Published online in http://ijam.co.in ISSN No: 0976-5921

International Journal of Ayurvedic Medicine, Vol 15 (1), 2024; 122-130

Efficacy of Integrated Ayurveda Treatment in Type 2 Diabetes mellitus with special reference to *Prameha:* A Randomised controlled Trial

Research Article

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Abstract

Background: Diabetes mellitus (DM) is marked by persistent hyperglycemia, often due to insulin resistance. Type 2 diabetes mellitus (T2DM) constitutes 90% of the cases and shares similarities with *Prameha*, a disorder characterised by frequent urination. Aims and objectives: This study aimed to compare Integrated *Ayurveda* Treatment (IAT) with standard diabetic treatment for *Prameha*. Materials and methods: A randomised, controlled open-label trial involved 200 T2DM subjects with HbA1C above 7%, taking metformin (≥1g /day). They were assigned to Standard Dietary Treatment (SDT) or IAT. SDT comprised metformin, dietary, and lifestyle modifications, while IAT included metformin with Ayurvedic medicine, specific Ayurveda diet, and yoga. Observation and result: Observations favoured Ayurveda treatment over standard diabetes treatment for most *Prameha* preliminary symptoms (*purvarupa*). Regarding *Prameha rupa* (symptoms), IAT significantly outperformed than SDT. Also, *Ayurveda* treatment group, led to improvements in HbA1C, fasting and postprandial blood sugar, and insulin resistance parameters compared to standard treatment group. Conclusion: Integrating *Madhumeha ghana vati*, *ayurveda* diet, and *yoga* with standard treatment yielded positive subjective and objective outcomes for *Prameha*, without significant adverse events. This suggests the potential benefits of combining *Ayurvedic* approaches with conventional care in managing *prameha.*

Keywords: *Prameha, Purvaroopas, Madhumehari ghana vati, Pathyahara,* Type 2 diabetes mellitus, Metformin.

Introduction

Diabetes mellitus (DM) is a chronic metabolic illness where persistent hyperglycemia is a hallmark. It might be brought on by decreased insulin secretion, resistance to insulin's peripheral effects, or both. Ninety percent of all instances of diabetes are caused by type 2 diabetes mellitus (T2DM) due to insulin resistance (1). Previous research considered insufficient diabetes control (uncontrolled T2DM) as glycated haemoglobin (HbA1C) of >7% (2). An estimated 462 million people worldwide suffer with T2DM (3). According to predictions from 2019, there were 77 million diabetics in India; by 2045, that number is predicted to reach over 134 million (4). The crucial elements of treatment for type 2 diabetes are lifestyle modification and goal-setting, pharmaceutical interventions, self-management and support (5). Anti-diabetic medications include biguanides like metformin, insulin secretagogues such as sulfonylureas, and insulin sensitisers such as thiazolidinedione's. Among these, metformin is the first-line pharmacotherapy for T2DM (6). However, following medications, which have potential side effects, makes treatment compliance difficult. *Ayurveda* classics define *Prameha* as a set of complex clinical disorders characterised by frequent abnormal micturition, with the aetiology involving genetic predisposition as well as improper diet and lifestyle. The clinical conditions described in *Prameha* have much in common with T2DM. Ayurveda classics describe etiological factors of *prameha* as sedentary activities, early introduction of milk and its products, animal feed cultivated especially in swampy areas, newly harvested grains and refined sugars etc. (7) which has have more similarity with aetiology of T2DM.

Ayurveda recommend different treatment modalities in *prameh*a such as *nidana parivarjana* (preventive strategies), *shodana* (Detoxification), *shamana* (internal medication) and *Pathyapathya* (diet and lifestyle restriction). In *Prameha*, aggravated *Kapha dosha* does vitiation of *medas* (adipose tissue), *mamsa* (muscle tissue) and *kleda* (fluid). Excessively aggravated *medas* leads to *Purvarupas* (premonitory symptoms) of *Prameha*. Vitiated *kleda* produces urinary symptoms(8). *Madhumehari ghana vati* [MGV], an Ayurvedic poly-herbal formulation which has 10

