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Glycemic and Metabolic Changes with Metformin Monotherapy in Newly Diagnosed Type 2 Diabetes Mellitus Patients

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Abstract

Background: Metformin is the first-line pharmacologic treatment for type 2 diabetes mellitus (T2DM), yet patient response can vary. Identifying clinical predictors of early glycemic response may help personalize therapy. The main objective of this study is to evaluate baseline predictors of glycemic response to metformin monotherapy in newly diagnosed patients with T2DM.

Methods: A prospective cohort study was conducted at Minia University Hospital involving 220 newly diagnosed T2DM patients. Participants initiated metformin monotherapy (500–2000 mg/day) and were followed for 3 months. Glycemic response was defined as achieving HbA1c < 7% at follow-up. Clinical, demographic, and laboratory data were collected at baseline and reassessed after 3 months. Logistic regression was used to identify independent predictors of treatment success.

Results: After 3 months, 65.5% of patients achieved HbA1c < 7%, with a significant mean reduction in HbA1c from 7.39% to 6.5% (p < 0.001). Body mass index (BMI) also decreased significantly (24.32 to 22.33 kg/m², p < 0.001). Younger age, lower BMI, and lower baseline HbA1c were significantly associated with better glycemic response (p < 0.001). However, in multivariable analysis, only baseline HbA1c remained a significant independent predictor (OR 0.12, 95% CI 0.05– 0.30, p < 0.001).

Conclusion: Lower baseline HbA1c is a strong predictor of short-term glycemic response to metformin monotherapy in newly diagnosed T2DM patients. These findings support early intervention and individualized treatment strategies to optimize outcomes.

Keywords: Metformin; Monotherapy; Type 2 Diabetes Mellitus; Glycemic; Metabolic.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and progressive beta-cell dysfunction (Galicia-Garcia et al., 2020). According to the latest edition of the International Diabetes Federation (IDF) Diabetes Atlas approximately 11.1% of the global adult population aged 20 to 79 years equivalent to 1 in every 9 adults is currently living with diabetes. This alarming prevalence highlights the continuing rise of diabetes as a global public health challenge, necessitating urgent efforts in prevention, early diagnosis, and effective management (International Diabetes Federation, 2025).

Effective management of T2DM is critical to prevent complications such as cardiovascular disease, nephropathy, and neuropathy. Metformin, a biguanide, is widely recommended as the first-line pharmacological therapy for T2DM due to its efficacy in lowering blood glucose, favorable safety profile, and cost-effectiveness (American Diabetes Association Professional Practice Committee, 2022). Its primary mechanisms include suppression of hepatic gluconeogenesis, enhancement of insulinmediated glucose uptake in skeletal muscle, and increased incretin secretion in the small intestine, collectively improving glycemic control without significant risk of hypoglycemia (Foretz et al., 2014; Rena et al., 2017) (Figure 1).

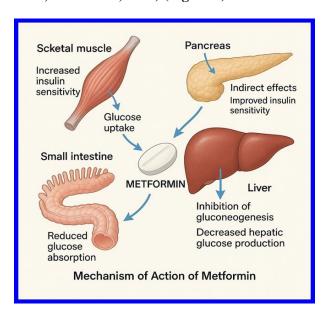


Figure 1. The mechanism of action of metformin

Despite its widespread use, individual responses to metformin monotherapy vary considerably, with some patients achieving optimal glycemic control (HbA1c < 7%) while others exhibit suboptimal responses, necessitating alternative or adjunctive therapies (**Zhou et al., 2014**). Factors such as age, body mass index (BMI), baseline HbA1c, and comorbidities like hypertension may influence metformin's efficacy, yet the precise predictors of response remain incompletely understood (**Becker et al., 2010**).

Previous studies have suggested that lower baseline HbA1c and younger age may be associated with better glycemic outcomes, but results are inconsistent, and few prospective studies have focused on newly diagnosed T2DM patients (Lee et al., 2021). Understanding these predictors is crucial for personalizing treatment strategies, optimizing therapeutic outcomes, and identifying patients who may require early intervention with alternative agents.

