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## Original Article

## Partitioning of radiological, stress and biochemical changes in pre-diabetic women subjected to Diabetic Yoga Protocol



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## ABSTRACT

**Background:** Yoga is an ancient system of wellness with *Asana* and *Pranayama* as its most popular and propagated modules for management of lifestyle disorders.

**Objectives:** The aim of the study was to characterise the liver abnormalities, biochemical changes, and stress levels after Yoga intervention in prediabetic females.

**Materials and methods:** 37 females were randomly divided into Yoga practising and non-practising control groups. The Yoga practising group performed Diabetic Yoga Protocol (DYP) for 3 months. Parameters including size of liver, fatty infiltration, and grade of severity were measured using ultrasonography along with biochemical parameters and stress levels at baseline and after Yoga practice.

**Results:** The glycosylated hemoglobin (HbA1c) and glucose levels were found significantly reduced in prediabetic ( $p = 0.015$ ) women after practising DYP, although cholesterol levels increased in menopausal women. No escalation of fatty liver was noted among women practising DYP.

**Conclusion:** DYP reduced the HbA1c and stress levels and therefore, could be a cost-effective tool for preventing prediabetes to diabetes progression.

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## 1. Introduction

Diabetes Mellitus (DM) [1] is a devastating metabolic disorder and a major cause of morbidity and associated life threatening risks [2]. The collateral damage becomes significant when Asian women,

considered the center of family maintenance, are affected. Over the past two decades, the global prevalence of DM has increased manifold. Furthermore, the numbers indicate that India will have the highest number of DM (women) individuals in the world by the end of 2035. Increased blood sugar levels, a condition termed as hyperglycemia, represent a pathological hallmark of DM, which results from lack of insulin release or insulin resistance [3]. DM is also related with other key hemodynamic and metabolic abnormalities including high blood pressure and diabetic dyslipidemia including increased serum cholesterol, low-density lipoprotein (LDL), and serum triglycerides [4]. Menopausal women, attained

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when ovaries naturally stop synthesising estrogen or are removed or injured [5], are prone to hyperlipidemia due to decreased estrogen levels [6]. This may increase the risk for cardiovascular diseases [5], often difficult to control without medication.

Apart from non-modifiable risk factors, lifestyle-related factors, particularly, physical inactivity, obesity, chronic stress are currently thought to be responsible in the pathogenesis of DM and current global diabetes epidemic. Thus, the central goal in DM management is the reduction of high blood glucose which, if left untreated, may lead to microvascular and/or macrovascular complications. Prolonged hyperglycemia, without appropriate timely management, may also cause serious complications including death. DM management involves both pharmacological and non-pharmacological options which require multifactorial consideration underlying the development of DM and its complications. Pharmacological treatment options available for DM are often costly and associated with adverse effects which results in decreased patient medication adherence and increasing healthcare costs to them. Metformin is an essential drug in the treatment of hyperglycemia and for maintaining blood glucose levels. On the other hand, it is also known to cause vitamin B12 deficiency induced neuropathy [7] with cognitive impairment [8].

In order to predict diabetes prevalence on the basis of risk factors, an Indian Diabetes Risk Score (IDRS) has been proposed as a simple, convenient, user friendly and economic method of screening the undiagnosed diabetes population. It was developed by Mohan *et al.* with their cohort, Chennai Urban Rural Epidemiology Study (CURES). IDRS screening is based on four factors (age, waist circumference, diabetes history, and physical activity) that contribute to a major portion of risk factors associated with metabolic syndrome and cardiovascular diseases. The simplified IDRS has been determined by adding the scores for each risk factor. The IDRS has a sensitivity of 72.5% and specificity of 60.1%, and is derived based on a large population-based study on DM in India CURES [9]. A larger, nationwide study called *Niyantrita Madhumeha Bharata* (NMB-2017) recently applied IDRS to screen a population of almost 1,70,000.

According to WHO classification, DM is categorised into three types: Type 1, type 2, and gestational DM. Type 1 DM is insulin-dependent and constitutes 5–10% of all cases of DM [10]. Type 2 DM is non-insulin dependent, which constitutes around 90% of all the cases [11,12]. The third type, namely gestational DM, is diagnosed in a few pre-partum cases. Usually this type of DM subsides post-partum. But women have a 20–50% chance for recurrence of type 2 DM thereafter. However, it is possible to prevent such women from developing type 2 DM with lifestyle modification. A number of studies have revealed that Yoga can be useful in management of metabolic disorders by improving the lipid profiles and gluconeogenesis [13]. Mind-body practices like Yoga, which is part of a traditional mind-body system originating in India, has been rising worldwide and its intervention is rapidly growing. A growing body of evidence suggests Yoga, which capitalizes on the ability of the mind to improve physical health and general well-being, can be beneficial for a range of physical health problems. It is believed to be beneficial via down-regulation of the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system (SNS). HPA and SNS are activated as a result of the release of cortisol and catecholamines in response to a physical or psychological stressors and repetitive activation of the HPA and SNS over time leading to dysregulation in the system, causing chronic diseases such as, obesity, diabetes, depression and cardiovascular diseases [14]. Nagarathna *et al.* conducted a randomized controlled trial and found Yoga to be more effective as compared to exercise in decreasing the requirement of oral hypoglycemic agents and LDL levels and increasing HDL levels in type 2 DM. A growing body of

evidence reveals that Yoga practice may also be effective in the high-risk populations such as those with prediabetes or metabolic syndrome.

