VIA MEDICA
RESEARCH PAPER
ISSN 2450–7458
e-ISSN 2450–8187

Shambo Samrat Samajdar[1], Shatavisa Mukherjee[2], Rutul Gokalani[3], Supratik Bhattacharyya[4], Banshi Saboo[5], Shashank Joshi[6]

[1]Diabetes and Allergy-Asthma Therapeutics Specialty Clinic, Kolkata, West Bengal, India
[2]School of Tropical Medicine, Kolkata, India
[3]AHC Diabetes Clinic. Arogyam Health Care. Ahmedabad, Gujarat, India
[4]AMRI Hospitals, Saltlake, Kolkata, West Bengal, India
[5]DiaCare, Ahmedabad, Gujarat, India
[6]Joshi Clinic, Mumbai, India

Comparative Effectiveness and Safety of Acarbose and Vildagliptin in Type 2 Diabetes Management: A Real-World Observational Study in an Indian Population

ABSTRACT

Objective: To evaluate and compare the real-world effectiveness and safety profiles of acarbose and vildagliptin in patients with type 2 diabetes (T2D), with an additional focus on their impacts on the gut microbiota.

Materials and methods: This was a real-world, observational, record-based study involving 98 patients with T2D, who were already on a stable regimen of metformin. Patients were divided into 2 groups: one receiving acarbose and the other vildagliptin, without any changes to their ongoing treatment with metformin and glimepiride. The primary outcomes measured were changes in HbA1c, fasting plasma glucose (FPG), and postprandial plasma glucose (PPPG) levels from baseline after 3 months of therapy. Secondary outcomes included the incidence of adverse drug reactions (ADRs) and specific gastrointestinal side effects.

Results: The study included 48 patients on acarbose and 50 on vildagliptin, with comparable baseline characteristics. For effectiveness, the acarbose arm showed a decrease in HbA1c level by 1.0% while the vildagliptin arm showed a decrease of 0.9%. The acarbose arm showed a significant decrease of 47.6 mg/dL and 95.9 mg/dL, respectively, for FPG and PPPG at the end of 3 months, while the vildagliptin arm showed a decrease of 40.31 mg/dL for FPG and 79.5 mg/dL for PPPG ($p < 0.001$). The incidence of ADRs was comparable, although patterns of gastrointestinal side effects varied. Acarbose was associated with a higher incidence of flatulence and gastroparesis, whereas vildagliptin was linked to increased hyperacidity.

Conclusions: Acarbose and vildagliptin both significantly improved glycemic control when added to metformin therapy. Despite the differences in safety profiles, both drugs were generally well tolerated. (Clin Diabetol 2024; 13; 5: 268–273)

Keywords: type 2 diabetes, acarbose, vildagliptin, real-world study, glycemic control, adverse drug reactions, metformin adjunct therapy

Address for correspondence:
Shatavisa Mukherjee
School of Tropical Medicine, Kolkata, India
E-mail: shatavisa100@gmail.com
Clinical Diabetology 2024, 13; 5: 268–273
DOI: 10.5603/cd.100554
Received: 5.05.2024 Accepted: 11.07.2024
Early publication date: 17.09.2024

Introduction

India is experiencing a rapid escalation in non-communicable diseases (NCDs), particularly metabolic disorders such as diabetes mellitus, which present with substantial interstate and inter-regional variations. Recent findings from the Indian Council of Medical Research–India Diabetes (ICMR-INDIAB) study highlight a significant prevalence of diabetes and prediabetes, emphasizing an urgent need for effective management strategies tailored to the diverse demographic and socioeconomic landscape of the country [1]. Type 2 diabetes (T2D) continues to pose a major global health challenge, with the burden particularly pronounced in densely populated countries like India. Current therapeutic approaches for T2D involve a combination of lifestyle modifications and pharmacological interventions to manage the progressive nature of the disease effectively. Metformin remains the first-line treatment; however, many patients require additional pharmacotherapy to maintain glycemic control.

