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Effect Of Pumpkin Seed Powder Supplementation On Metabolic Markers In Type 2 Diabetes Mellitus Patients

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Abstract

Background/Objectives: Diabetes mellitus is a metabolic disorder marked by hyperglycaemia from impaired insulin secretion or its action. Nowadays, the use of herbal medicine as an alternative treatment is increasing among patients with type 2 diabetes mellitus (T2DM). This study aimed to evaluate the effects of pumpkin seed powder supplementation on the BMI, BP, CBC, HbA1c, and lipid profile of T2DM patients. **Methods**: This open-label randomized trial was conducted on 52 T2DM patients aged 30 to 65 years, enrolled from the Department of Medicine. The patients were randomized into intervention (n=26) and control (n=26) groups, where the intervention group received 10 gm/day of pumpkin seed powder plus conventional T2DM medical treatment, while the control group received conventional T2DM medical treatment alone. Assessments were done at baseline and after 6 months. **Results**: In the intervention group, after follow-up, a significant decrease in BMI (p=0.0119) and decreased HbA1c level (6.8%) were found. The lipid profile showed a decrease in total cholesterol (2.6%), low-density lipoprotein (1.75%), very low-density lipoprotein (16.1%), a significant decrease in triglycerides (p=0.028), while an increase in high-density lipoprotein (3.24%). CBC levels did not significantly differ. However, there was no significant change in the control group from baseline to follow-up. **Conclusions**: The findings of this study indicate that in the intervention group, BMI was significantly reduced; a decrease in HbA1c and an improved lipid profile were also found after supplementation. This implies pumpkin seed powder supplementation could be an adjuvant nutrition for managing BMI, glycaemic and lipid profiles in T2DM patients.

Keywords: Nutritional supplement; Intervention; Diabetes Mellitus; Glycaemic Control; Metabolic Syndrome.

1. Introduction

Diabetes mellitus is a multifaceted metabolic disorder [1,2] characterised by a change in fat, protein and carbohydrate metabolism, resulting in defects in insulin secretion, insulin action or both, ultimately leading to chronic hyperglycaemia [3]. According to the World Health Organization (WHO) 2024 data published in The Lancet on World Diabetes Day, approximately 830 million people worldwide are living with diabetes [4]. India is home to an estimated 77 million people (over the age of 18 years) diagnosed with type 2 diabetes mellitus (T2DM) and nearly 25 million who are at the prediabetic stage, putting them at elevated risk of getting diabetes, as per WHO statistics [5]**.** Due to changes in lifestyle, the prevalence of diabetes has more than doubled worldwide over the past three decades [2,6]. Individuals with diabetes are two to three times more likely to experience heart attacks, strokes and other cardiovascular diseases [5]**.** Furthermore, T2DM impacts the kidneys and liver, increasing the risk of both acute and chronic kidney injury and liver cirrhosis [7], as well as small blood vessels,

jeopardizing microangiopathy (such as neuropathy, nephropathy, and retinopathy) along with the immune system, which may get dysfunction [1,2]. Therefore, diabetes has been considered a serious public health problem [8]. Treatment of T2DM is essential to prevent complications and worsening of the disease condition [9]. There is currently no permanent cure for diabetes, so patients have to rely on timely medication, a good lifestyle, and other interventions to prevent it and associated major health problems [8].

The major classes of conventional drugs for the treatment of T2DM include sulfonylureas, biguanides, peroxisome proliferator-activated receptor-γ (PPARγ) agonists and α-glucosidase inhibitors. These classes of drugs are either prescribed as monotherapy or combination therapy with other hypoglycaemics [10–12]. The use of certain antidiabetic therapies is frequently associated with adverse gastrointestinal issues such as dyspepsia, bloating, diarrhoea, nausea, vomiting, and sometimes constipation [13].

Also, the escalating cost of conventional diabetic medications has driven a growing consideration of alternative and complementary therapies for diabetes management. Some of the effective alternative therapies which have gained the limelight include medicinal plants, exercise therapy, diet and other lifestyle treatments for preventing T2DM [14].

Scientific literature has revealed that several plant species have hypoglycaemic qualities, and pumpkin is one of them [15–17]. Pumpkins (gourds) are related to the “Cucurbitaceae” family of the plant kingdom [18,19]. Pumpkin seed is a plentiful source of fibres, protein, minerals [17] (iron, zinc, manganese, copper, etc.) [20], unsaturated fatty acids and phytosterols. More than 95% of all fatty acids are found in pumpkin seeds, including linoleic, oleic, palmitic, and stearic acids. It also has a preventive effect against cardiovascular diseases [21]. Research shows that pumpkin seed oil can relieve high cholesterol and slow the progression of high blood pressure [22,23]. Overall, pumpkin seeds are an extraordinarily rich source of bioactive compounds with both nutraceutical and pharmaceutical properties, proving numerous health benefits [17].

