Journal of Ayurveda and Integrative Medicine 15 (2024) 100878

Contents lists available at ScienceDirect

Journal of Ayurveda and Integrative Medicine

journal homepage: elsevier.com/locate/jaim

'Vidangadi Lauha' for obese type 2 diabetes mellitus patients - An open-label randomized controlled clinical trial

Punam Khobarkar [a], Jayant Gulhane [b], Amit Nakanekar [b,*]

[a] All India Institute of Ayurveda, New Delhi, India
[b] Department of Kayachikitsa Government Ayurved College, Nagpur, India

ARTICLE INFO

Keywords:
Ayurveda
Vidangadi Lauha
Obese type 2 diabetes mellitus

ABSTRACT

Background: Type 2 diabetes mellitus in obese persons is becoming alarming due to the increasing prevalence of its microvascular and macrovascular complications. Multi-targeted treatment can be considered better than single-targeted treatment because of the multiple pathways involved in the pathogenesis of diabetes and its complications.
Objective: The study aimed to evaluate the efficacy of '*Vidangadi Lauha*' (*VL*) (an *Ayurveda* formulation) compared with Metformin for obese type II diabetes mellitus.
Methodology: This is an open-label randomized controlled clinical study.Participants were divided into two groups. The trial Group received *VL* 5 gm BID, and the control group received tablet metformin (MT) 500 mg BID for three months.
Results: VL showed reduction in HbA1c from 8.048(0.95) to 7.14(0.73), (CI, 0.7810 to 1.035; $p < 0.0001$) while MT showed reduction in HbA1C from 8.3(0.99) to7.18(0.67), (CI, 0.9220 to 1.305; $p < 0.0001$). *VL* showed improvement in the Quality of life instrument for the Indian Diabetes questionnaire(QOLID) score from 113.87 (11.36) to 136.47(8.703) (CI, −25.68 to −19.52; $p < 0.0001$) as compared to MT 128.57(7.9) to 102.32(7.9), (CI, 23.19 to 29.39; $p < 0.0001$) *VL* showed reduction in bowel symptom questionnaire 30.275(8.077) to 13.2 (1.265), (CI, 14.60–19.51; $p < 0.0001$) as compared to MT from 23.85(7.530) to 38.25(6.332), (CI, −15.99 to −12.80; $p < 0.0001$).
Conclusion: Both treatments were equally effective in reducing blood sugar fasting (F), post-meal (PM) glycated hemoglobin (HbA1C), and body mass index (BMI). *VL* is more effective than MT in reducing *Ayurvedic* symptoms, waist-hip ratio, cholesterol, quality of life, and bowel symptom questionnaire score.

1. Introduction

Obese patients with type 2 diabetes mellitus is a multifactorial, non-communicable disease challenge. It is caused by disturbances in carbohydrates, fat, and protein metabolism due to disturbed insulin secretion or its action. It is the most life-threatening disease due to its increasing microvascular and macrovascular complications prevalence.

A report by the Indian Diabetes Federation shows that nearly 463 million people are living with diabetes, which will increase to 578 million by 2030. It will go on increasing 700 million by 2045. This number will jump up to 700 million by 2045. The ratio of diabetic to healthy individuals was 1:11 in the 20–79 age group. Nearly 10 % of global expenditure is spent on diabetes. 3 out of 4 people with diabetes live in low- and middle-income countries [1].

The therapeutic approach for managing type 2 diabetes should not be limited to glycemic control but also to prevent complications due to diabetes. Currently, *Ayurveda* formulations are more popularly used as oral hypoglycemic agents with the belief of without any side effects and minimizing the risk of complications due to diabetes mellitus. Classical *Ayurveda* formulations have many phytochemicals that act symbiotically and exhibit pharmacodynamic actions [2]. Multi-targeted *Ayurveda* formulations can be essential to bring breakthroughs in treating type 2 diabetes if supported by scientifically designed clinical trials. The bedside-to-bench approach is also expected to be more suitable for various studies on Ayurveda formulations [3].

Quality of life is an essential domain in the treatment assessment of

Peer review under responsibility of Transdisciplinary University, Bangalore.
* Corresponding author.
E-mail address: amitnakanekar@gmail.com (A. Nakanekar).

https://doi.org/10.1016/j.jaim.2023.100878
Received 23 February 2023; Received in revised form 7 December 2023; Accepted 11 December 2023

Type 2 diabetes mellitus. It includes assessment of physical endurance, general health, treatment satisfaction, symptom botherness, financial worries, and emotional/mental health [4]. Gut health (gastrointestinal symptoms) and type 2 diabetes are closely related. The bowel symptoms questionnaire for Indian diabetes includes symptoms such as abdominal pain, abdominal bloating or distension, gastrointestinal reflux, dysphagia, diarrhea, straining, hard or very lumpy bowel movement, incomplete evacuation, anal blockage, manual assistance in fecal evacuation, less than three bowel movements a week [5].

