

Original research article

Impact of 8 Weeks of Yoga on Inflammatory Cytokine Markers in Uncomplicated Type 2 Diabetes Mellitus

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ABSTRACT

Objectives: To assess the effect of yoga on inflammatory cytokine markers in uncomplicated Type 2 Diabetes Mellitus (T2DM) patients when compared to routine conventional therapy alone. To compare inflammatory cytokine markers in T2DM patients before and after yoga.

Materials & methods:

Setting: It is a follow-up, randomized case–control study done in a tertiary care hospital.

Participants: Sixty Type 2 diabetic patients in the age group of 30-60 years, 0-10 years duration of DM were randomly divided into Yoga Group and Control Group, age and sex matched. Control Group received only conventional therapy for DM and Yoga Group received yoga therapy in the form of asanas and pranayama along with the conventional therapy for 8 weeks. Both groups were assessed twice (pre- and post-study).

Statistical Analysis: Data was analyzed using SPSS v 20.0. Repeated measure ANOVA followed by Tukey's test. $P < 0.05$ was considered significant. Results were expressed as mean \pm SD.

Results: After 8 weeks of yogic intervention, Yoga Group patients showed a significant reduction in their inflammatory markers.

Conclusion: Yoga can be used as an adjunct to the routine treatment for DM, for improvement of health as depicted by reduced inflammatory insult.

Keywords: Type 2 Diabetes Mellitus (T2DM), Blood Glucose, Inflammatory cytokine markers, Yoga, Prayanama

Introduction

Type 2 Diabetes Mellitus (T2DM) is characterized by the chronic state of hyperglycemia. Of particular concern are the co-morbidities associated with the development of T2DM, including microangiopathic and microvascular disease.

India is touted as the diabetes capital of the world. In 2019, diabetes was the direct cause of 1.5 million deaths, as per WHO report.¹ Prevalence among individuals aged over 50 years was found to be much higher (INDIAB Study).² The incidence of T2DM is also increasing with the increase in unhealthy dietary habits and sedentary lifestyle.³

A hypothesis was first proposed in 1997 that T2DM is associated with low - grade chronic inflammation resulting in part from the activation of the innate immune system.^{4,5} This activation leads to the release of pro-inflammatory cytokines such as Tumor Necrosis Factor- α (TNF- α) and Interleukin-6 (IL-6) which disrupt insulin homeostasis and action, finally resulting in increased insulin resistance and impaired blood glucose. Cytokines also show a gradual increase as the disease progresses to its complications⁵. Furthermore, exogenous administration of inflammatory markers results in insulin resistance⁶.

Core features of insulin resistance syndrome (IRS) are glucose intolerance, insulin resistance, visceral adiposity, atherogenic dyslipidemia and high blood pressure.^{7,8,9} Other abnormalities associated with the IRS and linked to the pathogenesis of T2DM include mainly hypercoagulation, chronic inflammation and endothelial dysfunction.¹⁰⁻¹² Increased sympathetic activity, reduced parasympathetic tone and enhanced cardiovascular reactivity have also been implicated in the development and progression of T2DM and related cardiovascular complications.^{13,14}

In addition, there is mounting evidence that chronic psychological stress and negative mood states are strongly associated, in a bidirectional manner, with other diabetic risk factors.^{15,16}

Accordingly, a holistic health care approach combining conventional medical treatment along with healthy lifestyle for the management is highly warranted¹⁷. Yoga, a Vedic science is one such mind - body approach which is highly appreciated and recommended and its health benefits are preventive as well as curative^{5,18}. It has been studied in diabetes as a means of decreasing stress-related hyperglycemia¹⁹⁻²¹, and may be more acceptable than sporting activity for some sectors of the population including the old age group.

Yoga increases parasympathetic control of the heart and reduces sympathetic activation via decreased stress levels, as well as reduces systemic inflammation²². Hence, the present study aimed to assess the role of yogic interventions on inflammatory cytokines in Type 2 diabetic patients on routine conventional therapy.

We hypothesized that the use of yogic intervention along with conventional drug therapy and diet modification for diabetes mellitus will reduce inflammation and thus, delay in complications. The primary objective of our study was to compare the inflammatory cytokine markers in T2DM patients on routine conventional therapy and in T2DM patients on both conventional + yoga therapy.

