

A cross-sectional study on the role of stress in hyperglycemia and the effect of *Mahatiktaka Kashaya* (an Ayurvedic formulation) in its management

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Abstract

Background: Stress is a potential contributor to chronic hyperglycemia. *Pitta Prakriti* (body constitution) individuals are more prone to stress and the prevalence of type 2 diabetes in stressed out individuals is much more. Aim of study was to evaluate the role of stress in hyperglycemia in individuals of *Pitta* predominant constitution and to assess the effectiveness of *Mahatiktaka Kashaya* in stress-induced hyperglycemia. **Methodology:** A cross-sectional study was carried out in 100 *Pitta* predominant patients having fasting blood sugar level greater than 140 mg/dl, to find the association of stress and hyperglycemia, using International Stress Management Association questionnaire followed by open labelled clinical trial with *Mahatiktaka Kashaya* (Decoction). Trial drug was administered at a dose of 15 ml twice daily for 14 days. Assessment was done before and after the treatment. **Observation and Analysis:** 80% of *Pitta* predominant individuals have reported stress-associated hyperglycemia. Overall effect of *Mahatiktaka Kashaya* in major domains of Stress Assessment Questionnaire, i.e., symptoms, stability and strategies was significant. Furthermore, the trial drug showed significant improvement in biochemical parameters of diabetes. **Conclusion:** The study concludes that there is significant association between stress and hyperglycemia in the individuals of *Pitta* constitution. *Mahatiktaka Kashaya* is found to be highly significant in stress-associated hyperglycemia in the above said group.

Keywords: Hyperglycemia, *Mahatiktaka Kashaya*, *Prakriti*, *Prameha*, stress, type 2 Diabetes

Introduction

“Stress” can be defined as any situation which tends to disturb the equilibrium between a living organism and its environment.^[1] Stress is a part of life and is necessary for providing challenge to physiological and psychological development. However, too much stress over a period of time combined with poor coping habits may cause physical, chemical and hormonal imbalances in the body, thus leading to disease and death if left unchecked.^[2] Stressors can be divided into two categories, external and internal causes. Family and relationship stressors, work stressors, etc., come under external causes and factors such as uncertainty or worries, low self esteem, self criticism, excessive anger and unrealistic expectations come under internal causes.^[3] Stress is a potential contributor to chronic hyperglycemia in *Madhumeha* (type 2 diabetes). Exposure to stress stimulates the hypothalamic–pituitary–adrenocortical (HPA) axis causing

release of various hormones, resulting in elevated blood glucose level.^[4] It has major effects on metabolic activity as well. Signs of stress can be defined at cognitive, emotional, physical or behavioral level.^[5]

In ayurvedic classics, *Prakriti* (psychosomatic constitution) is the sum total of anatomical, physiological and psychological factors, which plays an important role in the prognosis of disease and response to the treatment. It is a genetically transmitted trait.^[6] *Pitta* predominant constitutions are said to be more vulnerable to psychological stress.^[7] The prevalence of type 2 diabetes in stressed individuals is 2.6% in males

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and 2.1% in females. Significantly larger proportion of type 2 diabetes individuals had severe stress scores (23.4% vs. 10%; $P < 0.001$) compared to healthy controls.^[8]

Mahatiktaka is a *Ghrita Yoga* (ghee-based formulation) mentioned in *Kushtha Chikitsa*.^[9] In routine clinical practice also, the *Kashaya* (decoction) form of this formulation is found to be effective in *Madhumeha*, especially when associated with stress. Further, it is ideal to prescribe *Kashaya* form of any preparation for long-term usage, especially in *Kleda* (excretory portion of body fluids)-predominant clinical conditions. The *Kashaya* formulation ensures *Kleda Shoshana* (reduction of *Kleda*) by virtue of its inherent action of taste. *Mahatiktaka Kashaya* is also practised for long term effectively in major types of *Kushtha* (skin disorders) which is also a *Kleda* (liquid waste product) predominant disease. The *Kashaya Yoga* is found to be more cost-effective when compared with medicated *Ghrita* in routine clinical practice. *Amalaki* juice (*Embllica officinalis* Gaertn.) is the main ingredient in this formulation and is widely practiced for various mental illness. Details of the formulation are enlisted in Table 1.

