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Six-Month Glycemic Changes in Type 2 Diabetes: Insulin-Containing Versus Oral Regimens

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ABSTRACT

Type 2 diabetes mellitus (T2DM) requires regular evaluation of glycemic control, yet local evidence comparing insulin-containing and oral antidiabetic drug (OAD) regimens in routine care remains limited. This study compared the six-month change in glycated hemoglobin (HbA1c) and fasting blood glucose (FBG) between outpatients receiving OAD alone and outpatients receiving insulin combined with OAD. Because treatment was allocated by clinical indication rather than at random, the study describes treatment-associated glycemic change and does not establish causal treatment effects. An analytical observational study with a retrospective comparative design used medical records from the Internal Medicine Clinic of Universitas Sebelas Maret Hospital, Surakarta, Indonesia. Fifty-four patients were selected by purposive sampling (OAD, n = 27; insulin plus OAD, n = 27) and followed for six months. The primary endpoint was the between-group difference in ΔHbA1c and the secondary endpoint the between-group difference in ΔFBG, tested with the Mann–Whitney U test and summarized as a rank-biserial correlation (r) with 95% confidence intervals (CI); within-group change was tested with the Wilcoxon signed-rank test. Most patients were female (53.7%) and had comorbidities (94.4%). Mean HbA1c fell from 8.45% to 7.14% in the OAD group ($p = 0.005$) and from 10.46% to 9.21% in the insulin group ($p = 0.115$), while FBG fell from 146.19 to 129.44 mg/dL ($p = 0.089$) and from 187.56 to 173.96 mg/dL ($p = 0.614$), respectively. Baseline and six-month values were significantly higher in the insulin group (all $p < 0.05$). No statistically significant between-group difference in change was detected for HbA1c (difference in mean change +0.06 percentage points; rank-biserial $r = 0.03$; 95% CI −0.29 to 0.34; $p = 0.869$) or FBG (+3.15 mg/dL; $r = 0.05$; 95% CI −0.27 to 0.36; $p = 0.775$). These intervals are wide and do not establish equivalence between the regimens. Patients receiving insulin began and remained further from target, supporting structured follow-up and timely treatment intensification.

Keywords: Type 2 diabetes mellitus; Insulin; Oral antidiabetic drugs; HbA1c; Fasting blood glucose

INTRODUCTION

Diabetes mellitus (DM) is a chronic, non-communicable metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Type 2 diabetes mellitus (T2DM) is the most common form, accounting for approximately 90–95% of all diabetes cases worldwide (American Diabetes Association Professional Practice Committee, 2022). The global burden of diabetes continues to rise, and the number of adults living with diabetes is projected to increase substantially by 2045 (Cho et al., 2018; International Diabetes Federation, 2025). Indonesia is among the countries with the largest number of people with diabetes, making the optimization of T2DM management an important public health priority.

T2DM develops from insulin resistance in skeletal muscle, liver, and adipose tissue, followed by progressive pancreatic β-cell dysfunction. Its major risk factors include obesity, high-calorie diets, sedentary lifestyle, aging, family history, and genetic predisposition, and it frequently coexists with hypertension and dyslipidemia that aggravate cardiovascular and microvascular complications (Zheng et al., 2018). Management of T2DM therefore combines non-pharmacological measures, including healthy diet, regular physical activity, and weight reduction, with pharmacological therapy. Metformin is recommended as first-line therapy, whereas insulin is indicated when glycemic targets cannot be achieved with oral agents or when metabolic decompensation is present (Chaudhury et al., 2017; Davies et al., 2022).

Insulin therapy is highly effective in lowering blood glucose, particularly in patients with severe metabolic disturbances, but it carries risks of hypoglycemia and weight gain, requires more complex self-administration, and is more costly. Conversely, non-insulin regimens carry a lower risk of hypoglycemia and may support weight

reduction, although their glucose-lowering capacity is limited in patients with advanced β-cell failure (Davies et al., 2022; Hanefeld et al., 2020). Real-world comparisons have produced inconsistent findings. A retrospective matched cohort study reported that oral antidiabetic therapy was not inferior to early insulinization in newly diagnosed patients (Y.-M. Lee et al., 2024), while a study in Semarang, Indonesia, found that metformin–insulin reduced HbA1c by 1.06% compared with 0.21% for metformin–vildagliptin, without a statistically significant difference (p = 0.494) (Timur et al., 2024).

