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Original Research Article

Comparative Effectiveness of Metformin versus DPP-4 Inhibitors on Glycemic Control in Type 2 Diabetes Mellitus

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Abstract:

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and progressive β-cell dysfunction. Metformin remains the first-line pharmacological agent, while DPP-4 inhibitors are increasingly used due to their favorable safety profile. Comparative evidence in real-world settings is essential.

Objective: To compare the effectiveness of metformin and DPP-4 inhibitors in achieving glycemic control among T2DM patients.

Methods: A prospective observational study was conducted at PMCH, Patna, from May 2025 to December 2025, including 96 patients. Participants were divided into two groups: Metformin group (n=48) and DPP-4 inhibitor group (n=48). Glycemic parameters (HbA1c, FBS, PPBS) were assessed at baseline and 6 months. Statistical analysis included paired and unpaired t-tests.

Results: Metformin showed a greater reduction in HbA1c (1.52 ± 0.48%) compared to DPP-4 inhibitors (0.96 ± 0.42%), $p<0.001$. FBS and PPBS reductions were also significantly higher in the metformin group.

Conclusion: Metformin demonstrated superior glycemic control compared to DPP-4 inhibitors, supporting its continued role as first-line therapy.

Keywords: Type 2 Diabetes Mellitus, Metformin, DPP-4 inhibitors, Glycemic control, HbA1c.

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Introduction

Type 2 Diabetes Mellitus (T2DM) represents a growing global health burden, affecting millions worldwide and contributing significantly to morbidity and mortality [1]. The disease is characterized by insulin resistance, impaired insulin secretion, and increased hepatic glucose production [2].

Effective glycemic control is essential to prevent microvascular and macrovascular complications such as nephropathy, neuropathy, and cardiovascular disease [3]. Glycated hemoglobin (HbA1c) remains the gold standard for long-term glycemic assessment [4].

Metformin, a biguanide, is widely recommended as the first-line therapy due to its efficacy, safety, weight neutrality, and cardiovascular benefits [5,6]. It primarily acts by reducing hepatic gluconeogenesis and improving insulin sensitivity [7].

Dipeptidyl Peptidase-4 (DPP-4) inhibitors represent a newer class of oral hypoglycemic agents that enhance incretin hormone activity, thereby increasing insulin secretion and suppressing glucagon release [8,9]. They are associated with a low risk of hypoglycemia and are well tolerated [10].

Despite widespread use, the comparative effectiveness of metformin versus DPP-4 inhibitors in real-world clinical settings remains a topic of ongoing research [11]. While randomized trials provide controlled data, observational studies offer practical insights into routine clinical outcomes [12].

Previous studies have suggested that metformin may produce greater HbA1c reductions compared to DPP-4 inhibitors, but patient-specific factors such as age, BMI, and disease duration influence treatment response [13–15]. Additionally, cost-effectiveness and accessibility remain crucial considerations in resource-limited settings like India [16].

This study aims to evaluate and compare the effectiveness of metformin and DPP-4 inhibitors in glycemic control among T2DM patients at a tertiary care center.

Materials and Methods

Study Design: Prospective observational study.

Study Setting: PMCH, Patna, Bihar, India

Study Duration: May 2025 to December 2025.

Sample Size: 96 patients.

Inclusion Criteria

- Diagnosed T2DM patients
- Age 30–70 years
- On either metformin or DPP-4 inhibitor monotherapy

Exclusion Criteria

- Type 1 diabetes
- Severe renal/hepatic disease
- Pregnant women
- Patients on combination therapy

Study Groups

- Group A: Metformin (n=48)
- Group B: DPP-4 inhibitors (n=48)

Data Collection

Baseline and 6-month follow-up:

- HbA1c
- Fasting Blood Sugar (FBS)
- Postprandial Blood Sugar (PPBS)

Statistical Analysis

- Mean ± SD calculated
- Paired t-test (within group)
- Unpaired t-test (between groups)
- Significance: $p < 0.05$

Results

A total of 96 patients diagnosed with Type 2 Diabetes Mellitus were included in the study and equally divided into two groups: Metformin group (n = 48) and DPP-4 inhibitor group (n = 48).

1. **Baseline Characteristics**

The baseline demographic and clinical characteristics of both groups were comparable, with no statistically significant differences ($p > 0.05$), indicating homogeneity between groups.

