:

By conjugation, destruction, phagocytosis and antibody formation liver protects us in several ways. The stellate reticulo endothelial cells of liver phagocytize worn out RBC & WBC.

- **Storage**:

Liver stores glycogen, fat, Vitamin A, B, D, E and K, and minerals like Iron and Copper. It also participates in activation of Vit.D.

PITUITARY GLAND[70]

- The diabetogenic functions of pituitary are in relation with the growth hormone and adrenocorticotrophic hormone.
- The pituitary effect of growth hormone on carbohydrate metabolism is to promote its storage.
- Administration of growth hormone induces hyperglycemia & glycosuria.
- Administration of acth also produces similar effects
- Both hormones increases gluconeogenesis and reduces cell uptake of glucose.

ADRENAL GLAND[71]

- Adrenal function is mediated by the pituitary which, in turn, is regulated by the hypothalamus.
- Corticotropin releasing hormone released by the hypothalamus stimulates adrenocorticotrophic hormone release from the anterior pituitary which stimulates adrenal production of cortisol and to a lesser extent mineralocorticoids and androgenic steroids.
- Adrenal steroid hormones are synthesized from cholesterol.
- There are 3 principle hormone types produced by the adrenal cortex:

− Glucocorticoids, eg cortisol.

− Mineralocorticoids, eg aldosterone.

- Androgens.

- The adrenal medulla produces:
- Epinephrine (adrenaline).
- Nor-epinephrine (nor-adrenaline).

ACTH production

- ACTH production fluctuates in an apparently random manner in the dog whereas cats show a diurnal rhythm.
- The primary stimulus for ACTH production is stress which maybe physiological, emotional or chemical.
- High plasma ACTH concentrations also have a direct negative feedback effect on ACTH production.

Glucocorticoid production

- **Primary hormone: cortisol**.
- Cortisol is produced from cholesterol in the zona reticularisand zonafasciculata of the adrenal cortex.
- **Actions of glucocorticoids**
- Stimulate gluconeogenesis, Erythropoeisis, Maintain blood pressure
- Suppress peripheral uptake of glucose & Suppress inflammation
- Increase fat and protein catabolism.
- **Mineralocorticoid production**
- **Principle hormone: aldosterone.**
- Secretion of aldosterone is mainly under the control of the renin-angiotensin system.
- ACTH has some effects on aldosterone release.
- Hypovolemia causes renin release which stimulates angiotensin II synthesis from angiotensin I.
- Angiotensin II promotes aldosterone release which increases distal tubularresorption of sodium in exchange for potassium, thus increasing circulating volume and removing stimulus for further renin production.

- Increasing plasma potassium concentrations also directly increase aldosterone production.

Catecholamine production

In the normal animal catecholamines are released from the chromaffin cells of the adrenal medulla.

URINE FORMATION[72]

The rates at which different substances are excreted in the urine represent the sum of three renal processes.

1. Glomerular filtration
2. Reabsorption of substances from the renal tubules into the blood and
3. Secretion of substance from the blood into the renal tubules.

Urine formation begins when a large amount of fluid that is virtually free of protein is filtered from the glomerular capillaries into Bowman's capsule. Most substances in the plasma, except for proteins, are freely filtered, so that their concentration in the glomerular Bowman's capsule is almost the same as in plasma. As filtered fluid leaves Bowman's capsule and passes through the tubules, it is modified by reabsorption of water and specific solutes back into the blood or by secretion of other substances from the peritubular capillaries into the tubules. For each substance in the plasma, a particular combination of filtration, reabsorption and secretion occurs. The rate at which the substance is excreted in the urine depends on the relative rates of these three basic renal processes. In general tubular reabsorption is quantitatively more important than tubular secretion in the formation of urine, but secretion plays an important role in determining the amounts of potassium and hydrogen ions and a few other substances that are excreted in the urine. Most substances that must be cleared from the blood, especially the end products of metabolism such as urea, creatinine, uric acid, and urates are poorly reabsorbed and are therefore excreted in large amounts in the urine. Certain foreign substances and drugs are also poorly reabsorbed but, in addition, are secreted from the blood into the tubules so that their excretion rates are high. Conversely, electrolytes, such as sodium ions, chloride ions, and bicarbonate ions are highly reabsorbed, so that only small amounts appear in the urine. Certain nutritional substances, such as amino acids

and glucose are completely reabsorbed from the tubules and do not appear in the urine even though large amounts are filtered by the glomerular capillaries. Each of the processes glomerular filtration tubular reabsorption and tubular secretion is regulated according to the needs of the body.

SHAREERA KRIYA

Vata: '**पवनं अतिबलं अतिपारुष्यं अतिशीघ्र कारणं आत्ययिकं**'II[59]

Vata being the main *dosha* in *Madhumeha* is the cause for *mahatyayakaritava.*

Pitta: The *dosha* which is responsible for *dahana pachanadi kriya*. It's responsible for proper metabolism as the '**अग्निरेव शरीरे पित्तान्तर्गतः**'[73].

Kapha: **'सोम एव शरीरं श्लेष्मान्तर्गतं'[74].**

Chakrapani has said that *kapha dosha* is *jala devata*. In *prakritha avastha* it imparts *bala* to body & in *vikritha avastha* it becomes *mala*.

***Aapa dhatu*[55]:** *Aap dhatu* being considered as a *dhatu,* though not coming among *saptadhatu,* constitute major portion of the body and performs *sharira jeevana* and *kledana* but it is not an upadhatu. It is one of the main *dooshya* in *madumeha*. It is the main component of *udakavaha srotas & medovaha srotas*.

The *aap dhatu* forms a part of *pureesha, sweda, lasika, mutra* etc and *saptadhatu'*s such as *rasa, rakta, mamsa, meda, majja, sukra, twacha*. The *sweda* is the *mala rupa* expelled through *lomakoopa* and *lasika* is the liquid exudated from *vruna*.

Ojas*: Ojas* ie *apara ojas* is mainly vitiated in *Madhumeha*. Provoked *vata* due to its own aetiological factor or due to anger, hunger, worry, exertion carries ojas towards vasti and excrete through urine[75]. So symptoms of *ojo kshaya* manifests like *guru gatrata nidra tandra & daurbalya*[76].

AGNI

The synonyms of *Agni* are *kayagni, antaragni & koshtagni*. *Acharyas* explained 13 types of agnis in body. They are one *jatharagni*, 5 *bhootagni* & 7 *dhatwagni*. *Agni* or *jatharagni* is the cause for every parinama in body. *Dahana & paaka* are the main functions of *Agni.*

At *Jatharagni* level:

Consumed ahara first comes in the contact with *Jatharagni*. This *ahara* is not homogenous with *sharirika Bhava* (i.e. the Pancabhautika composition of consumed ahara is not homogenous to the *Pancabhautika* composition of *sharirika Bhavas*). *Jatharagni* transforms this ahara into subtle heterogenous nutrients.

At the level of *Bhutagni:*

Subtle heterogenous nutrients undergo modification by the influence of *Bhutagni* and a subtle homogenous matter form. But it's also required further processing. It means though the byproduct after Bhutagni influence is subtle and homogenous also but not so hence it go under the *Dhatwagni* function the ultimate factory of transformation.

At the level of *Dhatwagni*:

As the flame of the forest fire tends to increase or decrease according to the quantity of the *Indhana* (available in the proximity), so also in the case with *Dhatuparampara.* This D*hatuparampara* does continue due to the influence of each individual *Dhatwagni* on the out product of *Bhutagni* transformation. This *Atmiya Ahara Rasa* is utilised by the *Posya* or the *Sthayi Dhatus*, present in all parts of the body. Seven different kinds of *Dhatwagni* corresponding to seven types of *Dhatus* have been enlisted. They are *Rasagni*, *Raktagni,* etc. These Agnis are stated to mediate or catalyse metabolic transformations of nutrient substances before they are supplied to the seven types of *Dhatus viz. Rasa Rakta Mamsa Medas Asthi Majja Sukra* through their respective Srotamsi. Nutritional substances that nourish the *Dhatus* undergo *Paka* by the *Usma (Agni)* of the *Dhatus* and then, they are made available to the latter.

Dhatvaharas thus prepared confer upon the organism's strength, complexion, happiness, longivity and provide energy to the *Dhatus*. This *Paka* ultimately gives rise to two kinds of substances *Prasada* and *Kitta*. The two aspects anabolic and catabolic respectively constitute metabolism as a whole. The intermediary metabolism is only being performed due to the guidance of *Agni.*

Kloma* and *Talu

Kloma is said to be *kaphadhistana*[77] and both *kloma* and *talu* are the origin of *udakavaha srotas*[54]. Kloma probably is pancreas being included as a *kostha avayava. Kloma vikruti* brings about the imbalance and dysfunction of udakavaha srotas.

Vrukka

Vrukka's are kidneys and *moola* of *medovaha srotas,* as we do see in *Charaka samhita* that *medopradoshaja vyadhi's* produces *Prameha purvaroopa lakshanas*. In *Prameha* there is Polyuria, where kidneys secrete more and more urine. This reflects significance and connection of *medodhatu* and *vrukka*[78].

MUTRA

The *mutravaha srotas* deals with the urinary system. It is closely related to *udakavaha, rasavaha, raktavaha,* and *annavaha srotas*. Because the 'urine' is reckoned as one of the 3 major malas of the body, which depends on the condition of agni in *annavaha srotas* and *dhatus*. These srotas determine the quantity and quality of urine to be excreted out.

आहारस्य रसःसारः सारहीनो मलद्रवः l
शिराभिष्टात्जलं नयतं बस्तौ मूत्रत्वं आप्नुयात ll[79]

Sara bhaga of *ahara* is *rasa* and *Sara heena bhaga* is *mala*. This *jalaroopi mala* reaches the *basthi* through various siras and let out from here. *Sushruta* has explained the *mutra* formation in detail. The nadis which connect *pakvashaya & mutravaha srotas* absorb the *mutramsha* from *pakwashaya* and bring it to the *mutravaha srotas*. *Mutra* is continuously formed or supplied in the the *mootravaha srotas* by these *nadi's* like how thousand river continuously drain to form sea. The *mukhas* of these *nadi's* are so *sookshma* that its openings/ *mukha* are not visible. This function of formation of urine is carried out continuously irrespective whether the individual is sleeping or awaken. *Mutra* is formed continuously in the basti like how a pot is filled when dipped in water upto its *mukha*[80].

ETYMOLOGY OF *MADHUMEHA*

To understand the etiology, patho-physiology, complications and management methods is necessary to emphasize the disease *"Madhumeha".*

Vyutpatti:

The first and the foremost Vedic reference for the word *Meha* is found in the *Rigveda*[81].

Meha

"मेहयति सिंचति मूत्ररेतंसि इति मेहः"

This means to excrete: watering; wetting by the urination -*Halayudha Kosha*

The word *'Meha'* is derived from the root '***Miha***' which is employed in the sense of *sinchana* (to moisten) and *ksharana* (to flow) [82]. And word *Meha* has been used in the *prasrava* (excessive excretion) and as *a Prameha Roga Bheda (vachaspathyam)* also.

Nirukti:

Prameha

The word *Prameha* is formed by the *Sanskrit* root,

Prameha=Pra and ***Miha***

Pra:

Prefix -suggests excess or profuse in both Frequency and Quantity.

Miha*:*

Suffix- literally means to micturate. The verbal noun *Mehanam* signifies urination as well as act of passing any morbid urethral secretion.

Madhumeha

Madhumeha is a compound word composed of *Madhu* and *Meha*.

The word ***Madhu*** derived from the root

"मन्यंते विशेषेण जानति जन यस्मिन"

People are going to accept it as special. It refers to the meaning Honey, *Kshoudra, Madya, Pushparasa, Jala,* and *Madhurasa- Arunadatta*

`यस्मात कारणात मधु इव मेहति मधु सद्रुशं मेहति अस्मात कारणात मधुमेह संज्ञा ||'[83]

From above description the Etymology is concise which indicates that the diseases having excessive excretion of urine and similar qualities to *Madhu* in its color, taste, smell and consistency called as *Madhumeha.*

Paribhasha

PRAMEHA

'प्रकर्षेण मेहति क्षरति इति वीर्यदिरनेनिति प्रमेह'

Pra + miha +karane gnan roga visheshaha [84]

The disease in which the quantity as well as frequency of micturation increases is known as *Prameha*. On the above basis, explanation can be finding that *Prameha* is resultant of excessive excretion of *mutra*.

MADHUMEHA

Madhumeha is a disease in which urine of the patient is sweet like honey and quantitatively increased as well as *Kashaya rasa*, *Aruna Varna* and *Ruksha* in quality or guna. The whole body of *Madhumehi* becomes sweet[85].

Sushruta has defined *Madhumeha* by the term '*KSHAUDRA MEHA'* and stated that the urine in this condition resembles honey and acquires a sweet taste[86].

"कालेनोपेक्षिता सर्वे यद्यन्ति मधुमेहतमं || मधुरं यच्च सर्वेषु प्रायो मध्विव मेहति | सर्वे अपि मधुमेहाख्य माधुर्यच्च तनोरतः ||"

Vagbhata opine, if the patients of *Prameha* are not treated properly, all of them reach to the stage of '*Madhumeha*' which is *asadhya*[87].

Paryaya:

Meha: Is referred to as *Prameha*[88].

Mootradosha: A urinary disorder.

Bahumootrata: A disease where there is excessive urination.

Madhumeha: A condition characterized by excess urination, resembling honey either in colour or taste. This word has been used synonymously with *Prameha.*

Kshoudrameha: Kshoudra is a synonym of *Madhu* by *Sushruta.*

Ojomeha: Ojas is considered as sara or essence of all Dhatus, which is a *dushya* in *Madhumeha* hence *Ojomeha* has been used by *Charaka* to describe this disease.

Paushpameha: This term is used in *Anjananidana* to describe *Madhumeha* from all synonyms; we can suggest that all *Acharyas* mentioned the urine culture similar with *Madhu*[89].

ETYMOLOGY OF DIABETES MELLITUS

The word Diabetes is originated from the French word named "*Jiyabatis"* which means punctured pitcher or pitcher with leak, so that water sprinkles out of it.

Diabetes– ***Parashuram Shastry*.** The word Diabetes Mellitus contains two words i.e. Diabetes and mellitus. In Greek Diabetes means to run through a siphon and the term Mellitus means honey.

Definition of Diabetes Mellitus

Diabetes Mellitus is a metabolic disorder of multiple etiologies, characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both[90]. According to sir Jerold M Olefsky, type 2 DM is not a single disease process but, instead represents a heterogenous constellation of the disease syndrome all leading to a final common pathway hyperglycemia[91].

"Metabolic syndrome" refers to the phenomenon of risk factor clustering—an aggregation of metabolic traits occurring in the same individual with Frequencies greater than expected by chance, and presumably reflecting a unifying underlying pathophysiology. It has long been recognized that Type 2 Diabetes and cardiovascular disease (CVD) share many risk factors in common and that their co-occurrence is probably linked to insulin resistance and obesity[92].

NIDANA

The factor like ahita ahara and vihara which does dosha prakopana gets dooshita by itself and does dushana of dushyas to produce a disease is called Nidana or Hetu. Nidana is necessary to assess sadyasadhyata of a disease also its useful to do Vyadhi vyavacchedhana. It is the main indicator of present and forthcoming diseases[93]. Nidana Parivarjana is also one of the initial measures of treatment[94]. Only Charaka explains specific Nidanas for Madhumeha. The Samanya Nidana of Prameha and Vataja Prameha

may attribute to Madhumeha, as it is one of the types of Vataja Prameha. Kaphaja prameha nidanas may be considered in sthoola Madhumehi, as it is initial factor for the causation of all varieties of Madhumeha.

Ayurvedic classics elaborately describes about the general etiological factors of Prameha at the same time it is the highness of discretion elucidated by Acharya Charaka in relation to this disease which even though is Tridosha in origin but it is influenced by specific doshic etiologies which in turn decides the extent and strength of the corresponding disease pathology leading to Madhumeha latter –Vikara Vighata Bhava Abhava Prativishesha. Hence, classical etiologies mentioned for Prameha can be taken for Madhumeha also.

Etilogical factors of Prameha can be classified into *Sahaja* and *Apathyanimittaja*[95].

1. *Sahaja prameha:*

Sahaja prameha is further divided into two types *Kulaja* and *Garbhaja*.

a. *Kulaja prameha*: It is due to certain defects in *stree* and *pumbeeja* (ovum and sperm) which is said to be *matru-pitru beejadoshakrita, sahaja prameha* occurs. Regarding *beeja dosha,* it may have its origin from parents of either or both father and mother i.e., it may be inherited from generation to generation and thus is a unique example of hereditary disease.

b. *Garbhaja prameha*: *Acharya Charaka* mentioned that excessive intake of Madhura rasa by the pregnant lady is the chief cause for the changes and damages in the foetus. Over indulgence in Madhura rasa by mother during Pregnancy is likely to produce Prameha.

Table No.1: Showing the *Aharaja Nidanas* of *Madhumeha* according to different *Ayurvedic* Classics:

Sl.No	*Aharaja Nidanas*	*C.S*[96]	*Su.S*[97]	*A.H*[98]	*M.N*[9]	*Bhe.S*[100]	*B.P*[101]	*Y.R*[102]
1	*Dadhi sevana*	+	_	_	+	_	+	+
2	*Gramya rasa*	+	_	_	+	_	+	+
3	*Audaka rasa*	+	_	_	+	+	+	+
4	*Anupa rasa*	+	-	+	+	+	+	+
5	*Kshira sevana*	+	-	-	+	-	+	+
6	*Nava anna*	+		-	+	-	+	+
7	*Nava pana*	+	-	-	+	-	+	+
8	*Guda Vikara*	+	-	+	+	-	+	+
9	*Kaphakara Hetu*	-	+	+	+	+	+	+
10	*Sheeta*	-	+	+	-	-	-	-
11	*Snigdha*	+	+	+	-	+	-	-
12	*Madhura*	+		+	-	-	-	-
13	*Medovardhaka*	+	+	-	-	-	-	-
14	*Drava anna*	+	+	-	-	-	-	-
15	*Drava pana*	+	+	-	-	-	-	-
16	*Nava dhanya*	+	-	+	-	-	-	-
17	*Nava sura*	+	-	+	-	-	-	-
18	*Ikshu*	+	+	+	-	-	-	-
19	*Gorasa*	-	+	+	-	-	-	-
20	*Amla*	-	+	+	-	-	-	-
21	*Guru*	-	+	+	-	-	-	-
22	*Picchila*	-	+	+	-	-	-	-
23	*Mandaka dadhi*	+	+	-	-	-	-	-

Table No.2: Showing the *Viharaja Nidanas* of *Madhumeha* according to different Ayurvedic Classics

S.N	*Viharaja Nidanas*	*C.S*	*Su.S*	*A.H*	*M.N*	*Bhe.S*	*B.P*	*Y.R*
1	*Swapnasukha*	+	-	-	+	-	+	+
2	*Asyasukha*	+	-	-	+	-	+	+
3	*Divaswapna*	-	+	-	-	-	-	-
4	*Avyayama*	+	+	-	-	+	-	-
5	*Alasya*	-	+	-	-	-	-	-
6	*Ekasthanasana*	-	-	+	-	-	-	-
7	*Rathi*	-	-	-	+	-	-	-
8	*Vidhirahitashayana*	-	-	+	-	-	-	-
9	*Swapnaprasanga*	+	-	-	-	-	-	-
10	*Shayanaprasanga*	+	-	-	-	-	-	-
11	*Asanaprasanga*	+	-	-	-	-	-	-
12	*Sharirashodhana Varjya*	+	-	-	-	-	-	-

Table No.3 : Showing the *Vishista nidanas* of *Madhumeha* according to different *dosha*:

Nidana[97]	***Kapha***	***Pitta***	***Vata***
Ahara sambhandi	*Hayanaka, yavaka, chinaka uddalaka, naishada, ithakata, mukunda, mahavrihi, modaka, ughandaka, Sarpi, navaharenu, masha, Anupa, udaka, gramya mamsa, shaka, palala, tila, pistanna, payasa, krushara, vilepi, ikshu, sharkara, kshira, mandaka navamadhya, dadhi, madhura.*	*Ushna, amla, lavana, kashaya Katu,ajirna, vishamashana*	*Kashaya, Katu, Tikta, Rooksha, Laghu, Sheeta,*
Vihara sambhandi	*Mrujavarjana, avyayama, swapnashayana, aasanaprasanga*	*Atiatapasevana atapa, shrama, krodh*	*Atiyoga of Vyavaya, Vyayama, Vamana, Virechana,Ashtapana, Shiroovirechana, Sonita,Atisheka, Sandharana, Anashana, Atapa, Abhighata, Shokha Udvega, Jagarana, Vishamashareera, Asana, Upasevana.*

Nidanarthakara rogaja:

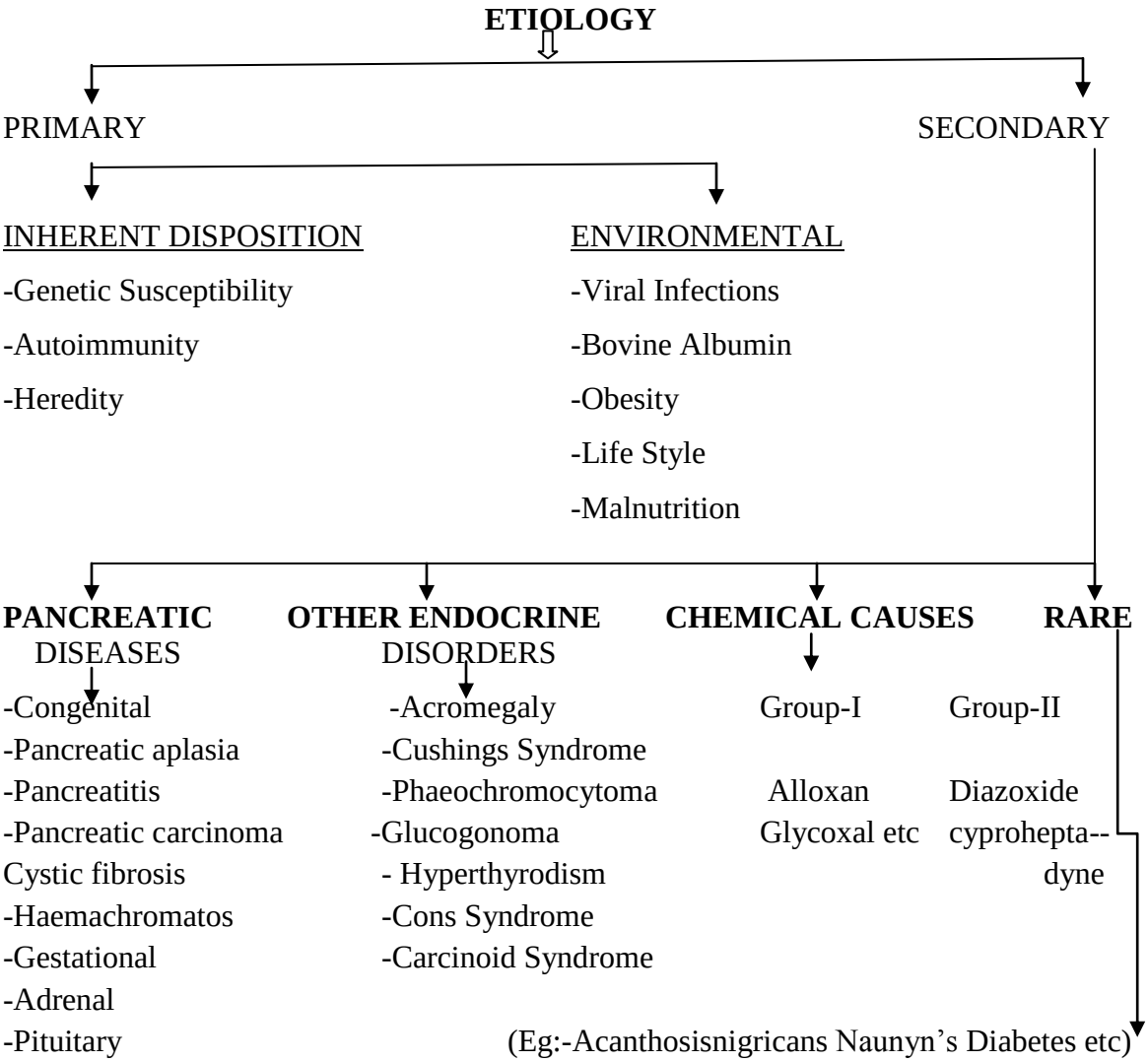
A. *Prameha*:

All the other types of mehas if neglected in its due course, lead into *Madhumeha*[98]. Pathogenesis and the srotas involved in *Prameha* and *Madhumeha* are similar. So, if the Prameha is not treated then it causes more strain on the same srothases and causes *Madhumeha.*

B. Sthoulya:

Sthoulya is *nidanarthakara roga* for *prameha*. It is obvious that the *samanya nidana* of *Sthoulya* and *Prameha* simulates each other. *Sushrutha* has stated that *apathyanimittaja Pramehis* are *Sthoola*[95].

Table no. 4: Schemetic diagram on aetiology of Showing the Etiology of Diabetes Mellitus



ETIOLOGY[105]

However, it is unlikely that a single factor is the cause of this heterogeneous disease. The etiology of Diabetes Mellitus has yet to be understood in spite of the advances made in the knowledge obtained with respect to various factors associated with the causation of Diabetes Mellitus.

Causes of Type-1Diabetes Mellitus

Type 1 Diabetes are caused by a lack of insulin due to the destruction of insulin-producing beta cells in the pancreas. In type 1 diabetes—an autoimmune disease—the body's immune system attacks and destroys the beta cells. In type 1 diabetes, beta cell destruction may take place over several years, but symptoms of the disease usually develop over a short period of time.

Latent autoimmune Diabetes in adults (LADA) may be a slowly developing kind of type 1 diabetes. Diagnosis usually occurs after age 30. In LADA, as in type 1 diabetes, the body's immune system destroys the beta cells. At the time of diagnosis, people with LADA may still produce their own insulin, but eventually most will need insulin shots or an insulin pump to control blood glucose levels.

Genetic Susceptibility

Heredity plays an important part in determining who is likely to develop type 1-diabetes. Many genes, as well as interactions among genes, are thought to influence susceptibility to and protection from type 1 diabetes. Variations in genes that affect more than 1 percent of a population group are called gene variants.

Certain gene variants that carry instructions for making proteins called human leukocyte antigens (HLAs) on white blood cells are linked to the risk of developing type 1 diabetes. The proteins produced by HLA genes help determine whether the immune system recognizes a cell as part of the body or as foreign material. Some combinations of HLA gene variants predict that a person will be at higher risk for type 1 diabetes, while other combinations are protective or have no effect on risk.

While HLA genes are the major risk genes for type 1 diabetes, many additional risk genes or gene regions have been found. Not only can these genes help identify

people at risk for type 1 diabetes, but they also provide important clues to help scientists better understand how the disease develops and identify potential targets for therapy and prevention.

Genetic testing can show what types of HLA genes a person carries and can reveal other genes linked to diabetes. However, most genetic testing is done in a research setting and is not yet available to individuals. Scientists are studying how the results of genetic testing can be used to improve type-1 Diabetes prevention or treatment.

Autoimmune Destruction of Beta Cells

In type 1 diabetes, white blood cells called T cells attack and destroy beta cells. The process begins well before Diabetes symptoms appear and continues after diagnosis. Often, Type 1 Diabetes is not diagnosed until most beta cells have already been destroyed. At this point, a person needs daily insulin treatment to survive. Finding ways to modify or stop this autoimmune process and preserve beta cell function is a major focus of current scientific research.

Recent research suggests insulin itself may be a key trigger of the immune attack on beta cells. The immune systems of people who are susceptible to developing type 1-Diabetes respond to insulin as if it were a foreign substance, or antigen. To combat antigens, the body makes proteins called antibodies. Antibodies to insulin and other proteins produced by beta cells are found in people with type 1 diabetes. Researchers test for these antibodies to help identify people at increased risk of developing the disease. Testing the types and levels of antibodies in the blood can help determine whether a person has Type 1diabetes, LADA, or another type of diabetes.

Environmental Factors

Environmental factors, such as foods, viruses, and toxins, may play a role in the development of type 1 diabetes, but the exact nature of their role has not been determined. Some theories suggest that environmental factors trigger the autoimmune destruction of beta cells in people with a genetic susceptibility to diabetes. Other theories suggest that environmental factors play an ongoing role in diabetes, even after diagnosis.

Viruses and infections

A virus cannot cause Diabetes on its own, but people are sometimes diagnosed with type-1 Diabetes during or after a viral infection, suggesting a link between the two. Viruses possibly associated with Type 1 Diabetes include coxsackievirus B, cytomegalovirus, adenovirus, rubella, and mumps. Scientists have described several ways these viruses may damage or destroy beta cells or possibly trigger an autoimmune response in susceptible people. For example, anti-islet antibodies have been found in patients with congenital rubella syndrome, and cytomegalovirus has been associated with significant beta cell damage and acute pancreatitis—inflammation of the pancreas. Scientists are trying to identify a virus that can cause Type 1 Diabetes so that a vaccine might be developed to prevent the disease.

Infant feeding practices

Some studies have suggested that dietary factors may raise or lower the risk of developing type 1-diabetes. For example, breastfed infants and infants receiving vitamin D supplements may have a reduced risk of developing Type 1 Diabetes, while early exposure to cow's milk and cereal proteins may increase risk. More research is needed to clarify how infant nutrition affects the risk for Type 1 Diabetes.

Causes of Type-2 Diabetes Mellitus

Type 2 Diabetes—the most common form of Diabetes—is caused by a combination of factors, including insulin resistance, a condition in which the body's muscle, fat, and liver cells do not use insulin effectively. Type 2-Diabetes develops when the body can no longer produce enough insulin to compensate for the impaired ability to use insulin. Symptoms of Type 2 Diabetes may develop gradually and can be subtle; some people with Type 2 Diabetes remain undiagnosed for years.

Type 2 Diabetes develops most often in middle-aged and older people who are also overweight or obese. Scientists think genetic susceptibility and environmental factors are the most likely triggers of type 2 diabetes.

Genetic Susceptibility

Genes play a significant part in susceptibility to type 2 Diabetes. The role of

genes is suggested by the high rate of Type 2 Diabetes in families and identical twins and wide variations in Diabetes prevalence by ethnicity. The known genes appear to affect insulin production rather than insulin resistance.

Studies have shown that variants of the TCF7L2 gene increase susceptibility to type 2-diabetes. For people who inherit two copies of the variants, the risk of developing type 2-Diabetes is about 80 percent higher than for those who do not carry the gene variant. However, even in those with the variant, diet and physical activity leading to weight loss help delay diabetes, according to the Diabetes Prevention Program (DPP), a major clinical trial involving people at high risk. Genes can also increase the risk of Diabetes by increasing a person's tendency to become overweight or obese. One theory, known as the "thrifty gene" hypothesis, suggests certain genes increase the efficiency of metabolism to extract energy from food and store the energy for later use. This survival trait was advantageous for populations whose food supplies were scarce or unpredictable and could help keep people alive during famine. In modern times, however, when high-calorie foods are plentiful, such a trait can promote obesity and type 2-diabetes.

Obesity and Physical Inactivity

Physical inactivity and obesity are strongly associated with the development of type 2 diabetes. People who are genetically susceptible to type 2-Diabetes are more vulnerable when these risk factors are present.

Central obesity, in which a person has excess abdominal fat, is a major risk factor not only for insulin resistance and type 2-Diabetes but also for heart and blood vessel disease, also called cardiovascular disease (CVD). This excess "belly fat" produces hormones and other substances that can cause harmful, chronic effects in the body such as damage to blood vessels.

The DPP and other studies show that millions of people can lower their risk for type 2-Diabetes by making lifestyle changes and losing weight. The DPP proved that people with pre-diabetes—at high risk of developing type 2-diabetes—could sharply lower their risk by losing weight through regular physical activity and a diet low in fat and calories.

Insulin Resistance

Insulin resistance is a common condition in people who are overweight or obese, have excess abdominal fat, and are not physically active. Muscle, fat, and liver cells stop responding properly to insulin, forcing the pancreas to compensate by producing extra insulin. As long as beta cells are able to produce enough insulin, blood glucose levels stay in the normal range. But when insulin production falters because of beta cell dysfunction, glucose levels rise, leading to pre-Diabetes or diabetes.

Abnormal Glucose Production by the Liver

In some people with diabetes, an abnormal increase in glucose production by the liver also contributes to high blood glucose levels. Normally, the pancreas releases the hormone glucagon when blood glucose and insulin levels are low. Glucagon stimulates the liver to produce glucose and release it into the bloodstream. But when blood glucose and insulin levels are high after a meal, glucagon levels drop, and the liver stores excess glucose for later, when it is needed. For reasons not completely understood, in many people with diabetes, glucagon levels stay higher than needed. High glucagon levels cause the liver to produce unneeded glucose, which contributes to high blood glucose levels.

Metabolic Syndrome

Metabolic syndrome, also called insulin resistance syndrome, refers to a group of conditions common in people with insulin resistance, including higher than normal blood glucose levels, increased waist size due to excess abdominal fat, high blood pressure, abnormal levels of cholesterol and triglycerides in the blood.

People with metabolic syndrome have an increased risk of developing type 2-Diabetes and CVD. Many studies have found that lifestyle changes, such as being physically active and losing excess weight, are the best ways to reverse metabolic syndrome, improve the body’s response to insulin, and reduce risk for type 2-Diabetes and CVD.

Cell Signaling and Regulation

Cells communicate through a complex network of molecular signaling pathways. For example, on cell surfaces, insulin receptor molecules capture, or bind, insulin molecules circulating in the bloodstream. This interaction between insulin and its receptor prompts the biochemical signals that enable the cells to absorb glucose from the blood and use it for energy.

Problems in cell signaling systems can set off a chain reaction that leads to Diabetes or other diseases. Researchers have identified proteins and pathways that transmit the insulin signal and have mapped interactions between insulin and body tissues, including the way insulin helps the liver control blood glucose levels. Researchers have also found that key signals also come from fat cells, which produce substances that cause inflammation and insulin resistance.

Beta Cell Dysfunction

Scientists think beta cell dysfunction is a key contributor to type 2 diabetes. Beta cell impairment can cause inadequate or abnormal patterns of insulin release. Also, beta cells may be damaged by high blood glucose itself, a condition called glucose toxicity.

Single gene defects lead to specific forms of Diabetes called maturity-onset Diabetes of the young (MODY). The genes involved regulate insulin production in the beta cells. Malnutrition early in life is also being investigated as a cause of beta cell dysfunction. The metabolic environment of the developing fetus may also create a predisposition for Diabetes later in life.

Gestational Diabetes Mellitus

Gestational Diabetes is caused by the hormonal changes and metabolic demands of pregnancy together with genetic and environmental factors.

Insulin Resistance and Beta Cell Dysfunction

Hormones produced by the placenta and other pregnancy-related factors contribute to insulin resistance, which occurs in all women during late pregnancy. Insulin resistance increases the amount of insulin needed to control blood glucose levels. If the pancreas can’t produce enough insulin due to beta cell dysfunction, gestational Diabetes

occurs. Overweight or obese women are at particularly high risk for gestational Diabetes because they start pregnancy with a higher need for insulin due to insulin resistance.

Family History

Having a family history of Diabetes is also a risk factor for gestational diabetes, suggesting that genes play a role in its development.

Future Risk of Type-2 Diabetes Mellitus

Because a woman's hormones usually return to normal levels soon after giving birth, gestational Diabetes disappears in most women after delivery. However, women who have gestational Diabetes are more likely to develop gestational Diabetes with future pregnancies and develop type 2-Diabetes and increase a child's risk for becoming overweight or obese and for developing type 2-Diabetes later on. Women with gestational Diabetes should be tested for persistent Diabetes 6 to 12 weeks after delivery and at least every 3 years thereafter.

Other Causes of Diabetes Mellitus:

Genetic Mutations Affecting Beta Cells, Insulin, and Insulin Action

Some relatively uncommon forms of Diabetes known as monogenic Diabetes are caused by mutations, or changes, in a single gene. Most of these gene mutations cause Diabetes by reducing beta cells' ability to produce insulin.

The most common types of monogenic Diabetes are neonatal Diabetes Mellitus (NDM) and MODY. NDM occurs in the first 6 months of life. MODY is usually found during adolescence or early adulthood but sometimes is not diagnosed until later in life. Other rare genetic mutations can cause Diabetes by damaging the quality of insulin the body produces or by causing abnormalities in insulin receptors.

Other Genetic Diseases

Diabetes occurs in people with Down syndrome, Klinefelter syndrome, and Turner syndrome at higher rates than the general population. The genetic disorders cystic fibrosis and hemochromatosis are linked to diabetes. The risk of Diabetes increases with age in people with cystic fibrosis. Hemochromatosis causes the body to store too much

iron. If the disorder is not treated, iron can build up in and damage the pancreas and other organs.

Damage to or Removal of the Pancreas

Pancreatitis, cancer, and trauma can all harm the pancreatic beta cells or impair insulin production, thus causing diabetes. If the damaged pancreas is removed, Diabetes will occur due to the loss of the beta cells.

Endocrine Diseases

Cushing's syndrome and acromegaly are examples of hormonal disorders that can cause preDiabetes and Diabetes by inducing insulin resistance. Cushing's syndrome is marked by excessive production of cortisol—sometimes called the "stress hormone." Acromegaly occurs when the body produces too much growth hormone. Glucagonoma, a rare tumor of the pancreas, can also cause diabetes. The tumor causes the body to produce too much glucagon. Hyperthyroidism, a disorder that occurs when the thyroid gland produces too much thyroid hormone, can also cause elevated blood glucose levels.

Autoimmune Disorders

Autoimmune disorders such as lupus erythematosus and stiff-man syndrome is associated with antibodies that attack the beta cells, similar to Type 1 Diabetes.

Medications and Chemical Toxins

Some medications, such as nicotinic acid and certain types of diuretics, anti-seizure drugs, psychiatric drugs, and drugs to treat human immunodeficiency virus (HIV), can impair beta cells or disrupt insulin action. Pentamidine, a drug prescribed to treat a type of pneumonia, can increase the risk of pancreatitis, beta cell damage, and diabetes. Also, glucocorticoids—steroid hormones that are chemically similar to naturally produced cortisol—may impair insulin action.

Chemical toxins for example, dioxin—a contaminant of the herbicide Agent Orange, used during the Vietnam War—may be linked to the development of type 2 diabetes. Also, a chemical in a rat poison no longer in use has been shown to cause Diabetes if ingested. Some studies suggest a high intake of nitrogen-containing chemicals

such as nitrates and nitrites might increase the risk of diabetes. Arsenic has also been studied for possible links to diabetes.

Lipodystrophy

Lipodystrophy is a condition in which fat tissue is lost or redistributed in the body. The condition is associated with insulin resistance and type 2 diabetes.

POORVA ROOPA:

It appears prior to manifestation of the disease and indicates the forth coming disease. The roopa is said to be in avyakta avastha as it is in the earlier stages of kriya kala. As Madhumeha is classified under the Vatika type of Prameha, Purvarupa of Prameha can be taken as Purvarupa of Madhumeha. Only samanya prameha poorva roopa is available[100]. Specific poorva roopa for Madhumeha has not been mentioned anywhere in classics.

Table No. 5: Showing *the Poorvaroopa of Madhumeha* in different *Ayurvedic* Classics

Sl.No	Poorva roopa	C.S[106]	S.S[107]	AS[108]	AH[109]	MN[110]	BP[112]	YR[113]
1	*Kesha nakha ati vriddi*	+	-	+	+	-	-	-
2	*Sheetala priyatva*	+	-	+	+	-	+	-
3	*Gala shosha*	+	-	+	+	-	+	-
4	*Talu shosha*	+	-	+	+	-	+	-
5	*Asya madhuryata*	+	-	+	+	-	+	+
6	*Kara Pada daha*	+	+	+	+	+	+	+
7	*Kesha jatili bhava*	+	+	+	+	-	+	-
8	*Mukha sosha*	+	-	-	-	-	-	-
9	*Pippasa*	+	+	+	-	+	+	+
10	*Anga supthi*	+	-	+	-	-	-	
11	*Sarva kaala nidra*	+	-	-	-	-	-	-
12	*Swasa*	-	+	-	-	-	-	-
13	*Dourgandya*	-	+	-	-	+	+	+
14	*Dantadinam maladyatvam*	-	+	-	-	-	-	-
15	*Taluni malotpatti*	+	-	+	-	-	-	-
16	*Visra gandha of muthra*		+	+	-	-	-	-
17	*Visra gandha of Shareera*	+	-	+	-	-	-	-
18	*Pichila gatrata*	+	+	+	-	-	-	-
19	*Snigdha gatrata*	+	-	+	-	-	-	-

20	*Shukla mootra*	+	-	-	-	-	-	
21	*Ati asana sukha*	+	-	+	-	-	-	-
22	*Kara pada supthi*	+	-	+	+	-	-	-
23	*Pippilika abhisarana*	+	-	-	-	-	-	
24	*Mootra abisarana*	+	-	+	+	-	-	
25	*Alasya*	+	-	+	-	-	-	-
26	*Kaye Malam*	+	-	+	-	-	-	-
27	*Sweda*	+	-	+	+	-	-	-
28	*Shithilangata*	+	-	-	+	-	-	-
29	*Ghanangata*	+	-	-	+	-	-	-
30	*Tandra*	+	+	+	-	-	-	-
31	*Madhura Mutrata*	-	+	-	-	-		
32	*Anga paridaaha*	+	-	-	-	-		
33	*Kayachidreshu Upadeha*	+	-	-	+	-		

The manifestation of the above mentioned prodromonal symptoms can be understood in co-relation to the stage of Sthanasamshraya where the already vitiated and dislodged bodily principles starts to find its substratum vide srotas and its appendages for the development of further pathogenesis within the latter and finally enabling the process of *Atura Samvedhya and Vaidya Samvedhya Lakshanas* which inturn helps the physician to assess the srotas and its appendages afflicted and plan for appropriate therapeutic measures based on the *Dushyadi Sameekshya Bhava* [114].

Pre-Diabetic States[115]

Sometimes a patient with abnormal hyperglycemia may not have full clinical symptoms of Diabetes Mellitus and often pre-diabetic states are asymptomatic. Mild symptoms if manifested go unrecognized but the identification of such stages can go a long way in prevention of an overt disease. The British Diabetic Association has suggested a classification that is accepted by W.H.O. expert committee on Diabetes. They are as follows:

Potential Diabetes:

These are persons who have high probability of developing Diabetes. They do not show any evidence of impaired glucose tolerance.

They include,

a) Identical twin of a diabetic,

b) Persons with both the parents diabetic,

c) Persons with one parent diabetic, the other non-diabetic parent having a diabetic parent or a diabetic sibling or their offspring having Diabetes.

Latent Diabetes:

a) Persons with a normal G.T.T. at present, but had an abnormal G.T.T. sometime in the past viz. during pregnancy, infection when under stress or when obese,

b) Persons with a normal G.T.T. under standard conditions but an abnormal one with provocative tests.

Asymptomatic Diabetes:

This stage is variously known as chemical, subclinical or subliminal Diabetes. They always show an abnormal G.T.T. but the fasting blood levels may be normal in the early stage. Later on, even these levels may be raised.

ROOPA:

Onset of *Roopas* marks the *Agama* of *Vikara* and they are usually pronounced manifestations of *Poorvaroopas.* These are characteristic of *Vyakta avastha* of a *Vyadhi* .The *Pratyatma roopas* are invariably encountered during this stage i.e., 5th kriyakala. *Acharya Gayadasa* opines that in case of *Prameha, poorvarupa* will manifest as *Rupa.* This type of manifestation is called '*Vyadhi prabhava'*. According to *Sushruthacharya,* the person should be diagnosed as Pramehi when complete or partial prodromal symptoms of *Prameha* accompanied by *prabhoota mootrata* and *avila mootrata* get manifested[115].

The *Roopas* can hence be studied under *Mootrasambandhi roopas* and Sarvadaihika roopas.

***Mootra Sambandhi Rupas*[116]:**

Mootrasambadhi roopas can be grouped into *Samanya Rupas* and *Vishishta rupas.*

A. *Samanya Roopas*:

1) ***Prabhoota Mootrata***

It is a result of *Dravaihi ekikarana* which means, there is an increased frequency of micturition with increased quantity of urine manifested due to the vitiation of *apana vayu* and increase of *Shareera kleda* respectively. It may be suggested that the *Prabhuta Mutrata* is more akin to metabolic changes. The excessive urination is due to an improper metabolism of carbohydrates, proteins and fats resulting in water and electrolytes imbalance.

2) ***Avila mootrata***

It has been described as *Samala mootra* or *Atyartha kalushita mootra*, which means, there is an abnormality in the density and turbidity of urine manifested due to *drava* and *guru guna vriddhi* of *kapha* and *medas*. *Avila Mutrata* is more akin to urinary pathology. This can be due to presence of phosphates, sugar, sperm, acetone, silicates, albumin, chyle, bile pigments and salts, blood, pus or casts etc. in the urine.

***B. VISHISHTA ROOPAS OF MADUMEHA[120]*:**

The classics describe the following *Rupas* as related to *Mootra* i.e.

- *Madhuryata*
- *Rookshata*
- *Panduta*
- *Kashayata and*
- *Madhu Sama lakshanas*

Chakrapani opines that *vata*, because of its *prabhava* converts *Madhura oja* into *Kashaya oja*. According to *Sushruta*, the urine of *Madhumehi* resembles with that of honey, as described above. Similar description is found in *Astanga hridaya* and *Astanga sangraha. Gangadhara* opines on this assertion that the *Madhura rasa* of Oja is displaced by *Kashaya rasa*. *Bhavaprakasha* clarify the controversy of the word *kashaya* as *kashaya Varna.* The implication of this term is still debatable. The presence of *madhura rasa* in *mutra* is mainly because of *ojas* in *mootra*, which can be easily understood by *pipeelika abhisarana. Rooksha guna* is due to vitiation of vata. *Pandu varnata* of *mootra* is because of *kleda dusti* which influences *Kapha* to attain more liquid state. *Madhusama mootra*

implies the colour, smell and taste of mootra similar to that of madhu. It has to be understood that along with the *samanya lakshanas madhusama mootra* is the *pratyatmaka lakshanas* of *Madhumeha*.

Sarvadaihika Rupas[121]:

The rupas of *madhumeha* can be explained in two ways a) *Sahaja prameha* b) *Apathya Nimitta*

Table No. 6: Showing the *Rupas* of *Madhumeha*

Sahaja Pramehi	***Apathyanimittaja***
*Krisha (*Asthenic*) Sthula (*obese)	*Sthula* (obese)
Ruksha (dry body)	*Snigdh*a (unctuous body texture)
Alpashi (consumes less food)	*Bahuashi* (consumes excessive food)
Bhrisha Pipasa (Excessive thirst)	*Shayyasanaswapnasheela* (likes to sit down and sleep always)
Parisaranshila (restless, always wants to wander)	*Kashyapa* has also narrated symptoms like *Gaurava* (Heaviness in the body), *Baddhata* (tightness) and *Jadata* (Steadiness, laziness). *Akasmat mutra nirgama, Makshika Akranta mutra, Shweta* and *Ghana mu*tra.

In ***Sahaja pramehi,*** the *Roopas* are interlinked as *Alpasheetva* leads to *Krushata & Rookshata* because of predominance of *vayu* as a result of *Vapavahana dushti*. These *Rupas* may be a cause for *Madhumeha* and will continue to deteriorate later as the disease progresses.

In ***Apathyanimittaja pramehi,*** the *Lakshana* like *bahvashee* leads to *snighdata* due to *kapha medo sanchaya* and sthoulya. Excess medas in sthoulya leads to reduced capacity to work as well as *alasya* hence the patient always tend to have *uttarottara shrama. Bahu ashitva* is due to desire/ nature of the individual, but later when excess *medo sanchaya* occurs, due to *margavroda samana vayu* gets aggravated causing *teekhnagni* leading to *bahu ashi*.

Shareera Madhurya: This special feature has been narrated only by *Vagbhata*. According to him, the body of *Madhumeha* patient becomes *Madhura* i.e. Sweet[122].

The *vishesha lakshanas* of individual *mehas*: According to physiochemical properties of urine, *Prameha* is divided in to 20 sub-types.

***Kaphaja Pramehas*[123]:**

01. ***Udakameha*:** - The person passes clear, whitish, cool, odorless and watery urine, in excessive quantity.

02. ***Ikshumeha*:** - The urine becomes sweet, cold, slightly viscid, turbid and resembling the juice of sugar cane.

03. ***Sandrameha*:** - The urine gets thickened, if kept overnight in a vessel.

04. ***Sandraprasadameha*:** -The character of urine manifests here partly dense and partly clear after keeping in a vessel.

05. ***Shuklameha:*** - Whitish urine is excreted and appears as if mixed with flour.

06. ***Shukrameha*:** - The person frequently passes urine, appears like white & mixed with shukra.

07. ***Sheetameha:*** - The person excretes large quantities of urine, which is exceedingly sweet and cold.

08. ***Sikatameha:*** - The person passes the urine, mixed with hard and small particles.

09. ***Shanairmeha*:** - There is Lack of force in the micturition and feels difficulty at the time of urination.

10. **Alalameha:** - There is sticky, slim and viscid urine.

***Pittaja Pramehas*[124]:**

01. ***Ksharameha*:** - The urine resembles like kshara in colour, taste and touch.

02. ***Kalameha*:** - The provocation of pitta transforms the urine as warm and black.

03. ***Neelameha:*** - The colour of the urine like the wings of jaybird and is acidic in reaction.

04. ***Lohitameha*:** - Urine smells like raw flesh, salty, warm and red in colour.

05. ***Manjishtameha*****:** - Person passes profuse quantity of urine, smells like *Manjishtodaka*.

06. ***Haridrameha***: - Urine looks like the colour of turmeric water and is pungent.

Vataja Pramehas[125]:

01. ***Vasameha*****:** -Urine mixed with fat or having the appearance of fat.

02. ***Majjameha***: - Urine mixed with majja frequently due to provoked vata.

03. ***Hastimeha*****:** -Passes excessive amount of urine without force like elephant.

04. ***Madhumeha*****:** - Passes urine, which is astringent and sweet in taste and resembles like Honey.

Pravritti of madhumehi**[126]:** Sushruta explained the pravritti of madhumehi as -

1. Gamanat Sthananichati.

2. Sthanat Asananichati

3. Asanat Shayyamichati

4. Shayanat Swapnamichati.

CLINICAL FEATURES OF DIABETES MELLITUS

The manifestations of symptomatic Diabetes Mellitus vary from patient to patient. Most often, symptoms are due to hyperglycemia (Polyuria, Polydipsia, Polyphagia), but the first event may be an acute metabolic decompensation resulting in diabetic coma. Occasionally, the initial expression is a degenerative complication, such as neuropathy, in the absence of symptomatic hyperglycemia. Typically, the clinical features of IDDM and NIDDM are distinctive.

Type I Diabetes Mellitus:

It usually begins before age 40 years. This type of Diabetes is characterized by a rapid onset, with symptoms such as Polydipsia, Polyuria, Polyphagia, loss of weight and strength. In the fulminating case, the most striking features are those of salt and water depletion i.e. loose dry skin, furred tongue, cracked lips, tachycardia, and hypotension and reduced intraocular pressure. Breathing may be deep and sighing due to acidosis, the breath is usually fetid and the sickly sweet smell of acetone may be apparent. Once the symptoms develop, Insulin therapy is required. Occasionally an initial episode of

Ketoacidosis is followed by a symptom free interval (the "honeymoon" period), during which no treatment is required.

Type II Diabetes Mellitus:

It usually begins in middle life or later. The typical patient is overweight. Symptoms begin gradually. Blurred or decreased vision due to retinopathy is found. Depression or loss of tendon reflexes at the ankles and impaired perception of vibration sensation distally in the legs indicate neuropathy. Hypertension and signs of atherosclerosis are common and may include diminished or impalpable pulses in the feet, bruits over the carotid or femoral arteries and gangrene of the feet. Signs of water and salt depletion with associated mental changes may be seen in cases with severe hyperglycemia[127].

1. Polyuria: Polyuria is due to the osmotic diuretic effect of glucose in the kidney tubules. There may be nocturia also.

2. Polydipsia: The diuresis in turn causes obligatory loss of electrolytes from the extra cellular fluid, which then causes compensatory dehydration of the intracellular fluid and hence produces Polydipsia.

3. Polyphagia: The failure of glucose utilization by the body because of deficiency and resistance of insulin produces and sends a message to the center, so digestive enzymes will be secreted more hence diabetic patient will have Polyphagia.

4. Weakness: The failure of glucose utilization, loss of electrolyte and loss of body protein Contributes to weakness.

5. Weight loss: Due to fluid depletion and the accelerated break down of fat and muscle secondary to insulin deficiency.

6. Glycosuria: Whenever the quantity of glucose entering the kidney tubules in the glomerular filtrate rises above approximately 225 mg/min, a significant proportion of the glucose begins to spill in to the urine and when the quantity increases above about 325mg/min which is tubular maximum for glucose. All the excess above this is lost in to the urine.

7. Dryness of Mouth and Throat: This is the effect of Polyuria.

8. Delayed healing of wounds: Studies in animal models of Diabetes implicate plasma glucose level greater than 200mg/dl and insulin deficiency as factor contributing to

impaired wound healing. Deficient formation of granulation tissue is one of the reasons for these findings.

9. Infections: Poorly controlled Diabetes entails increased susceptibility for skin, UTI & lung infection. Reason for susceptibility is chemo taxis and phagocytosis by polymorph nuclear leukocytes is impaired. Other reason may be reduced cellular immunity & poor blood supply to the vascular involvement.

SAMPRAPTI OF *MADHUMEHA*

Samprapti means the detailed description of all the morbid process that takes place in different stages of the disease to produce the anatomical and physiological changes in the target organs leading to the expression as a disease. That means, the evolution of a disease process from the beginning of *dōsika* vitiation caused by etiological factors and in the manifestation of signs and symptoms or in other words mutual interaction of *nidana, dosha, dooshya* under the influence of *prakrithi, desha, kala* & *bala* is the prime factor for the manifestation of disease. *Madhumeha* is considered as *Mahagada* and an *Anushangi Vyadhi*. This is because in *Madhumeha, Vyadhikshamatva* is the major factor. The *Charakacharya* introduced the concept of *Vikara Vighata Bhava Abhava Vishesha* in *Prameha Nidana*[128]. *Bala* derived from *Ojus* Characterizes *Vikara Vighata Bhava* and its deficiency characterizes *Vikara Vighata Abhava*. Hence the study of the involvement of *Ojas* in the disease warrants a top priority.

Ojas: *Ojas* plays an active part as *Dushya* in the *Samprapti* of *Madhumeha*.

Sushruta has mentioned that *Ojas* is a supreme extract of all the *Dhatus* & strength of the body. *Charaka* mentions that life depends on *Ojas* and therefore without *Ojas* one cannot live. Such *Ojas* remains in the heart and called as S*hareera Rasa Sneha*[129]. In the commentary *Chakrapani* has described two varieties of *Ojas* i.e., *Para* and *Apara Ojas. Para Ojas* is supreme and remains in the heart, while its *Pramana* is *Ashta Bindu. Apara Ojas* is of *Ardha Anjali Pramana* which is also called as *Shleshmika Ojas i.e. Shareera Bala*. Further *Chakrapani* explained that, in *Madhumeha Apara Oja Kshaya* occurs, which is *Sleshmika* in nature and not the *Para Ojas Kshaya*.

