

CHAPTER 6

STUDY 3: EFFICACY OF A YOGA-BASED LIFESTYLE PROGRAM ON GLYCEMIC CONTROL AMONG INDIANS WITH DIABETES

6.1 AIM AND OBJECTIVES

6.1.1 Aim of the study

To study the effect of the YLP on glycemic control among Indians with diabetes.

6.1.2 Objectives

- To study the effects of 12 weeks of YLP on the HbA1c levels among individuals with diabetes who are on standard care.

6.1.3 Rationale for the study

There is some evidence that the practice of Yoga can bring about reduction of blood sugar levels among individuals with diabetes. However, these effects have not been studied in a large community setting.

6.1.4 Hypothesis and Null Hypothesis

$$H_0: \mu_C = \mu_Y$$

$$H_1: \mu_C \neq \mu_Y$$

Where μ_C is the mean reduction in HbA1c level in the control group, and μ_Y is the mean reduction in HbA1c level in the Yoga group.

6.2 DESIGN OF THE STUDY

Study design of NMB 2017 has been described in section 4.2; the details of Phase 2, the data from which was used for this analysis, has been described in section 5.2.

6.2.1 Study Enrolment and Follow-up

The community level recruitment in Phase 1 of the screening for IDRS values included 240 clusters with 162,330 adult respondents. Of these 49,226 individuals belonging to 130 clusters (urban/rural) were found to eligible with high ≥ 60 IDRS scores; further 27,611 individuals responded to biochemical assessments. Among these, clusters with cohort population of an average of 50 individuals were invited for study. Accounting for a 24% loss for follow up, the final analyzed number was 3392, with 1820 in yoga and 1572 in the control arms of the study. The reasons for drop out were mostly time or work constraints, or unavailability of participants due to weather conditions.

6.2.2 Randomization and blinding

Overall, 80 clusters were randomly assigned in a 1:1 ratio to the control or the intervention arms by an independent statistician using a computer-generated randomization sequence. A total of 1820 (40 clusters) and 1572 (40 clusters) individuals were included in the intervention and control arms, respectively; an overall equivalent ratio of rural and urban location distributions was maintained (44 rural and 36 urban centres). Group allocation was concealed to the participants until the completion of the baseline assessment. Based on the nature of the intervention, other than the statisticians and the baseline data collection staff, the study participants or the field intervention yoga therapists or other investigators could not be blinded.

6.2.3 Data Collection

Assessments at baseline and after 3 months included study questionnaires, anthropometric measurements, and blood draw. Details of any adverse reactions or events were recorded including the time of occurrence, the severity and duration.

6.2.4 Procedure for biochemical measures

HbA1c assessment was done by high-pressure liquid chromatography using the Variant™ II Turbo machine (Bio-Rad, Hercules, CA) certified by the National Glycohemoglobin Standardization Program. The intra- and inter-assay coefficients of variation for the biochemical assays ranged within the target goals set by ADA's Standards of Medical Care.

6.3 METHODS

6.3.1 Participants and Outcomes

The study included individuals (age 19 - 80 years) who had been diagnosed with diabetes and whose blood HbA1c values were $\geq 6.5\%$. Individuals with severe obesity (BMI >40 Kg/m²), history of uncontrolled hypertension, coronary artery disease, renal disease, diabetes retinopathy, head injury, tuberculosis, reported psychiatric problems, major surgery, pregnancy in case of women, those planning to move out of the area within the next 3 months and those who had already done yoga for ≥ 3 months just before the dates of recruitment, were excluded from the study.

Informed consent was obtained from all the participants before screening and randomization. Details of recruitment of participants have been discussed in chapter 3, section 1 and in earlier reports (Nagarathna, et al., 2019; Nagendra et al., 2019).

The outcome was reduction in HbA1c levels after 3 months of intervention. The outcome was diagnosed based upon single time point assessment of blood HbA1c levels at baseline and at the end of 3 months.

