Original Article

# A Study of Lifestyle Modifications With and Without Metformin in Prediabetic Subjects

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## Abstract

**Purpose:** Prediabetes is a stage in the natural history of impaired glucose metabolism rather than as a distinctive clinical entity. The primary objective was to compare the effect of lifestyle modifications (LSMs) with and without metformin in prolonging the onset of diabetes mellitus in prediabetics. **Materials and Methods:** This study is an open label, parallel group comparative study conducted from 2016 to 2020. One hundred and four prediabetic subjects were assigned to two groups: group I (51) LSM and group II (53) metformin 500 mg along with LSM. Baseline investigations included fasting blood sugar (FBS), post-prandial blood sugar (PPBS), HbA1c, and lipid profile, followed up for 12 months. **Results:** The baseline parameters were comparable between the groups. In both the groups, there was a significant reduction in abdominal circumference, total cholesterol, triglycerides, low-density lipoprotein, FBS, PPBS, and HbA1c between baseline and 1 year. There was no significant difference between groups I and II in reduction of all the above-mentioned parameters. The outcomes of prediabetic subjects after 1 year of treatment in both the groups were comparable. Only one (2.1%) subject had more than 126 mmHg FBS in the LSM group. The adverse effects observed were dizziness, nausea, flatulence, myalgia, abdominal pain, and heart burn, which were mild to moderate in intensity and in most patients it subsided with time. **Conclusion:** LSM alone was equivalent to LSM along with metformin in effective control of blood sugars. Lipid profile and weight may be significantly reduced.

**Keywords:** Lifestyle modification, metformin, prediabetes, weight reduction

## Introduction

Diabetes mellitus (DM) as an epidemic continues to threaten the health of a large number of individuals in developing and developed countries.[1] Diabetes is associated with various macrovascular and microvascular complications, which accounts for excess morbidity, mortality, and healthcare costs. Thus diabetes is a critical public health challenge and gaining importance at the preventive level. Prediabetes is viewed as a stage in the natural history of impaired glucose metabolism rather than as a distinctive clinical entity.[2] Prediabetes is a condition which includes either impaired fasting glucose (IFG) where the fasting blood sugar (FBS) level is in the range of >100 to < 126 mg/dL or impaired glucose tolerance (IGT) where the 2-h glucose post-prandial blood sugar (PPBS) is in the range of >140 to <200 mg/dL.[2] In few people, both IFG and IGT can coexist. It is associated with risk factor presaging the development of diabetes and is associated with increased risks of cardiovascular complications.[3] The strategies developed to decrease the disease progression from IGT/IFG to type 2 DM can benefit to reduce the cardiovascular morbidity and mortality.[3] The transition from prediabetes to diabetes may take years but may also be rapid.[4] The risk of developing diabetes in prediabetics is 5–10% when compared with 0.7% in normoglycemics.[1,4,5]

Prediabetes is one of the components in metabolic syndrome as it is defined by the National cholesterol Education Program Adult Treatment Panel III (NCEP

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ATP III). According to this guideline, the metabolic syndrome is defined as the presence of three out of five risk factors that are obesity, hyperglycemia, low high-density lipoprotein (HDL) cholesterol, hypertriglyceridemia, and hypertension. The occurrence of metabolic syndrome is increasing globally more so in India due to sedentary lifestyle, easy economy, and modernization of diet.[6] Individual component in metabolic syndrome is an independent risk factor for type 2 DM.[7]

## Lacuna of Knowledge

Preventive measures at the prediabetes level are important. The most common intervention is diet and exercise. The pharmacological agents used for preventing diabetes during prediabetic stage are metformin, troglitazone, and acarbose.[6,8-10] Prevention of diabetes is of enormous value in the Indian scenario because the cost of diabetic care is high.[11,12] Metformin is approved by the Food and Drug Administration for the treatment of prediabetes, so has to prolong the onset of type 2 DM. Metformin is shown to reduce relative risk by 31% in the DPP-2002 study. Metformin was most effective in obese individuals with body mass index (BMI) of ≥ 35 kg/m$^2$, with reduction in incidence by 50%. The major side effects noted with metformin in these studies were gastrointestinal disturbances such as nausea, vomiting, and diarrhea.[8] The major drawback with metformin is its limited use in individuals with renal failure, hepatic failure, and congestive cardiac failure.[13]

