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Original Research Article

COMPARISON OF EARLY VERSUS DELAYED INITIATION OF INSULIN THERAPY IN NEWLY DIAGNOSED TYPE 2 DIABETES: GLYCEMIC CONTROL AND COMPLICATIONS

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a progressive metabolic disorder characterized by insulin resistance and β-cell dysfunction, often leading to inadequate glycemic control and long-term complications. Timely initiation of insulin therapy has been proposed as a strategy to overcome therapeutic inertia, improve glycemic control, and reduce the risk of diabetes-related complications. However, the clinical impact of early versus delayed initiation of insulin therapy in newly diagnosed patients remains debated. **Aim:** This study aimed to compare the effects of early versus delayed initiation of insulin therapy in patients with newly diagnosed T2DM in terms of glycemic control and the occurrence of diabetes-related complications.

Materials and Methods: A comparative observational study was conducted at a tertiary care hospital, enrolling 96 newly diagnosed T2DM patients. Participants were divided equally into two groups: early initiation (insulin started within one month of diagnosis) and delayed initiation (insulin introduced only if glycemic targets were not achieved with lifestyle and oral hypoglycemic agents). Baseline demographic, clinical, and biochemical parameters were recorded. Glycemic control (fasting plasma glucose [FPG], postprandial plasma glucose [PPG], glycated hemoglobin [HbA1c]) and complications were evaluated. Data were analyzed using SPSS version 26.0, with a p-value <0.05 considered statistically significant.

Results: Baseline characteristics, including age (51.23 ± 8.45 vs. 52.18 ± 9.12 years, p = 0.64), BMI (27.56 ± 3.12 vs. 28.04 ± 3.28 kg/m², p = 0.48), and HbA1c (8.92 ± 1.12 vs. 8.87 ± 1.15%, p = 0.81), were comparable between groups. At 6 months, early initiation significantly improved glycemic outcomes: FPG (118.54 ± 18.62 vs. 134.78 ± 20.41 mg/dL, p = 0.001), PPG (162.43 ± 28.17 vs. 181.64 ± 30.22 mg/dL, p = 0.002), and HbA1c (6.82 ± 0.72% vs. 7.34 ± 0.85%, p = 0.004). Target HbA1c <7% was achieved in 70.83% of early patients versus 47.92% in delayed (p = 0.02). Hypoglycemia (12.50% vs. 6.25%, p = 0.30) and weight gain (+1.24 vs. +0.72 kg, p = 0.19) were slightly higher with early insulin. Complications, though not statistically significant, were lower in the early initiation group.

Conclusion: Early initiation of insulin therapy in newly diagnosed T2DM provides superior glycemic control and trends toward fewer complications, supporting its role as a proactive strategy in diabetes management.

Keywords: Type 2 diabetes mellitus; insulin initiation; glycemic control; hypoglycemia; complications.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a rapidly expanding global health challenge that imposes substantial clinical and economic burdens on patients and health systems. Rising prevalence across regions, particularly in low- and middle-income countries, is driven by demographic aging, urbanization, sedentary lifestyles, unhealthy diets, and escalating obesity rates. The downstream effects of sustained hyperglycemia—ranging from retinopathy, nephropathy, and neuropathy to coronary heart disease and stroke—translate into reduced quality of life, excess mortality, and major health-care costs. Against this backdrop, strategies that achieve and maintain near-normoglycemia safely and promptly are central to minimizing both short-term metabolic decompensation and long-term vascular complications.[1,2]

International and national guidance has evolved toward more individualized, pathophysiology-informed care, emphasizing early achievement of glycemic targets while balancing risks, patient preferences, and comorbidities. The most recent ADA/EASD consensus underscores a person-centered approach, advocating timely intensification—including insulin—when individualized targets are not met, and prioritizing agents with established benefits on weight and cardio-renal outcomes when appropriate. These recommendations recognize that persistent exposure to glucotoxicity and lipotoxicity accelerates β-cell dysfunction, fostering a cycle of deteriorating glycemia that is harder to reverse later in the disease course. Within this framework, initiating insulin earlier in the therapeutic timeline is biologically plausible for rapidly correcting hyperglycemia, alleviating β-cell stress, and creating a metabolic milieu that favors durable control—provided it can be delivered safely and acceptably.[3]