MATERIAL AND METHODS

Study design:

The study we conducted was a follow-up, randomized case-control study. 116 Type 2 diabetic patients according to the revised American Diabetic Association (ADA) criteria, in the age group of 30-60 years, with duration of disease 0-10 years were selected from the Medicine outpatient department (OPD) of tertiary care hospital. All subjects underwent complete physical and clinical assessment at the onset of study. However, of total patients, 60 were selected. Blood samples of all the patients were taken to assess the baseline levels of inflammatory markers. Subjects were randomly divided into two groups: Yoga Group and Control Group. Simple randomization was done using a computer-generated random number table, and allocation was done by sealed envelope technique and matched for age, sex and duration of disease. . Hence, thirty subjects in each group were finally selected to participate in our study. Prior to participation, the purpose of the study was explained to all the subjects and their informed consent was taken according to the ethical principles of the Ethical Committee of our institution. Ethical clearance was taken from the Institutional Ethical committee for the study.

Inclusion Criteria :

- Age: 30-60 years.
- Duration of diabetes in the subjects was between 0 to 10 years.

Exclusion Criteria :

Patients with

- Type 2 DM with any known diabetic complication like nephropathy, retinopathy, peripheral neuropathy, coronary artery disease, cerebrovascular accident.
- Any other metabolic disease like hypothyroidism.
- Acute respiratory tract infection in preceding 3 weeks.
- Chronic respiratory diseases like Pulmonary cox, COPD, asthma.
- Any known interstitial lung disease.
- Alcoholism & Smoking
- Patients not able to do yoga.

Figure A depicts the plan of study.

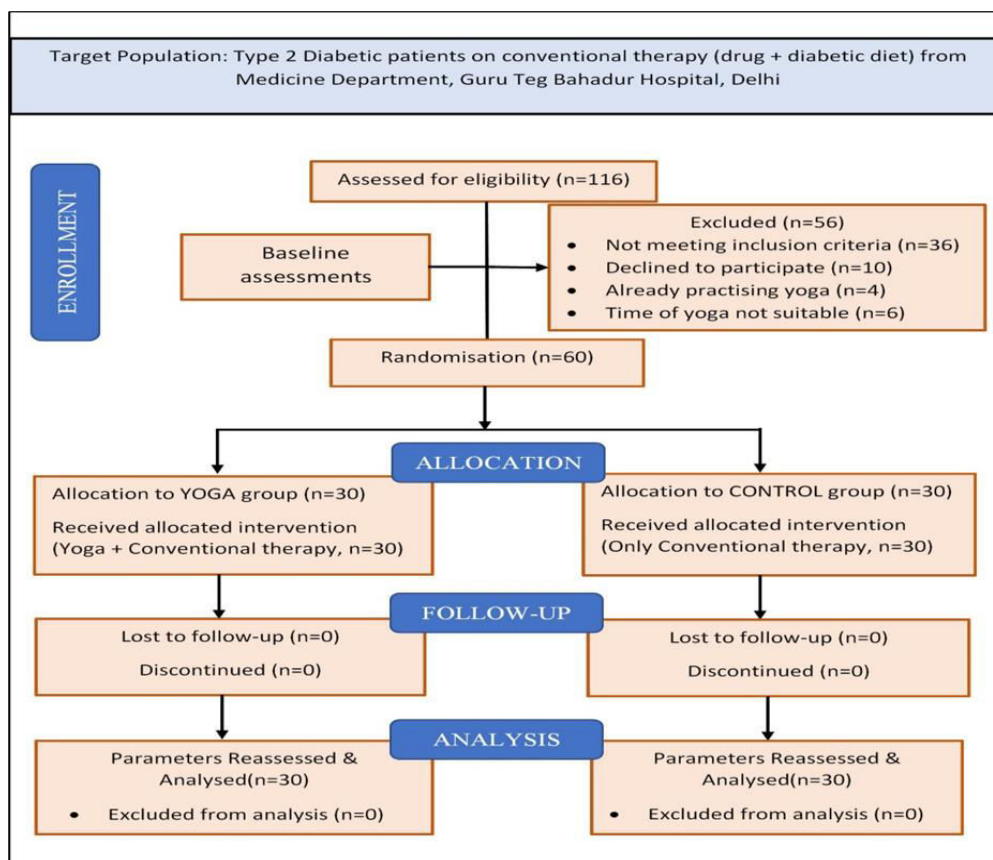


Figure A. CONSORT flow diagram of our study protocol over 8 weeks.

