



Research Article

CLINICAL EVALUATION OF A SIDDHA POLY HERBAL FORMULATION *AZHINJIYATHIKASHAYAM*
IN *MADHUMEGAM* (TYPE – 2 DIABETES) PATIENTS

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ABSTRACT

Azhinjiathikashayam is a herbo mineral Siddha poly herbal formulation said for the management of *Madhumegam* (Type-2 Diabetes mellitus) in ancient Siddha literature. The study drug was subjected to estimate the therapeutic efficacy in *Madhumegam* patients. A well designed study protocol was approved by Institutional Ethics Committee and the clinical study was conducted as an open clinical trial in OPD/IPD of Ayothidoss pandithar Hospital of National Institute of Siddha Chennai.

Based on the inclusion criteria 40 *Madhumegam* patients (Type -2 Diabetes mellitus) were enrolled in this study. Informed consent was obtained from each patient before study initiation. 60ml of *Azhinjiathikashayam* was administered orally before food twice a day for a period of 90 days and advised to follow the prescribed dietary regimen. All the baseline data, Laboratory investigations were recorded in the prescribed Case Report Form of each patient. Blood sugar level in fasting and postprandial was done once in 30 days and HbA1c was done before treatment (0th day) and after treatment (90th day). The clinical assessment was recorded once in 10 days.

Paired 't' test was used to test the significance of treatment using before and after treatment data on HbA1c, Clinical symptoms, Blood sugar fasting and postprandial. The level of significance probability 0.05 was used to test the treatment difference and the values are statistically significant. In this study there is statistically significant difference between before and after treatment on average HbA1c, average blood sugar of fasting and average clinical feature score ($p < 0.0001$).

KEYWORDS: *Madhumegam*, Type -2 Diabetes mellitus, *Azhinjiathikashayam*, Clinical trial, Siddha medicine.

INTRODUCTION

In Siddha system of medicine, *Madhumegam* is a type of *Meganeer* which is characterized by passing of sweet urine as per *Saint Yugi*. Based on the derangement of three vital humours, "*Meganeer*" is classified into twenty types in which four comes under *Vatham*, six under *Pitham* and ten under *Kabam*. The One called *Madhumegam* (Honey urine) comes under *Pitham* type. According to *Yugi* and *Agasthiyar*, the etiology of the disease is due to life style changes, food and deeds. Severity of the disease can be controlled by potent Siddha drugs with dietary regimen and Yoga therapy. As per *Yugi Vaithiyachinthamani* text, the signs and symptoms of *Madhumegam* is Polyuria (excessive urination), Polydypsia (excessive thirst), Polyphagia (excessive appetite), and often accompanied by unusual weight loss can be correlated with Type II Diabetes mellitus. The long term micro and macro vascular complications associated with Diabetes mellitus are responsible for a majority of its morbidity and mortality mentioned in modern science can also be

correlated as well as appreciated in *Yugi Vaithiyachinthamani* under *Avathaigal*.

According to International Diabetes Federation in 2013 globally 381 million people had diabetes. Its prevalence is increasing rapidly, and by 2030, this number is estimated to almost double. According to the International Diabetes Foundation, the disease affects more than 62 million Indians, which is more than 7.1% of India's adult population. An estimate shows that nearly 1 million Indians die due to Diabetes every year. The average age on onset is 42.5 years. The high incidence is attributed to a combination of genetic susceptibility plus adoption of a high-calorie, low-activity lifestyle by India's growing middle class.

The currently available oral anti-hyperglycemic agents for clinical use have characteristic profile of side effects when they administered regularly as a long duration. The management of Diabetes mellitus with agents devoid

of any side effects is still a challenge to the medical field. This had led to an increase in the demand of natural products with anti-hyperglycemic activity having fewer side effects.

Many poly herbal formulations are being practiced in Siddha system of medicine in the treatment of *Madhumegam*. One such formulation is *Azhinjiyathi Kashayam* which is said for *Madhumegam*.^[1] The ingredients present in this formulation is *Phyllanthus emblica* Linn, dried fruit (*Nellimulli*), *Cassia auriculata* Linn, Bark (*Aavarampattai*), *Salacia reticulata*. Wight, Bark (*Kadalazhinjilpattai*), *Terminalia bellirica* Roxb, Thol (*Thandrikkaithol*), *Smilax china* Linn, Bark (*Parangi pattai*) and *Strychnos potatorum* Linn.f, Seed (*Thaetran vithai*). Literature evidences had been identified for the antihyperglycemic activity in each ingredients of this formulation.