This prospective cohort study aims to identify baseline demographic, clinical, and laboratory factors associated with a good glycemic response (HbA1c < 7%) after 3 months of metformin monotherapy in newly diagnosed T2DM patients. By evaluating variables such as age, gender, BMI, hypertension, and baseline HbA1c, this study seeks to provide evidence-based insights to guide clinicians in tailoring treatment plans. Additionally, it will assess secondary outcomes, including changes in HbA1c, and BMI contributing to a comprehensive understanding of metformin's impact in this population.

2. Methods

2.1. Study Design and Setting

This study was designed as a prospective observational cohort study conducted at the diabetes outpatient clinic of Minia university hospital. The study aimed to identify baseline clinical and demographic predictors of glycemic response to metformin monotherapy in newly diagnosed patients with type 2 diabetes mellitus.

2.2. Participants

A consecutive sampling approach was utilized. Eligible participants were adult patients newly diagnosed with T2DM with HbA1c < 9. All participants were initiated on metformin monotherapy, starting at a dose of 500 mg twice daily. The dose was gradually titrated, with a

maximum dose of up to 2000 mg per day (administered as 1000 mg twice daily). Dose adjustments were made during routine follow-up visits to optimize glycemic control while minimizing adverse effects. No other antidiabetic medications were prescribed during the study period. Patients were included only if they had not received any prior antidiabetic therapy and were capable of providing informed consent.

The study flowchart shows the enrollment of 252 patients, of whom 235 met the eligibility criteria and were enrolled. After 3 months of metformin monotherapy, 15 patients were lost to follow-up, and 220 patients completed the study and were included in the final analysis. Inclusion and exclusion criteria were shown in the flow diagram of the study (**Figure 2**).

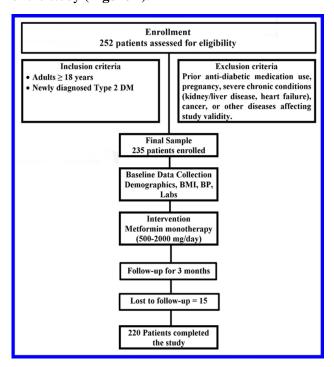


Figure 2. The Study Flow Diagram

2.3. Sample Size Calculation

The sample size was calculated based on an expected good glycemic response (defined as HbA1c <7% at 3 months) rate of 50%, with a 95% confidence level and a 7% margin of error. The minimum required sample size was determined to be 196. To account for potential dropouts or loss to follow-up, the sample size was increased to 220 participants.

2.4. Data Collection

Baseline data were collected at the time of enrollment and included demographic characteristics (age, sex, marital status, and residence), clinical history (hypertension, family history of diabetes, smoking status), anthropometric measurements (weight, height, and body mass index [BMI]), vital signs (blood pressure), and laboratory investigations (fasting plasma glucose, HbA1c, complete blood count, liver enzymes and estimated glomerular filtration rate [eGFR]).

Participants were followed for a period of 3 months during which they received standard metformin monotherapy. At follow-up, HbA1c, fasting glucose, and BMI were reassessed.

2.5. Outcome Measures

The primary outcome of the study was the assessment of glycemic response, defined as achieving an HbA1c level of less than 7% after 3 months of metformin monotherapy. Secondary outcomes included the evaluation of absolute and relative changes in HbA1c from baseline. The absolute change in HbA1c was calculated as the difference between baseline and follow-up values, while the relative change was calculated by dividing the absolute change by the baseline value and expressing the result as a percentage. Additionally, changes in BMI from baseline to follow-up were assessed as a secondary outcome.

These outcome measures were chosen to reflect both the effectiveness and tolerability of metformin in newly diagnosed patients with type 2 diabetes mellitus.

2.6. Ethical Considerations

This study was approved by the ethics committee of Minia University with an approval number (1460-02-2025). Written informed consent was obtained from all participants prior to enrollment.

2.7. Statistical Analysis

Descriptive statistics were used to summarize baseline characteristics. Continuous variables were presented as means ± standard deviation (SD) or medians with interquartile range (IQR), as appropriate. Categorical variables were expressed as frequencies and percentages. The paired samples

t-test was used to compare glycemic response parameters before and after three months of metformin monotherapy, while the chi-square test assessed the relationship between baseline categorical variables and treatment response. Multivariable logistic regression analysis was performed to identify independent predictors of good glycemic response, adjusting for potential confounders. A p-value < 0.05 was considered statistically significant. All analyses were conducted using SPSS software (version 26).