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ingredients such as *Meshashringi* (*Gymnema sylvestre* R. Br.), *Vijayasara* (*Pterocarpus marsupium* Roxb.), *Jambu* (*Syzygium cumini* Linn.), *Amalaki* (*Emblica officinalis* Gaertn.), *Hareetaki* (*Terminalia chebula* Retz.), *Vibheetaki* (*Terminalia belirica* Roxb.), *Haridra* (*Curcuma longa* Linn.), *Guduchi* (*Tinospora cordifolia* willd.), *Tamalapatra* (*Cinnamomum tamala* (Buch, Ham).) and *Daruharidra* (*Berberis aristata* DC.) which are known to have benefits in *prameha* by reversing the pathogenesis (9, 10). MGV, a poly-herbal formulation is a product of our affiliated pharmacy and has shown beneficial effects in our clinical settings. An experimental trial conducted on diabetes induced animals, administered with MGV for 28 days showed significant reduction of fasting blood glucose (FBG) compared to diabetic treated group animals (11). Herbs of MGV have anti-hyperglycaemic, lipid lowering (12), antioxidant (13) and insulin sensitising (14) properties. *Ayurveda pathyahara* contain food which are light to digest, *medohara* therapeutic food components and easy & have palatable nature. Yoga being lifestyle intervention proved beneficial in reducing body weight, useful in glycemic control. It also emphasises on relaxation, meditation, and deep breathing, may have special relevance with quality of life of T2DM (15). Hence, the current study was planned with the objective to evaluate the efficacy of Integrated *ayurveda* treatment [IAT] which contain Ayurveda medication [MGV], *Pathyahara* and *Yogic* intervention in *Premaha* with special emphasis on quality of life and subjective profile (*prameha purva rupa & laxana*).

Materials and methods

Participants

It was a randomised controlled trial conducted on 200 subjects at KLE *Ayurveda* hospital, Belagavi, Karnataka, India.

Inclusion criteria

a) Subjects with Type 2 diabetes who were between the ages of 18 and 70
b) Subjects with inadequate blood glucose control (HbA1c:7 to 10.5%) while receiving steady metformin medication (≥1g/day) were enrolled.
c) Participants quality of life and clinical condition assessment based on *Ayurveda* parameter was the main objective considered in this study (Table no.1).

Exclusion criteria

a) Subjects with cardiovascular disorders
b) Subjects with uncontrolled hypertension (≥140/90 mmHg)
c) Subjects with micro vascular complications of T2DM

The medical trial received approval from the KAHER ethical committee for human subjects (Ref ID: KAHER/EC/20-21/001/11) with prospective CTRI Registration Number: CTRI/2020/12/029762. The CONSORT statement guideline was followed when reporting the study's findings.

Table 1: *Prameha purva rupa* assessment parameter with grading

Si.no	*Purva rupa*	0	1	2	3
1	*Madhuryamasya* (Feeling sweetness in mouth)	None	Mild (Occasionally)	Moderate (Most time of the day)	Severe(Always)
2	*Anga Shaitilya*(flaccidity of muscles)	No anga shaithilya	Mild (shaithilya only few areas)	Moderate(flaccidity especially limbs)	Severe(Major areas)
3	*Alasya* (lazyness or indolence)	None does all routine and office work on time	Mild - tendency to postpone mildly	Moderate - tendency to postpone frequently	Severe – inability to carry on any work (office/ household) in time
4	*Shitapriyatwa* (Desire for cold food & environment)	No desire	Mild(occasionally)	Moderate(during hot climate/2-3 times of the day)	Severe(All the time)
5	*Anga gandha* (Body odour)	No odour	Bad odour but not offensive	Detectable offensive odour, tolerable	Very strong odour even after using fragrances (use of deodorants or perfumes)
6	*Shrama Swasa* (Dyspnoea on exertion)	No dyspnoea	Mild only when walking on an ascent or climbing steps more than 1 floor	Moderate when climbing one floor or walking for 500 mts on a flat surface	Severe cannot walk on flat surface more than 50 meters
7	*Swedadikyata* (perspiration)	Sweating only after heavy work and fast movement or in hot weather	Profuse sweating after moderate work and movement	Sweating after little work and movement (stepping ladder etc.)	Profuse sweating after little work and movement
8	*Angasada (*Physical Fatigability*)*	No fatigue	Fatigue on exercise	Fatigue on certain physical functioning	Fatigue at rest, interfering work family or social life

	***Prameha rupa* assessment parameter with grading**				
1	*Mutramadhurya* (Glycosuria)	Absence of glucose in urine	Traces of Glucose in urine	+ Glucose in urine	++ Glucose in urine
2	*Prabhuta Mutrata* (Polyuria) - Frequency of urination	3 – 5 times per day, rarely at night	6 – 8 times per day, 1 – 2 times per night	9 – 11 times per day 3 – 4 times per night	> 11 times per day > 4 times per night
3	*Pipasa-Adhikya* (Increased Thirst)	No thirst	Drinking water satisfy the thirst, dryness of mouth, throat	Frequent feel to drink water	Severe (Feeling of severe thirst, waking up night to drink)
4	*Kshudha-Adhikya* (Increased Appetite)	No appetite/very poor	Occasional hunger/ eating only few mouthful/one third plate	Two to three meals per day, comfortable, neither hungry nor full	Feeling hungry all the time with several hunger symptoms
5	*Klama* (mental fatigue)	No fatigue and mental effort not reduced	Fatigued quickly but still able to make some mental effort	Fatigue on certain physical functions	Fatigue at rest, interfering work family or social life
6	*Purishabaddhata* (Constipation)	Stool passes as per normal schedule	Passes stool with strain, sometimes takes purgative	Passes stool after more than 24 hours, frequently takes purgative	Passes stool after gap of one day, normal purgatives does not work

Research design

The research was a single-centric, open-label, parallel group, randomised, standard controlled trial. A block size of two was used for block randomisation. Random numbers produced by a computer were used to form allocation sequences. Based on statistical calculation, it was found that 80 participants in each group found sufficient. However, considering the 20% attrition rate, sample size of 100 in each group was taken within a 95% confidence interval and 5% correction error.