DM patients are known to develop fatty liver disease which is usually characteristic of high alcohol consumption. However, non-alcoholic fatty liver disease (NAFLD), a condition in which excess fat accumulates in the liver causing hepatomegaly, can develop in diabetes independent of alcohol intake. Provided the regular consumption of glucophagic drugs, DM patients, especially menopausal women, have been reported to have a higher susceptibility to liver enlargement, damage, and cirrhosis as compared to non-DM patients [15]. This may be due to insulin resistance and excessive accumulation of lipid within liver. Obesity and increased concentrations of fatty acid in plasma is a common risk factor for fatty liver, and these are also other factors associated with type 2 DM [13]. Death from liver failure is most common and it is estimated that 3–4% of diabetes population is affected by this [16]. In type 2 DM, there are a number of physiological alterations in the liver because of drug metabolism that also include increase in the levels of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), resulting in more than half of the population with liver abnormality [17]. As per the anthropometric classification of individuals, those with increased visceral fat are considered as unhealthy, irrespective of their BMI [18]. Visceral fat is notorious because it is metabolically active and hence can possibly attribute to the dysmetabolic syndrome [19]. It is reported that people with higher visceral fat have a higher risk of NAFLD [20] and resulting dysmetabolic disease or vice versa [21,22]. The fact whether visceral fat causes intrahepatic fat accumulation or otherwise is questionable. Studies have shown that intrahepatic fat and not visceral fat leads to insulin resistance in individuals within a wide range of age groups [23,24]. Therefore, it can be concluded that the dysmetabolic syndrome is caused because of the intrahepatic fat. Enhanced hepatic *De novo* lipogenesis (DNL) results in the aberration of lipid metabolism and causes steatosis. On the contrary, such phenomenon is completely absent in normal metabolism. However, we see that the complications of hepatomegaly, subsequent weight gain and impaired lipid metabolism are all a result of enhanced hepatic DNL in NAFLD [25]. There is sufficient evidence suggesting the role of anti-diabetic/glucophagic drugs in impaired metabolism, dysregulated vitamin assimilation, neuropathy and weight gain, etc. Mild to moderate exercise despite other lifestyle modifications can essentially affect lipid metabolism and can alleviate NAFLD effectively. Advancements in the understanding of Yoga with emphasis on *Asanas* can be beneficial for the treatment of DM and NAFLD. Aerobic exercises, which include Yoga and Pranayama, induce changes in the lipid profiles, reduce intrahepatic fat content, decrease hepatic oxidative stress and ameliorate hepatic inflammation by decreasing the pro-inflammatory cytokines [26,27]. There is a paucity of studies investigating beneficial effects of Yoga on the liver parameters among population group at high risk for developing NAFLD. The present study was undertaken to investigate this influence of Yoga on liver size, level of infiltration, and severity of disease via ultrasonography in high risk females after 3 months of Yoga. In addition, the biochemical parameters, stress scales after Yoga intervention were also analysed.

## 2. Methods

### 2.1. Participants

A total of 37 females were recruited from the national Yoga camp held in Chandigarh (NMB 2017) on the basis of IDRS under the National Diabetes Control Mission of Government of India. IDRS scores were derived from the age, physical activity, family history of

DM and waist circumference of the individual [9]. Females with IDRS score  $\geq 60$  (high risk group) were included in the study. Participants with IDRS  $< 60$  and glycosylated hemoglobin (HbA1c)  $< 5.7\%$ , prior Yoga practitioners, expecting mothers, and reluctant participants were excluded from the study. The participants were divided into two groups, out of which one group performed DYP for 3 months ( $n = 22$ ) and the other was waitlisted for this period ( $n = 15$ ). The study was approved by the S-VYASA Institutional Ethics Committee (RES/IEC-IYA/001). The registration number for this trial is CTRI/2018/03/012804. The following protocols, radiological and biochemical analysis done in this particular study follow the respective guidelines and regulations.

### 2.1.1. Yoga or treatment group

The pre-assessed female participants were trained to perform DYP (designed especially for subjects with diabetes and prediabetes) by certified Yoga practitioners, called the Yoga volunteers for DM management (YVDMs). The participants were trained for one week and then daily monitored for compliance to DYP for three months.

### 2.1.2. Control or non-treatment group

The participants under the control group were waitlisted and

did not perform DYP. They were counselled to carry on with their regular activities for three months and periodically monitored by YVDMs telephonically.