Pathological conditions regarding *Ojas* are of 3 types[130].

Ojokshaya - Murcha, Mamsa Kshaya, Moha, Pralapa, Marana

Ojovisramsa – Sandhi Vishlesha, Gatra Sada, Dosha Chyavana and *Kriyaasannirodha, Ojovyapath –Sthabda Gurugatrata, Vatashopha, Varna Beda, Glani, Tandra, Nidra*

1. Ojokshaya – *Murcha, Mamsa Kshaya, Moha, Pralapa, Marana***.**

In *Madhumeha Ojas* is excreted through the Urine leading to *Oja Kshaya,* so the symptoms of *Oja Kshaya* like *Murcha, Mamsa Kshaya, Moha* may manifest.*Vagbhata* has mentioned some additional symptoms of *Oja Kshaya* like *Bibheti* (excessive fear) *Abhikshna Daurbalya* (excessive weakness), *Vyathita Indriya, Rukshata* etc[131] .

In *Madhumeha* though the pathology regarding *Ojas* is of *Kshaya* nature, the other two pathological conditions may also be met with; if the *Samprapti* remain unbroken for prolonged period with continuous *Nidana Sevana* or due to improper treatment. Hence the pathological aspect of the *Ojas* is very necessary to be observed to know the severity of the disease.

The extent of this *Dosha Dushya Sammurchana* is dependent on the *Vikara Vighata Bhava* and its *Abhava. Ojas* is an important *Vikara Vighatakara Bhava* and one of the main *Dushya* in *Madhumeha,* which is eliminated through *Mutra* leading to *Dhatu Kshaya*. Hence *Madhumeha* is also called "*Ojomeha"*.

According to *Sushruta,* the excessive indulgence in the etiological factors related to *Prameha* results into *Aparipakva Vata, Pitta, Kapha* and *Meda,* which further proceed downward through the *Mutravaha Srotasa* to get localized at *Basti Mukha* and thus leading to disease *Prameha*[132]. *Sushruta* also asserted that, if all the *Pramehas* are treated improperly or ignored get terminated into *Madhumeha*[133]. Excessive *kleda dushti* leads to *ati mutra pravritti*. If further *mamsa* gets vitiated it ends up in *mamsa pidaka utpatti.*

Vagbhata narrated pathogenesis of *Madhumeha* very concisely. He indicated two types of pathogenesis i.e.

1) *Dahtukshayatmaka*

***2) Avaranatmaka*[134]**

Further, Vagbhata interpreted that in all types of *Prameha,* the *Dosha* and *Dushya* remain same but still the difference in *Mutra Pravritti* is due to specific type of *Samyoga* between specific *Dosha* and *Anukula Dushya*. *Vata vrudhi* in the disease produce due to two causes, where in the *Avarana* pathology produces the symptoms of the vitiated

Doshas in the *animitha* form (variable). The symptoms may sometimes very severe and sometimes mild[135].

Charaka has explained the pathogenesis in a detailed manner i.e.

1) *Samanya Samprapti of prameha*

***2) Vishesha Samprapti of Prameha*[136],[132]**

The later texts such as *Yogaratnakara, gada nigraha, bhavaprakasha, vangasena* and *Madhava Nidana* have followed the description of *Charaka Samhita* in explaining *saamanya samprapti*. But, in *Harita Samhita, Kashayapa, Bhela* and *Sharangadhara Samhita*, the description of *Samanya Samprapti* of *Prameha* is not present. *Vangasena* has mentioned the samprapti similar to *Vaghbatta*.

Samanya Samprapti

Charaka has mentioned *Prameha Samanya Samprapti* elaborately in *Nidana Sthana*[137]. It is explained on the basis of *Shatakriyakala*.

1. *Sanchaya*: The excessive indulgence in *Nidana Sevana* of *Guru, Snigdhadi Ahara* and *Avyayamadi Vihara* leads to *Kapha Dosha Sanchaya*.

It is important to mention that the *Kapha Dosha*, which gets *Sanchita* here, is having the quality of *Bahudravatva*[138]. In *Prakritavastha*, the *Kapha* remains in *Baddha* form i.e; solid form, but due to *Nidana Sevana* its *Prakrita Baddha* form changes to *Dravatva* form & that too in excess amount i.e. *Bahudravatva*.

2. *Prakopa*: These three factors *Nidana, Dosha* and *Dushya* get combined together in such a precise way that they lead to *Prakopa* of *Bahudrava Kapha* rapidly to form *Prameha* in future[115]. The *Bahudrava Kapha Dosha* is prone to develop *Prameha* and as it is already present in excess quantity from the beginning, hence it gets aggravated rapidly when the *Anukula Nidanas* are continued. This type of *Anukulatva* may be seen in person having *Kaphaja Prakriti* and who are having genetic predisposition for *Prameha*.

3. *Prasara:* In this stage, the provoked *Kapha* gets spread all over the body owing to *Sharira Shaithilya. Sharira Shaithilya* being one of the *Anukula* factors for *Nidana* towards the *Dosha.*

4. *Sthana Sanshraya:* *Vikrita Kapha* has affinity towards *Bahu-Abaddha Meda* due to their similar properties and gets lodged there. *Vikrita Kapha* after combining with *Bahu-*

Abadhdha Meda causes its vitiation[132]**.** The other important Dushyas are *Sharira Kleda* and *Mamsa,* which are already increased in large quantity, prior to vitiation of *Kapha*. The provoked *Kapha* with vitiated *Meda* gets combined with *Sharira Kleda or Mamsa or* both. This is an important stage because the prodromal symptoms of the disease are manifested in this stage. It is essential to diagnose the disease at this stage to prevent further progress of the disease for better prognosis[137]**.**

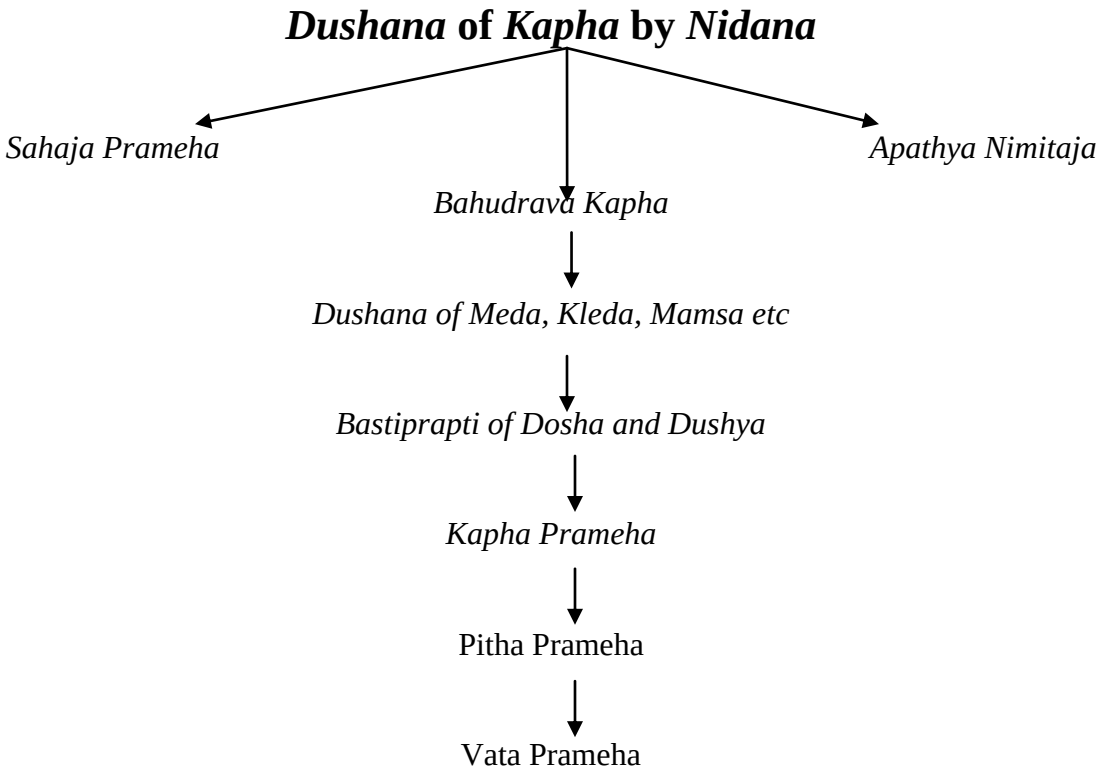
5. *Vyakta*: In this stage of *Vyaktavasta*, two types of manifestation will occur:

i. *Mutravaha Srotodushti* due to *Sharira Kleda Dushti* – When vitiated *Kapha* and *Meda* comes in contact with *Sahrira Kleda* and vitiates it, producing *Mutradushti.* The vitiated *Kapha* settles in *bastimukha* which are already filled with vitiated *Meda* and *Kleda*, thus producing the disease *Prameha.*

ii. *Puti Mamsa Pidika* due to *Mamsa Dhatu vitiation* – The vitiated *Kapha* and *Meda* combines with *Mamsa Dhatu* leading to *Puti Mamsa pidika*.

The above two manifestations of *Kleda* and *Mamsa Dushti* will occur simultaneously or in two stages[137].

6. *Bheda:* In this stage various complications of the disease manifest and the disease progresses towards Asadhyadta i.e. the disease becomes incurable. The Prameha disease attains *Sthairya* (stability) and *Asadhya* (incurability) status because of its *Prakriti* and *Vikriti*[137].



Flow Chart: Showing the *Samprapti* of *Madhumeha*

Vishesha Samprapti

***Kaphaja Prameha*:**

The etiological factors cause the aggravation of Kapha and this spreads all over the body rapidly due to Sharira shaithilya and then attracted by Abaddha Meda Dhatu due to similar properties, gets lodged and causes its vitiation. This combination of vitiated Meda and Kapha comes in contact with Sharira-Kleda and Mamsa, which are already in excess quantity resulting Puti mamsapidaka. Along within the vitiated Kleda gets converted into Mootra. The Kapha along with Meda and Kleda obstruct the openings of Mootravaha Srotas resulting into ten types of Kaphaja Prameha [139]. Classics explain different Dushyas in each Doshik type of Prameha and also narrated vitiation of Kapha along with Vata, Pita and Meda in Kaphaja Prameha[140].

Pittaja Prameha:

Due to its etiological factors provoked Pitta manifests as Pittaja Prameha. Here similar pathogenesis occurs as described in Kaphaja Prameha[141] depending on different properties of Pitta Dosha the Paittika Prameha develops into six types and also mentioned that the Pittaja Prameha is not entirely Paittika but it does have Pitta predominance. Raktha is also involved along with Vata, Kapha and Meda in the pathogenesis of Pittaja Prameha [140].

Vataja Prameha:

Here Vata gets provoked due to its own etiological factors and draws out Vasadi Dhatus from the body towards Mutravahi srotas resulting into four types of Vataja Prameha. When vitiated vata combines with vasa and moves into Mutravahi srotas, Vasameha is produced. When combines with lasika, Lasika meha is produced. When Mutra is expelled in huge quantity Hastimeha is diagnosed. When Oja is drawn towards Mutrashaya by the vitiated Vata, the natural Madhura Swabhava of Oja transformed into Kashaya Rasa due to the Ruksha Guna of Vata. This in turn leads to the manifestation of Madhumeha [142]

One more pathogenesis of Vataja Prameha is described in Charaka Chikitsa Sthana. Here provoked Vata along with the depletion of other two dosha (reduced in comparision to vata dosha) carries vital dhatus towards Basti, resulting into Vataja Prameha[136]. In the pathogenesis of Vataja Prameha, Kapha, Pitta, Meda, Vasa and Majja dushyas are involved[140].

1) ***Vishishta Anilatmaka Madhumeha Samprapti*****:**

"स प्रकुपित तद्विद शरीरे विसर्पान ओजः पुनर्मधुर स्वभावम तद यदा रौक्ष्यात वायुः कषायत्वेन अभिसंरुज्य मूत्राशये अभिवहति तदा मधुमेहम करोति तद्विदा शरीरे बहुद्रवश्लेष्म, बहव्बद्दमेध, बहुक्लेदयुक्त शरीर" [140]

The people who has genetic predisposition, Prakruti, or has sedentary habits, have the specific Meda Bahulyata preferably with Abaddhatva. If these patients consume excessive Vata provocative Ahara, Vihara or Mano Abhighatkara Bhava, then Vata gets provocated. This provocated Vata further gets implicated by Meda & leads to transfer of

Vasa, Majja, Lasika, Oja to Mutravaha Srotas. When Oja due to influence of Vata adopts Kashaya and Ruksha Guna and excrete through urinary tract is termed as Madhumeha.

2) *Dhatukshaya Janya Madhumeha Samprapti*:

"अपकर्षितेष्विति क्षीणेषु, क्षयस्तेषं प्रमेह आरंभकेन वातेनैव उपशोषणादिभि कर्षणाद वा क्रीयते"[143]

The Kshaya of Gambhira and Sarabhuta Dhatus like, Majja, Vasa, Oja and Lasika leads to Vata Prakopa. Vata Dosha gets vitiated leading to Ksharana of Sarabhuta Dhatus through Mutra Pravritti in such a quantity that this Ksharana of Sarabhuta Dhatus itself acts as etiological factor again for Vata Prakopa hence this vicious circle goes on. But due to Ashukaritva of Vata all the stages of Samprapti proceeds so fast that, it leads to Asadhya stage of the disease very quickly.

3) *Aprathikaritha Vatanubanditha Madhumeha Samprapti*:

This type of Madhumeha is actually not a separate entity but it is the further stage of Kaphaja or Pittaja Prameha due to Deerga Kalanubandha or this may be called as ignored stage of Prameha due to lack of proper treatment. Kaphaja and Pittaja Pramehas which are present from quite longer period they do get Anubandha of Vata due to chronicity i.e., they get converted into Vataja Prameha [142].

4) *Avarana Janya Madhumeha Samprapti*:

The description of Avarana Janya Samprapti of Madhumeha is a unique contribution of Charaka to the clinical medical knowledge. Here one can see that Nidana is same as that of Kaphaja Prameha but still the resulting disease is Madhumeha. Guru Snigdhadi Ahara, Avyayamadi Vihara etc., leads to provocation of Kapha and Pitta Dosha intern increases in quantity of Meda and Mamsa. All these increased factors obstruct the Gati of Vata leading to provocation of Vata. This provocated Vata withdraws Oja from the body and takes it towards Basti and leads to Madhumeha, which is Krichhrasadya for treatment due to its origin from Kapha and Pitta Doshas. The Vata, Pitta and Kapha Doshas start manifesting their symptoms intermittently depending on their extent of Dushti. Subsequently Pitta and Kapha attain Kshayavastha compared to Vata; due to Kshaya of Dhatus.

Samprapthi ghataka's

Dosha:

'वात पित्त भेदो भिरन्वितः श्लेष्म मेहान जनयति'[140]

Madhumeha is a tridoshaja vyadhi where sleshma has an important role of initiating the pathogenesis.

Sleshma: Sleshma is the mala of rasa dhatu. When a person indulges in Sleshmakara ahara vihara as in Madhumeha, which inturn causes jatragni mandhya leading to asamyak ahara parinama and formation of aparipakva sleshma. Dalhana commented on this: - 'aparipakva' as '**aparipakvaha amaha**'

The prakritha or paripakva sleshma is Ghana & sthira in nature and aparipakva is aghana. Chakrapani commented on sthira as 'ashaitilya', likewise asthira is shaitilya yuktha. This is the reason for shaitilyatha in the body of madumehi. Sharangadhara in kaphaja natmaja vikaras has mentioned bahumootrata, so it can be inferred that the apakva sleshma is one of the contributing factor for bahu mootrata. From the aetiological factors also its clear that kapha is the primarily & predominatly vitiated dosha [115] vitiates samana guna yuktha meda, mamsa, kleda, vasa, rasa & lasika and cause symptoms like shaitilya, alasya, atinidra gaurava, bahumootrata in madumehi.

Pitta:

A. *Vrudha*-in *Avaranjanya Madhumeha*

B. Kshina- in *Dhatukshayajanya Madhumeha*

Status of *Pitta Dosha* is *Vrudha* in *Avaranjanya Madhumeha*. In this state due to respective *Nidana, Vrudhi Lakshanas* will be manifested. In *Dhatukshayajanya Madhumeha, Vata dosha* is in the *Kupitha* state, so lakshanas related to *Pitta Dosha Vikruthi* and *Vata Dosha* is quite evident clinically.

Kshudha Adhikata, Atisweda etc. like *Pitta Vrudhi lakshanas* are evident in *Avaranajanya Madhu*meha and *Mandagni, Prabhahani* etc. like *Pitta Kshaya lakshanas* are found in *Dhatukshayajanya Madhumeha.*

Vata:

A. Avruta- in Avaranjanya Madhumeha

B. Vrudha-in Dhatukshayajanya Madhumeha

It possesses Gati and Yogavahi Svabhava. In Madhumeha the provocation of this dosha occurs in two ways i.e. Margavarodha and Dhatukshaya .This vitiated dosha then carries the vital dhatus like Vasa, Majja, Lasika and Oja to basti and results Madhumeha.

Role of Vyana and Apana [144]:

It is described that Vyana and Apana are the main culprits in Prameha-Madhumeha. Vyana being pervaded all over the body and Apana in Vankshana, Vyana acts as the collector of Kleda and Apana as Excretor. The provoked vata carries the dushyas like Vasa, Majja and Ojas towards Basti and excretes through urine. Again the excretion of dushyas exaggerates vata provocation and hence the vicious cycle goes on.

Dooshya: Charaka in chikitsa & nidana sthana explains the **ten** dooshya's. These are bahu abadha medas, raktha, shukra, ambu, vasa, lasika majja, rasa, oja, mamsa. Sushruta included the dooshya while explaining each type of prameha, vagbhatta included sweda as a dooshya.

Rasa: Apart from medas, this is another dhatu which is vitiated, because of close resemblance 'Raso api sleshmavath'[145]. Sushruta has explained **'रस निमित्तमेव स्थौल्यं कार्श्यं च'** Sthaulya and karshya are both found in Madhumeha, which shows the role of rasa in madumeha as a dooshya. Vitiated rasa shows manifestations like alasya, gaurava, klaibya & Agni nasha in context with Madhumeha.

Raktha: It mainly gets vitiated in pittaja prameha & plays a role in complications like pidaka, vidradi[146].

Mamsa: Mamsa & kapha have similar qualities, they both give strength to body. When it gets vitiated it looses its normal consistency and produce shaitilyatha. As an upadrava there is also production of pooti mamsa[147].

Medo dhatu: Medas is the dominant dooshya in the pathogenesis of Madhumeha. Medas & kapha are having samana guna due to which the same aetiological factor can do vriddi of both. Medo dhatu undergo vriddi qualitatively and quantitatively.Qualitatively in terms of abaddha medas. One of the karma of medo dhatu is to provide dhridatha to body, due

to this abaddhata there will be resulting shaitilyatha as it is unable to do its prakritha karma i.e. giving dridatha to body. The quantitative factor is the bahutha of medas. This vriddha medas along with kapha obstructs the srotas leading to vata vriddi; this vriddha vata ignites the Agni which is the cause for kshuda, so the patient eats more and more food causing excessive depletion of abaddha medas. Sthoulya where meda dhatu is the main culprit also exhibits ashta doshas which is also found in sthoola mehi showing the predominant role of medas as dooshya.

Majja dhatu: Majja is not vitiated much. It's thrown out of the shareera along with mutra causing its kshaya. This is one of the reasons why a madhumehi has klaibyatha[148].

Sukra dhatu: Shukra dhatu is responsible for deha bala. Sukra also gets vitiated in the pathogenesis producing symptoms like daurbalya & kruchra vyavayatha. Sushrutha has told that sukra dosha & prameha get precipitated due to vitiation of apana & vyana vata[144]**.** Thus one can easily understand the close relation of sukra dushti in madumeha.

Ojas: Ojas ie apara ojas is mainly vitiated in Madhumeha. Provoked vata due to its own aetiological factor or due to avarana carries ojas towards vasti and excrete through urine[149]. So the symptoms of ojo kshaya manifests like guru gatrata nidra tandra & daurbalya[150].

Kleda: The physiology of kleda is related with mutra, sweda & meda. Here bahu kleda causes shaitilyatha of dhatus and bahu mootrata.

Sweda: Sweda is mainly related with meda and kleda. Sweda vaha sroto dushti manifests as ati sweda, dauragandhya, pichila gatrata, snigdha gatrata. Sushruta mentions about the sweetness of sweda in Madhumehi[151].

Lasika: This is one of the liquid materials of body, present just beneath the skin. Lasika also get vitiated by vata resulting lasikameha. There is no direct reference related to vasa and lasika dushti.

Agni: There is no direct reference related to the avastha of Agni but both Agnimandya and tikshna Agni conditions are present in the pathogenesis.

Ama: Sushruta has illustrated the role of Ama in the pathogenesis of various disorders. He mentions that the Samprapti of Prameha takes its origin from the Aparipakva i.e. ama only. He states that is from the very beginning, Agnimandya has been developed due to Guru, Snigdhadi Ahara and Avyayamadi Vihara which leads to production of Ama.

Dalhana adds that not only Dosha but Meda Dhatu is in the ama form. Ama means Aparinamittaja. Anything which remains in undigested form, being harmful to the body is Ama.

***Srotas*:** In the *Samprapti* of *Madhumeha* there is reference of Mutravaha srotas, understood that there is also involvement of *Medovaha*, *Mamsavaha*, Swedavaha and Udakavaha Srotodushti. We can find out the Srotasa involvement according to the symptoms as follows

(1) Mutravaha Srotodushti - Prabhuta Avila Mutrata

(2) Medovahasrotodushti - Purvarupa of Prameha, Snigdhagatrata etc

(3) Mamsavaha Srotodushti - Putimamsapidaka

(4) Udakavaha Srotodushti - Pipasa, Mukha-Talu-Kantha Shosha.

Sroto dushti prakara: *Sanga, vimarga gamana, ati pravrutti.*

Udbhava sthana: *Amashaya, as it is the kapha sthana.*

Sanchara sthana: *Sarva shareera,* though pratyatma lakshna can be seen in mutra vaha srotas, as there is involvement of almost all dhatus and sarva daihika lakshana's are seen. So sarva shareera can be considered as *sanchara sthana*.

Vyaktha stana*: mutra vaha srotas*

Adhishtana*: Medovaha srotas*

Roga marga: *Trividha roga marga*

Vyadhi Svabhava: *Chirakari, Anushangi*.

Pathophysiology of NIDDM:

Three factors namely **insulin resistance**, **β cell dysfunction** and **HGO** underline the major defects which constitute the endocrine and metabolic profile subjects with NIDDM.

Peripheral insulin resistance

Insulin resistance is a metabolic state in which a normal concentration of insulin produces a less than normal biologic response. This decreased response to insulin can involve any of the multiple metabolic effects of insulin, but from the stand point of relevance to type 2 diabetes, resistance to insulin's effects on glucose metabolism have

been the most extensively studied. Because, the Insulin travels from the β cell through the circulation to the target tissue, events at any of these loci can influence the ultimate action of the hormone.

In general, insulin resistance can be due to

(1) An abnormal beta cell secretory product

(2) Circulation insulin antagonists

(3) Impaired access of insulin to target cells

(4) A target tissue defect in insulin action.

Abnormal β cell secretory product

Several patients have been described who secrete a structurally abnormal, biological defective insulin molecule resulting from a mutation in the structural gene for insulin. Others have familial hyperproinsulinemia caused by incomplete conversion of proinsulin to insulin within β cell secretory granule as a result of structural abnormalities at the proteolysis cleavage sites of the proinsulin molecule. Thus in these patients, they are resistant only to their endogenous insulin and not to exogenous insulin.

Circulating insulin antagonist

In general, insulin antagonists may be hormonal or nonhormonal.

HORMONAL ANTAGONISTS:

Hormonal antagonists include all the known counter regulatory hormones such as cortisol, growth hormone, glucagon and catecholamines. Islet amyloid polypeptide (IAPP), which is co-secreted with insulin from islet β cells, was found to inhibit insulin stimulated glucose uptake when pharmacologic doses were infused.

NONHORMONAL ANTAGONIST:

Free fatty acids-A number of years ago, Randle et al hypothesized that the elevated circulating level of free fatty acids (FFAs) found in obesity and Type 2 Diabetes impair peripheral glucose utilization. Substantial evidence indicates that FFA's may indeed contribute to insulin resistance, FFA's also play an important role in the regulation of HGO and may contribute to hepatic insulin insensitivity in obesity and type 2 diabetes.

Anti-Insulin Antibodies: Anti-insulin antibodies develop in essentially all patients treated chronically with insulin. By binding and trapping insulin within the plasma compartment, these antibodies can alter the usual time course of insulin action.

Insulin Receptor antibodies: A fascinating syndrome (type B insulin resistance) in which patients has antibodies directed against the insulin receptor.

Cytokines: Increased levels of cytokines such as tumor necrosis factor-α may contribute to the insulin resistance. TNF α have major effects on glucose and lipid metabolism.

Impaired Access of Insulin to Target Cells

Because insulin must travel from the circulation to target tissues to elicit biologic effects, any defect in this transfer could potentially lead to insulin resistance. The passage of insulin from the plasma compartment to tissue sites of action is marked by substantial delays, and insulin's in vivo effects to stimulate glucose disposal are well correlated with the appearance of insulin in the interstitial fluid. Lymph insulin levels are lower than those in plasma, which indicates that peripheral tissues are more sensitive to insulin than previously recognized. Furthermore, the possibility arises that either the rate or the amount of insulin transferring from the plasma to the interstitial compartment could be abnormal in type 2 diabetes.

Cellular Defects in insulin Action: Available evidence points to a target tissue defect as the major cause of insulin resistance in type 2 diabetes. Any defects in the mechanism of insulin propagation downstream from the activated insulin receptor to the various insulin-regulated enzymes, transporters, & insulin responsive genes to mediate its metabolic growth effects. If there is any alteration in theses mechanisms, it will lead to insulin resistance.

β- CELL DYSFUNCTION:

B-cell dysfunction in Type 2 Diabetes reflects the inability of these cells to adapt themselves to the long-term demands of peripheral insulin resistance and increased insulin secretion. In states of insulin resistance, insulin secretion is initially higher for each level of glucose than in controls. This hyperinsulinemic state is a compensation for peripheral resistance and can often maintain normal plasma glucose for years. Eventually, however, beta cell compensation becomes inadequate, and there is progression to overt diabetes. The underlying basis for failure of β cell adaption is not known although it is postulated that several mechanisms, including adverse effects of high circulating free fatty acids i.e. lipotoxicity or chronic hyperglycemia i.e. glucotoxicity may play a role, β

cell dysfunction in Type 2 Diabetes manifests itself as both qualitative and quantitative defects.

Qualitative β cell dysfunction is initially subtle, and seen as loss of the normal pulsatile, oscillating pattern of insulin secretion and attenuation of the rapid first phase of insulin secretion triggered by an elevation in plasma glucose.

Quantitative β cell dysfunction is reflected by a decrease in β cell mass, islet degeneration, and deposition of islet amyloid.

HGO (Hepatic Glucose Output):

A second metabolic stage is at the level of liver. One of the normal roles played by insulin is to promote hepatic storage of glucose as glycogen & suppress gluconeogenesis. In type 2 DM as a part of insulin resistance by peripheral tissues. Liver also shows insulin resistance i.e. in spite of hyperglycemia in the early stage of disease, gluconeogenesis in the liver is not suppressed. This results in increased hepatic synthesis of glucose which contributes to hyperglycemia. Subject with IGT have normal basal rates of HGO where as patients with fasting hyperglycemia have increased HGO, thus the capacity of liver to over produce glucose is an important contributory factor to the pathogenesis of type 2 DM.

Descriptively three phases can be recognized in the usual clinical sequence. In phase I, glucose levels are normal only because hyperinsulinemia compensates for the insulin resistance in muscle, liver and possibly other tissues. In phase II, insulin levels are somewhat diminished but are generally still higher than in individuals who are not diabetic. On the other hand the insulin levels in phase II are no longer sufficient to enhance glucose utilization by muscle and or restrict hepatic glucose production and postprandial glucose levels are increased as a result. Finally in phase III, plasma insulin levels fall even further as a result hyperglycemia occurs both in the fed and fasted states.

Pathogenesis of Type 1 Diabetes Mellitus

This type of Diabetes results from autoimmune destruction of β cell. Three interlocking mechanisms are responsible for the islet cell destruction. They are Genetic susceptibility, autoimmunity and an environmental factor. Genetic susceptibility is linked to specific alleles of the class II major histocompatability complex and other genetic loci that predispose certain persons to the development of autoimmunity against β-cell cells of

islets. The autoimmune reaction may develop spontaneously or is enhanced by an environment event like viral infections that alters β-cell cells, rendering them immunogenic. Overt Diabetes developed appears after most of the β- cell cells have been destroyed [152].

Pathogenesis of Type 1 Diabetes Mellitus as below:

Genetic Susceptibility
- Concordance in identical Twins 50%
-Susceptibility gene on HLA Region in chromosome 6

↓

Environmental factors
-Viral Infection
-Experimental induction With chemicals
-Geographic & seasonal variations
-Bovine milk proteins

↓

Autoimmune factors

1. Islet cell antibodies Insulitis
2. CD8+ T lymphocyte mediated selective destructon of beta cells

↓

Type 1 DM

Genetic factors
- Concordance in identical twins 80%
- Both parents diabetic 50% risk to the child

↓

Decreased insulin secretion
-Amylin
- Glucose toxicity of islets
- Lipotoxicity

↘

Constitutional factors
- Obesity
- Hypertension
- Low physical activity

↓

Insulin resistance
-Receptor & post Receptor defects.
- Impaired glucose utilization

↓

Increased hepatic glucose synthesis

↓

Hyper glycaemia

↓

Type 2 DM

FlowChart: Showing the Schematic Mechanisms Involved In Pathogenesis of Two Main Types of Diabetes Mellitus

CLASSIFICATION OF MADHUMEHA:

1. Classification based on Nidana (Etiology)

The root cause of disease has enough importance for the prognosis and treatment of the disease. The occurrence of Madhumeha according to this point of view is of two types [121].

A) Sahaja [Heriditary]

B) Apathyanimittaja [Acquired]

A) Sahaja

Sahaja Prameha occurs as a result of Beejadosha i.e. genetic origin. While describing prognosis, Acharya Charaka has narrated that Prameha or Madhumeha occurring due to Beeja dosha is incurable.

B) Apathyanimittaja

Apathyanimittaja type itself suggests its etiology. It occurs due to Ahitahara. On analyzing the Samprapti, Apathyanimittaja Madhumeha is of two types.

a) Santarpanjanya:

Santarpanjanya Madhumeha is due to intake of nutritious diet, which is having Kaphavardhaka properties. The excess intake of such substances will primarily lead to the vitiation of Kapha, Pita, Meda and Mamsa, which in turn cause Madhumeha by doing avarana of vata [149].

b) Apatarpanjanya:

If the substances which deplete the dhatu and aggravate vata are consumed then it leads to Apatarpanjanya Prameha. They act through vitiation of vata which in turn leads to the manifestation of Madhumeha.

2. Classification based on Dosha [Clinicopathological classification] [131]:

Twenty types of Prameha have been described by the different authors of Ayurvedic Classics. Among these, 10 are of Kaphaja type, 6 are of Pitaja type and 4 belong to Vataja type. They are enlisted below,

Table No.7: Showing the Classification of Prameha according to Doshas

Types	Charaka	Sushruta	Vagbhata	Madhava
Kaphaja Meha				
Udakameha	+	+	+	+
Ikshuvalikameha	+	+	Ikshumeha	Ikshumeha
Sandrameha	+	+	+	+
Sandraprasadameha	+	Surameha	Surameha	Surameha
Shuklameha	+	Pishtameha	Pishtameha	Pishtameha
Shitameha	+	Lavanameha	+	+
Sikatameha	+	+	+	+
Shanairmeha	+	+	+	+
Alalmeha	+	Phenameha	Lalameha	Lalameha
Shukrameha	+	+	+	+
Pitaja Meha				
Ksharameha	+	+	+	+
Kalameha	+	Amlameha	+	+
Nilmeha	+	+	+	+
Lohitameha	+	Shonitameha	Raktameha	Raktameha
Manjishtameha	+	+	+	+
Haridrameha	+	+	+	+
Vataja Meha				
Vasameha	+	+	+	+
Majjameha	+	Sarpimeha	+	+
Hastimeha	+	+	+	+
Madhumeha	+	Kshoudrameha	+	+

3. Classification based on Samprapti:

According to mode of Samprapti Prameha especially Madhumeha can be classified in to two types.

a) AvaranjanyaMadhumeha[154]

In Avaranjanya Madhumeha, Kaphavardhaka Nidanasevana leads to vata avarana, which in turn leads to Ojas Karshana which comes to the basti and patient passes Madhura, Kashaya, and Ruksha Mutra, which is said to be Madhumeha.

b) DhatukshayajanyaMadhumeha [155]

In Dhatukshayajanya Madhumeha, due to Vatavardhaka nidana, Vataprakopa occurs and the Madhuratva of Oja is displaced by Kashaya rasa and it is brought to the basti leading to Madhuvat Mutratyaga, leading to Madhumeha.

4. Prognostic Classification[156]:

Prognosis is an inevitable part of Chikitsa so far as a wise physician is concerned. Success of treatment depends on an unbiased prognosis. On the basis of the prognosis we can classify Prameha as follows.

Table No.:08 Showing the Sadhya Asadhyata of Prameha

Sadhya	**Yapya**	**Asadhya**
Kaphaja	Pitaja	Vataja
Sthula (Obese)	Usually not much obese	Krusha (Asthenic)
Apathyanimittaja (Acquired)	Acquired	Sahaja (Heriditary)
Early Stage	Acute Stage	Advanced Stage
Without complication	With Complication	with Complication

5. Classification of Prameha- based on physique[157], [121]:

Clinicopathological status of a disease has an invariable relation with physical constitution of the body in Madhumeha. This has to be taken into consideration when treatment is formulated. According to this, in Ayurveda, Madhumeha is of two types.

a) Sthula b) Krusha

6. According to Bhela Samhita[158] there is one more type of classification i.e.

a. Prakruti pabhava
b. Narasya swakrita.

Classification of Diabetes Mellitus: [As Per American Diabetes Association [159]:

I. **Type 1 Diabetes Mellitus** - 10% (Insulin dependent or juvenile onset Diabetes)
   Type 1A DM: Immune mediated
   Type 1B DM: Idiopathic
II. **Type 2 Diabetes Mellitus** - 80% (Non insulin dependent or maturity onset diabetes)
   a. Predominantly insulin resistance
   b. Predominantly insulin secretary defects
III. **Other specific types**
   A) Genetic defect of beta cell function
      a) Chromosome 12, HNF – 1 Alpha (MODY 4)
      b) Chromosome 07 Glucokinse (MODY 2)
      c) Chromosome 20 HNF 4 Alpha (MODY 1)
      d) Mitochondral DNA
      e) Others
   B) Genetic defects in insulin action: -
      Type 4 insulin resistances, Leprechaunism, Rabson Mendenhall Syndrome, Lipoatrophic Diabetes and others.
   C) Disease of exocrine pancreas: - Pancreatic pathology
      a) Pancreatitis
      b) Hemochromatosis

c) Fibrocalculous

d) Neoplastic Disease

e) Pancreactetomy

f) Cystic fibrosis and others.

D) Iaotrogenic: - Drug induced or chemical induced.

a) Glucocorticoids

b) Thiazides

c) Alpha – Interferon

d) Thyroid Hormone

E) Endocrinopathies: - Endocrine disease induced.

a) Cushing's Syndrome

b) Acromegaly

c) Thyrotoxicosis

d) Phaeo chromocytoma

e) Glucogonoma.

F) Infections: -

a) Congenital rubella

b) Cytomegalo virus and others

G) Other genetic syndromes sometimes associated with diabetes.

a) Dawn's syndrome,

b) Klenefelter's syndromes etc.

H) Gestational Diabetes Mellitus (GDM)

UPADRAVAS[147],[160]

Table No. 09: Showing the Samanya Upadravas of Prameha

Sl.No.	Name	Charaka	Bhela	Sl.NO.	Name	Ch	Bhela
1.	Trishna	+	+	10.	Aruchi	+	+
2.	Atisara	+	-	11.	Avipaka	+	-
3.	Jwara	+	-	12.	Angamarda	-	+
4.	Daha	+	-	13.	Kasa	-	+
5.	Putimamsa	+	-	14.	Bhrama	-	+
6.	Pidaka	+	+	15.	Shula	-	+
7.	Alaji	+	-	16.	Kandu	-	+
8.	Vidradi	+	-	17.	Tama	-	+
9.	Dourbalya	+	-				

Table No.10: Showing the Kaphaja meha Upadravas[161]

Sl.No.	Name	Su/YR	AH/BP	AS
1	Avipaka	+	+	+
2	Aruchi	+	+	+
3	Chardi	+	+	+
4	Nidradhikya	+	+	+
5	Kasa	+	+	+
6	Peenasa	-	+	-
7	Alasya	+	-	-
8	Makshikopasarpana	+	-	-
9	Mamsopachaya	+	-	-
10	Pratishyaya	+	+	+
11	Shaithilya	+	+	+
12	Kaphapraseka	+	-	-
13	Shwasa	+	-	-
14	Praseka	-	+	+

TableNo. 11: Showing the Pittaja meha Upadravas[162]

Sl.No.	Name	Su/YR	AH/BP	AS	Sl.No	Name	Su/YR	AS
1	Basti-mehana toda	+	+	+	9	Arochaka	+	-
2	Mushkavadarana	+	+	+	10	Vamathu	+	-
3	Jwara	+	+	+	11	Nidranasha	+	-
4	Daha	+	+	+	12	Panduroga	+	+
5	Trishna	+	+	+	13	Peeta vinmutra	+	-
6	Murcha	+	+	+	14	Hritshula	+	-
7	Vidbheda	+	+	+	15	Paridhumayana	+	-
8	Bastibheda	+	-	-	16	Amlodgara	+	+

Table No.: 12 Showing the Vataja meha Upadravas[162]

Sl.No.	Name	Su/YR	AH/BP	AS	Sl.No	Name	Su/YR	AH/BP	AS
1	Udavarta	-	+	-	7	Stambha	+	-	-
2	Kampa	+	+	+	8	Shula	+	+	+
3	Hridgraha	+	+	+	9	Baddhapureesha	+	-	+
4	Shosha	-	+	+	10	Rasalolupata	+	-	+
5	Kasa	-	+	+	11	Nidranasha	+	+	+
6	Shwasa	-	+	+					

Prameha pidakas:

If the disease (Madhumeha) is not treated or neglected, then it causes serious types of pidakas in subcutaneous, muscular area, vital parts and joints of the body. Hence pidaka can be termed as upadrava of Madhumeha[147].

There are difference of opinions among the acharyas, regarding the number and names of pidakas. They are as follows.

Table No. 13 showing the Prameha pidakas[163]

Sl.No.	Name	Charaka	Sushruta	B.P/A.H	Bhoja
1.	Sharavika	+	+	+	+
2.	Kacchapika(Kurmika)	+	+	+	+
3.	Jalini	+	+	+	+
4.	Sarshapi	+	+	+	+
5.	Alaji	+	+	+	+
6.	Vinata	+	+	+	+
7.	Vidradhi	+	+	+	+
8.	Putrini	-	+	+	+
9.	Masurika	-	+	+	-
10.	Vidarika	-	+	+	+
11.	Kulattika	-	-	-	+

Complications Of Diabetes Mellitus[164]:

Complications of Diabetes Mellitus fall into two major divisions i.e. Acute Complications and Chronic Complications. The complications resulting from the disease are associated with the damage or failure of various organs such as the eyes, kidneys and nerves.

Acute Complications:

Diabetic Ketoacidosis and Non Ketoic hyperosmolar state are the acute complications.

Chronic Complications:

(1) Macrovascular Complications:

- Coronary artery disease.
- Peripheral Vascular disease.
- Cerebro vascular disease.

(2) Microvascualar Complications:

- **Diabetic Eye disease**
  - Retinopathy (non-proliferative/proliferative)
  - Macular edema
  - Glaucoma
  - Cataracts
- **Diabetic Neuropathy**
  - Poly neuropathy /mono neuropathy
  - Autonomic neuropathy.

(3) Other

- Gastro intestinal [gastroparesis, diarrhoea]
- Genito urinary [uropathy /sexual dysfunction]
- Dermatologic infections.
- Diabetic foot.

(A) Acute Complications:

- **Diabetic Ketoacidosis [DKA]:**

Ketoacidosis is one of the most serious metabolic complications of diabetes, even if managed properly. It can be developed for individuals with type1 DM.The prognosis substantially worsened at the extremes of age and in the presence of coma and hypotension.

Clinical Features: Nausea, vomiting, thirst, polyuria, abdominal pain, altered mental function are the clinical features of DKA.

Physical Findings:

Tachycardia, Dry mucous membranes, reduced skin turgor, Dehydration, hypotension, Tachypnea, Kussmaul respirations, respiratory distress, abdominal tenderness, Fever, Lethargy, Obtundation, Cerebral edema and possibly coma are the physical findings of DKA.

Precipitating Factors:

Infection, Cerebrovascular Accident, Myocardial infarction, Alcohol abuse and discontinuation of or inadequate insulin is the main precipitating factors for DKA.

Treatment:

Correction of dehydration, hyperglycemia and electrolyte imbalances is the treatment modalities for DKA. Identification of precipitating factor and frequent patient monitoring are also important.

Non Ketoic Hyperosmolar State:

Clincial Features:

Polyuria, Orthostatic hypotension, Lethargy, Altered mental status, Obtundation, Seizure and Coma is the clinical features of NKHS.

Physical Findings:

Dehydration, Hyperosmolality, Hypotension, Tachycardia and Altered mental status are the main physical findings of NKHS.

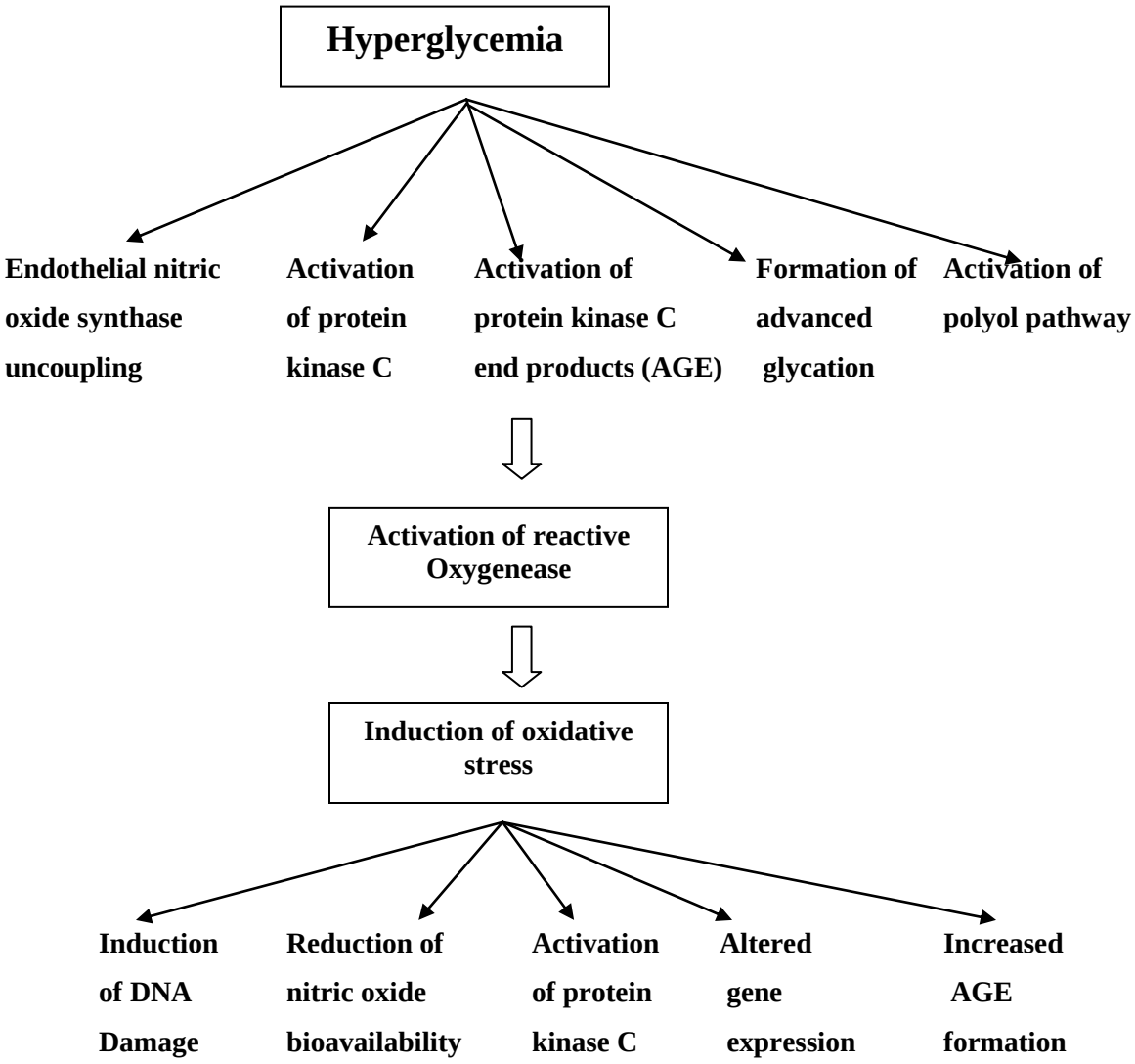
Precipitating Factors:

Concurrent illness such as myocardial infarciton, stroke, sepsis, pneumonia, debilitating conditions like dementia are found to be the main precipitating factors for NKHS.

Treatment:

Correction of dehydration, Insulin administration and Frequent Patient Monitoring are the treatment modalities.

(B) Chronic Complications[165]:



Flow Chart: Showing the Mechanism of developing chronic complications

Three theories have been proposed for the mechanism of complications:

The possible mechanism of complication is yet to be elucidated. One hypothesis proposes that increased intracellular glucose leads to inceased sorbitol which arise a polyol pathway. Some glucose converts into sorbitol by aldose reductase. Increased sorbitol concentrations leading to cellular dysfunction will exhibits the complication. Second hypothesis suggests that increased intra cellular glucose levels leads to the formation of Advanced Glycosylation End products (AGEs). AGEs modulate atherosclerosis, accelerate glomerular dysfunction, decrease nitric oxide synthesis, and

promote endothelial dysfunction which leads to complication by altered cell function. Third hypothesis has been explained in following manner. Increased hyperglycemia increases the formation of diacylglycerol which activates certain isoforms of protein kinase C, which leads to complications through altered gene expression or growth factors. Increased level of growth factors such as, Platelet derived growth factor, epidermal growth factor & vascular endothelial growth factor leads to complication of Diabetes Mellitus.

Glycemic control and Complications:

The DCCT (Diabetes Control and complications Trial) results postulated that improvement of glycemic control reduced non proliferative and proliferative retinopathy, micro albuminuria, clinical nephropathy and neuropathy. The United Kingdom Prospective Diabetes study results establish that retinopathy, nephropathy and neuropathy are benefited by lowering blood glucose levels in Type 2 Diabetes with intensive therapy. The overall complication rate was decreased by 60% with intense therapy and strict glyceamic control in patients with type1 Diabetes strict glyceamic control achieved a substantially lower HbA1c (7.2%) than individuals in the conventional Diabetes management group (HbA1c of 9%).

(i) Diabetic Retinopathy:

Diabetic Retinopathy is a most frequent cause of blindness among adults aged 20-74 yrs. Diabetic retinopathy is classified in to two stages proliferative and non proliferative. Non proliferative diabetic retinopathy usually appears late in the first decade or early in the second decade of the disease and is marked by retinal vascular micro aneurisms, blot hemorrhages and cotton wool spots. The appearance of neo vascularisation in response to retinal hypoxia is the hallmark of proliferative Diabetic retinopathy. They rupture easily and leading to vitrial hemorrhage, fibrosis and ultimately retinal detachment.

(ii) Diabetic Neuropathy:

Diabetic neuropathy occurs in approximately 50% of individuals with continuum of hyperglycemia in type 1 and Type 2 Diabetes Mellitus. It may manifest as polyneuropathy, mononeuropathy and autonomic neuropathy.

- **Polyneuropathy**

Manifestations:

Distal sensory loss, Hyperesthesia, Paresthesia, Pain [usually in lower extremities]

Physical findings: Sensory loss, Loss of ankle reflexes, abnormal position sense, Parethesia [sensation of numbness, tingling, sharpness or burning].

Diabetic polyradiculopathy is a syndrome characterized by severe disabling pain in the distribution of one or more nerve roots.

- **Mono neuropathy:**

It presents with pain and motor weakness in the distribution of a single nerve.

Involvement of the third cranial nerve is most common.

Physical findings:

Ptosis, Opthalmoplegia with normal papillary constriction to light can be noted. Peripheral mononeuropathies or simultaneous involvement of more than one nerve (Mononeuropathy multiplex) may also occur.

- **Autonomic neuropathy:**

Individuals with long standing type- 1 or type- 2 Diabetes may develop autonomic neuropathy involving multiple systems, like the cardiovascular system, genitourinary system, gastro intestinal tract, pseudo motor system and metabolic systems. Hyperhidrosis of the upper extremities and anhidrosis of the lower extremities result from sympathetic nervous system dysfunction. Anhidrosis of the feet can promote dry skin with cracking, which increases the risk of foot ulcers. Autonomic neuropathy may reduce counter regulatory hormone release, leading to an inability to sense hypoglycemia.

(iii) Diabetic nephropathy:

Diabetic nephropathy is an important cause for morbidity and mortality, and is now among the most common causes of end-stage renal failure (ESRF) in developing countries. As it is found with other microvascular and macrovascular complications, management is frequently difficult and the benefits of prevention are substantial. About 30% of patients with type1 Diabetes have developed diabetic neuropathy after 20 years and epidemiological data suggested that the overall incidents is declining as standards of glyceamic control. Increased microalbuminuria is an important indicator of risk developing nephropathy and more reliable for type1 Diabetes than type2 variety. Risk

factors for developing diabetic nephropathy includes poor control of blood glucose, long duration of diabetes, presence of other microvascular complications, family history etc.

(iv) Cardio vascular disease [166]

Cardiovascular disease is the leading cause of mortality for with diabetes.Type 2 Diabetes is an Independent risk factor for macrovascular disease and its common coexisting conditions i.e. hypertension & dyslipidemia.

Hypertension (blood pressure > 140/90 mmHg) is a common comorbidity of diabetes, affecting 20-60% of people with diabetes, depending on age, obesity and ethnicity. Lowering of blood pressure with regimens based on antihypertensive drugs, including ACE inhibitors, angiotensin receptor blockers (ARBs), B-blockers, diuretics & calcium channel blockers has been shown to be effective in lowering cardio vascular events. Patients with Type 2 Diabetes have an increased prevalence of lipid abnormalities. Which account for higher rates of CVD. The most common pattern of dyslipidemia in type 2 diabetic patients is elevated triglyceride levels. Type 2 diabetic patients typically have a preponderance of smaller, denser LDL particles, which possibly increases atherogenicity even if the absolute concentration of LDL is not significantly increased.

(v) Gastrointestinal Dysfunctions[167]:

Symptoms:

Delayed Gastric Emptying [gastroparesis], altered small & large bowel Motility [Constipation or diarrhoea], Anorexia, Nausea, Vomiting, Early satiety, Abdominal bloating.

(vi) Genito urinary Dysfunction:

- Cystopathy
- Erectile dysfunction
- Female sexual dysfunction
- Dyspareunia
- Vaginal Lubrication

(vii) Diabetic Foot[168]:

Foot ulcers and amputations are major causes for individuals with diabetes.The risks of ulcers or amputation increased in people who have had Diabetes > 10 years have poor glucose control have renal, retinal or cardio vascular complications. Clinical features include neuropathy and ischemia which presents with parasthesiae, pain, numbness, claudication, ulcer, gangrene, Osteomyelitis etc.

ARISTA LAKSHANA

Arista Lakshana are the signs and symptoms which indicates the oncoming death, just as the the smoke indicates the fire, flowers indicate the next coming fruit, and clouds the rain. There is no life after arista lakshanas appearance and death without arista lakshanas. Hence the physician should acquire the knowledge of the arista lakshanas. In classics a few references regarding the arista lakshanas of Madhumeha and Prameha are being explained.

- If the meeting of messenger and the physician occur near the pond or along with water then the prognosis is bad.
- If he is lethargic and obese ati snigdha and is a voracious eater, then death impends in the form of Prameha[169].
- After regular bath and the application of perfumes if the flies attack concurrently on a Madhumeha rogi, then he will die soon[170].
- If a person dreams of drinking various types of snehas in association with chandalas, then he dies of Prameha[171].
- If a Madhumehi dreams of consuming water then he dies of Prameha[172].
- If Madhumeha present with the upadravas it is to be considered as arishta[173].

***SADHYA – ASADHYATA* OF *MADHUMEHA*[173]:**

Madhumeha has been described as *Anushangi* which means it is *Punarbhavi,* in other words once a *Madhumehi,* will be so always throughout his life. Therefore one should make all efforts to prevent & control it.

(1) *Sadhya - Kaphaja Prameha*: *Nidana's* are same to that of *Dosha, Dushya* and having same qualities and same seat. So the treatment is same for both. Thus *Kaphaja Prameha* is *Sadhya.*

2) *Yapyatva - Pittaja Prameha*: Pittamehas are explained to be with this status. The disease is requiring continuous treatment. Its *vishamakriya* i.e. the disease is cured by *langhana* therapy but the associated vitiated dhatus are not. This also leads leads to *yapyatva.*

3) *Krichrasadhyatva & Asadhyatva - Vataja Prameha (Madhumeha)*

Here *vata* provocation might be due to *Sarvadhatukshaya* as it occurs after *kaphaja & pittaja pramehas*. The other important cause is *avarana*. When vata provocation is due to *dhatukshaya* it is included in *asadhya Madhumeha,* while the other produced by *avaranjanaya vata* is considered as krichrasadhya.

Asadhyata of *Vataja Prameha*: The four *Vataja Pramehas* are considered Asadhya due to the following reasons.

A) Mahatyayikatvat

B) Virudhopakramatvat

a) Mahatyayikatvat: The term Mahatyaya has following interpretations,

i) Mahata Gambhira Dhatunam Atyaya Nasho Yena Sa.

ii) Ashukaritva.

iii) Mahavyapattikatrukatva.

iv) Majja Prabruti Sarabhoota Dhatukshaya

v) Majjadi Gambhira Dhatu Apakarshakatvena

vi) Uttarottara Saratara Dhatu Sravakatvat.

The above interpretations indicate the fatality of the disease, where all the *Dhatus* including the *Gambhira Dhatus undergo Nasha, Kshaya, Sravana & Apakarshana. This* process involves multiple Srotases producing *Upadravas* and is hence

Mahavyapathikara, which means that the disease is much too fatal to sustain life. It is Ashukari and Sheegrakari which indicates the rapidity of the fatality in the patient.

b) Virudhopakramatvat: The Chikitsa of Vataja Prameha involves Virudhopakrama which means there is a mutual contradiction in the treatment modalities as use of Snigdha etc are Pathya for Vata but Apatya for Medas. Hence the disease is Asadhya.

OTHER SITUATIONS DETERMINING ASADHYATA OF MADHUMEHA:

It has been said by Charaka that if a disease in Roopavastha has all the Poorvaroopas manifested, and then the disease becomes Asadhya[175]. The severity of Asadhyata increases when associated with Poorvaroopas. Vataja Pramehas have already been described as Asadhya but this term has to be analytically interpreted in the two clinical types of Vataja Mehas, i.e., Dhatukshaya Janya & Margavarana Janya.