As stress has a significant impact on hyperglycemia, it needs to be addressed. Very limited research works are carried out in relation to *Prakriti*-based treatment strategy. Hence, a cross-sectional study was planned in this background to find the association between stress and hyperglycemia in individuals of *Pitta* constitution. A clinical study was also conducted in this milieu to evaluate the effect of *Mahatiktaka Kashaya* in stress-associated hyperglycemia in *Pitta*-predominant constitution.

Aims and objectives

1. To evaluate the role of stress in hyperglycemia in the individuals of *Pitta*-predominant constitution
2. To assess the effectiveness of *Mahatiktaka Kashaya* in stress-induced hyperglycemia.

Methodology

Two types of study design were used in the current work. A cross-sectional study and an open clinical trial were conducted in patients visiting the outpatient department of Kayachikitsa, Vaidyaratnam P.S. Varier Ayurveda College, Kottakal, Kerala, India.

Table 1: Ingredients of Mahatiktaka Kashaya

Sanskrit name	Botanical name	Part used	Quantity
<i>Saptacchadha</i>	<i>Alstonia scholaris</i> Linn	<i>Twaka</i> (bark)	1 part
<i>Parpata</i>	<i>Hedyotis corybosa</i> Linn	<i>Samoola</i> (whole plant)	1 part
<i>Aragwada</i>	<i>Cassia fistula</i> Linn	<i>Twaka</i> (bark)	1 part
<i>Katuki</i>	<i>Picrorhiza kurroo</i> Royle ex Benth	<i>Samoola</i> (Whole plant)	1 part
<i>Vacha</i>	<i>Acorus calamus</i> Linn	<i>Kanda</i> (rhizome)	1 part
<i>Haritaki</i>	<i>Terminalia chebula</i> Retz	<i>Phala Twaka</i> (fruit pericarp)	1 part
<i>Amalaki</i>	<i>Embllica officinalis</i> Gaertn	<i>Phala Twaka</i> (fruit pericarp)	2 part
<i>Vibitaki</i>	<i>Terminalia bellirica</i> Roxb	<i>Phala Twaka</i> (fruit pericarp)	1 part
<i>Padmakam</i>	<i>Prunus poddum</i> Franch	<i>Kashta</i> (stem)	1 part
<i>Patha</i>	<i>Cyclea peltata</i> Hook. Fil and Thoms	<i>Kanda</i> (rhizome)	1 part
<i>Haridra</i>	<i>Curcuma longa</i> Linn	<i>Kanda</i> (rhizome)	1 part
<i>Darvi</i>	<i>Coscinium fenestratum</i> (Gaertn) Colebr	<i>Kashta</i> (stem)	1 part
<i>Sariva</i>	<i>Hemidesmus indicus</i> Linn	<i>Mula</i> (roots)	1 part
<i>Shatavari</i>	<i>Asparagus racemosus</i> Willd	<i>KandhaI</i> (rhizome)	1 part
<i>Patola</i>	<i>Trichosanthes lobata</i> Roxb	<i>Patra</i> (leaves)	1 part
<i>Bramhi</i>	<i>Bacopa monnieri</i> Linn	<i>Samoola</i> (Whole plant)	1 part
<i>Vishala</i>	<i>Citrullus colocynthis</i> Linn	<i>Samoola</i> (Whole plant)	1 part
<i>Pippali</i>	<i>Piper longum</i> Linn	<i>Phala</i> (fruits)	1 part
<i>Gajapippali</i>	<i>Scindapsus officinalis</i> Schoott	<i>Mula</i> (roots)	1 part
<i>Nimba</i>	<i>Azadirachta indica</i> A. Juss	<i>Twaka</i> (bark)	1 part
<i>Chandana</i>	<i>Santalum album</i> Linn	<i>Sara</i> (heart wood)	1 part
<i>Yashimadhu</i>	<i>Glycyrrhiza glabra</i> Linn	<i>Kashta</i> (stem)	1 part
<i>Ashwattha</i>	<i>Ficus religiosa</i> Linn	<i>Twaka</i> (bark)	1 part
<i>Kutaja</i>	<i>Holarrhena antidysenterica</i> Roxb	<i>Twaka</i> (bark)	1 part
<i>Guduchi</i>	<i>Tinospora cordifolia</i> Willd	<i>Kashta</i> (stem)	1 part
<i>Kiratatikta</i>	<i>Swertia chirata</i> Linn	<i>Samoola</i> (whole plant)	1 part
<i>Ushira</i>	<i>Vetiveria zizanioides</i> Linn	<i>Mula</i> (roots)	1 part
<i>Vasa</i>	<i>Adhatoda vasica</i> Nees	<i>Patra</i> (leaves)	1 part
<i>Murva</i>	<i>Andrographis paniculata</i> Wall. Ex Nees	<i>Mula</i> (roots)	1 part
<i>Ativisha</i>	<i>Aconitum heterophyllum</i> wall	<i>Kanda</i> (rhizome)	1 part
<i>Musta</i>	<i>Cyperus rotundus</i> Linn	<i>Samoola</i> (whole plant)	1 part
<i>Duralabha</i>	<i>Fagonia cretica</i> Linn	<i>Samoola</i> (whole plant)	1 part