When this formulation is subjected to clinical trial in *Madhumegam* (Type 2 Diabetes) patients it is found significant result in reducing Blood sugar level and also the clinical signs and symptoms of *Madhumegam* (Type 2 Diabetes).

MATERIALS AND METHODS

The clinical study was conducted according to the standard protocol, after obtaining the approval of the Institutional Ethical Committee (IEC) (NIS/IEC/2011/3/01-24/12/2011). It is an Open Clinical Trial conducted in Ayothidoss Pandithar Hospital OPD.NO:1 Dept of Maruthuvam (Medicine), National Institute of Siddha, Tambaram sanatorium, Chennai.

Subject selection

Patients reporting at the OPD of Ayothidass Pandithar Hospital with symptoms of inclusion criteria will be subjected to screening test and documented by using screening proforma. After screening of 102 patients diagnosed as *Madhumegam* (Type 2 Diabetes mellitus), 40 cases were selected to this trial. Before enrollment into the trial the informed consent was obtained from all the study participants.

Inclusion criteria

- ❖ Age : 30-60Yrs
- ❖ Gender: Male & Female
- ❖ Patients with HbA1C level > 6.5%.

OBSEVATIONS

Age group

OP Cases	Sex	Age		
		30-40	41-50	51-60
Patients	Male	13	8	9
	Female	2	5	3
Total in number and Percentage		15 (37.5%)	13 (32.5%)	12 (30%)

The age group between 30 and 40 were 15 cases (37.5 %) between 41 and 50 were 13 cases (32.5 %) and between 51 and 55 were 12 cases (30 %).

- ❖ Patients who are willing to give blood sample.

Exclusion criteria

- ❖ IDDM (Insulin Dependent Diabetes Mellitus)
- ❖ Cardiac disease
- ❖ Chronic kidney diseases
- ❖ Thyroid dysfunction
- ❖ Gestational diabetes diseases

Withdrawal criteria

- ❖ Intolerance to the drug & development of any serious adverse reactions during drug trial.
- ❖ Poor patient compliance & defaulters.
- ❖ Patient turned unwilling to continue in the course of clinical trial.
- ❖ Increase in severity of symptoms.
- ❖ Uncontrolled blood sugar level

Conduct of the study

All the patients were given unique registration card in which patient's Registration number of the study, Address, Phone number and number etc. All the baseline data, vitals, clinical signs and symptoms (Increased frequency of Urination (polyuria), Thirst (polydipsia), Excessive hunger (polyphagia), Body pain, Tiredness, Burning feet, Generalized/genital pruritis, Dull pain in the testis, Yellow coloured urine) and laboratory data (Haematology, Blood biochemistry, Lipid profile, LFT& RFT, HbA1c, Urine analysis and *Ennvagaithervugal*) were recorded in the Case Report Form (CRF) before (i.e., 0th day), commencement of the trial.

The study drug packages contain 200 gms of *Azhinjiyathi Kashayam* powder sachets. Patients were advised to make *Kashayam* (10 gm powder was put in to 240 ml of water, then it was boiled until it reduces into 1/4th as Decoction) and take 60ml before food every day for two times for 90 days. At each visit (once in 10 days for 90 days) the patients were given the above drug packages for 10 days of treatment. At each visit the patients were advised to bring back the unconsumed drugs and return to the investigator. Each visit, the patient's vitals and clinical assessments were recorded in the case report form by the investigator. Laboratory investigations were done at the end of the treatment.

Sex Distribution

Patients	No of cases	Percentage (%)
Male	30	75%
Female	10	25%

Among 40 cases, 30 cases (75%) were Male and 10 cases (25%) were Female.

Educational Status

Education status	No of cases	Percentage (%)
Illiterate	14	35
Literate	26	65

14 patients (35 %) were Illiterate, 26 patients (65 %) were Literate.

