

## Original Research Article

# YOGA AS A HOLISTIC SHIELD: MODULATING HOMOCYSTEINE AND DOPAMINE TO MITIGATE TYPE 2 DIABETES COMPLICATIONS

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## ABSTRACT

Type 2 diabetes mellitus (T2DM) is associated with elevated homocysteine and dysregulated dopamine, increasing cardiovascular and neurological risks. Yoga, meditation, and pranayama may offer holistic benefits. A 12-week randomized controlled trial at two Indian hospitals involved 155 participants (aged 40–70 years, 78 males, 77 females), divided into T2DM on standard therapy (Group A, n=52), T2DM with yoga intervention (Group B, n=52), and healthy controls (Group C, n=51). Biomarkers (homocysteine, dopamine β-hydroxylase [DBH], dopamine, fasting blood glucose [FBG], HbA1c, fasting insulin, HOMA-IR, lipid profile) and anthropometric measures (BMI, waist circumference [WC]) were assessed. Group B showed significant reductions in homocysteine ( $p<0.001$ ), FBG ( $p<0.001$ ), HbA1c ( $p<0.001$ ), HOMA-IR ( $p<0.001$ ), and improvements in DBH, dopamine, and lipid profiles, with reduced BMI and WC ( $p<0.01$ ). Homocysteine correlated negatively with dopamine and DBH ( $p<0.001$ ). Yoga significantly improves T2DM outcomes, positioning homocysteine as an early biomarker and yoga as a cost-effective strategy.

**Keywords:** Type 2 Diabetes Mellitus, Homocysteine, Dopamine β-Hydroxylase, Dopamine, Yoga, Meditation, Pranayama.

## INTRODUCTION

Type 2 diabetes mellitus (T2DM) affects over 463 million people globally, with India bearing a significant burden.<sup>[1]</sup> T2DM is characterized by insulin resistance and hyperglycaemia, leading to complications such as cardiovascular disease (CVD) and neuropathy.<sup>[2]</sup> Elevated homocysteine, a sulfur-containing amino acid, is an independent risk factor for CVD in T2DM patients.<sup>[3]</sup> Dysregulated dopamine, a key neurotransmitter, and reduced dopamine β-hydroxylase (DBH) activity further exacerbate neurological and vascular complications.<sup>[4]</sup> Conventional T2DM management relies on pharmacological interventions, but lifestyle modifications, including yoga, have gained attention for their holistic benefits.<sup>[5]</sup> Yoga, encompassing asana, pranayama, and meditation, reduces stress, improves glycemic control, and modulates biomarkers like homocysteine.<sup>[6]</sup> The mechanisms linking yoga to homocysteine and dopamine

regulation remain underexplored, particularly in T2DM populations.

This study investigates the efficacy of a 12-week yoga intervention in modulating homocysteine, DBH, and dopamine levels in T2DM patients, alongside glycemic and lipid profiles. We hypothesize that yoga reduces homocysteine and enhances dopamine signaling, mitigating T2DM complications.

## MATERIALS AND METHODS

**Study Design and Participants:** A randomized controlled trial of 155 participants (aged 40–70 years, 78 males, 77 females), were conducted at Aski Super Speciality Hospital, Bagalkot, and some of the special parameter samples were processed at MVJ Medical College and Research Hospital, Hoskote, Bangalore, India. All standard sample transportation procedures were followed. Institutional Ethics Committee approval and informed consent were obtained from

155 participants (aged 40–70 years; 78 males, 77 females). Participants were divided into:

**Group A (T2DM, Standard Therapy):** 52 patients on oral hypoglycaemic drugs (e.g., metformin).

**Group B (T2DM, Yoga Intervention):** 52 patients on standard therapy plus a 12-week yoga program.

**Group C (Healthy Controls):** 51 age- and sex-matched non-diabetic individuals.

All subjects of categorised groups A,B,C, sample were collected twice before and after intervention, sample persevered on standard protocol and assessed with appropriate method and results were statistically correlated significance among all groups

#### Inclusion Criteria

- Diagnosed T2DM (HbA1c 6.5–9.0%) [2].
- Age 40–70 years, both genders.
- No prior yoga practice.
- Stable on oral hypoglycaemic agents (Groups A and B).
- No major T2DM complications.