3. Results

A total of 220 participants meeting the inclusion criteria were enrolled in the study. **Table 1** summarizes the baseline sociodemographic and clinical characteristics of the study population.

Table 1 shows that the included 220 newly diagnosed type 2 diabetes patients with a mean age of 47.16 years. Most participants were female (55%), married (72.7%), and lived in urban areas (70%). The majority were non-smokers (92.7%), and 37.3% had hypertension. Additionally, 35.9% reported a family history of diabetes. These baseline characteristics provide important context for analyzing predictors of glycemic response to metformin treatment.

Table 2 presents the baseline clinical and laboratory characteristics of the study population. The mean systolic and diastolic blood pressures and 130.98 mmHg 75.08 mmHg. respectively. The average BMI was 24.32 kg/m². Baseline fasting glucose and HbA1c levels were elevated, with means of 152.03 mg/dL and 7.39%, respectively, consistent with moderate hyperglycemia and reflective of recent diabetes onset.

Hematological parameters were largely within normal reference ranges, with mean hemoglobin at 14.47 g/dL, red blood cell count at $5.25 \times 106/\mu L$, white blood cell count at $7.63 \times 103/\mu L$, and platelet count at $307.97 \times 103/\mu L$, indicating no underlying anemia, infection, or thrombocytopenia in the cohort. Liver enzyme levels, including alanine aminotransferase (ALT) at 29.88 U/L and aspartate aminotransferase (AST) at 27.05 U/L, were within acceptable limits, suggesting preserved hepatic function. The eGFR averaged 86.11 mL/min/1.73 m², confirming that all participants had normal renal function at baseline, an important prerequisite for metformin use.

Table 3 demonstrates significant improvements in key metabolic parameters after 3 months of treatment. The data show a statistically significant

Table 1. Demographic characteristics of the study sample

| Sociodemographic characteristics | | | | |
|-----------------------------------|-------|--------------|--|--|
| Sociodeniographic characteristics | | | | |
| Age/year | | | | |
| Mean (SD) | 47.16 | 47.16 (5.43) | | |
| Gender, n (%) | | | | |
| Male | 99 | (45) | | |
| Female | 121 | (55) | | |
| Marital status, n (%) | | | | |
| Married | 160 | (72.7) | | |
| Single, divorced or widow | 60 | (27.3) | | |
| Residence, n (%) | | | | |
| Urban | 154 | (70) | | |
| Rural | 66 | (30) | | |
| Special habits, n (%) | | | | |
| Smokers | 16 | (7.3) | | |
| Non-Smokers | 204 | (92.7) | | |
| Hypertension | | · · · · · · | | |
| (-) | 138 | (62.7) | | |
| (+) | 82 | (37.3) | | |
| Family history of DM, n (%) | | · , | | |
| (-) | 141 | (64.1) | | |
| (+) | 79 | (35.9) | | |
| | | , | | |

Table 2. Baseline clinical and laboratory data in the study group

| Laboratory data | Mean (SD) |
|-----------------------------------------|----------------|
| Systolic B.P. (mmHg) | 130.98 (17.22) |
| Diastolic B.P. (mmHg) | 75.08 (9.42) |
| BMI (kg/m²) | 24.32 (4.71) |
| Fasting glucose (mg/dL) | 152.03 (12.50) |
| HbA1c (%) | 7.39 (0.56) |
| Hemoglobin (g/dL) | 14.47 (0.86) |
| Red Blood Cells (10 ⁶ /μL) | 5.25 (0.46) |
| White Blood Cells (10 ³ /μL) | 7.63 (2.18) |
| | |
| Platelets (10 ³ /μL) | 307.97 (87.41) |
| Alanine Aminotransferase (U/L) | 29.88 (3.03) |
| Aspartate Aminotransferase (U/L) | 27.50 (4.21) |
| eGFR (mL/min/1.73 m²) | 86.11 (6.20) |