### 2.2. Diabetic Yoga Protocol (DYP)

Three months of DYP was approved by Ministry of AYUSH (Government of India), which included a number of *Asanas*, meditations, *Pranayam*, and cyclic meditation that had never been tested before. Procedures of the DYP have been tabulated in [Table 1](#) ([Supplementary data](#)).

### 2.3. Estimation of liver size

Ultrasound was performed to estimate the size of liver, infiltration and grade of severity by a trained radiologist.

### 2.4. Biochemical analysis

Biochemical assessment was performed by measuring fasting blood sugar (FBS), post-prandial blood sugar (PPBS), HbA1c using standard laboratory procedures in an NABL accredited lab. FBS was estimated by measuring the blood glucose after at least 8 h of

**Table 1**  
Procedures of the Diabetic Yoga Protocol.

S. No	Name of Practice	Duration (in min)
1	<b>Starting Prayer:</b> <i>Asatoma Sat Gamaya</i> <i>Taraso Maa jyotir - garaya</i> <i>Mrtyor-Maa Amrtam gamaya</i> <i>Om Shaantih Shaantih Shaantih</i>	2
2	<b>Meaning:</b> From ignorance lead me to truth; From darkness, lead me to light; From death, lead me to immortality; Om peace, peace, peace. <b>Loosening Exercises</b> (Preparatory <i>Sukshma Vyayamas</i> and <i>Shithililarna</i> Practices): <b>1. Urdhahasthasana</b> (Upward Tree Position) (Hand Stretch Breathing 3 rounds at 90°, 135° and 180° each) <b>2. Kati-Shakti Vikasaka</b> (3 rounds) <b>a.</b> Forward and Backward Bending <b>b.</b> Twisting <b>3. Sarvangapushhti</b> (3 rounds clockwise, 3 rounds anticlockwise)	6
3	<b>Surya Namaskara (SN)</b> (Sun Salutation) <b>a.</b> 10 step fast <i>Suryanamaskara</i> (Fast Sun Salutation) 6 rounds <b>b.</b> 12 step slow <i>Suryanamaskara</i> (Slow Sun Salutation) 1 round Modified version Chair SN: 7 rounds	9
4	<b>Asanas (Pose/Posture)</b> (1 min per Asana) <b>1. Standing Position</b> (1 min per Asana) <i>Trikonasana</i> (extended triangle pose), <i>Parvritra Trikonasana</i> (revolved triangle pose), <i>Prasarita Padhasana</i> (Wide-Legged Forward Bend) <b>2. Supine Position</b> <i>Jatara Parivartanasana</i> (Master Revolved Abdomen Pose), <i>Pawanamuktasana</i> (Wind-Relieving Pose), <i>Viparitarani</i> (Upside-Down pose) <b>3. Prone Position</b> <i>Bhujangasana</i> (Cobra Pose), <i>Dhurasana</i> (Bow Pose) followed by <i>Pawanamuktasana</i> (Wind-Relieving Pose) <b>4. Sitting Position</b> <i>Mandukasana</i> (Frog Pose), <i>Vakrasana/ Ardhamatsayendrasana</i> (Half Spinal Twist Pose), <i>Paschimatanasana</i> (Seated Forward Bend), <i>Ardha Ushtrasana</i> (Half Camel Pose); At the end, relaxation with abdominal breathing in supine position ( <i>vishranti</i> ), 10-15 rounds (2 minutes)	15
5	<b>Kriya</b> (Outward Physical Manifestation) <b>a.</b> <i>Agnisara</i> (Abdomen Churning): 1 minute, <b>b.</b> <i>Kapalabhati</i> (Skull Shining Breathing Technique) (@60 breaths per minute for 1 minute followed by rest for 1 minute)	3
6	<b>Pranayama</b> (Breathing Techniques) <b>a.</b> <i>Nadishuddhi</i> (Alternate Nostril Breathing)]for 6 minutes, with <i>antarkumbhak</i> (Internal Breath Retention) and <i>jalandhar bandha</i> (Chin Lock) for 2 seconds], <b>b.</b> <i>Bhramari</i> (Humming Bee Breathing): 3 minutes	9
7	<b>Meditation</b> (for Stress, for deep relaxation and silencing of mind) Cyclic Meditation	15
8	<b>Closing Prayer:</b> <i>Sarvebhavantu Sukhina</i> <i>Sarve Santu Nirāmayaah</i> <i>Sarve Bhadrani Pasyantur</i> <i>Maa KaScid-Duhkha-Bhag-Bhavet</i> <i>Om Shaantih Shaantih Shaantih</i> <b>Meaning:</b> Let all be happy, free from diseases. Let all align with reality, let no-one suffer from miseries. Om peace, peace, peace. Total duration	1
		60

**Table 2**  
The baseline characteristics of patients.

Demographic Details	Yoga group	Control group
Sample Size (n = 37)	22	15
Known diabetes cases	10	9
New diabetes cases	12	6
Age (Years) M± (SD)	51.77 (8.37)	53.80 (8.30)
Height [28] M±(SD)	156.09 (5.17)	155.2 (5.5)
Weight (Kg) M±(SD)	68.22 (9.24)	67.93 (9.00)
BMI M± (SD)	27.99 (3.49)	28.16 (3.06)
Diabetes history (DYP n = 15; control n = 12)	Familial cases 11/15 (73.33%) Non familial cases 4/15 (26.66%)	Familial cases 5/12 (41.66%) Non familial cases 7/12 (58.33%)

overnight fasting. PPBS was estimated by measuring blood glucose levels after 2 h of taking 75 mg of glucose. HbA1c was measured to assess a 3 months historical sugar levels.