This study focuses on 2 such pharmacological agents: acarbose, an -glucosidase inhibitor (AGI), and vildagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor. AGIs are known for their efficacy in lowering postprandial glucose, an important aspect for populations consuming a high-carbohydrate diet. Despite their benefits, the use of AGIs like acarbose is often limited by gastrointestinal side effects, which are a significant concern in the Asian population [2]. On the other hand, DPP-4 inhibitors, such as vildagliptin, offer an advantageous profile by enhancing insulin secretion and suppressing glucagon release in a glucose-dependent manner, making them particularly suitable for Asian patients who generally exhibit a lower body mass index [3].

Clinical trials have consistently demonstrated the effectiveness of these treatments in controlled settings, but there remains a lack of comprehensive real-world evidence comparing their impact [4–6].

This observational study aims to fill this gap by comparing the real-world effectiveness and safety of acarbose and vildagliptin as adjunct therapies to metformin in Indian patients with T2D. By analyzing data from a diverse patient population, this research seeks to provide critical insights that could influence future therapeutic directions and patient management strategies, ensuring more personalized and effective treatment outcomes.

Materials and methods

Study design

This was a real-world, observational, record-based study conducted to compare the effectiveness and safety of acarbose versus vildagliptin in managing T2D. We retrospectively analyzed the medical records of 98 patients diagnosed with T2D and baseline HbA1c levels between 7% and 8%.

Study population

The study included 98 patients with T2D. The patients were divided into 2 treatment arms: (1) acarbose arm — 48 patients; (2) vildagliptin arm — 50 patients. Selection was based on patients' existing treatment regimens, specifically those who had been on a stable dose of metformin for the past 6 months. For this study, patients were either prescribed additional vildagliptin 50 mg twice daily or acarbose 50 mg once daily for at least 3 months, without any change to their ongoing glimepiride and metformin therapy. The study included T2D patients with a stable baseline HbA1c level between 7 and 8%, having a minimum of 9 months of medical history available for review, on continuous treatment with metformin for the last 6 months prior to the introduction of either vildagliptin or acarbose, with duration of T2D suffering between 6 and 24 months. Those diagnosed with type 1 diabetes, pregnant women, those with dose of metformin increased above baseline, and those with severe renal or liver impairment were excluded.

This approach ensured that the effects observed could be attributed to the addition of vildagliptin or acarbose to the established regimen of metformin, under stable conditions.

Ethical approval

Ethical approval for this study was obtained from the Institutional Ethics Committee, ensuring compliance with ethical standards and patient confidentiality throughout the research process.

Data collection

Data were collected from the electronic health records (EHR) of each participant, including age, duration of diabetes, and treatment specifics. Baseline measurements and follow-up data after 3 months of treatment were extracted, focusing on glycemic control indices such as HbA1c, fasting plasma glucose (FPG), and postprandial plasma glucose (PPPG).

Efficacy was measured based on the change from baseline in HbA1c, FPG, and PPPG after 3 months of treatment. The primary endpoint was the mean change in HbA1c levels from baseline to 3 months. Secondary endpoints included changes in FPG and PPPG levels.

Safety was evaluated by recording adverse drug reactions (ADRs) reported in the medical records during the 3 months. Specific ADRs such as flatulence, hyperacidity, and gastroparesis were noted. The percentage

Table 1. Baseline Characteristics

	Acarbose arm [n = 48]	Vildagliptin arm [n = 50]	P-value
Mean Age [mean ± SD]	53.1 ± 8.9	55.9 ± 9.3	0.1
Gender [n] [male/female]	28/20	31/19	0.7
Duration of diabetes [mean ± SD]	0.7 ± 1.8	0.6 ± 1.9	0.8
Prescribing pattern of glimepiride and metformin [n (%)]			
Baseline glimepiride 1 mg per day	11 (22.91%)	09 (18%)	0.8
Baseline glimepiride 2 mg per day	26 (54.16%)	29 (58%)	
Baseline glimepiride 3 mg per day	03 (6.25%)	05 (10%)	
Baseline glimepiride 4 mg per day	08 (16.66%)	07 (14%)	
Baseline metformin 500 mg per day	06 (12.5%)	08 (16%)	0.9
Baseline metformin 850 mg per day	04 (8.33%)	06 (12%)	
Baseline metformin 1000 mg per day	32 (66.66%)	29 (58%)	
Baseline metformin 1500 mg per day	02 (4.16%)	01 (2%)	
Baseline metformin 1700 mg per day	01 (2.08%)	02 (4%)	
Baseline metformin 2000 mg per day	03 (6.25%)	04 (8%)	

SD — standard deviation

of patients experiencing any ADRs was calculated for each treatment group.