Table 3. Parameters of glycemic response to metformin monotherapy at baseline and after 3 months

| Outcome | Baseline | At 3 months | P |
|------------------------------------------------------------|----------------|----------------|---------|
| Fasting glucose (mg/dL) | | | |
| Mean (SD) | 152.03 (12.50) | 129.77 (28.32) | < 0.001 |
| HbA1c (%) | | | |
| Mean (SD) | 7.39 (0.56) | 6.5 (0.99) | < 0.001 |
| Absolute Change in HbA1c from Baseline (percentage points) | | | |
| Median (IQR) | 0.9 | 0 (0.50-1.30) | |
| Relative Change in HbA1c from Baseline (%) | | | |
| Median (IQR) | 12.25 (6.2 | 9-19.12) | |
| | | | |

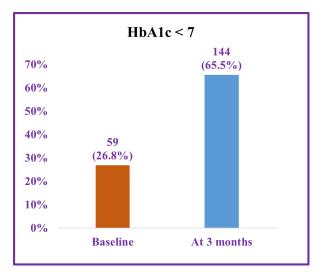


Figure 3. Glycemic response to metformin monotherapy at 3 months

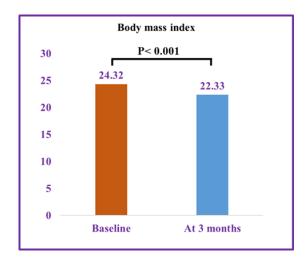


Figure 4. Change in mean BMI (kg/m^2) from baseline to 3 months following metformin monotherapy

reduction in fasting glucose levels, decreasing from a mean of 152.03 mg/dL (SD 12.50) to 129.77 mg/dL (SD 28.32) (p < 0.001), indicating improved glycemic control. The most notable finding is the reduction in HbA1c, dropping from a mean of 7.39% (SD 0.56) to 6.5% (SD 0.99) (p < 0.001). The median absolute change in HbA1c was 0.90 percentage points (IQR 0.50-1.30), and the relative change was 12.25% (IQR 6.29-19.12), further highlighting the efficacy of metformin in lowering glycemic levels.

Figure 3 illustrates the proportion of the patients achieving good glycemic control levels at baseline and after three months of metformin monotherapy. At baseline, 59 patients, representing 26.8% of the cohort, had an HbA1c < 7%. After 3 months of metformin monotherapy, there was a shift in glycemic control. The number of patients achieving good glycemic response (HbA1c < 7%) increased to 144 individuals, representing 65.5% of the cohort. This indicates a substantial improvement in glycemic control, with a large majority of patients (an increase of 38.7% from baseline) reaching the target HbA1c of less than 7% after three months of metformin monotherapy.

Figure 4 illustrates the change in BMI from baseline to 3 months following metformin monotherapy. At baseline, the average BMI of the study participants was 24.32 (kg/m²). After 3 months of metformin treatment, the average BMI showed a decrease to 22.33 (kg/m²). The observed reduction in BMI over the three-month metformin monotherapy period is consistent with the drug's established metabolic effects, which include promoting weight stability or modest weight loss in patients with type 2 diabetes mellitus. This finding reinforces metformin's role as a first-line therapy that addresses both glycemic control and weight management, key components of diabetes care.

Table 4 shows that younger age (< 50 years), lower baseline BMI (< 25 kg/m²), and lower baseline HbA1c (< 7.5%) are significantly associated with a good glycemic response (HbA1c < 7% after 3 months), each with p < 0.001. Younger patients (79.9% vs. 20.1%), those with lower BMI (76.4% vs. 23.6%), and those with lower initial HbA1c (61.8% vs. 38.2%) were more likely to achieve glycemic control. Gender, residence, smoking, hypertension, and family history of diabetes showed no significant association, suggesting age, BMI, and baseline HbA1c are key predictors for tailoring metformin treatment.