Sahaja Madhumeha and Madhumeha with Dhatu Kshaya have Vata as Anubandhya Dosha since the beginning, but in Margavarana Janya Madhumeha Vata is only Anubandha to Pitta & Sleshma and therefore the Chikitsa for Vataja Prameha have been designed keeping in mind the Anubandha Vata and not the Anubandhya Vata because in the later case it has been categorically stated that even thinking about managing this condition is a futile exercise. As in the former case the status of Vata can be controlled through the treatment, as it is still dependent on the status of Sleshma & Pitta. In this case the amenability of Vata to the treatment becomes less & less depending on with what severity the Poorvaroopas are associated.

01. The *Kaphaja and pittaja* groups of *prameha*, if they are developed after full expression of *poorvaroopa*s; they are *asadhya*[176].

02. *Kaphaja prameha* gradually develop in to *pittaja prameha* and they both transform in to *Vataja prameha*, which are incurable.

03. If *kaphaja prameha* gradually turns in to pittaja prameha these are yapya.

04. Even the *pittaja pramehas* are curable if there is no severe vitiation of *medas*[177].

05. *Jatha Madhumeha* is *Asadhya* due to *Beeja Dosha* as it is irreversible as the *Madhumeha arambaka Dosha Dusti* is since from the birth itself [177].

06. *Madhumeha* with *Pidakas* is *Asadhya*.

07. *Madhumehi* who has *Bala Mamsa Kshaya* can be left untreated.

08. All Pramehas if left untreated terminate into *Madhumeha,* which is *Asadhya.*

09. *Prameha* with *Upadravas* and *Atiprasruta Mutra* is *Asadhya*.

10. *Madhumeha* with *Arista Lakshanas is Asadhya*.

11. A patient who hates hygienic habits like Snana, Chankramana & one who has Manda Utsaha, who is *Atisthula, Snigdha & Mahashana* dies of *Madhumeha*[169].

Basavrajeeyum has mentioned a test for urine to know the prognosis of each dosha group. The urine of a Prameha patient has to be collected in a wide mouthed vessel and boiled on a mild flame till evaporation. The incurability of the disease depends upon the amount of residue. A *Vataja Prameha* is considered incurable if the residue is 1/5t h of the volume of urine taken for the test. *Pittaja Prameha* is incurable if the residue is 1/7t h and *kaphaja Prameha* is incurable if the residue is 1/9t h of the volume of urine in the test[178].

PROGNOSIS OF DIABETES MELLITUS[179]:

Good physical condition, obesity, favorable heredity, early diagnosis, prompt treatment, intelligent and co-operative patient, maintenance of body weight are good prognostic signs. Carelessness and coma are unfavorable prognostic signs.

The prognosis in Diabetes has improved steadily since the introduction of insulin, but even with its use the average exception life of diabetic is still less than that of non diabetics. It may be difficult to estimate the prognosis of an individual patient because so many variable factors have to be considered. The working capacity and longevity of a diabetic patient to a great extent depends on the timely recognition of the disease, its severity, complications, the age of patient and proper treatment. If Diabetes develops at early age it shortens the patient's life span.

The prognosis of Diabetes Mellitus is mainly determined by the degree of affection of the cardiovascular system. The commonest causes of the death in Diabetes Mellitus are pathological conditions of vessels like Myocardial infarction, thrombosis of cerebral vessels etc. The patients having mild Diabetes are capable in their works. In moderate and severe forms of the Diabetes the working capacity is assessed individually depending on the course of Diabetes Mellitus and concomitant diseases.

SAPEKSHA NIDANA

Acharya Charaka says that sometimes it is difficult to differentiate *Madhumeha* from *kaphaja mehas*, because the mutra in *Madhumeha* is having madhura rasa, picchila guna and appears like honey. In such a case we should consider the presence of roopa and nidanas. If there are symptoms of *dosha kshaya (kapha pittadi kshaya* in comparison to vata), then it is *vatika prameha* and if there is history of *santarpana nidana*, it is kaphaja prameha. This is important because if *Madhumeha rogi* is having less strength due to dhatukshaya and in that condition he is treated with *kaphamehopakramas*, it will be producing adverse results[**180**].

The term '*Sapeksha Nidana'* conveys the sense of differential diagnosis. A correct diagnosis should be made to distinguish from one disease to another, which will have similar signs and symptoms. Therefore further thorough investigations are necessary. A disease can be diagnosed by close study of the following factors[**181**]. Varna (Colour, complexion), *Rasa* (Taste), *Sparsha* (Touch), *Gandha* (Smell) etc.

An exact diagnosis of a disease is done while looking into all the *nidana panchakas* observed in the patient, which will help to differentiate it from other similar diseases. As discussed earlier *Prabhoota mootrata* and *avila mootrata* are the *lakshanas* which will manifest in all the twenty varieties of *Prameha's*. So as to differentiate *Madhumeha* from other *Prameha's* the study of them should be made according to *Varna, Rasa* etc, of the *Mootra* which is present in them. Until and unless *Haridra* and *Rudhira* coloured *Mutrapravritti* is not associated with the premonitory symptoms of *Prameha*, the disease cannot be diagnosed as *Prameha*, but it goes more in favor of *Raktapitta* [**182**]. Here more importance is given to *Poorvaroopa* of *Prameha* and not only to *Mutra Pravritti*. Regarding *Madhumeha*, it is to be specially emphasized that instead of only *Mutra Madhurya, 'Sharira Madhurya*[**122**] is also found which is not present in other types of Prameha. That is why to understand shareera lakshanas in roopavastha, the knowledge of Poorvaroopa's and the upadravas which are explained are important.

VYAVACCHEDAKA NIDANA

It plays a vital role in establishing exact identities of disease wherever identical signs & symptoms in two or more diseases, which is difficult for a true diagnosis.

Sthoola Madhumeha is considered as *Apathyanimittaja* variety, so it can be differentiated with *Sahaja type*[121]. In *Madhumeha* both *krisha* and *sthula* are affected. *Madumehi mutra* will be *kinchit usna, avilata, madhuryata* and *sharira* also having *madhuryata*, as well as *Madumeha* is of *Vataja Prameha bheda* where oja kshaya is seen which making the disease *chirakari, yapya and asadhya*. But in *Ikshuvalika* and Sheeta meha mostly stula person are affected. *Madhumehi mutra* will be *sheeta, avilata* but *sharira madhuryata* will not be seen. Both are of *Kaphaja prabheda* where oja kshaya is not seen which making the disease *ashukari and sadhya*[123].

Table No. 14: Showing the Differential Diagnosis of *Dhatukshayajanya and Avritajanya Meha*

Sl No	Factors	*Dhatukshayajanya*	*Avritajanya*
1.	Genetic factor s	+++	+
2.	Acquired factors	+	+++
3.	Pathogenesis	Destruction of tissues, increased *vata*	Excess diet & inactivity, increased *kapha, pitta, meda*; obstruction of vata & increased vata
4.	Dosha	*Pitta (-), kapha (-), vata (+ +)*	Pitta (+), Vata (+), Kapha (+ +)
5.	Clinical manifestations	V*ataja* type	Changing in nature – *vataja, pittaja & kaphaja* alternatively
6.	Appearance of patient	Thin and lean	Obese
7.	Prognosis	Incurable	Curable, if treated properly

Proper diagnosis is the foundation to the success of a treatment because many diseases affecting a srotas have similar manifestations, enough to confuse a physician but picking up threadbare with a little difference to clinch a diagnosis is an art aspired by all. Deep knowledge and untiring practice are the means to perfection as Vagbhata has rightly mentioned **"अभ्यासात प्राप्यते दृष्टिः कर्म सिद्धि प्रकाशिणि"**. Madhumeha is a mootra

atipravruttaja vikara with *prabhoota* and *Avila madhusama mootrata* as *pratyatma lakshana.* Although there are many diseases presenting with *Atipravrutti of mootra*, the diagnosis of *Madhumeha* is usually a straight forward proposition by differential diagnosis of the following with its sweet urination.

Table No. 15: Showing the Symptomatic evaluation of differential diagnosis in Madhumeha

MOOTRA LAKSHANA (Pravartana Nimitta)	**SYMPTOMS**
1) Abhikshnam (Muhurh muhurh, Punah punah : Subahushah, vikiranam)	*Ashmari (Cha. Chi. 26/38)*
	Mutratita (Su. Ut. 58/12)
	Ushna vata (A.H Ni. 9/36)
	Vatika Mootrakricchra (Cha. Chi 26/32)
2) Atipravrutti	*Ama jwara (Cha. Chi. 3/135)*
	Amavata (M. N. 25/9)
	Arsha poorvaroopa (A.S Ni. 7/7)
	Asadhya masurika (M. N. 54/27)
	Chidrodara (Cha. Chi. 13/44)
	Kaphaja arsha (Cha. Chi. 14/17)
	Mutra praseka (Su. Chi 7/36)
	Sahaja arsha (Cha. Chi. 14/8)
	Upasthita prasava (Su. Sha. 10/7)

DIFFERENTIAL DIAGNOSIS OF DIABETES MELLITUS[183]

Table No.16: Showing the Differential Diagnosis of Diabetes Mellitus

Characteristics	**Juvenile Onset -Type I (IDDM)**	**Adult or maturity onset type II (NIDDM)**
Age of onset	Childhood or young age	Middle age or later
Sex incidence	Equal	More in males
Mode of onset	Acute or rapid	Incidence
Symptoms	Present	Often absent
Body weight	Often lost	Often gained
Ketosis	Occurs easily	Absent
Insulin sensitivity	High	Low
Plasma insulin	Low	Normal or increased
Response to sulphonylurea	Poor	Good

1) Diabetes Mellitus & Endocrine disorders[184]:

a) Pituitary gland

1) Pituitary Diabetes due to growth hormone
2) Acromegaly
3) Diabetes insipidus

b) Adrenal Cortex

1) Cushing's Syndrome
2) Steroid Diabetes due to administration of steroids
3) Primary Hyperaldosteronism

c) Adrenal Medulla

1) Phaeochromocytoma
2) Addison's disease
3) Adrenalectomy

d) Thyroid

1) Hyperthyrodism
2) Myxoedema

2) Pancreatic Diabetes

1) Acute pancreatitis
2) Mumps (rarely)
3) Chronic pancreatitis
4) Haemochromatosis
5) Total pancreatectomy
6) Carcinoma of pancreas

3) Diabetes liver

1) Cirrhosis of liver
2) Gall Stones

4) Drugs & Diabetes

Thiazide, Chlorthalidone, frusemide, oestrogen containing oral contraceptives, â Blockers & catacholaminergic drugs

5) Miscellaneous

1) Type I glycogen storage disease

2) Down's syndrome

3) Turner's syndrome

4) Huntington's chorea

Conditions of polyuria

Polyuria should not be confused with prostratic hypertrophy or cystitis because here it is only increased frequency of micturition & not increased quantity.

1) **Polyurea due to water dieresis**

   Cranial or neurogenic Diabetes insipidus: This is due to an identifiable lesion in the hypo thalamus pituitary or both leading to failure of A.D.H. Nephrogenic Diabetes insipidus: Familial form seen in males only also as an accompaniment of Fanconi syndrome.

   Psychogenic polydipsia or compulsive water drinking this is a hysterical condition. There is clinically marked fluctuation here.

2) Polyurea due to increased solute load

   Diuretic therapy

   Chronic renal failure

PATHYAPATHYA

Pathya is that which is not harmful to Pathas [channels of the body] and is according to liking and which maintain the stability of physical and mental health are the *Pathya*. The *Ahara* & *Vihara* which produces the imbalance in the equilibrium of the *Dhosha*, *Dhatu*, *Mala* and *Mana* are considered as *Apathyas.* The physician who desires of success in the treatment should advise the Pathyapathya along with the medicine. If the patient follows the Pathya regularly and correctly then Pathya itself is capable in curing the diseases without medicine.

Pathya[185]:

A) Pathya Aahara:

Shook Dhanya: *Jeerna Shali, Shashtika, Kodrava, Yava, Godhuma, Uddalaka, Shyamaka*

Shimbi Dhanya: *Chanaka, Adhaki, Kulattha, Mudga*

Shaka Varga: The leafy vegetables with a predominance of *tikta-kashaya rasa,*

Patola, Karvellaka, Shigru

Phala Varga: *Jambu, Dadima, Shringataka, Amalaki, Kapittha, Tinduka, Kharjura, Kalinga, Navina Mocha.*

Mamsa Varga: *Vishkira mamsa, Pratuda, Jangala mamsa*

Taila Varga: *Danti, Ingudi, Sarshapa, Atasi*

Udaka Varga: *Sarodaka, Kushodaka, Madhudaka*

Kritanna Varga: *Apupa, Saktu, Yavodana, Vatya, Yusha*

Others: *Madhu, Hingu, Saindhava, Maricha, Lasuna.*

B) Pathya Vihara -

1. Vyayama

2. Pragadha Udvartana

3. Rukshana

4. Snana

5. Jalavaseka

6. Lepana of *Tvak, Ela, Agaru, Chandana*[186]

7. Niyuddha

8. Kridha

9. Gaja, Turaga, Padaticharya

10. Astropastra Abhyasa

11. Padatrana and *Chatrarahita Sanchara*[187]

12. Bhikshavritti Dharana

13. Live like a *Muni*[187]

14. Yojana ShatamVa Gacchet[188]

15. Mriga Sahavaset

16. Shiloccha Vritti Dharana

17. Dig the Jalashay[189]

18. Gobhireva Saha Bramet[188]

19. Nishi Jagarana

Apatya Ahara and Viharas-

Ahara - *Nava Annani, Dhadhi, Anupa mamsa, Nishpava, Pishtanna, Viruddha ashana, Kushmanda, Ikshu, Dushatambu, Svadu, Amla, Lavana, Abhishenda, Sura, Sauveera, Saktu, Taila, Kshara, Ghrita, Guda, Ksheera etc.*

Vihara- *Sada Asana, Diva Shayana, Mootra Vega Dharana, Dhoomapana, Sweda, Shonita Mookshana etc. Hareeta tells that Kshara, Amla, Katu, Divaswpa, Streedarshana, Vyavaya, Atyashana, Mootravirodha* are to be avoided.

MADHUMEHA CHIKITSA

In the *Brihattrayees i.e.Charaka, Susruta* and *Vagbhata* are considering the body constitution and strength of the body of the patient when dealing with the management aspect.

Charaka considers two types of patients; one is that with stout body structure and with strength and the other is thin and impaired strength. Susruta said that the sahaja meha (born diabetic) rogi will be krusha (thin) and apathyanimittaja rogi will be sthula (stout).

Chikitsa (Management Proper) and *Chikitsa sutra* (principles of treatments) are the two divisions of disease management. *Medoroga* context spoken managements are parallel to that of meha since the Dosha and dushyas are same to major extent. After considering all the factors in the management types it is emphasized as:

(1*) Samshodhana Chikitsa*

(2) Samshamana Chikitsa

are the common modalities of the *Madhumeha* management.

Factors which are responsible for the production of the diseases are eliminated and causative factors are prevented so the disease does not progress to offer complications. *Madhumeha* is said to be treated for long way although it is described as incurable. In *Madhumeha* and in such *Pratyakhyeya vyadhis*, symptomatic relief can offer better relief to patient along with proper management.

MANAGEMENT:

1) *KAPHAJA PRAMEHA*[189]

(i) *Samshodhana Chikitsa*

Charaka describes that *shodhana, Vamana* and *langhana* done at the proper time looking at the condition of the patient is able to cure *kaphaja meha*. For *Asthapana Basti Chikitsa Vagbhata* describes the utilization of *Surasadi gana kwatha*. After explaining the shodhana the palliative treatment given is *samshamana Chikitsa* in all types of *Madhumeha*. It is better to treat the patient with *Vamana* therapy as all *Prameha* are often with Kapha predominance.

(*ii) Samshamana Chikitsa:*

Charaka gives 10 combinations of drugs to all the mehas with *Kapha* predominance. According to *Susruta,* after proper s*amshodhana* the patient should use swarasa of *amalaki* with *Haridra* powder with *madhu. Susruta* in this context explains single drug decoctions with separate indications in 5 types of *kaphaja meha* and combinations in other 5 types.

Importance of *Apatarpana*:

Prameha and especially *Madhumeha* is a *santarpana janya vyadhi. Charaka* explains the cause of *Prameha* as due to increasing attitude of *kleda, meda, and Kapha.* So he emphasizes the role of *Apatarpana* in *kaphaja* and *Pittaja Prameha*. Different types of *vyayama, kshut, udvartana, dhara & snana* with churnas made of *Chandana, Aguru,* and *Ela* etc. are advised to use in *Kaphaja meha*.

2) *PITTAJA PRAMEHA*[189]

(i) Samshodhana Chikitsa

Virechana is best in *pittaja pramehas*. The drugs which are sufficient to eliminate morbid *Pitta* can be used with *sheeta* and other *tikta, kashaya rasa* in this. *Nyagrodhadi gana kwatha* is advised for *Asthapanbasti* by *Vagbhata*. *Susruta* has described that due to spreading of *medo dhatu* all over the body, *Madhumehi* subjects are *durvirechya*.

(ii) *Samshamana Chikitsa*

Charaka explains 10 *pada yogas* in this aspect to treat *pittaja pramehas*. *Susruta* has described 6 specific *kwatha yogas* for the specific type of *pittaja Prameha*.

The three *kwatha yogas* explained by *Vagbhata are*[190]:

(i) Ushiradi: Ushira, Lodhra, Arjuna, Chandana.

(ii) Patoladi: Patola, Nimba, Amalaki, Amrita

(iii) Lodhradi: Lodhra, Ambu, Kaleyaka, Dhataki.

3) *VATAJA PRAMEHA*[191]

Although vataja mehas are incurable still Charaka explains to induce certain treatment in Kapha Pitta anubandhi Vatika meha. Susruta has described that all types of Prameha if not treated properly in time, gets converted into Madhumeha. So the treatment described for vatika meha can be considered as treatment of Madhumeha.

MADHUMEHA[192]

Susruta has separately mentioned one chapter for the treatment of *Madhumeha*.

(i) *Samshodhana Chikitsa*

Considering *sthula* and *krusha pramehi, Samshodhana Chikitsa* should be administered only to the *sthula* and *Balvan Pramehi. Sarshapa, Nimba, Danti, Bibhitak & Karanja siddha Taila* or *Trikantakadya Sneha* (*Ghrita or Taila* according to *Dosha* predominance should be used for *Abhyantara Snehana*. Here while explaining the *Samshodhana, Charaka* describes to use the *Malashodhanayogas* from *Kalpa sthana* Both *Pitta and Kapha* are eliminated through *shodhana*. It may be *vamana* or *virechana*, because of *Pittantam Vamanam, Kaphantam Virechanam*. In *Virechana Pitta* is eliminated first, then *Samyak lakshana* of *virechana i*s *kaphadarshan*, so both *Pitta* and *Kapha* doshas which are vitiated are eliminated. Then the described *Anuvasana & Asthapana Basti Chikitsa's* are able enough to control the provocation of *Vata*. Like this all the d*oshas* are normalized to keep the *Dosha samyata*. *Anuvasana* with medicated oils and ghritas are prescribed in *Madhumeha.* After proper *Shodhana Chikitsa, Charaka*

details to give *santarpana Chikitsa* to the patients, to prevent the complications like *Gulma, Bastishula* etc.

(*ii)Samshamana Chikitsa*

Samshamana Chikitsa includes mainly *deepana* (appetizers), *Pachana*, (enhancing digestion), *Kshut* (Hunger maintenance), *Trit* (Maintenance of thirst), *Vyayama* (Exercise), *Atapa* (Having exposed to sunlight) and *Maruta* (Exposing oneself to wind). According to the conditions of vitiated *doshas* and *dushyas* , a physician has to suggest proper *Shamana Chikitsa* to the patient. Acharyas introduces different *tarpana upakramas* in *vatika mehas*. It is due to the less strength of the patient. *Acharya Charaka* & *Vagbhatta* says that the *kashaya yogas* should be enriched with *sneha* and given to *vatika mehas*.

Typical *Madhumeha Chikitsa*

In *Susruta* mentioned that *Shilajitu* should be taken after triturating with *Salsaradi gana Kasaya.* Quantity prescribed 1 Tula of *shilajatu*. Once it is digested patient should take *Jangala mamsa rasayukta Anna*.

Table No.17: Showing the *Yogas* used in Preparations Used In *Prameha*:

Charaka Samhita	*Phalatrikadi Kwatha, Lodrasava, Dantyasava, Bhallatakasava. Trikantakadya Sneha*
Sushruta Samhita	*Navayasa Loha, Ayaskriti, Loharista, Swarna Makshika, Rajata Makshika, Tuvaraka Taila, Dhanvatara Grita,*
Astanga Sangraha	*Mustadi Churna, Asanadi Kwatha, Dhanvantara Ghita, Lodrasava , Dashamularista*
Astanga Hrudaya	*Dhanvantara Grita , Navayasa Churna , Ayaskriti, Rodrasava, Shilajatu Rasayana, Aragvadadi Kashayam, Mdhukasavam, Mandura Vataka,*
Bhaishajya Ratnavali	*Shilajatu Prayoga, Salasaradi Leha, Kushavaleha, Dadimadhya Ghrita, Shukra Matruka Vati, Meha Mudgara Rasa,Vidangadi Loha, Panchana Rasa, Meha Kulantaka Rasa, Chandrakala Rasa, Trakeshwara Rasa, Vangeshwara Rasa, Vasanta Kusumakara Rasa, Chandra Prabha Vati, Prameha Mihira Taila, Somanath Rasa, Devadarvarista, Avipattikara Churna, Sarivadyasava,*
Bhava Prakhasha	*Nyagrodadya Churna, Trikatukadhya Modaka, Lohadi Churna, Trikatu Gutika, Dadimadhya Ghrita, Simhamrita Ghita,*
Sharangadhara Samhita	*Vatsakadi Kwatha, Varadi Kwatha, Nyagrodadi Kwatha, Triphala Churna, Triyushana Churna, Lavangadi Churna, Bahushala Guda, Suranadi Vataka, Triphaladi Vataka, Chandra Prabha Vati, Yoga Raja Guggulu, Kaishora Guggulu, Gokshuradi Guggulu, Triphaladi Ghrita, Shatavaryadi Taila, Ushirasava, Kumaryasava, Vidangarista, Devadarvarista, Babbularista, Dashmularista, Vasanta Kusumakara Rasa, Prameha Bhadda Rasa,*
Yoga Ratnakara	*Vangeshwara Rasa, Chandra Prabha Gutika, Devadarvarista, Pugapaka, Harishankara Rasa, Gokshuradi Guti, Mehantaka Rasa, Mehari Rasa, Meha Kunjara kEsari Rasa, Nisha Triphala Yoga, Saala Musta Yoga, Triphaladi Churna, Nyagrodadi Churna, Vasanta Kusumakara Rasa,*
Vangasena	*, Trikatukadya Gutika, Dadimadya Ghrita, Nyagrodadi Churna Gokshuradi churna, Dhanvantara ghrita, Arjunadya Ghrita, Saara Leha, Gokshuradyavaleha, Asanadi Yoga, Shilajatu Prayoga.*
Sahasra Yoga	*Madhusnuhi Rasayana*

DIAGNOSIS OF DIABETES MELLITUS[193]

Hyperglycemia remains the fundamental basis for the diagnosis of Diabetes Mellitus. In symptomatic cases, the diagnosis is not a problem and can be confirmed by finding glycosuria and random plasma glucose concentration above 200mg/dl. In asymptomatic cases, when there is a persistently elevated fasting plasma glucose level, diagnosis again poses no difficulty.

The problem arises in asymptomatic patients who have normal FBS but are suspected to have Diabetes on the other grounds and are subjected to have oral glucose tolerance test (OGTT). If abnormal GTT values are found, these subjects are said to have 'chemical diabetes'.

REVISED CRITERIA FOR DIAGNOSIS OF DIABETES MELLITUS

[As per WHO-AMERICAN DIABETES ASSOCIATION, 2000]

Table-18: Showing the Revised Criteria for Diagnosis of Diabetes Mellitus

Plasma Glucose Value	
Fasting (for > 8 hours) value:	
Below 100 mg/dl (< 5.6 mmol/L)	- Normal fasting value
100 – 125 mg/dl (5.6 -6.9 mmol/L)	-Impaired fasting glucose (IFG)
126 mg/dl (7.0 mmol/L) or more	- Diabetes Mellitus
Two hour after 75gm Oral Glucose Load:	
< 140 mg/dl (< 7.8 mmol/L)	- Normal post prandial GTT
140 -199 mg/dl (7.8 -11.1 mmol/L)	- Impaired post prandial glucose tolerance (IGT)
200 mg/dl (11.1 mmol/L) or more	-Diabetes Mellitus
Random value:	
200 mg/dl (11.1mmol/L) or more In a symptomatic patient	-Diabetes Mellitus

OTHER INVESTIGATIONS:

1. Urine testing

a. Glucosuria (Benedict's qualitative test)

• Renal glucosuria

• Alimentary (lag storage) glucosuria

b. Ketonuria

2. Glycosylated haemoglobin (HbA1C)

3. Glycated albumin

4. Extended GTT

5. Intravenous GTT

6. Cortisone primed GTT

7. Insulin assay

8. Proinsulin assay

9. C-peptide assay

10. Islet autoantibodies

Oral Glucose Tolerance Test (OGTT) [194]

In asymptomatic individuals, individuals with IFG and those with Random Plasma Glucose level between 100-200mg/dl an OGTT is strongly recommended for diagnosis.

Precautions

1. It should be done in the morning after unrestricted carbohydrate diet and usual physical activity for previous 72 hrs.

2. The subject should be fasting for at least 10 -16 hours before the test (may drink water).

3. The subject should not be smoking during the test.

4. Any concomitant medication, infection or inactivity must be recorded and be taken into consideration while interpreting the results.

Procedure:

1. The test should be performed with 75g of anhydrous glucose in 150 – 300 ml of water over the course of 5 minutes.
2. Children should be given 1.75gm/kg of body weight, up to a total of 75g glucose.
3. Blood should be collected in a tube containing sodium fluoride (6mg/ml of whole blood) and centrifuged properly to separate out the plasma. Two hours post glucose value of more than 200mg/ dl is considered diagnostic for diabetes, while values ranging between 140-200 mg/dl are considered Impaired Glucose Tolerance (IGT).

Glycosylated or Glycated Heamoglobin (HbA_1C) [195] :

In normal individuals a small proportion of hemoglobin combines with the circulating blood glucose and this fraction is called glycosylated or glycated Hb. This can be separated in to 3 types HbA1a, HbA_1b, and HbA_1c. More binding is to HbA_1c. The binding of glucose to Hb is a non-enzymatic process that occurs continuously throughout the lifespan of the RBC. Once glycated the elevated levels persists till the red cell dies. The amount of glycated Hb reflects the efficacy of glycemic control in a diabetic patient during the 8-12 week period before the blood was collected. Normal level of HbA_1C is below 7%. Elevation of HbA_1C above this value is evidence of a condition which is in need of glycemic control during the preceding 8-12 weeks. It reflects the radical changes in diet or modes of therapy approximately 3-4 weeks after the initiation of the change. HbA_1C is now considered as the most important diagnostic criteria which help in detecting an unknown hyperglycemic episode within a span of 2 yrs and the goal of the any treatment in type-2 Diabetes being achieving the HbA_1C level <7% along with Fasting and Post Prandial Blood Sugar Level between 90-130 mg/dl and below 180 mg/dl respectively.

Advantages:

1. It is useful for assessing long term blood sugar control.
2. The levels of the blood glucose can be easily manipulated by the patients by taking extra dose of the OHA or insulin or even missing meals on the day of test so that patient

can get good results but HbA_1C is unaffected by time, type of blood sample either venous or capillary, even fed or fasting state.

3. Highly indicative of susceptibility for short term and long term Micro vascular and Macro vascular complications.

Disadvantages:

1. It cannot help in diagnosing hypoglycemic episodes or even diabetic ketoacidosis.
2. It is sometimes possible to obtain normal values in patients suffering from frequent and dangerous episodes of hypoglycemia, if these are balanced by other episodes of excessive hyperglycemia.
3. It is highly dependent on the life span of the RBC.
4. If it is measured by electrophoretic method and patient who drink 30 or more units of ethanol per week then the values may be higher due to the acetaldehyde derived from the ethanol binds non-enzymatic ally to side chain of Hb which moves in same direction. This is overcome through electro endosmosis method.
5. It is not useful for day-to-day management and in adjusting the dose of insulin or oral anti diabetic drugs.

TREATMENT OF DIABETES MELLITUS:

The word treatment in Diabetes Mellitus seems incomplete instead management of Diabetes Mellitus is an appropriate term as the disease can only be controlled and constitutes a multidimensional approach namely Diet, exercise, oral hypoglycemic, insulin & patient education are vital aspect which require due consideration in the management of Diabetes Mellitus.

Life style modifications[196]

Life style measures which combines increased physical activity and dietary modifications are an important component in the management of both type 1 and Type 2 Diabetes Mellitus.

DIETARY THERAPY

The dietary planning is based on the type of diabetes, weight of the patient, activity profile, and presence of co-morbid conditions. Dietary macronutrient

composition is one of the important considerations for the dietary therapy in diabetes. Studies have shown that higher intakes of saturated and trans-fats are associated with an increased risk of diabetes, whereas higher intake of mono-unsaturated and poly-unsaturated fats is associated decreased risk of diabetes

The importance of consuming minimally processed foods with low glycemic index and glycemic load is recommended in the management of diabetes. Whole grain products such as whole wheat breads, brown unpolished rice, oats, and barley tend to produce lower glycemic and insulinaemic responses and are also rich in fibre, antioxidants, vitamins, and phytochemicals than highly processed refined grains.

The chief aims of diabetic diet are[197]:

a) Achieve good glycemic control

b) Reduce hyperglycemia and avoid hypoglycemia prevent hypoglycemia.

c) Obtain ideal body weight.

d) Reduce the risk of micro and macro vascular complications.

e) Ensure adequate dietary intake.

Type of Diet: Basically there are two types of diet:

Unmeasured Diet:

If Insulin or oral hypoglycemic agents are not required and marked obesity is not present it may not be necessary for the patient to follow such an accurate diet.

- ✓ Forbidden Foods: Sugar, Jam, Honey, Tinned fruits, Sweets, Chocolates, Glucose Drinks, Food made with Sugar, Cakes, Sweet Biscuits, Puddings, Rice and alcoholic drinks.
- ✓ Foods allowed in moderation: Chapattis made from wheat or millets, peas and backed beans, breakfast cereals and all fresh and dried fruits, custard.
- ✓ Free Foods: Eggs (not fried), vegetables such as cabbage, cauliflower, brinjal, lady's finger, French beans, cucumber, lettuce, tomato, spring onion, radish, and asparagus, lastly the saccharine for sweetening.

Measured Diet:

These are required for patients who are being treated with insulin or oral hypoglycemic agents and also for those who are overweight and are on anti obese regimen.

Vitamins and Minerals: As there is no evidence of benefit from it, vitamins and minerals are not advisable if person do not have underlying deficiencies.

Antioxidant: Routine supplementation of antioxidants is not advised because of uncertainties related to long term efficacy and safety.

Calorific Requirements: The approximate ratio in normal person's diet is protein 12%, fat 42% and carbohydrate 46%, but in diabetics it is usually needed to be modified as protein 15%, fat 35% and Carbohydrate 50%. In Insulin requiring Diabetics the distribution of calories is very important to avoid the hypoglycemia. A typical patient of IDDM usually require 20% of total calories for breakfast, 35% for lunch, 30% for the dinner and 15% for the late evening feedings[198].

EXERCISE THERAPY

Adequate physical activity helps in correcting obesity which is a major risk factor in type 2 DM. In addition, physical activity may independently enhance insulin sensitivity and glucose tolerance. It increases the skeletal glucose transporter protein GLUT4 which is responsible for insulin independent glucose transport into the skeletal muscle. Exercise causes a reduction in blood pressure, body fat and subsequently helps in maintenance of the weight.

Table No. 19: Showing the Exercise Recommendations for Patients with Type 2 Diabetes Mellitus

Recommend Exercise for Patients with Type 2 Diabetes Mellitus[199]	
Screening	Search for vascular and neurological complications including silent Ischaemic heart disease Stress electrocardiogram in patients >35 years of age or >10 years of diabetes
Exercise programme and type	Aerobic, Resistance, Yogic practices
Intensity	50% to 70% of maximum aerobic capacity
Duration	20 to 60 minutes with warm up and cool down
Frequency	Ideally daily or at least 5 times/week
Avoid	Careful selection of exercise type and intensity
Complications	Patient education

	Monitoring of blood glucose by patient and overall programme by medical personnel
Compliance	Make exercise enjoyable, Convenient location

Table No.20: Showing the Caloric Expenditure in Various Forms of Exercise

Caloric Expenditure in a 60 kg Individual Performing Various Forms of Exercise for 60 Minutes	
Type of Exercise	**Caloric expenditure**
Aerobics	450+
Cycling,moderate	450+
Jogging(5 m per hour)	500
Gardening,digging	500
Skipping with rope	700+
Running	700+
Swimming,active	500+
Waking (3 m per hour)	280
Table Tennis	290
Gardening	350
Tennis	350+

Oral Anti-Diabetic Drugs[200]

Classification of Oral Anti-Diabetic Drugs

1. Agents stimulating insulin release (secretagogues)
    A. Sulphonylureas
        a. First generation:tolbutamide
        b. Second generation: glibenclamide,glipizide and gliclazide
        c. Third generaton:glimepride
    B. Non-sulphonylureas
    -Meglitinides: repaglinide and nateglinide
    C. GLP-1 analogues

-Exenatide and liraglutide

D. DPP-4 inhibitors

-Sitagliptin,vildagliptin and saxagliptin

2. Agents lowering insulin resistance(sensitisers)
    A. Biguanides: metformin
    B. Thaizolidinediones: piogitazone
3. Agents reducing carbohydrate absorption
    A. Alpha-glucosidase inhibitors:acarbose,voglibose
4. Agents decreasing renal reabsorption of glucose

SGLT-2 Inhibitors

Sulphonylureas:

- These drugs stimulate production of Insulin initially but later on they act by their extra pancreatic actions.
- Sulphonylureas are mainly indicated for Maturity onset Diabetics of average weight not controlled by diet alone.
- The contraindication includes juvenile Diabetes, Ketosis, patients taking Insulin and presence of renal, hepatic, cardiovascular disease or alcoholic abuse.
- Hypoglycemia, dyspepsia, skin rashes, facial flushing after ingestion of alcohol are the most frequently encountered side effects with sulphonylureas.

Meglitinides

- These are helpful in controlling post prandial hyperglycemia. They must be taken just prior to meals can be combined with Sulphonyurea, Biguanides.

Biguanides:

- There major effect is to increase the peripheral uptake of glucose and in large doses to delay or decrease intestinal absorption.
- These are the drug of choice for the treatment of maturity onset obese diabetic patients who have failed to lose weight on diet.
- The adverse effects include metallic taste in mouth, anorexia, nausea, dyspepsia, diarrhea, malaise, weakness, drowsiness, lactic acidosis and lastly the vitamin B12 malabsorption after prolonged treatment.

Thiazolidinedione derivatives –

- These are useful in subjects with insulin resistance. They can be combined with Sulphonyurea, Biguanides and insulin. It is widely regarded as the drug of choice for overweight, obese patients with Type 2 Diabetes Mellitus. It can also be used in normal weight patients.

Alpha glucosidase inhibiters-

Alpha glucosidase inhibiters like acarbose are helpful in controlling post prandial hyperglycemia given along with meals. They can be combined with Sulphonyurea, Biguanides and insulin.

Insulin Therapy[201]

Insulin is one of the oldest, best studied and most effective treatments for diabetes. Insulin is a must and life saving for patients with Type 1 Diabetes while many patients with advanced duration of Type2 Diabetes also require insulin therapy for optimal glycemic control.

Insulin preparations

Conventional insulin

- Short acting insulin: Regular human insulin
- Intermediate-acting insulin: Neutral protamine Hagedorn, NPH(human)

Insulin analogues

- Rapid-acting insulin: lispro,Aspart,Glulisine
- Log acting insulin: Glargine,Detemir

Timings and Dosage of Insulin Therapy

Short acting regular human insulin needs to be injected 30 to 60 minutes prior to meals while rapid acting insulin can be injected 5 to 15 minutes prior to meals. Insulin NPH is to be injected once or twice a day usually with regular insulin 30 minutes prior to meals. It takes care of post- lunch hyperglycemia. Insulin glargine given once a day at fixed time, usually at 8pm or 8am. Insulin detemir needs to be injected twice a day. In fasting hyperglycemia, intermediate or long-acting insulin can be injected. If post Prandial glycemic control remains inadequate, short/rapid acting insulin is to be added either in the form of pre-mixed preparation or as basal bolus regimen. The usual

preparation used is 30:70 or 25:75 ratio of short/rapid acting insulin to intermediate acting insulin.

Table No. 21: Showing the Modalities of Treatment in Type 2 Diabetes Mellitus

Modalities of Treatment in Type 2 Diabetes Mellitus					
Drug	**Name**	**Mechanism of Action**	**HbA_{1C} Reduction**	**Advantage**	**Adverse Effects**
Incretin mimetics	Exenatide, Liraglutide	↑ Insulin, Glucagon ↓ -Slow gastric emptying	0.5% to 1.0%	Weight loss	Nausea, pancreatitis
Incretin enhancers	Sitagliptin, Vildagliptin, Saxagliptin	-Prolong endogenous -GLP-1 action -Care while using in renal failure	0.4% to 0.9%	Weight neutral, no hypoglycaemia	Nausea, Pancreatitis, dose reduction in renal failure
SGLT-2 inhibitors	Dapagliflozin	Inhibits glucose re-absorption	0.5% to 0.9%	Weight loss	Polyuria, genital infections
Amylin agonist	Pramlintide	-Slow gastric emptying, ↓ glucagon	0.3% to 0.5%	Reduce PPBS, weight oss	Nausea, Hypo glycemia

Prevention of Type 2 Diabetes Mellitus:

A large pool of diabetics remains undetected, ranging from 70%-80% which is a matter of concern all over world. Besides this there is a population with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) around 14% in our country. It is estimated that approximately 40% of the patients with IGT shall progress to Diabetes in

the next 5-10 years and therefore, provides a good opportunity for prevention of Diabetes and thus prevent morbidity.

Strategies for Prevention of Diabetes

Two main strategies have been evaluated for reducing of type 2 diabetes.

1. Life style interventions
    a. Medical nutrition therapy(MNT)
    b. Physical activity
2. Drugs
3. Others- Provide family help and support, failures is circumvented, close follow up.

The risk factors of Diabetes can be classified into modifiable and non modifiable risk factors. The modifiable risk factors are the subject matter of intervention.

Table No.22: Showing the Risk Factors for Type II Diabetes Mellitus

Risk Factors for Type 2 DM	
Modifiable factor	**Non-Modifiable factor**
Overweight and obesity	Ethnicity
Sedentary life style	Family history
Impaired glucose tolerance and impaired fasting glucose	Age
Metabolic syndrome: Elevated TG, reduced HDL, Hypertension	H/O gestational Diabetes Mellitus
	Gender
Dietary factors	PCOS
Intra-Uterine environment	
Inflammation	
Use of drugs like corticosteroids, diuretics	

BARIATRIC SURGERY[201]

Bariatric type of surgery (metabolic surgery) is emerging as the third arm of prevention. Bariatric surgery includes a variety of procedures done on persons who having obesity to lose weight who have health problems like Type 2 Diabetes Mellitus or Heart problems. Weight loss is achieved by reducing the size of the stomach with a gastric band or through removal of a portion of the stomach (sleeve gastrectomy or

biliopancreatic diversion with duodenal switch) or by resecting and re-routing the small intestine to a small stomach pouch (gastric bypass surgery). The basic clinical outcome of bariatric surgery is to reduce weight and this in turn has proved to be useful in the prevention of diabetes. Studies demonstrated that the patients who underwent bariatric surgery, the risk of Diabetes was reduced by 86% at 2 years and 75% at 10 years follow up. It also reported to induce a remission in diabetic patients. The patient selection has to be careful and surgery has to be considered in patients with BMI of more than 35 kg/m^2.

Role of Vitamin D in Prevention

Recent studies were observed that low levels of vitamin D are contributory to insulin resistance, reduced calcium mediated insulin secretion and higher incidence of diabetes. Asians have prevalence of vitamin D deficiency and vitamin D with calcium supplements is likely to improve B-cell function.

Pancreatic Islet Transplantation

The two types of pancreatic islet transplantation are

1. allo-transplantation
2. auto-transplantation

Pancreatic islet allo-transplantation is a procedure in which islets from the pancreas of a deceased organ donor are purified, processed, and transferred into another person. Pancreatic islet allo-transplantation is performed in certain patients with Type 1 Diabetes whose blood glucose levels are difficult to control. The goals of the transplant are to help these patients achieve normal blood glucose levels with or without daily injections of insulin and to reduce or eliminate hypoglycemia unawareness.

Pancreatic islet auto-transplantation is performed following total pancreatectomy in patients with severe and chronic pancreatitis that cannot be managed by other treatments. This procedure is not considered experimental. Patients with Type 1 Diabetes cannot receive pancreatic islet auto-transplantation.

The shortage of islets from donors is a significant obstacle to widespread use of pancreatic islet allo-transplantation. Financial barriers also prevent the widespread use of islet allo-transplantation. Until the transplantation technology is considered successful enough to be labeled therapeutic rather than experimental, the costs of islet allo-transplants must be covered by research funds.

Prevention of Type 1 Diabetes

Genetic susceptibility and environmental factors like infections, ingestion of bovine milk proteins, and infection during pregnancy are the main attributing factors. For an effective prevention strategy there is need for an efficient prediction strategy using genetic and immune markers (Islet antibodies, GAD antibodies).

DRUG REVIEW

In *"Padachatustaya" Oushadha* (drug) is in second position, next to the Bhisaka (Physician). *Hetu , Linga and Oushadha* are *Tri-sutra* of *Ayurveda* where Oushadha is in 3rd position. *Oushadha* has got place in the *Dasavidha Pariksha Bhava*[206] of *Charaka samhita* which plays a key role in the treatment of disease.

The vitiation of *Meda, Kleda, Vasa* and *Lasika* along with the *Oja* and *Majja dhatu kshaya* leads *Vata* provocation ultimately leads to *Madhumeha.* Hence the physician should select the drugs having above said *gunas* for *Samprati Vighatana*. In parlence with this the drug should have the qualities like Tikta and Kasaya Rasa along with *Kapha Vata hara, Medo hara, Kledaghna* and *Prameha hara* properties. Such a compound medicine explained in *Bhaishajya Ratnavali* the *Mustadi Kwatha* composed of the active ingredients like *Musta, Amalaki , Haritaki, Bibhitaki, Haridra, Devadaru, Moorva, Indrayana, Lodra* has been taken in this study.

The detail descriptions of these ingredients with respect to their nomenclature, Chemical Composition, Classical Pharmacological Properties and Actions along with their Therapeutic Effects, updated studies and authentication study etc. are explained here. The raw drugs components of *Mustadi Kwatha* will be collected as per API Standards as follows:-

Table No.23: List of drugs present in Mustadi Kwatha

Sl.No.	Name of the Drug	Latin name	Family	Parts used
1.	*Musta*[208]	*Cyperus rotundus* Linn	Cyperaceae	Dried Rhizome
2.	*Amalaki*[209]	*Embelica officinalis* Gaertn	Euphorbiceae	Dried fruit
3.	*Haritakia*[210]	*Terminalia chebula* Roxb	Combritaceae	Dried fruit
4.	*Bibhitaki*[211]	*Terminalia belerica* Retz	Combritaceae	Dried fruit
5.	*Haridra*[212]	*Curcuma longa* Linn	Zingiberaceae	Dried Rhizome
6.	*Devadaru*[213]	*Cedrus deodaro* Roxb Loud	Pinaceae	Heart wood (*Kanda sara*)
7.	*Murva*[214]	*Marsdenia tenacissima* Wight & Arn	Asclepidiaceae	Root
8.	*Endri*[215]	*Citrullus colocynthis* Schrad	Curcubitaceae	Root
9.	*Lodhra*[216]	*Symplocos racemosa* Roxb	Symplocaeae	Bark

Details of each ingredients of *Mustadi Kwatha* are discussed in context of *Rasa, Guna, Virya, Vipaka and Doshagnata*

1. MUSTA[206]

Musta is a Perennial slender herb, the base is nodular, thickened and suddenly constricted into hairy rhizome, subsolitary, triquestrous at top. The leaves are long often overtopping stem, flowers in compound umbel, seeds trigonus nuts. Details are explained below:

Family : Cyperaceae

Botanical Name : Cyperus rotundus Linn.

Paryaya : Mustaka, Varida, Kuruvinda.

Types : 3 Types -*Bhadramusta, Nagaramusta, Jalamusta*

Chemical composition : Cineol, cyperen, rotundone,cyperenole.

Therapeutic Action : *Pitakaphahara, Medhya, Deepana, Pacana, Trushnanigrahana, Jvaragna, Vishaghna, Krimigna, Tvak doshahara, Shotahara*

Therapeutic Uses	**:**	*Apasmara, Aruchi, Trushna, Krimi, Raktavikara, Mutrakriccha, Sootika roga, Jwara*
Parts Used	**:**	Kanda (Dried Rhizome)
Dosage	**:**	*Kwatha*: 50-100ml, *Churna*: 3-6gms
Gana:		
Charaka	**:**	Truptigna, Trushna Nigrahana, Lekhaniya, Kandugna, Stanya Shodhaka,
Sushruta	**:**	Mustadi, Vachadi
Vagbhata	**:**	Mustadi, Vachadi

RECENT STUDIES[218]

Musta has got Anti diarrheal activity. Ethanol extract of Musta (Cyperus rotundus) [219] has got the anti diabetic activity. It is also found that it has got Hepatoprotective activity, Anti Hyperlipidemic, Anti Inflammatory, Anti Oxidant, Hepatoprotective activity.

Table No. 24: Showing Raw drug Musta Authentication test result:

Description Macroscopic:		
Tests	**Limits (As Per API)**	**Results**
Parts	Rhizome	Rhizome
Colour	Dark Browm to Black	Dark Browm to Black
Odour	Pleasant	Pleasant
Taste	Bitter	Bitter
Physio Chemical Standards		
Tests	**Limits (As Per API)**	**Results**
Foreign Matter	Not more than 2%	Nill
Ash Value	Not more than 8%	3.627%
Acid Insoluble ash	Not more than 4%	1.146 %
Water soluble extractive	Not less than 11%	21.868 %
Alcohol Soluble extractive	Not less than 5%	1.864

2. AMALAKI[220]

Amalaki is a large deciduous tree has got greenish-grey or red bark, peeling off in scales. The leaves are pinnate, distichously close-set, linear-oblong, obtuse, flowers-densel fascicled along the branchlets, yellowish in colour. The males on slender pedicles, females sub-sessile. The fruits are berry type, depressed globose, succulent, yellow or pink colour when ripe, obscurely 6- lobed and seeds are trigonus.

Family	**:**	Euphorbiaceae
Botanical Name	**:**	*Emblica officinalis* Gaertn.
Paryaya	**:**	*Dhatri, Vayasya, Vrishya, Amritaphala*
Types	**:**	-
Chemical constituents	**:**	Ellagic acid, lupeol, oleanolic aldehyde, leucodelphinidin, procyanidin, tannin, vit-C, phyllemblin, Linolic acid, indole acetic acid, terchebin, corilgin, and salts.
Therapeutic Action	**:**	*Tridoshahara* especially *pittahara, Daahaprashamana,Chakshushya,Keshya Rasayana, Pramehagna, Vrushya*.
Therapeutic Uses	**:**	*Netraroga, Amlapitta, Raktapitta, Prameha, Trushna, Daaha, Mutra roga*.
Parts Used	**:**	*Phala* (Fruits)
Dosage	**:**	*Churna*: 3-6gms
Gana:		
Charaka	**:**	*Vayahsthapana, Virechanopaga*
Sushruta	**:**	*Triphala, Parusakadi.*
Vagbhata	**:**	*Parusakadi*

RECENT STUDIES[218]:

The Amalaki (Emblica officinalis) has got Anti Hyperglycemic, Anti Ulcerogenic, Anti Hyperlipidemic activity. It has also got the Nephroprotective, Neurotonic effect, Anti carcinogenic, Anti Oxidant, Anti Inflammatory activity.

Table No. 25: Showing the Raw drug Amalaki Authentication test result

Description Macrosopic:		
Tests	**Limits (As Per API)**	**Results**
Parts	Pericap of dried fruit	Pericap of dried fruit
Colour	Grayish to Black	Grayish to Black
Odour	Indistinct	Indistinct
Taste	Sour & Astringent	Sour & Astringent
Physio Chemical Standards		
Tests	**Limits (As Per API)**	**Results**
Foreign Matter	Not more than 3%	Nill %
Ash Value	Not more than 7%	3.583 %
Acid Insoluble ash	Not more than 2%	0.519%%
Water soluble extractive	Not less than 50%	57.871 %
A;cohol Soluble extractive	Not less than 40%	43.396

3. HARITAKI[217]

Haritaki is a large tree usually rusts coloured; the younger branches are silvery colour. The leaves are ovate, distant, 8-20cm long. The flowers are dull white or yellowish, strong offensive smells. Fruit is ovovoid in shape, glabrous, broad base. After drying fruits are in five ribbed. Fruiting season is in the month of November to January.

Family : Combretaceae

Botanical Name : Terminalia Chebula. Retz

Paryaya : Abhaya, Pathya, Kayastha, Haimavati, Vayastha, Rohini, Chetaki, Avyaktha.

Types : 7 Types

Chemical constituents : Fruit: chebulinic acid, tannic acid, vit C, glycoside. Fruit kernel: Krachivic, behelic, stearic acid

Therapeutic Action : Tridoshahara, Rasayana, Deepana, Balya Anulomana, Shotahara, Hridya, Kaphagna.

Therapeutic Uses : Vata Vyadhi,Nadi Dourbalya, Prameha, Vibandha, Aruci, Udavarta, Gulma, Udararoga, Arsha,

		Pandu, Shotha, Jeernajvara, Vishamajvara, Kasa, Tamaka Shwasa, Hrdroga.
Parts Used	**:**	Fruits
Dosage	**:**	3-6gms
Gana :		
Charaka	**:**	Prajasthapana, Jvaraghna, Kustaghna, Kasagna, Arshogna
Sushruta	**:**	Triphala, Amalakyadi, Parushakadi.
Vagbhata	**:**	Parushakadi.

RECENT STUDIES[218],[219]:

Haritaki has got Anti Hyperlipidemic, anti inflammatory, anti viral, anti Mutagenic and Cardioprotective activity. In other studies it shows Retinoprotective, Anti hemorrhagic and Anti parasitic activity.

Table No. 26: Showing the Raw drug Haritaki Authentication test result

Description Macrosopic:		
Tests	**Limits (As Per API)**	**Results**
Parts	Pericap of Dried fruits	Pericap of Dried fruits
Colour	Greenish to Yellowish	Greenish to Yellowish
Odour	Not specific	Not specific
Taste	Astringent	Astringent
Physio Chemical Standards		
Tests	**Limits (As Per API)**	**Results**
Foreign Matter	Not more than 1%	Nill
Ash Value	Not more than 5%	2.477%
Acid Insoluble ash	Not more than 5%	4.317 %
Water soluble extractive	Not less than 60%	64.428 %
A;cohol Soluble extractive	Not less than 40%	55.667 %

4. BIBHITAKI[222]

Bibhitaki (*Terminalia belerica* Roxb) is a large tree around 20-25mtr high with pubescence on younger branch lets. The leaves are clustered at the end of branch lets, pale beneath, broad elliptic or obviate in shape, interrupted 8-15cms long. The fruit are ovoid grey velvety in colour with 5 or more indistinct furrows.

Family	**:**	Combretaceae
Botanical Name	**:**	Terminalia belerica Roxb.
Paryaya	**:**	Bibitaka, Karshaphala, Aksha, Kalidruma, Bhuta Vasa.
Types	**:**	-
Chemical constituents	**:**	Galactose, glucose, mannitol, sitosterol,
Therapeutic Action	**:**	Tridoshahara especially Kaphahara, Vedanasthapana, Deepana, Anulomana, Trushna Nigrahana, Shothahara,
Therapeutic Uses	**:**	Jwara, Svarabheda, Abhishyanda, Kasa, Chardi, Krimiroga,Vibandha, Vatavyadhi, Agnimandya,Trushna.
Parts Used	**:**	Fruits
Dosage	**:**	3-6gms
Gana:		
Charaka	**:**	Jvarahara, Virechanopaga.
Sushruta	**:**	Triphala, Mustadi

RECENT STUDIES [223]:

Bibhitaki (Terminalia belerica Roxb) has got Anti Hyperlipidemic, Anti platelet aggregation activity of Terminalia belerica, Anti hyperglycemic, Anti inflammatory, Retinoprotective and Hepato protective activity.

Table No.27: Showing the Raw drug Bibhitaki Authentication test result

Description Macrosopic:		
Tests	**Limits (As Per API)**	**Results**
Parts	Fruits	Fruits
Colour	Grayish Brown or silvery grayish	Grayish Brown
Odour	Characteristic	Characteristic
Taste	Astringent	Astringent
Physio Chemical Standards		
Tests	**Limits (As Per API)**	**Results**
Foreign Matter	Not more than 2%	Nill
Ash Value	Not more than 7%	3.785%
Acid Insoluble ash	Not more than 1%	0.276 %
Water soluble extractive	Not less than 35%	49.812 %
A;cohol Soluble extractive	Not less than 8%	19.533%

5. HARIDRA[224]

Haridra (*Curcuma longa* Linn) is an annual herb. The rootstalk is large, ovoid, cenile. The tubers are thick cylindrical bright yellow inside. The leaves are long petiole oblong narrow at the base, the flowers are bracts pale green.

Family **:** *Zingiberacae*

Botanical Name **:** *Curcuma longa* Linn.

Paryaya **:** *Kanchani,Varavarnini, Nisha, Krimigna, Gouri, Yoshitapriya, Httavilasini*,

Types **:** -

Chemical constituents **:** Curcumin, curcuminol, curcone, curdione, cineole, curcumins,

Therapeutic Action	**:**	*Kaphavatahara, Shotahara, Vedanasthapana, Varnya, Lekhana, Vishagna, Anulomana, Mutrasangrahaniya, Pramehagna*
Therapeutic Uses	**:**	*Prameha, Kusta, kandu, Vibhandha, Kasa, Jeernajwara*
Parts Used	:	*Kandha* (Tubers)
Dosage	**:**	Swarasa: 10-20ml, Churna: 3-6gms
Gana:		
Charaka	**:**	*Kushtagna, Kandugna, Lekhaniya, Vishagna, Tiktaskandha, Shirovirechana*
Sushruta	**:**	*Haridradi, Mustadi*
Vagbhata	**:**	*Vachadi, Mustadi*

RECENT STUDIES[220], [225]:

Haridra (*Curcuma longa* Linn) Antidiabetic, Anti inflammatory, Hypolipidemic effect, Antioxidant, Antibacterial, Antimicrobial activity. It has been proven for Antidepressan and Anticarcinogenic activity also.