This clinical trial is designed to evaluate the comparative clinical efficacy of Ayurveda formulation' *VL'* (5 gm BD) against MT 500 mg in the treatment of newly diagnosed obese type 2 Diabetic patients for three months.

2. Methodology

2.1. Trial design

A randomized open-label parallel-group clinical trial with an allocation ratio of 1:1 was conducted as per the CONSORT statement for adherence to clinical trials. The study was conducted after approval from the Institutional Ethics Committee, Government Ayurveda College, Nagpur, India (approval number PGS/465/2018) and prospective registration in the Clinical Trials Registry government of India (CTRI/2019/02/017609). The study period included February 15, 2019, to May 31, 2020.

3. Trial participants

Initially, persons willing to be screened for diabetes were screened based on the Indian Diabetes Risk Score (IDRS). If IDRS> 50, they were advised to have blood sugar level (BSL) fasting and BSL post-meal. After that, they were enrolled/excluded per the inclusion and exclusion criteria.

3.1. Inclusion and exclusion criteria

People aged between 30 and 70 years, newly diagnosed obese type 2 diabetes mellitus (BMI 23–30 Kg/m2), fasting blood sugar level 126 mg/dl to 200 mg/dl and postprandial blood sugar level 200 mg/dl to 300 mg/dl, HbA1c up to 9 %, fulfilled criteria of diagnosis and had signs and symptoms of *Sthula Madhumeha* as per Ayurveda clinical evaluation, patients with controlled hypertension BP < 150/90 mm of Hg and those who were willing to give informed written consent included in the study were included in the study.

The exclusion criteria include diagnosis with diabetes mellitus (fasting blood sugar level >200 mg/dl and post-meal blood sugar level>300 mg/dl, HbA1c more than 9 %, BMI less than 23Kg/m2 and above 30Kg/m2.) Patients with insulin-dependent diabetes mellitus and juvenile diabetes; complications such as vasculopathy, nephropathy, retinopathy, and neuropathy; other systemic complications such as hepatic, renal, and cardiac problems; any complications arising during treatment or if any patient discontinued the treatment; poorly controlled blood pressure; lactating females; emergency cases in type 2 diabetes mellitus; and patients who were currently participating in any other clinical trials