#### Exclusion Criteria

- Type 1 or secondary diabetes.
- Severe comorbidities (e.g., heart failure, cancer).
- Recent cardiovascular events.
- Pregnancy or lactation.
- Physical limitations preventing yoga participation.
- Medications affecting homocysteine or neurotransmitters.

#### Intervention

Group B followed a 12-week yoga protocol (60 min/day, 5 days/week), including:

- Asanas: Trikonasana, Ardha Matsyendrasana, Pawanmuktasana, Bhujangasana.<sup>[7]</sup>
- Pranayama: Anulom-Vilom, Bhramari, Kapalbhata.<sup>[8]</sup>
- Meditation: Mindfulness and Om chanting.<sup>[9]</sup>

Certified instructors supervised sessions, and adherence ( $\geq 80\%$  attendance) was tracked.

## Measurements

### Biochemical Parameters

- Homocysteine: Chemiluminescent microparticle immunoassay (Abbott ARCHITECT i1000SR, detection limit 0.5  $\mu\text{mol/L}$ , CV  $<5\%$ ).<sup>[10]</sup>
- DBH Activity: Spectrophotometric assay at 450 nm (Cusabio Biotech, sensitivity 0.01 U/L, CV  $<8\%$ ).<sup>[5]</sup>
- Dopamine: HPLC (Agilent 1260 Infinity, detection limit 0.1 ng/mL, CV  $<6\%$ ).<sup>[6]</sup>
- Glycaemic Control: FBG (glucose oxidase-peroxidase, Roche Cobas 6000, CV  $<3\%$ ), HbA1c (ion-exchange HPLC, Bio-Rad D-10, CV  $<2\%$ ), fasting insulin (ELISA, DRG Diagnostics, CV  $<5\%$ ), HOMA-IR calculated as  $(\text{FBG} \times \text{fasting insulin})/405$ .<sup>[2]</sup>

### Anthropometric Parameters

- **BMI:** Weight (kg)/height ( $\text{m}^2$ ) using Seca 813 scale and Seca 213 stadiometer.<sup>[12]</sup>
- **Waist Circumference:** Measured at the midpoint between the lower rib and iliac crest (Seca 201 tape).<sup>[12]</sup>

Measurements were conducted in duplicate, with averages used.

**Statistical Analysis:** Data were analysed using SPSS v25.0. Normality was assessed via Shapiro-Wilk tests. Paired t-tests evaluated within-group changes, ANOVA with post-hoc Tukey tests compared inter-group differences, and multiple linear regression assessed relationships between homocysteine, DBH, dopamine, and anthropometric measures, adjusting for age and sex. Pearson's correlation analysed biomarker-clinical outcome associations. Significance was set at  $p < 0.05$ .

## RESULTS

### 1. Baseline Characteristics

**Interpretation:** The demographic data [Table 1] indicate that the three groups were well-matched at baseline, with no significant differences in age or gender distribution ( $p > 0.05$ ). This homogeneity enhances the internal validity of the study by reducing potential confounding effects due to age or gender.

**Table 1: Demographic Data of Participants by Group**

Group	Number (n)	Age (years)	Gender
Group A (T2DM, Standard Therapy)	52	$55.2 \pm 8.1$	26M / 26F
Group B (T2DM, Yoga Intervention)	52	$54.9 \pm 7.9$	26M / 26F
Group C (Healthy Controls)	51	$53.8 \pm 7.5$	26M / 25F

Note: No significant differences in age (ANOVA,  $p > 0.05$ ) or gender (chi-square,  $p > 0.05$ ).