The present study primarily focuses on the effect of pumpkin seed powder as a sole nutritional supplementation (devoid of combined supplementation with other seeds or seed powders) on T2DM patients. Thus, this study aims to evaluate the intervention’s impact on key metabolic markers and haematological parameters, including body mass index (BMI), blood pressure (BP), waist-hip ratio (WHR), glycated haemoglobin (HbA1c), lipid profile, and complete blood count (CBC) among T2DM patients.

2. Materials and Methods

The present study was conducted as an open-label randomized trial after approval by the Institutional Ethics Committee, which was then registered under Clinical Trial Registry India (website url: http://ctri.nic.in; registration number: CTRI/2024/05/067310). The study was conducted on T2DM patients attending the outpatient department (OPD) of the Department of Medicine at King George’s Medical University (KGMU), Lucknow, India.

This study was conducted in adherence to the Declaration of Helsinki. The written informed consent forms were obtained from patients before their inclusion in the trial. Patient enrolment was carried out based on the study’s inclusion criteria, which included male and female patients (aged 30 to 65 years) with less than or equal to a 10-year history of diabetes and ongoing conventional medical T2DM treatment as well as not being involved in any other research study or trial. As per exclusion criteria, the study excluded patients on insulin; those aged less than 30 years and more than 65 years; pregnant or nursing women; individuals with any other active medical conditions, endocrine disorders, hepatorenal complications, chronic illnesses, congenital disorders or neurological and psychiatric conditions; and patients already consuming pumpkin seed or any other commercially available nutritional supplements in the past 3 months.

A total of 100 T2DM patients were screened, out of which 68 were enrolled and randomized into two groups, i.e., 33 in the intervention group and 35 in the control group using randomized computer-generated random number table method. The study intervention included pumpkin seed powder consumption as a supplement (10 gm/day) for six months in addition to the patient's ongoing conventional T2DM medical treatment for the intervention group, while no intervention was provided to the control group in addition to their ongoing conventional T2DM medical treatment.

2.1. Baseline assessments (anthropometric, clinical and biochemical parameters)

Baseline anthropometric, clinical and biochemical assessments were conducted for both groups before intervention. Body weight and height were measured using an analogue weighing scale and stadiometer, respectively. A Standard formula was used to estimate BMI [weight (kg) / height (m^2)] and WHR [waist circumference / hip circumference]. BP and heart rate (HR) were recorded using an Omron BP monitor.

A blood sample (5 mL) was collected from patients (on an empty stomach) in the morning OPD for the baseline biochemical tests. The 5 mL blood sample was firstly split into 3 respective vials for a lipid profile (2 mL, plain), HbA1c (2 mL, EDTA) and CBC (1 mL, EDTA) in both groups. All tests were [CBC, HbA1c and lipid profile {total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL), very low-density lipoprotein (VLDL) and high-density lipoprotein cholesterol (HDL)}] carried out in accordance with the guidelines provided on the respective test kit by the manufacturer.

2.2. Study Intervention

In the intervention group, patients were instructed to consume 10 gm of pumpkin seed powder (5 gm half an hour before breakfast and 5 gm half an hour before dinner) in a day for six months. It was provided to the patients in a zip-lock pouch (2 pouches/month) alongside their standard conventional medical treatment. A daily dose of 10 gm was based on Food Safety and Standards Authority of India guidelines (FSSAI, 2016) [24,25]. The study's control group continued with their standard conventional medical treatment with no add-on intervention for six months. Pumpkin seeds used in the study were purchased quarterly (from Shudh Bharat, a unit of Ceyon Healthcare India Private Limited, Lucknow, India) and stored in a cool, dark place throughout the study. Pumpkin seeds were ground and then packed in zip-lock pouches (150 gm per pouch) before giving them to the patients.

2.3. Follow-up assessments

All assessments performed at baseline were repeated after six months during follow-up of both groups. In the intervention group, 26 patients had given their follow-up (n=7 lost to follow-up), and in the control group, 26 patients gave their follow-up (n=9 lost to follow-up).

2.4. Compliance of Intervention:

To assess and enhance compliance, patients of the intervention group received daily reminder messages via a WhatsApp group for pumpkin seed powder consumption. Compliance was also monitored through weekly phone calls and patient OPD-visits, every month for six months. During each visit, the patients collected their next supply of pumpkin seed powder pouches on returning the empty supplement pouches consumed in the previous month. This process continued throughout the six-month study period of each patient.