Table 4. Relationship between baseline data and glycemic response

| Variable | Poor glycemic response | Good glycemic response | P |
|---------------------------|------------------------|------------------------|---------|
| Age group, n (%) | | | |
| < 50 years | 30 (39.5) | 115 (79.9) | < 0.001 |
| ≥ 50 years | 46 (60.5) | 29 (20.1) | |
| Gender, n (%) | | | |
| Male | 36 (47.4) | 63 (43.8) | 0.61 |
| Female | 40 (52.6) | 81 (56.3) | |
| Residence, n (%) | | | |
| Urban | 55 (72.4) | 99 (68.8) | 0.58 |
| Rural | 21 (27.6) | 45 (31.3) | |
| Smoking, n (%) | | | |
| Non-smokers | 72 (94.7) | 132 (91.7) | 0.40 |
| Smokers | 4 (5.3) | 12 (8.3) | |
| Hypertension, n (%) | | | |
| (-) | 54 (71.1) | 84 (58.3) | 0.06 |
| (+) | 22 (28.9) | 60 (41.7) | |
| F.H. of DM, n (%) | | | |
| (-) | 54 (71.1) | 87 (60.4) | 0.12 |
| (+) | 22 (28.9) | 57 (39.6) | |
| BMI (kg/m²) degree, n (%) | | | |
| < 25 | 28 (36.8) | 110 (76.4) | < 0.001 |
| ≥ 25 | 48 (63.2) | 34 (23.6) | |
| Baseline HbA1c (%), n (%) | | | |
| < 7.5 | 15 (19.7) | 89 (61.8) | < 0.001 |
| ≥ 7.5 | 61 (80.3) | 55 (38.2) | |
| | | | |

| | Odd ratio | 95% C.I. | | P |
|--------------------------------|-----------|----------|-------|---------|
| | | Lower | Upper | |
| Age | 0.99 | 0.9 | 1.08 | 0.75 |
| Gender, Male | 1.10 | 0.54 | 2.23 | 0.79 |
| Residence, Urban | 1.31 | 0.64 | 2.70 | 0.46 |
| Special habits, Non-smoker | 2.09 | 0.51 | 8.59 | 0.31 |
| Hypertension, Non-hypertensive | 1.85 | 0.91 | 3.74 | 0.09 |
| F.H. of DM, (-) | 1.92 | 0.94 | 3.95 | 0.08 |
| Baseline BMI | 0.98 | 0.86 | 1.11 | 0.70 |
| Baseline HbA1c | 0.12 | 0.05 | 0.30 | < 0.001 |
| | | | | |

Table 5: Multivariable Logistic Regression for Predictors of Good Glycemic Response

Table 5 shows the logistic regression analysis identified baseline HbA1c as the sole statistically significant predictor of glycemic response to metformin therapy (OR 0.12, 95% CI 0.05-0.30, p<0.001), demonstrating that patients with lower initial HbA1c levels were significantly more likely to achieve treatment success. While no other variables reached statistical significance, non-hypertensive status (p=0.09) and absence of diabetes family history (p=0.08) showed borderline associations that may warrant further investigation. The lack of significant findings for demographic factors like age, gender, and residence suggests these characteristics may have limited influence on short-term metformin response.

4. Discussion

The demographic and clinical profile of the study population offers valuable insight into factors that may influence glycemic response to metformin monotherapy. In this cohort of 220 newly diagnosed T2DM patients, the mean age was approximately 47 years, with a predominance of female participants. This aligns with previous studies showing that middle-aged adults are commonly affected by T2DM, and women often exhibit higher healthcareseeking behavior, leading to earlier diagnosis and treatment initiation (Kautzky-Willer et al., 2016). The predominance of females may reflect differences in healthcare-seeking behavior, as women in our community are more likely to attend outpatient clinics and participate in screening programs, as well as potential sociocultural factors influencing referral patterns.

The relatively normal mean BMI values observed in this study may be attributed to the early detection of T2DM, facilitated through primary care referrals or other screening methods. Furthermore, residents of rural and semi-urban areas in the Minia governorate tend to engage in higher levels of physical activity and follow distinct dietary patterns, which may also influence BMI outcomes. In addition, the metabolically obese normal-weight (MONW) phenotype, characterized by normal BMI despite increased visceral adiposity and insulin resistance, has been documented in Middle Eastern populations and may partially explain our findings (Lee et al., 2015).

