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**ORIGINAL RESEARCH**

# Comparative Safety and Effectiveness of Metformin in Patients with Diabetes Mellitus and Heart Failure: A Study of 50 Patients

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## Abstract:

Background: Diabetes mellitus (DM) and heart failure (HF) frequently coexist, posing complex challenges for therapeutic management. Metformin, a commonly prescribed antidiabetic medication, has shown potential benefits beyond glycemic control, particularly in cardiovascular conditions. This study aimed to assess the safety and effectiveness of metformin in a cohort of patients diagnosed with both DM and HF.

Methods: A prospective observational study was conducted on a sample of 50 patients at Madhepura, Biharwith coexisting DM and HF. Patients were divided into two groups based on metformin use (Group A: Metformin users; Group B: Non-metformin users). Baseline demographic, clinical and laboratory data were collected for all participants. Primary outcomes included changes in glycemic control (HbA1c levels) and cardiac function (ejection fraction) over a 12-month period. Secondary outcomes encompassed hospitalization rates, adverse events, and changes in other relevant clinical parameters.

Results: Of the 50 patients, 25 were assigned to Group A (mean age: 65 ± 8.2 years) and 25 to Group B (mean age: 68 ± 7.9 years). Both groups exhibited similar baseline characteristics in terms of age, gender distribution, comorbidities, and baseline HbA1c levels. After 12 months, the metformin group demonstrated a statistically significant reduction in HbA1c levels compared to the non-metformin group ($p < 0.05$). Additionally, the metformin group exhibited a trend towards improved ejection fraction, although the difference was not statistically significant ($p = 0.08$). Hospitalization rates and adverse events were comparable between the groups.

Conclusion: This study suggests that metformin may be a safe and effective option for managing patients with coexisting DM and HF. Metformin demonstrated favorable effects on glycemic control, and a potential trend towards improved cardiac function was observed. The comparable safety profile and incidence of adverse events between metformin and non-metformin groups highlight its potential utility in this patient population. However, further

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large-scale randomized controlled trials are warranted to confirm these findings and establish optimal dosages and treatment durations.

Keywords: diabetes mellitus, heart failure, metformin, glycemic control, cardiac function, observational study, adverse events, therapeutic management.

**Introduction:**

Diabetes mellitus (DM) and heart failure (HF) are prevalent chronic conditions that often coexist, posing significant challenges for clinical management (1,2). The co-occurrence of DM and HF is associated with increased morbidity, mortality, and healthcare costs, emphasizing the need for effective therapeutic approaches (3). Metformin, a cornerstone of DM treatment, has garnered attention beyond its glycemic control properties due to its potential cardiovascular benefits (4). Despite its widespread use in DM management, concerns have been raised about the safety of metformin in patients with HF due to its potential to exacerbate lactate levels and worsen HF symptoms (5). Consequently, understanding the safety and effectiveness of metformin in individuals with both DM and HF is essential for guiding clinical decisions.

While some studies have explored the use of metformin in HF populations, there remains a gap in the literature regarding its comparative safety and effectiveness specifically in patients with coexisting DM and HF. Therefore, this study aims to assess the impact of metformin on glycemic control and cardiac function in a cohort of patients diagnosed with both DM and HF.

**Materials and Methods:**

Study Design and Participants: This prospective observational study enrolled 50 adult patients diagnosed with both DM and HF from Madhepura, Bihar. Patients were recruited based on specific inclusion criteria, including a confirmed diagnosis of type 2 DM and HF with reduced ejection fraction (HFrEF) or preserved ejection fraction (HFpEF). Exclusion criteria encompassed contraindications to metformin, severe renal impairment (glomerular filtration rate < 30 mL/min/1.73 $m^2$), and recent acute coronary syndrome or stroke.

Data Collection: Baseline demographic, clinical and laboratory data were collected for all participants. Demographic information included age, gender, and duration of DM and HF. Clinical parameters consisted of New York Heart Association (NYHA) functional class, medication history, and comorbidities. Laboratory data encompassed hemoglobin A1c (HbA1c) levels, serum creatinine, estimated glomerular filtration rate (eGFR), and brain natriuretic peptide (BNP) levels.

Study Groups: Patients were divided into two groups based on metformin use: Group a included patients receiving metformin in their treatment regimen, while Group B comprised patients not using metformin. The groups were matched as closely as possible for baseline characteristics.

Outcome Measures: The primary outcome measures included changes in HbA1c levels and cardiac function over a 12-month period. HbA1c levels were measured at baseline and at 12 months. Cardiac function was assessed using echocardiography to determine ejection fraction at baseline and 12 months. Secondary outcomes encompassed hospitalization rates due to worsening HF, adverse events related to metformin use, changes in NYHA functional class, and alterations in serum creatinine, eGFR, and BNP levels.

**Statistical Analysis**: Descriptive statistics were used to summarize baseline characteristics. Continuous variables were expressed as mean ± standard deviation (SD), and categorical

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variables as frequencies and percentages. The independent samples t-test and chi-square test were used to compare continuous and categorical variables between groups, respectively. Changes in HbA1c levels and ejection fraction were analyzed using paired t-tests within each group and independent t-tests between the groups. A p-value < 0.05 was considered statistically significant.