2.5. Statistical analysis

Data analysis was performed using GraphPad Prism 5 (GraphPad Software, La Jolla, CA). All data were presented as the mean, standard deviation (SD), number (n) and percentage (%). The normality of all parameters was checked using the D'Agostino and Pearson omnibus normality test. The differences between the two groups were evaluated using the unpaired t-test or Mann-Whitney U test, while the differences within the group were assessed using the paired t-test or Wilcoxon matched pair test. All the statistical tests with $p<0.05$ were considered statistically significant.

The study flowchart outlines the progression of the study from screening, recruitment, baseline assessments, supplementation, follow-up assessments upto data analysis (Figure 1).

Figure 1. Study flowchart.

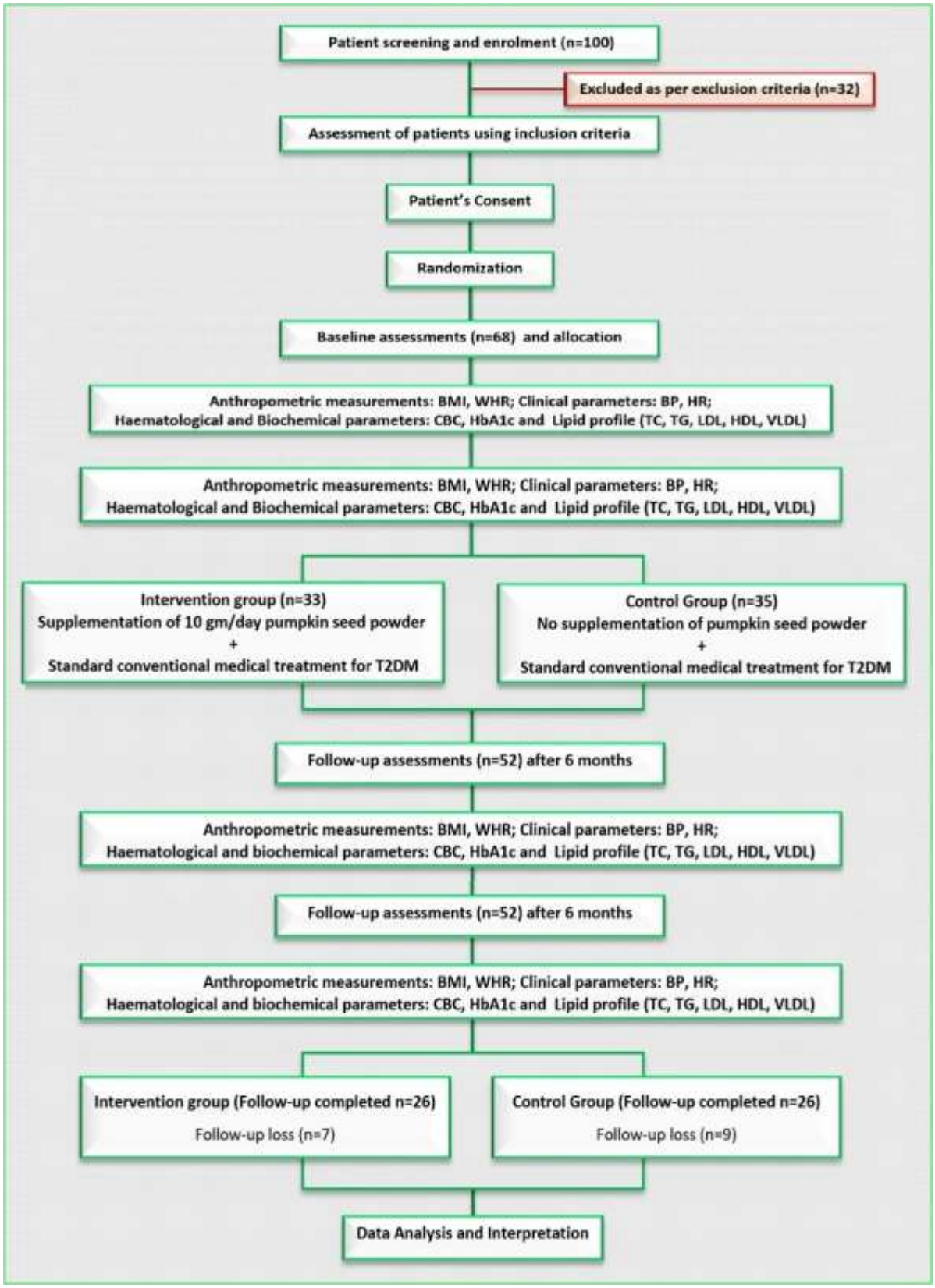

Figure 1. T2DM: Type 2 diabetes mellitus; BMI: body mass index; WHR: waist-hip ratio; BP: blood pressure; HR: heart rate; CBC: complete blood count; HbA1c: Glycosylated haemoglobin; TC: total cholesterol; TG: triglycerides; LDL: low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol; VLDL: very low-density lipoprotein.