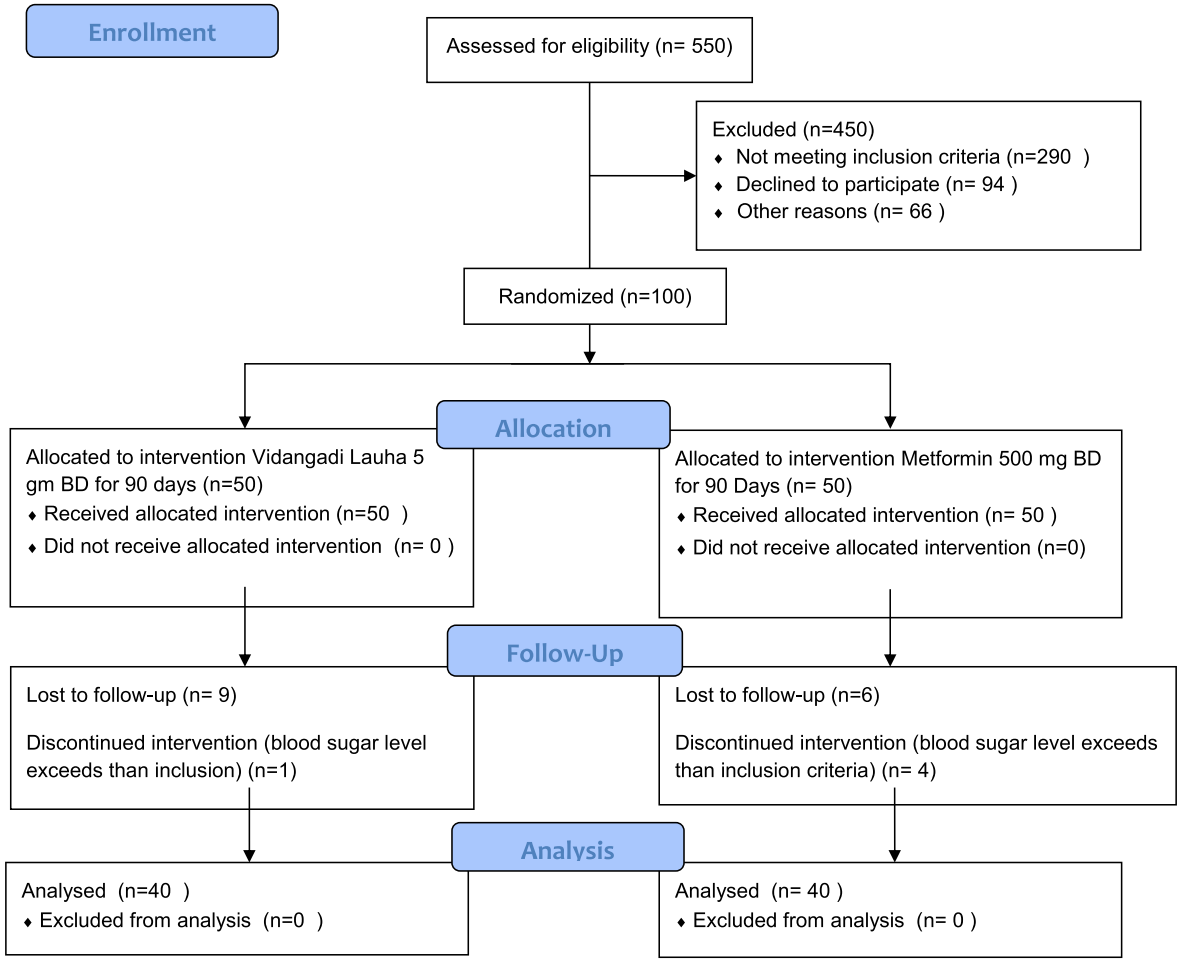

Fig. 1. CONSORT flow diagram.

(since last six months) were excluded from the study. Those unwilling to participate in the Trial and unwilling to give written consent were also excluded.

3.2. Study settings

Participants were recruited in the study through OPD, casualty, and various camps in the department of *Kayachikitsa* Government Ayurveda College, Nagpur, after written informed consent. Fig. 1 describes the flow chart of clinical Trials.

4. Intervention-

There were two groups for the study trial. The group was treated with the Ayurveda formulation *VL* (5 gm BD with Luke warm water), while the control group was treated with MT 500 mg BD orally. *VL* was given before meals, while MT was given after significant meals.

4.1. VL formulation-

'*VL*' is a classical Ayurveda formulation mentioned in '*Bhaishajya Ratnawali*' *(*A classical *Ayurveda* text*)*, prepared as per classical Ayurveda methods [6].

After identification of raw material for formulation, i.e., the fruit of *Embelia ribes* (Batch No-VF01), rhizome of *Piper nigrum* (Batch No-S01), *Cuminum cyminum* (Batch No-SJ01), the fruit of *Piper longum* (Batch No-PF01), rhizome of *Cyperus rotandus* (Batch No-MR01), fruit of *Emblica officinalis* (Batch No-AF01), fruit of *Terminalia chebula* (Batch No- HF01), fruit of *Terminalia bellerica* (Batch No-BF01), *Lauh*a *Bhasma (Batch No-LB01)* they were sent for standardization.

After raw material standardization, *VL* (Batch No-VL01) was prepared using the classical method. The prepared formulation was again standardized for finished product standardization. We ensured that the qualities of all the raw materials and final products matched the *Ayurvedic Pharmacopeia of India* (API) guidelines for the standardization of *Ayurvedic* medicine. Unijules Pharma Nagpur, India, prepared the formulation and its standardization.

5. Measuring trial outcomes-

The study's primary outcome was to evaluate the effect of *VL* and MT on HbA1c and blood sugar levels fasting and post-meal and compare the effect of both treatments.

The study's secondary outcome is to evaluate the efficacy of *VL* and MT on diabetes bowel symptom questionnaires and quality of life.

Initially, general and systemic examinations of the participants were performed. Clinical symptoms of obese type 2 diabetes mellitus were assessed and recorded in a case record form (CRF). Baseline investigations that included complete blood count with erythrocyte sedimentation rate, blood sugar level fasting and post-meal, glycated hemoglobin, urine routine, and microscopic lipid profile were performed.

Those in the MT were given metformin 500 mg twice daily (with meals) for 90 days. All the participants were advised to continue a routine diet but stopped direct sugar intake. A 1-month stock of medicine was provided to participants at each visit.

Participants were called every month (on the 30th, 60th, and 90th days) for follow-up after the baseline visit. Fasting and post-meal blood sugar levels were determined at each follow-up. General and systemic examinations, clinical assessments, BMI, abdominal circumference, and waist-hip ratio were performed at each follow-up. Complete blood count, ESR, HbA1c, routine urine tests, and microscopy were performed at baseline and after 90 days. Quality of life instrument for Indian Diabetes patients (QOLID) questionnaire [4] and bowel symptom questionnaire [5] for diabetes patients were taken at baseline and after the treatment. Each participant's observations were recorded in case record form at every follow-up. The participants were monitored for clinical improvement in clinical, physical, and pathological parameters and adverse drug effects.

