

# Conquering Prediabetes: Battle of Metformin Versus Lifestyle Makeover

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## ABSTRACT

**Background:** Prediabetes is a metabolic condition characterized by blood sugar levels higher than normal but below the diabetic range. The onset of microvascular complications may set in this phase, hence intervening during the prediabetic stage becomes crucial in halting the progression to irreversible diabetes. We compared blood sugar levels between lifestyle modification and metformin medication and identified which option is better for managing prediabetes.

**Methods:** A quasi-experimental study was done from January to October 2023 recruiting 150 prediabetic adults coming to Sikander Abad clinic through convenience sampling including 18 to 65 years of age while obese adults, those who had hypoglycemia within the past 3 months, and GDM women were excluded. Patients were divided into two groups and given a choice to choose pharmacotherapy (Metformin) or non-pharmacological measures (lifestyle modification). A thorough history and examination were done on all patients and Fasting Blood Sugar was done initially and after 3 months. SPSS version 21 was used. Independent and paired sample T-tests were used and chi-square was computed to see associations with the demographic factors. P-value <0.05 was considered significant.

**Results:** Prediabetes was better controlled with Metformin (FBS-3.2mg/dl) as compared to lifestyle modification (FBS-2.7mg/dl) in our study ( $p < 0.02$ ). Non-obese patients constituted a higher proportion of the cohort, with 91(60%) compared to 59(39.3%) obese patients. Additionally, 43.3% of the study participants aimed to delay or prevent the onset and complications of Diabetes Mellitus.

**Conclusion:** In our study, starting Metformin in the prediabetes phase, prevents or delays the progression to full-blown diabetes, contributing to a 0.5mg/dl reduction in glycemic control.

**Keywords:** Prediabetes, Hb A1c, Glycemic Control, Metformin.

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## INTRODUCTION

Diabetes mellitus (DM) is an endocrine disorder of chronic hyperglycemia diagnosed by fasting blood sugar levels of  $\geq 126$  mg/dL or glycated hemoglobin (HbA1c) levels of  $\geq 6.5\%$  while Pre-diabetes is labeled with FBS of 100-125mg/dl and HbA1C of 5.7-6.4%. The IDF Diabetes Atlas 2021 estimated the comparative adult (20–79 years) prevalence rate of DM in Pakistan to be 30.8%—the highest in the world<sup>1</sup>. Diabetes is considered a worldwide epidemic that is putting humans at risk of micro and macrovascular changes<sup>2</sup>. Intervening at the pre-diabetic stage can slow or stop the progression to diabetic stages, which is an irreversible condition that can only be controlled<sup>3</sup>. Research has been conducted on this topic and the prediabetic population has been advised to include physical activity with dietary modifications and weight reduction, it was suggested that Prediabetes /Diabetes care must be patient-centered<sup>4,5</sup>. Various RCTs have been conducted to get a better understanding of the effect of lifestyle changes and medication use to prevent full-blown diabetes<sup>5</sup>. In some, lifestyle modification was considered effective in controlling glycemic levels<sup>6</sup>. While in one of the other retrospective cohort studies, it was seen that Metformin was barely prescribed for Diabetes prevention<sup>7</sup>. While some studies clearly showed positive outcomes with Metformin treatment<sup>8</sup>. To identify individuals who are appropriate candidates for preventive interventions, we measure glycated hemoglobin (Hemoglobin A1C) or fasting plasma glucose (FPG) in adults  $\geq 45$  years, in women with a history of gestational diabetes, and in adults of any age with body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> ( $\geq 23$  kg/m<sup>2</sup> in Asian Americans) who have one or more additional risk factors for diabetes included family history of diabetes mellitus in a first-degree relative, Sedentary lifestyle and Hypertension<sup>9</sup>.