The high proportion of married individuals and urban residents may reflect lifestyle patterns, dietary habits, and access to medical care, which can affect diabetes risk and management outcomes (Kalra et al., 2024). The low prevalence of smoking is notable in the current study, despite the fact that smoking is a well-known risk factor for insulin resistance and poor glycemic control (Cho et al., 2022). Moreover, the presence of hypertension in over one-third of the participants is consistent with the frequent coexistence of hypertension and diabetes, both components of the metabolic syndrome (Cheung & Li, 2012). A family history of diabetes, reported by 35.9% of highlights patients, the role of genetic predisposition in disease development and possibly in treatment response (Ali, 2013; Goyal et al., 2023). These baseline characteristics are crucial in understanding which patient subgroups are more likely to benefit from metformin monotherapy, and they support the need for personalized treatment approaches.

The observed improvement in glycemic control following three months of metformin monotherapy

highlights its effectiveness as a first-line treatment in newly diagnosed T2DM patients. At baseline, only 26.8% of patients achieved the glycemic target (HbA1c < 7%), a threshold recommended by major diabetes associations to reduce the risk of long-term complications (American Diabetes Association Professional Practice Committee, 2024). After three months of treatment, this proportion more than doubled to 65.5%, representing a significant 38.7% increase in patients achieving adequate glycemic control. These findings are consistent with previous studies demonstrating metformin's robust glucoselowering effect, particularly in early-stage diabetes when β-cell function is still relatively preserved (UK Prospective Diabetes Study (UKPDS) Group, 1998; Mohamed et al., 2024). Metformin primarily improves insulin sensitivity and decreases hepatic glucose production, contributing to early and sustained HbA1c reduction (Rena et al., 2017). The relatively high response rate observed in the current cohort may also be attributed to the patients' recent diagnosis and treatment initiation, as early intervention is known to yield better metabolic outcomes (Warrilow et al., 2020). This glycemic response reinforces metformin's role as a foundational therapy in diabetes management and supports its continued use in clinical guidelines (Dutta et al., 2023).

The present study demonstrated that three months of metformin monotherapy led to significant improvements in several key metabolic parameters among newly diagnosed T2DM patients. A statistically significant reduction in BMI was observed, (p < 0.001). This weight reduction aligns with metformin's known mechanism of action, including enhancement of insulin sensitivity and decreased hepatic glucose output without promoting weight gain which is a common limitation of other antidiabetic therapies (Seifarth et al., 2013; Rena et al., 2017). Metformin has also been shown to reduce appetite and modulate gut microbiota, which may contribute to weight loss (Wu et al., 2017).

Glycemic parameters showed notable improvement. Fasting glucose levels significantly declined, indicating enhanced glucose homeostasis, and HbA1c levels dropped from 7.39% to 6.5% (p < 0.001). The median absolute reduction in HbA1c of 0.90% and a relative reduction of 12.25% are clinically meaningful and consistent with previous findings from large-scale studies, such as the UKPDS trial, which reported similar benefits of early metformin use (UK Prospective Diabetes Study (UKPDS) Group, 1998). Moreover, the

proportion of patients achieving the glycemic target (HbA1c < 7%) increased from 26.8% to 65.5%. emphasizing the effectiveness of metformin in achieving short-term glycemic control when initiated promptly after diagnosis (Hostalek & Campbell, 2021). These findings reinforce the role of metformin as the cornerstone of initial therapy in current T2DM and support guidelines recommending its use based on efficacy, weight neutrality or loss, and a favorable safety profile (American Diabetes Association Professional Practice Committee, 2024; 2025).

Findings from the current study highlight that younger age, lower BMI, and lower baseline HbA1c are strongly associated with a good glycemic response (HbA1c < 7% after 3 months) to metformin monotherapy in newly diagnosed T2DM patients, each with a highly significant pvalue of < 0.001. These results align with previous research indicating that younger patients and those with lower BMI may exhibit better insulin sensitivity and beta-cell function, facilitating metformin's action in reducing hepatic glucose production and enhancing peripheral glucose uptake (Rena et al., 2017; Nordklint et al., 2021). The strong association with lower baseline HbA1c suggests that initiating metformin therapy early, before significant hyperglycemia develops, may reduce the harmful effects of elevated blood glucose (Martono et al., 2015). In contrast, gender, residence, smoking status, hypertension, and family history of diabetes showed no significant association with glycemic response, consistent with studies suggesting these factors may have limited direct impact on metformin's pharmacodynamics (Zhou et al., 2014). These findings emphasize the importance of early intervention in younger, leaner patients with milder hyperglycemia optimize to metformin's effectiveness, guiding clinicians in personalizing T2DM treatment and identifying those who may require alternative therapies.