Occupation Status

Occupation	No of cases	Percentage (%)
Driver	5	12.5
Business man	16	40
House wife	10	25
Post man	2	5
Manual workers	7	17.5

Among 40 cases 5 patients (12.5 %) were Drivers, 16 patients (40 %) were Business man, 10 cases (25 %) were House wives, 2 patients (5 %) were Post men, and 7 patients (17.5 %) were Manual workers.

Marital Status

Marital status	No of cases	Percentage (%)
Unmarried	3	7.5
Married	37	92.5

Out of 40 cases 3 patients (8 %) were Unmarried, 37 patients (92.5 %) were married.

Socio- Economic Status

S.No	Economic status	No of cases	Percentage (%)
1.	Poor	8	20
2.	Middle class	26	65
3.	Rich	6	15

Among 40 patients, 8 cases (20 %) were under poor socio- economic status and 26 cases (65 %) were from middle class family and 6 cases (15 %) were from upper class.

Menopausal Status

Menopause	No of cases	Percentage (%)
Not yet attained	6	60
Attained	4	40

Among 10 female study participants, 6 patients (60 %) were not yet attained menopause and 4 (40 %) patients were Attained menopause.

Family History

Family history	No of cases	Percentage (%)
Family history	22	55
No family history	18	45

Among 40 Patients, 18 cases (45%) had positive family history of type 2 diabetes.

Personal Habits

Personal habits	No of cases	Percentage (%)
Smokers	6	15%
Alcoholic	12	30%
Non smokers & Non Alcoholic	22	55%

15% of patients (6) were smokers, 30% (12) patients were alcoholic, and 55% (22) cases were Non smokers & Non Alcoholic.

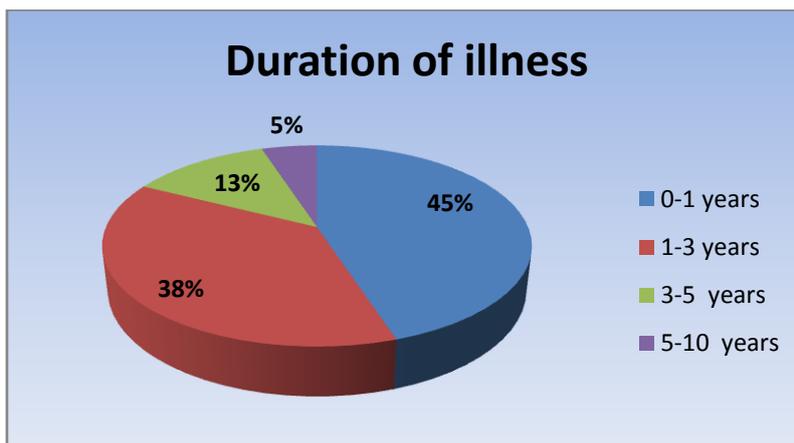
Food Habits

Food habits	No of patients	Percentage (%)
Vegetarian	10	25
Non vegetarian	30	75

75% of cases were Non vegetarians and 25 % were vegetarians.

Duration of Illness

Fig.1



Among the 40 known diabetic patients, 18 (45 %) cases were diabetic within 1 year. 15 (37.5 %) patients were between 1 and 3 years and 5 (12.5 %) patients were between 3 and 5 years and 2 (5 %) patients were between 5 and 10 years.

Clinical signs and symptoms

Among 40 cases, during 1st visit, polyuria was in 20 cases (50 %), Polydipsia in 16 cases (40 %), polyphagia in 15 cases (37.5 %), nocturia in 12 cases (30 %), Tiredness in 28 cases (70%) Body pain in 12 cases (30 %), Weight gain in 6 cases (15 %), pain and burning sensation of sole in 6 case (15 %) and pruritis in genitals in 1 case (2.5%).