Glycated hemoglobin (HbA1c) reflects average glycemia over the preceding two to three months and is closely related to the risk of chronic complications, whereas fasting blood glucose (FBG) reflects basal glucose regulation and is more sensitive to short-term variation (Sherwani et al., 2016). Evaluating both parameters therefore provides a more complete picture of treatment response than either measure alone, and both are recorded routinely in outpatient diabetes care, which makes them suitable indicators for evaluating regimens under real-world conditions.

Three gaps remain in the evidence available for this setting. First, most comparisons between insulin-containing and oral regimens come from clinical trials or from cohorts in which insulin was started early in the course of the disease (Y.-M. Lee et al., 2024), whereas in Indonesian hospital practice insulin is generally added only after oral agents have failed, so that the patients who receive it differ systematically from those who do not. Second, the Indonesian studies published so far have compared specific drug combinations in pharmacy-based evaluations rather than the two regimen categories as they are actually used in outpatient clinics (Timur et al., 2024). Third, the available reports present p-values for the comparison between regimens without effect estimates or confidence intervals, so the magnitude of difference that the data can reasonably exclude remains unknown. As a result, there is little quantitative evidence on how much HbA1c and FBG actually change under each regimen in routine hospital care in Indonesia.

The objective of this study was to measure and compare the six-month change in HbA1c and FBG among patients with T2DM treated at the Internal Medicine Outpatient Clinic of Universitas Sebelas Maret (UNS) Hospital, Surakarta, Indonesia, who received oral antidiabetic drugs alone and those who received insulin in combination with oral agents. The specific objectives were threefold: to quantify the within-group change in HbA1c and FBG after six months of therapy in each regimen group; to estimate the between-group difference in that change, expressed as an effect size with a 95% confidence interval; and to describe the extent to which each group reached the recommended HbA1c target. Because the regimen was determined by clinical indication rather than by randomization, the study was designed to describe and compare treatment-associated glycemic change; it cannot determine which regimen is causally more effective, and the results are not intended to rank the two regimens against each other.

METHODS

Study Design and Setting

This study was an analytical observational study with a retrospective comparative design, using secondary data obtained from medical records at a single center. The study was conducted at the Internal Medicine Outpatient Clinic of UNS Hospital, Surakarta, Indonesia, and data were collected from July to September 2025. Each patient was observed over a six-month treatment period, defined by two laboratory evaluations: a baseline measurement and a measurement after six months of continuous therapy under the same regimen category.

Study Groups and Operational Definition of the Regimens

Patients with T2DM were classified, according to the regimen recorded throughout the observation period, into two groups. The OAD group comprised patients who received one or more oral antidiabetic drugs without insulin. The insulin group comprised patients who received insulin in combination with at least one oral antidiabetic drug. No patient in this study received insulin as monotherapy, and the term "insulin group" is used in this combination sense throughout the manuscript. Patients whose regimen category changed during the six months were excluded, so that every patient was analyzed under a stable regimen category.

Population, Sampling, and Eligibility Criteria

The accessible population comprised all patients with T2DM treated at the Internal Medicine Outpatient Clinic of UNS Hospital during the study period. Subjects were selected by purposive sampling from the medical records that satisfied the eligibility criteria. Inclusion criteria were: (1) a documented diagnosis of T2DM; (2) age older than 18 years; (3) treatment with oral antidiabetic drugs alone or with insulin combined with oral agents; and (4) complete records of HbA1c, FBG, sex, body mass index (BMI) and comorbidity over a six-month treatment period. Exclusion criteria were: (1) loss to follow-up or irregular visits during the six consecutive months of observation; (2) incomplete medical records for any study variable; and (3) a change of regimen from oral agents to an insulin combination, or the reverse, during the observation period.