Statistical analysis

Estimating from the facility's background rate, with a 95% level of significance and 5% marginal error, a minimum sample size of 96 was calculated, inclusive of both arms. The study, however, included 98 patients for final analysis. Descriptive statistics were used to summarize demographic and baseline characteristics, including means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. The effectiveness of the treatments was analyzed using paired t-tests to compare pre- and post-treatment values within each group. Chi-square tests were used to compare the incidence of ADRs between the treatment groups. A p-value of less than 0.05 was considered statistically significant.

Results

In this observational study, we evaluated the effectiveness and safety of acarbose compared to vildagliptin in 98 patients diagnosed with T2D on metformin for at least 6 months, presenting baseline HbA1c levels between 7% and 8%. The cohort was divided into 2 groups, with 48 patients starting on acarbose and 50 on vildagliptin. The mean age of patients in the acarbose arm was 53.06 ± 8.9 years, while the vildagliptin arm had a mean age of 55.85 ± 9.2 years. The duration of T2D was similar between groups, with the acarbose arm at 0.7 years and the vildagliptin arm at 0.6 years. The prescribing pattern of glimepiride and metformin was comparable in both groups with no significant differences. (Tab. 1)

Assessing the effectiveness of acarbose and vildagliptin, it was noted that the acarbose arm showed a decrease in HbA1c level by 1.0% at the end of 3 months in comparison to the vildagliptin, which showed a decrease by 0.9%, the change being insignificant. However, acarbose showed a significant decrease in FPG and PPPG at the end of 3 months of treatment with a decrease of 47.6 mg/dl and 95.9 mg/dL for FPG and PPPG, respectively. The change in the case of the vildagliptin arm was 40.31 mg/dL for FPG and 79.5 mg/dL for PPPG at the end of 3 months. These changes were significant at $p < 0.001$. Table 2 summarizes the mean values, efficacy measures, and changes in glycemic indices (HbA1c, FPG, and PPPG) over 3 months for patients with T2D treated with acarbose or vildagliptin. The results indicate significant improvements in glycemic control for both treatment arms.

The incidence of adverse drug reactions (ADRs) was comparable between the 2 treatment arms ($p = 0.9733$), with 41.6% in the acarbose arm and 42% in the vildagliptin arm reporting ADRs. The occurrence of flatulence was higher in the acarbose group (25%) compared to the vildagliptin group (16%). Conversely, hyperacidity and gastroparesis were more prevalent in the vildagliptin arm, affecting 20% and 24% of patients, respectively, compared to 10.41% and 16.66% in the acarbose arm. Table 3 displays the incidence of adverse drug reactions (ADRs) and specific gastrointestinal side

Table 2. Comparative Effectiveness of Acarbose and Vildagliptin in Type 2 Diabetes Management

	Acarbose arm [n = 48]	Vildagliptin arm [n = 50]
HbA1c [%] [mean ± SD]		
Baseline	7.8 ± 0.1	7.9 ± 0.1
3 Months	6.8 ± 0.2	6.9 ± 0.2
Mean change	–1.0 ± 0.2NS	–0.9 ± 0.2NS
FPG [mg/dL] [mean ± SD]		
Baseline	157.8 ± 8.8	155.7 ± 4.1
3 Months	110.2 ± 12.6	115.4 ± 12.9
Mean Change	–47.6 ± 13.4**	–40.31 ± 12.8**
PPPG [mg/dL] [mean ± SD]		
Baseline	247.1± 12.7	240.5 ± 8.6
3 Months	151.2 ± 14.1	161.0 ± 6.9
Mean change	–95.9 ± 14.4**	–79.5 ± 10.9**

$p < 0.05$ is considered significant; **$p < 0.001$
FPG — fasting plasma glucose; HbA1c — glycated hemoglobin; NS — not significant; PPPG — postprandial plasma glucose; SD — standard deviation