Intensive LSMs have proved beyond doubt to reduce the blood sugar levels, hyperlipidemia, and obesity which are the risk factors for type II DM, which in turn increase cardiovascular mortality and morbidity.[3,7,8,14,15] Despite its efficacy, in Indian scenarios, the adherence to intensive lifestyle changes is challenging. The dietary advice which is flexible and more appropriate to the local population along with minimum exercise would be much easier for the people to adhere. If the adherence is better and effortless, these interventions will benefit the patient for a long duration. As per the literature search, studies comparing the effect of LSM with or without metformin in prediabetics in this region of the country are lacking. Hence, the present study was planned to compare the efficacy of LSM and metformin, prolonging the onset of DM in prediabetics.

## Materials and Methods

This is an open label, parallel group comparative study conducted from October 2016 to January 2020 at R L Jalappa Hospital and Research Center attached to Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research (SDUAHER), Kolar, Karnataka on participants with prediabetes. The study was approved by the Central Ethics Committee, SDUAHER, Kolar, Karnataka, India with No. SDUAHER/KLR/R&D/37/2016–17. The study was conducted in accordance with the ethical standards of the National Ethical Guidelines for Biomedical and Health Research involving Human Participants 2017 by Indian Council of Medical Research and registered in Clinical Trial Registry of India No. CTRI/017/09/009635.

Individuals with no history of diabetes visiting for other non-serious illness/general health check-up were tested for FBS or random blood sugar and confirmed prediabetes status from Department of General Medicine (outpatients and inpatients) and were screened for the inclusion criteria. The adults of either gender, aged between 20 and 70 years, BMI 18.5–29.9 kg/m$^2$ and with prediabetic status (American Diabetes Association, ADA 2011 guidelines), IFG (FBS >100 < 126 mg/dL), IGT (2-h glucose PPBS >140 <200 mg/dL), and HbA1c (5.7–6.4%) were counseled for the condition and explained regarding the study. Participants with contraindications to metformin (congestive cardiac failure, hepatic dysfunction, renal impairment, respiratory disease, glucocorticoid therapy, and hypersensitivity) were excluded from the study. The participants were handed over a participant information sheet and those who were willing to participate and adhere to 12 months' follow-up were recruited after obtaining written informed consent.

The participants were counseled for dietary habits such as avoiding sweet dishes, restricting rice to 1 cup/day, including wheat, finger millet (Nachini, Ragi), pearl millet (Bajra, Sajje), foxtail millet (Kangni, Navane), kodo millet (Kodra, Harka), little millet (Shavan, Saame), and sorghum millet (Jowar, Jola) daily in diet, preferably advised to use the millet grown locally, three major meals converted to five minor meals [50% food and 50% vegetables + fruits (optional and locally available)], include more protein-rich food such as pulses, legumes, egg, and lean meat, and physical activity (walking for 30 min per day for 5 days/week) by the principal investigator (PI) and physician. A dietary chart was planned in consultation with the dietician of the Academy and the same was provided to the patients. They were provided with a dairy to maintain the daily activity and adherence to advice such as dietary intake, physical activity, and drug intake. At each follow-up, the patients were requested to bring this chart and diary for verification by the PI.

The participants were explained about the various advantages and disadvantages for both interventions. Based on patients' choice, they were divided into group L and group M. Group L were advised dietary restriction and physical activity and group M received tab metformin 500 mg (Tab Melmet 500 mg, Micro Labs Ltd) once daily along with LSM for 1 year.

Patients' demographic, anthropometric data, and follow-up details were recorded in the case record form.

