

**Head-To-Head Comparison of Acarbose and Voglibose as Add-On Therapy to Metformin in Patients with Type 2 Diabetes**MasuramBharath Kumar<sup>1</sup>, Shalini Chandra<sup>2</sup>, KV Thimmaraju<sup>3</sup>, M Amruth<sup>4</sup><sup>1</sup>PhD Research Scholar, Department of Pharmacology, Rohilkhand Medical College, BIU, U.P., India<sup>2</sup>Professor & Head, Department of Pharmacology, Rohilkhand Medical College, BIU, U.P., India<sup>3</sup>Professor & Head, Department of Biochemistry, Varun Arjun Medical College, Shahjhanpur, U.P., India<sup>4</sup>Professor, Dept of Community Medicine, Varun Arjun Medical College & Shahjhanpur, U.P., India

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Corresponding author: MasuramBharath Kumar

Conflict of interest: Nil

**Abstract:****Objective:** To compare the effectiveness of Acarbose and Voglibose as add-on therapy to Metformin monotherapy in patients with type 2 diabetes mellitus.**Methods:** A prospective, non-random, open-label study was conducted at Varun Arjun Medical & Rohilkhand Hospital involving 76 patients divided into two groups. Group I received Metformin with Acarbose, and Group II received Metformin with Voglibose for three months. Glycemic parameters (HbA1c, FBS, PPBS) were evaluated at baseline and after three months. Medication adherence was calculated using the Morisky Medication Adherence Scale-8 (MMAS-8). The primary outcome was reduced HbA1c levels and secondary outcomes included changes in FBS and PPBS and medication adherence.**Results:** Both groups significantly reduced HbA1c, FBS, and PPBS levels ( $p < 0.0001$ ). Adding Acarbose to Metformin therapy showed slightly better effectiveness in reducing FBS and PPBS than adding Voglibose. Medication adherence was comparable in both groups.**Conclusion:** Acarbose and Voglibose, as add-on therapies to Metformin, showed significant effectiveness in glycemic control with a good adherence profile. Acarbose exhibited a slightly superior reduction in FBS and PPBS compared to Voglibose. Further randomised controlled studies are needed to validate these findings.**Keywords:** Metformin, Acarbose, Voglibose, Type 2 Diabetes, Medication Adherence.

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**Introduction**

Diabetes Mellitus, primarily type 2 diabetes, is a chronic metabolic disorder characterised by persistent hyperglycaemia and is a significant global health issue. The International Diabetes Federation estimates that over 463 million adults are living with diabetes, a number assumed to reach 700 million by 2045.[1] Diabetes is associated with severe complications, such as cardiovascular diseases, neuropathy, nephropathy, and retinopathy, which contribute significantly to morbidity and mortality.[2] Metformin, a biguanide derivative, is the first-line medication recommended for managing type 2 diabetes.[3] It reduces hepatic glucose production and improves insulin sensitivity, thereby reducing blood glucose levels without causing substantial weight gain or hypoglycaemia.[4] Despite its efficacy, many individuals with type 2 diabetes fail to achieve glycemic targets with metformin monotherapy.[5] Add-on therapies, including alpha-glucosidase inhibitors like Acarbose and Voglibose, have been

considered in such cases. Acarbose and Voglibose slow carbohydrate digestion and absorption in the intestines, thereby reducing postprandial hyperglycemia.[6] Clinical studies have demonstrated the effectiveness of these agents in reducing HbA1c levels when combined with metformin.[7,8] With this background, our study aims to compare the effectiveness of Acarbose and Voglibose as add-on therapies to metformin monotherapy. The rationale for this study is to provide data that might guide clinicians in personalising diabetes treatment, emphasising the importance of efficacy and medication adherence.

**Materials and Methods**

The Institutional Review Board approved the study protocol. All participants were provided informed consent before participation. The study was conducted under the Declaration of Helsinki and its later amendments. This was a prospective, non-randomised, open-label study conducted over three

months at Varun Arjun Medical & Rohilkhand Hospital, Uttar Pradesh And Associated with Rohilkhand medical college, Bareilly, 76 participants with type 2 diabetes mellitus (T2DM) on Metformin monotherapy were recruited for this study.