Intervention

As per the randomisation, 200 subjects equally divided into two groups: Group A has Standard diabetic treatment (SDT) and group B has Integrated Ayurveda treatment (IAT). SDT intervention had standard dietary advice, lifestyle intervention along with drug metformin (≥ 1g/day). Standard dietary advice was as approved by American diabetic association (ADA) (16) which was customised as per local and regional eating practices. A top dietician who has worked with diabetes for more than ten years approved the diet plan. Lifestyle change advice includes any sort of activity for at least 150 minutes per week (or 3 to 7 days per week, with no more than 2 days without exercise) (17). IAT group had metformin (≥ 1g/day), add on intervention of *Ayurveda* polyherbal drug called *Madhumehari ghana vati* (MGV) 3 grams per day administered as 500 mg *ghana* (thick extract) 2 tablet 3 times a day after meal with water, *Ayurvedic* therapeutic diet and yoga. MGV had 10 herbs procured from reliable sources and prepared **(Table no.2& 3)**. The tablets were manufactured at a recognised KLE *Ayurvedic* pharmacy using Good Manufacturing Practices (GMP) in compliance with normal procedures. As per the specified quantity, all coarse powders were taken in *khalva yantra* (mortar & pestle), and a homogenous mixture was prepared. The drug mixture was taken into a stainless steel container and soaked in eight parts of tap water for 12 hours. The overnight-soaked drug mixture was kept boiling on a moderate fire till it was reduced to one-fourth quantity. A pleasant odour of *kashaya* was observed during boiling. Filtered and kept aside. The *kashaya* was taken into a stainless steel vessel and kept for boiling. The boiling was continued until it attained a semisolid consistency. After attaining semisolid consistency, the vessel was removed from the gas. It was taken on a thick polythene sheet when it was warm and kept in the shade for drying. After drying completely, it was powdered to a size of 500 mg. The *Vati* was prepared and stored in an airtight container. In the Ministry of AYUSH-approved ASU (*Ayurveda, Siddha, Unani*) drug testing laboratory at KAHER's Shri BM Kankanwadi *Ayurveda* Institute Belagavi, raw drug authentication and physiochemical standards of tablets were conducted. *Ayurveda* dietary plan is prepared after a thorough literature review and with incorporation of local eating practices. This consists time restricted therapeutic eating, herbs processed drinks, and the millet based meals and integration of more greens with allowance of all tastes to make it more palatable and interesting. The following factors were taken into consideration when determining the *hitatwa* (wholesome) and *ahitatwa* (unwholesome) of food: *prakrati* (food nature), *karana* (processing method), *raashi* (quantity), *desham* (habitat), *kalam* (time or climatic factor), *samyoga* (combination), *upayoga samstha* (rules of food intake), and *upayokta* (user compatibility). Food which pacifies *kapha*, *kleda* and *medas* were incorporated. The diet regimen was more broadly appealing and focused on *dosha* balancing. [Table no.4].

Table 2: Botanical name, part used and proportion of the *Madhumehari ghana vati*

Sl.no	Sanskrit name	Botanical name	Part used	Proportion of the drug
1	*Meshashringi*	*Gymnema sylvestre* R. Br.	Leaves	1 part
2	*Vijayasara*	*Pterocarpus marsupium* Roxb.	Heart wood	2 part
3	*Jambu*	*Syzygium cumini* Linn.	Seed	2 part
4	*Haridra*	*Curcuma longa* Linn .	Rhizome	1 part
5	*Daruharidra*	*Berberis aristata* DC.	Stem	1 part
6	*Hareetaki*	*Terminalia chebula* Retz .	Fruit	1 part
7	*Vibhitaki*	*Terminalia belirica* Roxb.	Fruit	
8	*Amlaki*	*Emblica officinalis* Gaertn.	Fruit	
9	*Guduchi*	*Tinospora cordifolia* willd.	Leaves	1 part
10	*Tamala patra*	*Cinnamomum tamala* (Buch,Ham)	Leaves	1 part