Table No. 28: Showing the raw drug Haridra Authentication test result:

Description Macrosopic:		
Tests	**Limits (As Per API)**	**Results**
Parts	Rizome	Rizome
Colour	Yellowish to yellowish Brown	Yellowish
Odour	Characteristic	Characteristic
Taste	Bitter	Bitter
Physio Chemical Standards		
Tests	**Limits (As Per API)**	**Results**
Foreign Matter	Not more than 2%	Nill
Ash Value	Not more than 9%	5.343%
Acid Insoluble ash	Not more than 1%	0.759 %
Water soluble extractive	Not less than 12%	15.915 %
A;cohol Soluble extractive	Not less than 8%	16.456%

6. DEVADARU[226]

Devadaru is an evergreen tree growing up to 80m height. It has broad trunk and leaves slender dark green colour with wavy margins. The bark is thickened fissured at place. The wood is oily aromatic smell, hap wood white. The heart wood light yellowish brown in colour.

Family	**:**	Pinaceae
Botanical Name	**:**	*Cedrus deodara* Roxb Loud
Paryaya	**:**	*Bhadradaru, Suraburuha, Suradaru, Indradaru, Kilima*
Types	**:**	-
Chemical constituents	**:**	Essential oil from wood: p.methylacetophnone, atlantone. Stem bark: deodarin,toxifolin.
Therapeutic Action	**:**	Kaphavatahara, Shotahara, Kushtagna, Deepana, Krimigna, Lekhana, Raktaprasadana, Pramehagna
Therapeutic Uses	**:**	It is used in Sandhivata, Amavata, Grudrasi, Vibhandha, Kaasa, Peenasa, Mutrakricchra, Prameha, Medoroga,
Parts Used	**:**	Heart wood (Khandasaara) , Oil
Dosage	**:**	Churna: 3-6gms
Gana:		
Charaka	**:**	Stanya Shodhana, Anuvasanopaga,Katukaskanda
Sushruta	**:**	*Vatasamshamana*

RECENT STUDIES[221], [228]:

The Devadaru (Cedrus deodara) has got variety of actions like Antioxidant, Anticonvulsant, and Gastric anti secretory and antiulcer & anxiolytic activity. It has the other effect like Mild Antihyperglycaemic, Antimicrobial activity, Anti-inflammatory & Antiviral activity Activity.

Table No.29: Showing the raw drug Devadaru Authentication test result:

Description Macrosopic:		
Tests	**Limits (As Per API)**	**Results**
Parts	Heart wood	Heart wood
Colour	Yellowish Brown	Yellowish Brown
Odour	No distinct	Not distinct
Taste	Aromatic	Aromatic
Physio Chemical Standards		
Tests	**Limits (As Per API)**	**Results**
Foreign Matter	Not more than 1%	Nill
Ash Value	Not more than 2%	1.195%
Acid Insoluble ash	Not more than 1%	0.528 %
Water soluble extractive	Not less than 7%	16.872 %
A;cohol Soluble extractive	Not less than 1.5%	7.747 %

7. MURVA[229]

Murva **(***Marsdenia tenacissima* W. & A**)** is a perineal climber. It has purple or yellowish flower. It is one of the highly controversial plants.

Family **:** Asclepiadaceae

Botanical Name **:** *Marsdenia tenacissima* W. & A

Paryaya **:** Moorva,Tiktavalli,Piluparni, Madhurasa,

Types **:** -

Chemical constituents **:** Marsdenin, D-cymorose, Asclepobiose, D-canarose,linsugenin etc.

Therapeutic Action	**:**	Tridoshahara, Deepana, Pachana, Anulomana, Hridya, Pramehagna, Raktashodaka
Therapeutic Uses	**:**	Charnaroga, Amadosha, Shoola, Krimi, Prameha, Kusta, Vishamajwara
Parts Used	**:**	Roots
Dosage	**:**	Kwatha: 50-100ml
Gana:		
Charaka	**:**	Sthanyashodhana , Truptighna &Tiktaskanda,
Sushruta	**:**	Patoladi, Pittasamshamana,
Vagbhata	**:**	Varunadi, Aragvadadi, Vatsakadi

RECENT STUDIES [230], [231],[232]:

In recent study shows that the extract of Murava have Anti-angiogenic effect in vitro and in vivo study[230]. The ethanol extract has anti tumour and antipyretic activity.

Table No.30: Showing the raw drug Murva Authentication test result

Description Macrosopic:		
Tests	**Limits (As Per API)**	**Results**
Parts	Stem	Stem
Colour	Yellowish to Buff	Yellowish to Buff
Odour	Aromatic	Aromatic
Taste	Slightly bitter	Slightly bitter
Physio Chemical Standards		
Tests	**Limits (As Per API)**	**Results**
Foreign Matter	Not more than 2%	Nill
Ash Value	Not more than 5%	3.180 %
Acid Insoluble ash	Not more than 0.5%	0.376 %
Water soluble extractive	Not less than 14%	22.308 %
A;cohol Soluble extractive	Not less than 7%	14.388%

8. ENDRI [233]

Endri is a perineal climbing herb with angular stem and bifid tendril. The leaves are sinuately pinnate, flowers solitary axillary. The fruits are globose, smooth green in colour, bitters in taste. The seeds are many in numbers, white or light brown in colour.

Family	**:**	Cucurbitaceae
Botanical Name	**:**	*Citrullus colocynthis* Schrad
Paryaya	**:**	Gavakshi, Chitra, Gavadani, Indravalli, Indravarunika, Vishala,
Types	**:**	-
Chemical constituents	**:**	Alkaloids 1, 2, 3, cucurbitacin, cucurbitacin B, citrollic acid, cucurbitacin C, citrollol.
Therapeutic Action	**:**	Kaphapittahara, Vrunashotahara, Vishagna,Vamaka, Rechana, Pramehagna,Garbhashaya sankochaka
Therapeutic Uses	**:**	Gulma, Kamala, Amavata, Rajorodha, Kastaprasava, Prameha
Parts Used	:	Moola, Phala
Dosage	**:**	Moola churna: 1-3gms, Phala churna: 1/8-1/2gm

Gana:

Charaka	**:**	Virechana, Moolini
Sushruta	**:**	Adhobhagahara, Shyamadi
Vagbhata	**:**	-

RECENT STUDIES[227], [223], [225], [234]:

Indravaruni has gotiImmunostimulating activity; fruits have got anti diabetic effect, Anticarcinogenic activity and Antioxidant activity.

Table No.31: Showing the raw drug Endri (Indravaruni) Authentication test result:

Description Macrosopic:		
Tests	**Limits (As Per API)**	**Results**
Parts	Root	Root
Colour	Dull Yellow	Dull Yellow
Odour	Indistinct	Indistinct
Taste	Bitter	Bitter
Physio Chemical Standards		
Tests	**Limits (As Per API)**	**Results**
Foreign Matter	Not more than 2%	Nill %
Ash Value	Not more than 8%	3.630%
Acid Insoluble ash	Not more than 2%	0.982 %
Water soluble extractive	Not less than 40%	42.427%
A;cohol Soluble extractive	Not less than 6.5%	9.447%

9. LODRA[235]

Lodhra (*Symplocos racemosa* Roxb.) is a medium tree grows 6m high; the bark is dark grey in colour and rough. The leaves are elliptic oblong, acute, globus above. The flowers are white or whitish yellow. The fruit is drupe, purplish black in colour.

Family : Symplocaceae

Botanical Name : Symplocos racemosa Roxb.

Paryaya : Sthulavalkala, Tilvaka, Akshibhaishajya, Shavaraka,

Types : Many

Chemical constituents : Symposide, lopuridin, lopurin, colloturin.

Therapeutic Action : Kaphapittashamaka, Shotahara, Kushtagna, Raktasthambana,

Therapeutic Uses : Raktatisaara,Kaasa, Pradara, Jwara,

Parts Used	:	Twak
Dosage	**:**	Kwatha: 5-10ml, Churna: 1-3 Masha
Gana:		
Charaka	**:**	Shonita sthapana, Sandhaniya, Pureesha sangrahaniya, Kashaya skanda
Sushruta	**:**	Lodradi, Nyagrodadi
Vagbhata	**:**	Lodradi, Nyagrodadi

RECENT STUDIES[231], [227], [236]:

Lodhra has got hepatoprotective activity along with Gonadotropin releasing effect. It has also Antidiabetic, wound healing and antimicrobial activity.

Table No.32: Showing the raw drug Lodhra Authentication test result

Description Macrosopic:		
Tests	**Limits (As Per API)**	**Results**
Parts	Stem Bark	Stem bark
Colour	Grayish Brown to Gray	Grayish Brown
Odour	Not specific	Not Specific
Taste	Astringent & feebly bitter	Astringent & feebly bitter
Physio Chemical Standards		
Tests	**Limits (As Per API)**	**Results**
Foreign Matter	Nill	Nill
Ash Value	Not more than 12%	8.197 %
Acid Insoluble ash	Not more than 1%	0.631 %
Water soluble extractive	Not less than 15 %	24.490 %
A;cohol Soluble extractive	Not less than 9%	14.070 %

All the 09 ingredients of Mustadi Kwatha were authenticated in AYUSH approved Testing Laboratory for ASU Drugs at Central Research Facility at KLE's BMK Ayurved Mahavidyalaya, Belgaum, Karnataka.

1. Musta
[*Cyperus rotundus* Linn]

2. Amalaki
[*Embelica officinalis* Gaertn]

3. Haritaki
[*Terminalia chebula* Roxb]

4. Bibhitaki
[*Terminalia belerica* Retz]

5. Haridra
[*Curcuma longa* Linn]

Figure No. 1: Raw Drug Photos of Musta, Amalaki, Haritaki, Bhibhitaki & Haridra

6. Devadaru
[*Cedrus deodaro Roxb* Loud]

7. Endri
[*Marsdenia tenacissima* Wight & Arn]

8. Lodhra
[*Symplocos racemosa* Roxb]

9. Murva
[*Citrullus colocynthis* Schrad]

Figure No. 2: Raw Drug Photos of Devadaru, Endri, Lodhra & Murva

MUSTADI KWATHA CHURNA

MATERIALS & METHODS:

Source of Literature:

All the *Ayurvedic* treatises and information's available allopathic system of medicine for *Madhumeha* and Diabetes mellitus were consulted for literary source including *Ayurveda* Journals, Modern Journals and information available in different websites.

Source of Medicine (Drug):

The ingredients of the *Mustadi Kwatha* (*B.R Prameha rogadhika*ra Chapt.37) were collected by considering the standard mentioned in The Ayurvedic Pharmacopeia of India. Individual ingredients were authenticated in Central Research Facility at KAHER's *Ayurveda Mahavidyalaya*, Belgaum, Karnataka

Table No. 33: Showing the ingrediants of Mustadi Kwatha

Sl.No.	Name of the Drug	Scientific name	Family	Parts used
1.	*Musta* [204]	Cyperus rotundus *Linn*	Cyperaceae	Dried Rhizome
2.	*Amalaki*[205]	Embelica officinalis *Gaertn*	Euphorbiceae	Dried fruit
3.	*Haritakia*[206]	Terminalia chebula *Roxb*	Combritaceae	Dried fruit
4.	*Bibhitaki*[207]	Terminalia belerica *Retz*	Combritaceae	Dried fruit
5.	*Haridra*[208]	Curcuma longa *Linn*	Zingiberaceae	Dried Rhizome
6.	*Devadaru*[209]	Cedrus deodaro Roxb *Loud*	Pinaceae	Heart wood *(Kanda sara)*
7.	*Murva*[210]	Marsdenia tenacissima *Wight & Arn*	Asclepidiaceae	Root
8.	*Endri*[211]	Citrullus colocynthis *Schrad*	Curcubitaceae	Root
9.	*Lodhra*[212]	Symplocos racemosa *Roxb*	Symplocaeae	Bark

Procedure adopted for Preparation of *Mustadi Kwatha* [237]:

All the ingrediants of *Mustadi Kwatha* were collected individually and checked properly and coarse powder were prepared. After adding eight parts of water mixed with one part of *Mustadi kwatha choorna.* The entire medicine along with water were boiled till it was reduced to one part. After proper percolation of the filtrate i.e. boiled liquid content is called kwatha was taken for internal administration of patients.

While preparing the kwatha eight times of water was taken, because all the ingredients present *Mustadi kwatha yogas* were having medium in the type of hardness[237].

Study Sample (Patient):

The Patients who are approaching the outpatient department and inpatient department of Shri J.G.C.H Society's Sahakar Maharshi Shri B A Patil Ayurvedic Medical College Hospital, *Ghataprabha Karnataka*, suffering with classical symptoms of Madhumeha vis-a-vis Diabetes Mellitus (Type-II) both male and female patients by following the predesigned inclusion and exclusion criteria.

Method of data Collection:

This present study designed as single blind study with cross over. Two groups were done. **Group A 75** patients and **Group B 75** patients excluding the dropouts. After Completion of treatment in both the **Group A** (treated by Oral anti diabetic drug and *Mustadi Kwatha*) and **Group B** (treated by oral anti diabetic drug & placebo). The washout period was 90 days. During that period the patients were advised to continue only allopathic drug. Then crossover of the drug was done to both the groups.

Where **Group - A** were given Placebo along with oral anti diabetic drug and **Group - B** were given *Mustadi Kwatha* along with their previously continued oral anti diabetic drug.

Clinical signs & symptoms (subjective parameters) and all the objective parameters of *Madhumeha* vis-à-vis diabetes mellitus were collected predesigned case proforma in premeditations, during medications and post medications.

Criteria for Inclusion:

Patients having classical signs and Symptoms of *Madhumeha* vis-a-vis Type-II Diabetes Mellitus like:

- *Prabhootamootra* more than 3000ml in a day[236]
- *Avilamootra* [237], [238]
- *Ati Kshuda* [239]
- *Pippasa* [240]
- *Dourbalyata*[241]
- *Swedadhikata*
- *Shosa of Galatalu*
- *Klaibyata*
- *Purisha baddhata*
- Duration of illness *Madhumeha* not more than five years
- Patients having *Madhumeda* in both sexes
- Treated patients with allopathic drug during the age group of thirty to seventy years.
- Diabetic patients having [241a]
    - FBSL more than & equal to (≥) 126mg/100 ml of blood and less than and equal to (≤) 220mg/100 ml of blood,
    - PPBSL: more than & equal to (≥) 140mg/100ml of blood and less than and equal to (≤) 280mg/100 ml of blood
- Glycosylated Hb (HbA_1c)[241a] more than (≥) 6.5
- Diabetic receiving only oral anti diabetic will be taken in to the study.
- Patients having other systemic disorder which does not interfere present study

Criteria for Exclusion :

- *Madhumehi* with prameha pidaka (diabetic curbuncle)
- IDDM
- Patients who are having less than thirty years and more than 70 years of age
- Patient who are receiving insulin medication
- Patient having albuminurea

- Other diabetic severe complications of diabetes mellitus like neurological complications, cardiovascular complications, Nephropathy etc.
- Any systemic disorder Diabetes Mellitus which does not interfere with present medication.

Criteria for Assessment of result:

Assessment was done for the subjective & objective parameters before, during & after treatment with appropriate scoring of symptoms.

i. Subjective criteria:

Scoring of Symptoms:

Table No. 34: Showing the Scoring of subjective parameters of Madhumeha

Sl. No.	Subjective parameters	Score 0	Score 01	Score 02	Score 03
1.	*Prabhootamootra*				
	Quantity	Passing of normal quantity urine of up to 2 liters daily	Passing of more than normal quantity urine of daily from 2 liters to 03 liters daily	Passing of more quantity urine of daily from 03 liters to 3.5 liters daily	Passing profuse quantity urine of daily more than 3.5 liters
	Frequency	Frequency micturition three to six times daily, Rarely nocturia	Frequency micturition six to nine times daily Nocturia one to two times	Frequency micturition nine to twelve times daily, Nocturia three to four times	Frequency micturition more than twelve times daily, Frequent Nocturia
2.	*Avilamootra*	**Score 0**	**Score 01**	**Score 02**	**Score 03**
		Normal straw coloured urine	Mild cloudy in appearance	Visible alphabet though the urine kept in a beaker	Alphabet is not visible through the urine kept in a beaker.
3.	*Ati Kshuda*	**Score 0**	**Score 01**	**Score 02**	**Score 03**
		Normal intake food	Consumes food more than normal quantity of food	Consumes heavy amount of food	Consumes heavy amount of food any following any schedule

4.	*Pippasa*	**Score 0**	**Score 01**	**Score 02**	**Score 03**
		Consumes normal quantity of water	Consumes two to three liters of water daily	Consumes two to three liters of water daily	Consumes more than four liters of water daily
5.	*Dourbalyata*	**Score 0**	**Score 01**	**Score 02**	**Score 03**
		Can carry out normal work	Can do the work with some difficulty	Perform the work with difficulty	Can not perform regular work also
6.	*Swedadhikata*	**Score 0**	**Score 01**	**Score 02**	**Score 03**
		No sweating	Perspiration normal work	Excessive Perspiration even in normal as well as walking to some distance /stepping ladder	Excessive perspiration even after rest.
7.	*Shosa of Galatalu*	**Score 0**	**Score 01**	**Score 02**	**Score 03**
		No dryness of throat	Dryness of throat reduced after consumption of water	Dryness of throat reduced after consumption of more quantity of water	Dryness of throat does not subside even after consumption of more water.
8.	*Klaibyata*	**Score 0**	**Score 01**	**Score 02**	**Score 03**
		Normal	Diminished frequency but have normal sexual behavior	Decreased libido with reduced sexual behavior	Sexual frigidity
9.	*Purisha baddhat*	**Score 0**	**Score 01**	**Score 02**	**Score 03**
		Normal passes feces daily	Passes of feces with efforts sometimes needs stool softeners	Passes of feces in more than twenty four hours. Needs purgatives	Passes of feces after a gap of twenty four hours, conventional laxative not effective.

ii. Objective criteria

- Fasting Blood Sugar (FBS)
- Post Prandial Blood Sugar (PPBS)
- Glycoselated Hb (HbA1c)
- The entire study blood sugar & Glycoselated Hb (HbA1c) was estimated by using one instrument
- Urine Sugar was estimated.

Interventions:

Sample size: 150

At 95% C.I. with allowable error of 10%.

Study design:

The clinical study was carried out in 150 patients in a single blind crossover of groups. Two groups were made consisting 75 patients each.

Group A – diagnosed patients who are taking oral allopathic anti diabetic medicines along with *Mustadi Kwath* (Study group)

Group B– diagnosed patients who are taking oral allopathic anti diabetic medicines along with placebo (Control group).

After 90 days of treatment & 03 month washout period, the patient were crossed over where,

Group A were received placebo along with oral anti diabetic drugs and

Group B were received *Mustadi kwatha* along with oral anti diabetic drugs.

For Placebo Gum acacia tablet was used in a dose of 250 mg.

Posology[237a]:

The *Mustadi kwatha* were given in a dose of 48 ml twice daily as per the given schedule:-

Table No. 35: Showing the Posology of *Mustadi Kwatha* in *Madhumeh*a

Drug	Dosage with frequency	Duration (in days)
Mustadi Kwatha	48ml twice daily in empty stomach (02 pala in *Abhakta kala*)	90

Treatment duration:

The intervention of the trial drug was done for period of ninety days. Assessment of effect of trial drug were done on interval of Zero day, on fifteenth day, thirtieth day, forty-fifth day, sixtieth day, seventy-fifth day and ninetieth day.

Statistical analysis:

The data collected during clinical study were tabulated and statistically analyzed using ‘ z’ test, ‘t’ test & Statistical method like Parametric, Non parametric and ANOVA. The probability with $p< 0.05$ was considered as significant of result.

Investigations

Routine Investigations

Blood- Hb, TC, DC

Urine– Sugar, Albumin, Microscopic study

Special Investigations

- Blood Glucose Test – FBS, PPBS
- HbA1c
- Lipid Profile (Serum Cholesterol, Triglyceride, LDL. HDL, VLDL)
- Kidney profile (Serum creatinine, Serum Urea)

DEMOGRAPHIC STUDY:

Observations:

The present clinical study was conducted upon 150 patients of *Madhumeha,* were screened and diagnosed from Shri J.G.C.H.S *Ayurvedic* Medical College Hospital *Ghataprabha* and medical camps completed the treatment. Out of which 15 patients refused to take part in our study and 20 patients were discontinued in between. 150 patients had completed the full duration of treatment with follow up. All the relevant data were collected before and after treatment and analyzed statistically.

The total observations of this clinical study are compiled under the following two headings.

A. Demographic Data B. Clinical observational Data

A. Demographical Data:

Details of Age, Sex, religion, education, occupation, economic status and marital status wise distribution of 150 patients of *Madhumeha* are as follows:

Table 36: Showing Age wise distribution of 150 Patients *Madhumeha*:

Age group	Group A N=75		Group N=75		Total	Percentage
	No of patients	%	No of patients	%	No of patients	%
30-40	19	25.33%	06	8%	25	16.67%
41-50	16	21.33%	23	30.67%	39	26%
51-60	20	26.66%	27	36%	47	31.33%
61-70	20	26.66%	19	25.33%	39	26%

Among the 150 patients of *Madhumeha* in between age group of 30 to 70 years ,25.33% of the subjects were between the age group in 30- 41years, 21.33% patients were in 41-50 age groups , 26.66% patients were in between the age group 51-60 years and 26.66% patients were in between the age group of 61-70 years in group A. In group B 8% of the patients were between the age group of 30-40 years, 30.67% were in between 41-50 years, 36% patients were in between the age group of 51-60 years and 25.33% patients were in between the age group 61-70 years. Over all in group A and B 16.67% of the subjects were belonged in the age group between 30-40 years, 26% in between 41-50, 31.33% is in between 51-60 and 26% were in 61-70 years range (Fig. No 3).

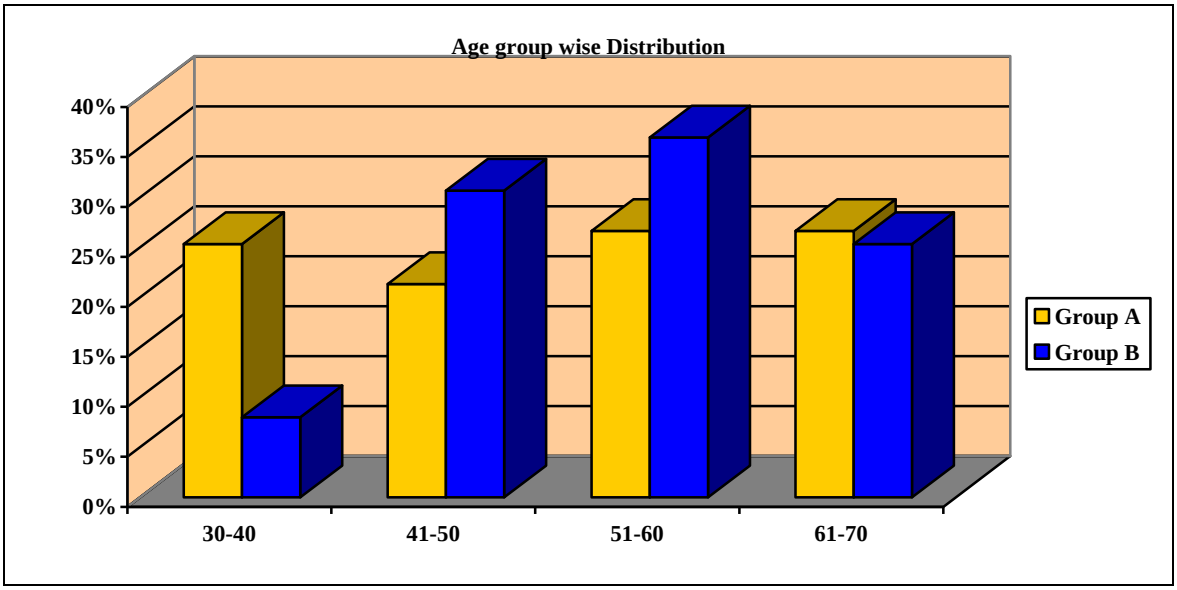


Fig.No.3: Showing Age group wise distribution of 150 Patients of Madhumeha

Table-37: Showing the sex wise distribution of 150 Patients of *Madhumeha*

Sex	Group A		Group B		Total	Percentage
	No of patients	%	No of patients	%	No of patients	%
Male	38	50.6%	53	70.6%	91	60.7%
Female	37	49.3%	22	29.3%	59	39.33%

Table 37 shows that out of 75 patients of madhumeha in each group 50.6 % of patients were males & 49.3% were females in group A. In group B there were 70.6 % were males & females of 29.3 % each. Total distributions of males were 60.7% & females were 39.33% .(Fig. No 4).

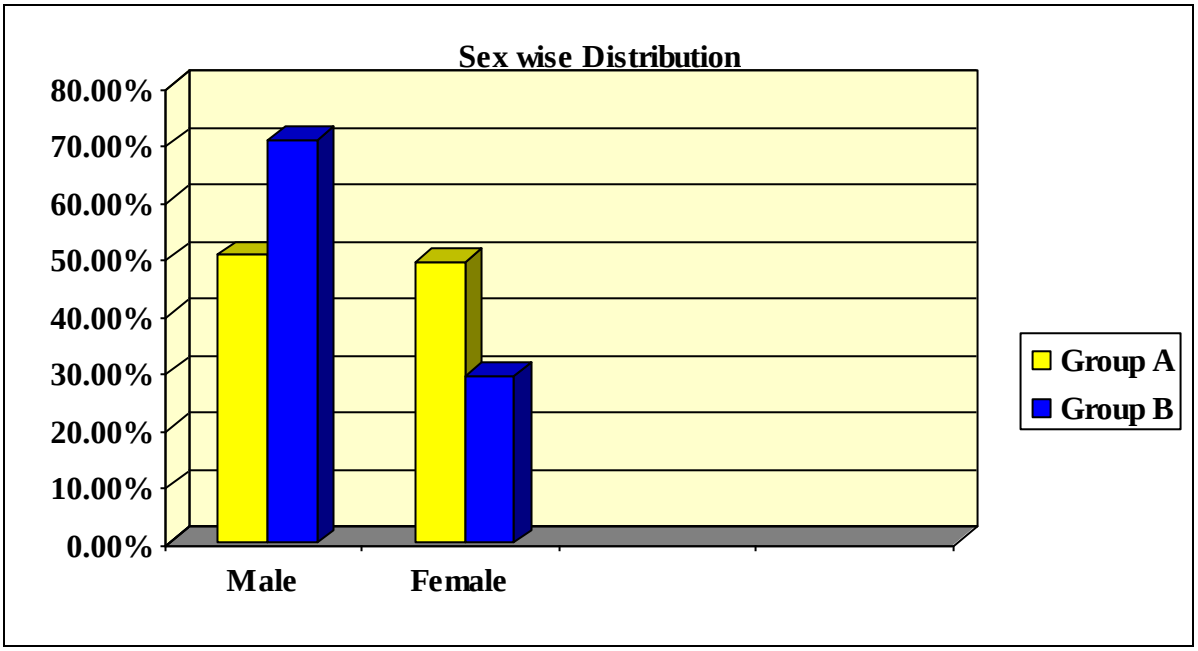


Fig.No.4: Showing the Sex wise distribution of 150 Patients of Madhumeha:

Table 38. Showing the Religion wise distribution of 150 Patients of Madhumeha:

Religion	Group A		Group B		Total	Percentage
	No of patients	%	No of patients	%	No of patients	%
Hindu	71	94.67%	69	92%	140	93.33%
Muslim	04	5.33%	02	2.67%	06	04%
Others (Christian, Jain)	0	0	04	5.33%	04	2.67%

Out of 150 patients of *Madhumeha* it was observed that 94.67 % were Hindus, 5.33% were Muslims in A group & in B group 92% were Hindus, 2.67% were Muslim. The total incidence being 93.33% patients from Hindu community, 4% from Muslim communoty, & 2.67 % from other community.(Fig. No 5).

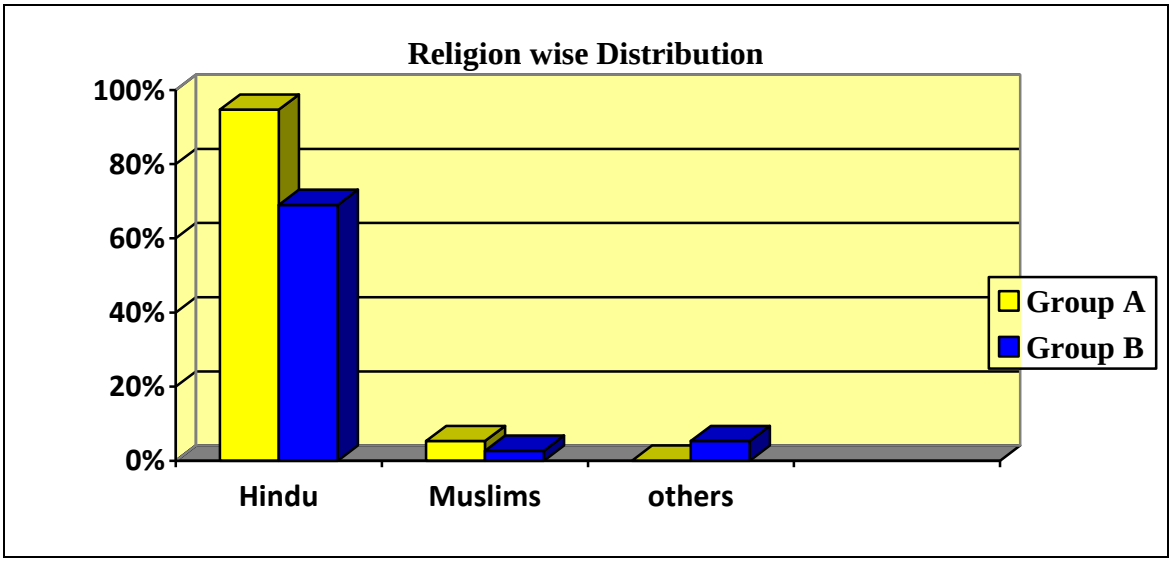


Fig.5: Showing the Religion wise distribution of 150 Patients of Madhumeha

Table-39: Showing the Marital Status wise distribution of 150 Patients of Madhumeha:

Marital Status	Group A		Group B		Total	Percentage
	No of patients	%	No of patients	%	No of patients	%
Married	71	94.67%	74	98.6%	145	96.67%
Unmarried	03	04%	01	1.33%	4	2.67%
Divorced	00	00%	00	00%	00	00%
Widow	01	1.33%	00	00%	1	1.33%

In this study it was found that 94.67% patients were married, 4% were unmarried and 1.33% were widow in group A. While in group B 98.6 % were married whereas 1.33 % were unmarried and 0% widows. Out of total 150 patients marital incidence being 96.67% married & 2.67% patients were unmarried, while 1.33% was widows.(Fig. No 6).

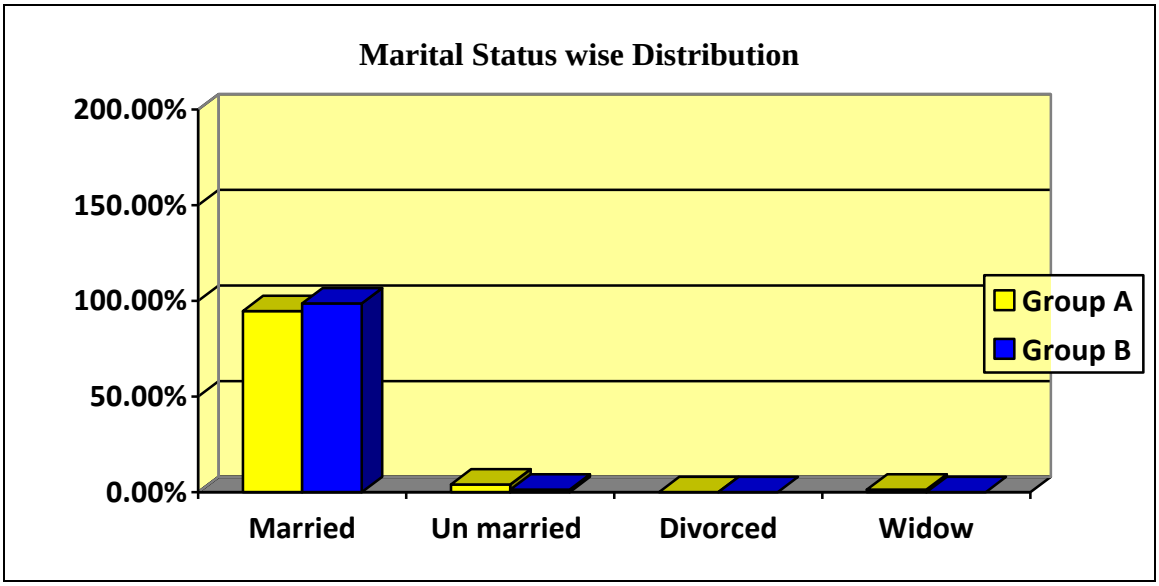


Fig.No.6: Showing the Marital Status wise distribution of 150 Patients of Madhumeha.

Table-40: Showing the Education Status wise distribution of 150 Patients of Madhumeha:

Educational status	Group A		Group B		Total	Percentage
	No of patients	%	No of patients	%	No of patients	%
Un Educated	05	6.67%	09	12%	14	9.3%
Primary School	39	52%	28	37.3%	67	44.67%
High School	25	33.33%	25	33.3%	50	33.3%
Under Graduate	06	8%	13	17.33%	19	12.67%
Post Graduate	00	00%	00	00%	00	00%

It is found in the study that out of 75 patients of Madhumeha in Group A 6.67 % patients were uneducated, 52% patients were of Primary school level, 3.33% were of High school level, 8% were educated up to the level of under graduate. In group B 12% patients were un educated, 37.33% were educated up to the level of Primary school, 33.33% were high school level and 17.33% patents were educated up to the level of undergraduate . Therefore overall 9.3% were uneducated, 44.67% patients were to the level of primary school. 33.33% were educated to the level of High school level, 12.67% patients were undergraduate level.(Fig. No. 7).

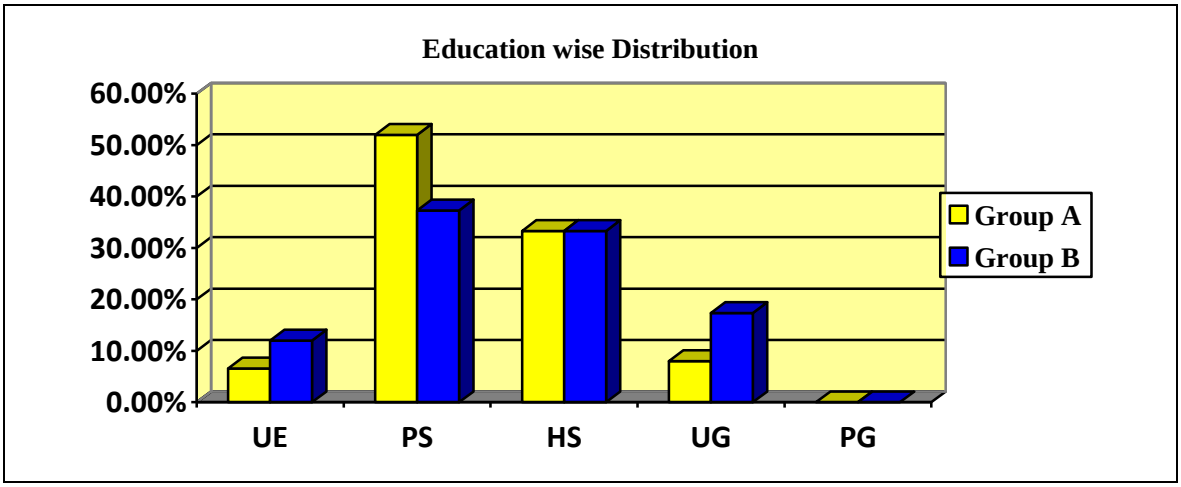


Fig. No. 7: Showing the Education Status wise distribution of 150 Patients of Madhumeha:

Table-41: Showing the Occupation wise distribution of 150 Patients of Madhumeha:

Occupation	Group A		Group B		Total	Percentage
	No of Patients	%	No of Patients	%	No of Patients	%
Sedentary	06	8%	07	9.33%	13	8.67%
Active	22	29.33%	34	45.33%	56	37.33%
Labour	14	18.67%	30	40%	44	29.33%
House work	33	44%	04	5.33%	37	24.66%

Out of 75 patients of Madhumeha in group A 8% patients having sedentary life style, 29.33% were having active work, 18.67% were having labour work and 44% were having house work. In group B 9.33 % were having sedentary life style, 45.33 % were having active work life, 40% were labour work and 5.33% were house workers. Over all out of 150 patients of Madhumeha 8.67 % were having sedentary life style, 37.33 % were having active work life, 29.33% were labor work and 24.66% were house worker.(Fig. No. 8).

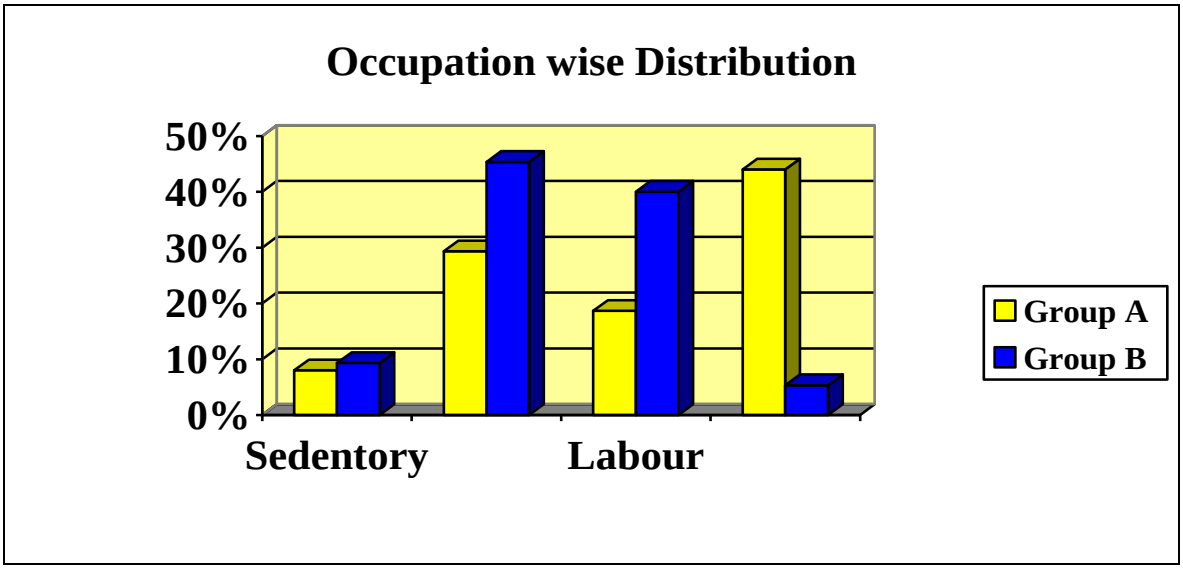


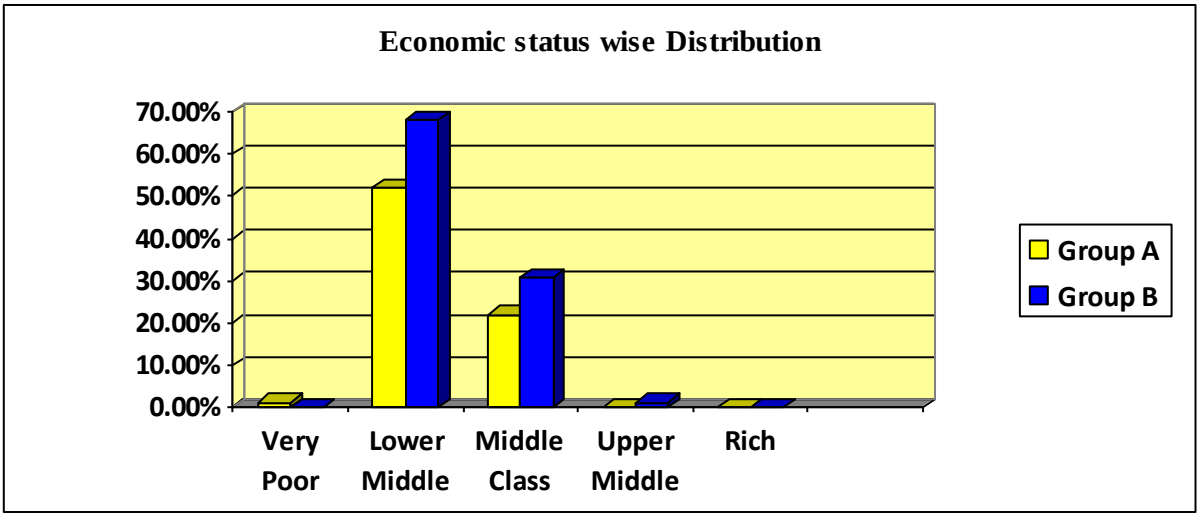
Fig. No. 8: Showing the Occupation status wise distribution of 150 Patients of Madhumeha

Table-42: Showing the Economic Status wise distribution of 150 Patients of Madhumeha

Economic Status	Group A		Group B		Total	Percentage
	No of Patients	%	No of Patients	%	No of Patients	%
Very poor	01	1.33%	00	00%	01	0.66%
Lower middle	52	69.33%	51	68%	103	68.66%
Middle class	22	29.33%	23	30.66%	45	30%
Upper middle	00	00%	01	1.33%	01	0.66%
Rich	00	00%	00	00%	00	00%

It was found that in group A only 1.33% were very Poor, 69.33% came from lower middle class , 29.33% middle class family, upper middle class and rich class. In group B, no patients from very poor category, 68% from lower middle class, 30.66% from upper middle class, only 1.33% from upper middle class & again 0% rich class. Therefore out of total 150 patient of Madhumeha 0.66% is from very poor category, 68.67% from lower middle class group, 30% from middle class, 0.66% from upper middle class and 0% from rich class .(Fig. No 9).

Fig.No. 9: Showing the Economic Status wise distribution of 150 Patients of Madhumeha



B. Clinical Data:

Table-43: Showing the Family history wise distribution of 150Patients of Madhumeha:

Family history	Group A		Group B		Total	Percentage
	No. of Patients	%	No. of Patients	%	No. of Patients	%
Present	39	52%	42	56%	81	54%
Absent	36	48%	33	44%	69	46%

Out of 75 patients of Madhumeha in Group A 52% patients were having family history and 48% were not having family history. In Group B 56% patients were havin family history and 44% patients were not having family history. Over all 150 patients 54% patients were having family history and 46% patients without family history.(Fig. No.10).

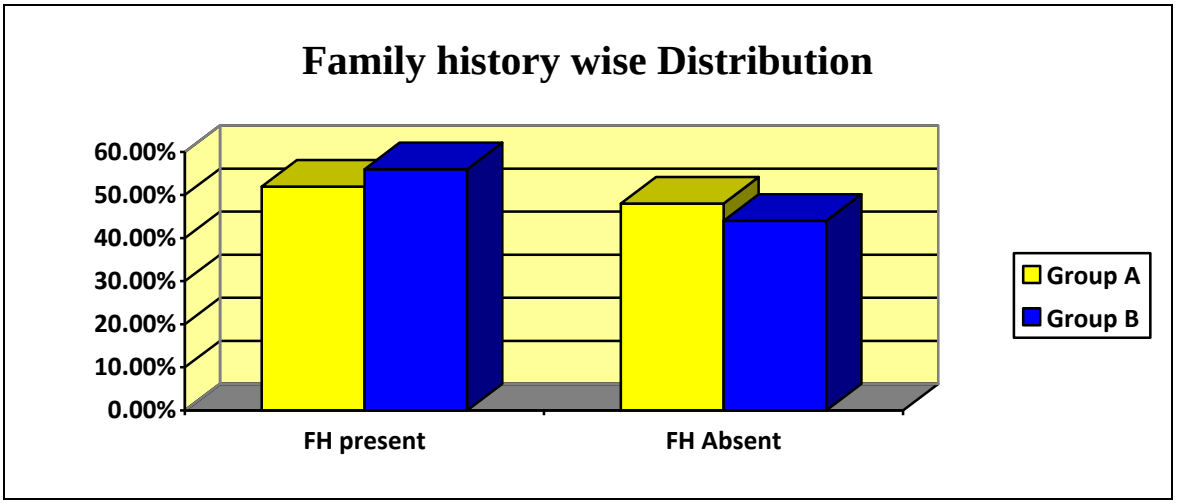


Fig. No.10: Showing the Family history wise distribution of 150 Patients of Madhumeha:

Table-44: Showing the Nature of Diet wise distribution of 150 Patients of Madhumeha

Diet	Group A		Group B		Total	Percentage
	No of Patients	%	No of Patients	%	No of Patients	%
Vegetarian	24	32%	27	36%	51	34%
Mixed food	51	68%	48	64%	99	66%

In group A out of 75 patients 32 % were having vegetarian food habit & 68% were having mixed food habit. In group B 36% patient were having vegetarian diet and 64% patients were having mixed food habit. Overall in 150 patients of group A & B 34% patients were having vegetarian diet and 66% patient were having mixed diet habit.(Fig. No.11).

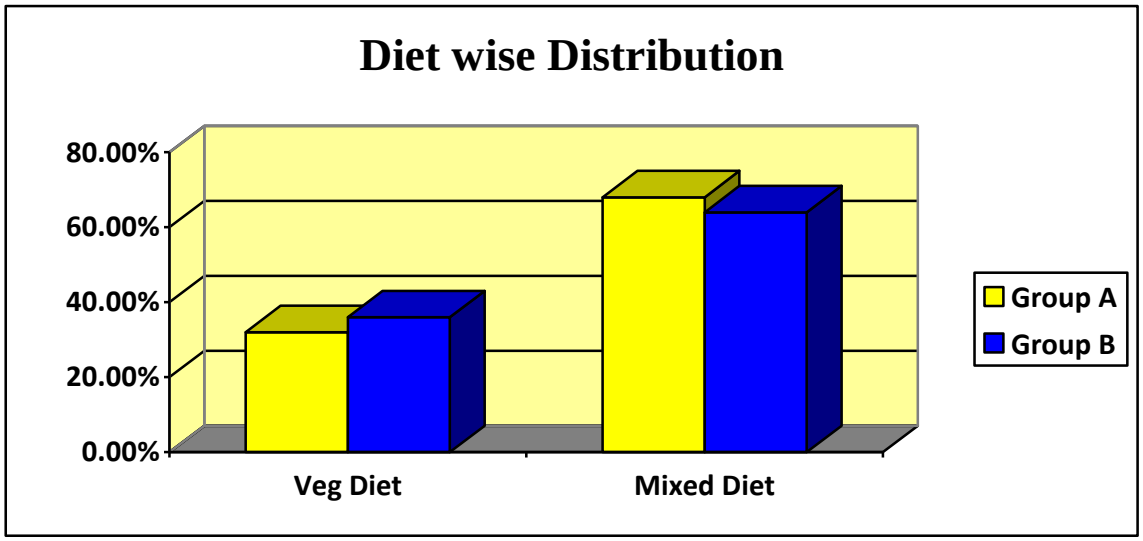
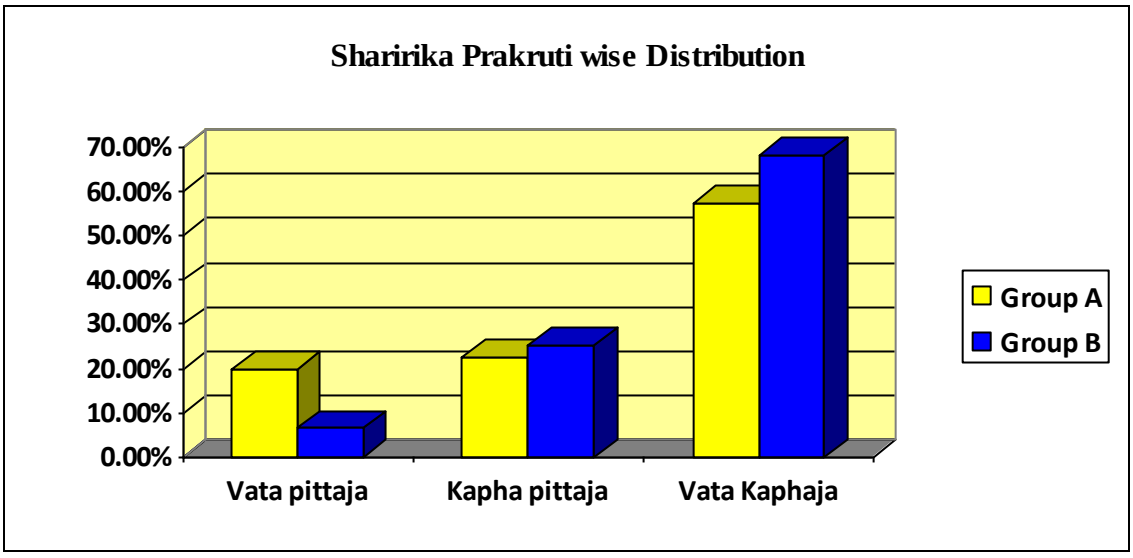


Fig.No.11: Showing the Nature of Diet wise distribution of 150 Patients of Madhumeha

Table-45: Showing the *Sharirika Prakruthi* wise distribution of 150 Patients of *Madhumeha*

Sharirika Prakruthi	Group A		Group B		Total	Percentage
	No of Patients	%	No of Patients	%	No of Patients	%
Vata pittaja	15	20%	05	6.67%	20	13.33%
Kapha Pittaja	17	22.67%	19	25.33%	36	24%
Vata Kaphaja	43	57.33%	51	68%	94	62.67%

In this clinical study out of 75 patients of *Madhumeha* 20% subjects were having *Vatapittaja prakruti*, 22.67% of *Kaphapittaja prakruti* and 57.33%% were of *Vatakaphaja prakruti* in group A. Out of 75 patients of Madhumeha in group B, 6.67% subjects were having *Vata kaphaja prakruti*, 25.33% patients were having *Kaphapittaja* and 68% patients were of *Vatakphaja prakriti*. So over all out of 150 patients of Madhumeha 13.33 % of *Vatapittaja prakruti*, 24% of *Kaphapittaja prakruti* and 62.67% subjects were having *Vatakaphaja prakruti*.(Fig. No.12).



F.No.12: Showing the *Sharirika Prakru*thi wise distribution of 150 Patients of *Madhumeha*

Table- 46: Showing the *Manasika Prakruthi* wise distribution of 150 Patients of *Madhumeha*.

Manasika Prakruthi	Group A		Group B		Total	Percentage
	No of Patients	%	No of Patients	%	No of Patients	%
Sattva	15	20%	24	32%	39	26%
Raja	21	28%	19	25.33%	40	26.67%
Tama	39	52%	32	42.67%	71	47.33%

In the present study of of 75 patients of *Madhumeha* in Group A 20% patients were having *Sattva prakruti*, 28% of *rajas prakruti* and 52% were having *Tamas prakruti*. Out of 75 patients of Group B, 32% subjects were having *Sattva prakruti*, 25.33% were having *Raja prakruti* and 42.67% patients were having *tamas prakruti*. So over all total 150 patients of *madhumeha* of 26% of *Sattva prakruti*, 26.67% of *Raja prakruti* and 47.33% subjects were having *tamas prakruti* (Fig. No. 13).

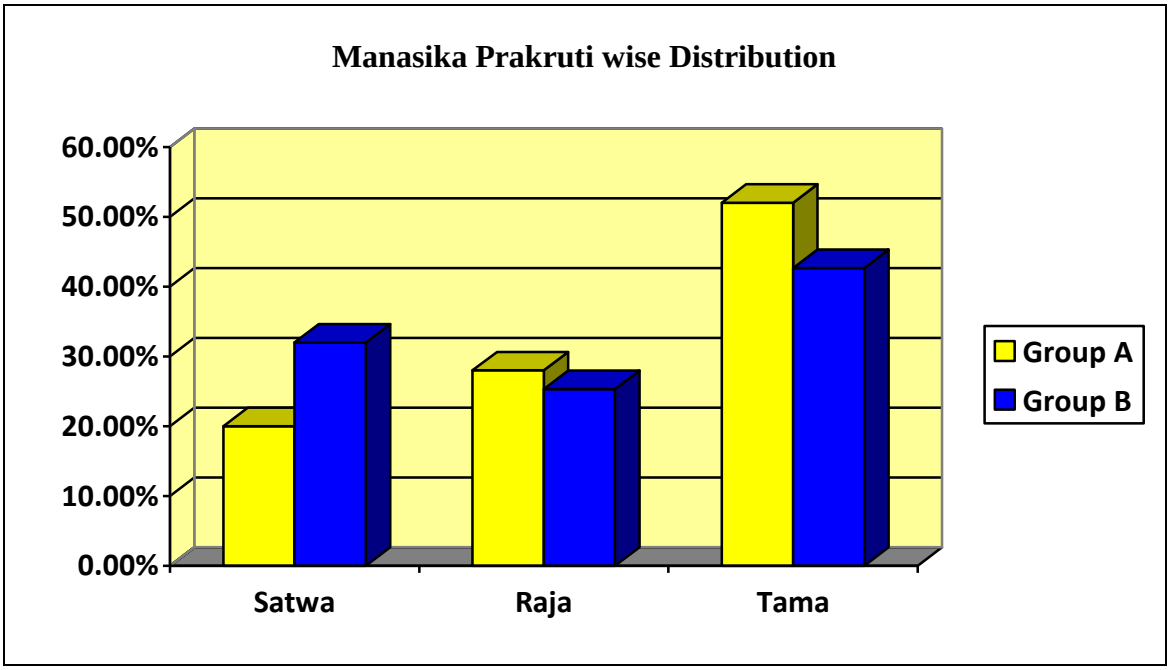


Fig.No 13: Showing the Manasika Prakruthi wise distribution of 150 Patients of Madhumeha

Table-47: Showing the Samhanana wise distribution of 150 Patients of Madhumeha

Samhanana	Group A		Group B		Total	Percentage
	No of Patients	%	No of Patients	%	No of Patients	%
Pravara	21	25%	26	34.67%	47	31.33%
Madhyama	40	55%	45	60%	24	56.67%
Avara	14	20%	04	5.33%	08	24%

In this present study out of 75 patients of *Madhumeha* of Group A, 25%% subjects were having *Pravara samhanana*, 55% subjects were having *Madhyama* and 20% subjects were having *Avara samhanana*. Out of 75 patients in Group B 34.67% subjects were having *Pravara samhanana*, 60% were having *Madhyama samhanana* and 5.33% patients were having *Avara samhanana*. Out of total 150 patients of madhumeha 31.33% patients were having *Pravara samhanana*, 56.67% subjects were having *Madhyama samhana*and 24% patients were having Avara samhanana.(Fig. No 14).