Cross-sectional study design

This was carried out to find the association of stress and hyperglycemia among *Pitta*-predominant individuals.

Sample size

One hundred patients (25–60 years age group).

Inclusion criteria

- *Pitta*-predominant individuals with fasting blood sugar (FBS) level above 140 mg/dl
- Age between 25–60 years irrespective of gender and religion
- With informed consent.

Exclusion criteria

Patients having psychiatric illness and undergoing antipsychiatric medication.

Survey tools

1. Specially formulated questionnaire for *Prakriti* analysis It includes 10 major characters of all the three constitutions
2. International Stress Management Association (ISMA) questionnaire.^[10]

To calculate the stress score, ISMA questionnaire containing 25 questions was used. According to the symptoms present in the individuals, the score is given. The score above 14 is suggestive of stress and stress-related diseases.

Open labelled clinical trial

The trial drug *Mahatiktaka Kashaya* was given for 14 days in 30 patients. Assessment was done before and after the treatment. Total scores before and after the medication were statistically analyzed.

Study design – Open labelled randomized clinical trial.

Age group – 30–60 years.

Dose – 15 ml.

Administration – With 45 ml lukewarm water twice daily before food.

Investigations

- FBS
- Postprandial blood sugar (PPBS).

Inclusion criteria

- Patients having blood sugar level (FBS 140–200 mg/dl) fulfilling criteria for *Pitta*-predominant constitution after getting informed consent
- ISMA stress score >14
- Age between 30 and 60 years.

Exclusion criteria

- Patients having psychiatric illness and under antipsychiatric medications
- Gestational diabetes
- Juvenile diabetes
- FBS >200 mg/dl
- Pregnant and lactating women.

Assessment

1. Evaluation of stress through Stress Assessment Questionnaire (SAQ) before and after the treatment
2. Assessment of biochemical parameters like FBS and PPBS before and after the treatment.

Interpretation of the data

The outcome was measured, and data were statistically analyzed using student “*t*”-test with two-tailed paired sampling.

Ethical clearance – IEC/CL/06/12 dated 19/05/12.

Observation and analysis

Cross-sectional study

One hundred individuals of *Pitta*-dominant *Doshika* constitution were selected for the study. Of the 100 individuals, 55 had FBS in-between 140 and 160 mg/dl, 29 within the range 160–180 mg/dl and 16 within the range of 180–200 mg/dl of FBS. Majority of the individuals were having FBS in-between 140–160 mg/dl. Fifty-five percent had PPBS within the range 200–225 mg/dl, 20% within the range of 225–250 mg/dl, 14% within the range 250–275 mg/dl and 11% within the range of 275–300 mg/dl of PPBS, respectively. Of 100 people, 80% had ISMA stress score >14 and the remaining 20% had stress score <14.

Among 85% of total *Pitta* predominance *Prakriti* persons (with *Pitta* character ≥ 7), 18% were having FBS >170 and 67% were having FBS between 170 and 120. Among them, 76% were having stress score >14 and 9% <14. Forty-nine percent of the *Pitta Prakriti* with stress score ≥ 14 were having FBS ≥ 170 and 31% of *Pitta Prakriti* with stress score ≥ 14 were having FBS between 170 and 120 (mg/dl). In the present study, the association between stress and hyperglycemia and between *Pitta Prakriti* and hyperglycemia was calculated and a significant association was observed. 80% of *Pitta*-predominant individuals have reported stress-associated hyperglycemia [enlisted in Tables 2-4].