They were divided into two groups of 38 each. included patients aged 30-65 years, diagnosed with T2DM, and on metformin monotherapy for at least three months. Patients with severe complications of diabetes, liver or kidney diseases, and those who were pregnant or lactating were excluded. Baseline data were recorded at the start of the study, including HbA1c, FBS, and PPBS. These parameters were re-evaluated at the end of the three months. Medication adherence was monitored and calculated using the Medication adherence, as calculated by the Morisky Medication Adherence Scale-8 (MMAS-8). The Statistical Package for the Social Sciences (SPSS Version 25) was used for analysis of the data. Unpaired T-tests were used to compare the baseline characteristics between the two groups, and paired T-tests were used to compare the changes within each group from

baseline to three months. A p-value less than 0.05 was regarded as statistically significant.

### Intervention

The first group continued with Metformin and received add-on acarbose therapy, while the second group continued with Metformin and received add-on voglibose therapy. The specific dosages were determined according to standard clinical guidelines and the patient's needs.

### Outcome Measures

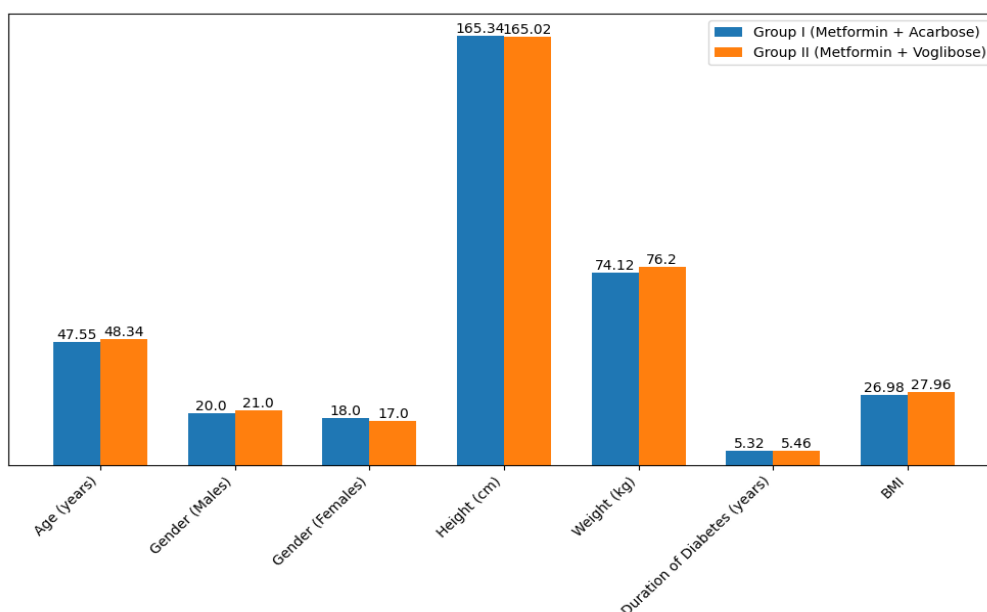
The primary outcome was reduced HbA1c levels from baseline to the conclusion of the study period. Secondary outcome measures included changes in fasting blood sugar (FBS), postprandial blood sugar (PPBS), cost-effectiveness evaluated using the incremental cost-effectiveness ratio (ICER), and medication adherence over the three months.

### Results

There were no significant differences in age, gender, height, weight or duration of diabetes between the two groups. All parameters' p-values remained above 0.05, except BMI (p = 0.013).

**Table 1: Baseline Demographic Characteristics**

Variables	Group I (Metformin + Acarbose) (38)	Group II (Metformin + Voglibose) (38)	P-Value
Age (years)	47.55 ±6.96	48.34±8.64	0.661
Gender	Males	20	0.810
	Females	18	
Height (cm)	165.34±4.78	165.02±3.34	0.742
Weight (kg)	74.12±7.70	76.20±6.58	0.209
Duration of Diabetes (years)	5.32±1.95	5.46±1.58	0.721
BMI	26.98±1.72	27.96±1.65	0.013*