**Results**:

Baseline Characteristics:

The study included a total of 50 patients, with 25 patients in each group (Group A: Metformin users; Group B: Non-metformin users). Baseline demographic and clinical characteristics are presented in Table 1. Both groups were comparable in terms of age, gender distribution, duration of DM and HF, NYHA functional class, and comorbidities.

**Table 1: Baseline Characteristics**

| **Characteristics** | **Group A (Metformin Users)** | **Group B (Non-Metformin Users)** |
|---|---|---|
| Age (years, mean ± SD) | 65 ± 8.2 | 68 ± 7.9 |
| Gender (Male/Female) | 13/12 | 14/11 |
| DM Duration (years) | 9.4 ± 3.1 | 8.8 ± 2.7 |
| HF Duration (years) | 5.7 ± 2.6 | 5.9 ± 2.8 |
| NYHA Functional Class | | |
| - I | 4 (16%) | 3 (12%) |

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| | | |
|---|---|---|
| - II | 15 (60%) | 17 (68%) |
| - III | 6 (24%) | 5 (20%) |
| Comorbidities | | |
| - Hypertension | 22 (88%) | 21 (84%) |
| - Coronary Artery Disease | 8 (32%) | 9 (36%) |
| - Chronic Kidney Disease | 10 (40%) | 11 (44%) |

Glycemic Control:

At baseline, both groups had similar HbA1c levels (Group A: 7.9% ± 0.6%; Group B: 7.8% ± 0.5%). After 12 months, Group A exhibited a statistically significant reduction in HbA1c levels to 7.1% ± 0.5% ($p < 0.05$), while Group B showed a modest decrease to 7.7% ± 0.4% ($p = 0.12$). The difference in HbA1c reduction between the groups was statistically significant ($p < 0.01$).

Cardiac Function:

The ejection fraction at baseline was comparable between the groups (Group A: 38.2% ± 4.8%; Group B: 37.5% ± 4.6%). After 12 months, Group A exhibited a trend towards improved ejection fraction (39.8% ± 4.5%, $p = 0.08$), while Group B showed a minimal change (37.6% ± 4.4%, $p = 0.63$). However, the difference in ejection fraction improvement between the groups was not statistically significant ($p = 0.14$).

Hospitalization and Adverse Events:

Hospitalization rates due to worsening HF were comparable between the groups (Group A: 6 (24%); Group B: 7 (28%)). The incidence of adverse events related to metformin use was minimal, with only 3 patients in Group A reporting mild gastrointestinal symptoms.

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The study's findings suggest that metformin use in patients with coexisting DM and HF may lead to improved glycemic control and potentially enhanced cardiac function. However, further large-scale randomized controlled trials are needed to validate these results and establish optimal treatment strategies for this patient population.

**Discussion**:

The coexistence of diabetes mellitus (DM) and heart failure (HF) presents a complex clinical scenario, demanding careful consideration of therapeutic strategies. In this study, we aimed to assess the safety and effectiveness of metformin in a cohort of patients diagnosed with both DM and HF. Our findings contribute to the growing body of evidence exploring the potential benefits of metformin beyond glycemic control in patients with cardiovascular conditions.

The observed reduction in hemoglobin A1c (HbA1c) levels among metformin users aligns with previous studies demonstrating its efficacy in improving glycemic control (1,2). Metformin's mechanism of action, involving hepatic glucose output reduction and improved insulin sensitivity, likely contributes to these results. The modest decrease in HbA1c levels among non-metformin users emphasizes the importance of comprehensive DM management strategies in patients with coexisting HF.

Although the improvement in ejection fraction observed in the metformin group was not statistically significant, it suggests a potential trend towards enhanced cardiac function. This is consistent with emerging research indicating metformin's cardiovascular benefits beyond glycemic control (3,4). The mechanisms underlying these effects could involve mitochondrial modulation, anti-inflammatory properties, and potential hemodynamic improvements (5). However, larger and longer-term studies are necessary to establish metformin's definitive impact on cardiac function in this specific patient population.

The comparable safety profiles and incidence of adverse events between metformin and non-metformin groups are reassuring. Concerns regarding metformin's potential to worsen heart failure symptoms through lactate accumulation and volume overload have been raised (6). Our study's minimal adverse events related to metformin align with recent studies demonstrating its safety in HF populations (7-11).

This study's limitations include its observational design and relatively small sample size. Randomized controlled trials are essential to validate these findings and provide more robust evidence. Moreover, considering the heterogeneity of heart failure and DM populations, subgroup analyses based on HF etiology, ejection fraction, and comorbidities could yield further insights.

**Conclusion**

In conclusion, our study suggests that metformin may offer a safe and effective option for managing patients with coexisting DM and HF. The improvements in glycemic control and potential trends in cardiac function warrant further investigation in larger, well-controlled trials. Metformin's role in cardiovascular disease management underscores the need for a holistic approach to treating patients with complex comorbidities.

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