RESULTS

Table 1: Clinical symptoms of *Madhumegam* before treatment and after treatment

Clinical features	No of cases		Improvement (%)	
	Before treatment	After treatment	Before treatment	After treatment
Polyurea	37	20	92.5	50
Nocturia	32	12	80	30
Polydipsia	28	16	70	40
Polyphagia	30	15	75	37.5
Body pain	28	12	70	30
Weight gain	6	2	15	5
Tiredness	38	28	95	70
Burning feet	16	6	40	15
Genital pruritus	5	1	10	2.5

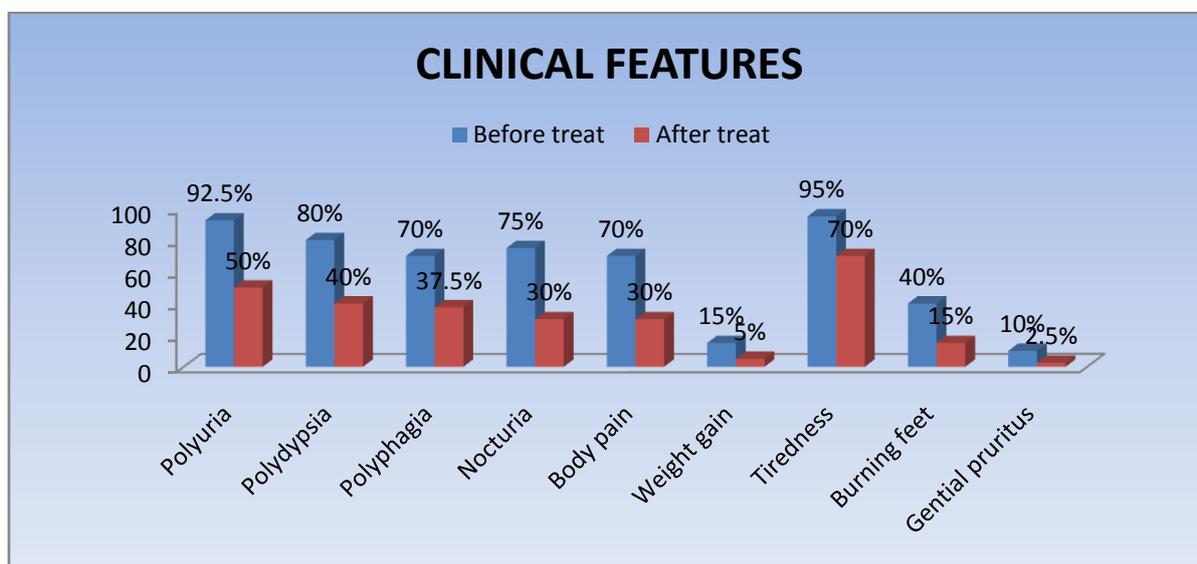
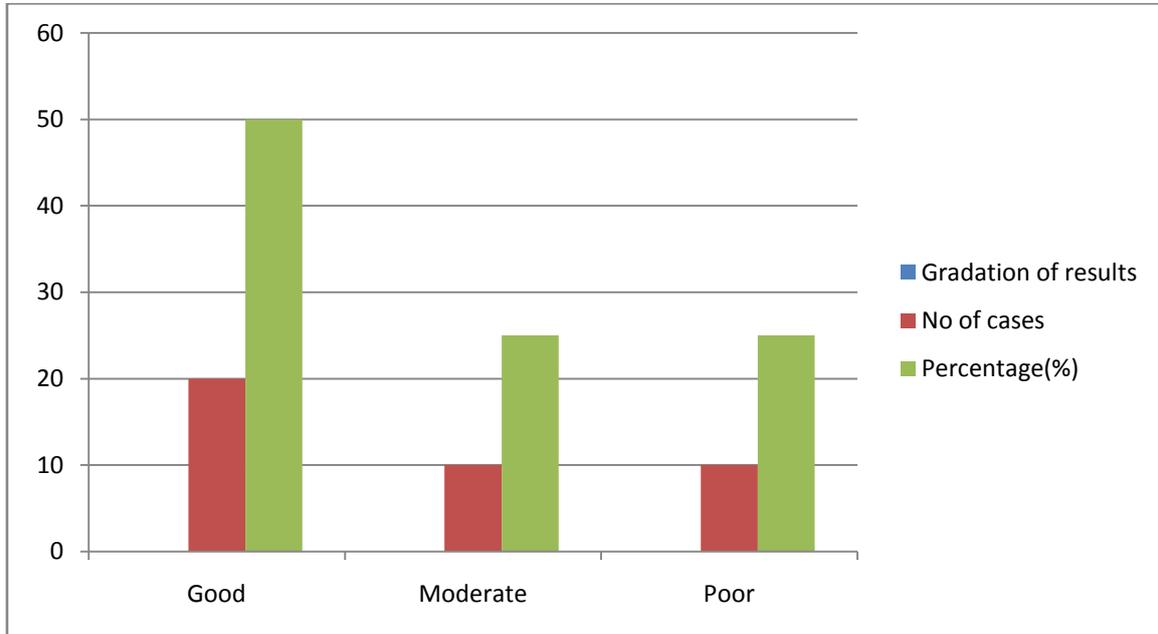