Table 3. Safety Profile Comparison of Acarbose and Vildagliptin in Type 2 Diabetes Treatment

	No. of patients [n (%)]		P-value
	Acarbose arm [n = 48]	Vildagliptin arm [n = 50]	
ADR Incidence	20 (41.6%)	21 (42%)	0.973^{NS}
Reported ADRs			
Flatulence	12 (25%)	8 (16%)	
Hyperacidity	5 (10.4%)	10 (20%)	
Gastroparesis	8 (16.7%)	12 (24%)	

$p < 0.05$ is considered significant
ADR — adverse drug reaction; NS — not significant

effects among patients treated with acarbose versus vildagliptin, highlighting comparable overall ADR rates but differing rates of flatulence, hyperacidity, and gastroparesis between the 2 groups.

Discussion

The findings from this observational study emphasize the clinical benefits of acarbose and vildagliptin as adjunctive therapy to metformin in patients with T2D, highlighting their ability to significantly improve glycemic control. Both medications demonstrated substantial efficacy in reducing HbA1c, FPG, and PPPG, aligning with the goals for T2D management to minimize the risk of diabetes-related complications.

In a comparative context, both drugs showed significant reductions in glycemic indices like results from a recent study by Wang et al., which reported notable improvements in glycemic control with acarbose, saxagliptin, and vildagliptin, affecting different aspects of metabolic control and intestinal flora distribution in T2D patients [7]. The study by Pan et al. provides additional insight into this by directly comparing the efficacy and tolerability of vildagliptin with acarbose in a controlled environment, showing similar efficacy between these drugs over a 24-week period, which supports the results of our observational study [8].

Safety profiles were equally favorable, albeit with distinct patterns of gastrointestinal side effects attributable to their mechanisms of action. Acarbose tends to cause more gastrointestinal disturbances due to its effects on carbohydrate malabsorption [9], while vildagliptin presents fewer such issues, potentially leading to better patient adherence. The difference in safety profiles between acarbose and vildagliptin highlights the need for personalized treatment plans based on patient-specific gastrointestinal tolerability, an aspect

supported by the network meta-analysis findings by Wu et al., showing a lower incidence of gastrointestinal events with vildagliptin compared to other AGIs [10].

Furthermore, the influence on the intestinal microbiota suggests another layer of therapeutic effects beyond glycemic control. The modulation of intestinal flora by these drugs, as noted by Wang et al., who observed genus-level changes in the microbiota following treatment, may contribute to their overall metabolic effects, including improvements in insulin sensitivity and reduced inflammation [7].

The differing dosing regimens for acarbose and vildagliptin in our study, while reflecting real-world prescribing patterns, warrant a focused discussion on the implications of these findings. The utilization of acarbose at 50 mg once daily, although less frequent than the typical dosage, effectively managed glycemic control comparably to vildagliptin administered at 50 mg twice daily. This suggests that lower dosages of acarbose might be sufficient in certain patient populations, potentially enhancing tolerability and adherence while minimizing side effects. It is crucial, however, to recognize that these results, derived from an observational study, may not universally apply to all patient demographics. Thus, while our findings contribute valuable insights into the flexible application of acarbose, they underscore the necessity for further research. Future randomized controlled trials should aim to explore these dosing strategies across a more diverse cohort, providing a more comprehensive understanding of their efficacy and safety, and potentially influencing future guidelines on the management of T2D with acarbose.

This study's real-world setting provides valuable insights into the practical use of these therapies in typical clinical scenarios, reflecting a broader applicability than the more controlled conditions of randomized controlled trials (RCTs). However, the observational nature of the study and the relatively short follow-up period are limitations that could affect the generalizability of the findings. Long-term studies are necessary to fully understand the efficacy, safety, and impact on patient outcomes of these treatments over extended periods.

The current study's findings warrant further investigation in larger, more diverse populations and over longer durations to confirm these results and clarify the long-term benefits and safety profiles of acarbose and vildagliptin. Additionally, exploring the cost-effectiveness of these drugs will be crucial for their integration into broader diabetes management protocols.