**Table 1: Demographic and biochemical characteristics at baseline**

| Parameters | Group 1 (LSM) (mean±SD) *n*=51 | Group 2 (LSM+Met) (mean±SD) *n*=53 | *P*-value |
|---|---|---|---|
| Age (years) | 48±9.04 | 46.57±9.65 | 0.597 |
| Gender (female/male) | 20/31 | 29/24 | 0.121 |
| Place (rural/urban) | 27/24 | 30/23 | 0.843 |
| Weight (kg) | 71.24±10.59 | 69.37±10.37 | 0.587 |
| Height (m) | 1.62±0.07 | 1.60±0.05 | 0.06 |
| BMI | 26.81±2.96 | 26.96±3.74 | 0.432 |
| Abdominal circumference (cm) | 91.17±11.25 | 89.58±13.92 | 0.122 |
| FBS (mg/dL) | 104±13.1 | 107.89±12.39 | 0.618 |
| PPBS (mg/dL) | 151±22.6 | 158.5±25.16 | 0.237 |
| HbA1c | 6.15±0.22 | 6.25±0.21 | 0.07 |
| Lipid profile | | | |
| Total cholesterol | 187.68±49.28 | 192.28±37.36 | 0.176 |
| Triglycerides | 176.03±76.01 | 207.11±85.07 | 0.306 |
| LDL | 119.74±4429 | 125.45±47.09 | 0.898 |
| HDL | 43.58±16.83 | 41.81±18.29 | 0.890 |
| Liver function test | | | |
| AST | 30.84±14.5 | 29.60±14.94 | 0.650 |
| ALT | 31.92±15.1 | 31.73±17.27 | 0.408 |
| GGT | 27.58±12.47 | 29.20±17.68 | 0.670 |
| Alkaline phosphatase | 92.47±45.17 | 96.54±26.81 | 0.990 |
| Total bilirubin | 0.74±0.21 | 0.68±0.27 | 0.874 |
| Direct bilirubin | 0.35±0.11 | 0.39±0.21 | 0.785 |
| Serum creatinine | 0.95±0.28 | 0.91±0.26 | 0.920 |
| Blood urea | 23.82±5.21 | 25.52±5.18 | 0.837 |

Values: mean±SD

The baseline characteristics between the groups were comparable. Majority of the participants in both the groups were from the rural area

**Table 2: Blood sugar values in group I (LSM)**

| Parameters | Baseline *n*=49 (mean±SD) | 3 months *n*=49 (mean±SD) | 6 months *n*=49 (mean±SD) | 1 year *n*=49 (mean±SD) | *P*-value |
|---|---|---|---|---|---|
| FBS | 103.8±10.6 | 101.8±10.8 | 100.7±10.9 | 98.8±9.54 | 1 $\alpha$2 = 1.00<br>1 $\alpha$3 = 0.91<br>1 $\alpha$4 = 0.16<br>2 $\alpha$3 = 1.00<br>2 $\alpha$4 = 0.76<br>3 $\alpha$4 = 1.00 |
| PPBS | 149±22.5 | 143.6±16.5 | 140.6±19.8 | 125.04±21.8 | 1 $\alpha$2 = 0.14<br>1 $\alpha$3 = 0.02<br>1 $\alpha$4 = 0.001<br>2 $\alpha$3 = 1.00<br>3 $\alpha$4 = 0.001 |
| HbA1c | 6.15±0.22 | 6.00±0.20 | 6.00±0.17 | 6.08±1.08 | 1 $\alpha$2 = 0.04<br>1 $\alpha$3 = 0.04<br>1 $\alpha$4 = 0.12<br>2 $\alpha$3 = 1.00<br>3 $\alpha$4 = 0.07 |

Baseline investigations included FBS, HbA1c, lipid profile, blood collection including 12 h fasting and method PPBS after 2 h of food intake. All the participants who completed 1-year follow-up along with one of the two follow-ups in between on 3rd and 6th months were included for the analysis. Annually electrocardiogram, fundoscopy, liver function test (LFT), serum creatinine, and blood urea were done to rule out complications. At 3 and 6 months of follow-up, FBS, PPBS, HbA1c, and after 12 months FBS, PPBS, HbA1c, and lipid profile were done.