Table 2: Gradation Of Results

S.No.	Gradation of results	No of cases	Percentage (%)
1.	Good	20	50
2.	Moderate	10	25
3.	Poor	10	25
Total		40	100



Inference

Diagram shows that 50% (20) of cases had good control, 25% (10) of cases had moderate and 25% (10) of cases had poor control.

Good control: HbA1c - 6.1%-7% (20 cases i.e., 50%)

Moderate control: HbA1c- 7.1%-8% (10 cases i.e., 25%)

Poor control: HbA1c- >8% (10 cases i.e., 25%)

Statistical Analysis

All collected data were entered into computer using MS Excel software. The data entry was cross-checked manually with CRF. The data was analyzed using SPSS version 18.0 software. The probability value 0.05 was taken as significant level. Paired 't' test was employed to determine the significance of blood sugar at before and after treatment.

Table 3: Mean ± Standard deviation of HbA1c - Before and after treatment

Treatment status	Mean ±Std deviation	Significance
HbA1c – before	8.39 ±1.41	t = 11.4, p <0.0001 Significant
HbA1c – after	7.45 ±1.24	

The average HbA1c at the start of treatment and after the treatment were 8.39 and 7.45 respectively and it is significant.

Table 4: Mean ± Standard deviation of Blood sugar at FA- Before and after treatment

Treatment status	Mean ±Std deviation	Significance
FA – before	162.15 ±48.11	t = 2.6002, p <0.0128 Significant
FA – after	147.74 ±40.92	

The average blood sugars (FA) at the start of treatment and after the treatment were 162.15 and 147.74 respectively and it is significant.

Table 5: Mean ± Standard deviation of Blood sugar at PP- Before and after treatment

Treatment status	Mean ±Std deviation	Significance
PP – before	248.35 ± 59.86	t = 0.560, p =0.058
PP – after	244.75±66.24	

The average blood sugars (pp) at the start of treatment and after the treatment were 248.35 and 244.75 respectively.

Table 6: Mean ± Standard deviation of clinical feature score - Before and after treatment

Treatment status	Mean ±Std deviation	Significance
Clinical feature – before	5.37 ±1.49	t = 8.411, p <0.0001 Significant
Clinical feature– after	3.47 ±1.46	

The average clinical feature score at the start of treatment and after the treatment were 5.37 and 3.47 respectively and it is significant.

There is statistically significant difference between before and after treatment on average HbA1c, average blood sugar of FA and average clinical feature score (p<0.0001).

DISCUSSION

Diabetes is a common disease, with major global health consequences. World wide prevalence is expected to increase 300 million people by 2025; 90% of these people will have type 2 diabetes. It is the most common type of diabetes representing about 85% of cases in most caucasion populations and western countries, but more than 95% of diabetes in developing countries.^[2] India is now the country with the most diabetic people, and Indian migrants in many parts of the world have a higher frequency of diabetes than the indigenous population has.

There has been a progressive rise in the prevalence of diabetes in India since the 1970s, with increase from about 2% to 12% in urban populations. In many regions, diabetes is more common in urban than in rural populations. Type 2 Diabetes is usually a disease of the middle aged or elderly. Most subjects are diagnosed after the age of 40 years, the peak age of onset in developing countries being about 60 - 70 years.

Various clinical risk factors are associated with the disease, such as increasing age, obesity, physical inactivity a family history of diabetes and racial and geographical variations in the frequency. Social deprivation, unemployment and poverty in city dwellers may cosegregate with diabetogenic lifestyle factors, such as decreased physical activity, westernized diet and obesity.