The average age of the intervention group was 49.27±6.70 years, and of the control group, it was 51.19±11.02 years, which did not show any significant difference on comparison at baseline. In the intervention group there were 61.5% males and 38.5% females, whereas in the control group there were 57.7% males and 42.3% females at baseline. There was no discernible gender difference between the two groups (intervention and control group) at the baseline level (p=0.777). The parameters, such as history of diabetes, weight, BMI, WHR, systolic blood pressure (SBP), diastolic blood pressure (DBP) and HR, were found to be non-significant when compared in both groups at baseline. The baseline (demographic, anthropometric and clinical) parameters of the study are given in Table 1.

Table 1. Baseline demographic, anthropometric and clinical parameters of both groups.

Parameters (Baseline)	Intervention group (n=26) Mean±SD	Control group (n=26) Mean±SD	p-value
Demographic parameters			
Age (years)	49.27±6.70	51.19±11.02	0.4507
History of diabetes (years)	3.37±3.6	4.67±4.44	0.3190
Anthropometric parameters			
Weight (kg)	66.58±14.32	70.48±12.38	0.2975
BMI	26.52±4.3	27.07±4.85	0.4975
WHR	0.99±0.05	0.99±0.07	0.4790
Clinical parameters			
SBP (mmHg)	130.8±14.34	133.9±20.89	0.5997
DBP (mmHg)	82.38±8.66	82.71±9.94	0.9026
HR (beats/min)	84.92±10.38	85.08±7.92	0.9510

Data are expressed in mean±SD; p>0.05: non-significant
n: number of patients; SD: standard deviation; BMI: body mass index; WHR: waist-hip ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate

In the intervention group, on comparison between baseline and follow-up data, there was a 2.5% reduction in weight, a significant decrease of 4.9% in BMI ($p<0.05$), and a 2% reduction in WHR. Additionally, the SBP and DBP decreased by 2.9% and 3.8%, respectively, while HR showed a slight decline of 1%, though these were not statistically significant when baseline was compared to follow-up in the intervention group. Even though the control group also showed no significant differences in any of the measured anthropometric and clinical parameters on comparing baseline to follow-up. Likewise, none of the anthropometric and clinical parameters exhibited significant change when follow-ups of both groups were compared (Table 2).

Table 2. Comparison within the group (from baseline to follow-up) and between the two groups

Parameters	Intervention group (n=26)		Control group (n=26)		p-value		
Anthropometric	**Baseline Mean±SD**	**Follow-up Mean±SD**	**Baseline Mean±SD**	**Follow-up Mean±SD**	**p^{I}**	**p^{II}**	**p^{III}**
Weight (kg)	66.58±14.32	64.88±12.88	70.48±12.38	70.44±12.57	0.0898	0.9094	0.1216
BMI	26.52±4.30	25.22±4.26	27.07±4.85	27.15±4.94	0.0119*	0.9586	0.0774
WHR	0.99±0.05	0.97±0.05	0.99±0.07	0.99±0.05	0.7745	0.981	0.3759
Clinical							
SBP (mmHg)	130.8±14.34	126.9±15.25	133.9±20.89	133.7±22.93	0.2352	0.8616	0.3862
DBP (mmHg)	82.38±8.66	79.24±8.82	82.71±9.94	83.24±11.7	0.1003	0.4165	0.1786
HR (beats/min)	84.92±10.38	84.08±10.58	85.08±7.92	86.14±9.15	0.7423	0.3339	0.7571

Data are expressed in mean±SD; p>0.05: non-significant; *: p<0.05 (significant)
n: number of patients; SD: standard deviation
p^{I}: Comparison between the mean baseline and follow-up of intervention group; p^{II}: comparison between the mean baseline and follow-up of control group; p^{III}: comparison between the follow-ups of the two groups; BMI: body mass index; WHR: waist-hip ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate

(follow-ups) of anthropometric and clinical parameters.

The CBC parameters showed no significant difference between the two groups when compared at baseline. All the CBC parameters exhibited a slight variation in mean values from baseline to follow-up in both groups, but the changes were not upto the significant levels. The follow-up comparisons of both groups were also found to be non-significant (Table 3).