Intervention

Both groups received conventional therapy in the form of oral hypoglycemic agents mainly metformin as drug therapy and specific dietary modifications. Yoga group along with conventional therapy also underwent regular supervised yogic regimen which included OM ucharan, asanas, pranayamas and shavasana etc. [Figure B] for 5 times a week for 8 weeks under expert guidance of highly efficient yoga trainers possessing MD/PhD in yoga (with 5–10 years' experience in teaching yoga) and running a yoga center in the Physiology Department, UCMS under Central Council for Research in Yoga and Naturopathy. All the subjects practicing yoga came empty stomach and were thoroughly supervised by the

instructors to carry out yoga postures and breathing correctly. Compliance of patients was recorded by maintaining regular daily attendance of the subjects by the instructors. Yoga sessions were performed in a quiet environment from 9 to 10 am.

1. **Om Ucharan** [3 times]

2. **Asanas** were done for 15– 20 minutes and followed the sequence:

- *Tadasana* (Palm tree Pose): [2 times-each cycle for 15 seconds]
- *Trikonasana* (Triangular Pose): [2 times-15 seconds hold on each side]
- *Paschimottanasana* (Front Leaning Pose): [3 times- 15 seconds to 1 minute hold at a time]
- *Shavasana* (Corpse pose): [2 minutes]
- *Mandukasana* (Frog pose): [3 times- 1 minute hold]
- *Pawanmuktasana* (Wind Relieving Pose): [3 times- 30 seconds to 1 minute hold]
- *Bhujangasana* (Cobra Pose): [3 times- 15 seconds hold]
- *Shavasana* (Corpse pose): [2 minutes]

3. **Pranayama** was done for 18-20 minutes and had following deep breathing exercises:

- *Bhastrika* (bellows breath): 4 min (inhalation: exhalation=1:1, slowly done)
- *Kapalbhati* (frontal brain cleansing): 6 min. (forceful but controlled contraction of abdominal muscles during exhalation)
- *Anulom-vilom*: 8 min. (Inhalation/retention/exhalation- initially 1:1:1, gradually increasing to 1:2:2)

4. **Dhyana** (Meditation)

- Omkar meditation: 10 minutes

Figure B. Detailed Yogic regimen consisting of asana, pranayama and dhyana followed by the yoga group.

Assessment:

Serum inflammatory marker levels (TNF- α & IL-6) were measured using commercial Human ELISA kits from Diaclone, Gen-Probe. Both groups (Yoga and Control) underwent assessment for the outcome measures at the beginning as well as after 8 weeks of respective therapy. ELISA is based on the solid phase enzyme linked immunosorbent assay. The assay system utilizes a unique highly specific antibody (capture antibody) directed against cytokine (TNF- α or IL-6) molecule coated to the wells of the microtiter strip plate and anti TNF- α or anti IL-6 secondary antibody (detection antibody). The capture antibody is used for solid phase immobilization as it binds and immobilizes the antigen upon incubation with the antigen sample. There was development of the final yellow colored complex and intensity of the colored complex was directly proportional to the concentration of cytokine present in the samples and standards. The absorbance was read with a spectrophotometer at 450 nm and the amount of cytokine in each sample was determined by extrapolating optical density (OD) values against standard concentrations using the standard curve.

STATISTICAL ANALYSIS

Data analysis was done by IBM SPSS Statistics 20 software (by IBM Corporation, USA). Two factors repeated measure ANOVA followed by Tukey's test at 5% level of significance were used. One factor was group (Yoga and Control) and another factor used was time (pre, post) for comparison of inflammatory cytokine marker levels before and after intervention between the groups and within the group that is pre- and post-comparison for each group.