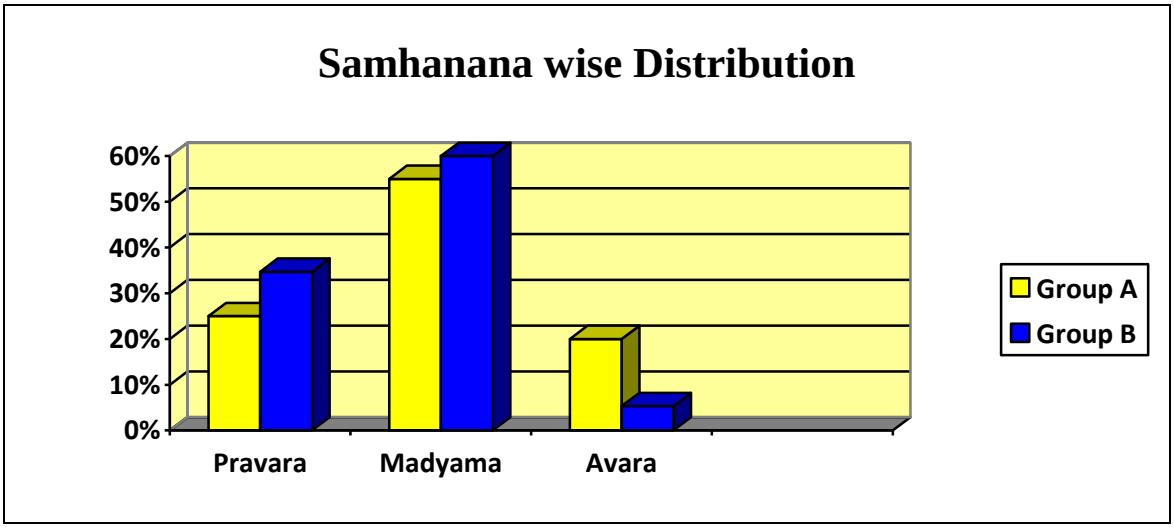


Fig.No 14: Showing the Samhanana wise distribution of 150Patients of Madhumeha:

Table-48: Showing the Pramana wise distribution of 150 Patients of Madhumeha:

Pramana	Group A		Group B		Total	Percentage
	No of Patients	%	No of Patients	%	No of Patients	%
Pravara	16	21.33%	08	10.67%	24	16%
Madhyama	42	56%	51	68%	93	62%
Avara	17	22.67%	16	21.33%	33	22%

In this present study out of 75 patients of *Madhumeha* in Group A, 21.33% subjects were having *Pravara pramana*, 56% patients were having Madhyama pramana and 22.67% patients were having *avara pramana*. Out of 75 patients of *Madhumeh*a in Group B 10.67% subjects were having *Pravara pramana*, 68%% were having *Madhyama pramana* and 33% were having *Avara pramana*. So out of total 150 patients of Madhumeha 16% of the patients were having *Pravara pramana*, 62% patients were having *Madhyama* and 22% having A*vara pramana*.(Fig. No 15).

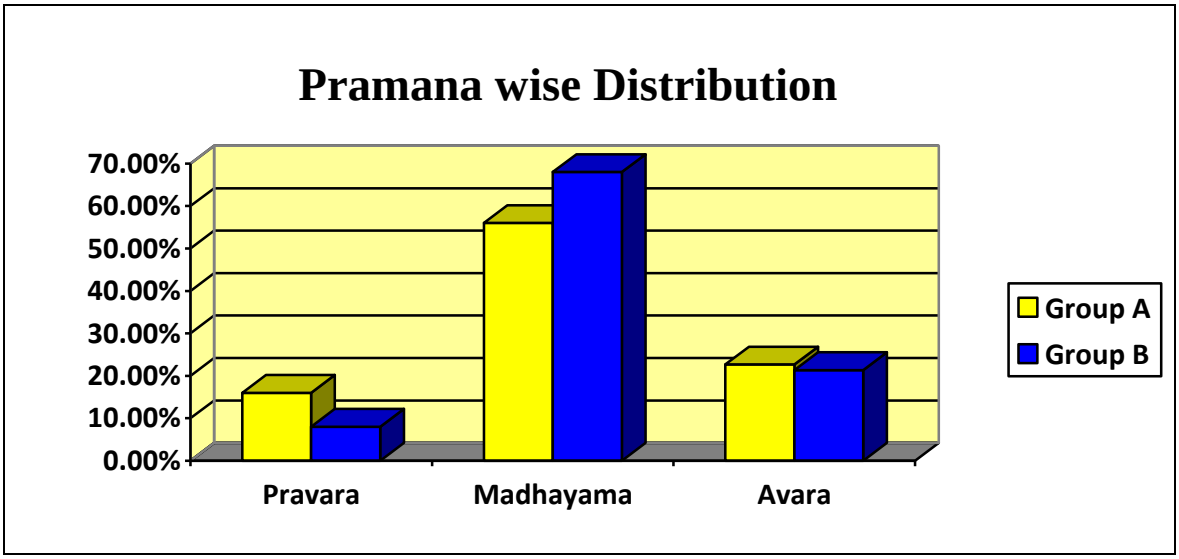


Fig.No.15: Showing the Pramana wise distribution of 150 Patients of Madhumeha

Table No. 49: Showing the Satva wise distribution of 150 Patients of Madhumeha

Satva	Group A		Group B		Total	Percentage
	No of patients	%	No of patients	%	No of patients	%
Pravara	05	06.67%	14	18.66%	19	12.67%
Madhyama	28	37.33%	29	38.66%	57	38%
Avara	42	56%	32	42.67%	74	49.33%

In the present study out of 75 patients of Madhumeha in Group A, 6.67% subjects were having Pravara satva, 37.33% were having Madhyama Satva and 56% patients were having Avara satva. Out of 75 patients of Madhumeha in Group B, 18.67% patients were having Pravara satva , 38.66% were having Madhyam satva, 42.67% were having Avara satva. So in total 12.67% patients were having Pravara satva, 38% patients were having Madhyama sattva and 49.33% were having Avara satva.(Fig. No.16).

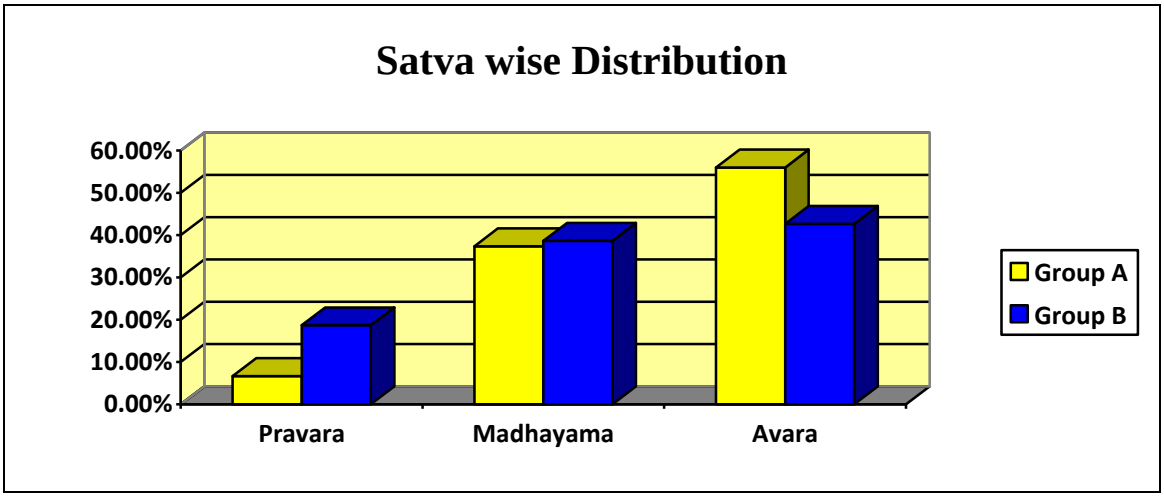


Fig.No.16: Showing the Satva wise distribution of 150 Patients of Madhumeha

Table-50: Showing the Vyayama Shakthi wise distribution of 150 Patients of Madhumeha

Vyayama Shakthi	Group A		Group B		Total	Percentage
	No. of Patients	%	No. of Patients	%	No. of Patients	%
Pravara	08	10.67%	10	13.33%	18	12%
Madhyama	20	26.67%	25	33.33%	45	30%
Avara	47	62.67%	40	53.33%	87	58%%

Out of 75 patients in Group A, 10.67% patients were having Pravara vyayama shakti, 26.67% were having Madhyama Vyayama shakti and 62.67% patients were having Avara vyayama shakti. Where as out of 75 patients of madhumeha in Group B 12% patients were having Prvara vyayama shakti, 33.33% were having Madhyama vyayama shakti and 53.33% patients were having Avara vyayama shakti . So out of total 150 patients of Madhumeha 12% subjects were Pravara vyayama shakti, 30% were having Madhyama vyayama Shakti, 58% subjects were having Avara vyayama shakti .(Fig. No.17).

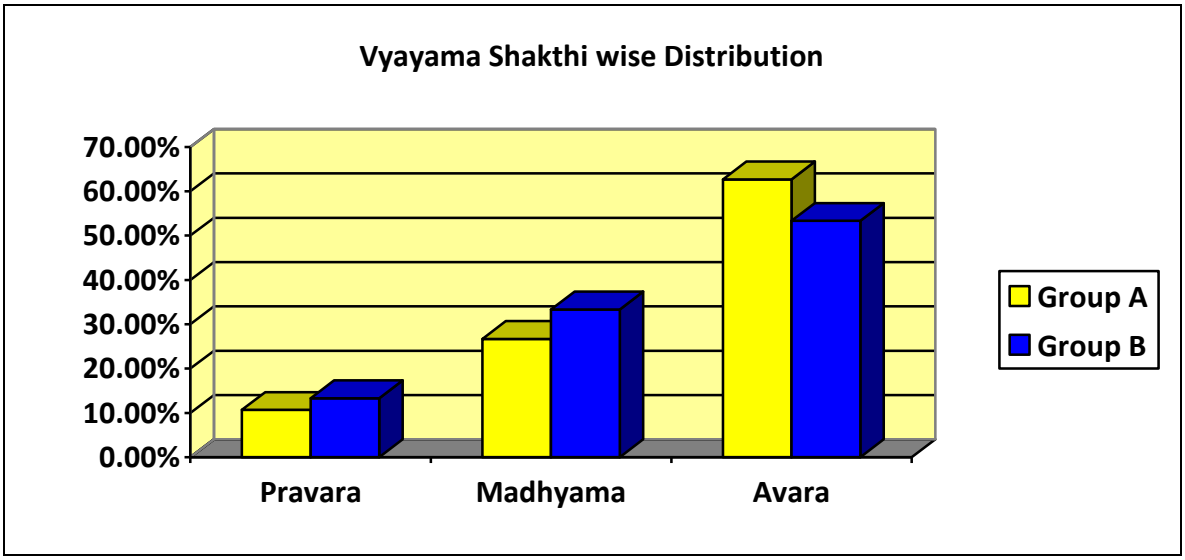


Fig. No.17: Showing the Vyayama Shakthi wise distribution of 150 Patients of Madhumeha

Table-51: Showing the *Vaya* wise distribution of 150 Patients of Madhumeha:

Vaya	Group A		Group B		Total	Percentage
	No of Patients	%	No of Patients	%	No of Patients	%
Baala	00	00%	00	00%	00	00%
Madhyama	51	68%	47	62.66%	98	65.33%
Vrudda	24	32%	28	37.33%	52	34.67%

Out of 75 patients of Madhumeha in Group A 68% Patients were in the Madhyamavastha, 32% patients were observed to be in Vruddavasta. Out 75 patients of Madhumeha in Group B 62.67% patients were observed in Madhyamavastha, 37.33% patients were in Vruddavasta. So over all 65.33% subjects were observed in Madyhamavasta, 34.67% subjects were observed in Vruddavasta.

00% was observed in Baalavasta as baala, as patients were not included in the study.(Fig. No.18).

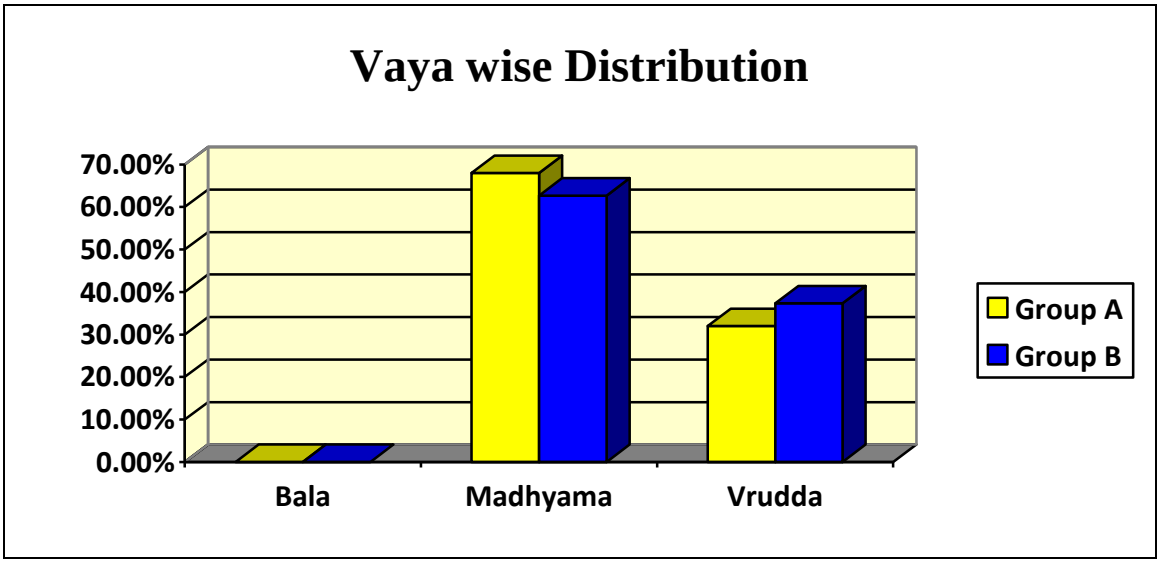


Fig.No.18: Showing the Vaya wise distribution of 150 Patients of Madhumeha

Table- 52: Showing the Ahara -Abhyavarana Shakthi wise distribution of 150 Patients of Madhumeha:

Ahara Abhyavarana shakthi-	Group A		Group B		Total	Percentage
	No of patients	%	No of patients	%	No of patients	%
Pravara	30	40%	25	33.33%	55	36.67%
Madhyama	31	41.33%	39	52%	70	46.67%
Avara	14	18.67%	11	14.67%	25	16.66%

In the present study out of 75 patients of Group A, 40% subjects were having Pravara Ahara Abhyavarana Shakti, 41.33% were having Madhyama and 18.67% were having Avara Ahara Abhyavarana Shakti. Where as in Group B out of 75 patients 33.33% patients were having Pravara Ahara Abhyavarana Shakti, 52% were having Madhyama Ahara Abhyavarana Shakti and 14.67% were having Avara Ahara Abhyavarana Shakti. Out of 150 patients of Group A & B, 36.67% subjects were having Pravara Ahara Abhyavarana Shakti, 46.67% Patients were having Madhyama and 16.67% were having Avara Ahara Abhyavarana Shakti (Fig. No.19).

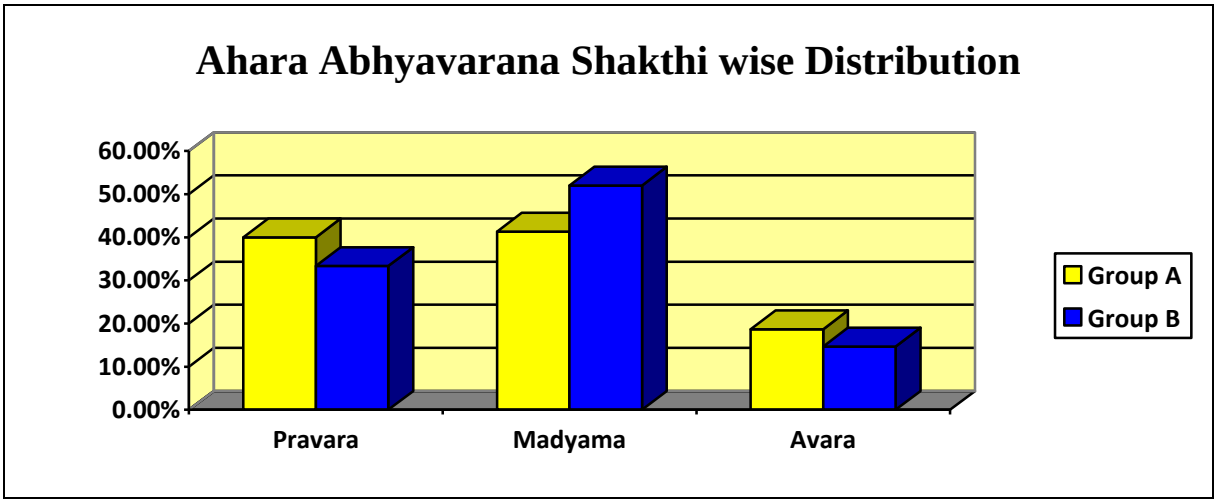


Fig.No.19: Showing the Ahara -Abhyavarana Shakthi wise distribution of 150 Patients of Madhumeha:

Table-53: Showing the Ahara -Jarana Shakthi wise distribution of 150 Patients of Madhumeha:

Ahara Jarana shakthi-	Group A		Group B		Total	Percentage
	No. of patients	%	No. of patients	%	No. of patients	%
Pravara	11	14.67%	17	22.67%	28	37.33%
Madhyama	46	61.33%	36	48%	82	54.67%
Avara	18	24%	22	29.33%	40	26.67%

In this present study out of 75 patients of Group A, 14.67% Patients were having Pravar Ahara Jarana Shakti, 61.33% were having Madhyama Jarana Shakti and 24% were having Avara Ahara Jarana Shakti. In Group B 22.67% subjects were having Pravara Ahara Jarana Shakti, 48% patients were having Madhyama Ahara Jarana Shakti and 29.33% were having Avara Jarana Shakti. Out of 150 patients of Group A & B 37.33% patients were having Pravara Ahara Jarana Shakti, 54.67% subjects were having Madhyama and 26.67% patients were having Avara Ahara Jarana Shakti (Fig. No.20).

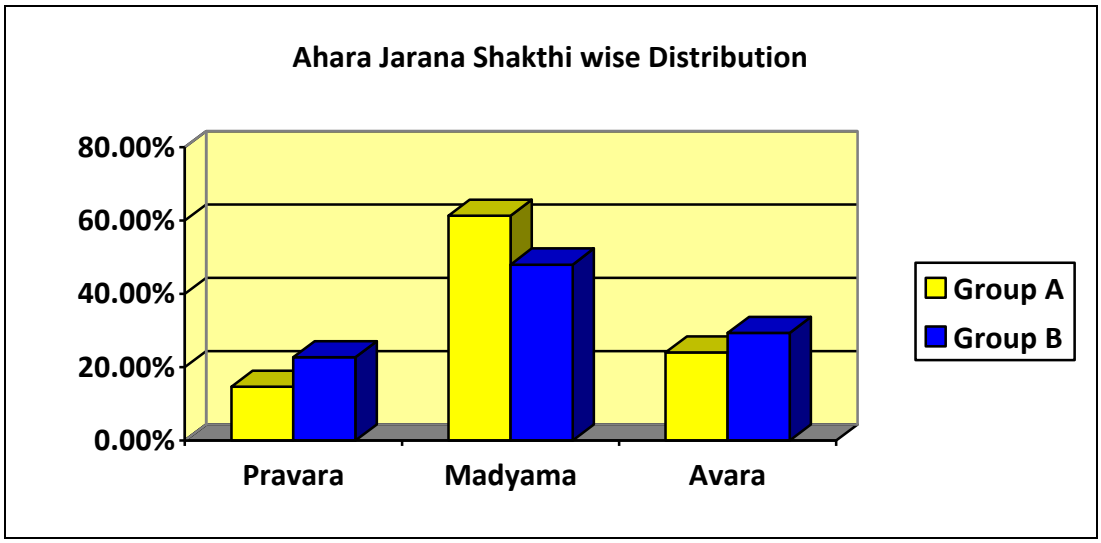


Fig.No.20: Showing the Ahara -Jarana Shakthi wise distribution of 150 Patients of Madhumeha:

Table No.54: Distribution of Blood Pressure in 150 Patients of Madhumeha by as follows:

Blood Pressure	Group A N=75		Group B N=75		Total 150	Percentage
	No. of patients	%	No. of patients	%	No. of patients	%
110/70 mm of Hg	11	14.67%	16	21.33%%	27	18%
120/80 mm of Hg	15	20%	08	10.67%	23	15.33%
130/80 mm of Hg	13	17.33%	09	12%	22	14.67%
140/80 mm of Hg	11	14.67%	15	20%	26	17.33%
150/90 mm of Hg	25	33.33%	27	36%	52	34.67%

Out of 75 patients of Madhumeha in Group A, 14.67% patients were having Blood pressure in the range of 110/70 mmHg, 20% patients were having 120/80 mmHg, 17.33% patients each were having 130/80 mmHg, 14.67% patients were having blood pressure in the range of 140/80 mmHg, and 33.33% patients were having the blood pressure 150/90 mmHg.

Out of 75 patients of Madhumeha in Group B, 21.33% patients were having Blood pressure in the range of 110/70 mmHg, 10.67% patients were having the blood pressure in the range of 120/80 mmHg, 12% patients were having the blood pressure in the range of 130/80 mmHg, 20% patients were having the blood pressure in the range of 140/80 mmHg, and 36% patients were having the blood pressure in between the range of 150/90 mmHg.

So over all 150 patients of Madhumeha in Group A & B, 18% patients were having Blood pressure in the range of 110/70 mmHg, 15.33% patients were having the blood pressure in the range of 120/80 mmHg, 14.67% patients were having the blood pressure in the range of 130/80 mmHg, 17.33% patients were having the blood pressure in the range of 140/80 mmHg, and 34.67% patients were having the blood pressure in between the range of 150/90 mmHg (Fig. No. 21).

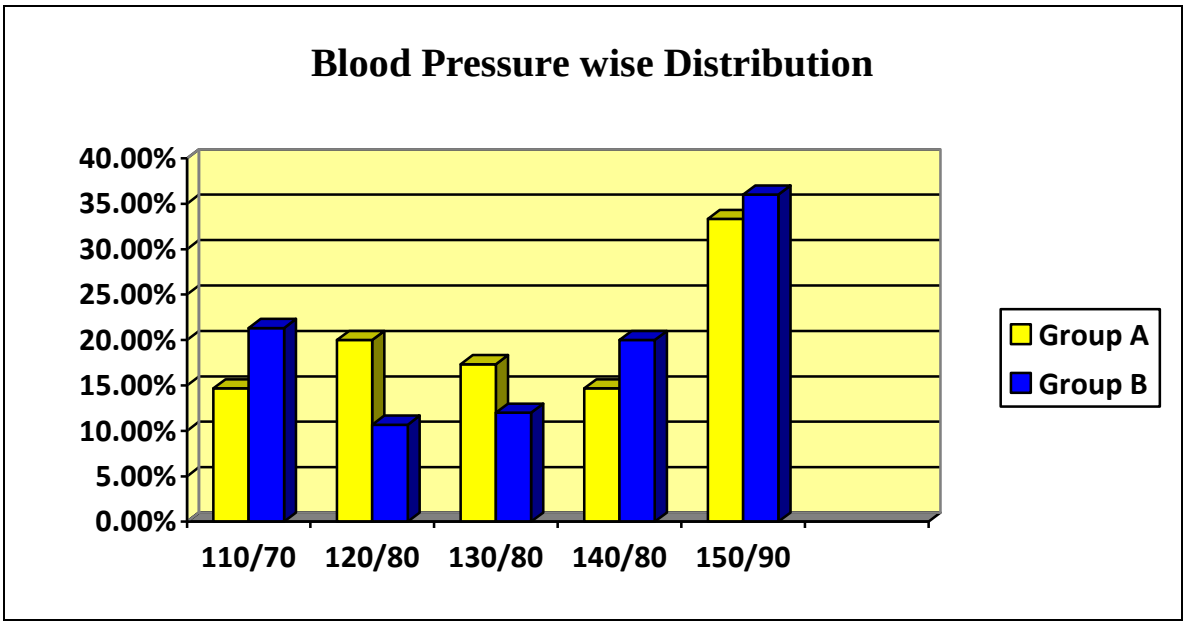


Fig. No. 21: Showing the Blood Pressure wise distribution of 150 Patients of Madhumeha:

Table No.55: Showing the History of Past illness wise distribution of 150 Patients of Madhumeha:

History of Past Illness	Group A		Group B		Total	Percentage
	No. of patients n=75	%	No of patients n=75	%	No. of patients n=150	%
HTN	26	34.66%	21	28%	51	34%
Cardiac	00	00%	00	00%	00	00%
Asthma	00	0%	00	00	00	00%
Tuberculosis	02	2.67%	03	4%	05	3.33%
Jaundice	00	00%	00	00%	00	00%

In the Group A out of 75 patients of Madhumeha 34.66% patients were having history of Hypertension, 2.67% patient each were having history of Tuberculosis and 05 were having Cardiac problem, Asthma, and Jaundice.

In the Group A out of 75 patients of Madhumeha, 28% were having history of Hypertension, 4% were having history of Tuberculosis, 0% subjects each were having history of cardiac problem,Asthma and Jaundice.

So overall 150 patients, 34% patients were having subjects were having history of Hypertension, 3.33% patients were having history of Tuberculosis (Fig. No.22).

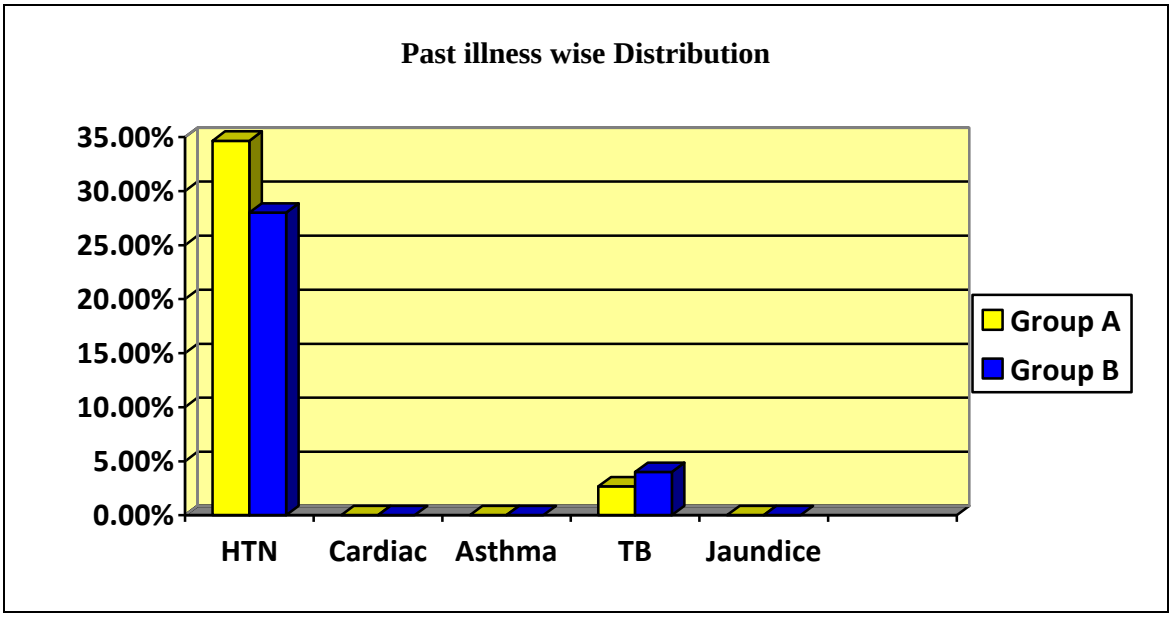


Fig. no.22: Showing the History of Past illness wise distribution of 150 Patients of Madhumeha:

Table-56: Showing the Aharaja Nidhana wise distribution of 40 Patients of Madhumeha:

Sl.No	Aharaja Nidhana	Group A		Group B		Total	Percentage
		No of patients n=75	%	No of patients n=75	%	No of patients n=150	%
1	Navanna pana	55	73.3%	32	42.6%	87	58%
2	Guda	34	45.3%	23	30.66%	57	38%
3	Guda vikruthi	40	45%	35	46.6%	75	50%
4	Dugdha	60	40%	55	73.3%	115	76.6%
5	Dadhi	55	75%	45	60%	100	66.6%
6	Dugdha vikruthi	42	70%	40	53.3%	82	54.6%
7	Mamsa rasa	30	55%	23	30.6%	53	35.3%
8	Sura	12	30%	10	13.3%	22	14.6%

In group A out of 75 patients 75% subjects were taking Dadhi, 73.3 % subjects were having history of taking Navanna Pana,70% patients were having history of taking Dugdha Vikriti, 55% subjects were having history of taking mamsa Rasa, 45.3% patients were having history of taking Guda, 45% patients were having history of taking Guda vikriti, 40% subjects were taking Dugdha and 30% subjects were taking Sura.

In group B out of 75 patients 73.3% subjects were taking Dugdha, 60 % subjects were having history of taking Dadhi,53.3% patients were having history of taking Dugdha Vikriti, 46.6% subjects were having history of taking Guda vikruthi, 42.6% patients were having history of taking Navanna, 30.6% patients were having history of taking Guda, 30.6% subjects were taking Mamsa Rasa, and 13.3% subjects were taking Sura.

Over all in total 150 patients 76.6%% subjects were having the history of taking Dugdha, 66.6 % subjects were having history of taking Dadhi, 54.6% patients were having history of taking Dugdha Vikriti, 50% subjects were having history of taking Guda Vikruthi, 38% patients were having history of taking Guda, 35.3% patients were having history of taking mamsarasa, 14.6% subjects were taking Sura (Fig. No.23).

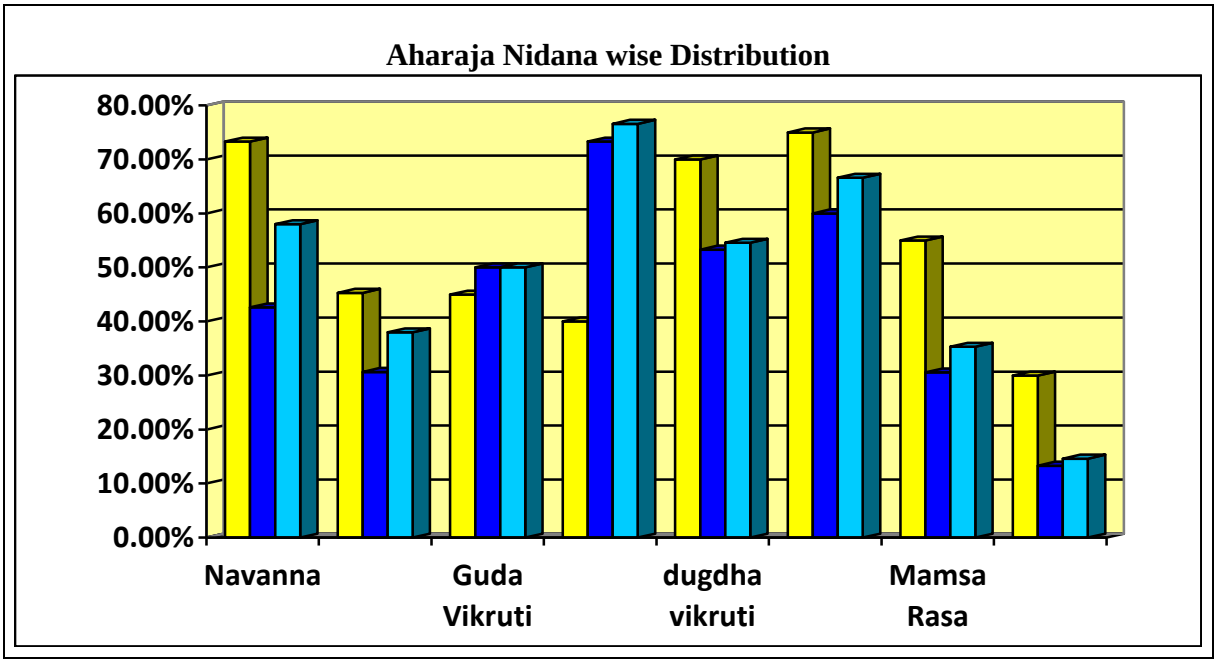


Fig.23: Showing the overall Aharaja Nidhana wise distribution of 150 Patients of Madhumeha

Table No.57: Showing the Viharaja Nidhana wise distribution of 150 Patients of Madhumeha:

Sl.No.	Viharaja Nidhana	Group A		Group B		Total	Percentage
		No. of patients n-75	%	No. of patients n=75	%	No. of patients n=150	%
1.	Swapna Sukha	32	42.6%	28	37.3%	60	40%
2.	Diva swapna	11	14.6%	15	20%	26	17.3%
3.	Manasika chinta	12	16%	11	14.6%	23	15.3%
4.	Avyayama	20	26.6%	21	28%	41	27.3%

In this study out of 75 patients in Group A, 42.6% patients were having the history of Swapna sukha, 26.6% patients were having the history of Avyayama, 16% patients were having the history of Divaswapna and 14.6% patients were having the history of Diva Swapna.

Again in Group B out of 75 patients, 37.3% patients were having the history of Swapna sukha, 28% patients were having the history of Avyayama, 20% patients were having the history of Diva Swapna and 14.6% patients were having Manasika chinta.

Overall in 150 patients of Madhumeha 40% patients were having the history of Swapna sukha, 27.3% patients were having the history of Avyayama, 17.3% patients were having the history of Diva Swapna and 15.3% subjects were having Manasik Chinta (Fig. No.24).

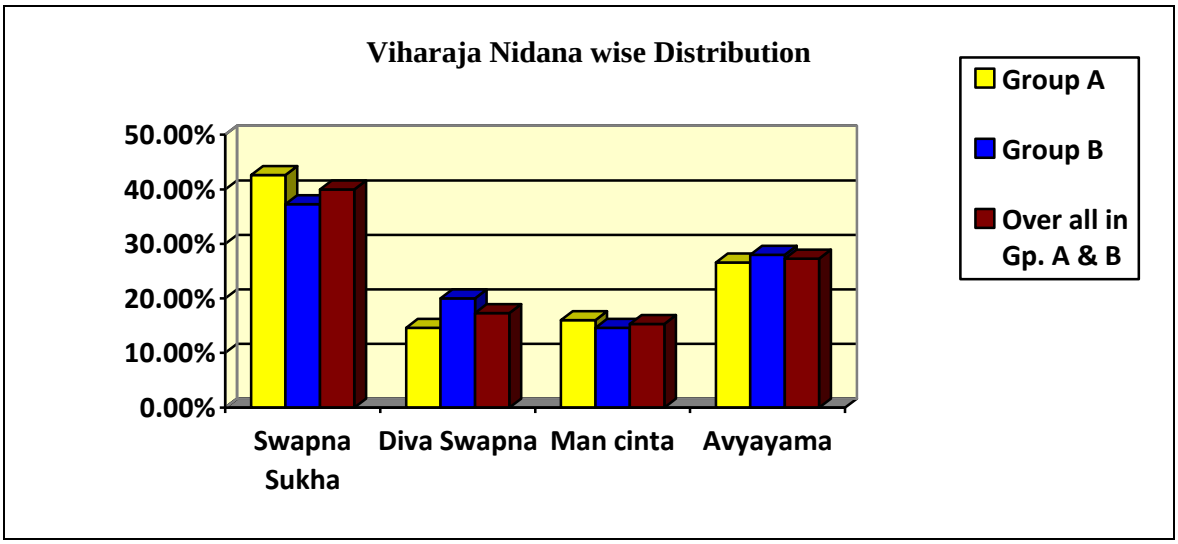


Fig. No. 24: Showing the Viharaja Nidhana wise distribution of 150 Patients of Madhumeha:

Table no. 58: Showing the Habit wise distribution of 150 Patients of Madhumeha:

Sl. No	Habits	Group A		Group B		Total	Percentage
		No. of patients n-75	%	No. of patient n-75	%	No. of patients n-150	%
1	Tea	70	93.3%	72	96%	142	94.6%
2	Coffee	15	20%	12	16%	27	18%
3	Alcohol	14	18.6%	10	13.3%	24	16%
4	Tobacco	12	16%	18	24%	30	20%
5	Smoking	19	25.3%	15	20%	34	22.66%
6	Soft drinks	5	6.6%	09	12%	14	09.3%

In this study out of 75 patients in Group A , 93.3% Patients having the addiction habit of Tea, 20% patients having the addiction habit of coffee, 18.6% patients having the addiction habit of Alcohol, 16% subjects having the addiction habit of Tobacco, 25.3% subjects having the addiction habit of Smoking and 5% of soft drinks.

Again in Group B out of 75 patients, 96% Patients having the addiction habit of Tea, 16% patients were having coffee, 13.3% patients having the addiction habit of

Alcohol, 24% subjects having the addiction habit of Tobacco, 20% subjects having the addiction habit of Smoking and12% of soft drinks.

Overall in group A and B, 94.6% Patients having the addiction habit of Tea, 18% patients were having coffee, 16% patients having the addiction habit of Alcohol, 20% subjects having the addiction habit of Tobacco, 22.66% subjects having the addiction habit of Smoking and 9.3% of soft drinks (Fig. No.25).

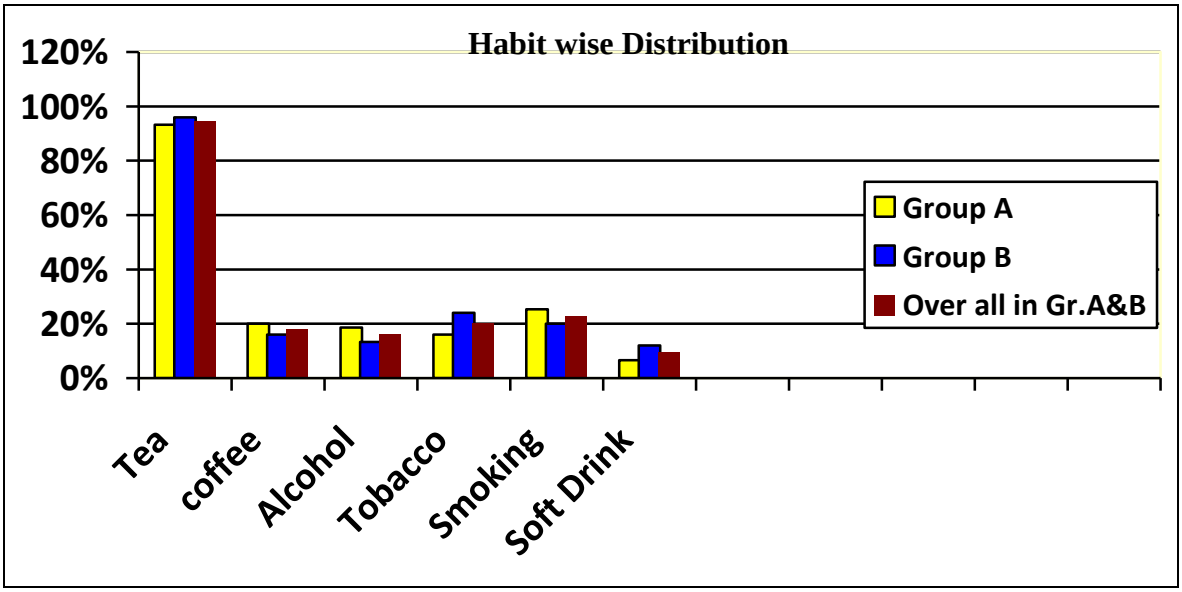


Fig No.25: Showing the Habits wise distribution of 150 Patients of Madhumeha:

RESULTS:

EFFECT OF *MUSTADI KWATHA* ON *MADHUMEHA*

The clinical study was conducted for 150 patients of *Madhumeha*. The 150 patients were divided in two groups. Each group was having 75 patients, completed the full protocol of treatment of duration 90 days.

The effect of *Mustadi kwatha* in both Group A and B before and after treatment at period at 0 days and 90 days are collected in study case proforma. The data obtained from subjective and objective parameters were collected in the specially designed proforma and the results were analyzed by using the statistical method like z test, independent‘t’ test and Maan whitney U test. The statistical analytic results are tabulated as below.

Group A (n-75) - Treated with oral Anti Diabetic drug and *Mustadi Kasaya*

Group B (n-75) - Treated by Oral Anti Diabetic drug and Placebo (Gum acacia tablet)

Table No.59: Showing the comparative effect of two study group A & B with respect of *Prabhoota mootra*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	*Prabhoota Mootra*	2.44 ± 0.499	0.53± 0.502	78.2%	23.369	< 0.05 *
Group B		2.61± 0.490	2.00 ± 0.493	23.37%	7.600	< 0.05*

*indicates p<0.05 is significant
n = Number of patient
Z = z value
BT = Before treatment
p = value represent significance
SD = Standard Deviation
t =Test probability difference level
AT = After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Prabhuta mootra* the mean value before treatment 2.44 changes to 0.53 with 78.2% relief. Where as in Group B also shows a significant (p<0.05) changes was observed in *Prabhoota Mootra* , with the before treatment value 2.61 changes to 2.00 with 23.37% relief of symptoms. (Fig.26)

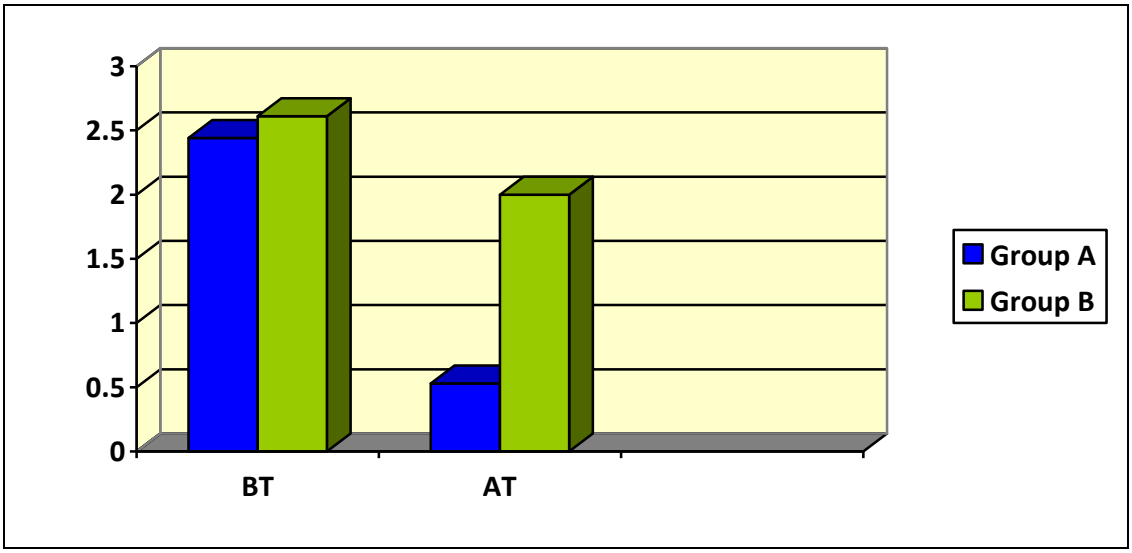


Fig. No.26: Showing the comparative effect of two study group A & B with respect of *Prabhoota mootra*

Table No.60: Showing the comparative effect of two study groups A & B with respect of *Avila mootra*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	*Avila Mootrata*	2.33 ± 0.474	0.13± 0.342	94.4%	32.596	< 0.001*
Group B		2.32± 0.469	0.36 ± 0.650	84.4%	21.176	< 0.01*

*indicates p<0.05 is significant

n= Number of patient

SD= Standard Deviation

Z= z value

t=Test probability difference level

BT= Before treatment

AT=After treatment

p = value represent significance

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Avilamootra* the mean value before treatment 2.33 changes to 0.13 with 94.4% relief. Where as in Group B also shows a significant (p<0.05) changes was observed in *Avilamootra*, the before treatment value 2.32 changes to 0.36 with 84.4% relief of symptoms. (Fig.27)

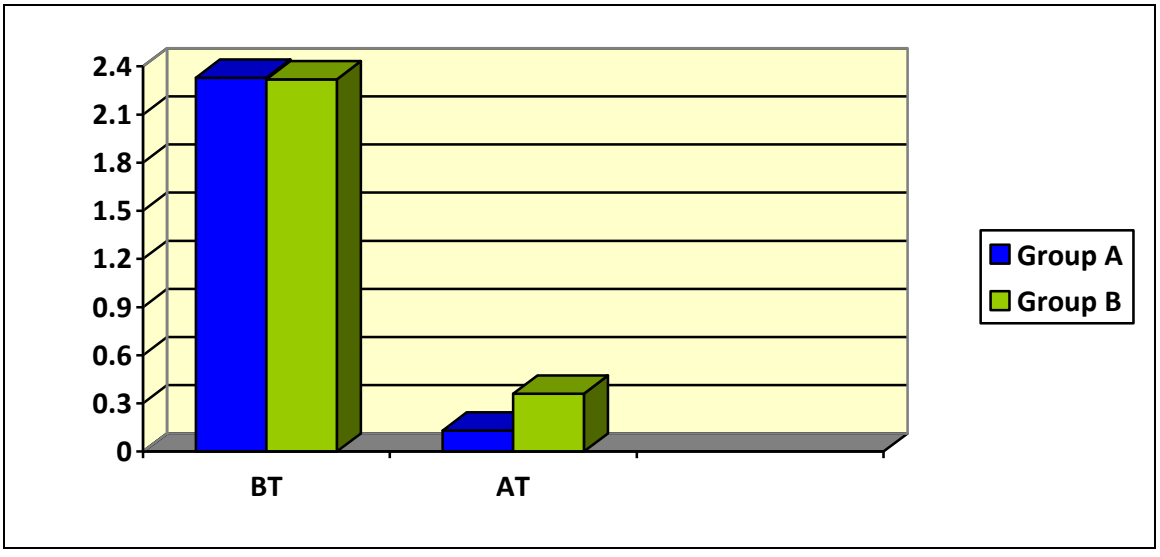


Fig. No.27: Showing the comparative effect of two study group A & B with respect of *Avila mootrata*

Table No. 61: Showing the comparative effect of two study group A & B with respect of *Kshudhadikya*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	*Kshudhadikya*	1.65 ± 0.528	0.13± 0.342	92.2%	21.062	< 0.05*
Group B		1.67± 0.469	0.13 ± 0.342	92.1%	21.176	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Kshudhadikya*, the mean value before treatment 1.65 changes to 0.13 with 92.2% relief. Where as in Group B also shows similar significant (p<0.05) changes was observed in *Kshudhadikya*, the before treatment value 1.67 changes to 0.13 with 92.1% relief of symptoms. (Fig.28)

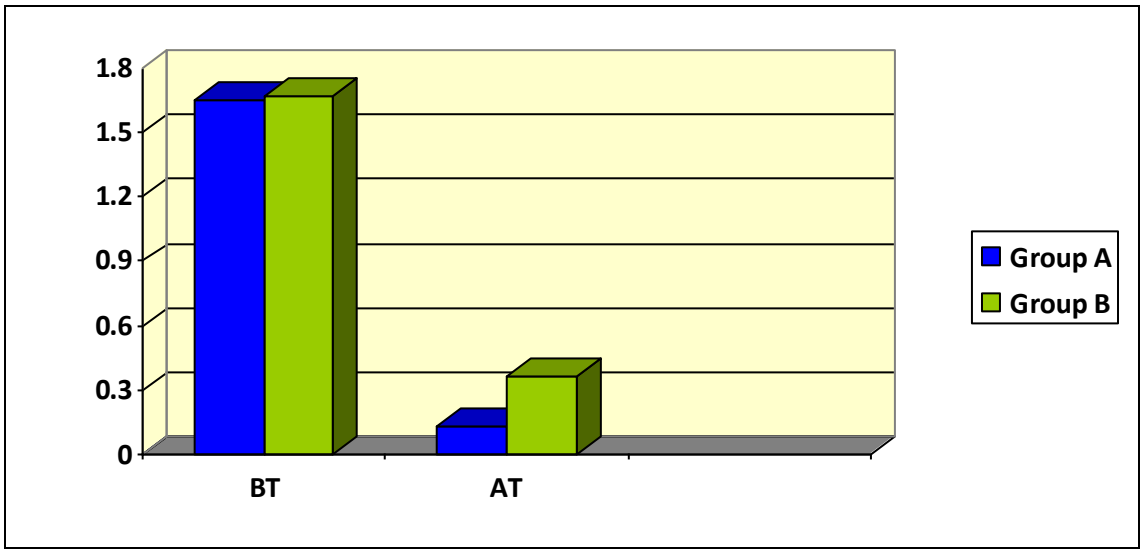


Fig. No.28:Showing the comparative effect of two study group A & B with respect of *Kshudhadikya*

Table No.62: Showing the comparative effect of two study group A & B with respect of *Pipasadikya*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	*Pipasadikya*	2.47 ± 0.502	0.08± 0.273	96.7%	36.221	< 0.05*
Group B		2.45± 0.501	0.99 ± 0.115	59.6%	24.597	< 0.05*

*indicates p<0.05 is significant

n= Number of patient

SD= Standard Deviation

Z= z value

t=Test probability difference level

BT= Before treatment

AT=After treatment

p = value represent significance

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Pipasadikya*, the mean value before treatment 2.47 changes to 0.08 with 96.7% relief. Where as in Group B also shows significant (p<0.05) changes was observed in *Pipasadikya*, the before treatment value 2.45 changes to 0.99 with 59.6% relief of symptoms. (Fig.29)

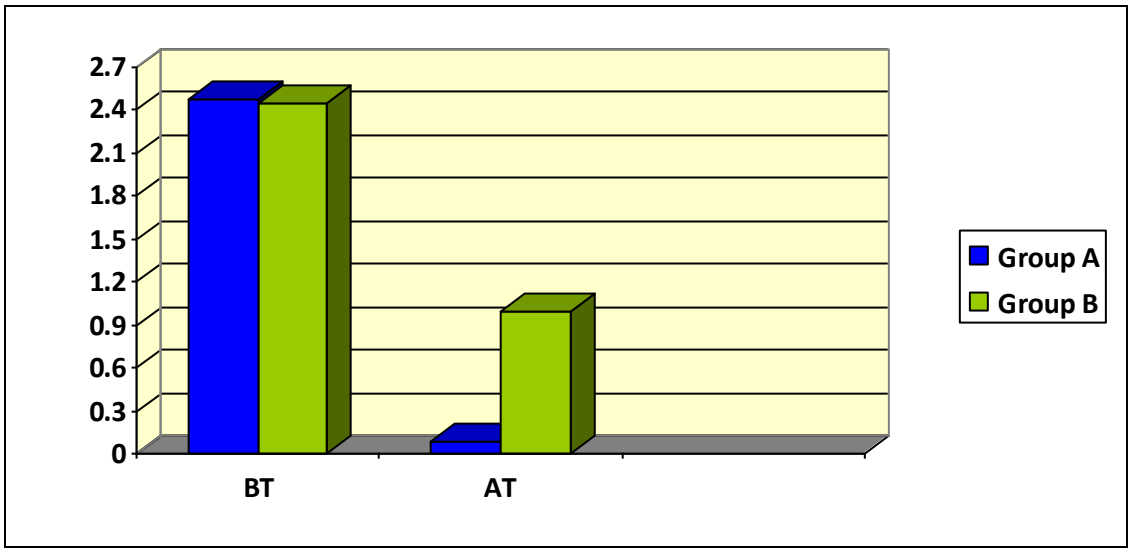


Fig. No. 29: Showing the comparative effect of two study group A & B with respect of *Pipasadikya*

Table No.63: Showing the comparative effect of two study group A & B with respect of *Dourbalya*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	*Dourbalya*	2.29 ± 0.458	0.13± 0.342	94.3%	32.725	< 0.05*
Group B		2.29± 0.458	0.97 ± 0.162	57.6%	23.531	< 0.05*

*indicates p<0.05 is significant

n= Number of patient

SD= Standard Deviation

Z= z value

t=Test probability difference level

BT= Before treatment

AT=After treatment

p = value represent significance

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Dourbalya* , the mean value before treatment 2.29 changes to 0.13 with 94.3% relief. Where as in Group B also shows significant (p<0.05) changes was observed in *Dourbalya,* the before treatment value 2.29 changes to 0.97 with 57.6% relief of symptoms. (Fig.30)

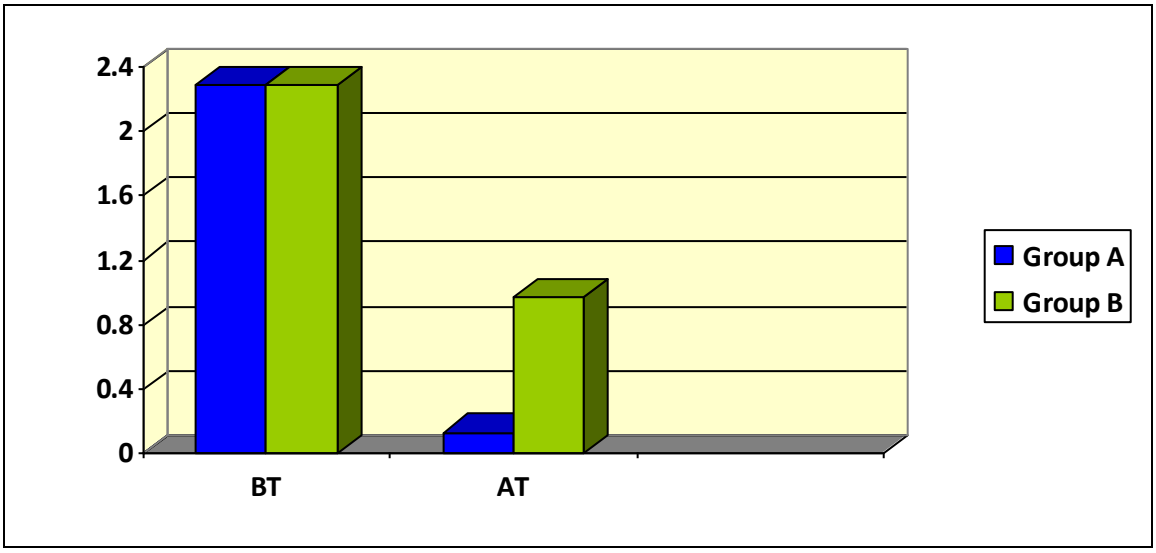


Fig. No. 30: Showing the comparative effect of two study group A & B with respect of *Dourbalya*

Table No.64: Showing the comparative effect of two study group A & B with respect of *Swedadhikya*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p-value
		BT	AT		(Zc – 1.96)	
Group A	*Swedadhikya*	2.15 ± 0.425	0.01± 0.115	99.5%	42.093	< 0.05*
Group B		2.13± 0.414	1.01 ± 0.115	52.58%	22.573	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Swedadhikya* , the mean value before treatment 2.25 changes to 0.01 with 99.5% relief. Where as in Group B also shows significant (p<0.05) changes was observed in *Swedadhikya*, the before treatment value 2.13 changes to 1.01 with 52.58% relief of symptoms. (Fig.31)

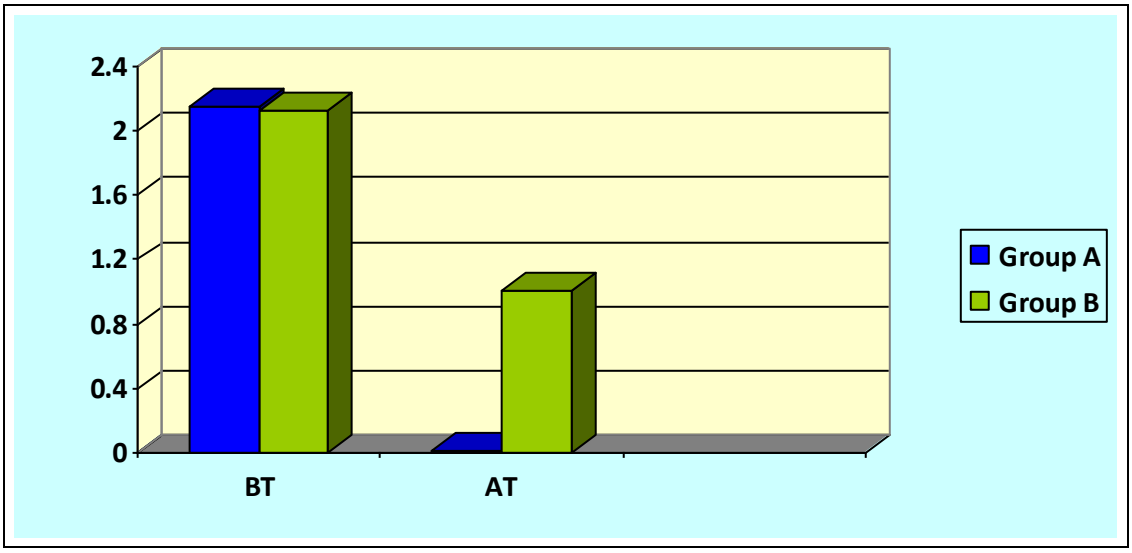


Fig. No.31: Showing the comparative effect of two study group A & B with respect of *Swedadikya*