Sample Size and Statistical Power

The minimum sample size was calculated using the formula for paired numerical analytical studies, $n = [(Z\alpha + Z\beta) \times S / (X_1 - X_2)]^2$, with $Z\alpha = 1.96$, $Z\beta = 0.842$, a standard deviation of 0.91 obtained from a previous randomized trial of basal insulin therapy in older adults with type 2 diabetes, and a clinically meaningful mean difference of 0.5, yielding a minimum of 26 subjects per group; 27 patients per group were obtained. This formula addresses the within-patient (paired) comparison and therefore justifies the precision of the within-group estimates only; it does not correspond to the primary between-group endpoint of the present analysis. With 27 patients per group, a two-sided α of 0.05 and 80% power, the study could detect only a large standardized between-group difference of approximately 0.76 SD, or about 0.78 SD for the rank-based test actually used. Smaller but clinically meaningful between-group differences could

therefore have escaped detection, and this limited power is reflected in the width of the confidence intervals reported below.

Variables and Endpoints

The independent variable was the type of antidiabetic regimen (oral agents alone, or insulin combined with oral agents). The dependent variables were HbA1c (%) and FBG (mg/dL), measured at baseline and after six months of treatment. FBG was defined as plasma glucose measured after fasting for at least eight hours. Sex, BMI (kg/m^2) and the presence of comorbidity were recorded as potential confounding variables. Glycemic change was expressed as the within-patient difference (Δ) between the six-month and the baseline value, so that a negative value denotes improvement.

The primary endpoint was the between-group difference in ΔHbA1c; the secondary endpoint was the between-group difference in ΔFBG. Comparisons of baseline and six-month values between the groups were descriptive and served to document the baseline imbalance between the regimens rather than to estimate a treatment effect. Because a single primary endpoint was specified, no formal adjustment for multiple comparisons was applied; a Bonferroni-corrected threshold for the six between-group tests ($p < 0.008$) would leave the differences in baseline HbA1c, six-month HbA1c and six-month FBG significant and would render the baseline FBG difference ($p = 0.026$) non-significant, without altering the conclusion drawn for the primary endpoint.

Data Collection Procedure

Data were extracted from the outpatient medical records of eligible patients onto a standardized extraction form containing the study variables only. For each patient, the baseline and six-month HbA1c and FBG results were recorded together with sex, BMI and documented comorbidity. Patient identity was replaced by a study code at the point of extraction, and no identifying information was retained in the analysis dataset.

Laboratory Measurement and Quality Control

All HbA1c and FBG determinations were performed in the clinical laboratory of UNS Hospital, which applied the same routine assay and the same internal quality-control procedures to every sample throughout the study period, so that the baseline and six-month measurements of a given patient are directly comparable. Laboratory values were analyzed exactly as recorded in the medical record; no value was excluded, truncated or modified. The highest HbA1c observed was 19.4%, which lies within the reportable range of routine HbA1c assays and is consistent with severe uncontrolled hyperglycemia at presentation; a value of this magnitude occurred in both groups, so the extreme observations are not concentrated in one arm. Because every comparison reported here is rank-based, the analyses are insensitive to such extreme values, and medians with interquartile ranges are presented alongside means for the same reason.

Data Analysis

Univariate analysis was performed using frequency distributions for categorical variables and mean, standard deviation (SD), median, interquartile range (IQR), range, and 95% confidence interval (CI) for numerical variables. Normality was tested using the Shapiro–Wilk test because each group contained fewer than 50 subjects. Most variables departed from normality ($p < 0.05$) and the distributions were markedly right-skewed, as were both change scores (ΔHbA1c, $p < 0.001$; ΔFBG, $p = 0.002$); results are therefore reported as mean ± SD together with median and IQR, and non-parametric tests were applied.