To assess the effect of medicines on *Ayurvedic* clinical symptoms index was used as per Nakanekar et al. [7] Ayurveda symptoms of *Sthula Madhumeha* includes *Mukhamadhurya, Supti, Daha, Trishnadhikya, Aalasya, Nidradhikya, Mutradhikya, Aavilmutrata, Kshudhadhikya, Durbalata, Dantadina Maladhyatwam, Swedadhikya, Swapna Sukherati, Shitpriyatwa, Shithilangata, Tandra, Durgandhi Sharira, Medadhikya, Anutsah*

6. Sample size

A sample size of 80 (40 in each group) was calculated considering the hypothesis of an equivalence trial. The sample size was calculated on the basis of data generated by Munishwar N. (2015 MD Thesis); using the formula $N = 2t2a\,(S2) \div d2$ [8]. We hypothesized that *VL* and MT would be equally effective in reducing HbA1c at the end of 3 months with a 95 % confidence interval and at least 80 % power of the study.

7. Randomisation-

A computerized random number table was used to randomize participants to either the VL or the MT.

7.1. Withdrawal criteria

If post-meal blood sugar is more than 300 mg/dl due to any because patients were withdrawn from the study. If the subject in the study suffers from any other disorder that has to be managed prior, like ischemic heart disease or any other major systemic illness, they were dropped from the study mid-while and referred to the appropriate center for management.

7.2. Statistical analysis

Numbers and proportions were used to describe the sociodemographic data of this study. Continuous data of this study were described by using means and standard deviations. A p-value of 0.05 or below was considered statistically significant. Statistical analysis was performed using Graph Pad Instat 5. The parametric test was a paired *t*-test, the Unpaired *t*-test, the non-parametric test was the Wilcoxon signed-rank test, and the Bonferroni multiple comparison test was used for the data analysis. Statistical analysis is mentioned in Tables 1 and 2.

7.3. Safety parameters

Treatment-related adverse events were evaluated. Blood sugar levels determine glycemic control. Notable variations or glycemic control issues were noticed and assessed. A higher risk of cardiovascular problems is frequently connected with diabetes. As a result, variables related to cardiovascular safety, including blood pressure and heart rate, were assessed. Diabetes can affect kidney function and liver function. Liver markers such as SGPT SGOT and renal markers like serum creatinine were done in 12 patients of the trial group.

8. Results

8.1. Study population

550 participants were screened to assess eligibility. Of these 46 patients who withdrew their consent, two hundred ninety met the exclusion criteria and were excluded. Among these 120 eligible participants, 100 were selected for the randomized computer-generated method. Participant distribution is shown in the CONSORT flowchart (Fig. 1).

Table 1
Effect of Therapy before and after treatment.