Table 3. Comparison within the group (from baseline to follow-up) and between the two groups (follow-ups) of haematological parameters.

Complete blood count	Intervention group (n=26)		Control group (n=26)		p-value		
	Baseline Mean±SD	**Follow-up Mean±SD**	**Baseline Mean±SD**	**Follow-up Mean±SD**	**p^{I}**	**p^{II}**	**p^{III}**
HGB (gm/dL)	13.35±1.74	13.37±1.28	13.32±1.75	13.13±1.59	0.9656	0.4746	0.4768
TLC (cells/mm^3)	8818±1180	8878±3106	8892±2112	8825±1996	0.6013	0.8509	0.4371
GRAN %	70.58±5.99	68.55±7.81	68.65±7.20	66.38±8.28	0.0591	0.0729	0.3558
LYM %	24.15±5.94	25.11±5.68	25.35±6.76	26.71±6.48	0.0937	0.0724	0.3901
MID %	5.27±1.41	4.77±1.30	6±1.35	5.47±1.3	0.2376	0.338	0.0669
PLT (Lac cells/mm^3)	1.44±0.66	1.61±0.73	1.34±0.53	1.49±0.48	0.068	0.0588	0.5036

MPV (fL)	15.7±7.71	15.4±8.45	13.97±1.32	13.68±1.59	0.2236	0.4464	0.5517
PCT (%)	0.19±0.08	0.20±0.08	0.18±0.07	0.18±0.06	0.7086	0.7984	0.2442
LPCR (%)	55.53±9.00	53.8±7.74	54.78±9.05	53.84±8.71	0.0884	0.4888	0.9873
PDW (%)	15.58±2.11	16.2±2.56	15.41±1.73	15.81±2.22	0.0749	0.315	0.5651
RBCs (Million cells/µL)	4.49±0.43	4.50±0.43	4.54±0.43	4.4±0.71	0.7637	0.5895	0.5543
MCV (fL)	86.18±8.65	85.61±9.74	88.68±11.38	87.48±10.65	0.1858	0.0995	0.6376
MCH (pg)	28.5±3.24	28.06±3.07	29.95±4.01	29.68±4.13	0.074	0.1207	0.1755
MCHC (gm/dL)	32.87±2.20	33.72±1.99	33.78±1.71	34.63±1.60	0.1129	0.0521	0.0818
RDWA (fL)	64.44±10.58	60.8±9.64	68.64±11.24	66.16±10.62	0.0514	0.2695	0.0702
RDWR (%)	12.74±1.88	13.77±1.94	12.61±1.56	13.58±1.85	0.0571	0.0578	0.7252
HCT (%)	40.05±5.96	38.6±5.79	40.33±6.17	37.33±5.63	0.0573	0.1417	0.4621

Data are expressed in mean±SD; p>0.05: non-significant
n: number of patients; SD: standard deviation; p^{I}: Comparison between the mean baseline and follow-up of intervention group; p^{II}: comparison between the mean baseline and follow-up of control group; p^{III}: comparison between the follow-ups of the two groups; HGB: haemoglobin; TLC: total leukocyte count; GRAN: granulocytes; %: percentage; LYM: lymphocyte; MID: mid cell; PLT: platelets; MPV: mean platelet volume; PCT: plateletcrit; LPCR: platelet-large cell ratio; PDW: platelet distribution width; RBC: red blood cell; MCV: mean cell volume; MCH: mean cell haemoglobin; MCHC: mean corpuscular haemoglobin concentration; RDWA: red cell distribution width; RDWR: red cell distribution width ratio; HCT: haematocrit

The mean values of the HbA1c were non-significant at baseline among both the groups. In the intervention group, the mean value of the HbA1c level at baseline was 6.72±1.3%, which decreased to 6.26±1.01% after follow-up, while in the control group, negligible change was found from 6.68±1.59% at the baseline to 6.60±1.5% after the follow-up. The follow-up comparisons of both groups were also found to be non-significant (Figure 2).