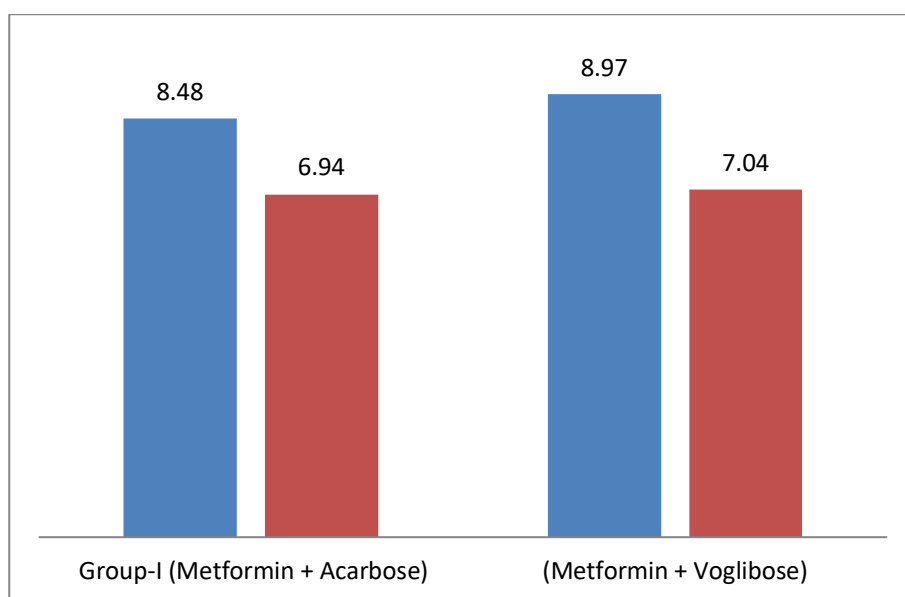


**Figure 1: Baseline Demographic Characteristics**

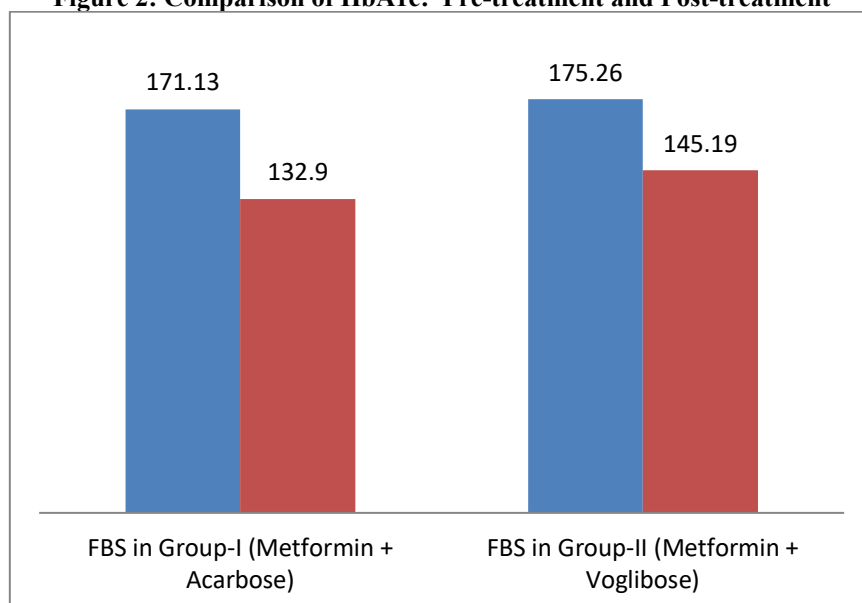
The comparison of the pre-treatment and post-treatment glyceimic parameters is shown in Table 2. In both groups, there was a significant reduction in HbA1c, FBS, and PPBS ( $p < 0.0001$  in all cases). Group I (Metformin + Acarbose) significantly reduced FBS and PPBS morethan Group II (Metformin + Voglibose).