Table 2: Association between *Pitta Prakriti* and fasting blood sugar level

FBS	<i>Pitta</i> character		Total	χ^2	P
	>7	<7			
>170	18	04	22	13.82	<0.001
<170	67	11	78		
Total	85	15	100		

FBS: Fasting blood sugar

Table 3: Association between stress and fasting blood sugar level

FBS	<i>Pitta</i> character		Total	χ^2	P
	>7	<7			
>170	49	04	53	10.82	<0.001
<170	31	16	47		
Total	80	20	100		

FBS: Fasting blood sugar

Open labelled clinical trial

Effect of therapy showed significant result in biochemical values. 11.87% and 14.6% relief were observed in FBS and PPBS respectively [Table 5].

Overall effect in major domains of SAQ are 5.85% relief in symptoms, 4.76% improvement in stability and 16.34% improvement in strategies, respectively. Mean BT score was reduced from 21.21 to 19.96 with 5.85% relief. The improvement found in this domain is mainly due to the psychological counseling (psycho-education) given to the patient during the period of intervention [Tables 6, 7 and Graph 1].

Discussion

Stress and hyperglycemia

Role of stress in the onset of type 2 diabetes in individuals predisposed to diabetes and in blood glucose control in people with established diabetes is already proved.^[11] Activation of HPA axis causes release of increased amounts of glucocorticoids, in particular cortisol, enhances gluconeogenesis in the liver and diminishes cellular glucose uptake. It also leads to immunosuppression.^[12] Stress-induced release of growth hormone can also decrease glucose uptake and fi-endorphin will suppress insulin secretion and elevate glucose levels.^[13] Therefore, stressful stimuli has impact on glucose levels through numerous pathways. Eventually, elevated blood glucose levels by themselves impair the ability of pancreas to respond to glucose stimulus.^[14] Stress management and progressive muscle relaxation have been shown to be very effective in the treatment of disorders with a psychophysiological component.^[15]

Discussion on demographic data

Cross-sectional study

Among 100 participants, majority of participants (48%) belong to 40–50 years of age group. Female participants accounts for 53% and male participants constitute 47% of survey population. Moreover, the prevalence of moderate stress was estimated to be highest in the 40–44 years age group. The major stress sources were parenting, relationship, incident and work.

A significant association between stress and hyperglycemia was detected in individuals of *Pitta* constitution. Among the

three types of constitution, *Pitta Prakriti* individuals are more prone to stress and other emotional disturbances, as they are described as *Klesha Asahishnava* (inability to face difficult situation) and *Kshiprapraprasada* (short tempered and easily delighted).^[16] Among various types of *Pitta*, mainly *Saadhaka Pitta* plays a role in immediate response and has a close association with the psychological functioning of

Table 4: Association of blood sugar level with *Pitta Prakriti* and stress

Parameters	Score (%)	FBS level (mg/dl)
<i>Pitta</i> character >7	49	≥170
Stress score >14	39	120-170

FBS: Fasting blood sugar

Table 5: Percentage of improvement in blood sugar level

Parameters	Mean score		SD	Percentage of relief	t	P
	BT	AT				
FBS	166.03	146.33	13.56	11.87	7.96	<0.001
PPBS	232.43	199.17	25.73	14.3	7.08	<0.001

BT: Before trial, AT: After trial, SD: Standard deviation, FBS: Fasting blood sugar, PPBS: Postprandial blood sugar

Table 6: Effects of *Mahatiktaka Kashaya* in major domains of stress assessment questionnaire

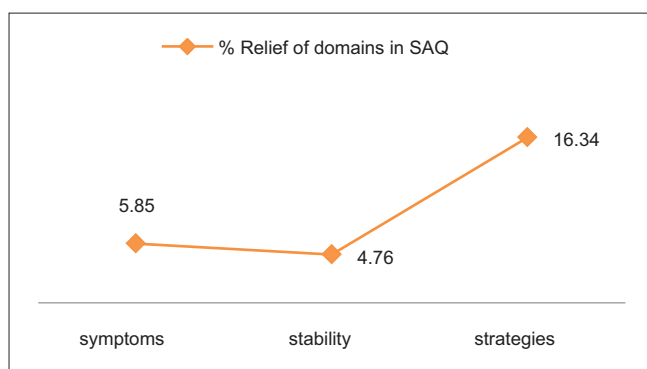
Parameters	Mean score		SD	Percentage of relief	t	P
	BT	AT				
Symptoms						
Emotion	6.83	5.4	1.22	20.94	6.42	<0.001
Behavior	7.16	5.20	0.99	27.45	10.78	<0.001
Physical	7.33	5.57	0.89	24.11	10.78	<0.001
Stability						
Procrastination	7.06	5.73	1.09	17.5	6.68	<0.001
Perfectionism	6.73	5.53	1.09	17.83	6	<0.001
Self-esteem	7.27	5.8	5.8	7.27	7.07	<0.001
Depression	7.43	5.46	0.85	26.47	12.69	<0.001
Anxiety	7.43	5.57	1.07	25.12	9.52	<0.001
Strategies						
Social support	4.06	6	1.46	47.89	7.25	<0.001
Self-regulation	4.28	5.93	1.24	39.06	7.36	<0.001
Problem-solving	4.57	6.53	1.33	43.07	8.12	<0.001
Distraction	4.27	6.27	1.44	46.87	7.61	<0.001
Health	4.7	7.7	1.8	63.83	9.12	<0.001