In Pakistan, work has been done to reflect lifestyle changes and medications' effects on prediabetic patients separately but not much data is available to compare the effect of lifestyle modification vs Metformin in the prediabetic population. It is necessary to explore and find ways to delay the progression of this deadly precursor to full-blown diabetes. Worldwide, both lifestyle modification and Metformin use showed hope in either the prevention or treatment of prediabetes. Especially, the incidence of Diabetes was decreased post-lifestyle modifications<sup>9</sup>. In Karachi, not many studies have been done so far in this context. Given the emerging trend of diabetes in Karachi, Pakistan, it's beneficial to understand the tools for the prevention of this condition. For instance, Metformin helps in decreasing glucose production in the liver, decreasing insulin resistance in the body as well as enhancing absorption of glucose that finally helps in lowering blood sugar levels<sup>10</sup>. However, some

patients are not convinced to start pharmacotherapy for Prediabetes. They support lifestyle modifications as an effective way to delay the progression of Prediabetes. That's why, with this inclining load of diabetes in our population, it is crucial to find some proven and applicable ways to tackle well with the ailment and aftereffects.

After the staggering rise in DM in Pakistan, it is imperative to make a DM management protocol for our population whether to introduce metformin early in the diabetes phase and prevent Type-2 DM or stick with the sequential therapy of lifestyle modification first and then introduce pharmacotherapy, promoting therapeutic inertia. Hence, we aimed to analyze the better management option for managing prediabetes through lifestyle modification or Metformin medication.

## METHODS

A quasi-experimental study was conducted in the primary care community clinics of Sikander Abad, Karachi, the majority inhabiting the Pushtun community, from January to October 2023. Out of 150 subjects, recruited through convenience sampling, two groups were made (75 each), Metformin users and those opting for lifestyle modification. Group A received Metformin 500 mg twice a day while Group B was advised for lifestyle modification such as 30 minutes of brisk walk or running on a treadmill on most of the days or at least 150 minutes in a week. Both groups were advised to follow up in the clinic every week to see their condition and adherence to the correct instructions. Relevant history and examination were recorded. Fasting blood glucose and HbA1C was done at the time of their participation in the study, then after 3 months. All relevant data and detailed information including demographic data and glycemic history etc. were documented for the selected cases after obtaining ethical approval from the institute. All adults 18 to 65 who have FBS of 110 – 125 mg/dl or HbA1C of 5.7 to 6.4 were included in the study while obese adults and GDM women were excluded. The study was approved (ERC: 6590123HJFM) by the Institutional Review Board, Karachi. By elucidating the benefits and risks associated with both Metformin and lifestyle modification, we want to be aware of the best option for the Pakistani population.

The data was analyzed by using SPSS version 21. Mean and standard deviation were calculated for the quantitative variables such as FBS and age and frequency and percentage of qualitative variables such as HTN, family history of DM, regular exercise, and glycemic monitoring. Post 3 months, a greater reduction in Mean FBS was considered more effective in the management of prediabetes.

Stratification was completed and a post-stratification independent t-test was applied for mean comparison. A paired t-test was also applied. The Chi-square test was put in to observe the influence of modifiers such as age and gender on the outcome. P value  $\leq 0.05$  was considered as significant.

## RESULTS

Out of 150 cases, 77 (51.3%) were males and 73 (48.7%) were females. The age was categorized into different groups from 1-4 (from below 40 to above 61 years of age). Most of the patients were from group 1.59 (39.3%). Non-obese patients were reported in a higher percentage 91(60%) as compared to obese patients 59(39.3%). According to the BMI scale, patients included in this study were reported as overweight 61(40.7%). Waist circumference in males

and females was also supported by the BMI scale which was recorded as 21.3% in both genders. History of Hypertension and Diabetes Mellitus was recorded as (69)46% and (43)64.7% in both genders respectively. A significant number of the targeted population (31.3%) was interested in maintaining their body toning and body weight; therefore, they do regular exercise. About 39.3% of patients were aware of the complications of Diabetes Mellitus (DM). Hence, they were checked for Fasting Blood Sugar Levels (FBS). A total of 22% of female study participants had a history of DM during pregnancy (Gestational Diabetes) in their last pregnancy. A significant number of study participants (43.3% want to achieve the goal of delaying or preventing the onset and complications of Diabetes).