Concurrently, yearly updates to the Standards of Care reinforce thresholds and clinical signals for insulin initiation or intensification. These include marked hyperglycemia at presentation (e.g., very high HbA1c or glucose), symptomatic hyperglycemia, catabolic features, or failure to reach targets with non-insulin therapy despite adherence. While many patients can attain goals with modern non-insulin combinations—especially those that confer cardiovascular and renal protection—insulin remains indispensable for prompt correction of significant hyperglycemia and for those with progressive β-cell failure. Nevertheless, gaps persist between recommendations and practice, and the optimal timing of insulin in newly diagnosed patients remains variably implemented.[4]

Evidence from major glucose-lowering outcome trials informs the debate on how soon and how intensively to normalize glycemia. Although these studies were not designed specifically around "early versus delayed insulin," they collectively underscore two complementary messages: first, that sustained improvements in glycemia reduce microvascular risk; and second, that in high-risk populations, very aggressive HbA1c targets achieved rapidly with intensive regimens may not always translate into macrovascular benefit and can introduce safety trade-offs. The ACCORD trial, for instance, targeted near-normal HbA1c and was stopped early due to excess mortality in the intensive arm, highlighting the importance of prudent target setting and careful therapy selection—particularly in individuals with long-standing disease and extensive comorbidity.[5]

In contrast, other large studies using more moderate glycemic targets demonstrated clear microvascular advantages with improved glycemic control. In ADVANCE, intensive control (mean HbA1c 6.5%) reduced major microvascular events—especially nephropathy—versus standard care. These data complement the broader understanding that earlier attainment of reasonable targets is beneficial for microvascular protection, while cardiovascular risk modification often hinges on a broader risk-factor strategy beyond glucose alone (lipids, blood pressure, antiplatelet therapy, weight management, and smoking cessation). This nuance is highly relevant when contemplating earlier insulin initiation: the aim is swift, safe control within individualized targets rather than indiscriminate pursuit of normoglycemia.[6,7]

MATERIALS AND METHODS

This was a comparative observational study conducted at a tertiary care hospital, involving patients with newly diagnosed type 2 diabetes mellitus (T2DM). A total of 96 patients were recruited and categorized into two groups based on the timing of insulin initiation: the early initiation group and the delayed initiation group. The study was designed to evaluate glycemic control outcomes and diabetes-related complications between the two groups.

Patients included were adults (≥18 years) with newly diagnosed T2DM, confirmed by American Diabetes Association (ADA) diagnostic criteria. Exclusion criteria comprised patients with type 1 diabetes, gestational diabetes, secondary causes of diabetes, severe systemic illnesses, chronic kidney disease stage ≥3, hepatic failure, history of prior insulin use, or those unwilling to provide consent. All eligible participants provided informed written consent prior to inclusion in the study.

Methodology

Participants were divided into two groups of 48 patients each. The early initiation group received insulin therapy within the first month of diagnosis, while the delayed initiation group was managed initially with lifestyle modification and oral hypoglycemic agents, and insulin therapy was introduced only if glycemic targets were not achieved after the initial treatment period. Both groups

received standardized dietary and exercise counseling, and adherence to therapy was reinforced at follow-up visits.

Baseline demographic characteristics (age, sex, body mass index, family history of diabetes, and blood pressure) were recorded. Laboratory parameters included fasting plasma glucose (FPG), postprandial plasma glucose (PPG), glycated hemoglobin (HbA1c), lipid profile (total cholesterol, triglycerides, LDL-C, HDL-C), serum creatinine, and estimated glomerular filtration rate (eGFR). Follow-up assessments were carried out at regular intervals to monitor glycemic control and detect any emerging microvascular or macrovascular complications.