**Table 2: Comparison of Pre-treatment and Post-treatment Glyceimic Parameters**

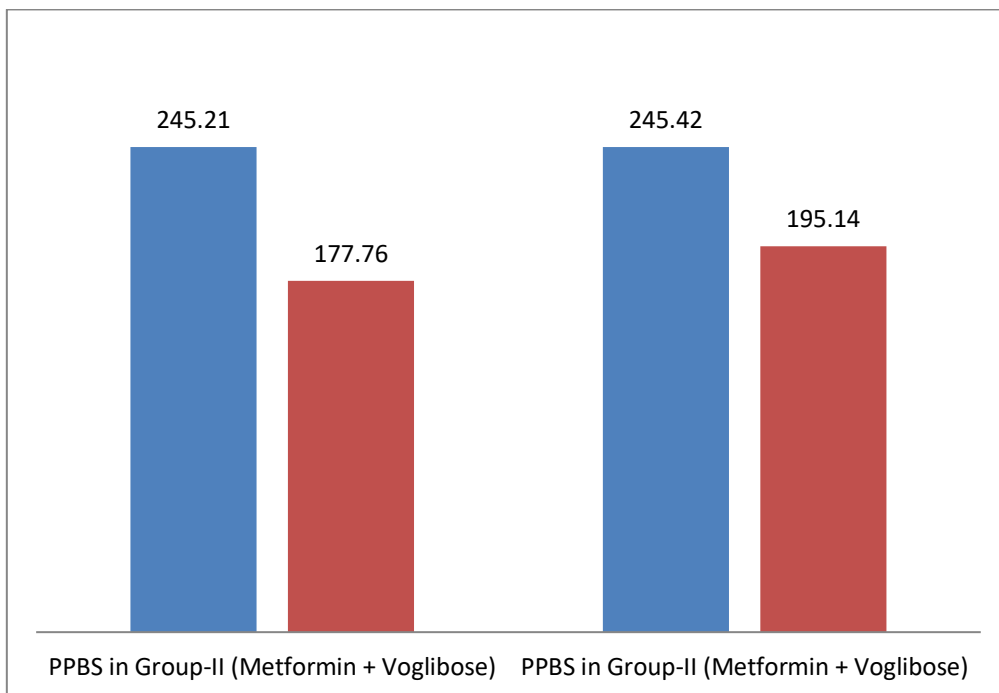
Comparison	Pre-Treatment Mean $\pm$ SD	Post-Treatment Mean $\pm$ SD	P-value
HbA1c in Group I (Metformin + Acarbose)	8.48 $\pm$ 0.43	6.94 $\pm$ 0.31	0.0001*
HbA1c in Group II (Metformin + Voglibose)	8.97 $\pm$ 0.54	7.04 $\pm$ 0.41	0.0001*
FBS in Group I (Metformin + Acarbose)	171.13 $\pm$ 22.61	132.90 $\pm$ 13.08	0.0001*
FBS in Group II (Metformin + Voglibose)	175.26 $\pm$ 21.27	145.19 $\pm$ 19.03	0.0001*
PPBS in Group I (Metformin + Acarbose)	245.21 $\pm$ 23.92	177.76 $\pm$ 18.11	0.0001*
PPBS in Group II (Metformin + Voglibose)	245.42 $\pm$ 20.67	195.14 $\pm$ 17.08	0.0001*



**Figure 2: Comparison of HbA1c: Pre-treatment and Post-treatment**



**Figure 3: Comparison of FBS: Pre-treatment and Post-treatment**

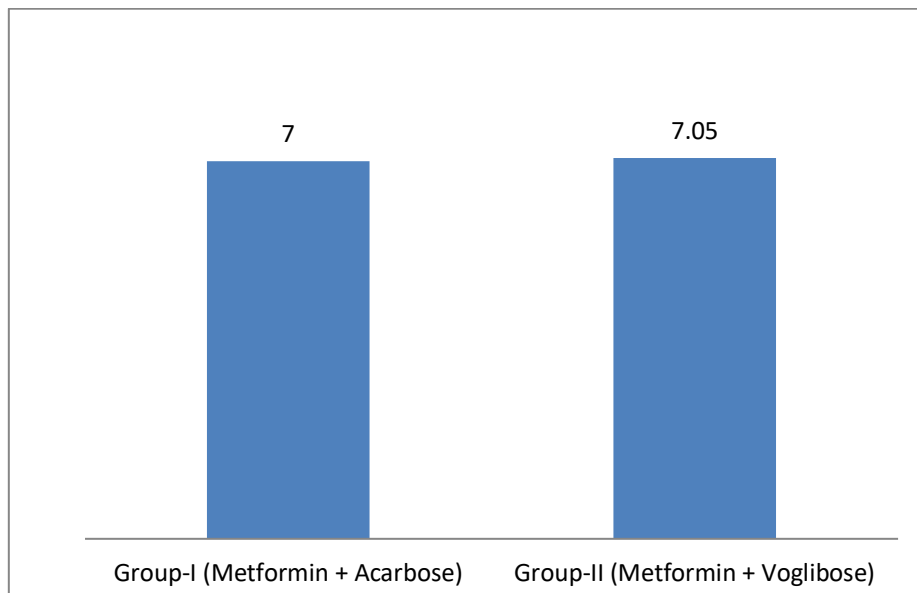


**Figure 4: Comparison of PPBS: Pre-treatment and Post-treatment**

As measured by the Morisky Medication Adherence Scale-8 (MMAS-8), medication adherence did not differ significantly between the two groups ( $7.0 \pm 0.80$  vs.  $7.05 \pm 0.83$ ,  $p=0.78$ ), as shown in Table 3.