Within-group change was tested with the Wilcoxon signed-rank test and summarized with the matched-pairs rank-biserial correlation. Between-group comparisons were tested with the Mann–Whitney U test and summarized as the rank-biserial correlation with its 95% CI, derived from the U statistic; effect sizes were computed with the simple difference formula (Kerby, 2014). Because the change scores were not normally distributed, the rank-biserial correlation and its interval are the primary expression of precision. To express the same result in the original measurement units, a deliberately conservative 95% CI for the difference in mean change was also computed, taking the standard deviation of the change score as the square root of (SD of the baseline value squared + SD of the six-month value squared), which corresponds to zero correlation between the two measurements and therefore yields the widest interval compatible with the observed data; any positive within-patient correlation narrows it. No covariate-adjusted model was fitted, for the reasons set out among the limitations. Statistical significance was set at $p < 0.05$, and all analyses were performed using SPSS.

Ethical Approval

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Sebelas Maret (No. 93/UN27.06.11/KEP/EC/2025), and research permission was granted by UNS Hospital (No. 1409.6/UN27.46/TA.04.19/2025). Patient confidentiality was maintained throughout data collection and analysis.

RESULTS AND DISCUSSION

A total of 54 patients met the study criteria, consisting of 27 patients in the OAD group and 27 patients in the insulin group. The characteristics of the participants are presented in Table 1.

Table 1. Characteristics of Patients With Type 2 Diabetes Mellitus by Treatment Group

Characteristic	OAD (n = 27)	Insulin + OAD (n = 27)	Total (n = 54)
Sex, n (%)			
Male	13 (48.1)	12 (44.4)	25 (46.3)
Female	14 (51.9)	15 (55.6)	29 (53.7)
Comorbidity, n (%)			
Present	25 (92.6)	26 (96.3)	51 (94.4)
Absent	2 (7.4)	1 (3.7)	3 (5.6)
BMI (kg/m^2), mean ± SD	25.91 ± 5.32	25.49 ± 4.09	–
BMI (kg/m^2), median (IQR)	25.39 (6.20)	25.35 (5.12)	–

Note: OAD: oral antidiabetic drugs; BMI: body mass index; SD: standard deviation; IQR: interquartile range. The insulin group received insulin in combination with at least one oral antidiabetic drug; no patient received insulin monotherapy.

Female patients slightly outnumbered male patients (53.7% vs. 46.3%), with a comparable sex distribution in both groups. This pattern is consistent with evidence that declining estrogen after menopause reduces insulin sensitivity and promotes visceral fat accumulation, thereby increasing the risk of T2DM in older women (Ahmed et al., 2022). Men, in contrast, tend to develop T2DM at a younger age and at a lower BMI, whereas premenopausal women are relatively protected by estrogen (Kautzky-Willer et al., 2023). Differences in population characteristics, dietary habits, and physical activity patterns may explain variations in sex distribution across studies.

Almost all patients (94.4%) had at least one comorbidity, with similar proportions in the OAD (92.6%) and insulin (96.3%) groups. Multimorbidity is common in T2DM; a study in the United Arab Emirates reported dyslipidemia in 93.4%, hypertension in 83.4%, and overweight or obesity in 90.5% of patients, largely attributed to suboptimal glycemic control (Jelinek et al., 2017). Comorbid metabolic disorders aggravate insulin resistance through oxidative stress and chronic low-grade inflammation, which disturb insulin signaling and impair β-cell function (Tangvarasittichai, 2015). The mean BMI in both groups fell within the overweight range (25.91 and 25.49 kg/m^2). Excess adiposity increases circulating free fatty acids, which trigger oxidative and endoplasmic reticulum stress, inflammation, and ultimately β-cell exhaustion (Dludla et al., 2023), linking excess body weight to poorer glycemic control and a smaller response to therapy.