	Trial Group (Vidangadi Lauha n = 40)		Control Group (Metformin,n = 40)		t	P value
Variables	BT	AT	BT	AT		
Median Age(IQR)	54.5 (35–70)	–	59 (32–70)	–	–	–
Male: Female (%)	14:26 (35–65)	–	20:20 (50-50)	–	–	–
Mean HbA1c (SD)	8.048 (0.9542)	7.14(0.73)[b]	8.3 (0.9923)	7.18 (0.67)[b]	0.2898 (0.2671–0.3581)	[a] 0.7227
Mean BSL-Fasting(SD)	151.65 ± 26.25	117.2 ± 19.428	157.5 ± 27.51	117.2 ± 19.428	7.188 (-5.487 to 11.53)	[a] 0.4766
Mean BSL-Post meal(SD)	248.3 ± 28.699	162.92 ± 42.85	247.52 ± 32.67	162.92 ± 42.85	6.489 (-63.13 to −33.51)	[a] <0.0001
Mean Total leucocyte count	6967 (1755)	7031 (1340)	7682 (1600)	7624 (1245)	2.050 (17.5–1168.9)	[a]0.0437
Mean haemoglobin	11.84 (1.292)	11.95 (1.19)	11.87 (1.558)	12.20 (1.376)	0.8584 (-0.3265–0.8215)	[a]0.3933
Mean ESR	17.85 (13.35)	11.55 (4.846)[b]	15.57 (5.52)	12.85 (5.077)[b]	1.171 (0.9092–3.509)	[a]0.2450
Mean Total cholesterol	192.32 (43.39)	160.07 (44.81)[b]	165.84 (34.72)	150.87 (27.94)[b]	1.102 (-25.82–7.426)	[a]0.2741
Mean HDL	43.03 (9.15)	45.41 (10.73)[b]	43.75 (11.06)	46.52 (11.40)[b]	0.4483 (-3.820–6.040)	[a]0.6552
Mean LDL	105.30 (31.61)	99.73 (38.93)	107.79 (32.92)	104.53 (24.72)	0.6586 (-9.715–19.32)	[a]0.5121
Mean VLDL	43.72 (35.54)	35.82 (26.54)[b]	30.94 (14.33)	26.33 (12.11)	2.059 (-18.68–0.3132)	[a]0.0429
Mean Triglycerides	183.42 (78.72)	145.72 (52.80)[b]	153.11 (60.46)	143.24 (47.91)	0.2196 (-24.92–19.96)	[a]0.8267
Mean Abdominal circumference	94.3 (7.940)	91.96 (7.778)[b]	93.525 (6.571)	92.39 (6.178)[b]	0.2738 (-2.697–3.557)	[a]0.7850
	BT (n = 12)	AT(n = 12)				
SGOT	38.52 ± 12.89	37.09 ± 7.92	Not Done	Not Done	6.337 (-3.545–6.411)	0.5392
SGPT	31.64 ± 15.31	35.66 ± 11.83	Not Done	Not Done	1.52 (-9.85–1.80)	0.1566
Billirubin Total	0.69 ± 0.25	0.64 ± 0.16	Not Done	Not Done	0.8693 (-0.9–0.2)	0.4051
Billirubin direct	0.186 ± 0.091	0.16 ± 0.069	Not Done	Not Done	0.7848 (-0.05–0.10)	0.45
Blood Urea	20.06 ± 7.85	15.1 ± 4.61	Not Done	Not Done	2.233 (0.1210–9.802)	0.045
Creatinine(N = 13)	0.98 ± 0.28	0.87 ± 0.21	Not Done	Not Done	3.744 (0.0508–0.1958)	0.0032
Uric Acid	5.1 ± 1.4	4.81 ± 1.54	Not Done	Not Done	0.6378(-0.539–0.9252)	0.5356
Bowel Symptom Score	30.275 ± 8.077 [b]	13.2 ± 1.265 [b]	23.85 ± 7.530	38.25 ± 6.332	(36.22–40.27)	[a]<0.0001
Quality of Life Score	113.87 ± 11.36 [b]	136.47 ± 8.703 [b]	128.57 ± 7.9	102.32 ± 7.9	99.78–104.87)	[a]<0.0001

[b] P < 0.05 for baseline verses after 90 days within the group. Data are mean ± standard deviation (95 % confidence interval).
[a] Comparison of change between trial group and control group after 90 days.

Table 2
Effect of Therapy on Follow-up parameters.

	Follow up period	Baseline	30th day	60th day	90th day	t (CI)	P value
Trial group	Fasting	151.6 ± 26.2	139.3 ± 25.1	132.4 ± 19.7	117.2 ± 19.4	11.1 (27.81–40.24)	[b] 0.0001
	Post meal	248.3 ± 28.6	227.05 ± 27.397	189.77 ± 20.59	162.9 ± 42.8	11.18 (69.49–100.17)	[b] 0.0001
	BMI	26.195 ± 2.5	25.866 ± 2.5	25.153 ± 2.4	24.45 ± 2.5	1.54–1.9	[b] 0.0001
	Ayurveda Symptom score	29.12 ± 6.68	22.3 ± 4.4	14.7 ± 2.8	6.625 ± 2.9	19.79–25.11	[b] 0.0001 (Wilcoxon)
	Waist hip ratio	0.9325 ± 0.075	0.9195 ± 0.074	0.865 ± 0.1536	0.8687 ± 0.05	0.039–0.07	[b] 0.0001
Control Group	Fasting	157.5 ± 27.51	146.9 ± 25.0	135.62 ± 20.1	114.9 ± 19.2	13.09 (36.266–49.53)	[b] 0.0001
	Post meal	247.52 ± 32.67	224.5 ± 25.30	182.1 ± 26.8	161 ± 22.6	17.835 (76.71–96.34)	[b] 0.0001
	BMI	25.96 ± 2.196	25.78 ± 2.160	25.44 ± 2.1	25.133 ± 2.3	0.42–1.25	[b] 0.0001
	Ayurvedic Symptom score	33.05 ± 7.528	28.325 ± 6.285	21.125 ± 4.5	17.875 ± 4.8	13.36–16.98	[b] 0.0001
	Waist hip ratio	0.88 ± 0.058	0.8795 ± 0.057	0.838 ± 0.20	0.874 ± 0.05	0.001–0.01	[b] 0.0073

[a]Comparison of change between trial group and control group after 90 days.
[b] P < 0.05 for baseline verses after 90 days within the group. Data are mean ± standard deviation (95 % confidence interval).