6.3.2 Sample Size

NMB-2017 was a study with multiple objectives, the sample size calculations for which have been detailed in Chapter 4, Section 1. To verify the sufficiency of sample size for our study, we assumed a small standardized effect size. Since the study variable was a difference in means, Cohen's *d* was used, and following Cohen's definition of a small effect size (Cohen J., 1988), $d = 0.2$ was assumed. Following the method described by Hajian-Tilaki K in (Hajian-Tilaki, 2011), it was found that a sample size of 392 in each group was sufficient to detect even small effect sizes.

6.3.3 Analysis

A two-sided *P* value < 0.05 was considered statistically significant for all analyses. Mean reduction in HbA1c values was calculated for each group, and the pooled variance was determined. Independent samples *t*-test was applied to find if the results were statistically significant. 95% confidence intervals were calculated for the mean reduction.

Heterogeneity of treatment effects were calculated for the subgroups with poor glycemic control (defined as individuals with HbA1c ≥ 7.6 at baseline) and fair glycemic control (defined as individuals with HbA1c < 7.6 at baseline), and tests of interaction were conducted according to the methods described by Altman (Altman & Bland, 2003).

Intervention adherence was assessed by evaluating (a) class attendance and (b) regularity of practice of yoga during the period of study.

All analyses were done using Python v.3.7. Pandas v.0.23 was used to import data. t-tests and interaction tests were performed using Statsmodels v.0.10.1.

6.4 INTERVENTION

All participants in the intervention group received core initiation camps of 2-hours daily for 9 days. The intervention group received the standardized yoga-based lifestyle modification protocol (YLP) along with educational meetings to emphasize the role of adherence to yoga-based lifestyle to prevent diabetes. The intervention protocol was developed by a team of 16 experts including senior yoga masters from different yoga traditions (member institutions of Indian Yoga Association [IYA]), yoga researchers and diabetologists. The protocol (Appendices 3 and 4) was comprised of selected practices for lifestyle diseases, extracted from traditional sources. It included 30 minutes of physical postures (sun salutation and asanas) equivalent to mild to moderate physical activity and 30 minutes of breathing practices (kapalabhati kriya and pranayama), meditation and relaxation techniques. Evidence-based dietetic advice was also provided to promote healthy choices, rich in fiber and lower in fat and carbohydrate content. Group/individual lectures on concepts of ethical principles (yamas and niyamas), stress and nutrition for diabetes management were also held for 20 minutes.

Roles and responsibilities of the study staff were discerned. The intervention was conducted at the study sites by the volunteers designated as yoga volunteers for diabetes movement (YVDM). These YVDMs were certified yoga instructors from different member organizations of Indian Yoga Association (IYA). After these core intervention camps, participants were asked to continue self-practice (group or individual) daily for 3 months. Supervised weekly follow up classes for 2-hours were also conducted. After 3 months, post data was collected from both groups. The YVDMs planned and conducted weekly 2-hours Sunday morning group classes where yoga camps were conducted, and social media groups were also created. This

facilitated the communications on interactive review follow-up classes, monitoring their compliance of daily practices, and their health-related issues. There were no major issues reported by the participants during the 3-month period.

Participants assigned to the control group received continued their current treatment regimen, and received standard of care through printed handouts and one day interactive group presentation on structured lifestyle (diet physical activity, tobacco cessation etc.) change for glycemic control, by a team consisting of a physician, a dietitian, and a fitness trainer. This was followed by weekly visit to the site by the volunteer to interact and answer queries by the control group participants.

Attendance was maintained in each class, with house-visits or phone calls being done to remind those who missed a class. These procedures reduced the number of dropouts from the study.

6.5 RESULTS

6.5.1 Description of Data

A total of 3392 individuals participated in the trial. The distribution of the demographic and clinical characteristics between the two arms was fairly even with non-significant difference between groups ($p > 0.05$) (Table 12, Figs 15-18).