Table 3: *Rasa panchaka* of *Madhumehari ghana vati*

Sanskrit name	*Rasa*	*guna*	*Veerya*	*Vipaka*	*Karma*	*Indication*
Meshashringi	*Kashaya,Tikta*	*Laghu,Ruksha*	*Ushna*	*Katu*	*Kaphavata shamaka*	*Madhumeha, Ikshumeha Agnimandya,*
Vijayasara	*Kashaya,Tikta*	*Laghu,Ruksha*	*Ushna*	*Katu*	*Kaphapitta shamaka*	*Madhumeha, Prameha, Sthoylya*
Jambu	*Kashaya, madhura, amla*	*Laghu,Ruksha*	*Sita*	*Katu*	*Pitta shamaka*	*Madhumeha, Prameha, Sthoulya Raktapitta, Raktavikara.*
Haridra	*Katu, Tikta*	*Laghu, Ruksha*	*Ushna*	*Katu*	*Kapha pitta shamaka*	*Prameha,agnimandya*
Daruharidra	*Tikta, kashaya*	*Ruksa, Laghu*	*Ushna*	*Katu*	*Tridosha shamaka.*	*Vibandha,Prameha*
Hareetaki	*Pancharasa*	*Laghu, Ruksha*	*Ushna*	*Madhura*	*Tridoshashamaka*	*Prameha,Vatarakta, Agnimandya*
Vibhitaki	*Kashaya*	*Laghu, Ruksha*	*Ushna*	*Madhura*	*Tridoshashamaka*	*Prameha,Vatarakta, Agnimandya*
Amlaki	*Pancharasa (alavana) Amla (Pradhana)*	*Laghu, Ruksha, Sita*	*Sita*	*Madhura*	*Tridoshashamaka, especially Pittashamaka.*	*Daha, Daurbalya, meha,*
Guduchi	*Kashaya*	*Laghu, Ruksha*	*Ushna*	*Madhura*	*Tridoshashamaka*	*Vibandha, doubalya, rasayana, Prameha*
Tamala patra	*Madhura, Katu*	*Laghu, picchila, tikshna*	*Ushna*	*Katu*	*Kapha vata shamaka*	*Medoroga*

Table 4: *Ayurveda* dietary plan

Timing Food Diary	Menu
Morning Drink B/w 6.30 am to 7 am (Any One)	1. Herbal Infused Drink (Lemon Added)-150 ml (1 Glass) 2. Ginger Lemon water -100 ml 3. Cinnamon water (lemon added)-100 ml 4. Fenugreek water-100ml 5. Herbal Juice-100 ml
8 am to 9 am Breakfast options (Any one)	1. Gram floor Dosa(Tomato Omlette)-1 in no + Herbal Chatni-2 tsf + Sambar-1 wati 2. Millet Dosa 1 to 2 in no/Millet Idli-2-3 in no + Herbal/ coconut Chatni-2 tsf + Sambar -1 wati 3. Millet Vegetable Upma-1 bowl/1 plate 4. Moong dosa-1 to 2 in no. + Herbal / coconut Chatni-2 tsf + Sambar-1 wati 5. Dhokla-2 pieces + Herbal chatni-2 tbsp 6. Barley kichdi-1 bowl Breakfast with Herbal /Cardamom/Green Tea without sugar-1 cup
Mid-Morning Snack(Optional) 11.30 am to 12 pm	1. Medicated Buttermilk (Spiced with Ginger, Pepper, Rock salt and Jeera)- 1 Glass(150ml)
Lunch 1pm to 2 Pm	Mix Veg Salad (Raw-spiced with pepper powder and Rock Salt)-1 bowl + Unripe guava (1), Any citrous fruit(1),Berries(3 to 4) + Jowar/Bajra Roti-1 to 2 in number + Vegetable Sabji-1 wati + Boiled Pulses Sabzi/ Junka /moong Dal-/4th katori + Peanut/Methi/Flax Chatni-2 tsf + Dahi (Added with Rock salt or pink salt)

Mid-Evening Snack(optional) 4.30 pm to 5 pm (Option-Any one)	1. Almond-6 to 8 + Walnut-4 + Roasted /Soaked Peanuts-1 handful + Green Tea/Lemon tea without Sugar-1 handful
	1. Boiled black Chana chat-1 cup +Almond -6 +Walnut-3 + Green Tea/Lemon tea without Sugar-1 cup
	2. Boiled Peanut Chat or unsalted peanuts- 1 plate/1 handful + Green Tea/Lemon tea without Sugar-1 cup
	3. Mix sprout bhel (lemon and rock salt added)- 1 bowl + Green Tea/Lemon tea without Sugar-1 cup
	4. Moong usali/chana dal tikki/green gram vada/veg cutlet/karela fry/Moong dal tikki (any one)- 1 plate + Green Tea/Lemon tea without Sugar-1 cup
Dinner (7 pm to 8 Pm)	1. Salad (spiced with lemon, pepper, rock salt)-1 bowl + Jowar /Bajra Roti-1 + Veg Sabzi-1 bowl + Millet Rice/millet pulav -1/2 wati + moong dal -1/2 katori + Herbal Raita-1 wati

Outcome measures

Subjective outcomes on *Prameha* as *purvaroopa* and *laxana* assessment and diabetes quality of life measured on 0th, 30th, 60th and 90th day of intervention. Subjective outcomes were graded based on severity

Anthropometric measures (weight, BMI) were assessed on 0th, 30th, 60th and 90th day of intervention.