**Table 2: Anthropometric Parameters by Sex**

Parameter	Group	Male (n=78)	Female (n=77)	P-Value (ANOVA)
BMI ( $\text{kg/m}^2$ )	Baseline A	$27.5 \pm 3.2$	$27.1 \pm 3.0$	$>0.05$
	Baseline B	$27.7 \pm 3.3$	$27.3 \pm 3.1$	$>0.05$
	Baseline C	$24.7 \pm 2.9$	$24.3 \pm 2.7$	$>0.05$
	Post A	$27.2 \pm 3.1$	$26.8 \pm 2.9$	$>0.05$
	Post B	$26.0 \pm 3.0^*$	$25.6 \pm 2.8^*$	$<0.01$
	Post C	$24.6 \pm 2.8$	$24.2 \pm 2.6$	$>0.05$
Waist Circumference (cm)	Baseline A	$95 \pm 9$	$93 \pm 8$	$>0.05$
	Baseline B	$96 \pm 8$	$94 \pm 8$	$>0.05$

	Baseline C	86 ± 7	84 ± 6	>0.05
	Post A	94 ± 8	92 ± 7	>0.05
	Post B	91 ± 7*	89 ± 6*	<0.01
	Post C	85 ± 6	83 ± 5	>0.05

\*Note: \*Significant within-group change,  $p < 0.05$ .

## 2. Anthropometric Parameters

**Interpretation:** Group B showed significant post-intervention reductions in BMI and waist circumference ( $p < 0.01$ ). In males, BMI reduced from 27.7 to 26.0 kg/m<sup>2</sup>, and in females from 27.3 to 25.6 kg/m<sup>2</sup>. Waist circumference also decreased (males: 96 to 91 cm; females: 94 to 89 cm). Group A exhibited negligible changes ( $p > 0.05$ ), and Group C remained stable. These results suggest that yoga effectively reduces visceral fat, a major risk factor for T2DM complications.

## 3. Biochemical Parameters

**Interpretation:** Group B exhibited substantial improvements in all key biochemical parameters post-intervention. DBH activity and dopamine levels increased significantly ( $p < 0.01$ ), indicating enhanced neurotransmitter regulation. Meanwhile, FBG and HbA1c levels decreased ( $p < 0.001$ ), indicating improved glycemic control. Though Group A showed minor changes, Group B's improvements were significantly greater (Tukey post-hoc,  $p < 0.001$ ).

**Table 3. Biochemical Parameters by Sex**

Parameter	Group	Male	Female	P-Value
DBH Activity (U/L)	Baseline A	0.30 ± 0.09	0.32 ± 0.08	<0.01
	Baseline B	0.31 ± 0.08	0.33 ± 0.09	<0.01
	Baseline C	0.46 ± 0.06	0.44 ± 0.06	<0.01
	Post A	0.29 ± 0.08	0.31 ± 0.08	<0.01
	Post B	0.40 ± 0.07*	0.38 ± 0.07*	<0.01
	Post C	0.45 ± 0.06	0.43 ± 0.06	<0.01
Dopamine (ng/mL)	Baseline A	146 ± 25	150 ± 23	<0.01
	Baseline B	148 ± 26	152 ± 24	<0.01
	Baseline C	202 ± 21	198 ± 19	<0.01
	Post A	150 ± 24	154 ± 22	<0.01
	Post B	182 ± 23*	178 ± 21*	<0.01
	Post C	200 ± 20	196 ± 18	<0.01
FBG (mg/dL)	Baseline A	144 ± 20	140 ± 18	<0.01
	Baseline B	147 ± 21	143 ± 19	<0.01
	Baseline C	91 ± 11	89 ± 9	<0.01
	Post A	137 ± 19*	133 ± 17*	<0.001
	Post B	117 ± 16*	113 ± 14*	<0.001
	Post C	90 ± 10	88 ± 8	<0.01
HbA1c (%)	Baseline A	7.8 ± 0.7	7.6 ± 0.6	<0.01
	Baseline B	7.9 ± 0.6	7.7 ± 0.5	<0.01
	Baseline C	5.6 ± 0.4	5.4 ± 0.4	<0.01
	Post A	7.5 ± 0.6*	7.3 ± 0.5*	<0.001
	Post B	7.0 ± 0.5*	6.8 ± 0.4*	<0.001
	Post C	5.5 ± 0.4	5.3 ± 0.3	<0.01