Table No.65: Showing the comparative effect of two study group A & B with respect of *Galatalu Shosa*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	*Galatalu Shosa*	2.43 ± 0.497	0.59 ± 0.495	75.7%	22.716	< 0.05*
Group B		2.33± 0.996	0.57 ± 0.498	75.5%	14.465	< 0.05*

*indicates p<0.05 is significant
N = Number of patient
Z = z value
BT= Before treatment
p = value represent significance
SD = Standard Deviation
t = Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Galatalu Shosa*, the mean value before treatment 2.43 changes to 0.59 with 75.7% relief. Where as in Group B also shows similar significant (p<0.05) changes was observed in *Galatalu Shosa*, the before treatment value 2.33 changes to 0.57 with 75.5% relief of symptoms. (Fig.32)

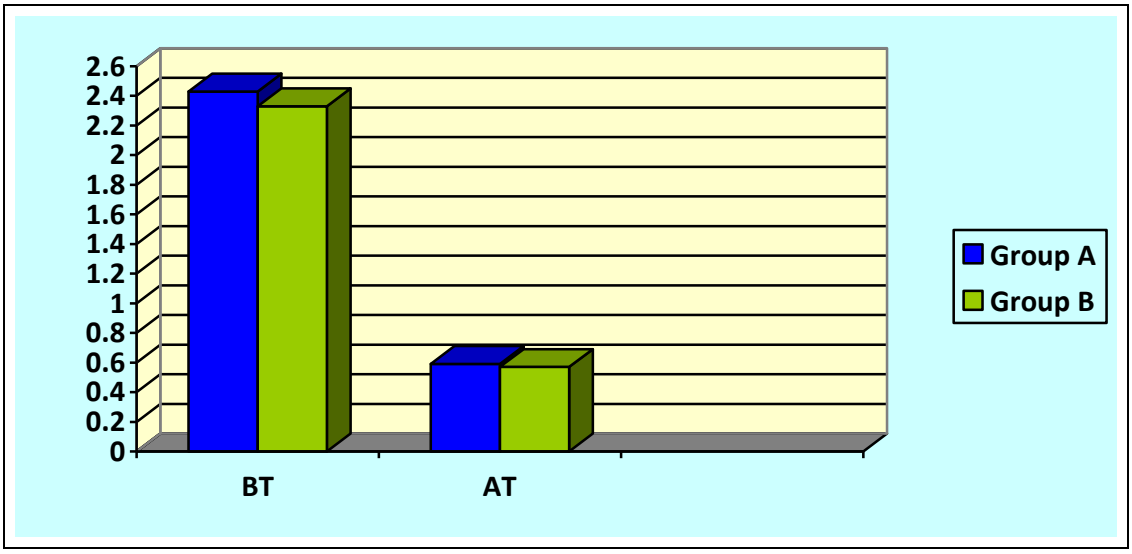


Fig. No.32: Showing the comparative effect of two study group A & B with respect of *Galatalu Shosa*

Table No.66: Showing the comparative effect of two study group A & B with respect of Klaibya

Treatment Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc 1.96)	
Group A	*Klaibya*	2.97 ± 0.162	0.95 ± 0.226	68.01%	62.912	< 0.05*
Group B		2.95± 0.226	1.89 ± 0.311	35.9%	22.904	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance

SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Klaibya* , the mean value before treatment 2.97 changes to 0.95 with 68.01% relief. Where as in Group B also shows significant (p<0.05) changes was observed in *Klaibya*, the before treatment value 2.95 changes to 1.89 with 35.9% relief of symptoms. (Fig.33)

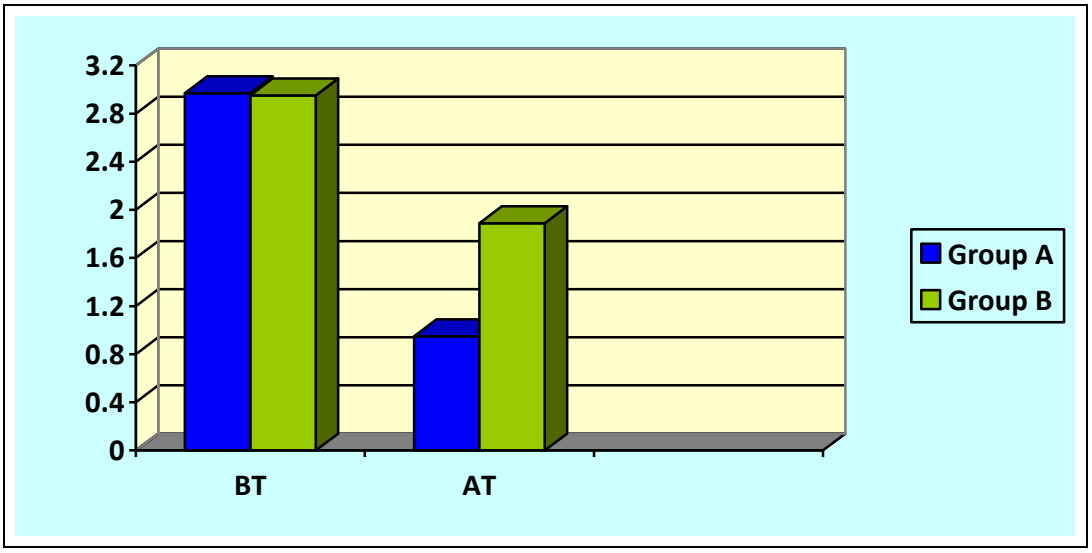


Fig. No.33: Showing the comparative effect of two study group A & B with respect of *Klaibya*

Table No.67: Showing the comparative effect of two study group A & B with respect of *Purisha Bhadhata*

Treatment Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	Purisha Bhadhata	2.83 ± 0.381	0.17 ± 0.381	93.8%	62.912	< 0.05*
Group B		2.72± 0.452	1.21 ± 0.412	55.51%	21.381	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e. *Purisha Bhadhata*, the mean value before treatment 2.83 changes to 0.17 with 93.8% relief. Where as in Group B also shows significant (p<0.05) changes was observed in *Purisha Bhadhata*, the before treatment mean value 2.72 changes to 1.21 with 55.51 % relief of symptoms. (Fig.34)

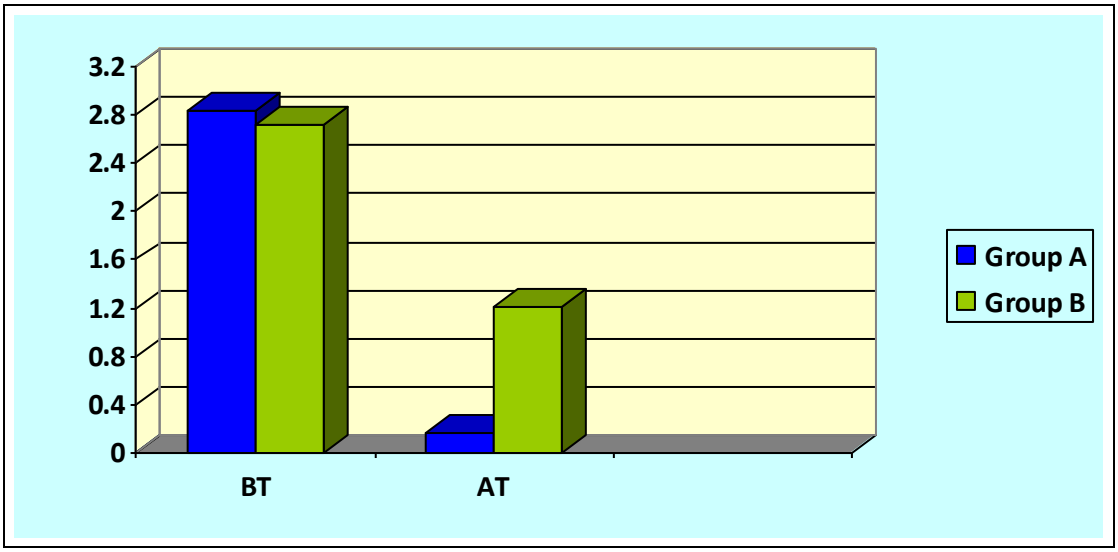


Fig.No.34: Showing the comparative effect of two study group A & B with respect of *Purishabadhata*

Table No.68: Showing the comparative effect of two study group A & B with respect to FBSL (Fasting blood Sugar level)

Treatment Group	Objective Parameter n=75	Mean ± SD		% of relief	Z - Value	p-value
		BT	AT		(Zc – 1.96)	
Group A	FBSL	166.25 ± 11.495	130.61 ± 6.375	21.43%	23.481	< 0.05*
Group B		170.69± 11.495	140.76 ± 8.424	17.53%	18.187	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the Fasting Blood sugar(FBSL), the mean FBS level before treatment 166.25 reduced to 130.61 with 21.43% relief. Where as in Group B also shows significant (p<0.05) changes was observed in Fasting Blood sugar (FBSL), the before treatment the mean FBS level was 170.69 reduced to 140.76 with 17.53% reduction. (Fig.35)

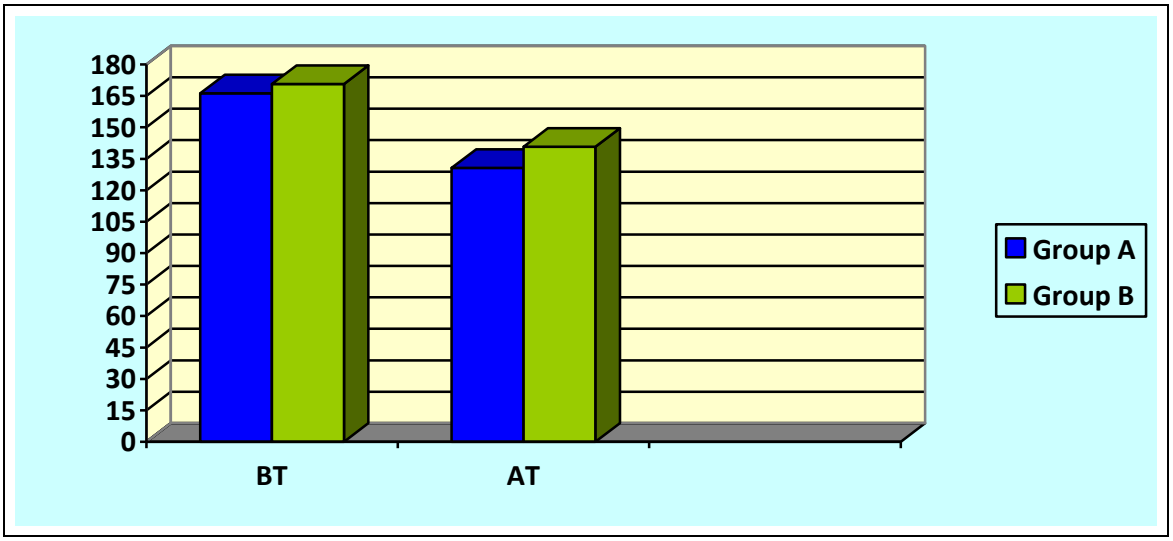


Fig. No.35: Showing the comparative effect of two study group A & B with respect to FBSL (Fasting blood Sugar level)

Table No. 69: Showing the comparative effect of two study group A & B with respect to PPBSL (Post Prandial blood Sugar level)

Treatment Group	Objective Parameter n=75	Mean ± SD		% of relief	Z -Value	p-value
		BT	AT		(Zc – 1.96)	
Group A	PPBSL	259.01 ± 21.371	152.77 ± 6.29	41.01%	41.300	< 0.05*
Group B		276.96± 24.00	157.44± 5.173	43.1%	21.381	< 0.05*

*indicates p<0.05 is significant
N = Number of patient
Z = z value
BT = Before treatment
p = value represent significance

SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the Post Prandial Blood sugar level (PPBSL), the mean PPBSL level before treatment 259.01 reduced to 155.77 with 41.01% relief. Where as in Group B also shows significant (p<0.05) changes was observed in Post Prandial Blood sugar level (PPBSL), the before treatment the mean PPBS level was 276.96 reduced to 157.44 with 43.1% reduction. (Fig.36)

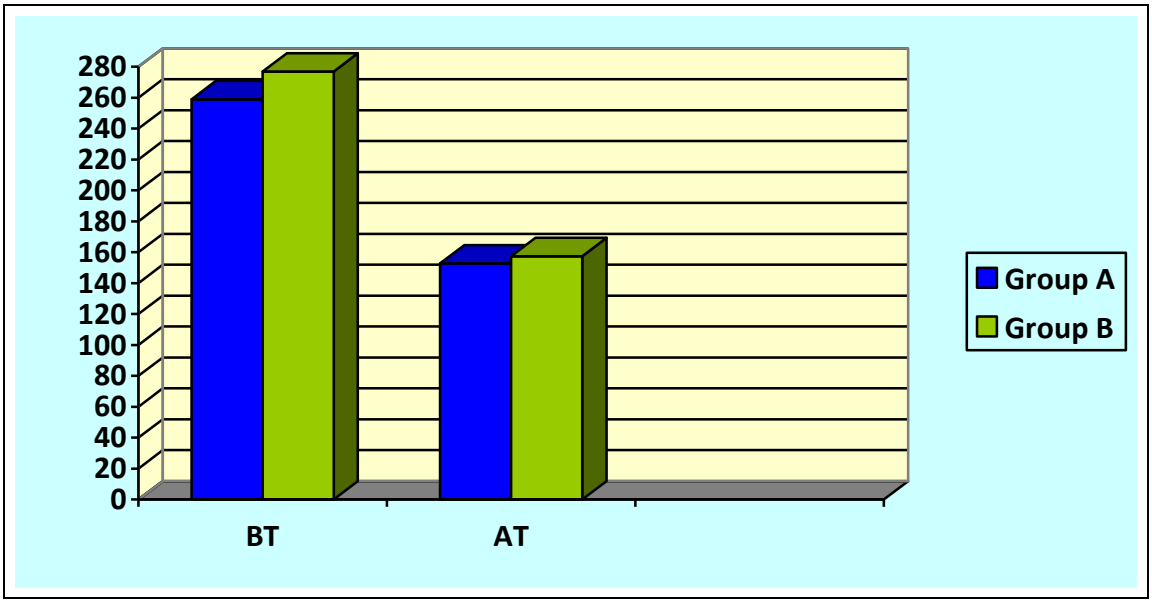


Fig.No. 36: Showing the comparative effect of two study group A & B with respect to PPBS (Post Prandial blood Sugar level)

Table No. 70. Showing the comparative effect of two study group A & B with respect to HbA_{1c}

Treatment Group	Objective Parameters	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	HbA_{1c}	8.94 ± 0.397	6.52 ± 0.349	**27.1%**	39.648	< 0.05*
Group B		9.11± 1.072	7.07 ± 0.348	22.39%	61.761	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the HbA_{1c}, the mean HbA_{1c} level before treatment 8.94 reduced to 6.52 with 27.1% relief. Where as in Group B also shows significant (p<0.05) changes was observed in HbA_{1c} but lesser than group A, the before treatment the mean Hb_1AC level was 9.11 reduced to 7.07 with 22.39% reduction. (Fig.37)

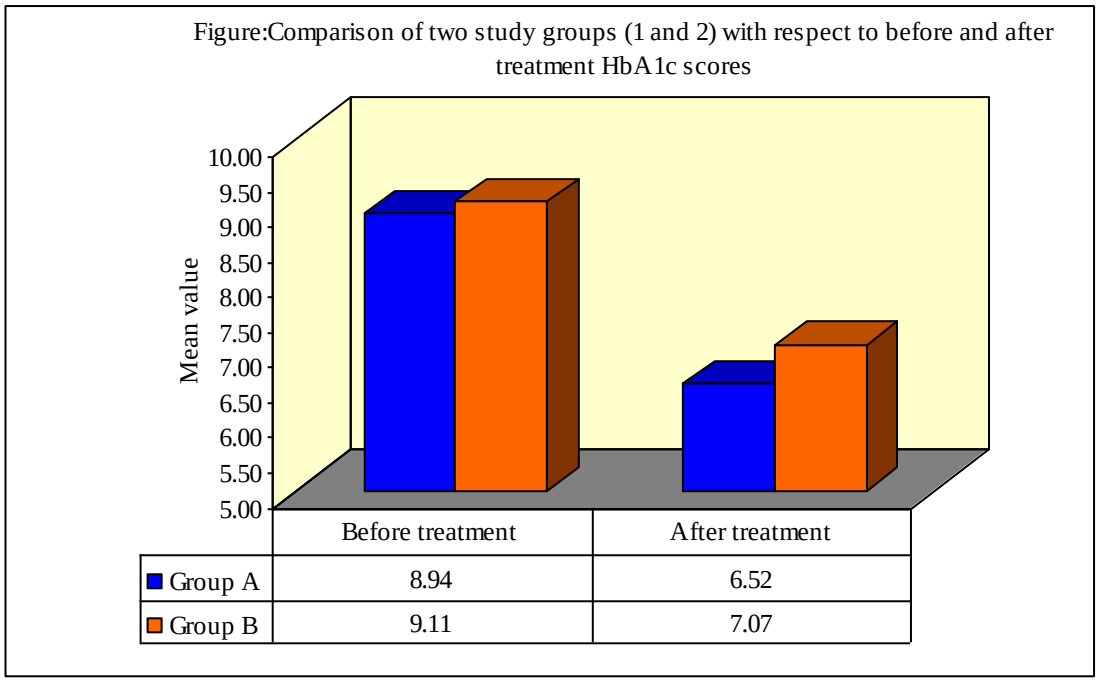


Fig. No.37: Showing the comparative effect of two study group A & B with respect to HbA_{1c}.

Table No.71: Comparison of two study groups (A and B) with respect to before and after treatment HbA1c scores by independent t test

Treatment	Groups	Mean	SD	SE	t-value	p-value
Before	Group A	8.94	0.38	0.03	-1.5597	0.1199
	Group B	9.11	0.81	0.07		
After	Group A	6.52	0.34	0.03	-6.0353	0.0001*
	Group B	7.07	0.39	0.04		
Difference	Group A	2.42	0.39	0.03	2.0376	0.0425**
	Group B	2.04	0.89	0.07		

*p<0.01, **p<0.05

In Group A statistically significant (p<0.01) changes was observed in the HbA_{1c}, the mean HbA_{1c} level before treatment 8.94 reduced to 6.52 . Where as in Group B also statistically significant (p<0.01), the mean HbA_{1c} level before treatment 9.11 reduced to 7.07. In comparison in group A and B the HbA_{1c} in Group A shown statistically significant (p<0.05) reduction of HbA1c than Group B.

Table No.72: Comparison of before and after treatment serum Creatinine scores in two study groups (A and B) by paired t test

Groups	Treatment	Mean	SD	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A	Before	1.19	0.17	0.10	0.11	8.42	11.1430	0.0001*
	After	1.09	0.13					
Group B	Before	1.28	0.17	0.15	0.21	11.99	9.0801	0.0001*
	After	1.13	0.16					

*indicates p<0.01 is significant
N = Number of patient
Z = z value
BT= Before treatment
p = value represent significance
SD = Standard Deviation
t = Test probability difference level
AT=After treatment

In this study the serum creatinine score in both the group were in changing trend towards normal value. In Group A the mean serum creatinine level before treatment 1.19 changes to 1.09 after treatment on 90th day which statistically significant at p<0.001. Again in Group B the mean serum creatinine level before

treatment 1.28 changes to 1.13 after treatment on 90th day which was statistically significant at p<0.001. However both the groups the changes almost similar.

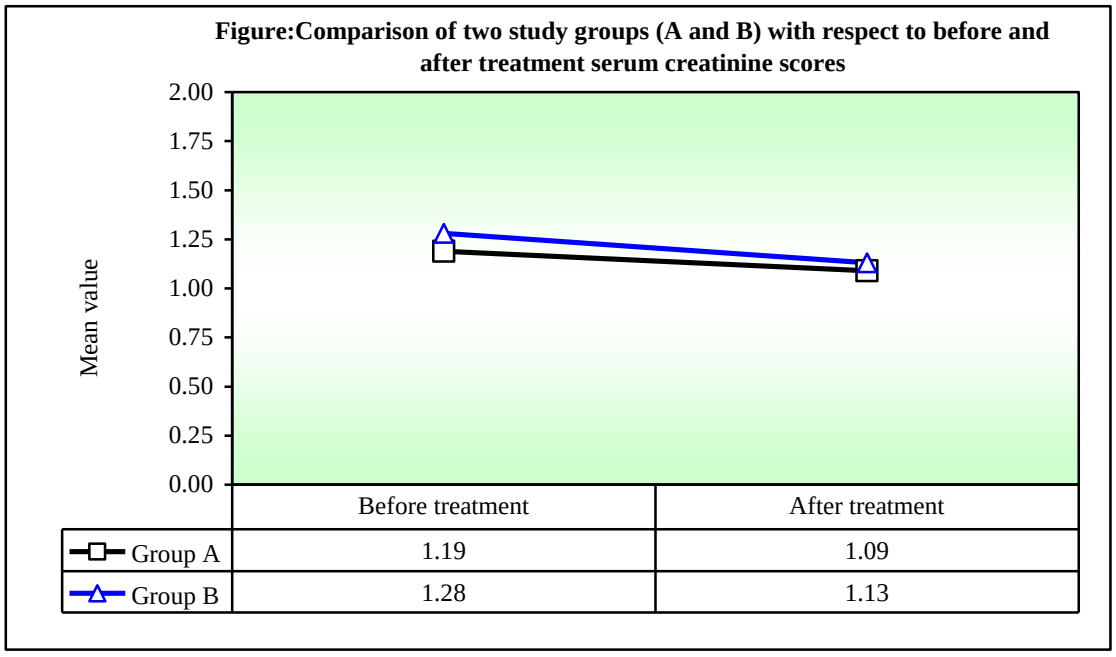


Fig. No.38: Comparison of before and after treatment serum Creatinine scores in two study groups (A and B)

Table No.73: Comparison of before and after treatment serum urea scores in two study groups (Aand B) by paired t test

Groups	Treatment	Mean	SD	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A	Before	17.33	3.53	2.50	0.66	14.4	9.3597	0.0001*
	After	14.83	3.36					
Group B	Before	18.81	3.28	2.12	3.63	11.30	7.1730	0.0001*
	After	16.69	3.24					

*indicates p<0.01 is significant
N = Number of patient
Z = z value
BT= Before treatment
p = value represent significance
SD = Standard Deviation
t = Test probability difference level
AT=After treatment

In this study the serum urea score in both the groups were in changing trend. In Group A the mean serum Urea level before treatment 17.33 changes to 14.83 after treatment on 90th day which statistically significant at p<0.01. Again in Group B the mean serum Urea level before treatment 18.81 changes to 16.69 after treatment on 90th day which was also statistically significant at p<0.01. However in comparison in both the groups the changes in percentage in group A is 14.4% than group B i.e. 11.30 (Fig.No. 39)

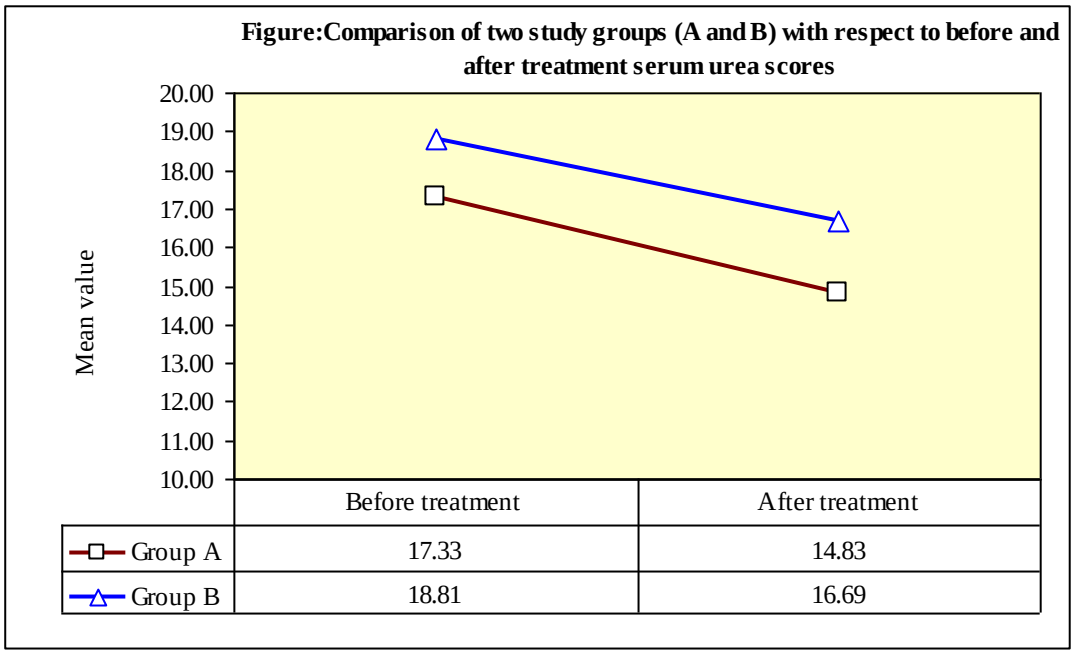


Fig. No.39: Comparison of before and after treatment serum urea scores in two study groups (A & B)

Table No.74: Comparison of before and after treatment serum Cholesterol scores in two study groups (A and B) by paired t test

Groups	Treatment	Mean	SD.	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A	Before	200.76	23.18	17.21	15.11	8.57	13.9559	0.0001*
	After	183.55	13.23					
Group B	Before	192.15	20.75	10.13	14.07	5.27	8.8128	0.0001*
	After	182.03	12.25					

*indicates p<0.01 is significant
N = Number of patient
Z = z value
BT= Before treatment
p = value represent significance

SD = Standard Deviation
t = Test probability difference level
AT=After treatment

In this study the serum Cholesterol level in Group A the mean scorel before treatment 200.76 changes to 183.55 after treatment on 90th day which was statistically significant at p<0.01. Again in Group B the mean serum Cholesterol level before treatment 192.15 changes to 182.03 after treatment on 90th day which was also statistically significant at p<0.01. However in comparison in both the groups the changes in percentage in group A is more i.e. 8.57% than group B i.e. 5.27.(Fig. No.40)

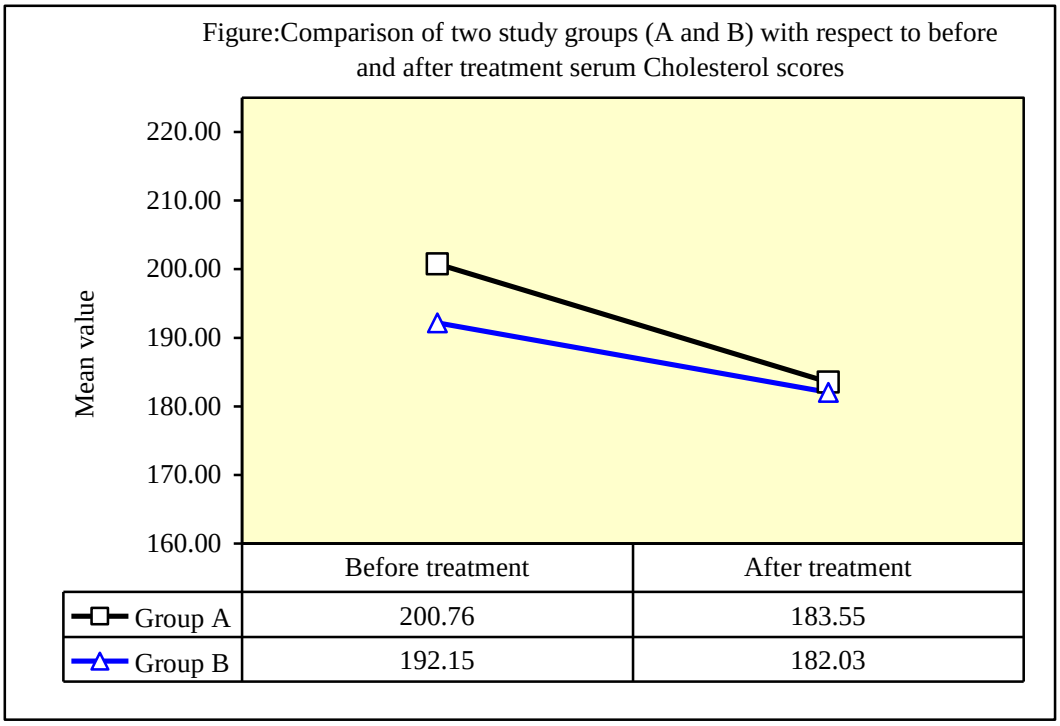


Fig. No.40: Comparison of before and after treatment serum Cholesterol scores in two study groups (A and B)

Table No 75: Comparison of before and after treatment serum Triglyceride scores in two study groups (A and B) by paired t test

Groups	Treatment	Mean	Std.Dv.	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A	Before	143.19	18.33	9.81	17.92	6.85	6.7019	0.0001*
	After	133.39	12.89					
Group B	Before	154.67	15.67	22.95	15.78	14.84	17.8114	0.0001*
	After	131.72	12.69					

*indicates p<0.01 is significant
N = Number of patient
Z = z value
BT= Before treatment
p = value represent significance

SD = Standard Deviation
t = Test probability difference level
AT=After treatment

In this study the serum Triglyceride level in Group A the mean score before treatment 143.19 changes to 133.39 after treatment on 90th day which was statistically significant at p<0.01. Again in Group B the mean serum Trglyceridel level before treatment 154.67 changes to 131.72 after treatment on 90th day which was also statistically significant at p<0.01. However in comparison in both the groups the changes in percentage in group A is less i.e. 6.85% than group B i.e. 14.84.

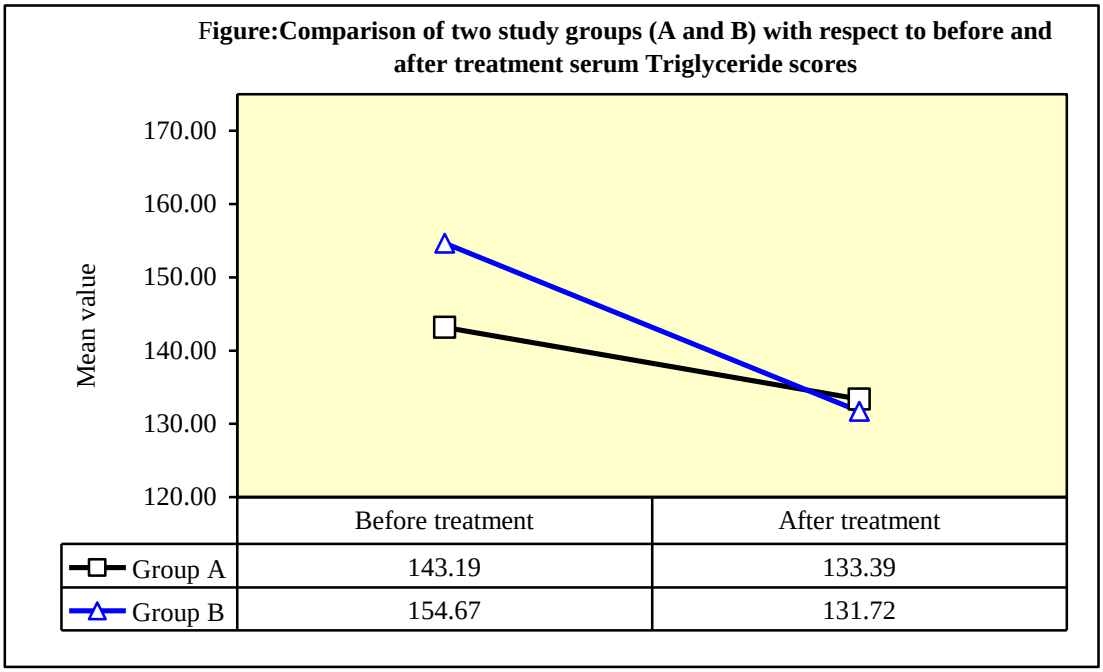


Fig.No.41: Comparison of before and after treatment serum Triglyceride scores in two study groups (A and B)

Table No.76: Comparison of before and after treatment LDL scores in two study groups (A and B) by paired t test

Groups	Treatment	Mean	Std.Dv.	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A n-75	Before	143.56	13.69	27.73	15.47	19.32	21.9493	0.0001*
	After	115.83	10.21					
Group B n-75	Before	144.56	12.69	18.75	14.42	12.97	18.9320	0.0001*
	After	125.81	11.21					

*indicates p<0.01 is significant
N = Number of patient
Z = z value
BT= Before treatment
p = value represent significance
SD = Standard Deviation
t = Test probability difference level
AT=After treatment

In this study the serum LDL level in Group A the mean score before treatment 143.56 changes to 115.83 after treatment on 90th day which was statistically significant at p<0.01. Again in Group B the mean serum LDL level before treatment 144.56 changes to 125.81 after treatment on 90th day which was also statistically significant at p<0.01. However in comparison in both the groups the changes in percentage in group A is more i.e. 19.32% than group B i.e. 12.97.

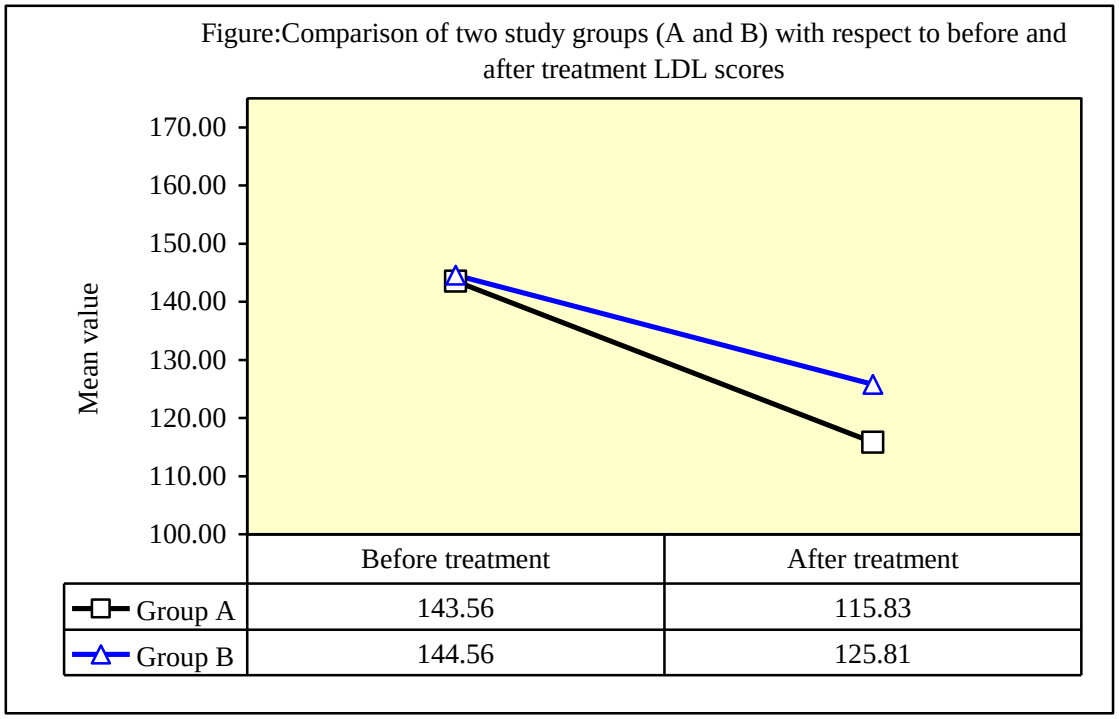


Fig. No.42: Comparison of before and after treatment LDL scores in two study groups (A and B).

Table No.77: Comparison of before and after treatment HDL scores in two study groups (A and B) by paired t test

Groups	Treatment	Mean	SD	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A n-75	Before	52.37	6.55	-4.59	6.40	-8.76	-8.7735	0.0001*
	After	56.96	5.53					
Group B n-75	Before	47.47	5.41	-3.31	4.13	-6.97	-9.8089	0.0001*
	After	50.77	4.16					

*indicates p<0.01 is significant
N = Number of patient
Z = z value
BT= Before treatment
p = value represent significance

SD = Standard Deviation
t = Test probability difference level
AT=After treatment

In this study the serum HDL level in Group A the mean score before treatment 52.37 changes to 56.96 after treatment on 90th day which was statistically significant at p<0.01. Again in Group B the mean serum HDL level before treatment 47.47 changes to 50.77 after treatment on 90th day which was also statistically significant at p<0.01. However in comparison in both the groups the changes in percentage in group A is more i.e. 8.67% than group B i.e. 6.97 (Fig.No.43)

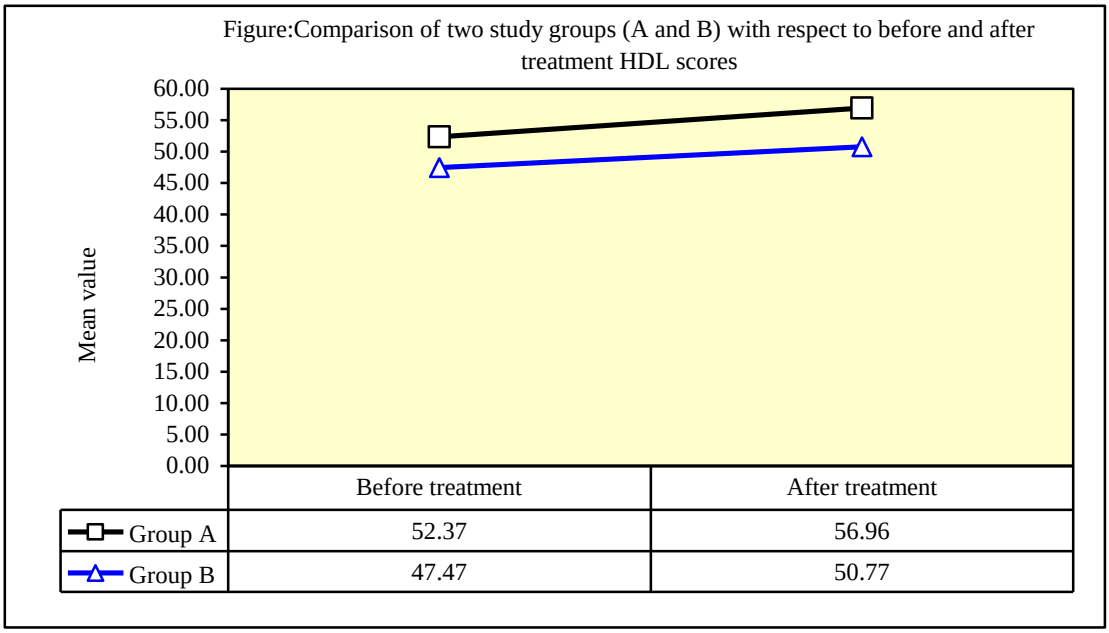


Fig.No.43: Comparison of before and after treatment HDL scores in two study groups (A and B) by paired t test

CROSSOVER STUDY:

After Completion of treatment in both the Group A (treated by Oral anti diabetic drug and *Mustadi Kwatha*) and Group B (treated by oral anti diabetic drug & placebo). The patents were kept for washout period of 90 days. During that period the patients were advised to continue only allopathic drug.

The crossover of the drug was done to both the groups.

Group - A were given Placebo along with oral anti diabetic drug and

Group - B were given *Mustadi Kwatha* along with their previously continued oral anti diabetic drug. The results after 90 days of treatment are tabulated as below:

Table No.78: Showing the comparative effect after crossover of two study group A & B with respect of *Prabhoota mootra*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	*Prabhoota Mootra*	2.29 ± 0.731	0.56 ± 0.499	75.5%	16.927	< 0.05 *
Group B		2.40± 0.805	0.08 ± 0.273	96.6%	23.637	< 0.05*

*indicates p<0.05 is significant
N = Number of patient
Z = z value
BT = Before treatment
p = value represent significance
SD = Standard Deviation
t =Test probability difference level
AT = After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Prabhoota mootra* the mean value before treatment 2.29 changes to 0.96 with 58.1% relief. Where as in Group B also shows a significant (p<0.05) changes was observed in *Prabhoota Mootra*, with the before treatment value 2.40 changes to 0.08 with 96.6% relief of symptoms. (Fig.44)

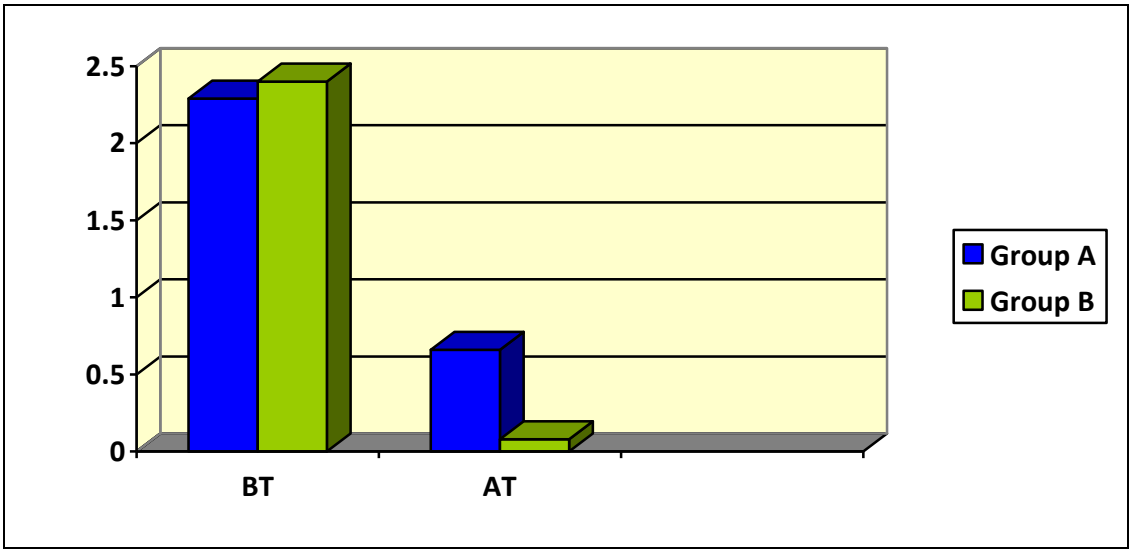


Fig. No.44: **Showing the comparative effect after crossover of two study group A & B with respect of *Prabhoota mootra***

Table No.79: Showing the comparative effect after crossover of two study group A & B with respect of *Avila mootrata*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	*Avila Mootrata*	2.32 ± 0.469	0.13± 0.342	94.4%	32.674	< 0.001*
Group B		2.17± 0.685	0. 09 ± 0.293	96%	24.178	< 0.01*

*indicates p<0.05 is significant

n= Number of patient

SD= Standard Deviation

Z= z value

t=Test probability difference level

BT= Before treatment

AT=After treatment

p = value represent significance

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Avilamootrata* the mean value before treatment 2.32changes to 0.09 with 94.4 % relief. Where as in Group B also shows a significant (p<0.01) changes was observed in *Avilamootrata*, the before treatment value 2.17 changes to 0.36 with 96% relief of symptoms. (Fig.45)

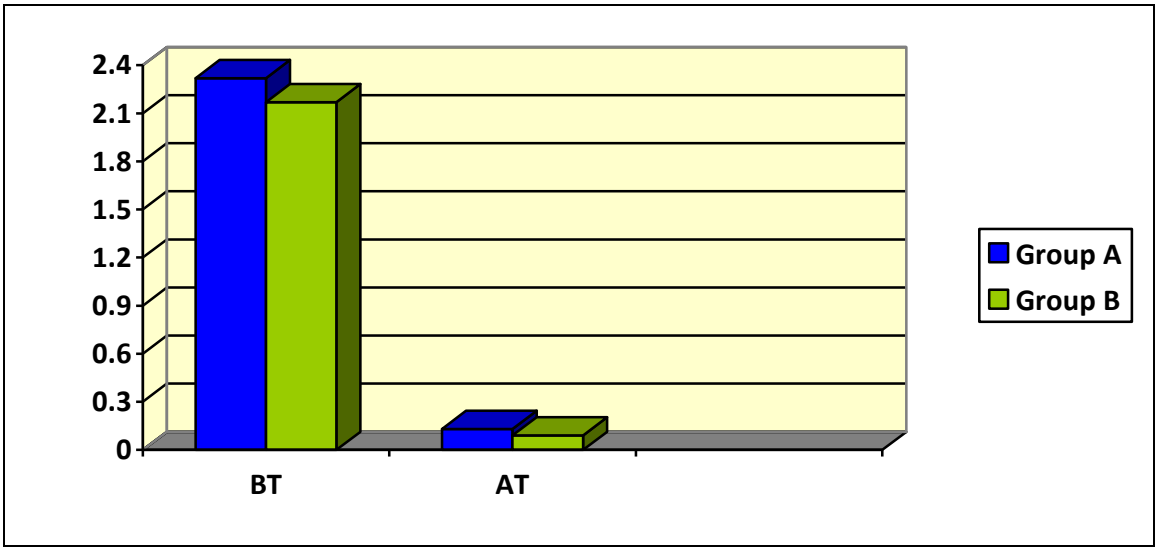


Fig. No. 45: Showing the comparative effect after crossover of two study group A & B with respect of *Avila mootrata*

Table No.80: Showing the comparative effect after crossover of two study group A & B with respect of *Kshudhadikya*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	*Kshudhadikya*	1.65 ± 0.532	0.13± 0.342	92.5%	20.813	< 0.05*
Group B		1.96± 0.528	0.04 ± 0.197	98.1%	24.897	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e. *Kshudhadikya*, the mean value before treatment 1.65 changes to 0.13 with 92.2% relief. Where as in Group B also shows more significant (p<0.05) changes in *Kshudhadikya*, the before treatment value 1.96 changes to 0.04 with 98% relief of symptoms. (Fig.46)

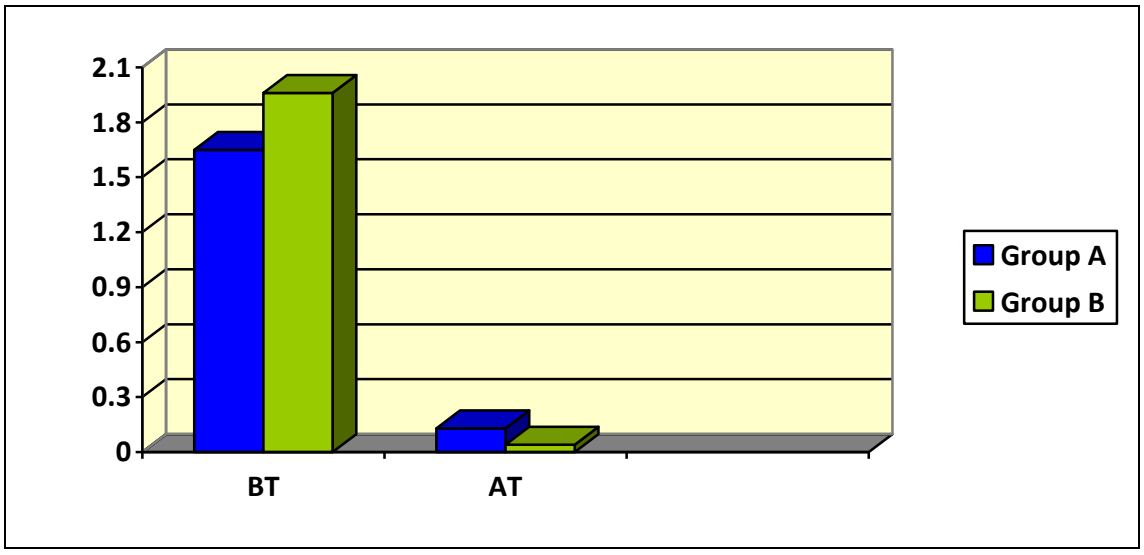


Fig. No.46: Showing the comparative effect after crossover of two study group A & B with respect of *Kshudhadikya*

Table No.81: Showing the comparative effect after crossover of two study group A & B with respect of *Pipasadikya*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p-value
		BT	AT		(Zc – 1.96)	
Group A	*Pipasadikya*	2.47 ± 0.502	0.15± 0.356	93.9%	36.674	< 0.05*
Group B		2.45± 0.501	0.09 ± 0.292	95.5%	32.245	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Pipasadikya*, the mean value before treatment 2.47 changes to 0.15 with 93.9% relief. Where as in Group B also shows significant (p<0.05) changes was observed in *Pipasadikya*, the before treatment value 2.45 changes to 0.09 with 95.5% relief of symptoms. (Fig.47)

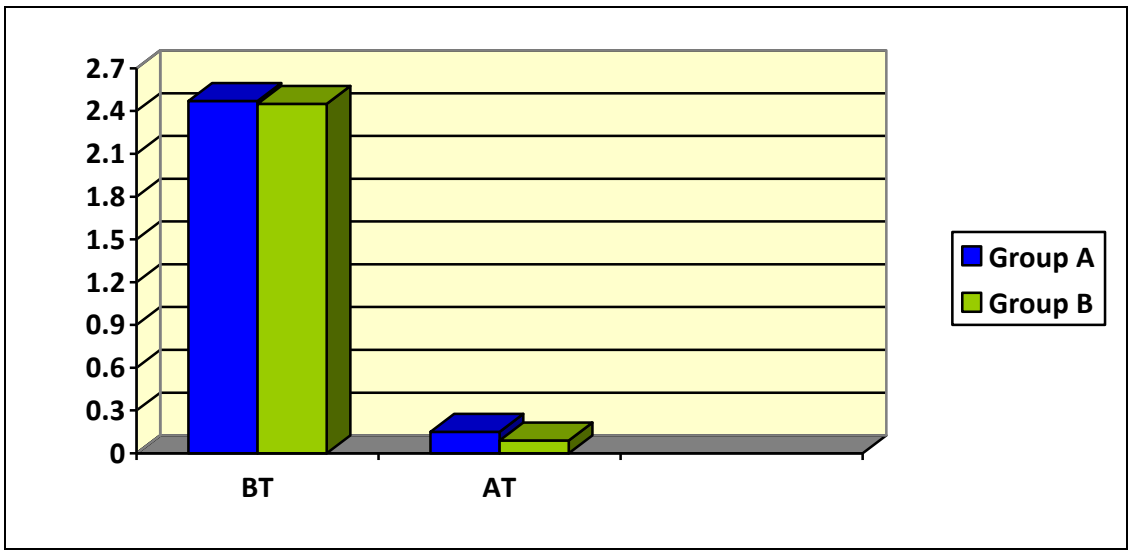


Fig. No. 47: Showing the comparative effect after crossover of two study group A & B with respect of *Pipasadikya*

Table No.82: Showing the comparative effect after crossover of two study group A & B with respect of Dourbalya

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	*Dourbalya*	2.29 ± 0.458	0.92± 0.273	59.8%	22.251	< 0.05*
Group B		2.30± 0.458	0.57 ± 0.162	75.1%	21.258	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Dourbalya* , the mean value before treatment 2.29 changes to 0.92 with 59.8% relief. Where as in Group B also shows significant (p<0.05) changes was observed in *Dourbalya*, the before treatment value 2.30 changes to 0.57 with 75.1% relief of symptoms. (Fig.48)

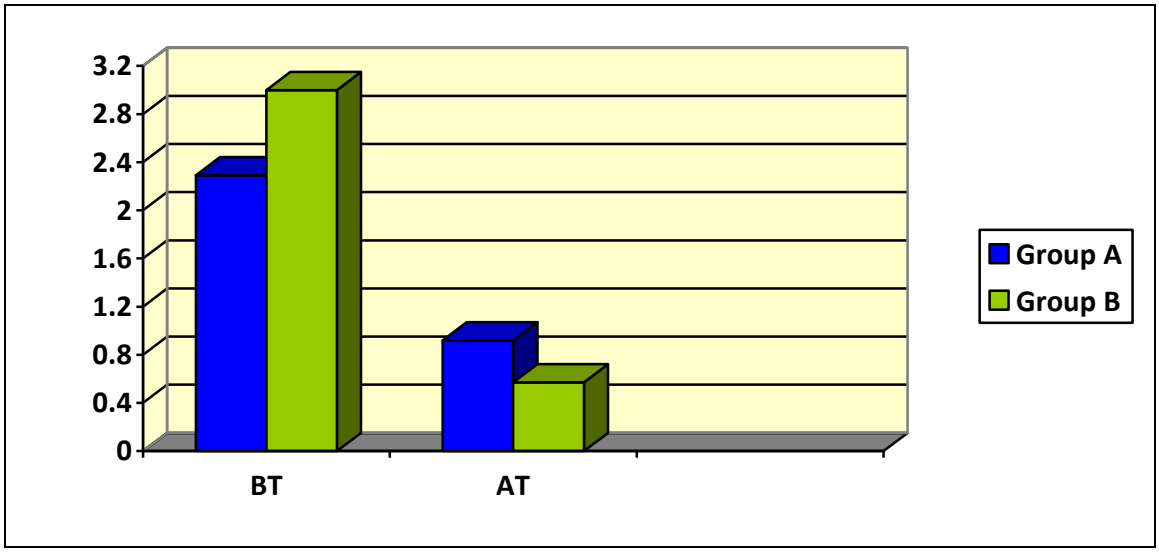


Fig. No.48: Showing the comparative effect after crossover of two study group A & B with respect of *Dourbalya*

Table No. 83: Showing the comparative effect after crossover of two study group A & B with respect of *Swedadhikya*

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p-value
		BT	AT		(Zc – 1.96)	
Group A	*Swedadhikya*	2.15± 0.425	0.95± 0.226	55.8%	21.590	< 0.05*
Group B		2.13± 0.414	0.43 ± 0.497	79.8%	22.573	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Swedadikya* , the mean value before treatment 2.15 changes to 0.95 with 55.8% relief. Where as in Group B also shows more significant (p<0.05) changes in *Swedadikya*, the before treatment value 2.13 changes to 0.43 with 79.8% relief of symptoms. (Fig.49)