BT: Before trial, AT: After trial, SD: Standard deviation

Table 7: Overall effect of *Mahaatiktakam Kashayam* on symptoms, stability and strategies

Features	BT	AT	SD	Percentage of relief	t	P
Symptoms	21.21	19.96	0.58	5.85	11.6	<0.001
Stability	35.52	33.82	1.01	4.76	9.06	<0.001
Strategies	21.79	25.34	2.11	16.34	9.05	<0.001

BT: Before trial, AT: After trial, SD: Standard deviation



Graph 1: Percentage relief of domains in SAQ (in open trial)

the body.^[17] Moreover, in the etiopathogenesis of *Paittika Prameha*, involvement of *Santapa* (grief), *Shrama* (exertion) and *Krodha* (anger) are explained.^[18] Anger, particularly anger temperament, is associated with the onset of type 2 diabetes. Due to the abovesaid reasons, *Sadhaka Pitta* gets vitiated very faster, which is directly connected with the formation of *Ojas* and leads to *Ojakshaya*. In this situation, the person cannot respond appropriately to a given situation, named stress. Continuous stress alters the quality of *Apara Ojas* (innate immunity). This will result in the faster manifestation of *Pittaja Prameha* (stress diabetes) due to *Ashukaritwa* (rapid action) of *Pitta*.^[19]

Clinical trial

Maximum number of patients were in 40–50 years age group. 100% of participants reported fluctuating FBS level and 80% were free from family history of diabetes. 70% had unhealthy food habits and low exercise levels.

Mahatiktakakashaya is found to be highly significant in stress-associated hyperglycemia in *Pitta* constitution. *Mahatiktaka Gritha* is effective in various ailments including *Unmaada* (insanity), *Apasmara* (epilepsy), *Kushtha* (skin disease), *Hridroga* (heart disease), and in all *Pitta Vikaara* (disorders due to imbalance in *Pitta Dosha*). This is widely practiced for psychological conditions as well. In a dissertation study on the efficacy of *Mahatiktaka Gritha* in *Krodha* (anger) with special reference to *Paittika Unmaada* (insanity), significant effect was noticed.^[20] As the current work is on *Madhumeha*, it is better to administer the above *Yoga* in *Kashaya* form. In *Madhumeha* (*Prameha*) where the patient is not suitable for *Shodhana* (purification), *Shamana chikitsa* (pacification), in the form of *Kashaya* or *Mantha* can be administered.^[21] Hence, *Mahatiktaka Gritha* formulation was modified to *Kashaya Kalpana* and administered. As the *Yoga* has *Sheeta* (cold) and *Kleda Shoshana* (obserption of waste liquid) property, it can alleviate the *Ushna* (hot in potency) and *Tikshna Gunavridhhi* (penetrating property) of *Pitta*. Furthermore, while addressing the *Pitta Kopa* (vitiating of *Pitta*) the correction of *Dravarupa Pitta Vridhhi* (increased state of *Pitta*) is met along with *Kledasamaavastha*. Further *Samprapti* leading to the development of hyperglycemia can be arrested by normal functioning of *Sadhaka Pitta* and *Ojas*.

Conclusion

In this current era, stress has a key role in the etiopathogenesis of diabetes. The present study proves that hyperglycemia which occurs in individuals of *Pitta* constitution is primarily stress induced. Furthermore, the effectiveness of the trial drug “*Mahatiktaka*” which is indicated in mental disorders is highly significant in stress-associated hyperglycemia in *Pitta* constitution. This shows the importance of stress evaluation while treating a diabetic patient. The treatment varies depending on the factors such as nature of the stress and *Prakriti* of the individuals.

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Conflicts of interest

There are no conflicts of interest.

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