Obesity contributes to diabetes by causing insulin resistance, the best relationship being with the amount of visceral fat. About 80% of type 2 diabetic patients are obese. Obesity and under activity are maior risk factors for developing this type of diabetes. A BMI >35 KG/M2 increases the risk of type 2 diabetes developing over a 10 year period by 80 fold, as compared with those with a BMI <22 kg/m2. type 2 diabetes is now becoming a problem in children with an increasing frequency in many countries that is paralleled by the increase in ors,

though many have positive family history of type 2 diabetes.

Irrespective of personal habits the disease affects all groups such as smokers, alcoholic, non smokers and non alcoholic. Cigarette smoking markedly enhances CVD risk in diabetes and should be discouraged vigorously. Stopping smoking is at least as effective in reducing CVD in diabetes as reducing cholesterol and controlling blood pressure and glycaemic. Regular exercise can reduce long – term mortality by 50-60% in type2 diabetic people compared with patients with poor cardio respiratory fitness. In long duration type 1 diabetes nephropathy and heart disease are common, whereas in type 2 diabetes most deaths are due to cardio vascular disease.

Glycated haemoglobin percentage is a measure of integrated glycaemic control over the preceding 2 -3 months, and especially the last month. In clinical practice, HbA1c provides a objective measure of long term glycaemic control in a single measurement.

The ingredients of *Azhinjiyathi Kashayam* namely *Phyllanthus emblica* Linn, dried fruit (*Nellimulli*), *Cassia auriculata*. Linn, Bark (*Aavarampattai*), *Salacia reticulata*. Wight, Bark (*Kadalazhinjilpattai*), *Terminalia bellirica* Roxb, Thol (*Thandrikkaithol*), *Smilax china* Linn, Bark (*Parangi pattai*) and *Strychnos potatorum*. Linn.f, Seed (*Thaetran vithai*), have been identified for the antihyperglycemic activity in various research articles. *Phyllanthus emblica* possesses anti-oxidant, hypoglycaemic, antihyperlipedimic effects. Chandrashekar CN, et al^[3] reported that *Salacia reticulata* extract of bark or core root alone are more effective in decreasing blood glucose level in alloxan induced diabetic rats. *In vitro* studies confirmed scavenging activity of free radicals, superoxide and hydrogen peroxide. Oral administration of methanolic extract of *Cassia auriculata* bark of 250 mg/kg showed a significant reduction was observed in the blood glucose level of streptozotocin induced diabetic rats^[4].

Mahendra Shiradkar et al^[5] reported that, the methanolic extract of *Cassia auriculata* bark were found to posses promising anti-diabetic, antimutagenic and anti-fertility activities in streptozotocin induced diabetic rats. *Terminalia*

bellirica extract (100mg/kg, body weight) significantly decreased serum glucose level in hyperglycaemic animals^[6]. The hydro alcoholic and aqueous extract of *Smilax china* Linn (1g/kg) produces a significant reduction in blood glucose levels in alloxon- induced diabetic rats^[7]. Biswas A et.al^[8] evaluated the antidiabetic effect of seeds of *Strychnos potatorum* Linn. in a model of diabetes mellitus using streptozotocin (40 mg/kg b.w., i.p.). The antidiabetic effects were compared with glipizide as the reference hypoglycemic drug. *Strychnos potatorum* Linn. (100 mg/kg p.o.) Significantly reduced fasting blood sugar, the effects being comparable with glipizide (40 mg/kg, p.o.), an established hypoglycemic drug. The anti diabetic effect of each ingredient in this formulation is due the presence of potent phytoconstituents.

CONCLUSION

In this clinical study, the Siddha medicine *Azhinjiyathikashayam* a poly herbal formulation was effective in reducing the Blood sugar level in *Madhumegam* (Type-2 diabetes) patients, and did not produce any adverse drug reactions during long term administration in diabetes patients. This may also prevent the development of complications in Diabetes as the drug is purely a herbal based medicine and it is safe to administer in chronic cases.

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Conflict of interest: None Declared

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