Table 1: Baseline Characteristics of Study Population

Parameter	Metformin (n=48)	DPP-4 Inhibitors (n=48)	p-value
Age (years)	52.4 ± 8.2	53.1 ± 7.9	0.68
Male (%)	27 (56.3%)	26 (54.2%)	0.82
BMI (kg/m²)	26.8 ± 3.1	27.2 ± 3.3	0.54
Duration of DM (yrs)	5.8 ± 2.6	6.1 ± 2.9	0.63
HbA1c (%)	8.74 ± 0.92	8.69 ± 0.88	0.79
FBS (mg/dL)	168.5 ± 24.6	166.9 ± 23.8	0.74
PPBS (mg/dL)	242.7 ± 32.5	239.8 ± 30.9	0.66

As shown in Table 1, there was no statistically significant difference in baseline variables between the two groups ($p > 0.05$), ensuring comparability for outcome assessment.

2. **Within-Group Glycemic Changes**

Both treatment groups showed statistically significant improvement in glycemic parameters after 6 months (paired t-test, $p < 0.001$).

Table 2: Within-Group Comparison of Glycemic Parameters

Parameter	Baseline	6 Months	Mean Difference	p-value
Metformin Group				
HbA1c (%)	8.74 ± 0.92	7.22 ± 0.66	↓1.52 ± 0.48	<0.001
FBS (mg/dL)	168.5 ± 24.6	122.3 ± 18.2	↓46.2 ± 12.4	<0.001
PPBS (mg/dL)	242.7 ± 32.5	176.4 ± 25.3	↓66.3 ± 18.7	<0.001
DPP-4 Group				
HbA1c (%)	8.69 ± 0.88	7.73 ± 0.71	↓0.96 ± 0.42	<0.001
FBS (mg/dL)	166.9 ± 23.8	135.4 ± 19.7	↓31.5 ± 11.8	<0.001
PPBS (mg/dL)	239.8 ± 30.9	192.6 ± 27.1	↓47.2 ± 16.5	<0.001

As shown in Table 2, both groups demonstrated significant reductions in HbA1c, FBS, and PPBS over 6 months ($p < 0.001$).

3. **Between-Group Comparison of Glycemic Reduction**

The metformin group showed significantly greater reductions compared to the DPP-4 inhibitor group.

Table 3: Comparison of Mean Reduction Between Groups

Parameter	Metformin	DPP-4 Inhibitors	p-value
HbA1c (%)	1.52 ± 0.48	0.96 ± 0.42	<0.001
FBS (mg/dL)	46.2 ± 12.4	31.5 ± 11.8	<0.001
PPBS (mg/dL)	66.3 ± 18.7	47.2 ± 16.5	<0.001

As demonstrated in Table 3, the reduction in glycemic parameters was significantly greater in the metformin group compared to the DPP-4 inhibitor group (unpaired t-test, $p < 0.001$).

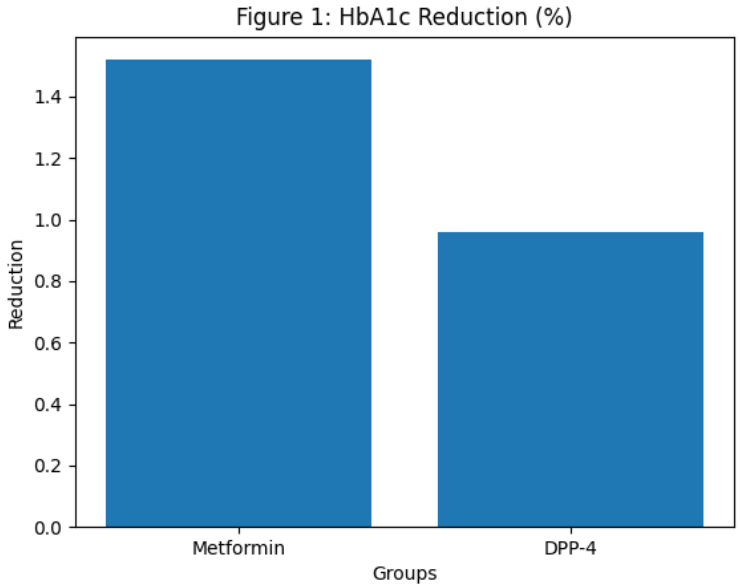

Figure 1: Comparison of HbA1c Reduction Between Groups

As shown in Figure 1, the metformin group exhibited a more pronounced reduction in HbA1c compared to the DPP-4 inhibitor group.