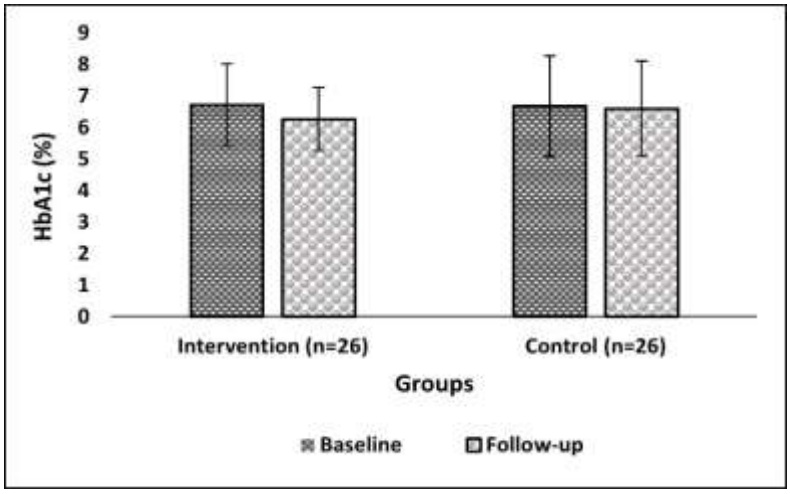

Figure 2. Glycosylated haemoglobin (HbA1c) values of the intervention and control group.

Data are expressed in mean±SD; p>0.05: non-significant
n: number of patients; HbA1c: glycosylated haemoglobin; %: percentage

Figure 3 represents lipid profile parameters with no significant differences when the baseline values of both the groups were compared. The mean value of total cholesterol in the intervention group was 179.8±47.21 mg/dL at baseline, which decreased to 175.1±47.34 mg/dL after follow-up. While in the control group, it was 173.5±32.62 mg/dL at baseline, which decreased to 171±26.01 mg/dL after follow-up. Besides this, triglycerides in the intervention group exhibited a significant decrease ($p<0.05$) from baseline to follow-up, while in the control group, an increase from baseline to follow-up values was found but not upto significant levels.

Moreover, the mean values of HDL in the intervention group increased by 3.24% from baseline (53.09±8.86 mg/dL) to follow-up (54.87±9.14 mg/dL), whereas in the control group, it decreased from 52.05±11.1 mg/dL at baseline to 49.34±6.38 mg/dL after follow-up. Furthermore, in the intervention group the mean LDL value was decreased by 1.75% from baseline (86.66±32.43 mg/dL) to follow-up (85.14±26.47 mg/dL), and VLDL was decreased by 16.1% from baseline (40.61±19.64 mg/dL) to follow-up (34.07±12.17 mg/dL). But, in the control group, both LDL and VLDL showed an increase after the follow-up. Undeniably, HDL, LDL and VLDL did show changes in both groups but were not found to be significant. The follow-up comparisons of both groups among respective parameters of lipid profile were also found to be non-significant (Figure 3).

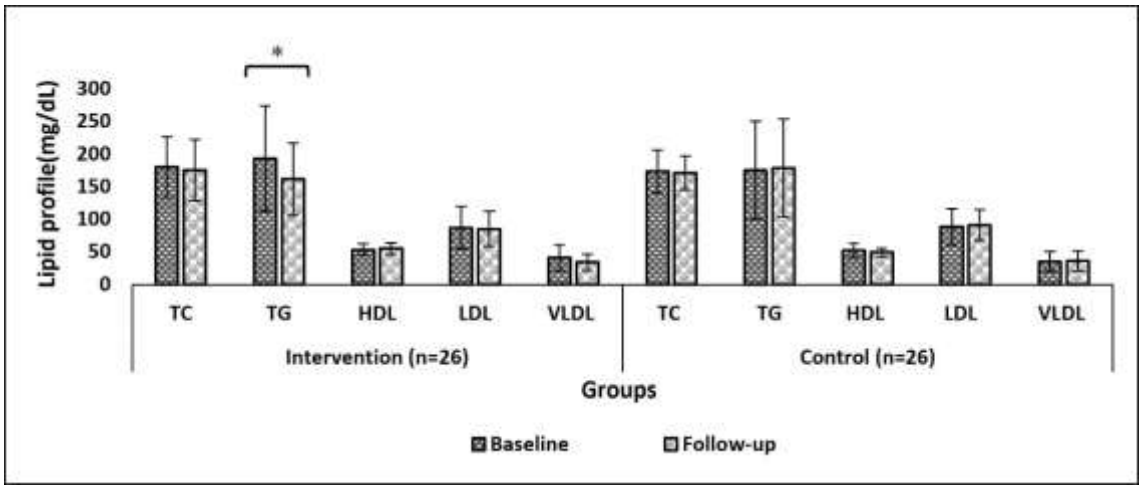

Figure 3. Lipid profile of the intervention and control group.