### 2.5. Statistical analysis

Changes in the radiological and biochemical variables in the experimental and the control group were tested by using SPSS version 21.0, before and after Yoga intervention. The comparisons were tested by using paired *t*-test as the data followed the normal distribution. The level of significance (*p*) below 0.05 was considered for testing the hypothesis.

## 3. Results

### 3.1. Participant characteristics

The participants were divided into two groups, out of which one group performed DYP for 3 months and the other was waitlisted for this period.

A total of 37 females with IDRS  $\geq 60$  were recruited based on willingness to undergo ultrasound examination and after obtaining informed consent. 15 out of 22 females in the Yoga practising group completed the 3 months of DYP with average attendance of 52.7 days. 12 out of 15 females in the wait-listed group for Yoga were followed up and served as control group. Females with known diabetes status of either group continued their medication and lifestyle throughout the study period. The subjects were grouped on the basis of IDRS and HbA1c for further analysis. It must be noted that the levels of HbA1c and mean plasma glucose (MPG) were found to be comparable at the baseline. The follow ups were carried out according to the unique identification number provided to each individual. Data compilation and analysis was conducted in the GLP compliant facility recognised by Quality Council of India. The characteristics of the participants are provided in Table 2.

### 3.2. Effect of DYP on liver size

The liver size did not show any significant changes in both the

Yoga group (*p* = 0.648) and the control group (*p* = 0.937) (Table 3) (Supplementary data). However, net change in liver size after 3 months revealed that no changes were observed in 4/14 (28.58%) females who performed DYP in comparison with 4/12 (33.33%) in the control group. In 5/14 (35.71%) Yoga performing high risk females, the liver size was found increased with the mean change of  $-0.88$  in comparison with 4/12 (33.33%) with the mean change of  $-1.12$  (Table 4). The extent of mean increase in the liver size of control group was found to be more as compared to the Yoga group. Females in both the Yoga and the control group showed a reduction in the liver size (Table 4). However, the extent of reduction was less in the Yoga group 5/14 (35.71%) with a mean reduction of 0.44 when compared to the control group 4/12 (33.33%) with the mean reduction of 1.86 (Table 4). Considering both the subject wise changes as well as the familial background of DM in these subjects (Table 2), it can be argued that Yoga intervention helps in maintaining systemic homeostasis despite impaired gluconeogenesis in the liver.

### 3.3. Effect of DYP on glycemic and lipid profile

The comparison of glycemic profile in individuals with IDRS  $\geq 60$  after 3 months of DYP revealed a statistically significant reduction in HbA1c (*p* = 0.005) with reduced mean HbA1c levels of 6.00% and mean MPG of  $125.51 \pm 44.75$  (*p* = 0.005), whereas, no statistically significant difference was found in the control group. Cholesterol was found to be enhanced in the Yoga group after three months (*p* = 0.003) whereas the control group did not show any statistical difference. The glycemic and lipid profiles of individuals with IDRS  $\geq 60$  have been shown in Table 5 (Supplementary data)

### 3.4. Effect of DYP on prediabetic and diabetic females

HbA1c based analysis in response to DYP in the prediabetes and diabetes experimental group revealed that diabetic as well as prediabetic females improved with respect to the HbA1c levels. Three months follow up of DYP performing high risk females with baseline HbA1c (%)  $\geq 6.4$  showed reduction from mean 7.25%–6.39% (Table 6). Similarly, prediabet females (HbA1c <6.4%)

**Table 3**  
Changes in liver size after 3 months of Yoga.

Ultrasound	Control group			Yoga group		
	Pre	Post	p-value	Pre	Post	p-value
	M±SD	M±SD		M±SD	M±SD	
Liver Size	14.52 ± 1.40	14.39 ± 1.37	0.937	13.69 ± 1.66	13.78 ± 1.39	0.648
Liver Size (HbA1c <6.4%)	14.47 ± 1.76	15.20 ± 1.85	0.787	13.48 ± 1.44	13.66 ± 1.12	0.413
Liver Size (HbA1c $\geq 6.4$ %)	14.54 ± 1.44	13.90 ± 1.00	0.213	13.54 ± 2.04	13.68 ± 1.7	0.687

**Table 4**

Net change in the liver size after 3 months in Yoga and Control group.