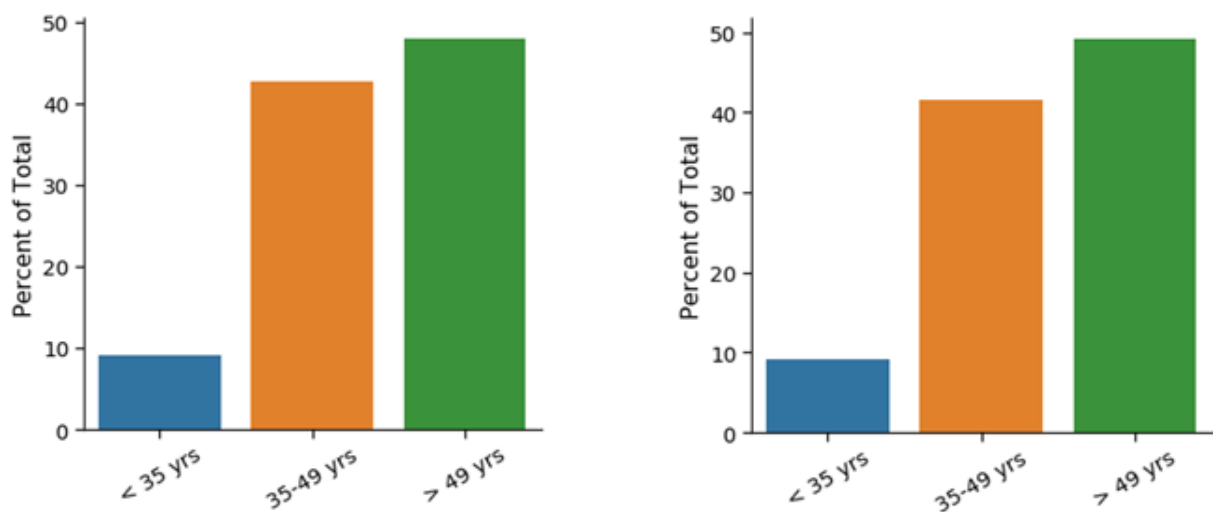


Fig 15: Control group age distribution

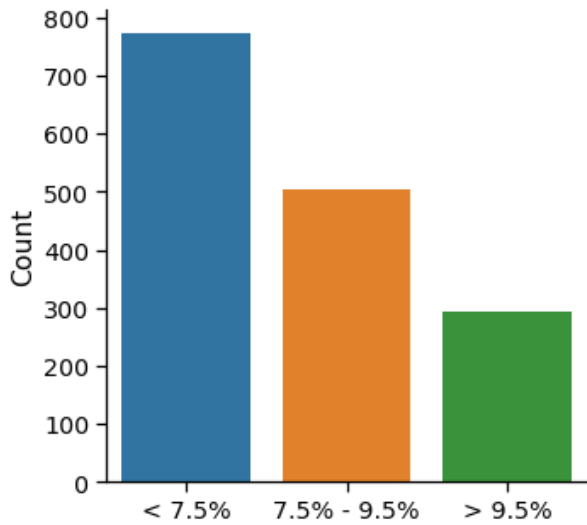


Fig 16: Yoga group age distribution

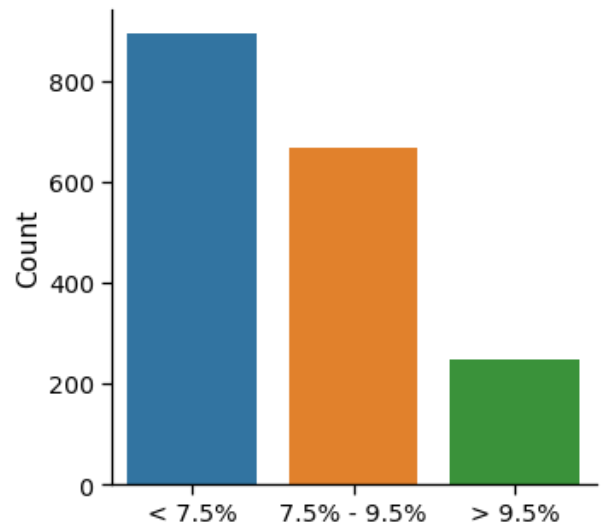


Fig 17: Control group HbA1c distribution

Fig 18: Yoga group HbA1c distribution

They varied in age from 19 - 80 years ($\mu = 48.54$, $\sigma = 10.86$). 55.60% (n=1886) were females, and 44.40% (n=1506) were males; 64.56% (n=2190) were urban and 35.44% (n=1202) were rural. HbA1c levels varied from 6.5% to 15.6% ($\mu = 8.04$, $\sigma = 1.56$).