Glycemic parameter assessment

HbA1C (in %) assessed on 0th and 90th day of intervention. Fasting blood glucose (FBS in mg/dl), Post prandial blood glucose (PPBS in mg/dl) were assessed on 0th, 30th, 60th and 90th day of intervention.

Lipid profile parameters assessed on 0th and 90th day of intervention.

Insulin resistance parameter: Fasting insulin (in miU/l) and Homa IR (Homeostatic model for assessment for Insulin resistance) measured on 0th and 90th day.

Statistical methods

Baseline data including demographic data and patient profile between the groups was analyzed using $\chi 2$ test. Result of the intervention at different time point between the groups was analyzed by Mann-Whitney U test. Wilcoxon matched pairs and Friedman's ANOVA test used to analyse within the group results at different time point.

Results

Demographic profile

Total 200 patients eligible for the study were randomised into SDT group and IAT group. In SDT group, among 100 subjects, total 8 subjects were dropped out and in IAT group among 100 subjects, 12 subjects were dropped due to various reasons. In this study, age wise distribution of subjects reveals, majority were above 61years (43%) followed by 51 to 60 years (34%) in SDP group and in IAP, maximum were between 41 to 50 years (41%) to above 61 years (35%). Gender wise, above 53% were male and 47% were females in SDT and 54% were male & 46% were female in IAT. Majority were from Hindu religion. Maximum subjects were graduated (37%) followed by primary school education (31%) in SDT and 33% graduates followed by 31% have primary education in IAT. Majority of subjects were married. Family history of diabetes found in 44% of participant's in SDT and 36% participants in IAT. Physical activity of subject's revealed moderate (50%) to sedentary (44%) activity with 50 and 44% respectively in SDT and 61 to 34% in IAT **(Table no.5).** Personal history of subjects revealed majority had good bowel habit (i.e 72% in SDT and 71% in IAT), normal appetite (61% in SDT and 60% in IAT).Mixed dietary pattern is seen in both SDT (66%) and IAT (57%) group. Around 47% in SDT and 43% in IAT had *vata pitta prakrati* (constitution) followed by *pitta kapha prakriti* in 26% of participants in SDT and 31% participants in IAT. *Sara* (essence) of the subjects revealed majority had *medosara* (essence of adipose tissue) i.e. 90% in SDT and 88% in IAT group.

Subjective outcome

In this study, based on classical reference, assessment of clinical features of *prameha* was classified into two different parameters as *poorvaroopa* (premonitory symptoms) and *Rupa* (symptoms). *Poorvaroopa* assessment parameters included are *madhuryamasyata* (feeling sweetness in mouth), *angashaitilya* (flaccidity of muscles), *alasya* (indolence), *shitapriyatva* (desire for cold things), *angaganda* (body odour), *shramashwasa* (dysnoea on exertion), *swedadikyata* (perspiration) and *angasada* (physical fatigability).

Effect of intervention on *prameha poorva roopa* outcome showed significant difference favoring IAT group in *angashaitilya*, *alasya*, *shitapriyatva*, *angaganda*, *swedadikya* and *angasada* features. In *angashaitilya*, significant difference was observed on 60th ($p<0.05$) and 90th ($p<0.05$) day of intervention. In *alasya* and *angaganda* changes were seen on 60th ($p<0.05$) and 90th ($p<0.01$) day of intervention. In *shramashwasa* and *angasada,* statistical significance was observed on 60th and 90th day of intervention ($p<0.001$).In *swedadikya*, difference was observed on 60th ($p<0.01$) and 90th ($p<0.001$). No difference was observed between the group in *madhuryamasya* but significant changes shown within the SDT ($p=0.001$) and IAT ($p<0.001$) (Table no.06)

Impact of intervention on *Prameharoopa* parameter showed significant difference towards IAT in *mutramadhurya, prabhutamutrata*, *pipasa* from 60th day of intervention with p value<0.001.In *Khsudadikyata*, between the group comparison showed that, significance in IAT was found on 60th ($p<0.05$) and 90th day ($p<0.01$). In *klama*, difference was observed between the group from 30th ($p<0.05$), 60th ($p<0.001$) day to 90th ($p<0.001$) day of intervention favoring IAT group. In *Purishabaddata*, between the group comparison showed that, IAT was significant on 90th day ($p<0.05$) (Table no.07)

Table 5: Comparison of Group A and Group B with demographic characteristics using chi-square test