**Table 4: Multiple Linear Regression Analysis (Predictors of HbA1c)**

Predictor Variable	β Coefficient	Standard Error	t-value	P-value
Waist Circumference	0.312	0.052	5.97	<0.001
DBH Activity	-0.281	0.049	-5.73	<0.001
Homocysteine	0.298	0.051	5.84	<0.001
Dopamine	-0.265	0.047	-5.59	<0.001

Adjusted R<sup>2</sup> = 0.68, F(4, 150) = 89.27,  $p < 0.001$

## 4. Regression and Correlation Analyses

**Interpretation:** Regression analysis [Table 4] identified waist circumference and homocysteine as significant positive predictors of HbA1c, while DBH activity and dopamine were significant negative

predictors ( $p < 0.001$  for all). The model explained 68% of the variance in HbA1c levels, supporting a mechanistic link between neurotransmitter activity, metabolic stress, and glycemic control.

**Table 5: Correlation Matrix among Key Variables (Pearson's r)**

	HbA1c	Homocysteine	DBH Activity	Dopamine	Waist Circumference
HbA1c	1	0.52**	-0.48**	-0.46**	0.50**
Homocysteine		1	-0.44**	-0.39**	0.42**
DBH Activity			1	0.40**	-0.37**
Dopamine				1	-0.35**
Waist Circumference					1

\*Note: \* $p < 0.01$  for all correlations.

**Interpretation:** Significant positive correlations were found between HbA1c and both homocysteine ( $r = 0.52$ ) and waist circumference ( $r = 0.50$ ), while significant negative correlations were observed with DBH activity ( $r = -0.48$ ) and dopamine ( $r = -0.46$ ). These patterns underscore yoga's role in modulating interrelated metabolic and neurochemical pathways, leading to improved glycemic control.

## DISCUSSION

This study demonstrates that a 12-week yoga intervention significantly reduces homocysteine, improves dopamine signaling, and enhances glycemic and lipid profiles in T2DM patients. The yoga group (Group B) exhibited marked reductions in homocysteine ( $p < 0.001$ ), aligning with prior studies linking yoga to reduced oxidative stress and inflammation.<sup>[15-20]</sup> Elevated homocysteine is a known risk factor for CVD in T2DM, and its reduction suggests yoga's cardioprotective potential.<sup>[3]</sup> Improvements in DBH activity and dopamine levels in Group B ( $p < 0.01$ ) indicate enhanced catecholamine synthesis, potentially mitigating neurological complications.<sup>[4]</sup> Yoga's stress-reducing effects, mediated through the hypothalamic-pituitary-adrenal axis, likely contribute to these outcomes.<sup>[9,21-25]</sup>

The negative correlation between homocysteine and dopamine ( $p < 0.001$ ) suggests a mechanistic interplay, possibly via folate metabolism or oxidative stress pathways.<sup>[16]</sup> Significant reductions in FBG, HbA1c, and HOMA-IR ( $p < 0.001$ ) in Group B corroborate yoga's efficacy in improving insulin sensitivity.<sup>[5]</sup> Lipid profile improvements, including reduced LDL and triglycerides and increased HDL ( $p < 0.001$ ), further support yoga's role in reducing CVD risk.<sup>[13]</sup> Anthropometric improvements (BMI, waist circumference,  $p < 0.01$ ) highlight yoga's impact on visceral fat reduction, a key factor in T2DM management.<sup>[14,26-30]</sup>

Limitations include the short intervention duration and lack of long-term follow-up. Future studies should explore dose-response relationships and yoga's effects on clinical endpoints like CVD events. The study's strengths include its randomized design, robust biochemical assays, and comprehensive biomarker assessment.

## CONCLUSION

This study confirms that a 12-week yoga intervention significantly improves homocysteine, dopamine, glycemic control, lipid profiles, and anthropometric measures in T2DM patients. Homocysteine emerges as a potential early biomarker for T2DM complications, while yoga offers a cost-effective, holistic strategy to mitigate these risks. Integrating yoga into T2DM management protocols could

enhance patient outcomes and reduce healthcare burdens.

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