Table 2. Glycemic Parameters Before and After Six Months of Treatment

Parameter	OAD (n = 27)		Insulin + OAD (n = 27)	
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)
HbA1c before (%)	8.45 ± 2.95	7.80 (2.3)	10.46 ± 2.96	9.90 (3.6)
HbA1c after (%)	7.14 ± 1.22	6.80 (1.6)	9.21 ± 2.34	8.80 (2.6)
FBG before (mg/dL)	146.19 ± 52.79	132.0 (66)	187.56 ± 75.02	178.0 (112)
FBG after (mg/dL)	129.44 ± 37.68	121.0 (47)	173.96 ± 67.63	154.0 (95)

Note: Range — OAD: HbA1c before 5.5–19.4, after 5.4–11.4; FBG before 81–349, after 65–228. Insulin: HbA1c before 7.1–19.4, after 5.6–16.0; FBG before 95–367, after 80–331. 95% CI of the mean — OAD: HbA1c before 7.28–9.62, after 6.66–7.63; FBG before 125.30–167.07, after 114.54–144.35. Insulin: HbA1c before 9.29–11.63, after 8.28–10.14; FBG before 157.88–217.23, after 147.21–200.72. Medians and IQR are reported because all four distributions were right-skewed (Shapiro–Wilk $p < 0.05$ for most variables). FBG: fasting blood glucose; IQR: interquartile range; OAD: oral antidiabetic drugs.

Both groups showed lower HbA1c and FBG after six months of therapy (Table 2). Mean HbA1c fell by 1.31 percentage points in the OAD group and by 1.25 percentage points in the insulin group, and median HbA1c fell from 7.80% to 6.80% and from 9.90% to 8.80%, respectively; mean FBG fell by 16.75 and 13.60 mg/dL. The two distributions were strongly right-skewed, which is why medians are reported alongside means. The clinical meaning of these changes differs between the groups: in the OAD group the median six-month HbA1c was below the conventional target of 7%, whereas in the insulin group both the mean and the median remained well above 8%, so that a numerically similar reduction left the two groups in very different clinical positions. A reduction of this order is nevertheless clinically relevant in both groups, since each 1% increment in historical mean HbA1c has been associated with a 22% higher risk of cardiovascular events and a 26% higher risk of diabetes-related death (Lind et al., 2021). Expressed in terms of target attainment, the median six-month HbA1c of 6.80% in the OAD group implies that at least half of these patients were below the recommended threshold of 7%, whereas the median of 8.80% in the insulin group implies that fewer than half reached it; the same reduction therefore translated into a very different level of clinical benefit in the two groups.

Table 3. Within-Group Changes in HbA1c and Fasting Blood Glucose (Wilcoxon Signed-Rank Test)

Group	Parameter (after − before)	Decreased n (mean rank)	Increased n (mean rank)	Unchanged n	Z	r	p-value
OAD	HbA1c	19 (14.03)	6 (9.75)	2	−2.800	0.64	0.005*
	FBG	17 (14.26)	9 (12.06)	1	−1.702	0.38	0.089
Insulin + OAD	HbA1c	16 (15.91)	11 (11.23)	0	−1.574	0.35	0.115
	FBG	14 (15.00)	13 (12.92)	0	−0.505	0.11	0.614

Note: *Significant at $p < 0.05$. r: matched-pairs rank-biserial correlation, computed from the sums of the positive and negative ranks; higher values indicate a more consistent decrease. FBG: fasting blood glucose; OAD: oral antidiabetic drugs.

Within the OAD group, HbA1c decreased significantly after six months ($Z = -2.800$; $p = 0.005$; matched-pairs rank-biserial $r = 0.64$), with 19 of 27 patients showing a reduction, whereas the decrease in FBG was smaller and not statistically significant ($Z = -1.702$; $p = 0.089$; $r = 0.38$) (Table 3). A plausible explanation for the reduction in HbA1c is the complementary action of the agents commonly used in this setting: metformin suppresses hepatic glucose production and improves peripheral insulin sensitivity (Bailey, 2024), sulfonylureas stimulate endogenous insulin secretion by closing ATP-sensitive potassium channels in β-cells (Kalra et al., 2018), and dipeptidyl peptidase-4 inhibitors enhance incretin activity (Artasensi et al., 2020; Gallwitz, 2019). Because the class, dose and combination of the drugs actually prescribed were not recorded in a form that could be analyzed, this explanation could not be tested in the present data and is offered as a hypothesis only. The

smaller change in FBG is consistent with the fact that a single fasting measurement fluctuates with dietary intake, sampling time, physical activity, stress and adherence, whereas HbA1c integrates glycemia over two to three months (Sherwani et al., 2016).