8.2. Baseline characteristics

The overall median age of the participants in the VL was 54 years (interquartile range [IQR] – 35–70), and that of the participants in the MT was 59 (IQR 32–70). Twenty-six percent were females in the trial group, and 20 % were in the control group. In this study, it was observed that in the trial group, 32.5 %, 32.5 %, 15 %, 10 %, 10 %, 5 %, and in the Control Group, 37.5 %, 35 %, 15 %, 7.5 %,0 %, 5 % patients were belonging to Undergraduate, higher secondary, primary, illiterate, high School, post-graduate educational status respectively. In the trial group, 5 % of patients had a positive family history of diabetes, while 11 % of patients in the MT had a family history.

Most participants in the VL had *Kapha-Pitta Prakriti (13 %),* while most participants in the MT had *Vat-Pitta Prakriti* (11 %). Most participants in the trial and control groups had *Vishamagni* (17 % and 21 %, respectively).

8.3. Effect analysis

VL showed reduction in HbA1c from 8.048(0.95) to 7.14(0.73), (CI, 0.7810 to 1.035; p < 0.0001) while Metformin showed reduction in HbA1C from 8.3(0.99) to7.18(0.67), (CI, 0.9220 to 1.305; p < 0.0001). *VL* improves QOLID score from 113.87(11.36) to 136.47(8.703), (CI, −25.68 to −19.52; p < 0.0001) as compared to Metformin 128.57(7.9) to 102.32(7.9), (CI, 23.19 to 29.39; p < 0.0001). *VL* shows reduction in bowel symptom questionnaire score 30.275(8.077) to 13.2(1.265), (CI, 14.60–19.51; p < 0.0001) as compared to MT from 23.85(7.530) to 38.25(6.332), (CI, −15.99 to −12.80; p < 0.0001).

Mean fasting and post-meal blood sugar levels in both groups decreased significantly over three months of treatment. There was a significant reduction in glycated hemoglobin in both groups. The mean waist-hip ratio before *VL* treatment was 0.9235, with a standard deviation of 0.0751. The mean waist-hip ratio dropped to 0.880 after treatment, indicating that the participant's waist-hip ratio had improved. The after-treatment measures' standard deviation is 0.058, indicating lower variability than the pre-treatment measurements. The P-value of 0.0058 indicated a statistically significant difference between the waist-hip ratios before and after Treatment of *VL*. The VL was more effective in reducing the waist-hip ratio than the MT. Both groups were equally effective in reducing body mass index.

There was a significant reduction in the Ayurveda clinical score in the VL compared to the control group, which suggests more symptomatic relief in VL participants.

No adverse events were observed in the VL and MT participants.

Among the VL participants, nine patients had lost follow-up, and one patient discontinued the intervention due to blood sugar levels exceeding the inclusion. Among the MT participants, six patients had lost follow-up, and four discontinued the intervention due to blood sugar levels exceeding the inclusion.

9. Discussion

In *Ayurveda*, obese type II diabetes mellitus patients can be correlated with *Sthul Madhumeha*. *Ayurveda* assumes the pathogenesis and treatment of obese type 2 diabetes mellitus through a gut-centric approach. There are two main vitiation factors: *Agni* and *Rasa Dhatu*. *Agni* (metabolic power) is a physiological phenomenon in the body responsible for the digestion, absorption, and bio-assimilation of all micronutrients. As per *Ayurveda* classics, *Aama* (toxic material) is produced when there is a disturbance in *Agni* (Digestion). *Rasa Dhatu* is the first primary base for forming all tissues in the body during the process of Digestion. According to *Ayurveda*, all cascades of the pathogenesis of diabetes start in the gut, and disturbances in the formation of *Rasa* occur in the gut [9].

Antidiabetic action of Metformin occurs by reducing and suppressing hepatic glucose production and modulating glucagon-like peptide 1 [10]. If MT is given for a longer duration, there are side effects. Some research papers provide evidence that MT affects the status of vitamins B1, B12, D, folic acid, and magnesium and causes disruption to the microbiome, all of which may, to some extent, predict the desired outcomes with this medication. Given that the status of these micronutrients in patients with T2DM is already likely to be suboptimal and that these deficiencies are variously associated with diabetic complications such as compromised endothelial, microvascular, vascular, and neurological function [11].

VL showed a reduction in bowel symptoms questionnaire score compared to MT. *VL* improves gut health in obese type 2 diabetes mellitus patients. Published research articles showed that the administration of processed herbal medicine lowers the gut microbiota and improves gut health [12]. *VL* improves gut health and acts as hepatoprotective, as no changes were found in the liver function test after three months of treatment.