**Table 3: Blood sugar values in group II (LSM+ metformin)**

| Parameters | Baseline *n*=48 (mean±SD) | 3 months *n*=48 (mean±SD) | 6 months *n*=48 (mean±SD) | 1 year *n*=48 (mean±SD) | *P*-value |
|---|---|---|---|---|---|
| FBS | 107.5±12.39 | 105.2±13.31 | 100.8±12.03 | 96.9±8.20 | 1 $\alpha$2 = 0.95<br>1 $\alpha$3 = 0.01<br>1 $\alpha$4 = 0.001<br>2 $\alpha$3 = 0.95<br>2 $\alpha$4 = 0.14<br>3 $\alpha$4 = 0.05 |
| PPBS | 158.4±25.9 | 151.2±22.9 | 140.5±22.8 | 130.3±19.8 | 1 $\alpha$2 = 0.11<br>1 $\alpha$3 <0.001<br>1 $\alpha$4 <0.001<br>2 $\alpha$3 = 0.003<br>2 $\alpha$4 <0.001<br>3 $\alpha$4 <0.001 |
| HbA1c | 6.25±0.03 | 6.02±0.02 | 6.00 | 6.00 | 1 $\alpha$2 <0.001<br>1 $\alpha$3 <0.001<br>1 $\alpha$4 <0.001<br>2 $\alpha$3 = 1.00<br>2 $\alpha$4 = 1.00<br>3 $\alpha$4 = 1.00 |

**Table 4: Comparison of weight, BMI, and lipid profile between baseline and 1 year: group I**

| Parameters | Baseline | 1 year | *P*-value |
|---|---|---|---|
| Weight | 71.04±10.7 | 66.22±8.9 | <0.001 |
| BMI | 26.68±2.9 | 25.0±2.7 | <0.001 |
| AC | 92.04±10.3 | 88.7±11.2 | 0.043 |
| Lipid profile | | | |
| Total cholesterol | 187.16±50.06 | 174.61±45.27 | 0.004 |
| Triglycerides | 173.08±76.0 | 163.2±64.0 | 0.071 |
| LDL | 120.5±44.7 | 116.22±41.21 | 0.019 |
| HDL | 43.92±17.1 | 48.06±5.56 | 0.073 |
| FBS | 103.82±12.9 | 98.8±13.7 | 0.027 |
| PPBS | 149.8±22.5 | 125.0±21.8 | <0.001 |
| HbA1c | 6.15±0.22 | 6.08±0.20 | 0.078 |

**Table 5: Comparison of weight, BMI, and lipid profile between baseline and 1 year: group II**

| Parameters | Baseline | 1 year | *P*-value |
|---|---|---|---|
| Weight | 69.25±9.59 | 67.10±9.41 | 0.31 |
| BMI | 27.05±3.3 | 26±3.49 | 0.116 |
| AC | 90.62±12.94 | 86.51±10.4 | 0.025 |
| Lipid profile | | | |
| Total cholesterol | 195.2±58.6 | 184.2±55.6 | 0.003 |
| Triglycerides | 210.3±87.9 | 185.7±55.6 | <0.001 |
| LDL | 126.7±47.7 | 118.2±36.8 | 0.003 |
| HDL | 41.6±19.2 | 46.3±6.2 | 0.072 |
| FBS | 107.56±12.38 | 96.9±8.28 | <0.001 |
| PPBS | 158.48±25.9 | 130.38±19.8 | <0.001 |
| HbA1c | 6.25±0.25 | 6 | <0.001 |

At the end of 1 year, the participants were categorized as normal (FBS <100 mg/dL), 2-h glucose PPBS (<140 mg/dL and HbA1c <5.6%), prediabetic (FBS >100 <126 mg/dL) or 2-h glucose PPBS (>140 to <200 mg/dL or HbA1c 5.7–6.4%), and diabetic (FBS>126 mg/dL or 2-h glucose PPBS >200 mg/dL and HbA1c >6.5%).

Patients were advised to report any side effects/adverse effects as soon as they occur if it was serious in nature or were suggested to note down in their dairy and report the same when they come for follow-up. Adverse drug reactions were documented and assessed using the WHO causality assessment scale. The events were classified as certain (if it has a plausible time relationship to drug intake and if the adverse effect subsided on withdrawal of the drug and rechallenge is positive), probable (if it has a reasonable time relationship to drug intake, if adverse effect subsides on withdrawal of the drug), possible (if there is reasonable time relationship to drug intake if adverse effect can be explained by disease or other drugs), unlikely (if it has an improbable time relationship to drug intake if the adverse effect can be explained by disease or other drugs), conditional (if more data for assessment are required), and unassessable (if data cannot be supplementary or verified).