**Table 1: Demographics of the study participants.**

| Variables   | Metformin Group<br>n (%) | Lifestyle Modification<br>n (%) | Chi-square | p-value |
|---|--------------------------|---------------------------------|------------|---------|
| Age (years)   |                          |                                 |            |         |
| ≤40   | 20(33.9)                 | 40(66.1)                        | 22.024     | < 0.001 |
| 41-50   | 21(56.1)                 | 19(43.9)                        |            |         |
| 51-60   | 17(54.8)                 | 15(45.2)                        |            |         |
| ≥61   | 17(94.7)                 | 1(15.3)                         |            |         |
| Gender  |                          |                                 |            |         |
| Male  | 31(44.2)                 | 45(55.8)                        | 3.9        | 0.019   |
| Female  | 44(60.3)                 | 30(39.7)                        |            |         |
| Obesity   | 40(67.8)                 | 19(32.2)                        | 10.18      | 0.001   |
| Junk food user  | 29(50.9)                 | 28(49.1)                        | 0.046      | 0.481   |
| Hypertension  | 42(60.9)                 | 27(39.1)                        | 4.02       | 0.18    |
| Family history of DM                                    | 56(57.7)                 | 41(42.3)                        | 3.6        | 0.042   |
| Regular exercise  | 15(31.9)                 | 32(68.1)                        | 11.06      | 0.001   |
| Glycemic monitoring regularly                           | 34(47.9)                 | 37(52.1)                        | 1.02       | 0.045   |
| Women having Gestational Diabetes in the last pregnancy | 18(54.5)                 | 15(45.5)                        | 7.14       | 0.072   |

With Metformin control results were significantly better (FBS -3.2mg/dl) as compared to lifestyle modification (FBS -2.7mg/dl) in controlling prediabetes, (p-value 0.02) as a mean reduction in FBS was more with Metformin as compared to lifestyle modification. Table 1 demonstrates the demographics of the study population and Table 2 demonstrates the mean difference in FBS in both groups.

**Table 2: Glycemic control of lifestyle modification vs Metformin**

| FBS mg/dl      | Lifestyle<br>$X \pm SD$ | Metformin<br>$X \pm SD$ | Mean<br>Difference | p-value* |
|----------------|-------------------------|-------------------------|--------------------|----------|
| Baseline       | 113.4 $\pm$ 6.9         | 116.4 $\pm$ 8.4         | 2.7                | 0.021    |
| After 3 months | 107.2 $\pm$ 7.4         | 104.02 $\pm$ 9.9        | 3.2                | 0.024    |
| p-value**      | <0.001                  | <0.001                  | -                  | -        |

*independent sample t-test, p-value\*\* paired sample t-test*

## DISCUSSION

When given the chance to clarify their values and deliberate the choice of a diabetes management strategy, we found that when relevant evidence regarding diabetes prevention options was presented, medication like metformin control was significantly preferable and more effective (FBS-3.2mg/dl) than lifestyle modification (FBS: 2.7mg/dl) in controlling prediabetes, (p-value 0.02). Fewer than 4% of patients with prediabetes received metformin prescriptions, according to previous analyses using large-group health plan data. Interestingly, studies showed that exercise with Metformin was more effective than exercise alone<sup>12</sup>. However, in a trial on the overweight/obese Japanese population with impaired fasting glucose levels, lifestyle modification alone could prevent type 2 Diabetes<sup>13</sup>.

Management of pre-diabetes requires shared decision-making between physician and patient. It is difficult to maintain lifestyle modification long-term<sup>14</sup>. However, maintaining lifestyle modification with diet and exercise can revert pre-diabetes and there will be lesser chances of occurrence of DM<sup>15</sup>. Today, diabetes has become a threat worldwide<sup>16</sup>. These studies and collected data have become crucial for the diabetes-free population<sup>17</sup>. In the current study, patients with higher BMIs and with a family history of diabetes were more likely to choose both options, such as exercise/lifestyle modification and metformin, to achieve the overall goal of obtaining a healthy lifestyle (27.3%), prevent/delay diabetes (43.3%), and lose weight (14%). Another study revealed that younger patients were more likely to use metformin, and patients with higher BMIs were more likely to select either approach over standard treatment.