Table 4. Between-Group Comparison of HbA1c and Fasting Blood Glucose (Mann–Whitney U Test)

Variable	Mean rank OAD	Mean rank Insulin	U	r (95% CI)	p-value
HbA1c before	20.61	34.39	178.5	−0.51 (−0.82 to −0.20)	0.001*
HbA1c after	18.72	36.28	127.5	−0.65 (−0.96 to −0.34)	<0.001 *
FBG before	22.72	32.28	235.5	−0.35 (−0.67 to −0.04)	0.026*
FBG after	21.56	33.44	204.0	−0.44 (−0.75 to −0.13)	0.005*
ΔHbA1c	27.85	27.15	355.0	0.03 (−0.29 to 0.34)	0.869
ΔFBG	28.11	26.89	348.0	0.05 (−0.27 to 0.36)	0.775

Note: *Significant at $p < 0.05$. Δ: change between baseline and six months. r: rank-biserial correlation derived from the Mann–Whitney U statistic; negative values indicate lower values in the OAD group. FBG: fasting blood glucose; OAD: oral antidiabetic drugs.

In the insulin group, neither HbA1c ($Z = −1.574$; $p = 0.115$; $r = 0.35$) nor FBG ($Z = −0.505$; $p = 0.614$; $r = 0.11$) changed significantly, although 16 and 14 of 27 patients, respectively, showed a decrease. This differs from a prospective observational study in which adding basal insulin to oral agents significantly improved HbA1c after six months (Brož et al., 2019). Several mechanisms could account for a smaller response among insulin users — longer diabetes duration, reduced residual β-cell secretory capacity (Abdelgani et al., 2021), more severe insulin resistance associated with obesity and elevated free fatty acids (Wondmkun, 2020), a greater burden of metabolic comorbidity (Boels et al., 2021), conservative insulin titration, and imperfect adherence. None of these variables was measured in this study, and they are therefore presented as possible explanations to be tested in future work rather than as findings of the present analysis.

Between-group comparisons showed that HbA1c and FBG were significantly higher in the insulin group than in the OAD group both before and after treatment, with large rank-biserial effect sizes whose confidence intervals excluded zero (Table 4). This difference should not be read as a difference in treatment response. Insulin is initiated in patients who have not reached glycemic targets on oral therapy and whose disease is therefore more advanced (B.-W. Lee et al., 2017), so treatment assignment in an observational study of this kind is determined by disease severity — the situation known as confounding by indication. The baseline gap was substantial, corresponding to about 0.68 SD for HbA1c and 0.64 SD for FBG, and it is the most likely explanation for the higher six-month values in the insulin group. Real-world data similarly indicate that patients with HbA1c above 9% at insulin initiation are less likely to reach target and need longer to do so, particularly when diabetes duration is long and several oral agents have already been used (Blonde et al., 2018). For the same reason, the observation that insulin users remained further from target cannot be interpreted as evidence that insulin was less effective.

Table 5. Between-Group Difference in Six-Month Glycemic Change (Primary and Secondary Endpoints)

Endpoint	Mean Δ, OAD	Mean Δ, insulin + OAD	Difference in mean Δ (insulin − OAD), 95% CI[a]	r (95% CI)	p
ΔHbA1c (%)	−1.31	−1.25	+0.06 (−1.86 to +1.97)	0.03 (−0.29 to 0.34)	0.869
ΔFBG (mg/dL)	−16.75	−13.60	+3.15 (−43.2 to +49.5)	0.05 (−0.27 to 0.36)	0.775

Note: Δ: six-month value minus baseline value; negative values indicate improvement. [a]Conservative interval: the SD of the change score was taken as the square root of the sum of the squared baseline and six-month SDs, which assumes zero within-patient correlation and therefore gives the widest interval compatible with the data; any positive correlation narrows it. r: rank-biserial correlation with 95% CI derived from the Mann–Whitney U statistic; values near zero indicate no tendency for one group to change more than the other. All intervals are wide and include clinically important effects in both directions, so they indicate absence of evidence for a difference and not evidence of equivalence. FBG: fasting blood glucose; OAD: oral antidiabetic drugs.