## Statistical analysis

The sample size was calculated using relative risk reduction by metformin 40% in previous studies. Assuming 15% relative risk reduction with LSM alone, we calculated a sample size of 42 in each arm with a power of 80% and an $\alpha$ error of 5%. Keeping 5% dropout rate, our sample size is 45 in each arm. The total number of samples was 90 subjects. The statistical analysis was done using GraphPad software online (GraphPad Prism version 7, QuickCalcs) and SPSS version 20, IBM SPSS Statistics for Windows, Version 20.0, IBM Corp., Armonk, NY, USA. Analysis was done as per intention to treat protocol. Normality

**Table 6: Comparison of anthropometric and biochemical parameters between the groups**

| Parameters | Group I | Group II | *P*-value |
|---|---|---|---|
| At 3 months | | | |
| FBS | 101.8 ± 10.8 | 105.2 ± 13.31 | 0.437 |
| PPBS | 143.6 ± 16.5 | 151.2 ± 22.9 | 0.017 |
| HbA1c | 6.00 ± 0.20 | 6.02 ± 0.02 | 0.042 |
| At 6 months | | | |
| FBS | 100.7 ± 10.9 | 100.8 ± 12.03 | 0.778 |
| PPBS | 140.6 ± 19.8 | 140.5 ± 22.8 | 0.158 |
| HbA1c | 6.00 ± 0.17 | 6.00 | 0.197 |
| At 1 year | | | |
| Weight | 66.22 ± 8.9 | 67.10 ± 9.41 | 0.441 |
| BMI | 25.0 ± 2.7 | 26 ± 3.49 | 0.288 |
| AC | 88.7 ± 11.2 | 86.51 ± 10.4 | 0.341 |
| Lipid profile | | | |
| Total cholesterol | 174.61 ± 45.27 | 184.2 ± 55.6 | 0.208 |
| Triglycerides | 163.2 ± 64.0 | 185.7 ± 55.6 | 0.639 |
| LDL | 116.22 ± 41.21 | 118.2 ± 36.8 | 0.631 |
| HDL | 48.06 ± 5.56 | 46.3 ± 6.2 | 0.369 |
| FBS | 98.8 ± 13.7 | 96.9 ± 8.28 | 0.354 |
| PPBS | 125.0 ± 21.8 | 130.38 ± 19.8 | 0.238 |
| HbA1c | 6.08 ± 0.20 | 6 | 0.148 |

of distribution was assessed using the Kolmogorov–Smirnov test. The demographic data were analyzed using descriptive statistics. The biochemical parameters were expressed as mean with standard deviation. Significance of the difference between the groups with or without metformin was evaluated using Student's *t*-test. The biochemical parameters within the group were analyzed using repeated-measures analysis of variance. The adverse effects were analyzed using the $\chi^2$ test. A *P*-value of less than 0.05 will be considered as statistically significant.

## Results

Patients recruited initially in our study were 124, out of which 104 were allocated to two groups. A flow chart summarizing the study recruitment and follow-up is shown in Figure 1. The baseline characteristics were comparable between the groups as shown in Table 1.

In comparison to baseline, there was a significant fall in PPBS and HbA1c at 1 year as shown in Figures 2 and 3. There was a decrease in FBS from baseline to 1 year but not statistically significant.

In comparison to the baseline, there was a significant fall in FBS, PPBS, and HbA1c at 1 year as depicted in Tables 2 and 3.

With LSM in group I, there was a significant reduction in weight, BMI, total cholesterol, LDL, and PPBS between baseline and 1 year as shown in Table 4.

With LSM and tablet metformin in group II, there was a significant reduction in abdominal circumference, total cholesterol, triglycerides, LDL, FBS, PPBS, and HbA1c between baseline and 1 year as shown in Table 5.