Characteristics	Group SDT		Group IAT		Total		c^2	p-value
	n	%	n	%	n	%		
Age groups								
≤40yrs	7	7.00	17	17.00	24	12.00	9.0860	0.0280*
41-50yrs	16	16.00	25	25.00	41	20.50		
51-60yrs	34	34.00	23	23.00	57	28.50		
61yrs	43	43.00	35	35.00	78	39.00		
Gender								
Male	53	53.00	54	54.00	107	53.50	2.8200	0.4200
Female	47	47.00	46	46.00	93	46.50		
Religion								
Hindu	92	92.00	86	86.00	178	89.00	2.8200	0.4200
Muslim	3	3.00	3	3.00	6	3.00		
Christian	1	1.00	4	4.00	5	2.50		
Jain	4	4.00	7	7.00	11	5.50		
Education Status								
Illiterate	6	6.00	1	1.00	7	3.50	8.4900	0.1310
Primary School	31	31.00	31	31.00	62	31.00		
High School	21	21.00	22	22.00	43	21.50		
Diploma	0	0.00	3	3.00	3	1.50		
Graduate	37	37.00	33	33.00	70	35.00		
Post graduate	5	5.00	10	10.00	15	7.50		
Occupation								
Agriculture	6	6.00	5	5.00	11	5.50	1.9550	0.8550
Business	18	18.00	23	23.00	41	20.50		
Officer	29	29.00	22	22.00	51	25.50		
Home maker	32	32.00	35	35.00	67	33.50		
Teacher	5	5.00	4	4.00	9	4.50		
Labor	10	10.00	11	11.00	21	10.50		
Marital Status								
Married	94	94.00	83	83.00	177	88.50	8.1600	0.0430*
Unmarried	0	0.00	6	6.00	6	3.00		
Divorced	1	1.00	2	2.00	3	1.50		
Widowed	5	5.00	9	9.00	14	7.00		
Family history of T2DM								
Positive family history	44	44.00	36	36.00	80	40.00	1.3330	0.2480
Negative family history	56	56.00	64	64.00	120	60.00		
Physical activity								
Highly Active	6	6.00	5	5.00	11	5.50	2.4630	0.2920
Moderate	50	50.00	61	61.00	111	55.50		
Sedentary	44	44.00	34	34.00	78	39.00		

*p<0.05

Table 6: Effect on *Pramehapurvaroopa* variables using Mann-Whitney U test (between the groups) and Wilcoxon matched pairs (within the group). Expressed in mean and standard deviations (SD)
*** p < 0.05, **p < 0.01, ***p < 0.001**

Si.no	Parameter	Intervention	Baseline	30th day	60th day	90th day	P value	BL-30th	BL-60th	BL-90th
1	*Madhuryamasya*	SDT	0.5±0.9	0.5±0.8	0.5 ±8	0.5±8	0.55	<0.05*	<0.05*	<0.05*
		IAT	0.7±0.9	0.50±8	0.40±7	0.40±7		<0.001*	<0.001*	<0.001*
2	*Angashaitilya*	SDT	1.5±1.0	1.4±10	1.4±10	1.41±0	<0.05*	0.1614	0.1097	0.35
		IAT	1.3±1.0	1.2±1.0	1.1±1.0	1.0±0.9	<0.05*	0.0010*	0.0001*	0.0001*
3	*Alasya*	SDT	1.7±0.8	1.4±0.8	1.3±0.8	1.3±0.8	0.0012*	0.0001*	0.0001*	0.0001*
		IAT	1.9±0.8	1.4±0.8	1.0±0.8	0.9±0.8		0.0001*	0.0001*	0.0001*
4	*Shitapriyatwa*	SDT	1.1±0.9	1.0±0.9	0.9±0.9	0.9±0.9	0.0011*	0.0117*	0.0003*	0.0002*
		IAT	0.9±1.0	0.7±0.8	0.5±0.6	0.4±0.6		0.0010*	0.0001*	0.0001*
5	*Angagandha*	SDT	1.1±0.9	0.9±0.8	0.8±0.8	0.7±0.8	0.0059*	0.0001*	0.0001*	0.0001*
		IAT	1.10.9	0.80.8	0.50.7	0.40.6		0.0001*	0.0001*	0.0001*

6	*Shramashwasa*	SDT	1.4±0.9	1.2±0.8	1.1±0.9	1.1±0.9	0.0001*	0.0022*	0.0001*	0.0001*
		IAT	1.3±0.9	1.0±0.8	0.5±0.6	0.5±0.6		0.0001*	0.0001*	0.0001*
7	*Swedadikyata*	SDT	1.5±0.8	1.3±0.8	1.1±0.8	1.1±0.8	0.0001*	0.0001*	0.0001*	0.0001*
		IAT	1.6±0.8	1.3±0.9	0.7±0.8	0.6±0.8		0.0001*	0.0001*	0.0001*
8	*Angasaada*	SDT	1.7±0.8	1.5±0.8	1.3±0.9	1.3±0.8	0.0001*	0.0004*	0.0001*	0.0001*
		IAT	1.8±0.7	1.4±0.8	0.9±0.8	0.8±0.8		0.0001*	0.0001*	0.0001*

Table 7: Effect on *Prameha roopa* variables using Mann-Whitney U test (between the groups) and Wilcoxon matched pairs (within the group). Expressed in mean and standard deviations (SD)
*** p < 0.05, **p < 0.01, ***p < 0.001**