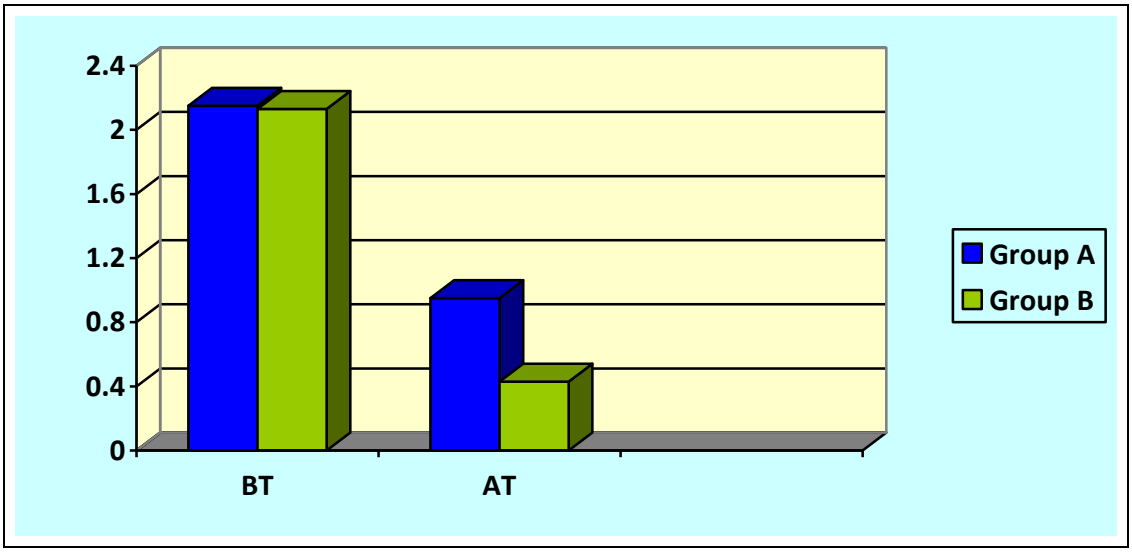


Fig. No.49: Showing the comparative effect after crossover of two study group A & B with respect of *Swedadikya*

Table No.84: Showing the comparative effect after crossover of two study group A & B with respect of Galatalu Shosa

Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p-value
		BT	AT		(Zc – 1.96)	
Group A	*Galatalu Shosa*	2.43 ± 0.498	0.91 ± 0.226	62.5%	22.782	< 0.05*
Group B		2.53± 0.451	0.29 ± 0.458	88.53 %	27.391	< 0.05*

*indicates p<0.05 is significant
N = Number of patient
Z = z value
BT= Before treatment
p = value represent significance
SD = Standard Deviation
t = Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Galatalu Shosa*, the mean value before treatment 2.43 changes to 0.91 with 62.5 % relief. Where as in Group B also shows significant (p<0.05) changes in *Galatalu Shosa*, the before treatment value 2.53 changes to 0.29 with 88.53% relief of symptoms. (Fig.50)

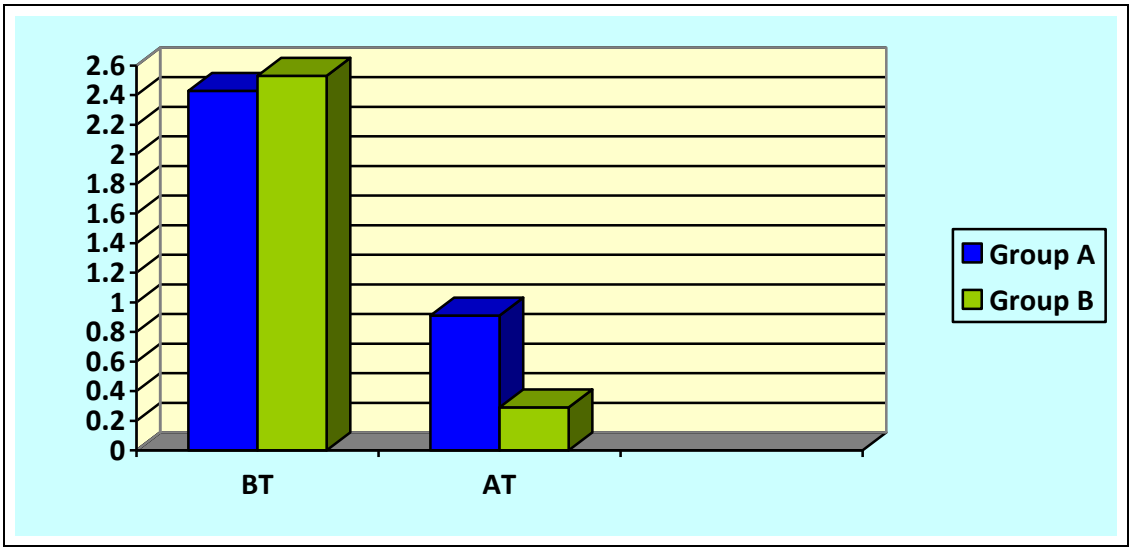


Fig. No.50: Showing the comparative effect after crossover of two study group A & B with respect of *Galatalu Shosa*

Table No. 85: Showing the comparative effect after crossover of two study group A & B with respect of *Klaibya*

Treatment Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc 1.96)	
Group A	*Klaibya*	2.88 ± 0.327	1.43 ± 0.498	50.34%	21.078	< 0.05*
Group B		2.42± 0.251	0.93 ± 0.251	61.6.%	11.594	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e *Klaibya* , the mean value before treatment 2.88 changes to 1.43 with 50.34% relief. Where as in Group B also shows significant (p<0.05) changes was observed in Klaibya, the before treatment value 2.42 changes to 0.93 with 61.6 % relief of symptoms. (Fig.51)

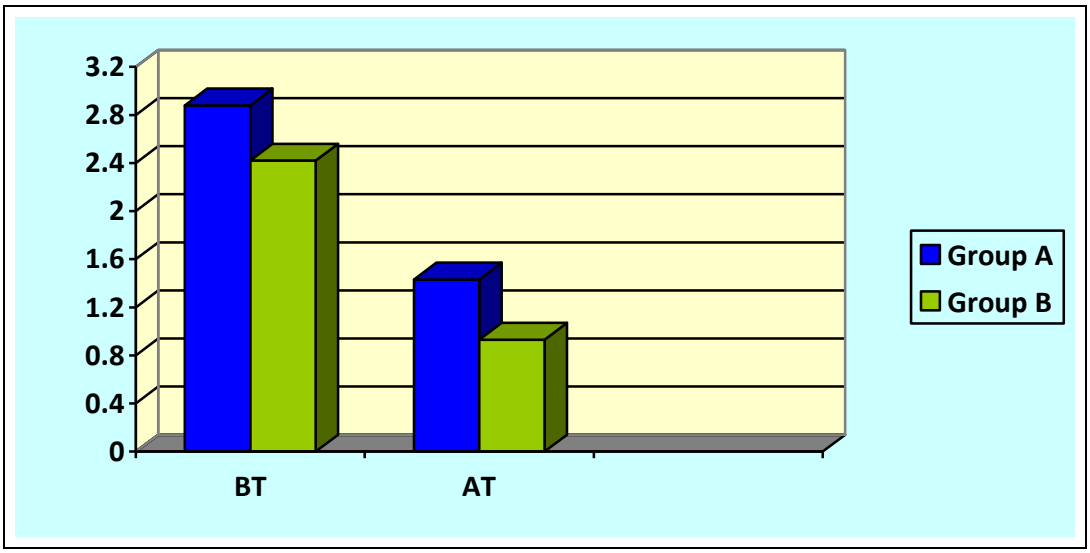


Fig. No.51: Showing the comparative effect after crossover of two study group A & B with respect of *Klaibya*

Table No.86: Showing the comparative effect after crossover of two study group A & B with respect of *Purisha Bhadhata*

Treatment Group	Symptoms n=75	Mean ± SD		% of relief	Z -Value	p- value
		BT	AT		(Zc – 1.96)	
Group A	*Purisha Bhadhata*	2.77 ± 0.421	0.8 ± 0.381	71.1%	39.655	< 0.05*
Group B		2.81± 0.392	0.52 ± 0.503	81.4%	31.098	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the subjective symptoms i.e. *Purisha Bhadhata*, the mean value before treatment 2.77 changes to 0.8 with 71.1% relief. Where as in Group B also shows significant (p<0.05) changes was observed in *Purisha Bhadhata*, the before treatment mean value 2.81 changes to 0.52 with 81.4 % relief of symptoms. (Fig.52)

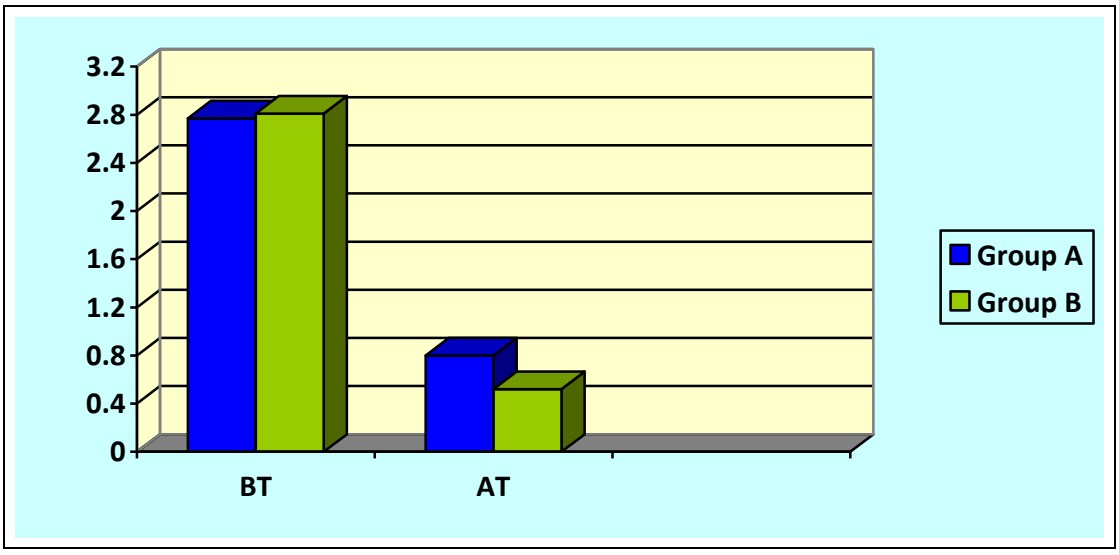


Fig.No. 52: Showing the comparative effect after crossover of two study group A & B with respect of *Purishabadhata*

Table No.87: Showing the comparative effect after crossover of two study group A & B with respect to FBSL (Fasting blood Sugar level)

Treatment Group	Objective Parameter n=75	Mean ± SD		% of relief	Z - Value	p-value
		BT	AT		(Zc – 1.96)	
Group A	FBSL	166.23 ± 11.507	146.43 ± 6.420	11.91%	23.429	< 0.05*
Group B		170.96 ± 11.495	140.76 ± 8.424	17.66%	17.560	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the Fasting Blood sugar level (FBSL), the mean FBSL level before treatment 166.25mg/100ml of blood reduced to 140.61 mg/100ml of blood with 15.41% relief. Where as in Group B shows significant (p<0.05) changes was observed in Fasting Blood sugar level (FBSL), the before treatment the mean FBSL was 170.96 mg/100ml of blood reduced to 140.76 mg/100ml of blood with 17.66% reduction. (Fig.53)

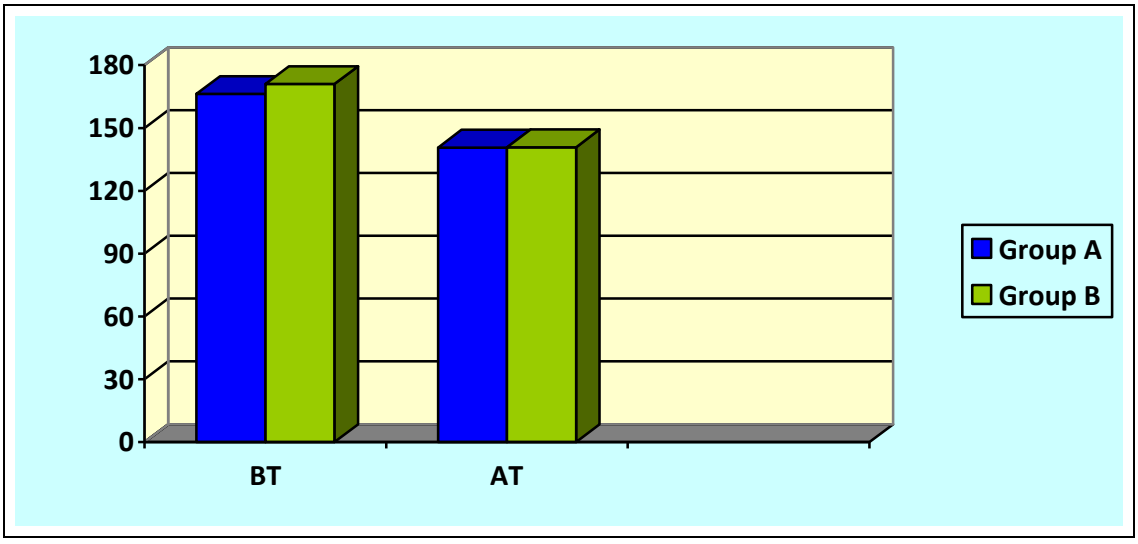


Fig. No. 53: Showing the comparative effect after crossover of two study group A & B with respect to FBS (Fasting blood Sugar)

Table No.88: Showing the comparative effect after crossover of two study group A & B with respect to PPBS (Post Prandial blood Sugar)

Treatment Group	Objective Parameter n=75	Mean ± SD		% of relief	Z -Value	p-value
		BT	AT		(Zc – 1.96)	
Group A	**PPBSL**	260.57 ± 20.937	157.77 ± 6.372	39.45%	42.230	< 0.05*
Group B		277.96± 24.04	157.44 ± 5.173	43.51%	42.160	< 0.05*

*indicates p<0.05 is significant
N = Number of patient
Z = z value
BT = Before treatment
p = value represent significance

SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the Post Prandial Blood sugar level (PPBSL), the mean PPBS level before treatment 260.57 mg/100ml of blood reduced to 157.77 mg/100ml of blood with 39.45% relief. Where as in Group B also shows significant (p<0.05) changes was observed in Post Prandial Blood sugar level (PPBSL), the before treatment the mean PPBS level was 277.96 mg/100ml of blood reduced to 157.44 mg/100ml of blood with 43.51% reduction. (Fig.54)

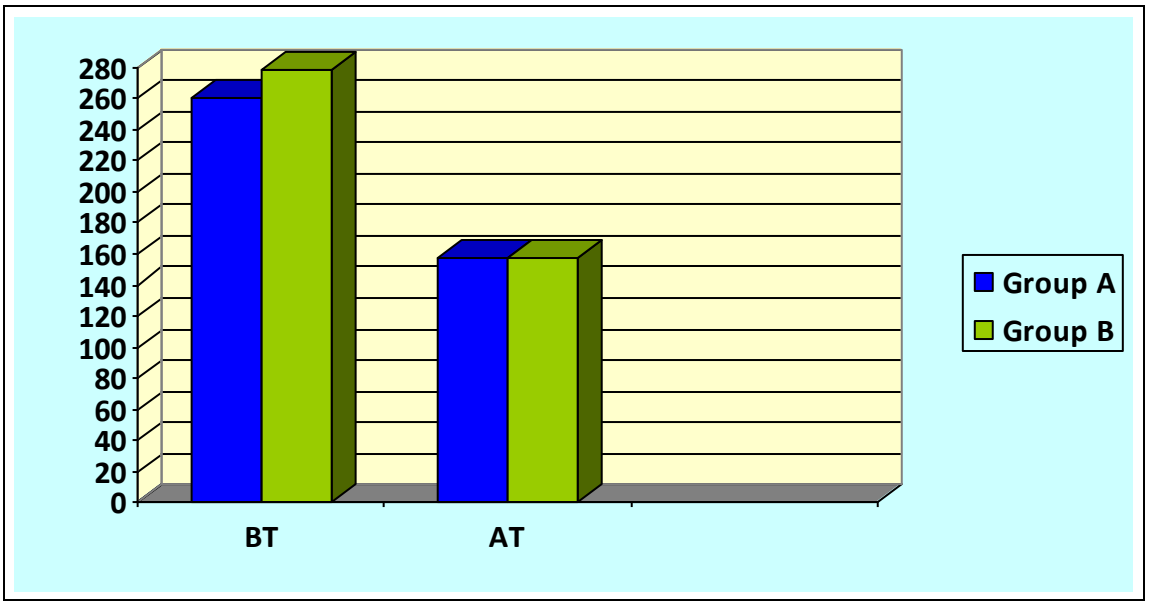


Fig.No. 54: Showing the comparative effect after crossover of two study group A & B with respect to PPBSL (Post Prandial blood Sugar level)

Table No. 89: Showing the comparative effect after crossover of two study group A & B with respect to HbA_{1c}

Treatment Group	Objective Parameters	Mean ± SD		% of relief	Z -Value	p-value
		BT	AT		(Zc – 1.96)	
Group A	HbA_{1c}	8.95 ± 0.832	7.01 ± 0.344	**21.6%**	39.648	< 0.05*
Group B		9.23± 1.072	6.20 ± 0.367	32.8%	61.761	< 0.05*

*indicates p<0.05 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance

SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In Group A statistically significant (p<0.05) changes was observed in the HbA_{1c}, the mean HbA_{1c} level before treatment 8.95 reduced to 7.01 with 21.6% relief. Where as in Group B also shows significant (p<0.05) changes was observed in HbA_{1c} but more than group A, the before treatment the mean Hb_1AC level was 9.23 reduced to 6.20 with 32.8% reduction. (Fig.55)

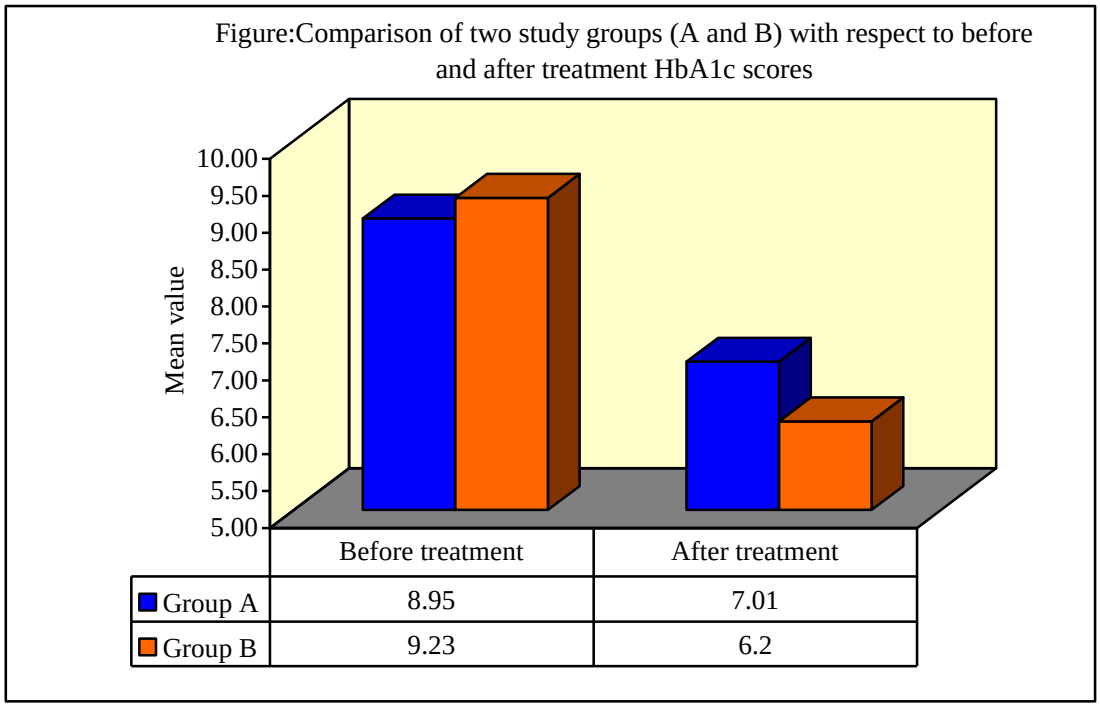


Fig. No.55: Showing the comparative effect after crossover of two study group A & B with respect to HbA_{1c}

Table No.90: Comparison of before and after treatment serum creatinine scores in two study groups (A and B) by paired t test after cross over

Groups	Treatment	Mean	Std.Dv.	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A	Before	1.29	0.17	0.20	0.11	15.50	11.143	0.0001*
	After	1.09	0.13					
Group B	Before	1.38	0.17	0.27	0.21	19.56	09.115	0.0001*
	After	1.11	0.16					

*indicates p<0.01 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

After the cross over in this study the serum Creatinine level in Group A the mean score before treatment was 1.29 changes to 1.09 after treatment on 90th day which was statistically significant at p<0.01. Again in Group B the mean serum Creatinine level before treatment 1.38 changes to 1.11 after treatment on 90th day which was also statistically significant at p<0.01. However in comparison in both the groups the changes in percentage in group A is 15.50% and group B i.e. 19.56 (Fig. No.56)

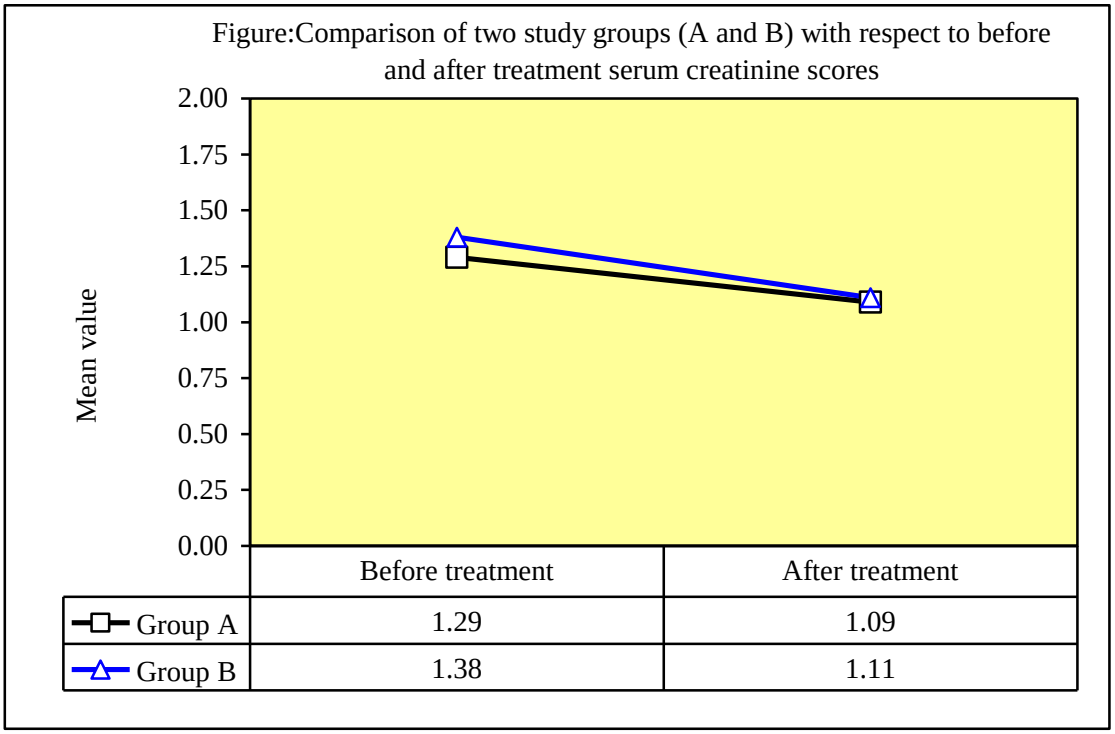


Fig. No. 56: Comparison of before and after treatment serum creatinine scores in two study groups (A and B) after cross over.

Table No. 91: Comparison of before and after treatment serum urea scores in two study groups (A and B) by paired t test after cross over

Groups	Treatment	Mean	Std.Dv.	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A	Before	17.33	3.52	1.5	1.66	8.6%	9.2137	0.0001*
	After	15.83	3.38					
Group B	Before	18.00	3.29	2.32	3.60	12.88%	7.538	0.0001*
	After	15.68	3.55					

*indicates p<0.01 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

After the cross over in this study the serum Urea level in Group A, the mean score before treatment was 17.33 changes to 15.83 after treatment on 90th day which was statistically significant at p<0.01. Again in Group B the mean serum Urea level before treatment 18.00 changes to 15.68 after treatment on 90th day which was also statistically significant at p<0.01. However in comparison in both the groups the changes in percentage in group A is 8.6% and Group B it is 12.88% (Fig. No.57)

Figure:Comparison of two study groups (A and B) with respect to before and after treatment serum urea scores

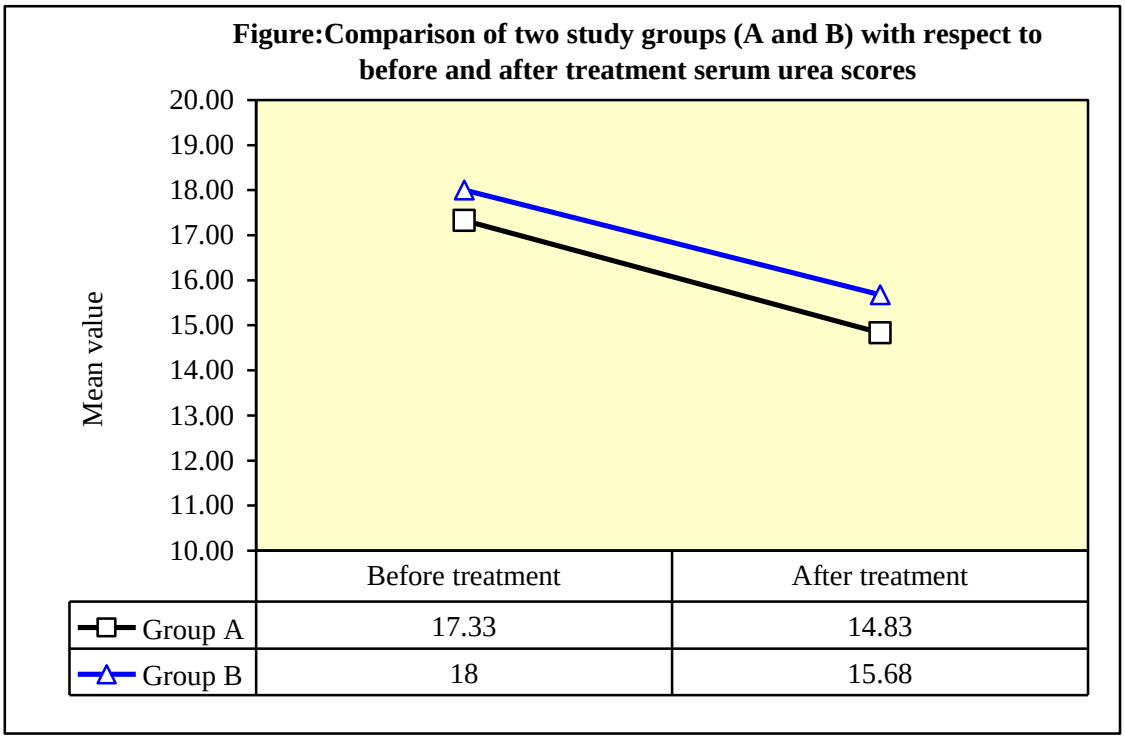


Fig. No. 57: Comparison of before and after treatment serum urea scores in two study groups (A and B) after cross over.

Table No. 92: Comparison of before and after treatment serum Cholesterol scores in two study groups (A and B) by paired t test after cross over

Groups	Treatment	Mean	Std.Dv.	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A	Before	198.10	20.12	18.07	14.07	9.12	8.2162	0.0001*
	After	180.03	13.25					
Group B	Before	202.71	22.18	22.2	15.11	10.95	11.321	0.0001*
	After	180.51	12.21					

*indicates p<0.01 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

After the cross over in this study the serum Cholesterol level in Group A, the mean score before treatment was 198.10 changes to 180.03 after treatment on 90th day which was statistically significant at p<0.01. Again in Group B the mean serum Cholesterol level before treatment 202.71 changes to 180.51 after treatment on 90th day which was also statistically significant at p<0.01. However in comparison in both the groups the changes in percentage in group A is 9.12% and Group B it is 10.95% (Fig. No.58).

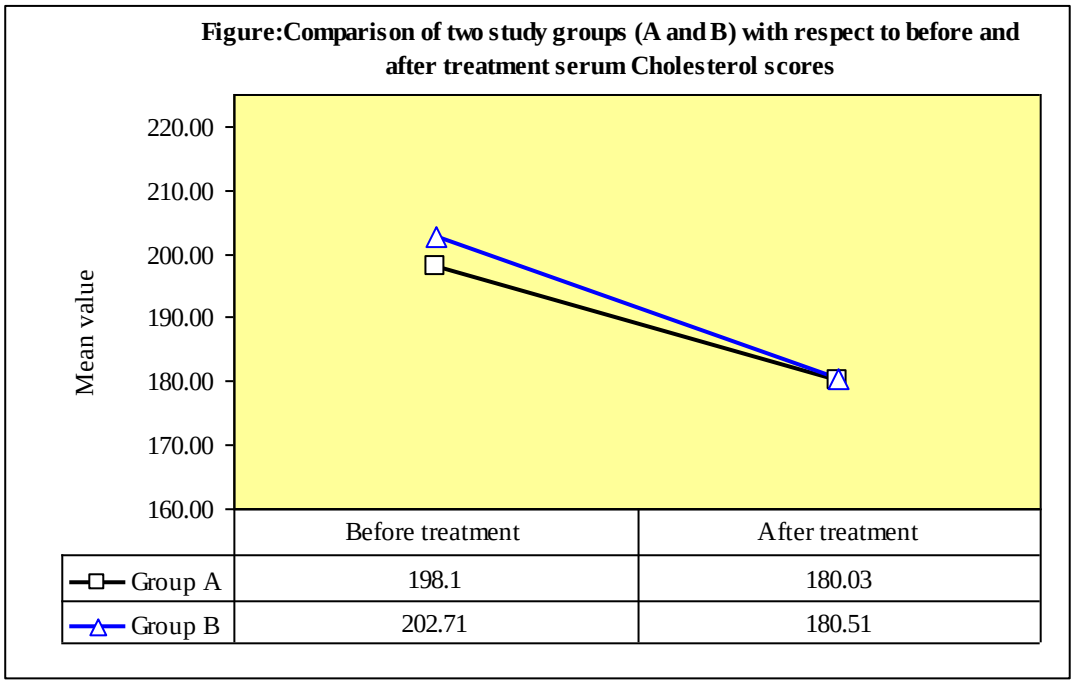


Fig no.58: Comparison of before and after treatment serum Cholesterol scores in two study groups (A and B) after cross over.

Table No.93: Comparison of before and after treatment serum Triglyceride scores in two study groups (A and B) by paired t test after cross over

Groups	Treatment	Mean	Std.Dv.	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A	Before	140.21	17.31	3.83	17.92	2.73%	6.712	0.0001*
	After	136.38	11.88					
Group B	Before	152.62	14.61	18.3	15.78	11.99%	16.831	0.0001*
	After	134.32	12.60					

*indicates p<0.01 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance

SD= Standard Deviation
t=Test probability difference level
AT=After treatment

After the cross over in this study the serum Triglycerides level in Group A, the mean score before treatment was 140.21 changes to 136.38 after treatment on 90th day which was statistically significant at p<0.01. Again in Group B the mean serum Triglycerides level before treatment 152.62 changes to 134.32 after treatment on 90th day which was also statistically significant at p<0.01. However in comparison in both the groups the changes in percentage in group A is 2.73% and Group B it is 11.99% (Fig No.59).

Figure:Comparison of two study groups (A and B) with respect to before and after treatment serum Triglyceride scores

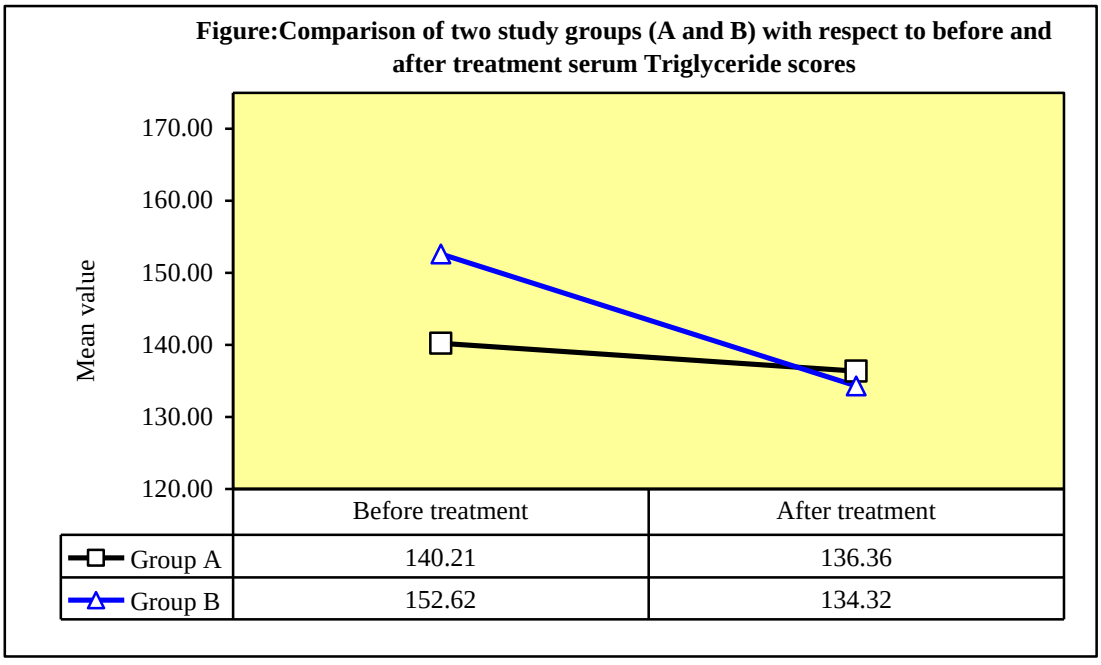


Fig. No.59: Comparison of before and after treatment serum Triglyceride scores in two study groups (A and B)

Table No 94: Comparison of before and after treatment LDL scores in two study groups (A and B) by paired t test after cross over.

Groups	Treatment	Mean	Std.Dv.	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A	Before	143.55	13.68	27.73	15.47	19.31	21.9493	0.0001*
	After	115.82	10.22					
Group B	Before	144.55	14.19	26.72	14.49	18.48	20.8492	0.0001*
	After	117.83	10.72					

*indicates p<0.01 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In this study the serum LDL level in Group A, the mean score before treatment was 143.55 changes to 115.82 after treatment on 90th day which was statistically significant at p<0.01. Again in Group B the mean serum LDL level before treatment 144.55 changes to 117.83 after treatment on 90th day which was also statistically significant at p<0.01. However in comparison in both the groups the changes in percentage in Group A was 19.31% and Group B it was 18.48%.(Fig No.60)

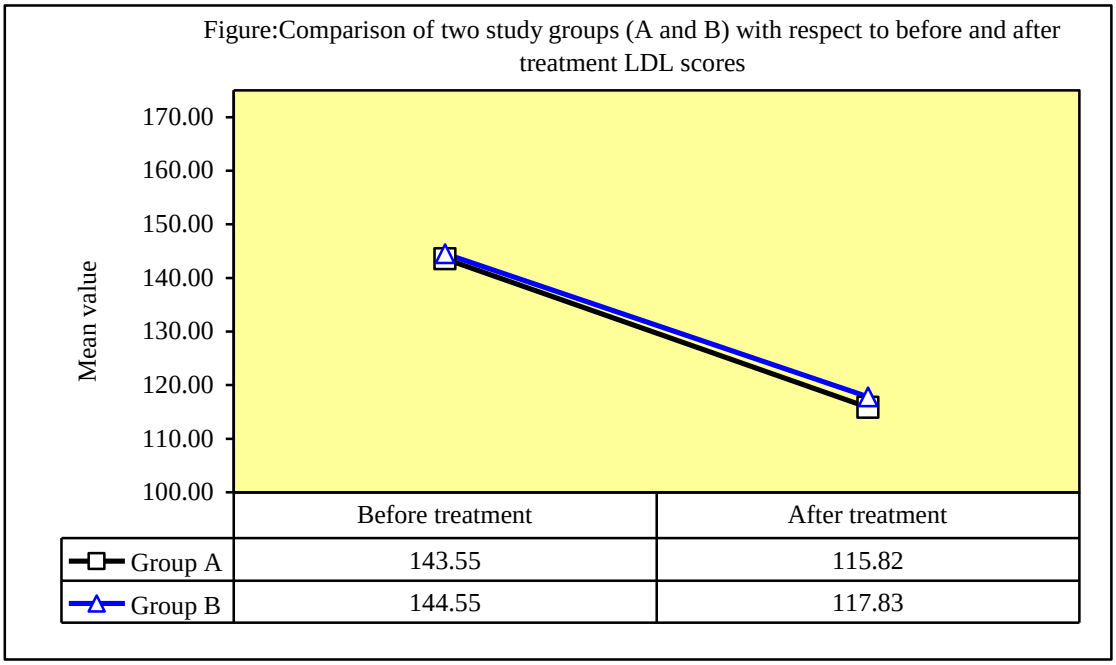


Fig. No.60: Comparison of before and after treatment LDL scores in two study groups (A and B) after cross over.

Table No.95: Comparison of before and after treatment HDL scores in two study groups (A and B) by paired t testafter cross over

Groups	Treatment	Mean	Std.Dv.	Mean Diff.	SD Diff.	% of change	Paired t	p-value
Group A	Before	54.32	6.55	-3.69	6.40	-6.79	-8.2245	0.0001*
	After	58.01	5.53					
Group B	Before	49.20	5.41	-3.75	4.13	-7.62	-9.9324	0.0001*
	After	52.95	4.16					

*indicates p<0.01 is significant
n= Number of patient
Z= z value
BT= Before treatment
p = value represent significance
SD= Standard Deviation
t=Test probability difference level
AT=After treatment

In this study the serum HDL level in Group A, the mean score before treatment was 54.32 increases to 58.01 after treatment on 90th day, which was statistically significant at p<0.01. Again in Group B the mean serum HDL level before treatment 49.20 increases to 52.95 after treatment on 90th day , which was also statistically significant at p<0.01. However in comparison in both the groups the changes in percentage in Group A was 6.79% and Group B it was 7.62%(Fig No.61)

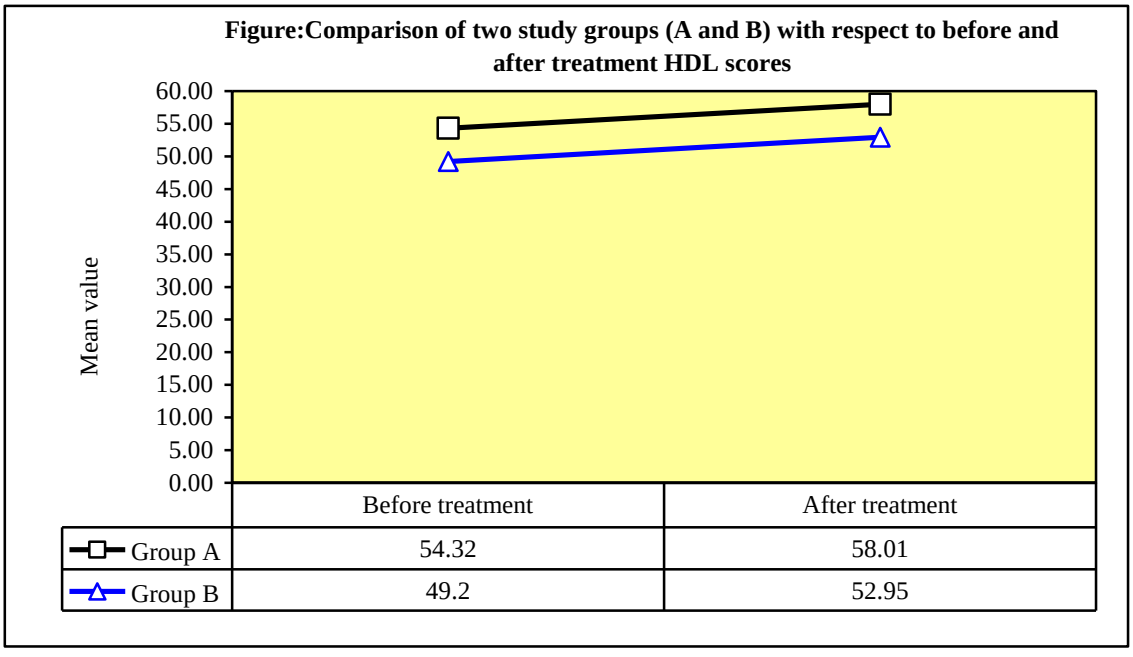


Fig. No.61: Comparison of before and after treatment HDL scores in two study groups (A and B) after cross over.

DISCUSSION:

Ayurveda is the most ancient system of Medicine among the different traditional existing in the present world. *Ayurveda* develops the primary concept by describing the tridosa theory which makes pivotal role in health and diseases. Since from the time immemorial human being is constantly trying to control over different ailments which were evolved time to time. The very concept of *Swasthswa swastha rakshana* and *Aturasya vikara prasamana* explained for the same reason. Different types of non-communicable diseases are explained in *Ayurveda* where *Madhumeh*a is one among the oldest documented disease. Gradually the prevalence of non communicable diseases are increasing day by day due to today's stressful environment leading to more challenges to the health care system. Because of this life style disorders are increasing; out of which *Madhumeha* (Diabetes mellitus) is one.

The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014. The global prevalence of diabetes among adults over 18 years of age has increase from 4.7% in 1980 to 8.5% in 2014[245]. The prevalence has been rising more rapidly in middle and low-income countries. Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation. In the year 2016, an estimated 1.6 million deaths were directly caused due to diabetes. Another 2.2 million deaths were attributable to high blood glucose in 2012. Almost half of all deaths attributable to high blood glucose occur before the age of 70 years. WHO estimates that diabetes was the seventh leading cause of death in 2016. Healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use are ways to prevent or delay the onset of type 2 diabetes mellitus. Diabetes mellitus can be treated and its consequences avoided or delayed with diet, physical activity, medication and regular screening and treatment for complications[246]**.**

In worldwide as estimation by 2017 there are 451 million (age 18-99 years) people with diabetes. These figures were expected to increase to 693 million by 2045. It was estimated that almost half of all people (49.7%) living with diabetes are undiagnosed. Moreover, there was an estimated 374 million people with impaired

glucose tolerance (IGT) and it was projected that almost 21.3 million live births to women were affected by some form of hyperglycaemia in pregnancy. In 2017, approximately 5 million deaths worldwide were attributable to diabetes in the 20-99 years age range. The global healthcare expenditure on people with diabetes was estimated to be USD 850 billion in 2017 [247].

Present era "*Madhumeha"* i.e. Diabetes Mellitus has is one of cause to visit hospital regularly. Because of difficult nature of the disease Madhumeha is always considered as a *asadhya vyadhi* and denoted as '*Mahatyaya*' for *Chikitsa*[245] because vata dosha effects the *vasa, majja,Oja* and *Lashika* etc *dhatus* and cause their *kshaya* leads to different complications. Timely intervention with diet, exercise and medicine the lifespan of a *Madhumehi* can be maintained and morbidity can be reduced. For this in different *Ayurveda* treatises explained lots of formulations to overcome the morbidity and early mortality. This encompasses this study has been taken with the drug *Mustadi Kasaya* for effective management of Madhumeha vis-vis diabetes mellitus.

In '*Madhumeha'* where the person excretes excessive quantity of urine which is similar to that of *Madhu*. According to modern concept Diabetes mellitus can be correlated with *madhumeha* having many similarities. Literally where diabetes means siphoning of water and mellitus means honey. The word "meha" is attributed to Madhumeha. Prameha word is applied to all types of *"Prameha"* where *Madhumeha* is one type of *Vataja Prameha*.

The causes of *Madhumeha* is divided in to two types *sahaja & apathyanimittaja*. It is described that *Sahaja madhumeha* is due Matru Pitru bija doshskrits i.e. genetic factor. *Apathayaja nimitta* one is due to faulty foods & habits, lack of exercise[246]. Present days it can be seen that due to use of refined food with high amount of carbohydrates & use of different machines people are less active & leads sedentary lifestyle leads to *Madhumeha*. *Aasya sukham* and *swapna sukham* were said to be the Nidanas of *Madhumeha* along increasing stressful envionmentcauses episodes of being eating more leading to *Madhumeha*. *Madumeha* is *kapha pradhanaja tridoshaja vyadhi*. *Avrutta Vata* along with *bahudrava Shlesma* leads to *Madhumeha*. IDDM (Type I Diabetes mellitus) is similr to *dhatukshayajanya, apatarpanajanya* type of *Madhumeha* while the NIDDM

(Type II Diabetes mellitus) is similar to *avaranajanya, santarpanajanya* type of *Madhumeha* as described in *Ayurveda*. In dhatukshayajanya / Apatarpanajanya *Madhumeha vata dosha* gets vitiated either due to its own etiological factors or by *dhatukshaya*. In *avaranajanya* and *santarpanajanya Madhumeha* the *kapha* and *pitta dosha* get vitiated due to etiological factors, which causes the obstruction of *Srotas* causing provocation of Vata & leading to the manifestation of the disease Madhumeha. The *ahara* and *vihara* which increases the *Kapha dosha* are considered under *apathyakara ahara* for *prameha rogi*. Intake of excessive *madhura rasa* causes the Medo *vriddhi, Shleshmaja vriddhi, Sthoulya,* and *Meha kara*[250].

Madhumeha caused due to excessive consumption of *Dugdha, Dadhi, Guda, Navanna, Sheeta Ahara, Madhura-Amla-Lavana Rasa, Surapana, avyayama, swapnasukha, mrujavarjana. Among mamsa sevana,* most of the patients mainly indulge the *Gramya* and *oudaka mamsa*[251]. Food which are having the qualities like *Guru, drava, abhisyandi* causes vitiation of *kapha* & *meda.* Modern science advocates that intake of excessive carbohydrate rich food and processed foods, non vegetarian products, packed foods, preserved foods which will lead to increase in total consumption of high calories ultimately resulting in 'obesity'. *Ayurveda* and Modern medicine have accepted role *sthoulyata* as one of the cause for *Prameha*.

The *Rupa* and *Purvarupa* of *Madhumeha* which are explained in our *samhita* are similar to the clinical features of Diabetes Mellitus. *Sarva kaala nidra, dantadinam maladyatvam, kaya chidreshu upadeha , ati asana sukha, alasya, ghanangata, tandra, ashya madhuryata, madhura mootrata, Pippilika abhisarana, Mootra abisarana,* Shithilangata are some of the *purvarupas of Madhumeha* related with the *prakupita kapha dosha*[249].

Kapha Dosha is *dominant* factor in the pathogenesis of *Madhumeha.* It gets primarily vitiated because of its close resemblance with the etiological factors. *Kapha* having qualities like *guru, sheeta, snigda, madhura, sthira, picchila* and *tamogunaadhika,* i.e. *kapha prakopakara ahara* and *vihara* does the vitiation of concordant body elements and respective *srotasas* like *Rasa, Mamsa, Meda, Kleda, Vasa,*

Lasika and *oja* etc[253]. The vitiation of *Kapha dosha* takes the main role for vitiation of other dushyas.

Dantadidanam Maladhyatvam, Kaye malam and kesha nakha ativruddi are usually due to excessive formation of defective *medadhatu* formation, is the main *dushya* in *Kaphaja Prameha*.

Tandra & *Nidra, alasya, guru gatrata, shitilangata* are laxanas due to kapha and dushyas like *Rasa dhatu, mamsa dhatu, meda dhatu & Oja* with their respective srotas as involvement. *Rasadhatu, Meda dhatu* and *Kapha dosa* are having close resemblance with regard to functions as well as qualitative parameters, as said by *Vagbhata 'Raso api shleshmavat'*[123]. So the role of Rasa Dhatu is very much important in the precipitation of the disease. The vitiation of meda dhatu is common and along with *dominant Dushya* in the *samprapti of Madhumeha*. *Meda* is to provide *snigdata a*nd *drudata* to the *sharira*, but due to *asanghatana* of *meda* leading to *Shaithilyatha* of body. *Mamsa dhatu* is also one of the main dushya, vitiated especially in *Kaphaja Prameha* and *Avaranjanya Madhumeha,* as *Mamsa* and *Kapha* have same qualities. They both give strength to the body. When get vitiated, *Mamsa* losses it's normal consistency and develops *shaithilyatha* and provide space in between for the accumulation of morbid matter. In modern parlance tiredness, fatigue, lethargy can be correlated.

Kara pada supthi and Kara Pada daha, Peripheral Neuropathies and vasculopathis which are quite in accordance with the late complications of Diabetes Mellitus in modern science. *Karapada suptata* is due to *Ashayapakarshaka Gati of K*apha and its relationship with the Vata dosha as explained in the context of *Avarana* by *Charakacharya. Karapada daha* is due to *pittadosha. Pitta Dosha* is not so dominant factor in the pathogenesis of *Prameha.* By the vitiation of *Pitta, Avaranjanya Samprapti* of *Madhumeha* resulted. *Rakta Dhatu* has no much involvement in the manifestation of the *Madhumeha.* It is mainly getting vitiated in *pittaja Prameha*. Not initially but in later stage *Rakta* also get vitiated prominently causing complication like *karapada daha*[148]. It may be also due to loss of *Ambu* which is *sheeta* in property and required for *preenana,* failing to which results in *Daha*. Vascular and neural diseases are closely related with 4 factors in pathogenesis. Vasoconstriction leads to capillary basement membrane

thickening and endothelial hyperplasia which causing Hypoxia and Neuronal Ischemia. An elevated glycated end product at the cellular end activates polyol pathway or sorbitol/aldose reductase pathway which decreases the level of glutathione and nitric oxide which is an important vasodilator in turn increase in reactive O_2 radicals. This sorbitol cannot cross cell membrane accumulation of which causes osmotic stress on cells by drawing water into cells causing inflammation. This whole pathology leads to vascular and neural degeneration with manifesting symptoms like pain, pricking, throbbing, burning sensations, and numbness of peripheral nerve endings [43].

*Prabhoota mootrat**a*** means increased in quantity as well as frequency of urination. In *samprapti* there is involvement of vitiated *kapha, meda* and *kleda* and *mutravaha srotodusti*. Due to *kaphakara Nidhana sevana prakrita kapha* which is in *bhadda* form gets vitiated to *bahudrava rupa*. The physiology of *Kleda* is mainly related with *Mutra* and *Sweda* along with *Meda*. Thus when *Kleda* is involved then it directly affects the above factors. *Kleda* proper in quantity is important to maintain the *snigdhata* in between the tissues. *Vikrita Kapha* has affinity towards *Bahu-Abaddha Meda* due to their similar properties and gets lodged there. When vitiated *Kapha* and *Meda* come in contact with *Sahrira Kleda* and vitiate it, producing *Mutradushti*. The vitiated *Kapha* settles in *bastimukha* which are already filled with vitiated *Meda* and *Kleda*, thus producing excessive quantity of urine[141].

Polyuria the established pathophysiological theory behind this clinical feature is excessive fluid loss through urination along with glucose causing severe extracellular and to some extent in the intracellular dehydration resulting in both Polyuria and also Polydypsia in Diabetes Mellitus is due to decreased renal threshold by the Kidneys brought about by higher glucose concentration of the blood. This leads to increased Glomerular Filtration Rate (GFR) by the kidneys, which is stated as Polyuria in Diabetes Mellitus. Another established theory on increased urination is due to the consequence of osmotic diuresis secondary to the sustained hyperglycemia during which along with the loss of glucose,free water and various electrolytes are also lost.

Madhusama mootra or *madhura mootra* is because of *ojadhatu kshrana* through *mootra* which can be easily understood by *pipeelika abhisarana*. These symptoms

indicate the glycosuria. Whenever the quantity of glucose entering the kidney tubules in the glomerular filtrate rise above approximately 180 mg/100 ml a level that is called the blood "threshold" for the appearance of glucose in the urine.

In *Avila mootrata* there is an abnormality in the density and turbidity of urine manifested due to *drava* and *guru guna vriddhi* of *kapha* and *medas*. *Kleda, Lasika, Dhatugata mala* and vitiated *dosha* circulating in the blood and getting excreted out by imparting the *Samalatva* to the urine along with the *Ojus*. This can be due to presence of phosphates, sugar, sperm, acetone, silicates, albumin, chyle, bile pigments and salts, blood, pus or casts etc. in the urine.

Pipasa Adhikata, muka talu shosha establishes the *Udakavaha Srothodushti* and is due to *Rukshaguna* of *vata* & also due to loss of *sheetata* & *snigdata* caused by *Udakakshya*. It is one among the cardinal features of *Madhumeha* which is termed as Polydypsia in Diabetes Mellitus. The *Srotomula* of the *Udakavaha Srothas* is stated as *Kloma*. Massive loss of fluid in the urine, causing dehydration of the extracellular fluid, which in turn causes compensatory dehydration of the intracellular fuid[213]. This probably can be referred to Adrenal Glands[64] which is responsible for the fluid balance of the body. Any disturbance in the homeostasis of these glands will results in multi systemic dysfunction and one among which is severe cellular dehydration, which may be the reason for *Pippasa Adhikata* in *Madhumeha*.

Kshudadhikata has been mentioned as a l*akshana* in *apathyanimittaja Madhumeha. Patha* of *vata* is obstructed by vitiated kapha and medas. As a result samana vata get vitiated and produces *theekshnagni*. So patients develop bahukankshatha towards food. Failure to use the glucose for energy leads to increased utilization and decreased storage of proteins as well as fat. Therefore, a person with severe untreated diabetes mellitus suffers rapid weight loss and *asthenia* (lack of energy) despite eating large amounts of food (polyphagia). Without treatment, these metabolic abnormalities can cause severe wasting of the body tissues and death within a few weeks.

Another important characteristic feature of the disease is *Swedapravruthi*. When pitta and kapha gets provoked, it undoubtedly causes the vitiation of dusyas like rakta, meda, kleda, sweda and lasika leading to *sweda vruddhi, visra sharira gandha, panidaha, pipasa* and *sosha* indirectly *Agni vaisyama* too. Only *Vagbhata* mentioned *sweda* as a *dushya* along with above *dushyas*.

Daurbalya: In *Madhumeha Ojus* is concerned it is always the *Apara ojus* which is *Ardhanjali Pramana* which gets disturbed along with other vitals and the same circulates all over the body according to the explanatory theory of *Acharya Chakrapani*[107]. Oja as Dushya mainly involved in *Vataja Prameha* i.e. *Ojomeha.* Provoked Vata due to its own etiological factors or due to *Avarana* carries Oja towards basti and excrete outside through urine. Pathological conditions regarding Oja are of 3 types. So the symptoms of Oja kshaya like *Murccha, Mamsakshaya, Moha, Daurbalya* (excessive weakness), *Vyathita Indriya, Rukshata, Gurugatrata, Nidra, Tandra* etc may manifest. It is already mentioned that aparipakwa dhatus will not nourish the body properly and hence causes weakness and klama. From the modern parlance, the role of T-cell mediated tissue damage in type-2 diabetes mellitus is well established and it is the T-cell mediated immunity which takes the pivotal role during the progression of the disease pathology through various stages of inflammation and its corresponding tissue injury which leads to osmotic changes within the tissues when glucose concentration in the blood increases. The failure of glucose utilization, loss of electrolyte and loss of body proteins causes weakness.

Netragaurava, Angagauravata in *Madhumehi* patient is due to vitiated *Vata* with involvement of *Majja Dhatu. Majja dhatu* is not vitiated in maximum extent but *Vata prakopa* causes its *Ksaya* producing the above symptoms.

Prameha is a *Kulaja Vikara* and occurs as result of Beeja dosha. *Susruta* described that *Sukra Dosha* and *Prameha* get precipitate because of the vitiation of *Vyanavata* and *Apanavata*. *Vata* causes depletion of *Shukra Dhatu* leading to *daurbalyata,* **kruchra vyavayata**, and also *Shukrameha*. So, one can appreciate the

importance of *Shukra Dushti* in *Prameha*. With this it is understood that the relation of *Sukra Dushti* as a component of Prameha formation.