Haw et al. stated that lifestyle change was a viable long-term diabetes prevention strategy based on a review of collected trials, however, the long-term efficacy of these trials is not still established; nevertheless, its prolonged protective benefits depended on maintenance treatments, even intermittent ones<sup>18</sup>. This was in line with earlier findings that suggested lifestyle changes could help delay the onset of diabetes in some cases<sup>18</sup>. Furthermore, because weight loss appears to be the primary factor linked to a slower course of diabetes, decreases in BMI, body weight, waist, and hip circumference brought on by lifestyle interventions are likely to improve individual physical conditions. Also, promising results were seen in the prevention of metabolic syndrome development<sup>19</sup>. The linked risk reduction of changing one's lifestyle by eating healthy food, including exercise in the daily schedule, and losing weight, is more pronounced than the influence of any one component alone<sup>19</sup>.

In the current study, in comparison to Metformin, more people were not willing to choose lifestyle modification and exercise (78 out of 150, 52%) as a preventive measure and among them mostly were females (44 out of 78, 56.4%). While out of 150, 72 individuals (48%) were willing to exercise and wanted to modify their lives and most of them (43) were males (out of 72, 59.7%).

Primary prevention or prevention of the first kind is vital and cost-effective due to the chronic nature of the disease and the rising trend of diabetes. Therefore, we decided to investigate whether metformin therapy may be a more effective treatment or whether lifestyle changes are more effective in lowering long-term diabetes<sup>20</sup>. Findings showed that, compared to metformin, a lifestyle modification approach for more than six months following a pre-diabetic diagnosis can be successful in lowering the incidence of type II diabetes and lowering the incidence of diabetes by 25%<sup>20</sup>. Our findings showed that our elderly targeted population mostly preferred Metformin as compared to lifestyle modification and exercise while persons less than 50 years of either gender preferred exercise, nutritional change, and lifestyle modification to reduce blood sugar level<sup>21</sup>. In this era, where Diabetes has become a global threat any of these two therapies can be used jointly or separately, depending on the person's condition and level of acceptance<sup>22</sup>.

However, regarding the cultural settings and resources, we advise that preventative diabetes incidence plans be built on localized lifestyle adjustments. Lifestyle modifications, on the other hand, typically involve changes in diet, exercise, and other healthy habits aimed at preventing or managing prediabetes and type 2 diabetes. While lifestyle modifications can have significant benefits in terms of overall health and well-being, including weight management and cardiovascular health, some individuals might still struggle to achieve optimal glycemic control through lifestyle changes alone. Current medical guidelines typically recommend lifestyle modifications as the first-line approach to managing prediabetes. Medication, such as metformin, might be considered in specific cases, especially when lifestyle changes are not effective or feasible. More real-world studies are required to comment concretely on how early Metformin can be started in the diabetes journey.

## CONCLUSION

Prediabetic patients are generally making diabetes prevention decisions that are consistent with suggestions and anticipated advantages from the published literature. Strong evidence backs up the idea that taking metformin and changing one's

lifestyle can lower the risk of developing diabetes in persons with pre-diabetes. In our study, metformin was more effective in achieving glycemic control compared to lifestyle modifications alone; it suggests that the medication had a positive impact on reducing blood sugar levels in individuals with prediabetes. This could be due to metformin's ability to improve insulin sensitivity, reduce glucose production in the liver, and enhance the uptake of glucose by cells.

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#### CONFLICT OF INTEREST

There was no conflict of interest among the authors.

#### ETHICS APPROVAL

The study was approved by the ethical review committee (ERC code# ERC: 6590123HJFM).

#### PATIENT CONSENT

Written consent was taken from all participants. Anybody who wished to drop in the middle of the study was allowed to do so.

#### AUTHORS CONTRIBUTION

HAJ: Principal Investigator, Design research study, concept making, manuscript writing, benchwork, and draft making. FJ: Conceptualization; Design methodology and supervised the findings of this work, Resolved the problems of accuracy or integrity of the work, and data interpretation for the work. FFA: Acquisition of data, statistical analysis, verified the analytical methods, Implementation of critical experimental protocols, Draft making, proofreading. NH: Resolved the problems of accuracy or integrity of the work, and data interpretation for the work. MA: Data analysis, data interpretation, critically reviewed the manuscript, to investigate the cases, Implementation of critical experimental protocols. TA and FRA: Gathered and compiled data.

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