Si.no	Parameter	Intervention	Baseline	30th day	60th day	90th day	P value	BL-30th	BL-60th	BL-90th
1	*Mutramadhurya*	SDT	1.8±2.0	1.6±2.0	1.4±1.0	1.3±1.0	0.0001*	0.0001*	0.0001*	0.0001*
		IAT	2.0±2.0	1.4±1.0	0.8±1.0	0.7±0		0.0001*	0.0001*	0.0001*
2	*Prabhuta Mutrata*	SDT	1.6±1.0	1.3±1.0	1.2±1.0	1.1±1.0	0.0001*	0.0001*	0.0001*	0.0001*
		IAT	1.6±2.0	1.2±1.0	0.6±1.0	0.5±0.0		0.0001*	0.0001*	0.0001*
3	*Pipasaadhikya*	SDT	1.7±2.0	1.4±1.0	1.3±1.0	1.2±1.0	0.0001*	0.0001*	0.0001*	0.0001*
		IAT	1.8±2.0	1.3±1.0	0.8±1.0	0.6±0.0		0.0001*	0.0001*	0.0001*
4	*Kshudhaadhikya*	SDT	1.7±2.0	1.5±2.0	1.3±1.0	1.3±1.0	0.0002*	0.0001*	0.0001*	0.0001*
		IAT	1.9±2.0	1.6±2.0	1.0±1.0	0.8±1.0		0.0001*	0.0001*	0.0001*
5	*Klama*	SDT	1.5±1.0	1.4±1.0	1.3±1.0	1.2±1.0	0.0001*	0.0117*	0.0001*	0.0001*
		IAT	1.4±1.0	1.1±1.0	0.8±1.0	0.7±1.0		0.0001*	0.0001*	0.0001*
6	*Purishabaddhata*	SDT	0.6±0.0	0.5±0.0	0.4±0.0	0.3±0.0	0.0252*	0.0051*	0.0002*	0.0001*
		IAT	0.6±0.0	0.4±0.0	0.2±0.0	0.1±0.0		0.0001*	0.0001*	0.0001*

Glycaemic outcome

The impact of the intervention on HbA1c revealed a significant difference (p<0.001), with the mean percentage change in IAT (16.58%) being higher than that of SDT (4.82%), favouring the IAT group. In FBS parameter there is a significant difference between the group (p=0.001). The IAT group shown changes from 30th (p=0.001), 60th (p<0.001), and 90th (p<0.001) day of the intervention in group analysis. In SDT group, changes were evident on the 90th (p<0.001) day of the intervention. In FBS parameter, there is a significant difference between the groups (p=0.001). Individual group analysis revealed that there were changes in the IAT group on the 30th (p=0.001), 60th (p<0.001), and 90th (p<0.001) day of the intervention, where as in SDT group changes visible on 90th day of intervention (p<0.001). The result of intervention on PPBS showed significant difference between the group (p<0.001) which is favouring to IAT group had shown changes on 30th, 60th, and 90th day of intervention (p<0.001)

Lipid profile outcome

In lipid profile parameter both the group shown significant changes in Total cholesterol (p=0.007 in SDT & p=0.001 in IAT), very low density lipoprotein ((p = 0.001in SDT and p<0.001 in IAT group) and serum triglycerides (P<0.001 in both SDT and IDT group). High density lipoprotein and low density lipoprotein had not shown any results in this study.

Anthropometric measure outcome

From the baseline to the 30th, 60th, and 90th day of the intervention, in weight and BMI, there was a substantial decrease in both SDT and IAT group (P < 0.001).Mean changes in weight was from 69.30 kg's to 68.67 kg's in SDT and 71.43 to 68.39 kg's in IAT group.

Insulin resistance outcome

Result of intervention on serum insulin showed significant change between the group (p<0.05), with the IAT group had superior improvement (p<0.001). Intervention outcome on HomaIR showed significant difference (p=0.001). Within the group, IAT had shown more improvement (p<0.001).

Diabetes quality of life

Diabetes quality of life domains are satisfaction, impact and concern (Social and diabetes specific).Results on quality of life with above domains showed that group IAT had good improvement (p<0.001) at all-time points of the study i.e on 30th, 60th and 90th day of the study.

Discussion

This study revealed that, Integrated Ayurveda treatment (IAT) showed beneficial outcome compared to Standard Diabetic treatment (SDT) in maximum parameters of *prameha purvarupa* except in *madhuryamasya*. In *Prameha rupa*, all the parameters showed statistical significance favouring to IAT group. Ayurveda treatment group showed benefits in HbA1c, FBS, PPBS and Insulin resistance parameters. Both the group had shown results in weight, BMI and few components of lipid profile (i.e Total cholesterol, VLDL and Triglycerides).