Data are expressed in mean±SD; p>0.05: non-significant; *: p<0.05 (significant)
n: number of patients; TC: total cholesterol; TG: triglycerides; HDL: high-density lipoproteins; LDL: low-density lipoproteins; VLDL: very low-density lipoproteins

4. Discussion

Pumpkin seeds have demonstrated promising antidiabetic effects in animal studies, particularly in diabetic rats and mice. A limited number of human trials have also examined the effect of pumpkin seeds and related products, including pumpkin seed oil, flour, and extract, either alone or in combination with other seeds or ingredients. Although numerous review papers have highlighted the antidiabetic and antilipidemic potential of pumpkin seeds based on their rich nutritional profile, there remains a significant gap in clinical evidence, particularly regarding long-term human intervention studies. To date, no studies have specifically evaluated the effect of six months of pumpkin seed powder

supplementation among type 2 diabetes patients in the Indian population. Therefore, this study was primarily focused on evaluating the effect of pumpkin seed powder consumption on the weight, BMI, WHR, BP, CBC, glycaemic and lipid profiles of T2DM patients.

The present randomized study after supplementation of pumpkin seed powder (10 gm/day) to T2DM patients showed a reduction in weight (2.5%) and the BMI ($p<0.05$) was found to decrease significantly, while WHR (2%) without any significant decrease from baseline to follow-up in the intervention group. Meanwhile, the control group did not show any significant differences in weight, WHR and BMI between baseline and their follow-up values. In the same context, a study conducted on T2DM patients by replacing grain-based flour with seed-based flour (pumpkin seeds, sunflower seeds, watermelon seeds, soya, and flaxseeds) for a 12-week period reported a mean weight reduction (11%), which was statistically significant ($p<0.001$) [26]. Besides human trials, in an animal study, treatment with Cucurbita maxima seed extracts for 21 days resulted in a significant reduction in body weight gain among diabetic rats, compared to control rats [27]. While, in another human study where 5 gm of pumpkin seed intervention was given for 60 days to women (diagnosed with metabolic syndrome), there was a reduction reported in body weight, waist circumference, and BMI. However, these changes were non-significant when compared with their counterparts [24]. Substantial evidence suggests that the pumpkin seeds may aid weight regulation due to their high crude fibre content [28], which promotes satiety, delays gastric emptying, and improves insulin sensitivity [29]. On top of that, their rich oleic acid content may help regulate BMI by activating adenosine monophosphate-activated protein kinase (AMPK) signalling in the hypothalamus, which decreases appetite and energy expenditure [30], ultimately leading to a reduction in BMI.

Moreover, a human study (with medical conditions including dyslipidaemia, hypertension, diabetes, and obesity) in which the cases received 1000 mg of pumpkin seed oil daily in addition to counselling for a healthy diet and lifestyle for 90 days highlighted the antihypertensive potential of pumpkin seed oil in the case group as evidenced by a significant reduction in DBP [31]. Similarly, our findings depict a reduction in SBP of 3.9±0.91 mmHg (2.9%) and DBP of 3.14±0.16 mmHg (3.8%) in the intervention group but without a significant decrease after comparing baseline to follow-up. This implies that pumpkin seed consumption may help lower BP because of their existing vasodilatory properties due to the presence of the cucurbitin protein compound in them [32]. Mechanistically, pumpkin seeds exert antihypertensive effects by reducing malondialdehyde and increasing nitric oxide levels in endothelial cells which promote vascular relaxation [33,34]. Also, protein hydrolysates derived from pumpkin seed protein inhibit angiotensin-converting enzyme (ACE) activity, thereby reducing angiotensin II production and promoting vasodilation, which can help lower BP [35–37]. Additionally, essential nutrients such as magnesium, potassium, and unsaturated fatty acids found in the pumpkin seed contribute to cardiovascular health and also aid BP regulation [35,38]. To our surprise, our study follow-ups on comparison with the baseline of CBC parameters in both the groups were found to be non-significant.

Furthermore, the Indian study demonstrated that carbohydrate reduction achieved by replacing grain-based flour with a seed-based flour mixture (pumpkin seeds, sunflower seeds, soya, watermelon seeds, and flaxseeds) showed a major drop in HbA1c from an average of 8.65% to 6.31%, i.e., an average reduction of 2.34% in HbA1c ($p<0.01$) after 12 weeks of intervention among T2DM patients [26]. In an animal study where pumpkin seeds and their oil were given to diabetic rats for 1 month in varying amounts, the blood glucose and HbA1c levels were found to be significantly reduced along with a significant elevation in insulin level [22]. In line with this finding, our result also showed a decreased HbA1c level by 6.8% in the intervention group after comparing its baseline values to the follow-up values, but the reduction was found to be non-significant. While in the control group, negligible change was found from baseline to follow-up. The hypoglycaemic action of pumpkin seeds is due to the tocopherols, flavonoids, phenolic compounds [39,40] and saponins [15,27] present in them. Tocopherols act as antioxidants that reduce oxidative stress, flavonoids improve glucose metabolism by enhancing insulin sensitivity, phenolic compounds protect β-cells through antioxidant activity, and saponins stimulate β-cells to boost insulin secretion [15,27] which altogether reduces blood sugar levels. Also, polysaccharides in pumpkin seeds are acclaimed to increase pancreatic β-cells, activate

phosphoinositide 3-kinase/serine/threonine-specific protein kinase (PI3K/Akt) and trigger insulin signalling, thereby reducing β-cell dysfunction, showing their strong antidiabetic effects [41,42].