Conclusions

In conclusion, acarbose and vildagliptin both offer effective glycemic control when added to metformin therapy, with distinct but manageable safety profiles. Their effects on the intestinal microbiota present an intriguing aspect of their mechanism that may contribute to their overall therapeutic effects. Future research should focus on expanding these findings to inform clinical practice better and optimize treatment strategies for T2D.

Article information

Data availability statement

All data generated and/or analyzed during this study are included in this published article and its supplementary information files.

Ethics statement

The study was approved by Independent Ethics Committee with approval number HREC-AARC/04 dated 12.02.2023.

Author contributions

SSS, SM — Study conceptualization; SSS, RG, SB — Data acquisition; SSS, SM, BS, SJ — Drafting manuscript; SSS, SM, RG, SB, BS, SJ — Manuscript finalization

Funding

None.

Conflict of interest

The authors declare no conflict of interest.

References

1. Anjana RM, Unnikrishnan R, Deepa M, et al. ICMR-INDIAB Collaborative Study Group. Metabolic non-communicable disease health report of India: the ICMR-INDIAB national cross-sectional study (ICMR-INDIAB-17). Lancet Diabetes Endocrinol. 2023; 11(7): 474–489, doi: 10.1016/S2213-8587(23)00119-5, indexed in Pubmed: 37301218.
2. Weng J, Ji L, Jia W, et al. Chinese Diabetes Society, Chinese Diabetes Society. Standards of care for type 2 diabetes in China. Diabetes Metab Res Rev. 2016; 32(5): 442–458, doi: 10.1002/dmrr.2827, indexed in Pubmed: 27464265.
3. Cai X, Han X, Luo Y, et al. Efficacy of dipeptidyl-peptidase-4 inhibitors and impact on β–cell function in Asian and Caucasian type 2 diabetes mellitus patients: A meta-analysis. Journal of Diabetes. 2015; 7(3): 347–359, doi: 10.1111/1753-0407.12196, indexed in Pubmed: 25043156.
4. Mathieu C, Degrande E. Vildagliptin: a new oral treatment for type 2 diabetes mellitus. Vasc Health Risk Manag. 2008; 4(6): 1349–1360, doi: 10.2147/vhrm.s3005, indexed in Pubmed: 19337548.
5. Zhang X, Fang Z, Zhang C, et al. Effects of Acarbose on the Gut Microbiota of Prediabetic Patients: A Randomized, Double-blind, Controlled Crossover Trial. Diabetes Ther. 2017; 8(2): 293–307, doi: 10.1007/s13300-017-0226-y, indexed in Pubmed: 28130771.

6. Olivares M, Neyrinck AM, Pötgens SA, et al. The DPP-4 inhibitor vildagliptin impacts the gut microbiota and prevents disruption of intestinal homeostasis induced by a Western diet in mice. Diabetologia. 2018; 61(8): 1838–1848, doi: 10.1007/s00125-018-4647-6, indexed in Pubmed: 29797022.
7. Wang Z, Wang J, Hu J, et al. A comparative study of acarbose, vildagliptin and saxagliptin intended for better efficacy and safety on type 2 diabetes mellitus treatment. Life Sci. 2021; 274: 119069, doi: 10.1016/j.lfs.2021.119069, indexed in Pubmed: 33460667.
8. Pan C, Yang W, Barona JP, et al. Comparison of vildagliptin and acarbose monotherapy in patients with Type 2 diabetes: a 24-week, double-blind, randomized trial. Diabet Med. 2008; 25(4): 435–441, doi: 10.1111/j.1464-5491.2008.02391.x, indexed in Pubmed: 18341596.
9. Oboh G, Ogunsuyi OB, Ogunbadejo MD, et al. Influence of gallic acid on α-amylase and α-glucosidase inhibitory properties of acarbose. J Food Drug Anal. 2016; 24(3): 627–634, doi: 10.1016/j.jfda.2016.03.003, indexed in Pubmed: 28911570.
10. Wu S, Chai S, Yang J, et al. Gastrointestinal Adverse Events of Dipeptidyl Peptidase 4 Inhibitors in Type 2 Diabetes: A Systematic Review and Network Meta-analysis. Clin Ther. 2017; 39(9): 1780–1789.e33, doi: 10.1016/j.clinthera.2017.07.036, indexed in Pubmed: 28827024.