**Table 7: Outcomes among prediabetic subjects after 1 year**

| Parameter | Group I, *n*=49 | Group II, *n*=48 |
|---|---|---|
| FBS | | |
| ≥126 | 1 | Nil |
| 100–125 | 15 | 16 |
| <100 | 33 | 32 |
| PPBS | | |
| ≥200 | Nil | Nil |
| 140–199 | 19 | 19 |
| <140 | 30 | 29 |
| HbA1c | | |
| ≥6.5 | Nil | Nil |
| 5.7–6.4 | 46 | 47 |
| <5.7 | 03 | 01 |

There is no significant difference between groups I and II in reduction of all the above-mentioned parameters except PPBS and HbA1c as shown in Table 6.

The outcomes of prediabetic subjects after 1 year of treatment in both the groups are comparable as shown in Table 7. Most of the patients had normal FBS and PPBS after 1 year of treatment. Only three patients and one patient in groups I and II had normal HbA1c, respectively.

The adverse effects observed were dizziness, nausea, flatulence, myalgia, abdominal pain, and heart burn, as depicted in Table 8. These were mild to moderate in intensity and in most patients it subsided with time.

## Discussion

Type 2 DM is the most common chronic metabolic disorder characterized by chronic hyperglycemia, which has a major impact on health status of people and burdens nation's healthcare system.[7] Prevention of DM is one of the best strategies to reduce this problem. In this line, identification and treatment of prediabetes (IFG or IGT) are crucial. The progress of prediabetes to type 2 DM is quicker and accounts for 5–10%.[16] There are a plenty of drugs available to treat diabetes among which few are tested to prevent DM. LSM has a prime role in preventing the progression of prediabetes to diabetes. The studies have shown that intense LSM has better outcomes compared with drug.[4,5,7,15,17,18] The adherence to the intense LSM is a major challenge in developing countries like India where the majority of population is from the rural setup. In the present study, LSM including dietary alterations specific to the local region was tried and it was compared with metformin along with LSM. The influence of locally modified LSM on prediabetic subjects was not studied in this region. To best of our knowledge and as per literature search, this is one of the fewer studies in which local modification of LSM is studied and this is the only study in this part of the country.