In this study, the majority of subjects were over 41 years old; however, currently, it is observed that type 2 diabetes can develop at a young age, usually driven by insulin resistance due to obesity and ethnicity. Religion-wise, the distribution of subjects revealed that Hindu

subjects were predominant in both groups. This may be due to the maximum population of Hindu subjects in the study area. Subjects in the graduated and primary school categories of educational status were found which shows that prevalence is not strongly related to the educational status of the subjects. Different occupation distributions were found, so no conclusion could be drawn about the prevalence of the disease. Subjects with a sedentary lifestyle to moderate physical activity were found, revealing that lifestyle has a stronger role to play in disease manifestation.

Ayurveda herbs are extensively used for different health conditions and general welfare. MGV has ten herbs i.e *Meshashringi* (Gymnema Sylvestre Retz.), *Jambu* (Syzygium cumini L.), *Triphala* (a blend of *Emblica officinalis* Gaertn, *Terminalia chebula* Retz, *Terminalia belirica* Roxb.), *Vijayasara* (*Pterocarpus marsupium* Roxb), *Haridra* (*Curcuma longa* Linn), *Guduchi* (*Tinospora cordifolia* willd,) *Tamala patra* (*Cinnamomum tamala* (Buch,Ham) and *Daruharidra* (*Berberis aristata* DC). All the herbs have *pramehagna* property hence showed significant benefits in glycaemic outcomes. Drugs such as *Jambu, Asana, Haridra* are having potent anti-diabetic activity, also they are having *pitta* mitigating property, hence might helped in symptoms of *Pipasadikyata*, *kshudadikyata* etc. An open label clinical trial conducted in 4 centres of India to see the efficacy of *vijayasara* (*Pterocarpus marsupium* Roxb.) in non-insulin dependent diabetes mellitus had shown reduction in glycaemic parameters and lipid changes (18). The research done on the extract from *syzygium cumini* demonstrates the existence of phenolic compounds with anti-oxidant and anti-glycation properties that can mediate their anti-diabetic benefits (12). A meta-analysis of various studies have shown the beneficial effects of curcumin and its preparation in asian pre-diabetes and T2DM patients by reducing HbA1c (19). *Meshashringi*, *Tamala patra*, *Daruharidra* have *kapha medohara* and *lekhana* (scrapping) action might help in reversing the pathogenesis (9, 10). A clinical trial on T2DM, administered with 500 mg of *Meshashringi* (*Gymnema sylvestre* R. Br.) along with diet for a period of 90 days shown beneficial effect in polyphagia and other symptoms (20). Patients with T2DM who received 1 mg of *daruharidra* fruit extract showed results in blood glucose regulation (21). An oral administration of an ethanolic extract of *Cinnamon tamala* (200 mg/kg body weight) for 40 days resulted in a significant reduction in blood glucose levels and the maintenance of body weight and lipid profile parameters close to normal in diabetes induced experimental animals. *Guduchi* and *Triphala* have added *rasayana* advantages (22, 23) in addition to the aforementioned ones, which may have an impact on *Angashitilya*, *Sada*, and *Klama*.

The Ayurvedic diet planned here consists of millet-based meals, plant-based food treated with herbs, time-restricted eating with 2 to 3 meal method, and avoids processed and junk food. Time restricted eating have benefits in body weight and fat mass (24), improves glucose tolerance hence showed results in this study. The *Ayurvedic* concept of dietary recommendations for lifestyle diseases is *guru cha aatarpana,* i.e., food that is heavy and rich in nutrients without causing over nourishment (25) and avoids excess fat storage, like foods made of millet. This theory helps to balance the metabolism and prevent overeating, which is why this study found the effective outcomes. This diet contained majority of plant-based food. A meta-analysis of six randomised controlled trials (N = 255) found that plant diets were associated with a 0.4% larger drop in glycated haemoglobin (HbA1c) than other suggested dietary patterns for diabetic people (26). Review on benefits of yogasana's reveal that, ten minutes of yoga intervention combined with standard medical care for 10 minutes helped to improve metabolic health significantly. Combined effect of *Madhumeha ghana vati* with *pathyahara* and integration of yoga showed benefits in type 2 diabetes without causing any adverse events.

Conclusion

This study evaluated efficacy of integrated Ayurveda treatment which consist of an Ayurveda poly herbal formulation *Madhumehari ghana vati* along with diet and *yoga* showed beneficial effect in majority of parameters of *Prameha poorvaroopa* and *roopa* in a duration of *90* days. The efficacy result was also noticed in diabetes quality of life parameters. Study showed benefits in glycaemic outcomes compared to standard control group. Comparable results were observed in lipid profile and anthropometric measures. Study conducted with adequate sample size is strength of this study. Long term intervention is needed to see the better results. No any adverse events seen in this study.

Acknowledgements

The authors are thankful to the Staff of KAHER's Shri BMK Ayurveda hospital for their support in completing this study.

Financial support: Nil

Ethics statement

Authors certify that appropriate patient consent was taken

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