S. No	Yoga group (n = 14)					Control group (n = 12)				
	Number	%	Pre M	Post M	Net Change	Number	% People	Pre M	Post M	Net Change
No change	4/14	28.58	14.05	14.05	0	4/12	33.33	13.72	13.72	0
Increased	5/14	35.71	11.98	12.86	−0.88	4/12	33.33	14.32	15.45	−1.12
Decreased	5/14	35.71	14.62	14.08	0.44	4/12	33.33	15.52	14	1.86

**Table 5**Biochemical and lipid profile of individuals with IDRS $\geq$ 60, pre and post 3 months of DYP.

	Control group			Yoga group		
	Pre	Post	p-value	Pre	Post	p-value
Glycemic Variables	M $\pm$ SD	M $\pm$ SD		M $\pm$ SD	M $\pm$ SD	
BMI (kg/m <sup>2</sup> )	28.11 $\pm$ 3.01	27.89 $\pm$ 3.00	0.410	28.24 $\pm$ 3.39	27.26 $\pm$ 2.86	0.136
Post Prandial Glucose (mg/dl)	195.92 $\pm$ 85.97	214.33 $\pm$ 65.98	0.347	112.57 $\pm$ 21.50	114.43 $\pm$ 23.85	0.806
Fasting Blood Glucose (mg/dl)	142.67 $\pm$ 42.81	138.08 $\pm$ 47.64	0.715	119.07 $\pm$ 40.69	127.57 $\pm$ 88.23	0.589
HbA1c (%)	7.63 $\pm$ 1.46	7.23 $\pm$ 1.59	0.089	6.64 $\pm$ 1.22	6.00 $\pm$ 1.56	<b>0.005</b>
Mean Plasma Glucose (mg/dl)	172.14 $\pm$ 41.88	160.89 $\pm$ 45.69	0.089	143.94 $\pm$ 34.97	125.51 $\pm$ 44.75	<b>0.005</b>
Lipid Profile	M $\pm$ SD	M $\pm$ SD	p-value	M $\pm$ SD	M $\pm$ SD	p-value
Triglycerides (mg/dl)	147.58 $\pm$ 47.30	171.08 $\pm$ 57.93	0.049	141.50 $\pm$ 99.36	181.14 $\pm$ 138.61	0.133
Cholesterol (mg/dl)	180.83 $\pm$ 28.88	190.92 $\pm$ 34.99	0.190	177.36 $\pm$ 37.15	194.29 $\pm$ 33.55	<b>0.003</b>
High Density Lipoprotein (mg/dl)	45.75 $\pm$ 8.05	45.08 $\pm$ 8.30	0.548	49.43 $\pm$ 10.90	51.07 $\pm$ 12.69	0.392
Low Density Lipoprotein (mg/dl)	172.33 $\pm$ 64.31	202.17 $\pm$ 86.59	0.025	100.07 $\pm$ 30.26	109.29 $\pm$ 32.15	0.101
Very Low Density Lipoprotein (mg/dl)	100.75 $\pm$ 20.33	105.50 $\pm$ 25.51	0.455	99.50 $\pm$ 31.10	107.00 $\pm$ 33.31	0.073

**Table 6**Pre and post glycemic and lipid profile of Yoga group (IDRS  $\geq$ 60 & HbA1c  $\geq$  6.4% and <6.4%) and control (non-Yoga) group (IDRS  $\geq$ 60 & HbA1c  $\geq$  6.4%).

Parameters	Yoga group (HbA1c $\geq$ 6.4%)			Yoga group (HbA1c < 6.4%)			Control group (HbA1c $\geq$ 6.4%)		
	Pre M $\pm$ SD	Post M $\pm$ SD	p-value	Pre M $\pm$ SD	Post M $\pm$ SD	p-value	Pre M $\pm$ SD	Post M $\pm$ SD	p-value
HbA1c (%)	7.25 $\pm$ 1.33	6.39 $\pm$ 1.94	<b>0.024</b>	5.93 $\pm$ 0.26	5.45 $\pm$ 0.60	<b>0.015</b>	8.08 $\pm$ 1.29	7.63 $\pm$ 1.63	0.198
Mean Plasma Glucose (mg/dl)	161.36 $\pm$ 38.31	136.65 $\pm$ 55.70	<b>0.024</b>	123.35 $\pm$ 7.47	109.71 $\pm$ 17.16	<b>0.025</b>	185.06 $\pm$ 36.90	172.13 $\pm$ 46.79	0.197
Cholesterol (mg/dl)	163.50 $\pm$ 33.14	180.13 $\pm$ 38.80	0.064	188.50 $\pm$ 34.85	208.13 $\pm$ 28.22	<b>0.025</b>	182.13 $\pm$ 33.78	195.38 $\pm$ 38.44	0.194
Triglycerides (mg/dl)	125.50 $\pm$ 80.51	201.75 $\pm$ 173.20	0.066	139.75 $\pm$ 114.02	143.13 $\pm$ 73.97	0.878	178.38 $\pm$ 77.08	221.25 $\pm$ 98.97	<b>0.009</b>
HDL (mg/dl)	51.38 $\pm$ 14.01	54.00 $\pm$ 17.50	0.118	51.00 $\pm$ 9.09	52.50 $\pm$ 8.72	0.637	47.00 $\pm$ 9.50	45.63 $\pm$ 9.61	0.375
LDL (mg/dl)	86.75 $\pm$ 32.17	85.75 $\pm$ 32.94	0.871	109.50 $\pm$ 25.06	127.00 $\pm$ 24.26	<b>0.001</b>	99.63 $\pm$ 23.60	105.63 $\pm$ 28.67	0.496
BMI (kg/m <sup>2</sup> )	28.09 $\pm$ 3.84	27.93 $\pm$ 3.04	0.751	28.37 $\pm$ 3.209	26.67 $\pm$ 2.76	0.071	27.65 $\pm$ 2.90	17.31 $\pm$ 13.07	0.071
Liver Size (cm)	13.48 $\pm$ 1.44	13.66 $\pm$ 1.12	0.413	13.53 $\pm$ 2.04	13.67 $\pm$ 1.75	0.151	14.54 $\pm$ 1.45	13.90 $\pm$ 1.01	0.213