Interestingly, an animal study performed on diabetic rats with elevated total cholesterol and triglycerides demonstrated that after supplementation of a flax and pumpkin seed mixture for 14 days, the total cholesterol levels in plasma and liver decreased by 47% and 45%, respectively, LDL reduced by 63%, and HDL increased by 33% [43]. Another study on diabetic rats, divided into nine groups and fed with three different forms of pumpkin powder (peel, flesh, and seed) in varying doses of 5, 10, and 15 g for 28 days, exhibited a significant reduction in serum total cholesterol, triglyceride, and LDL along with a significant increase in HDL level [44]. Consistently, Abd-elnoor and E. V. (2019) found that supplementation of either 1% or 3% pumpkin seed powder/oil among diabetic rats presented a substantial decrease in total cholesterol, triglycerides, and LDL as well as VLDL and improved HDL levels when compared to the diabetic control group [22]. Furthermore, an Egyptian study stated that pumpkin seed and sunflower seed supplementation for 1 month resulted in decreased overall lipid profile levels in diabetic rats [45]. Undeniably, our study observations in T2DM patients indicate notable changes in lipid profile parameters [total cholesterol (2.6% decrease), LDL (1.75% decrease), VLDL (16.1% decrease), decreased triglycerides ($p<0.05$), and increased HDL (3.24%)] after comparing baseline to follow-up in the intervention group. While no significant changes in the control group (from baseline to follow-up) were found. A potential reason for the hypolipidemic effect of pumpkin seed is due to its protein, vitamins, and unsaturated fatty acid (mainly omega-6) rich content [46,47]. Also, the arginine-rich extract in pumpkin seeds enhances nitric oxide (NO) production, reducing LDL oxidation, inflammation, and Vascular Cell Adhesion Molecule (VCAM) expression [48,49], thus helping in mitigating the risk of plaque buildup in arteries and eventually supporting cardiovascular health.

Some of the limitations of this study were that it was an open-label study, i.e., with no blinding or inclusion of a placebo group. The study also involved a small sample size, and the time of consumption of the supplement was not in the control of the investigator, as the meal timings varied from patient to patient.

For future research, the inclusion of blinding and a placebo group could be considered. Additionally, an increase in sample size would improve the statistical power and allow the finding to be generalized to a large population. Overall, this study indicates that incorporating pumpkin seed powder into the diet may help improve BMI, HbA1c, and lipid profile in patients with T2DM, demonstrating its potential as a supportive strategy for managing diabetes mellitus.

5. Conclusions

Our study concludes that pumpkin seed powder supplementation for six months among T2DM patients has shown a significant decrease in BMI and reduced HbA1c. In the case of the lipid profile, a significant decrease in triglycerides as well as a slight increase in HDL levels were also found. This implies pumpkin seed powder supplementation in addition to the ongoing/conventional medical treatment is an adjuvant nutrition for managing obesity and glycaemic as well as lipid profiles in T2DM patients.

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Abbreviations

The following abbreviations are used in this manuscript:

AMPK	Adenosine monophosphate-activated protein kinase
ACE	Angiotensin-converting enzyme
BMI	Body mass index
BP	Blood pressure
CBC	Complete blood count
DBP	Diastolic blood pressure
FSSAI	Food Safety and Standards Authority of India guidelines
HbA1c	Glycated haemoglobin
HDL	High-density lipoprotein cholesterol
HR	Heart rate
ICMR	Indian Council of Medical Research
KGMU	King George's Medical University
LDL	Low-density lipoprotein cholesterol
n	Number
NO	Nitric oxide
OPD	Outpatient department
PPARγ	Peroxisome proliferator-activated receptor-γ
SBP	Systolic blood pressure
SD	Standard deviation
TC	Total cholesterol
TG	Triglycerides
T2DM	Type 2 diabetes mellitus
VCAM	Vascular cell adhesion molecule
VLD	Very low-density lipoprotein
WHO	World health organization
WHR	Waist-hip ratio

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