Some herbs used in the formulation *VL* formulation have alpha-glucosidase inhibitory activity [13], antidiabetic [13,14], anti-dyslipidemia [15,16], hypoglycaemic [17], and beta cell protective activity [18]. Prevention of platelet aggregation and thrombus [19] formation, inhibited the activities of αamylase, α-glucosidase, dipeptidyl peptidase-4 [20], anti-obesity [21], endothelial dysfunction, oxidative stress, and systemic inflammation [22]. Thus, '*VL*' is effective for managing obese type 2 diabetes mellitus and can be helpful in the prevention of multiple complications of type 2 diabetes.

Quality of life is an important assessment tool in diabetes treatment modality. It assesses the patient's physical, mental, and social health status of the patient. *VL* improves the quality of life in type 2 diabetes mellitus diabetes patients. A published study shows the efficacy of various Ayurveda formulations for type 2 diabetes mellitus with reference to glycated hemoglobin and anthropometric parameters [23]. Published evidence for the efficacy of Ayurveda formulations for improving gut health assessed by diabetes bowel symptom questionnaire is lacking. This Trial provides evidence of improvement in gut health of obese type 2 diabetes patients by *VL* as compared to Metformin.

9.1. Limitations of the study

Only a small number of patients had liver and kidney function tests performed. Inflammatory biomarkers in obesity, such as adiponectin, leptin, ghrelin, ferritin, and C-reactive protein, were not measured before and after treatment due to economic constraints. In this study, blood sugar levels were measured at 0, 30, 60, and 90 days of treatment, as the blood sugar level is a variable parameter that should be done frequently, or the CGM system should be used for blood sugar monitoring.

9.2. Future scope

This study is conducted in the Indian population. There is a need to conduct studies in different populations to determine genetic variation or the effect on genetics.

In developing countries, the maximum number of type 2 diabetes cases is in the 40–60 age working group. Cost-effective, safest *Ayurveda* medicine is beneficial to this age group. According to *Ayurveda,* the treatment varies according to *Prakriti* and the status of *Dosha*, *Dushya*, and *Mala* in patients. There is future scope to conduct this study in different kinds of *Prakriti* patients and see the genetic correlation between this.

As type 2 diabetes mellitus is a chronic disease, it is evident that most diabetic patients are diagnosed when complications develop. Complications in type 2 diabetes mellitus develop after five years. Early intervention with VL may prolong diabetic complications;studies this direction can be done in future.

10. Conclusion

VL can be a potential formulation with multi-targeted action for treating newly detected obese type 2 diabetes.

Author credits-

Data Collection, Supervision, and Monitoring- PK, JG.
Conceptualization- AN, PK, JG.
Drafting protocol, drafting the manuscript, Critical Edits, Statistical analysis- AN.

Data availability statement

Trial registered with CTRI. A summary of data is available on CTRI.

Source of funding

We have not received any funding for this study.

Declaration of generative AI and AI-assisted technologies in the writing process

While preparing this work, the author(s) used ChatGPT to edit language. After using this tool/service, the author(s) reviewed and edited the content as needed. The authors take full responsibility for the publication's content.

Declaration of competing interest

Nil.

References

[1] International diabetes federation.IDF diabetes atlas. ninth ed. 2019 Brussels, Belgium https://www.diabetesatlas.org.
[2] Suvarna R, Shenoy RP, Hadapad BS, Nayak AV. Effectiveness of polyherbal formulations for the treatment of type 2 Diabetes mellitus - a systematic review and meta-analysis. J Ayurveda Integr Med 2021;12(1):213–22. https://doi.org/10.1016/j.jaim.2020.11.002.
[3] Banerjee S, Debnath P, Rao PN, Tripathy TB, Adhikari A, Debnath PK. Ayurveda in changing scenario of diabetes management for developing safe and effective treatment choices for the future. J Compl Integr Med 2015;12(2):101–10. https://doi.org/10.1515/jcim-2014-0012.
[4] John R, Pise S, Chaudhari L, Deshpande PR. Evaluation of quality of life in type 2 diabetes mellitus patients using quality of life instrument for Indian diabetic