Table 12. Baseline data for trial participants

Characteristics	Overall (n=3392)	Control (n=1572)	Yoga (n=1820)
Age, years, $\mu \pm \sigma$	48.55 \pm 10.86	48.35 \pm 10.96	48.72 \pm 10.78
HbA1c, $\mu \pm \sigma$	8.02 \pm 1.56	8.00 \pm 1.62	8.04 \pm 1.50
Area, n (%)			
Urban	2190 (64.56)	894 (56.87)	1296 (71.21)
Rural	1202 (35.44)	678 (43.13)	524 (28.79)
Gender, n (%)			
Female	1886(55.60)	882(56.11)	1004 (55.16)
Male	1506(44.40)	690 (43.89)	816 (44.84)

6.5.2 Glycemic control

Over a follow-up period of 3 months, the intervention arm showed a significantly greater reduction HbA1c levels ($\mu=1.31$, $\sigma=1.40$) compared to control arm ($\mu=0.45$, $\sigma=0.55$); $t(\infty) =$

22.68, $p < 0.001$. These results suggest that the addition of YLP to standard care can bring about better glycemic control among individuals with T2DM than standard care alone.

Table 13: Mean HbA1c reduction in control and yoga arms

	N	HbA1c at baseline ($\mu \pm \sigma$)	HbA1c at end of trial ($\mu \pm \sigma$)	HbA1c Reduction ($\mu \pm \sigma$) ¹	95% CI ¹
Control	1572.0	8.00 \pm 1.62	7.55 \pm 1.86	0.45 \pm 0.55	0.43 – 0.48
Intervention (Yoga)	1820.0	8.04 \pm 1.50	6.73 \pm 1.61	1.31 \pm 1.40	1.25 - 1.38

¹ CIs for difference in mean calculated according to (Altman, 1991)

Reduction in HbA1c levels were compared between individuals with poor glycemic control at baseline (defined as HbA1c ≥ 7.6) to individuals with fair glycemic control at baseline (defined as HbA1c < 7.6). Yoga intervention was found to be more effective in reducing HbA1c levels among individuals with poor glycemic control at baseline ($\mu=1.85$, $\sigma=1.66$) compared to standard care ($\mu=0.24$, $\sigma=0.61$), $t(\infty) = 22.72$, $p < 0.001$. Among individuals with fair glycemic control at baseline, yoga intervention still showed significant reduction in HbA1c levels ($\mu=0.94$, $\sigma=1.05$) compared to standard care ($\mu=0.59$, $\sigma=0.46$), $t(\infty) = 9.6$, $p < 0.001$. The estimated interaction effect was the difference in mean reduction of HbA1c, which was found to be 1.26 ($p < 0.001$). These results suggest that YLP can be very valuable clinically as an adjunct treatment for individuals whose serum glucose levels are not responding well to standard care.

Table 14: Effect of Yoga intervention on groups with poor vs fair glycemic control

	N Control, HbA1c reduction μ (CI)	N Yoga, HbA1c reduction μ (CI)	Diff in Mean HbA1c Reduction μ (CI)	Interaction (Effect difference) ¹
All	1572.0 0.45 (0.42–0.48)	1820.0 1.31 (1.25-1.38)	0.86 (0.78 - 0.93)	
Glycemic control at baseline				
Fair (< 7.6)	960.0 0.59 (0.56-0.62)	1084.0 0.94 (0.88-1.01)	0.35 (0.28 - 0.43)	1.26, Z=15.73, $p < 0.001$
Poor (≥ 7.6)	612.0	736.0		

	0.24 (0.19-0.29)	1.85 (1.73-1.97)	1.61 (1.47 - 1.75)
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1 Subgroup interaction effects calculated according to methods described by (Altman & Bland, 2003)

6.5.3 Adverse effects

There were no major adverse events or mortality during these 3 months of follow-up. Some participants reported mild pain in the lumbar or dorsal region during the yoga classes which was relieved by the end of the core practice session after practicing corrective posture (*pavanamuktasana* lumbar stretch for back pain), deep relaxation in supine posture, pranayama and meditation.