**Table 7A**

Pre-post analysis of menopausal diabetic females in DYP and control groups.

Groups	Cholesterol (mg/dl) Pre M $\pm$ SD	Cholesterol (mg/dl) Post M $\pm$ SD	t-value	p-value
Menopausal DYP	170.44 $\pm$ 21.01	193.44 $\pm$ 35.31	−2.967	0.018
Menopausal Control	175.86 $\pm$ 30.08	194.71 $\pm$ 40.45	−1.877	0.110

presented a statistically significant reduction from mean 5.93%–5.45% (Table 6) (Supplementary data). In contrast to the increase in the cholesterol levels of prediabetic females, no difference was observed in the diabetic females. The remaining variables are represented in Table 6.

### 3.5. Effect of DYP on cholesterol

In order to understand the cause of increased cholesterol, the menopausal status of females was revisited. Levels of cholesterol were found to be significantly enhanced in the DYP group ( $p = 0.018$ ) after three months of Yoga intervention (Table 7A) (Supplementary data). Due to the unexpected increase in the cholesterol levels among the menopausal DYP individuals (Table 5), a separate data set was randomly selected from the primary study site for the purpose of analysis. Menopausal and non-menopausal

women with diabetes, undergoing DYP for 3 months, were compared. It also showed a significant increase in cholesterol levels in menopausal women as shown in Table 7B.

### 3.6. Effect of DYP response on stress

VSS and PSS analysis indicated an increase in the severity of

**Table 7B**

Group comparison between menopausal and non-menopausal diabetic females of different locations.

Group	Cholesterol (mg/dl) Mean $\pm$ SD	Cholesterol (mg/dl) Mean $\pm$ SD	t-value	p-value
Menopausal	194.9 $\pm$ 37.7	207.85 $\pm$ 47.52	−2.027	0.051
Non-Menopausal	176.33 $\pm$ 30.73	176.53 $\pm$ 28.33	−0.312	0.761

stress in control group in contrast with the Yoga group where one person moved from severe stress to moderate one (Table 8). Similarly, PHQ scoring indicated the conversion of severely stressed and moderately severe diabetic females to moderate levels.

#### 4. Discussion

The research team investigated the effect of practising DYP in high risk diabetic women for a period of three months. The intervention of DYP in these patients resulted in negligible change in their liver size or infiltration, as seen by ultrasound. However, biochemical analysis revealed that the HbA1c levels were significantly reduced, providing proof of principle for potential of DYP to halt or delay the conversion of prediabetes into diabetes. This should be re-analysed after a longer intervention of DYP, using both ultrasonography and biochemical analysis because molecular changes precede ultrasonographic changes. The control group, which did not undergo any Yoga intervention, showed no statistical difference between liver size and/or level of infiltration, i.e., grade I (mild), grade II (moderate) and grade III (severe). However, there were some individuals in the Yoga practising group who showed positive changes, but they had a family history of DM or were minimally compliant to DYP. Considering both the subject wise changes as well as the familial background of DM in these subjects (Table 2), it can be argued that Yoga intervention helps in maintaining systemic homeostasis despite impaired gluconeogenesis in the liver [29]. These could also be ascribed to their unique psychometric profile borne out their personality traits, often termed as *Prakriti* or personality type, which were not analysed in this study.