For the primary endpoint, the magnitude of change did not differ significantly between the groups: ΔHbA1c differed by 0.06 percentage points (rank-biserial $r = 0.03$; 95% CI −0.29 to 0.34; $p = 0.869$) and ΔFBG by 3.15 mg/dL ($r = 0.05$; 95% CI −0.27 to 0.36; $p = 0.775$), favoring neither regimen (Table 5). On the original measurement scale, the conservative interval around the difference in mean change runs from −1.86 to +1.97 percentage points of HbA1c and from −43.2 to +49.5 mg/dL of FBG. These intervals are wide and include effects that would be clinically important in either direction, so the correct interpretation is that no between-group difference was detected, not that the two regimens are equivalent. Demonstrating equivalence or non-inferiority would require a pre-specified margin and a sample size several times larger than the one available here. The result is nevertheless compatible with a matched cohort study in which oral therapy was not inferior to early insulinization in newly diagnosed patients (Y.-M. Lee et al., 2024), and with an Indonesian study that found no significant difference between metformin–insulin and metformin–vildagliptin (Timur et al., 2024). Read together with the baseline imbalance described above, the data are most consistent with the interpretation that the two groups differed mainly in disease severity at entry, while the observed six-month change was of similar magnitude in both — a descriptive statement about this cohort rather than a general claim about the two treatment strategies.

The clinical implication concerns follow-up rather than choice of regimen. Both groups improved by roughly one percentage point of HbA1c, but only the OAD group approached the recommended target, while the insulin group ended the observation period above 9% on average. A statistically non-significant within-group change in the insulin group should therefore not be read as therapeutic failure, nor should the statistically significant change in the OAD group be read as superiority; what the data show is that patients who start insulin in this setting remain far from target after six months and need closer monitoring. Current guidelines recommend an individualized approach in which glycemic targets, hypoglycemia risk,

comorbidities, adverse-effect profile, cost and the patient's ability to adhere to the regimen are all weighed (American Diabetes Association Professional Practice Committee, 2024; Davies et al., 2022); the present findings support that approach and, specifically, argue for structured titration and timely intensification in patients receiving insulin.

Several limitations must be taken into account when reading these results. The design is retrospective and non-randomized, so the regimen was determined by clinical indication: patients with more advanced disease received insulin, and the groups were consequently very different at baseline. Effectiveness was therefore assessed from the within-patient change rather than from absolute six-month values, identical inclusion and exclusion criteria were applied to both groups, and patients whose regimen changed during the observation period were excluded, so that every patient was analyzed under a stable regimen. These measures reduce, but do not remove, confounding by indication, because a change score still depends on the baseline value and on regression to the mean when the baseline is extreme. Sex, BMI and comorbidity were identified in advance and are reported for both groups, but no covariate-adjusted model was fitted, for three reasons. First, with 27 patients per group and both change scores departing from normality (Shapiro–Wilk $p < 0.001$ for ΔHbA1c and $p = 0.002$ for ΔFBG), a linear model containing the baseline value and three further covariates would have been estimated from approximately five observations per parameter, and its distributional assumptions could not be satisfied. Second, outside a randomized design, analysis of covariance does not simply remove a baseline imbalance: the baseline value is itself part of the reason the treatment was chosen, so the adjusted estimate answers a different question from the unadjusted change, and simulation work has shown that in non-randomized studies it carries more bias than the change score it is meant to improve on (Van Breukelen, 2006). Third, the covariates available were limited to sex, BMI and comorbidity, so any adjustment would still have left the principal determinants of treatment allocation — diabetes duration and prior treatment history — unmeasured. We therefore report the unadjusted change with its effect size and confidence interval and state the imbalance openly. An adjusted analysis in a larger sample with a richer set of covariates, or propensity-score matching with an explicit assessment of common support, remains the appropriate way to address the imbalance, and is a task for a future study rather than an analysis that could have been performed reliably in these data.