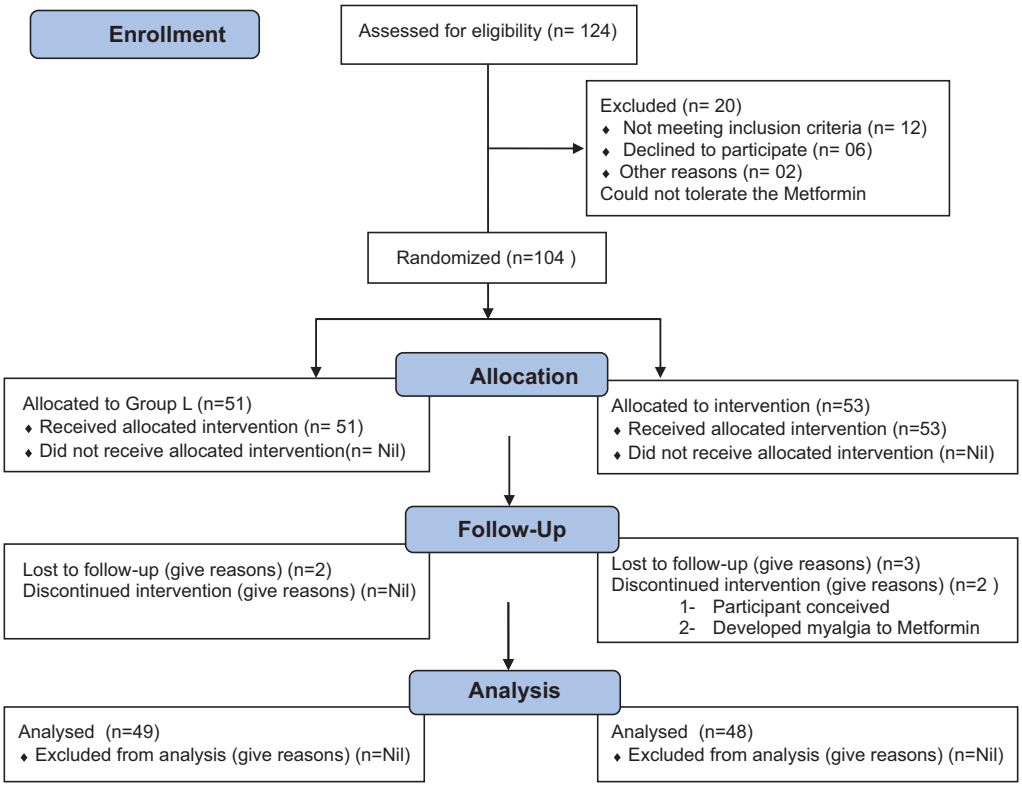


**Figure 1:** Flow chart detailing the participation and allocation of subjects in the treatment group

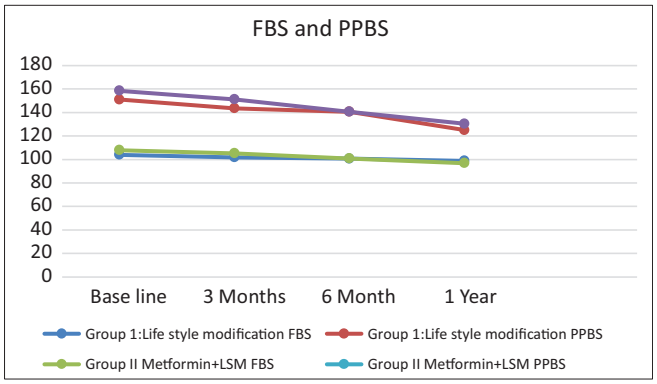


**Figure 2:** Comparison of fasting blood sugar and post-prandial blood sugar within and between the groups

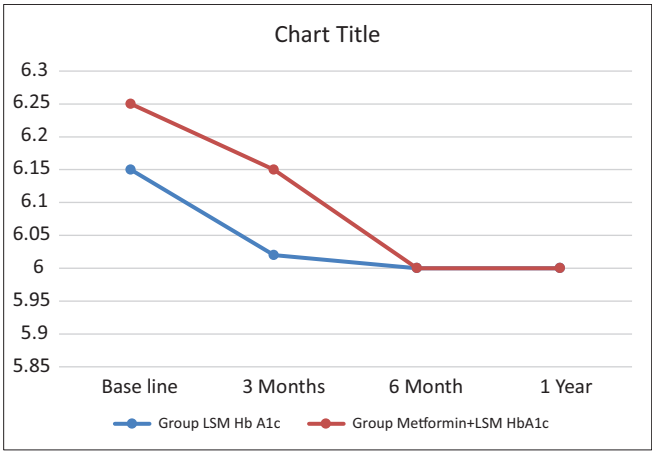


**Figure 3:** Comparison of glycated hemoglobin (HbA1C) within and between the groups

Majority of the participants in our study were from rural areas, yet the dietary habits in participants from rural and urban areas were similar to a great extent as they preferred local food. The blood sugar parameters such as FBS, PPBS, and HbA1c constantly reduced over a period of 1 year in both the groups. In the metformin + LSM group, there was a significant reduction in all the three parameters when compared with the LSM group in which a significant reduction was seen in PPBS only. This improvement was similar to the earlier studies conducted in the USA, Italy, Iran, and Saudi Arabia,[7,19-21] but the reduction was less compared to these studies. The reduction in blood sugar parameters was slightly better in the group LSM+metformin when compared with LSM alone but the difference was not significant.

LSM was reformed according to the preference and convenience of the local population. The dietary alteration included complete or partial replacement of rice with available local millets [finger millet (Nachini, Ragi), pearl millet (Bajra, Sajje), foxtail millet (Kangni, Navane), kodo millet (kodra, Harka), little millet (Shavan, Saame), and sorghum millet (Jowar, Jola)]. Instead of intense workout, brisk walk for 150 min per week was introduced. They were counseled to include more protein rich-food such as legumes, pulses, egg, and lean meat in their diet. These transformations

**Table 8: Adverse effects in prediabetic subjects in both the groups**

| Groups | Adverse effects | WHO causality assessment scale | |
|---|---|---|---|
| | | Possible | Unlikely |
| Group I (LSM), *n*= 49 | Dizziness | 05 | 02 |
| | Flatulence | 04 | 02 |
| | Myalgia | Nil | 02 |
| | Abdominal pain | Nil | 02 |
| Group II (LSM+metformin), *n*=48 | Dizziness | 07 | 02 |
| | Nausea | 06 | 01 |
| | Diarrhea | 05 | 01 |
| | Flatulence | 04 | Nil |
| | Myalgia | 02 | Nil |
| | Abdominal pain | 02 | 02 |
| | Heart burn | 02 | 01 |

helped in reduction of blood sugar parameters in group I and addition of metformin further enhanced the reduction.