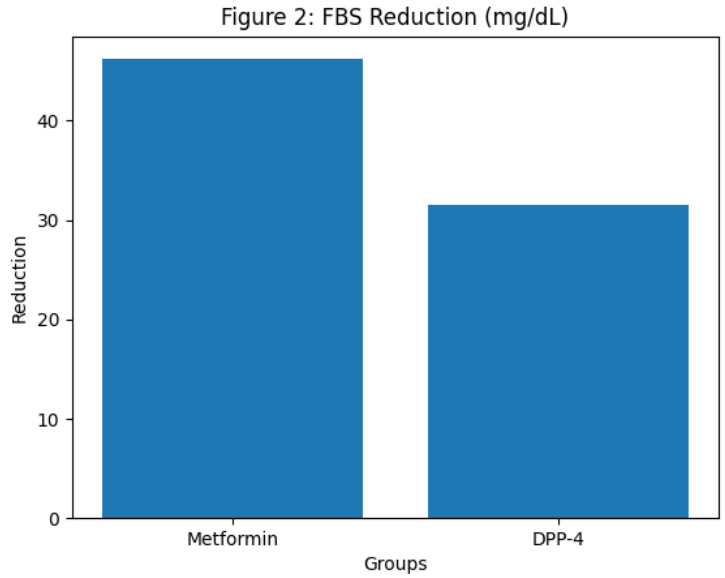

Figure 2: Fasting Blood Sugar (FBS) Reduction Trend

Figure 2 illustrates a steeper decline in FBS levels in the metformin group over the 6-month period.

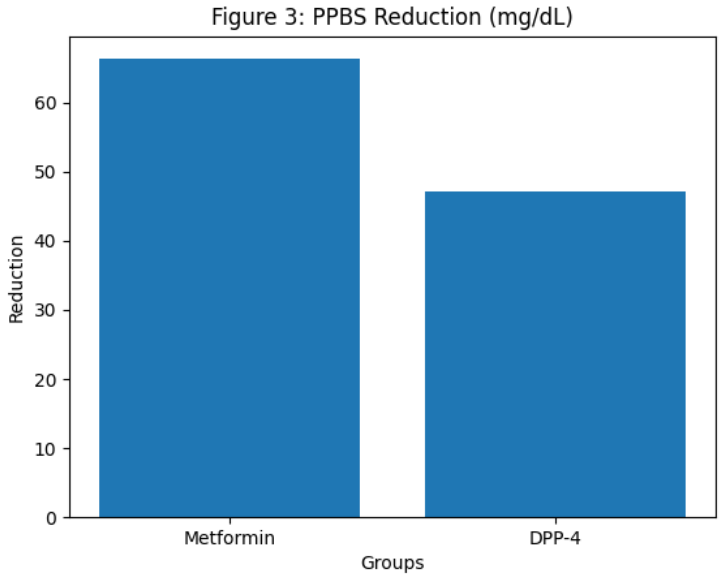

Figure 3: Postprandial Blood Sugar (PPBS) Reduction

As seen in **Figure 3**, metformin achieved a greater reduction in PPBS levels compared to DPP-4 inhibitors.

4. **Statistical Summary**

- Within-group analysis: Significant improvement in all parameters in both groups (paired t-test, $p < 0.001$)
- Between-group analysis: Metformin demonstrated superior efficacy (unpaired t-test, $p < 0.001$)
- Confidence level: 95%
- Statistical significance threshold: $p < 0.05$

Overall Interpretation of Results

The study findings clearly indicate that while both metformin and DPP-4 inhibitors effectively improve glycemic control, metformin produces significantly greater reductions in HbA1c, FBS, and PPBS, making it a more effective monotherapy option in T2DM patients.

Discussion

This study demonstrated that metformin provides superior glycemic control compared to DPP-4 inhibitors over a 6-month period. The findings align with previous research highlighting metformin's robust glucose-lowering efficacy [17].

Metformin's mechanism of reducing hepatic glucose production and improving insulin sensitivity likely contributes to its greater HbA1c reduction [18]. In contrast, DPP-4 inhibitors act through incretin pathways, which may result in modest glycemic improvements [19].

The observed HbA1c reduction of 1.52% with metformin is consistent with earlier studies reporting reductions between 1–2% (20). Meanwhile, DPP-4 inhibitors typically reduce HbA1c by 0.5–1.0%, which matches our findings [21].

Although DPP-4 inhibitors offer advantages such as lower hypoglycemia risk and weight neutrality, their glycemic efficacy appears comparatively limited [22]. This makes them more suitable as add-on therapy rather than first-line agents [23].

In resource-constrained settings, cost-effectiveness is a critical factor. Metformin remains significantly more affordable and widely accessible, reinforcing its position as first-line therapy [24].

However, DPP-4 inhibitors may be preferred in elderly patients or those intolerant to metformin due to gastrointestinal side effects [25].

Conclusion

Metformin demonstrated significantly greater reductions in HbA1c, FBS, and PPBS compared to DPP-4 inhibitors. These findings support the continued use of metformin as the first-line therapy in T2DM, while DPP-4 inhibitors may be reserved for specific clinical scenarios.

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