The study was also limited in size and scope. Fifty-four patients recruited by purposive sampling from a single hospital restrict generalizability, and the available power allowed only a large between-group difference to be detected, which is why the confidence intervals around the primary endpoint are wide. Several determinants of glycemic response were not documented in the medical records and could not be analyzed: diabetes duration, the class, dose and combination of oral agents, the type, dose and titration of insulin, treatment adherence, diet, physical activity, and renal function. Any of these could differ systematically between the groups and act as a source of residual confounding, and the absence of information on regimen composition in particular means that the two groups should be understood as pragmatic categories of routine care rather than as standardized treatments.

Finally, the outcomes examined were narrow. Effectiveness in diabetes care also depends on hypoglycemia, body weight, adverse effects, adherence, quality of life and treatment cost, none of which were available in this dataset; a comparison restricted to HbA1c and FBG therefore captures only part of what distinguishes an insulin-containing regimen from an oral one. Six months is long enough for two consecutive HbA1c measurements to reflect the response to therapy, but too short to assess durability, the development of complications, or long-term safety. These gaps can only be closed by prospective data collection, as outlined below.

CONCLUSIONS

Among patients with T2DM treated at UNS Hospital, HbA1c and FBG were lower after six months in both treatment groups, and the within-group reduction in HbA1c reached statistical significance only in the OAD group. Patients receiving insulin in combination with oral agents had significantly higher HbA1c and FBG both before and after treatment, consistent with more advanced disease at the time insulin was started. No statistically significant difference in the magnitude of change in HbA1c or FBG was detected between the two groups in this small retrospective sample, and the confidence intervals were too wide to exclude clinically important differences in either direction; these findings therefore do not establish that the two regimens are equivalent. The results are specific to this single-center cohort and indicate that patients who begin insulin in this setting remain far from the recommended glycemic target after six months, which argues for structured follow-up and timely intensification rather than for a general preference between the two strategies.

SUGGESTION

For research, future studies should adopt a prospective, multicenter design with primary data and consecutive sampling, with the sample size calculated for the between-group difference in HbA1c and FBG change and the results reported as effect estimates with 95% confidence intervals. Baseline imbalance between regimens should be handled statistically, for example through analysis of covariance adjusted for the baseline value or through propensity-score matching, and an equivalence or non-inferiority design with a pre-specified margin would be required if the question of comparable effectiveness is to be answered directly. Diabetes duration, drug class and dose, insulin type and titration, adherence, diet, physical activity and renal function should be recorded prospectively, and effectiveness should be assessed more broadly, including hypoglycemia, body weight, lipid profile and treatment cost, with follow-up extended to at least 12 to 24 months.

For clinical practice, the finding that both regimens produced a comparable magnitude of improvement, while insulin users remained far from target, supports structured follow-up rather than a change of regimen alone. Patients receiving insulin need scheduled dose titration, education on injection technique and hypoglycemia recognition, self-monitoring of blood glucose, and HbA1c measurement every three months, with timely intensification when the target is not reached. For the hospital, a diabetes registry that routinely records regimen, adherence, HbA1c, FBG, body weight and hypoglycemic events would allow continuous evaluation of treatment effectiveness and support better-designed studies in the future.

DECLARATIONS

Ethics Approval and Consent to Participate

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Sebelas Maret (No. 93/UN27.06.11/KEP/EC/2025), and research permission was granted by UNS Hospital (No. 1409.6/UN27.46/TA.04.19/2025). Because the study used anonymized secondary data from medical records, individual informed consent was not required.

Consent for Publication

Not applicable. This article does not contain any individual person's identifiable data.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Author Contributions

RSK: conceptualization, data collection, formal analysis, and writing – original draft; NAP: conceptualization, methodology, supervision, and writing – review and editing. All authors read and approved the final manuscript.

Artificial Intelligence (AI) Usage Statement

During the preparation of this manuscript, the authors used an AI-assisted tool solely to improve language and readability. No AI tool was used to generate data, perform statistical analyses, or interpret the findings. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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