In the present study, while younger age and lower BMI were associated with better outcomes in univariate analysis, only baseline HbA1c remained statistically significant after adjusting for potential confounders in the logistic regression model. Baseline HbA1c identified as the sole independent predictor of glycemic response to metformin monotherapy, with lower initial HbA1c levels significantly increasing the likelihood of achieving treatment success. This finding aligns with a study

demonstrating that patients with higher baseline HbA1c tend to experience a greater absolute reduction in HbA1c with antidiabetic medications. but those with lower baseline HbA1c are more likely to reach glycemic targets (Sherifali et al., 2010; Al-Qerem et al., 2022). A meta-analysis by Sherifali et al. (2010) found that baseline HbA1c was a strong predictor of HbA1c reduction with metformin, with higher baseline values associated with larger absolute drops. However, achieving an HbA1c target of <7% is more feasible for individuals starting closer to this goal. The current study underscores the importance of early diagnosis and intervention in T2DM, as patients initiating metformin with lower HbA1c levels are more likely to achieve optimal glycemic control within a short timeframe.

In the present study, while non-hypertensive status (p=0.09) and absence of diabetes family history (p=0.08) showed borderline associations with glycemic response, these did not reach statistical significance. The relationship between hypertension and metformin response is complex; some studies suggest metformin may have beneficial effects on blood pressure, particularly in certain populations, but a direct impact on glycemic response in hypertensive T2DM patients is not consistently reported (Muntzel et al., 1999; Thomopoulos et al., 2017).

Similarly, a family history of diabetes, while indicating a genetic predisposition to the disease, does not consistently predict individual response to specific pharmacotherapies like metformin (**Dujic et al., 2017**). These borderline findings warrant further investigation in larger cohorts to determine if these factors play a more subtle, yet clinically relevant, role in metformin efficacy.

Conversely, demographic factors such as gender and residence did not emerge as significant predictors of short-term metformin response in the current study. This is consistent with some previous research indicating that while these factors can influence overall diabetes progression management, they may not directly dictate the immediate glycemic efficacy of metformin monotherapy (Zhou et al., 2016; Kalka et al., 2021). However, other studies have reported ageand gender-dependent effects on metformin differences response, often related to pharmacokinetics or physiological responses (Krentz & Bailey, 2005; Kalka et al., 2021). The lack of significance in the present cohort might be attributed to the relatively homogenous nature of

newly diagnosed T2DM patients or the specific duration of follow-up. Future studies with longer follow-up periods and more diverse populations may reveal more nuanced associations.

5. Limitations

This study has several limitations. First, the follow-up period was limited to 3 months, which may not capture the long-term glycemic durability of metformin therapy. Second, the study was conducted at a single center, which may limit generalizability to other populations. Additionally, potential confounders such as dietary habits, physical activity, and socioeconomic factors were not comprehensively evaluated. Future studies with longer follow-up and multicenter designs are warranted.

6. Conclusion

This study confirms metformin's efficacy in newly diagnosed T2DM, with 65.5% achieving HbA1c <7% within 3 months. Baseline HbA1c emerged as the strongest predictor of treatment success, emphasizing the importance of early intervention. Younger age and lower BMI further enhanced glycemic response, while demographic factors (e.g., gender) showed negligible impact. The modest weight reduction observed aligns with metformin's metabolic benefits. Borderline associations with hypertension and family history suggest avenues for future research. These findings support tailored metformin therapy based on baseline characteristics to optimize outcomes in T2DM management.

7. Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

This study was approved by the research ethical committee of Minia University with an approval number (1460-02-2025). Written informed consent was obtained from the study participants after describing the study's goals and advantages.

Human Ethics

All study steps were performed in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Data availability

All data generated or analysed during this study are included in this published article.

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Authors' contributions

Asmaa S. Mohamed and Fatma M.M. Kamel developed the study concept and design. Fatma M.M. Kamel collected the data. Asmaa S. Mohamed and Hosam M. A. Refaei drafted the manuscript. All authors read, reviewed, and approved the final manuscript.

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