patients: a cross-sectional study. J Midlife Health 2019;10(2):81–8. https://doi.org/10.4103/jmh.JMH_32_18.
[5] Quan C, Talley NJ, Cross S, et al. Development and validation of the diabetes bowel symptom questionnaire. Aliment Pharmacol Ther 2003;17(9):1179–87. https://doi.org/10.1046/j.1365-2036.2003.01553.x.
[6] Shastri A, editor. Bhaishajya ratnavali,Pramehachikitsa, verse 191. first ed. Varanasi: Chaukhamba prakashan; 2019. p. 737.
[7] Nakanekar A, Kohli K, Tatke P. Ayurvedic polyherbal combination (PDBT) for prediabetes: a randomized double blind placebo controlled study. J Ayurveda Integr Med 2019;10(4):284–9. https://doi.org/10.1016/j.jaim.2018.05.004.
[8] Nisha Munishwar. A clinical study on the management of Sthula Madhumeha vis-A-vis type ii diabetes mellitus with special reference to the effect of herbal compound on blood sugar level. MD Thesis. Nashik: Submited to Maharashtra University of Health Sciences; 2014-2017.
[9] Thottapillil A, Kouser S, Kukkupuni SK, Vishnuprasad CN. An 'Ayurveda-Biology' platform for integrative diabetes management. J Ethnopharmacol 2021;268:113575. https://doi.org/10.1016/j.jep.2020.113575.
[10] Foretz M, Guigas B, Viollet B. Understanding the glucoregulatory mechanisms of metformin in type 2 diabetes mellitus. Nat Rev Endocrinol 2019;15(10):569–89. https://doi.org/10.1038/s41574-019-0242-2.
[11] Wakeman M, Archer DT. Metformin and micronutrient status in type 2 diabetes: does polypharmacy involving acid-suppressing medications affect vitamin B12 levels? Diabetes Metab Syndr Obes 2020;13:2093–108. https://doi.org/10.2147/DMSO.S237454. 2020 Jun 18.
[12] Mane S, Dixit KK, Lathwal N, et al. Rectal administration of buttermilk processed with medicinal plants alters gut microbiome in obese individuals. J Diabetes Metab Disord 2021;20(2):1415–27. https://doi.org/10.1007/s40200-021-00879-z. Published 2021 Aug 20.
[13] Chen X, Gao M, Jian R, et al. Design, synthesis and α-glucosidase inhibition study of novel embelin derivatives. J Enzyme Inhib Med Chem 2020;35(1):565–73. https://doi.org/10.1080/14756366.2020.1715386.
[14] Nalamolu KR, Nammi S. Antidiabetic and renoprotective effects of the chloroform extract of Terminalia chebula Retz. seeds in streptozotocin-induced diabetic rats. BMC Compl Alternative Med 2006;6:17. https://doi.org/10.1186/1472-6882-6-17. 2006 May 7.
[15] Nabi SA, Kasetti RB, Sirasanagandla S, Tilak TK, Kumar MV, Rao CA. Antidiabetic and antihyperlipidemic activity of Piper longum root aqueous extract in STZ induced diabetic rats. BMC Compl Alternative Med 2013;13:37. https://doi.org/10.1186/1472-6882-13-37. 2013 Feb 18.
[16] Bhandari U, Kanojia R, Pillai KK. Effect of ethanolic extract of Embelia ribes on dyslipidemia in diabetic rats. Int J Exp Diabetes Res 2002;3(3):159–62. https://doi.org/10.1080/15604280214278.
[17] Purohit A, Vyas KB, Vyas SK. Hypoglycaemic activity of Embelia ribes berries (50% etoh) extract in alloxan induced diabetic rats. Ancient Sci Life 2008;27(4):41–4.
[18] Bhandari U, Jain N, Pillai KK. Further studies on antioxidant potential and protection of pancreatic beta-cells by Embelia ribes in experimental diabetes. Exp Diabetes Res 2007;2007:15803. https://doi.org/10.1155/2007/15803.
[19] Li JY, Chen RJ, Huang LT, Lee TY, Lu WJ, Lin KH. Embelin as a novel inhibitor of PKC in the prevention of platelet activation and thrombus formation. J Clin Med 2019;8(10):1724. https://doi.org/10.3390/jcm8101724. 2019 Oct 18.
[20] Majeed M, Majeed S, Mundkur L, et al. Standardized Emblica officinalis fruit extract inhibited the activities of α-amylase, α-glucosidase, and dipeptidyl peptidase-4 and displayed antioxidant potential. J Sci Food Agric 2020;100(2):509–16. https://doi.org/10.1002/jsfa.10020.
[21] Salunke M, Deshpande M, Bhalerao S. Experiential documentation of Trimad for its anti-obesity potential: a survey of Ayurvedic physicians from Pune city. J Ayurveda Integr Med 2017;8(3):190–3. https://doi.org/10.1016/j.jaim.2017.03.004.
[22] Pingali U, Nutalapati C, Illendulla VS. Evaluation of the effect of fish oil alone and in combination with a proprietary chromium complex on endothelial dysfunction, systemic inflammation and lipid profile in type 2 diabetes mellitus - a randomized, double-blind, placebo-controlled clinical study. Diabetes Metab Syndr Obes 2020;13:31–42. https://doi.org/10.2147/DMSO.S220046. 2020 Jan 7.
[23] Chattopadhyay K, Wang H, Kaur J, et al. Effectiveness and safety of ayurvedic medicines in type 2 diabetes mellitus management: a systematic review and meta-analysis. Front Pharmacol 2022;13:821810. https://doi.org/10.3389/fphar.2022.821810. 2022 Jun 8.