**Table 3: Medication Adherence Over Three Months**

Group	Number of Patients	Average MMAS-8 Score	P-Value
I (Metformin + Acarbose)	38	$7.0 \pm 0.80$	0.78
II (Metformin + Voglibose)	38	$7.05 \pm 0.83$	



**Figure 5: Medication Adherence Over Three Months**

**Discussion**

Managing type 2 diabetes mellitus (T2DM) remains a global health concern, and adequate glycemic control is critical to managing this chronic disease. Metformin is a cornerstone of T2DM management due to its efficacy, tolerability, and low cost. However, many patients fail to achieve glycemic targets on metformin monotherapy and require additional treatment

options.[9] Combination therapies using Metformin with other antidiabetic drugs have emerged as effective strategies to achieve better glycemic control.[10] This investigation evaluated the efficacy of two combination therapies, Metformin plus Acarbose and Metformin plus Voglibose. Acarbose and Voglibose are alpha-glucosidase inhibitors that help control postprandial hyperglycemia, a significant aspect of T2DM

management.[11]Acarbose has shown effectiveness in preventing T2DM and offers additional cardiovascular benefits.[12,13]

Voglibose, an alpha-glucosidase inhibitor, improves the postprandial state and reduces oxidative stress markers and soluble adhesion molecules in obese type 2 diabetic patients.[14]

The study's primary objective was to evaluate and compare the efficacy of the two combination therapies in controlling glycemic parameters in T2DM patients. We found a significant reduction in HbA1c, FBS, and PPBS in both groups, indicating that both combinations effectively control glycemic parameters. Furthermore, we assessed medication adherence using the MMAS-8 score and found no significant difference between the two groups. Medication adherence is critical to T2DM management as non-adherence to antidiabetic medication has been linked to poor glycemic control, increased morbidity and mortality, and increased healthcare costs.[15]

These findings have implications for primary care physicians. While both combination therapies are effective, the choice between Acarbose and Voglibose as add-on therapy to Metformin should be individualised based on patient characteristics, tolerability, cost considerations, and preference. It is also essential to note that despite the positive results, the study has several limitations. For instance, the study's non-random nature may induce selection bias. Future randomised controlled trials are needed to confirm these findings.

### Conclusion

In conclusion, adding Acarbose or Voglibose to Metformin substantially decreased HbA1c, FBS, and PPBS levels in patients with type 2 diabetes. Both combinations showed effective glycemic control, indicating their potential as viable treatment options. Medication adherence was comparable in both groups. The findings of this study highlight the significance of individualising therapy according to patient characteristics, tolerability, cost considerations, and personal preference. More extensive, randomised controlled trials are needed to substantiate these findings further and guide clinicians in optimising diabetes management strategies.

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### References

1. International Diabetes Federation. IDF Diabetes Atlas, 9th ed. Brussels, Belgium: International Diabetes Federation, 2020.
2. Cho NH, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res Clin Pract.* 2018;138:271–281.
3. American Diabetes Association. Standards of Medical Care in Diabetes—2020. *Diabetes Care.* 2020;43(Suppl. 1):S1–S212.
4. Bailey CJ, Turner RC. Metformin. *N Engl J Med.* 1996;334(9):574–579.
5. Turner RC, et al. Glycemic control with diet, sulfonylurea, Metformin, or insulin in patients with type 2 diabetes mellitus. *JAMA.* 1999;281(21):2005–2012.
6. Van de Laar FA, et al. Alpha-glucosidase inhibitors for patients with type 2 diabetes. *Cochrane Database Syst Rev.* 2005;(2):CD003639.
7. Holman RR, et al. Addition of biphasic, prandial, or basal insulin to oral therapy in type 2 diabetes. *N Engl J Med.* 2007;357(17):1716–1730.
8. Pan C, et al. Efficacy of Acarbose in Chinese subjects with impaired glucose tolerance. *Diabetes Res Clin Pract.* 2003;61(3):183–190.
9. DeFronzo RA. Pharmacologic therapy for type 2 diabetes mellitus. *Ann Intern Med.* 1999; 131(4):281-303.
10. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med.* 2008;359(15):1577-1589.
11. Standl E, Schnell O, Ceriello A. Postprandial hyperglycemia and glycemic variability: should we care? *Diabetes Care.* 2011;34(Supplement 2):S120-S127.
12. Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. *Lancet.* 2002; 359(9323): 2072-2077.
13. Hanefeld M, Schaper F. Acarbose: oral anti-diabetes drug with additional cardiovascular benefits. *Expert Rev Cardiovasc Ther.* 2008;6(2):153-163.
14. Satoh N, Shimatsu A, Yamada K, Aizawa-Abe M, Suganami T, Kuzuya H, Ogawa Y. An alpha-glucosidase inhibitor, Voglibose, reduces oxidative stress markers and soluble intercellular adhesion molecule 1 in obese type 2 diabetic patients. *Metabolism.* 2006 Jun;55(6):786-93.
15. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care.* 2004;42(3):200-209.