Yoga, exercises, and liver size has been studied earlier along with biochemical parameters. For instance, Sharma *et al.* studied the role of Yoga on liver functions and found that the practice of Yoga significantly reduced the level of globulin and alkaline phosphatase when compared to controls [30], suggesting the beneficial biochemical effects of Yoga in the treatment of liver diseases. However, this study did not investigate the changes in liver size, nor did it trace back the changes with family history, personality traits, or compliance level of individuals; thus, leaving a void in literature. It is pertinent to note that patients with diabetes, especially menopausal women, have a higher risk of developing NAFLD, exacerbated by sedentary lifestyle [31,32]. This results in insulin insensitivity, increase in body fat deposition, and increase in free fatty acid uptake by the liver [33]. Inclusion of Yoga or any other form of exercise in day to day life may circumvent the occurrence or progression of metabolic disorders, hepatic steatosis and cardiovascular diseases; however, customised Yoga protocols are particularly recommended. According to previous reports, steatohepatitis, which is characterised by lipid accumulation and an

increase in inflammatory cytokines and infiltrates in the liver, can be managed through regular exercise [34,35]. Incorporation of both aerobic and resistance exercise (akin to DYP) is known to control glucose levels and the risk of developing cardiovascular disease besides microvascular complications of DM [36,37]. Zelber-Sagi *et al.* has also investigated the effect of resistance training on NAFLD patients and found reduced hepatic steatosis on ultrasonography [38]; however, despite positive changes, none of these studies around the world have a nationally standardised protocol, developed in consensus with Yoga classical literature, such as DYP, that could be mainstreamed for translation for use in the clinic.

Recently, Sullivan *et al.* demonstrated that aerobic exercise and Yoga result in a significant reduction in intrahepatic triglyceride content in NAFLD patients [39]. Similar reports have demonstrated the beneficial effects of exercise in reducing steatosis, inflammation and insulin resistance in NAFLD patients [40]. These studies did not examine the biochemical parameters among the non-working women at risk for lifestyle disorders. Regardless, some studies have still shown a reduction in intrahepatic lipids, improvement in insulin resistance, inflammation, liver enzymes and steatosis [41,42]. Although these studies did not describe the familial background of these subjects, the cholesterol levels in the DYP group point towards a strong genetic context of Yoga practising subjects (Tables 5 and 6), which could be irreversible. However, this could not be confirmed. Other related studies have shown that NO-mediated vasodilatation is ameliorated through aerobic exercises in NAFLD patients [43]. It has also been reported that the body fat content is reduced in DM and NAFLD patients with the help of aerobic exercise [44]. A corresponding waist hip ratio of DYP group might have explained the results but we were not able to collect this information from the participants. Briefly, NAFLD continues to be an important co-morbidity of DM as much as it has a strong association with cognitive impairment [45,46] and thus requires an early intervention. Knowing that Yoga aids in improving blood supply to the muscles and brain, it is possible that it enhances insulin receptor expression, causing increased glucose uptake, thus reducing blood sugar levels [47]. Briefly, the increase in secretion of hepatic lipase after Yoga practice enables increased uptake of triglycerides by adipose tissues, thereby lowering their levels [48,49].

Our report showing a decrease in MPG level after DYP is consistent with current reports that show that Yoga therapy decreases FBS, PPBS, HbA1c and LDL cholesterol with increased HDL cholesterol among diabetic patients [39]. This could be important in assessing whether the conversion of prediabetes into diabetes is possible by a cost-effective intervention. The inclusion of long-term Yogic practice by diabetic patients in their daily routine may ameliorate insulin sensitivity, lower glycemic index and even lipid profile, especially among patients with non-familial diabetes [50].

**Table 8**  
The proportion of female participants in various stress categories of VSS, PSS, and PHQ scales in Yoga and control groups.

Scale		Yoga group (n = 15)		Z- score	p-value	Control group (n = 11)		Z- score	p-value
		Pre n (%)	Post n (%)			Pre n (%)	Post n (%)		
VSS	Mild	9 (60%)	11 (73.3%)	-0.77	0.44	6 (54.54%)	8 (72.72%)	-0.88	0.373
	Moderate	6 (40%)	4 (26.66%)	0.77	0.44	5 (45.45%)	2 (18.18%)	1.37	0.170
	Severe	0	0	NA	NA	0	1 (9.09%)	-1.02	0.30
PSS	Mild	6 (40%)	6 (40%)	0	1	4 (26.66%)	5 (45.45%)	-0.43	0.66
	Moderate	8 (53.33%)	9 (60%)	-0.36	0.711	7 (73.33%)	5 (45.45%)	0.85	0.38
	Severe	1 (6.66%)	0	1.09	0.30	0	1 (9.09%)	-1.0	0.30
PHQ	Minimum	5 (33.3%)	5 (33.3%)	0	1	6 (54.54%)	7 (63.63%)	-0.43	0.66
	Mild	6 (40%)	5 (33.3%)	0.378	0.703	3 (27.27%)	3 (27.27%)	0	1
	Moderate	1 (6.6%)	5 (33.3%)	-1.82	0.06	2 (18.18%)	1 (9.09%)	0.62	0.53
	Moderate severe	1 (6.6%)	0	1.01	0.30	0	0	NA	NA
	Severe	2 (13.33%)	0	1.4	0.14	0	0	NA	NA

However, the optimum intensity and duration of exercise recommended to reduce the levels of cholesterol, LDL and increase in the levels of HDL is not achievable by many patients [51,52] because of which a simplified DYP was developed as a national effort. The high cholesterol can also be ascribed to the female study participants attaining menopause. Menopause is associated with a progressive decline in blood estrogen levels, which has been described to cause high blood cholesterol [53,54]. It is possible that DYP may not have a direct effect on the cholesterol levels in the menopausal and post-menopausal women. This was confirmed by comparing it with an independent data set of non-menopausal women. Unlike our study which showed an increase in cholesterol levels, the subjects included in most studies were both men and non-menopausal women [55,56]. Besides, DYP is not a very dynamic protocol that could impact cholesterol levels as significantly as HbA1c.