Discussion *on Samprapti*: *Charaka* stated that, when *tridosha* which are in *bahudravatva* form get affected due to *ahita Nidhana sevana* it does *dushana* of *meda, mamsa, kleda* etc, the morbidity would be driven to urinary system to bring about *Prameha* of corresponding kinds. The Dushyas included are *Meda, Mamsa, Sharira Kleda, Shukra, Shonita, Majja, Lasika,Rasa* and *Oja*[115]. The special characteristic features of these Dushyas are in bahvabadha form.

From the modern parlance the following pathophysiological theories in relationship with the type -2 Diabetes Mellitus are well established.

1. Type 2 DM is a more complex multifactorial disease.
2. There is greater role of genetic defect and heredity.
3. The two main mechanisms for hyperglyceamia in type 2 DM- insulin resistance and impaired insulin secretion are interlinked.
4. Obesity plays a role in pathogenesis of insulin resistance; impaired insulin secretion may be from many constitutional factors.
5. Increased hepatic synthesis of glucose in initial period of disease contributes to hyperglycemia.

These pathological theories are invariably supportive for the condition termed as **Metabolic Syndrome**.

Discussion on *Upadrava*: The esteemed emeritus foresight of the Ayurvedic seers over the *Upadrava* of this condition *Madhumeha* enlisted approximately thousand years identified and named as *Prameha pidakas*[142] i.e., Diabetic Carbuncles are now well justified with various explanatory theories based on the Altered Platelet Function along with the Coagulating and Fibrinolytic factors, Endothelial Dysfunction and increased Oxidative Stress. Recent DCCT studies reveal that these altered functions with varied degree can manifest both in the early as well as in the advanced stage of this condition but commonly noticed diabetic complications are CAD, diabetic nephropathy and diabetic retinopathy. *Prameha pidakas* later leads to a clinical condition termed as

Putipuyamamsa - Diabetic Gangrene. Other *samanya upadravas* are *Trushna, Arochaka, Avipaka, Atisara, Jwara, Daaha* etc.

Discussion on *Arishtalakshana*: Severe persistent hyperglycemic condition leads to cell destruction with restricted elimination of the toxins causing fruity odour which attracts flies even after the bath of the subjects which in turn is a sure prognostic sign of death mentioned for *Prameha*[149]. The fruity breath odor of acetone further suggests the diagnosis of Diabetic Ketoacidosis. This extensive hyperglycemic condition may produce diabetic coma and lead to death.

Clinical study:

The clinical study was conducted to assess the efficacy of Mustadi Kwatha in the management of *Madhumeha* vis-à-vis Diabetes Mellitus. The herbal formulations was taken in to consideration as the formulation contains potent ingredients like *Musta, Amalaki, Haritaki, Bibhitaki, Haridra, Devadaru, Murva, Endri* and *Lodhra* has got disease specific action and *pramehaghna* action. These ingredients were easily available with minimum controversies.

The dose of the Polyherbal formulations is fixed as 48ml in divided doses twice daily in *Abhukta kaala* keeping in view that dose specification of *Kwatha Kalpana* is fixed to be as 2 *Pala* per day.

In the present study we have totally 190 patients were screened and diagnosed as *Madhumeha* as per the inclusion criteria at Shri JGCHS Ayurvedic Medical College & Hosptal, Ghataprabha, Dist. Belagavi, Karnataka and by conducting medical camp. Out of 190 patients 150 patients completed the treatment protocol in both group A and B. After one month gap the same groups were crossed over. During the entire treatment period 40 patients were dropped out at different level due to various reasons.

The single blind cross over study were be done in 150 patients (n=75 for each group) after getting written consent. Group-A diagnosed patients who are taking oral allopathic anti diabetic medicines along with *Mustadi Kwath* (Study group). Group- B diagnosed patients who are taking oral allopathic anti diabetic medicines along with placebo (Control group).

After 90 days of treatment & 03 month washout period, the patient were crossed over where, Group A were received placebo along with oral anti diabetic drugs and Group B were received *Mustadi kwatha* along with oral anti diabetic drugs for 90 days.

In this clinical trial totally 150 patients were completed treatment observed features in the patients during the clinical study were recorded in the case proforma and these observations were analyzed and tabulated. These observational findings are discussed below.

AGE**:** It was observed that majority of the patients were distributed primarily between the age ranges 51-60 years i.e. 31.36% in Group A and B, 26% patients were from the age group 41-50 and 61-70 years. 16.67% patents were from the age group 30-40 years age group. This reflects that almost all the age groups diabetes is prevalent, WHO data of age occurrence of type -2 Diabetes Mellitus are seen from middle age group. Sedentary life style and stressful factors are more common in middle age .

SEX: Out of 150 patients *madhumeha* in both the group the majority of the patients were males i.e. 60.7% and 39.33% were females. It is evident that males are more susceptible for diabetes mellitus than female. However male and female are having nearly equal risk of getting Diabetes Mellitus as now a day's both are equally managing responsibilities of their life.

RELIGION**:** Religion incidence of Madhumeha shows that 93.33% were from Hindu community, 04% from Muslim community and only 2.67% from other community. It cannot be concluded that only Hindus are more susceptible madhumeha; it may be because of the locality where Hindu population is more.

MARITAL STATUS**:** In this study data of marital status shows that 96.67% patients are married. 92.5% married, 2.67% are unmarried & 1.33% were widows. Nothing specific conclusion could be put forth from this data related to the disease; however married community are more susceptible for more stress.

EDUCATIONAL STATUS**:** In this study higher percentage from Primary school level educated i.e. 44.67%, 33.33% from high school educated, 12.67% undergraduate and only 9.3% patients are uneducated. It signifies that educated people have awareness about the health.

OCCUPATION: In this present study patients from different occupation were registered. The majority of the subjects i.e. 37.33% were active worker, 29.33% were labourer, 24.66% house work and remaining 8.67% patients were having sedentary life style. This may probably due to the occupational ratio of this region. All types of occupations are susceptible for *Madhumeha*. So, evident that only the people having sedentary life style are prone to *Madhumeha*.

ECONOMIC STATUS**:** It was observed that majority of the patients were belonging to lower middle class (68.66%) , middle class (30)% and 0.66% patients were upper middle class. Though DM is called as disease of higher economic status but this study didn't support this statement. This shows that diabetes mellitus has a changing trend which effects all class of people. These findings also reflects that this hospital fully located in rural area. It may be assumed that lower middle class because of their jobless attitude produces psychological upset.

CLINICAL DATA:

FAMILY HISTORY: Out of the subjects i.e. 150 patients in both Groups 54% patients' were having the positive family history of Madhumeha and remaining 46% patients were not having any family history of Madhumeha. This signifies that madhumeha is having strong relation with genetic predisposition. Ayurveda also advocates that madhumeha occurs due to Bija dosa.

NATURE OF DIET: It was observed that majority of the subjects were having history of taking mixed food 66% and 34% patients were Vegetarian. It to some extent indicate that intake of excessive fatty substances, spicy and less fiber content food can lead to manifestation of the disease.

*SHARIRIKA PRAKRUTHI***:** In this study it was observed that majority i.e. 62.67% of the patients were belonging to *vata-kaphaja* category, 24% from *Kapha Pittaja prakriti* and 13.33% patients from Vata pittaja. Here *Vata-kaphaja prakruthi* showed maximum tendency of getting *Madhumeha* and subsequently by *Kaphapitha* and *Vatapita Prakruti*. The vitiated state of *Vata* along with *Kapha* takes major role in progression of disease.

*MANASIKA PRAKRUTI***:** In this study it was observed that majority of the patients were belonging to *Tama prakriti* i.e 47.33% in total , subsequently *rajasa prakruthi* i.e. 26.67% and *Sattva prakruthi* i.e. 26%. It signifies that *vata dosa* takes important role in the pathogenesis of disease.

*SAMHANAN*A**:** In this study out of 150 patients majority of the patients were having *Madhyama samhanana* i.e. 56.67%, subsequently *pravara* 31.33% and 24% in *avara samhanana.*

PRAMANA: In this study out of 150 patients that majority of the subjects were having *Madhyama pramana* 62%, then *avara pramana* 22% and 16% patients were *avara pranama.*

*SATVA***:** In this study out of 150 patients maximum number of subjects were having *avara satva* i.e. 49.33%, 38 % were from *Madhyam Sattva* and 12.67% from *Pravara sattva*. This signifies that person having avara sattva are kaphaja prakriti will contribute the disease.

VYAYAMA SHAKTHI: In this study out of 150 patients maximum number of patients i.e.58% were having *avara Vyayama shakthi*, 30% were havig *madhyama Vyayama Shakti* and 12% patients were having *Pravara vyayama Shakti*. People does not perform adequate physical exercise are prone for Diabetes mellitus. The lack of physical exercise is one of important contributory factor which was explained by our all *acharyas*.

*VAYA***:** Out of 150 patients registered in this study majority of the patients were belonging to the group *Madhyama vaya* i.e. 65.33% ,34.67% patients were from *Vriddha avastha*. This signifies that *madhumeha* is seen in commonly in middle age group.

*AHARA ABHAVARANA SHAKTHI***:** It was observed that majority of the subjects were having *Madhyama abhyavarana shakhti* i.e. 46.67%, 36.67% patients were having *pravara bhyavarana shakthi* and 16.66% were having *Avara janana shakti*.

*AHARA JARANA SHAKTHI***:** In this study was observed that majority of the subjects i.e. 54.67% were having *Madhyama jarana shakhti*, 37.33% patients were having *Pravara Jarana shakti* and 26.67% were having *avara Jarana Shakti*. Usually in diabetes mellitus due to loss of calories the appetite increases.

BLOOD PRESSURE**:** Blood pressure in majority of the cases i.e. 34.67% were 150/90 mmHg, 18% were having blood pressure of 110/70 mmHg, 17.33% were having blood pressure of 140/80 mmHg, 15.335 were having blood pressure 120/80 mmHg and rest i.e 14.67% patients were having blood pressure 130/80mmHg. This distribution of blood pressure are normal according to these age groups found in the study. Higher percentage blood pressure i.e 34.67% may be because diabetes mellitus is common in middle age group.

HISTORY OF PAST ILLNESS: It was evident that average 34% patients were suffering from hypertension. It may be due to continuous suffering by high blood sugar leads to increase the stress of individual leads to hypertension.

*AHARAJA NIDANA***:** Distribution of *Aharaj nidana* where 76.6% patients were having intake of *Dougdha*, 66.6% subjects were taking *Dadhi*, 58% patients were having intake *Navanna*, 54.6% patients were havig history of *dugdha Vikriti*, 50% were havig history of intake of *Gudavikruthi*, 38% patients were having the history of taking *Guda,* 35.3% patients were having *Mamsa Rasa*, and 14.6% patients were having the of taking Sura. This distribution of food habit suggest that *Nidana* described in our classics are foud similar in this study leads to *Madhumeha*

*VIHARAJA NIDANA***:** Overall 40% subjects were having *Swapna sukha*, 27.3% subjects were having *Avyayama*, 17.3% subjects were having the history of *Diva Swapna* and subjects were having *manasik Chinta*. It suggests that *viharaja Nidana* are eually responsile for creation of *madhumeha.* First four factors are responsible for kapha *Vriddhi* and *mansik chinta* causes provocation of Vata leads to the *prameha samprapti*.

HABITS: In the present study it was found that 94.6% subjects were taking Tea, 22.66% subjects were addicted to Smoking, 20% subjects were addicted to Tobacco, 18% were taking Coffee, 16% were addicted to alcohol. 09.3% were taking Soft drinks

As WHO reports mentioned that persons consume regularly in Smoking, Chewing tobacco and alcohol are more susceptible for diabetes mellitus. Addictions leads to reduced immunity & also provocate vata leading to the manifestation of DM. Caffeine present in the coffee and tea are potent enough to trigger and accelerate the rate of inflammation and thus the tissue injury due to long term consumption leads to persistent

hyperglycemic condition which is also supportive for reduced insulin sensitivity and increased insulin resistance.

Response of treatment over Cardinal feature of Madhumeha

The responses of the drug *Mustadi kasaya* on 90 days of treatment period the subjective symptoms of *Madhumeha* is appreciable. In the comparison in Group A treated by *Mustadi Kasaya* shows better improvement than the Group B treated by Placebo in subjective parameters like *Prabhoota mootrata* in Group A shows 78.2% where as group B shows 33.37% relief; in *Avila mootrata* in Group A shows 94.4% where as in group B shows 84.4%, *Kshudhahikya* in Group A shows 92.2 % relief where as in group B also similar relief of 92.1%, *Pipasadhikya* in Group A shows 96.7% relief where as group B shows 59.6% relief, *Dourbalya* in Group A shows 94.3% relief where as in group B shows 57.6% relief, in *Swedadhikya* in Group A shows 99.5% relief where as group B shows 52.58% relief, in *Galatalu shosa* shows 75.7% relief where as Group B also shows 75.5% relief, in *Klaibya* Group A shows 68.01% relief where as Group B shows 35.9% relief and in *Purisha Badd*hata in Group A 93.8% relief where as Group B shows 55.51% relief.

Group A and Group B shows statistically significant improvement of subjective parameters at the level $p<0.01$, $p<0.05$ except the symptoms *Ksudhadhikya* and *Galatalu* shosa shows equal response which were statistically significant ($p<0.05$). All the subjective symptoms are well controlled in Group A than Group B in the treatment of *madhumeha.* In other words, the difference between the average of the A and B populations is big enough to be statistically significant.

The responses of the drug *Mustadi kasaya* on 90 days of treatment period the objective parameters are very promising. In Group A mean fasting blood sugar 166.25 mg/dl reduced to 130.61 mg/dl, where as Group B fasting blood sugar 170.69 mg /dl reduced to 140.76 mg/dl with 21.43% and 17.53% changes respectively.

In Group A mean postprandial blood sugar 259.01mg/dl reduced to 152.77mg/dl, where as Group B postprandial blood sugar 276.96mg /dl reduced to 157.44 mg/dl with 41.01% and 43.1% changes respectively.

In Group A mean HbA_{1c} 8.94 reduced to 6.25, whereas in Group B mean HbA_{1c} from 9.11 reduced to 7.07 with 27.1% and 22.39% changes respectively. However both the group shows statistically significant ($p<0.01$, $p<0.05$) but group A shows better improvement than group B. It suggests that the *Ayurvedic* intervention in the mamnagement of *madhumeha* shows an added effect in controlling the subjective parameters and Objective parameters.

All the patients of Group A and Group B before and after treatment were undergone Serum urea, serum creatinine and lipid profile before cross over The results very much promising both the time of intervention.

In Group A mean serum creatinine level before treatment 1.19 changes to 1.09 whereas in Group B 1.28 changes to 1.1 after treatment on 90^{th} day which statistically significant at $p<0.001$ with 8.42% and 11.99% changes respectively.

In Group A mean serum urea level before treatment 17.33 changes to 14.83 whereas in Group B 18.81 changes to 16.69 after treatment on 90^{th} day which statistically significant at $p<0.001$ with 14.4% and 11.30% changes. This suggests that during entire treatment the drug does not show any toxicity to patients and reduces the morbidity of kidney.

In Group A mean serum Cholesterol level before treatment 200.76 changes to 183.55 whereas in Group B 192.15 changes to 182.03 after treatment on 90^{th} day which statistically significant at $p<0.001$ with 8.57% and 5.27% changes respectively. In Group A mean serum Triglyceride level before treatment 143.19 changes to 133.39 whereas in Group B 154.67 changes to 131.72 after treatment on 90^{th} day which statistically significant at $p<0.001$ with 6.85% and 14.84% changes respectively. In Group A mean serum LDL level before treatment 143.56 changes to 115.83 whereas in Group B 144.56 changes to 125.81 after treatment on 90^{th} day which statistically significant at $p<0.001$ with 19.32% and 12.97% changes respectively. In Group A mean serum HDL level before treatment 52.37 increases to 56.96 whereas in Group B 47.47 changes to 50.77 after treatment on 90^{th} day which statistically significant at $p<0.001$ with 8.76% and 6.96% changes respectively.

This above observation it is evident that the intervention of Mustadi Kasaya shows positive added result in Lipid profile than group B except in Triglyceride.

Test of hypothesis:

Following formulas were used to test different samples of the study for testing of hypothesis.

Null and Alternative Hypotheses

The following null and alternative hypotheses need to be tested:

Ho: $\mu 1 = \mu 2$

Ha: $\mu 1 \neq \mu 2$

Rejection Region

Based on the information the significance level is $\alpha = 0.05$, and the critical value for a two-tailed test is $zc = 1.96$. The rejection region for this two-tailed test is R = {z: |z| > 1.96\}

Two sample z-test test, using Normal distribution (two-tailed)

1. H0 hypothesis

Since p-value < α (0.05), H0 is rejected.

The average of the A's population is considered to be not equal to the average of the B's population.

In other words, the difference between the average of the A and B populations is big enough to be statistically significant.

2. P-value

P-value equals 0.0352794, (p (x ≤ Z) = 0.0176397). This means that the chance of type1 error (rejecting a correct H0) is small: 0.03528 (3.53%)

The smaller the p-value the more it supports H1

3. The statistics

The test statistic Z equals -2.105137, is not in the 95% critical value accepted range: [-1.9600: 1.9600] x1-x2=-0.17, is not in the 95% accepted range: [-0.1600: 0.1600]

4. Effect size

The observed standardized effect size is medium (0.34). That indicates that the magnitude of the difference between the average and average is medium

Decision about the null hypothesis

Since it is observed that $|z| = 2.105 > z_c = 1.96 |z| = 2.105 > zc = 1.96$, it is then concluded that *the null hypothesis is rejected.*

Using the P-value approach: The p-value is p=0.0353, and since p = 0.0353 < 0.05, it is concluded that the null hypothesis is rejected.

Assessment of significance of the treatment Group A and Group B before treatment and after treatment:

Table No.: Showing the before and after treatment score of Subjective parameter and Objective Parameter of Hypothesis testing

Subjective Parameters								
Parameters	**Mean**			**SD**		**Z Value**	**P Value**	**H_o Hypothesis**
		Group A	Group B	Group A	Group B			
Prabhoota Mootrata	BT	2.44	2.61	0.499	0.490	02.105	0.035	Rejected
	AT	0.53	2.00	0.502	0.493	18.093	0.000	
Avilamootrata	BT	2.33	2.32	0.474	0.469	00.129	0.896	Rejected
	AT	0.13	0.36	0.342	0.650	02.711	0.0067	
Ksudhadikya	BT	1.66	1.66	0.528	0.528	00.000	1.000	Accepted
	AT	0.13	0.13	0.342	0.342	00.000	1.000	
Pipasadikya	BT	2.47	2.45	0.502	0.501	00.807	0.244	Rejected
	AT	0.08	0.99	0.273	0.115	26.603	0.000	
Dourbalya	BT	2.29	2.29	0.458	0.458	00.000	1.000	Rejected
	AT	0.13	0.97	0.342	0.162	19.223	0.000	
Swedaadikya	BT	2.15	2.13	0.425	0.414	00.291	0.770	Rejected
	AT	0.01	1.01	0.115	0.115	53.249	0.000	
Galatalu Shosha	BT	2.43	2.43	0.497	0.996	00.000	1.000	Accepted
	AT	0.59	0.57	0.495	0.498	00.246	0.805	
Klaibya	BT	2.97	2.95	0.162	0.226	00.622	0.533	Rejected
	AT	0.95	1.89	0.226	0.311	21.175	0.000	
Purisha Bhadhata	BT	2.83	2.72	0.381	0.452	01.611	0.107	Rejected
	AT	0.17	1.21	0.381	0.412	16.049	0.000	
Objective Parameters								
FBS	BT	166.25	170.69	11.495	11.495	02.365	0.018	Rejected
	AT	130.61	140.76	6.375	8.424	08.320	1.11	
PPBS	BT	259.01	276.96	21.371	24.000	04.837	0.000	Rejected
	AT	152.77	157.44	6.29	5.173	04.966	6.833	
HbA1c	BT	8.94	9.11	0.397	1.072	01.287	0.197	Rejected
	AT	6.52	7.07	0.349	0.349	09.650	2.221	

In this study it is evident that in comparison of group A and B in all the subjective parameters except *Kshudhikya* and *Galatalu shosa* and Objective parameters the null hypothesis is rejected, which implies that the Group A more effective than Group- B. That means the patient treated by *Mustadi kasaya* shown added effect in *madhumeha.*

Analysis of results after Cross over:

The effect of the drug Mustadi kasaya after the cross over were analyzed showing similar results as before cross over.

In the comparison in Group A treated by placebo along oral antidiabetic drug with Group B treated by *Mustadi Kasaya* shows better improvement in subjective parameters like *Prabhoota mootra* in Group B shows 96.6% where as group A shows 75.5 % relief; in *Avila mootra* in Group B shows 96% where as in group A shows 94.4%, *Kshudhahikya* in Group B shows 98.1 % relief where as in group A also similar relief of 92.5%, *Pipasadhikya* in Group B shows 95.5 % relief where as group A shows 93.9 % relief, *Dourbalya* in Group B shows 75.1% relief where as in group A shows 59.8% relief, in *Swedadhikya* in Group B shows 78.8% relief where as group A shows 55.8% relief, in *Galatalu shosa* shows 88.53 % relief where as Group A also shows 62.5% relief, in *Klaibya* Group B shows 61.6% relief where as Group A shows 50.34% relief and in *Purisha Badd*hata in Group B 81.4% relief where as Group A shows 71.1% relief.

After crossover of groups also Group A and Group B shows statistically significant improvement of subjective parameters at the level $p<0.01$, $p<0.05$). All the subjective symptoms are well controlled in Group B than Group A in the treatment of *madhumeha.* In other words, the difference between the average of the B and A populations is big enough to be statistically significant.

The responses of the drug *Mustadi kasaya* on 90 days of treatment period the objective parameters are very promising. In Group B mean fasting blood sugar 170.96 mg/dl reduced to 140.76 mg/dl, where as Group A fasting blood sugar 166.23 mg /dl reduced to 146.43 mg/dl with 17.66% and 11.91% changes respectively.

In Group B mean postprandial blood sugar level 277.96 mg/dl reduced to 157.44mg/dl, where as Group A postprandial blood sugar level 260.57mg /dl reduced to 157.77mg/dl with 43.51% and 39.45% changes respectively.

In Group B mean HbA_{1c} 9.23 reduced to 6.20, whereas in Group A mean HbA_{1c} from 8.95 reduced to 7.01 with 32.8% and 21.6% changes respectively. However both the Group shows statistically significant ($p<0.05$) but Group B shows better improvement than Group A.

It suggests that the *Ayurvedic* intervention in the management of *madhumeha* shows an added effect in controlling the subjective parameters and objective parameters.

All the patients of Group A and Group B before and after treatment were undergone Serum urea, serum creatinine and lipid profile after cross over. The results very much promising after the intervention.

In Group B mean serum creatinine level before treatment 1.38 changes to 1.11 whereas in Group A 1.29 changes to 1.09 after treatment on 90^{th} day which both statistically significant at $p<0.001$ with 19.56% and 15.50% changes respectively.

In Group B mean serum urea level before treatment 18.00 changes to 15.68 whereas in Group A 17.33 changes to 15.83 after treatment on 90^{th} day which statistically significant at $p<0.001$ with 12.88% and 08.6% changes respectively. This suggests that during entire treatment the drug does not show any toxicity to patients and reduces the morbidity of kidney.

In Group B mean serum Cholesterol level before treatment 202.71 changes to 180.51 whereas in Group A 198.10 changes to 180.03 after treatment on 90^{th} day which statistically significant at $p<0.001$ with 10.95% and 9.12% changes respectively. In Group B mean serum Triglyceride level before treatment 152.62 changes to 134.32 whereas in Group A 140.21 changes to 136.38 after treatment on 90^{th} day which statistically significant at $p<0.001$ with 11.99% and 2.73% changes respectively. In Group B mean serum LDL level before treatment 144.55 changes to 117.83 whereas in Group A 143.55 changes to 115.82 after treatment on 90^{th} day which statistically significant at $p<0.001$ with 18.48% and 19.31% changes respectively. In Group B mean serum HDL level before treatment 49.20 increases to 52.95 whereas in Group A 54.32 changes to 58.01 after treatment on 90^{th} day which was statistically significant at $p<0.001$ with 7.62% and 6.79% changes respectively.

This above observation it is evident that the intervention of Mustadi Kasaya (Group B) shows positive added result in Lipid profile than group A except in LDL.

Table No.: Showing the before and after treatment score of Subjective parameter and Objective Parameter of Hypothesis testing after cross over:

Subjective Parameters								
Parameters	**Mean**			**SD**		**Z Value**	**P Value**	**Ho Hypothesis**
		Group A	Group B	Group A	Group B			
Prabhoota Mootrata	BT	2.29	2.40	0.731	0.805	0.876	0.380	Rejected
	AT	0.56	0.08	0.499	0.273	7.308	2.14	
Avilamootrata	BT	2.32	2.17	0.469	0.685	1.564	0.118	*Accepted*
	AT	0.13	0.09	0.342	0.293	0.769	0.441	
Ksudhadikya	BT	1.65	1.96	0.532	0.528	0.115	0.908	Rejected
	AT	0.13	0.04	0.342	0.197	1.974	0.048	
Pipasadikya	BT	2.47	2.45	0.502	0.501	0.244	0.807	*Accepted*
	AT	0.15	0.09	0.356	0.292	1.128	0.259	
Dourbalya	BT	2.29	2.30	0.458	0.458	0.000	1.000	Rejected
	AT	0.92	0.57	0.273	0.497	5.345	9.020	
Swedaadikya	BT	2.15	2.13	0.425	0.414	0.292	0.77	Rejected
	AT	0.95	0.43	0.226	0.497	8.248	8.882	
Galatalu Shosha	BT	2.43	2.53	0.498	0.498	0.000	1.000	Rejected
	AT	0.91	0.29	0.293	0.458	9.875	4.441	
Klaibya	BT	2.88	2.42	0.327	0.251	1.05	0.29	Rejected
	AT	1.43	0.93	0.498	0.251	7.609	2.820	
Purisha Bhadhata	BT	2.77	2.81	0.421	0.392	0.602	0.547	Rejected
	AT	0.80	0.52	0.498	0.251	7.609	2.820	
Objective Parameters								
FBS	BT	166.23	170.96	11.507	12.283	2.434	0.149	Rejected
	AT	146.43	140.76	6.420	8.424	8.446	0.000	
PPBS	BT	260.57	276.96	20.937	24.00	4.728	0.000	Rejected
	AT	157.77	157.44	6.372	5.173	4.84	0.000	
HbA1c	BT	8.95	9.23	0.832	0.367	2.666	0.007	Rejected
	AT	7.01	6.20	0.344	0.349	9.543	9.992	

In this study it is evident that in comparison of group B and A in all the subjective parameters except Avila mootrata and Pipasadhikya and Objective parameters the null hypothesis is rejected, which implies that the Group B (trated by Mustadi Kasaya) more effective than Group- A

PROBABLE MODE OF ACTION *OF MUSTADI KWATHA*

a. Mode of action on *Prabhutamutrata*: *Mootra sangrahaniya guna of Musta, Haridra* and *Lodra* might possibly have helped in regulating the amount and frequency of micturation. *Bahudravata* will be reduced by the absorption of excessive fluid from the body. When *bahudravata* reaching *basti* reduces then *prabhoothamootrata pratyatma lakshana* of *Prameha* also reduces which may reverse the pathological conditions like decreased renal threshold and osmotic diuresis caused due to persistent hyperglycemic condition[214].
b. Mode of action on *Avilamutrata* : *Tridoshahara* and *Shothahara* property of *Triphala, Musta* and *Moorva, Rasayana* property of *Haritaki, Amalaki*, and *Amadoshahara guna* of *Moorva, Mala shodhana guna* of *Triphala, Laghu, Ruksha guna*, of almost all drugs might possibly have helped in rectifying the *Samalatva* of *Mutra* to *Nirmalatva.*
c. Mode of action on *Pippasaadhikyata*: *Trushna Nigrahana Kriya* of *musta, Vibhitaki, Amalaki* and *Daruharidra,* and the *Qwatha Kalpana* itself might have possibly helped in regulating the above symptom. Also when *Prabhoota mootrata* reduces in turn reducing the above symptom which on the other side supports the theory of regulating the fluid and electrolytic balance by inhibiting inflammation induced excessive cellular dehydration and subsequent fluid and electrolyte loss caused due to persistent hyperglycemic condition.
d. Mode of action on *Kshudaadhikata*: Both *Agnimandya* and *Teekshagni* leads to *Kshudaadhikata*. Here *Deepana, Amapachana karma* of *Musta, Haritaki, Vibhitaki, Daruharidra*, and *Moorva* drugs, *Medohara guna* of *Musta, Daruharidra, Devadaru* removes *avarana* of *Kapha* and *Meda* around *Vata* there by correcting the *samana vata* vitiation and reducing the symptom. On the contrary it may have altered metabolic activities and thereby increasing hepatic and intestinal glucose uptake in the system.

e. Mode of action on *Dourbalya*: It is *dhatvagnimandhyjanya vyadhi*. This metabolic disease demands *medadhatvagnivriddhi*. When any agni is not proper, *dhatus* are not produced properly. Having *deepana & pachana* and *Rasayana gunakarma* of almost all the drugs and *tikta rasa, ushna virya* encounters *dhatvagnimandya* & help in *ama-pachana* thereby alleviates *aparipakwa ama*. That in turn helps to form the dhatu's in proper proportion with s*amyak* qualities. There by it ensures *sarvadhatuposhana* including oja hence pacifies *Dourbalya.* These above said properties might have helped in promoting enhanced insulin sensitivity and reduced insulin resistance, followed by proper utilization of glucose by the peripheral tissue.

f. Mode of action on *Shareerabalahaani: Madhumeha* is one of the *Vataja* types of *Prameha* where *oja* plays vital role in *samprapti.* Here mainly *Rasayana* property of *Triphala* help to overcome this symptom. Moreover *Pramehahara guna* of these drugs might have rectified the overall metabolic activities of carbohydrate, fat and proteins bringing them to normal equilibrium state thus increasing the T-cell mediated immunity there by increasing the strength of body.

g. Mode of action on *Karpadadaaha*: *Tridoshahara guna* of *Triphala*, and *Tikta kashaya rasa pradhana* of all other drugs of polyherbal formulations, especially *Daahaprashamana guna* of *Amalaki, Rakta prasadana guna* of *Devadaru, Rakta shodhana guna* of *Moorva*, might have helped in bringing back the *Dosha* to their normal site and perform normal physiological function thereby rectifying Karapada Daha which on the other side reducing the vascular tissue injury and endothelial degeneration.

PROBABLE MODE OF ACTION OF *MUSTADI KWATHA* IN OBJECTIVE PARAMETERS like PPBSL, FBSL and HbA_1c

a. EFFECT ON FASTING BLOOD SUGAR LEVEL: It signifies the enhanced process of hepatic gluconeogenesis which is hampered due to persistent hyperglycemic level.

b. EFFECT ON POST PRANDIAL BLOOD SUGAR LEVEL: It signifies the process of glucose uptake by the peripheral tissues especially skeletal muscles induced by reduced insulin resistance.

c. EFFECT ON HbA1C: Long term control of blood sugar level it signifies the accumulation of advanced glycation end products (AGEs).

PROBABLE MODE OF ACTION BASED ON *RASA PANCHAKA*

a) Probable mode of action based on the Rasa: The drug Mustadi Kwatha due to presence of *Lavanavarjita Pacharasa Yukta Oshadhi Dravya* like *Amalaki* and *Haritaki* the formulation is dominated by *Kashaya* and *Tikta rasa* which are potent enough to bring back *Prakupita Kaphapitta Dosha*, which are responsible for *Margavarana* of the *vata dosha* to its equilibrium state.

b) Probable mode of action based on *Guna*: The drugs in both the Polyherbal formulations are possessing *Laghu* and *Ruksha Guna* in common may help in doing *kapha medo hara, kledagna, srotoshodhana* altogether.

c) Probable mode of action based on *Virya*: The drugs *Mustadi Kwatha* possess *Ushna* and *Sheeta Virya* in the ratio 6:3 which is quite supportive for not only for the reduction of *Kleda* an *Lasika* but also for maintaining the normal homeostatic nature of *vata dosha* by amplifying *Tridoshahara* and *Medohara* effect and thus break up the vicious cycle of pathology of the disease *Madhumeha*. At the same time, it promotes the formation of *Prashasta Dosha*, *Dhatu* and thus restores *Dhatu Samyatva*.

d) Probable mode of action based on *Vipaka*: The drugs *Mustadi Kwatha* possess *Madhura* and *Katu Vipaka* in the ratio 6:3 which is quite supportive for promoting and restoring the normal functions of the damaged *Dhatu* by nullifying and rejuvenating the *Dhatu* from the effect of *Prakupita Dosha* and thus restore *Dhatu Samyatva.*

e) Probable mode of action based on Karma: The drugs Mustadi Kwatha possess Kaphapitahara and Tridoshahara activity in the ratio 6:3 also with *Shotha hara, Mootra Sangrahaniya, Kledopashoshana, Sangrahi, Anuloma, Jvaragna, Medohara, Chakshushya, Hridya, Trushnanigrahana, Kandugna, Kushtagna, Tridoshahara, Stanya Shodaka, Virechnopaga, Rasayana* and *Vajeekarana* activities altogether responsible for restoration of *Dhatu Samyatva*.

Mode of action based drug Research

1. *Triphala:* Anti Hyperlipidemic, Anti Inflammatory, Anti viral, Cardio hapatoprotective Anti hemorrhagic, Retinoprotective , Anti hyperglycemic , Nephroprotective, Anti carcinogenic and Anti Oxidant property are potent enough to reduce the vicious cycle of pathology. It reduces the insulin resistance and increases the insulin sensitivity of the peripheral tissues by stimulating Adiponectin, a potent Insulin Sensitizer. The above description can be justified with the following reference "*Triphala Kapha Pitagni Mehakushtahara Apara Chakshushya Dipani Vrushya Vishama Jvara Nashini*"[215].
2. *Musta*: Anti diarrheal, Anti Diabetic activity of hydro-ethanolic extract of Cyperus rotundus, Anti Hyperlipidemic, Hepatoprotective, Anti Bacterial Anti Inflammatory and Anti Oxidant activities which are already established – are supportive enough to bring about the glycemic control by correcting the cellular dehydration and osmotic dieresis.
3. *Daruharidra*: Anti diarrheal, Anti-spasmodic, Anti-microbial, and hypoglycemic activity altogether promotes glycemic control.
4. *Haridra*: Anti inflammatory, Antibacterial, Hypolipidemic, Antidepressant, Antioxidant, Antimicrobial, Anticarcinogenic, Antidiabetic activity of curcumin. Hypoglycemic effect might be due to increased utilization of peripheral glucose, decreased hepatic synthesis or increased insulin secretion (Tank R et al, 1989). Curcumin might have improved diabetes induced endothelial dysfunction significantly in relation to its potential to decrease superoxide production. Even researches proved its other activities such as Anti inflammatory, Anti oxidant property in boosting immune system thus combating Diabetes Mellitus. The

above description can be justified with the following reference "*Haridra pramehaharaanaam"*

5. *Devadaru* : Antioxidant, Gastric anti secretory and antiulcer activity, Anticonvulsant and anxiolytic activity, Mild Antihyperglycaemic, Antimicrobial, Anti-inflammatory, Antiviral activity are quite supportive for glycemic control and reduction in common symptoms of Diabetes Mellitus. Hypoglycemic effect may be probably brought about by pancreatic mechanism by enhancing regeneration of islets in the pancreas and restoration of normal cellular size of islet with hyperplasia.
6. *Moorva:* Anti-angiogenic effect: The main features of angiogenesis are increased vasculature and over expression of vascular endothelial growth factor (VEGF). So by inhibiting this process indirectly it might have helped in controlling sugar level in the blood.
7. *Indrayana moola*: Anti Diabetic effect, Immunostimulating activity, Antioxidant activity of Indrayana drug acts as major defense mechanism by protecting the damages caused by free radicals thus it might be beneficial in attenuating the elevated sugar levels in the subjects.
8. *Lodra:* Hepatoprotective activity, Gonadotropin releasing effect, Anti Diabetic effect, wound healing property; Antimicrobial activity might have helped in regeneration of b- cells of pancreas and production of insulin secretion and thus might have brought glycogen level near to normal which aided in bringing back the raised sugar values.

CONCLUSION:

The present research work was mainly aimed to explore the efficacy of *Mustadi Kwatha* in the management of *Madhumeh*a. After the detailed clinical observations, discussion and results, the following conclusions are drawn:

- The clinical trial on *Madhumeh*a in both Group A and Group B showed significant relief in both subjective and objective parameters.
- *Mustadi Kwatha* showed significant relief in the objective criteria's like Fasting blood Sugar level (FBSL), Post Prandial blood sugar level (PPBSL) & Glycated hemoglobin -HbA_{1C} after 90 days of treatment in the patients treated along with modern drugs.
- This study it is evident that *Mustadi Kwatha* has got an added effect in all the subjective as well as objective parameters of Madhumeha.
- The serum Cholesterol, Triglyceride, LDL.HDL well controlled during the study treated by Mustadi Kwatha.
- During entire study the serum creatinine and seum urea remains in downward trend towards the normal level, indicates that the indigenous compound does not have any adverse effect in kidney.

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Tilak Maharastra Vidya Peeth, Pune

Ph.D. RESEARCH WORK CASE REPORT FORM

Study Centre: SHRI J.G.C.H. S Sahakar Maharshi Shri BA Patil AYUREDIC MEDICAL COLLEGE & HOSPITAL GHATAPRABHA-591310

Topic: Evaluation Of The Effect Of Mustadi Kwatha In The Management Of Madhumeha Vis-a-Vis Diabetes Mellitus (NIDDM)

Ph.D. Scholar: Dr. Jatyanta Kumar Sarma, M.D (Ayu).

Guide: Dr. Vineeta Deshmukh, M.D. Ph.D

Name of the patient:	**GROUP A/B-**
	SL NO:
Father/Husband name:	DATE:
Age	ADMISSION DATE:
Sex-	DISCHARGE DATE:
Address	Ward No:
	Bed No:
Religion- H/M/CH/S/J/Others	**DISEASE-**
	Schedule
Education –UE/E/PS/HS/UG/PG	**Initiation:**
Occupation: Sedentary ☐	**Completion:**
Labour ☐	**RESULT:**
Active ☐	Marked Response
House Work ☐	Moderate Response
	Mild Response
Economic Status-VP/LM/M /UM /R	Poor/No Response
	Discontinued
Marital Status: M/UM/D/W	

Tilak Maharastra Vidya Peeth, Pune

Study Centre: SHRI J.G.C.H. S Sahakar Maharshi Shri B A Patil AYUREDIC MEDICAL COLLEGE GHATAPRABHA-591310

Ph.D Scholar Scholar: Dr. Jatyanta Kumar Sarma

Guide: Vd. Vineeta Deshmukh, M.D. Ph.D

CONSENT OF PATIENT

I_____hereby willingly agree to participate in the clinical trial on "Madhumeha" and affirm that there is no mandatory inducement in my will as patient. I am convinced that it is for the benefit of the science and mankind. I have been told about the intervention & risks involved.

Date: Signature of Patient

Criteria for Inclusion

	Yes	No
1. Age bet 30-70 Yrs	☐	☐
2. FBS ≥126 mg/dl ≤ 220 mg/dl	☐	☐
3. PPBS ≥140 mg/dl ≤ 280mg/dl	☐	☐
4. $HBA_1C > 6.5$	☐	☐
5. Within 5yrs of Onset	☐	☐
6. Fresh Case	☐	☐
7. Treated Case.	☐	☐

Criteria for Exclusion

1. Age bet < 30->70Yrs	☐	☐
2. Diabetic Carbuncle	☐	☐
3. Urine Albumin	☐	☐
3. Retinopathy	☐	☐
4. Nephropathy	☐	☐
5. Chronic DM > 5 Yrs of Onset	☐	☐
6. Malignant HTN	☐	☐
7. CVS Disorder like IHD	☐	☐

8. CNS Disorder ☐ ☐

9. Pregnant women with Diabetes ☐ ☐

10. Lactating Mother ☐ ☐

11. Patient receiving Insulin Therapy ☐ ☐

12. Others (specify)

Chief Complaints:

Prabhoota mootrata	Score 0	Score 1	Score 2	Score3
Duration-	Normal	Slightly Increased	Increased	Markedly Increased
Quantity	Passing of normal quantity urine of up to 2 liters daily	Passing of more than normal quantity urine of daily from 2 liters to 03 liters daily	Passing of more quantity urine of daily from 03 liters to 3.5 liters daily	Passing profuse quantity urine of daily more than 3.5 liters
0^{th} Day				
15^{th} Day				
30^{th} Day				
45^{th} Day				
60^{th} Day				
75^{th} Day				
90^{th} Day				
Frequency	Frequency micturition three to six times daily, Rarely nocturia	Frequency micturition six to nine times daily Nocturia one to two times	Frequency micturition nine to twelve times daily, Nocturia three to four times	Frequency micturition more than twelve times daily, Frequent Nocturia
0^{th} Day				
15^{th} Day				

30th Day				
45th Day				
60th Day				
75th Day				
90th Day				

Avila Mootrata	Score 0	Score 1	Score 2	Score3
Duration-	Normal straw coloured urine	Mild cloudy in appearance	Visible alphabet though the urine kept in a beaker	Alphabet is not visible through the urine kept in a beaker.
0th Day				
15th Day				
30th Day				
45th Day				
60th Day				
75th Day				
90th Day				

Kshudadhikya	Score 0	Score 1	Score 2	Score3
Duration-	Normal intake food	Consumes food more than normal quantity of food	Consumes heavy amount of food	Consumes heavy amount of food any following any schedule
0th Day				
15th Day				
30th Day				
45th Day				
60th Day				
75th Day				
90th Day				

Pippasa adhikya	Score 0	Score 1	Score 2	Score3
Duration-	Consumes normal quantity of water	Consumes two to three liters of water daily	Consumes two to three liters of water daily	Consumes more than four liters of water daily
0th Day				
15th Day				

30th Day				
45th Day				
60th Day				
75th Day				
90th Day				

Dourbalya	Score 0	Score 1	Score 2	Score3
Duration-	Can carry out normal work	Can do the work with some difficulty	Perform the work with difficulty	Can not perform regular work also
0th Day				
15th Day				
30th Day				
45th Day				
60th Day				
75th Day				
90th Day				

Swedadhikya	Score 0	Score 1	Score 2	Score3
Duration	After heavy work/Hot weather/Fast Movement	Excessive sweating by normal work	Excessive sweating even by normal to some distance /stepping ladder	Excessive sweating even at rest.
0th Day				
15th Day				
30th Day				
45th Day				
60th Day				
75th Day				
90th Day				

Gala Talu Shosa	Score 0	Score 1	Score 2	Score3
	No dryness of throat	Dryness of throat reduced after consumption of water	Dryness of throat reduced after consumption of more quantity of water	Dryness of throat does not subside even after consumption of more water.

0th Day				
15th Day				
30th Day				
45th Day				
60th Day				
75th Day				
90th Day				
Klaibya	Score 0	Score 1	Score 2	Score3
	Normal	Diminished frequency but have normal sexual behavior	Decreased libido with reduced sexual behavior	Sexual frigidity
0th Day				
15th Day				
30th Day				
45th Day				
60th Day				
75th Day				
90th Day				
Purisha badhatta	Score 0	Score 1	Score 2	Score3
	Normal passes feces daily	Passes of feces with efforts sometimes needs stool softeners	Passes of feces in more than twenty four hours. Needs purgatives	Passes of feces after a gap of twenty four hours, conventional laxative not effective.
0th Day				
15th Day				
30th Day				
45th Day				
60th Day				
75th Day				
90th Day				

	Score 0	Score 1	Score 2	Score3	Score 4
HBA_1C	**<6.5%**	**6.5-8%**	**8.1-9%**	**9-10%**	**>10%**
0th Day					
90th Day					

	Score 0	Score 1	Score 2	Score3
FBS	**70-110mg/dl**	**110-170mg/dl**	**171-220mg/dl**	**>220mg/dl**
0th Day				
15th Day				
30th Day				
45th Day				
60th Day				
75th Day				
90th Day				

	Score 0	Score 1	Score 2	Score3
PPBS	**126-180mg/dl**	**181-230mg/dl**	**231-280mg/dl**	**>280mg/dl**
0th Day				
15th Day				
30th Day				
45th Day				
60th Day				
75th Day				
90th Day				

Blood RE:

Hb%

TC

DC: N: L: B: E: M:

Urine: Sugar Albumin:

Microscopic Study:

History of present Illness

Disease was detected- As Accidental ☐

In Regular Check up ☐

By Suspicion ☐

History of past Illness
HTN
Cardiac problem
Asthma
T.B
Jaundice
Others

Treatment History

Menstrual History
Rajo darshana: Rajonivrutti:

Ritu chakra: Regular / Irreglar / Days

Ritusrava: moderate /severe / reduced

Prasava vruttanta: **G/P/L/A** **TL-** YES/NO **Hyterectomy-** YES/NO

Menorrhagia / Metrorrhagia / Dysmenorrhoea / Leucorrhoea.

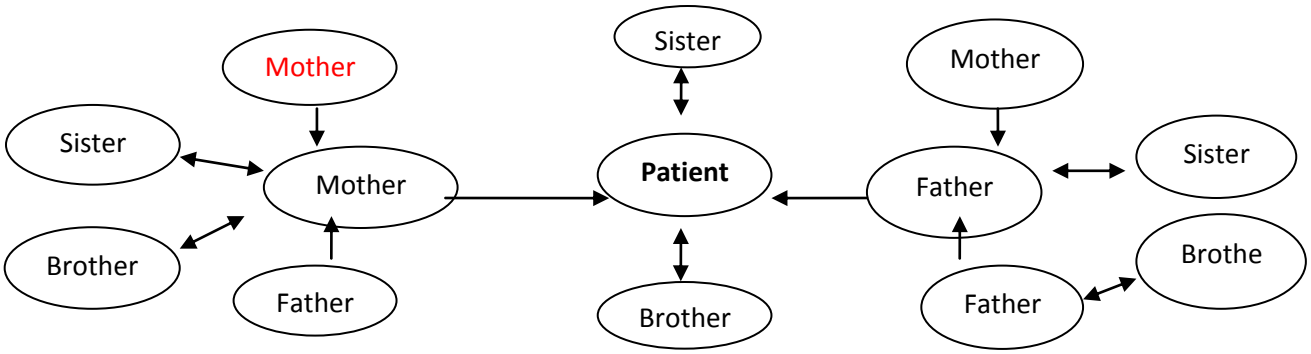
Upashaya	**P/A**	**Anupashaya**	**P/A**
Usna Ahaara		Sheeta Ahaara	
Tikta rasa		Madhura rasa	
Vyayama		Divaswapna	

	Purvaroopa	**Duration**	**Present**	**Absent**
1.	Sweda adhikata			
2.	Shitilangata			
3.	Shayyashana swapna sheela			
4.	Hridaya jihwa netra karna upadeha			
5.	Sthoulyata			
6.	Kesha Nakha ativriddi			
7.	Utsaha haani			
8.	Sheeta priyata			
9.	Mukha Talu Gala Shosha			
10.	Asya madurya			
11.	Kara paada tala daha			
12.	Mutra pipilikahisarana			
13.	Kesha jatilibhava			
14.	Kara paada tala suptata			
15.	Pippasa			
16.	Anga ghandha			

17.	Nidradhikya			
18.	Guru gatrata			
19.	Snigdangata			
20.	Mutra pandu varna			

Upadrava	**P/A**	**Upadrava**	**P/A**
Trishna		Prameha Pidaka	
Atisaara		Chardi	
Jwara		Kaasa	
Daaha		Pratishyaya	
Arochaka		Others	
Avipaka			

Family History



Personal History

Ahaara	Veg	Mix				
Frequency of intake/Day						
Quantity	alpa	pramita	sama	Ati pramana		
Dominant of Rasa	M	A	L	K	T	KS
Dominant of Guna	Guru	Laghu	Snigda	Ruksha	Sheeta	Ushna
Diet Habit	Samashana	Adyashana	Vishamashana	Atyashana		
Agni	Sama	Manda	Teekshna	Vishama		
Koshta	Mrudu	Madya	Teekshna			
Pureesha	Normal	Constipated	Loose			
Mootra	Normal	Obstructed	Incontinence			

Aaharaja Nidhana		P/A			P/A
1	Madhura		16	Dadhi Fresh	
2	Guru Aahara		17	Mandaka dadhi	
3	Picchila		18	Dravanna paana	
4	Sheeta		19	Matar	
5	Snigdha		20	Udad dal etc	
6	Navaanna		21	Sugar	
7	Sughandaka(basmati)		22	Sura(New)	
8	Pistanna		23	Mamsa rasa	
9	Payasa		24	Amla lavana ahara	
10	Krushara		25	katu ahara	
11	Guda		26	Ushna ahara	
12	Guda vikruti		27	Ajeerna Bhojan	
13	Ikshu		28	Vishama ahara	
14	Dugda		29	Ruksha laghu ahara	
15	Dugdha vikruti		30	Others	

ADDICTIONS	Quantity	Frequency	Duration
Tea			
Coffee			
Soft drinks			
Alcohol			
Tobacco			
Smoke			

Viharaja Nidana

Nidra	Duration			
	Normal	Less	Excessive	
Disturbed due to				
Vyayama	No	Less	Normal	Excessive

Nature of Profession					
Physical strain	Standing	Sitting	Sedentary	Moderate	Heavy
Mental strain					
Involves Both					

Emotional Status	Normal	Jolly	Tense	Anxiety	Depressive

General Examination

Vital Signs	**0th day**	**15th day**	**30th day**	**45th day**	**60th day**
Pulse					
B.P					
Temp					
H.R					
R.R					
Ht					
Wt					

Built- Lean /Medium / well built Skin- Normal / Pallor / Edema / Dry / Oily

Tongue- Pink / Coated /Pale / Cyanosed Eyes- Normal / Pallor / Icterous / Redness

Systemic Examinations:

Respiratory System

Digestive System

Urinary System

Cardiovascular System

Arterial Pulse- Tachycardia /Bradycardia / Normal

Rhythm-Normal/Irregular/Missed Bruits-P/A

Abnormal Heart Sound-
Murmur-
Peripheral pulses of Upper Limb- Normal / Abnormal / absent
Peripheral pulses of Lower Limb- Normal / Abnormal / absent

Central Nervous System

Mental Stage- Gait-
Cranial nerves
Fundii- Pappiloedema-P / A

Optical Atrophy-Normal / Abnormal

Hypertensive changes / Uremic changes / Diabetic Changes

Motor Changes- Sensory Changes-

Finger / Toes-Normal / Abnormal

Pin prick test of Limbs & Face- Normal / Abnormal

Response to Light & Touch- Positive / Negative.

Dashavida pareeksha

Prakruti-	**Sharirika**	V	P	K	VP	VK	KP	SAMA
	Manasika	Satva	Raja	Tama				
Saara	Twak	Rakta	Mamsa	Meda	Asthi	Majja	Shukra	Satva
Samhanan	Pravara	Madyama	Avara					
Pramana	Pravara	Madyama	Avara					
Satva	Pravara	Madyama	Avara					
Satmya		3	2	1				
	Ahara	Most of Edible Suitable	few edibles suitable	Very few edibles suitable				
	Desha	Never trouble some	Sometimes troublesome	Always trouble some				
	Kala	Never trouble some	Sometimes troublesome	Always trouble some				
Ahara Shakti	**Abhyavarana Shakti**	P	M	A				
	Jarana Shakti	P	M	A				
Vyayama	P	M	A					
Vaya	Balya	Madya	Vridda					
Vikruti	Vata	Kshaya	Vriddi	Prakopa				
	Pitta	Kshaya	Vriddi	Prakopa				
	Kapha	Kshaya	Vriddi	Prakopa				

STROTAS PAREEKSHA

Udaka vaha	**Put x/**	**Mutravaha**	**Put x/**
Osta Jiwha Talu shosha		Adhika mootrata	
Pravridda Pippasa		Mutra rodha	
tama		Alpa mutrata	
Rasavaha	**Put x/**	Sashula mootrata	
Shithila gatrata		Basti stabdhata	
Kara pada suptata		**Annavaha**	**Put x/**
Klyvya		anannabhilasha	
Shrama		Asya vyrasya	
Agnimandya,Aruchi		Avipaka	
Gourava		chardi	
Atinidra		Admana	
Asyamadhurya		Shoola	
Arasangjata		Anna dwesha	
Alasya		pippasa	
Raktavaha	**Put x/**	**Mamsavaha**	**Put x/**
Kara pada suptata		Ghana gatrata	
Daha		Anga shaithilya	
Raktasrava		Arbuda	
Pidika		Arsha	
Vidradi		Mamsa shosha	
Khota		Sira granthi	
Muka paka			
Medovaha	**Put x/**	**Asthivaha**	**Put x/**
Swedadhikya		Kesha jatilibhava	
Snigdangata		Nakha vriddi	
Stula shophata		Danta mala sanchaya	
Pippasa			
Shwasa			
Alasya			
Majjavaha	**Put x/**	**Sukravaha**	**Put x/**
Anga gourava		Apraharsha/klyvya	
Pureeshavaha	**Put x/**	**Swedavaha**	**Put x/**

Vibhanda		Ati sweda	
Atisaara		Twak parushya	
Admana		Sparsha vaigunya	
Anaha		Paridaaha	
atopa		Durgandita sweda	
		Loma harsha	
		Ati slakshna	

Samprapthi

1. **Dosha-**

Vata	Prana	Udana	Samana	Vyana	Apana
Pitta	Pachaka	Ranjaka	Alochaka	Brajaka	Sadhaka
Kapha	Tarpaka	Bhodaka	Kledaka	Sleshaka	Avalambaka

2. **Dooshya's**

Rasa Majja Rakta Shukra Mamsa
Vasa Meda Lasika Asthi Oja

3. **Agni**

Sama Vishama Teekshna Manda

4. **Ama**
5. **Strotas**

Prana Anna Udaka Rasa Rakta Mamsa Meda Asthi Majja Shukra Mutra Pureesha Sweda Arthava

6. **Sroto dusti prakara** Ati Pravrutti / Sanga / Vimarga Gamana / Siraja Granti

7. **Udbhava Sthana**

8. **Sanchara Sthana**

9. **Vyakta Sthana**

10. **Adhisthana**

11. **Roga Marga** Bahya Madyama Abhyantara

Vyadhi Swaroopa

Chirakari Ashukaari

Mrudu Daruna
Navina Jeerna

Diagnosis- Madhumeha

Treatment Started On- **Treatment Ended On-**

Follow Up Started On- **Follow Up Ended On-**

Medicine: Mustadi Kwatha **Quantity-48 ml** **Dose-B.D Before food**
Treatment Duration- 90 Days

(Signature of Ph.D Scholar) (Signature of Guide)

KEY TO MASTER CHART

Sex	**:**	M-Male, F-Female
Religion	**:**	H-Hindu, M-Muslim, C-Christian
Marital Status	**:**	M-Married, U-Unmarried, W-Widow, D-Divorcee
Educational Status	**:**	U-Uneducated, PS-Primary school, HS-High school, UG-Undergraduate, PG- Postgraduate
Socio-economic	**:**	VP-Very poor, LM-Lower middle, MC-Middle class,
Status	**:**	UM-Upper middle, R-Rich
Diet	**:**	V-veg, M-mixed
Prakruti	**:**	V-vataja, P-pittaja, K-kaphaja, VP-vatapittaja, VK-vatakaphaja, PK-pittakaphaja,