RESULTS:

Both yoga and control groups were matched for age, sex and duration of DM. The mean age in Yoga and control group was 44.533 ± 5.178 and 45.4 ± 5.315 respectively. Yoga group had 15 female and 15 male subjects. Number of females and males were 13 and 17 in the control group. Duration of DM in yoga and control group was 4.817 ± 1.178 and 4.75 ± 1.12 respectively.

Inflammatory Cytokines

a. Tumor Necrosis Factor- α (TNF- α)

In our study, Yoga Group showed a significant reduction (p-value < **0.01**) in TNF- α levels pre yoga (73.937 ± 12.259) and post yoga (52.17 ± 17.416) at the end of 8 weeks. However, in controls there was a slight increase in TNF- α levels when pre-study (74.822 ± 11.300) and post-study (76.694 ± 10.132) levels were compared [TABLE 1].

Table 1. Comparison of TNF- α .

Tumor Necrosis Factor- α (TNF- α)	pg/ml (mean \pm SD)		P-value (F test)	Tukey's significance
	Pre	Post		
Yoga Group	73.937 ± 12.259	52.17 ± 17.416	<0.01	Significant
Control Group	74.822 ± 11.300	76.694 ± 10.132	0.502	Non-significant
P-value (F test)	0.772	<0.01		
Tukey's significance	Non-significant	Significant		

b. Interleukin-6 (IL-6)

There was a significant reduction (p-value < **0.01**) in IL-6 levels in the yoga group at the end of our study from pre yoga (94.275 ± 8.201) to post yoga levels (72.29 ± 13.655). However, IL-6 levels in the control group at the end of our study showed a slight non-significant (p-value=0.783) increment from 92.449 ± 9.462 to 93.100 ± 8.765 [TABLE 2].

Table 2. Comparison of IL-6.

Interleukin-6 (IL-6)	pg/ml (mean \pm SD)		P-value (F test)	Tukey's significance
	Pre	Post		
Yoga Group	94.275 ± 8.201	72.29 ± 13.655	<0.01	Significant
Control Group	92.449 ± 9.462	93.100 ± 8.765	0.783	Non-significant

P-value (F test)	0.428	<0.01		
Tukey's significance	Non-significant	Significant		

Discussion

Within the last decade, a hypothesis was proposed to explain the pathogenesis of T2DM that connects the disease to a state of subclinical chronic inflammation^{4,5,6}. As a result there was increased release of pro-inflammatory cytokines like TNF- α and IL-6²². In this study, there was a 29% decrease in TNF- α levels and IL-6 levels reduced by 23% in the yoga group, contrary to the 2.5% and 0.7% increase in the respective levels in the control group. (TABLE 1 depicts a comparison of TNF- α before and after 8 weeks of intervention in Yoga Group and Control Group. Changes in IL-6 levels in two groups before and after 8 weeks of study are shown in TABLE 2). This observation is in accordance with a recent randomized trial that suggested yoga might have positive benefits on inflammation; nine heart failure patients randomized to a 2-month hatha yoga intervention showed a 22% reduction in IL-6 compared with minimal change in the ten patients who received standard medical care²³. Yoga is known to cause reductions in sympathetic nervous system tone^{24,25} and increase in vagal activity directly²⁵, both of which could result in decreased inflammation.

Conclusion

In our study, yoga group on assessment showed a significant decrease in inflammatory markers (TNF- α and IL-6). In the control group, the levels of inflammatory markers were found to be raised after 8 weeks. Therefore, it can be concluded that inflammatory markers increase with the progression of diabetes mellitus in spite of taking convention therapy. Yoga may reduce the effects of stress by promoting feelings of well-being, and reduced systemic inflammatory responses. Thereby, yoga would be beneficial to the patients of T2DM in terms of better glycemic and inflammatory control. So, it can be postulated that yoga can be used as an adjunct to the conventional therapy for the treatment of DM as it slows the progression of the disease.

Limitations of our study

The study was conducted in a limited time period on a small sample size. Better results would have been obtained with a larger sample size. Information extracted from a small sample size tends to be slightly skewed. In this study, the assessment of the parameters was done only twice i.e. before and after study, and therefore the changes during the time period could only be deduced. Had the study been of longer duration, multiple time assessments would have been possible and then the trend of changes could also be determined.

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Conflicts of interest

There are no conflicts of interest in our study.

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