The weight, BMI, and abdominal circumference were reduced significantly in the group LSM, whereas only abdominal circumference was reduced significantly in the group LSM with metformin at the end of 1 year when compared with baseline. The findings were similar to the studies reported from Saudi Arabia, Jordan, and Bangladesh.[7,22,23] Though metformin has action on glucose metabolism, helps in reduction in blood glucose, and reduces appetite, the weight reduction was not significantly reduced. The participants with only LSM could have been highly motivated in weight reduction.

The lipid profile parameters such as total cholesterol, triglycerides, LDLs, and HDLs were improved, that is, reduction in total cholesterol, triglycerides, and LDL and increase in HDL in both the groups. However, the reduction was better in the metformin +LSM group but not statistically significant. This finding was in line with two other studies.[22,23] The LSM including the alteration in dietary could improve lipid profile. The inclusion of metformin does not contribute to the additional improvement in lipid profile.

In our study, the incidence of diabetes in the LSM group was 2.1% and none in the metformin +LSM group. The participants on metformin had better glucose reduction and none among the total enrolled participants had progressed to type 2 DM. This finding was supported by a recent study from Bangladesh.[23] In the past two decades, multiple studies have proved the benefits of intense LSM and dietary restrictions in delaying the progression of prediabetes to type 2 DM. The reduction rate of risk for developing DM ranges from 42% to 58% over 4–6 years in long-term studies, which was reported from different countries.[8,24,25] Thus the LSM along with dietary restriction forms the main stay treatment for people with IGT and IFG. The drugs used for the treatment of prediabetes to prevent DM onset are metformin, acarbose, voglibose, orlistat, troglitazone, rosiglitazone, sitagliptin, and canagliflozin.[8-10,26,27]

These studies have proved marginal advantage of drugs as add-on to LSM with dietary restriction in preventing the incidence of DM. Intense LSM is the most ideal for preventing DM in people with prediabetes, but the implementation of the same for long-term is difficult, especially in rural areas and in some people in urban areas due to their busy schedule. In rural setups, the tailor made alterations in LSM with dietary improvement would be ideal, which is easier to follow as it includes the native food. Adding a drug to prevent DM would be an option if there is a defect in the action or secretion of insulin. If there are contraindications to the exercise or if the person is unable to walk due to trauma or any defect, the dietary restriction along with medication is advisable to prevent DM.

Around 10 participants in each group were followed up for 2 years. In the LSM group, 5/10 had developed DM, based on FBS and HbA1c values, whereas only 2 out of 9 had progressed to DM in group II. The long-term adherence and efficacy of LSM were relatively poor, compared with the metformin group. In case of low adherence to LSM, starting metformin would be beneficial in preventing the onset of diabetes.

The occurrence of adverse effects and their causality assessment showed that LSM had few adverse effects when compared with metformin+LSM. There were no serious adverse effects in either groups. Patients tolerated the adverse effects which subsided gradually. These findings were similar to another study in which gastrointestinal and musculoskeletal adverse effects were common in both groups which were tolerable and self-limiting. The limitations of our study include the restricted region of the country; hence, the results cannot be generalized, the dietary alterations were not uniform for everybody, it was personalized for each patient according to which their food habits with few common measures and the physical activity could have been tracked digitally through fit bands, but due to lack of understanding in the usage of fit bands/smart watches/smart phones among participants, it was not done. Despite all these limitations, the participants were enthusiastic and showed their filled dairy to ensure adherence in medications and physical activity.

## Conclusion

The LSM with or without metformin for a period of 12 months significantly reduces blood sugar and other parameters in prediabetic subjects.

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## Conflicts of interest

None.

## Ethical approval

The approval was obtained from the Central Institutional Ethics Committee, SDUAHER.

## Informed consent

Written informed consent was obtained from all participants and documented.

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