Previous reports suggest that 50–70% of maximum aerobic capacity must be practised three to five times a week for at least half an hour to control DM [57,58]; however, the DYP is a non-dynamic version of Yoga, which is not recommended for menopausal or polycystic ovary syndrome with high cholesterol, even though it was practiced for a period of three months.

The increase in the HDL level in the Yoga practising group is, however, consistent with another study [55]. As mentioned, DYP significantly reduced HbA1c levels in the experimental group. As discussed, these results are also consistent with previous findings [40,47,59]. A community based study involving diabetic patients demonstrated the beneficial effect of Yoga therapy in lowering the HbA1c levels as compared to controls [60]; however, no protocol has been tested as a nationwide trial with the scale and audacity of NMB. It will not be out of context to highlight the study of Jagtap *et al.*, who reported the effect of aerobic exercises on HbA1c level in diabetic patients and found that their levels were found reduced after the intervention of 'walking and Yoga', which suggests the positive and significant influence of Yoga in these patients [61] even though there was no standardised protocol or large sample size. A recent limited study investigated the effect of Yoga on HbA1c levels among diabetic subjects and found significantly reduced levels in diabetic patients who practised Yoga [62]. Therefore, the participants were segregated with respect to HbA1c, namely participants with IDRS  $\geq 60$  & HbA1c  $\geq 6.4\%$  and HbA1c  $\leq 6.4\%$  for simplification. As the results have shown significantly improved levels of HbA1c in the above groups, the progression of prediabetes to diabetes, estimated to be 37% within 4 years, may be halted if not left untreated [63,64]. Since the intervention of DYP lasted for only 3 months within the prediabetes group, the HbA1c levels decreased significantly ( $p < 0.015$ ), approaching baseline HbA1c. Therefore, DYP intervention can aid the prevention of conversion of prediabetes into diabetes if a larger public health intervention program is established through a national scheme.

The findings in this study provide evidence for undertaking longitudinal studies that not only assess the NAFLD outcome but also test cognitive functions consequent to DYP intervention. The incorporation of Yoga into their lifestyle can benefit patients struggling with non-communicable diseases like DM, hypertension, or stroke before being integrated into mainstream therapy. Most experts argue that Yoga should be practised with utmost care and under the supervision of a qualified and well-trained person. It is exemplified by a report of a female practitioner who suffered stroke after practising Yoga. This happened because she adopted an unusual and incorrect neck posture during Yoga practice [28]. It must be noted that India is undertaking the standardisation of Yoga protocols, some of which include Common Yoga Protocol, DYP and Cancer Yoga Protocol after United Nations (UN) declared June 21 as the International Yoga Day. Concurrently, Level I and Level II accreditation programs have been launched by the country for Yoga

professionals worldwide. Such programs will facilitate multi-centric studies based on a scientifically-derived Yoga protocol.

## 5. Conclusions

The HbA1c levels and stress were significantly altered after 3 months of DYP intervention but no change in liver size was noted. The cholesterol levels were increased in the menopausal women. A comparative study, with cholesterol lowering Common Yoga Protocol, is imperative.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.dsx.2019.07.007>.

## Author contribution statement

AS contributed with acquisition and compilation of data, and writing of the manuscript.

NK contributed with acquisition of data, and writing of the manuscript.

SK contributed with compiling and validation of data.

RT contributed with writing of the manuscript and statistical analysis.

DM contributed with writing, validation of data and statistical analysis.

MS contributed with analysis of lipid profile in postmenopausal women, and writing and submission of the manuscript.

VP contributed with analysis of lipid profile in postmenopausal women, and writing, submission and proof reading of the manuscript.

KM contributed to the collection of data and writing.

SB contributed with editing and compilation of data.

SM contributed with the editing of the manuscript.

RK contributed with validation of the data.

KS contributed to the collection of data.

AA<sup>1</sup> contributed with acquiring and interpretation of radiological data.

NM contributed with co-conceptualization of the manuscript.

VB contributed with clinical inputs of the acquired data.

RN is the principal investigator, contributed with editing and approval of the manuscript.

HR contributed with co-conceptualization, editing and approval of the manuscript.

AA<sup>2</sup> contributed with co-conceptualization and editing of the manuscript, and assigning tasks to the authors.

## Conflicts of interest

The authors declare no competing interests.

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