The primary outcome was improvement in glycemic control, assessed by changes in HbA1c, FPG, and PPG levels. Secondary outcomes included the occurrence of hypoglycemic episodes, weight changes, treatment adherence, and development of complications such as diabetic retinopathy, nephropathy, neuropathy, ischemic heart disease, and cerebrovascular events.

Statistical Analysis

All clinical and laboratory data were collected using a structured case record form and entered into a secure database. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent t-test or Mann–Whitney U test, depending on the distribution of data. Categorical variables were expressed as frequencies and percentages and analyzed using the chi-square test or Fisher's exact test where appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS

Baseline Demographic and Clinical Characteristics (Table 1)

The baseline demographic and clinical characteristics of the study population were comparable between the early and delayed insulin initiation groups. The mean age of patients was 51.23 ± 8.45 years in the early initiation group and 52.18 ± 9.12 years in the delayed initiation group (p = 0.64), showing no significant difference. The gender distribution was also similar, with males comprising 58.33% of the early initiation group and 54.17% of the delayed group (p = 0.69). Body mass index (BMI) was nearly identical across groups (27.56 ± 3.12 vs. 28.04 ± 3.28, p = 0.48). A positive family history of diabetes was present in 39.58% of patients in the early initiation group and 43.75% in the delayed group (p = 0.68). Blood pressure parameters, both systolic (132.46 ± 12.15 mmHg vs. 134.27 ± 11.83 mmHg, p = 0.45) and diastolic (83.72 ± 8.41 mmHg vs. 84.63 ± 7.92 mmHg, p = 0.61), were not significantly different. These findings confirm that both groups were well-matched at baseline without any significant demographic or clinical imbalance.

Baseline Biochemical Parameters (Table 2)

Similarly, baseline biochemical investigations did not reveal any significant differences between the two groups. Mean fasting plasma glucose (FPG) levels were 176.38 ± 32.24 mg/dL in the early initiation group and 178.92 ± 34.18 mg/dL in the delayed group (p = 0.72). Postprandial plasma glucose (PPG) levels were also comparable (251.46 ± 44.32 mg/dL vs. 254.18 ± 42.87 mg/dL, p = 0.68). Glycated hemoglobin (HbA1c) values were nearly the same between the groups (8.92 ± 1.12% vs. 8.87 ± 1.15%, p = 0.81). Lipid profile parameters including total cholesterol, LDL-C, HDL-C, and triglycerides showed no significant differences, with p values ranging from 0.57 to 0.68. These results demonstrate that the two groups were biochemically comparable before initiation of therapy, ensuring unbiased follow-up outcomes.

Glycemic Control at Follow-Up (Table 3)

At the 6-month follow-up, significant differences were observed in glycemic control between the two groups. The early insulin initiation group showed a markedly lower mean FPG (118.54 ± 18.62 mg/dL) compared to the delayed initiation group (134.78 ± 20.41 mg/dL), which was statistically significant (p = 0.001). Similarly, postprandial glucose values were significantly better in the early group (162.43 ± 28.17 mg/dL) compared to the delayed group (181.64 ± 30.22 mg/dL, p = 0.002). HbA1c levels also demonstrated a significant reduction in the early initiation group (6.82 ± 0.72%) compared to the delayed group (7.34 ± 0.85%, p = 0.004). Furthermore, 70.83% of patients in the early initiation group achieved the target HbA1c <7%, compared to only 47.92% in the delayed group (p = 0.02). These findings clearly indicate that early initiation of insulin therapy results in superior glycemic control.

Hypoglycemia and Weight Changes (Table 4)

The frequency of hypoglycemic episodes was higher in the early initiation group (12.50%) compared to the delayed initiation group (6.25%), although this difference was not statistically significant (p = 0.30). With respect to weight changes, both groups experienced modest weight gain during the study period. The mean weight increase was +1.24 ± 1.82 kg in the early initiation group and +0.72 ± 1.65 kg in the delayed initiation group, with no significant difference between the groups (p = 0.19). These results suggest that while early insulin initiation may slightly increase the risk of hypoglycemia and weight gain, the differences were not clinically or statistically significant.

Diabetes-Related Complications (Table 5)

The incidence of microvascular and macrovascular complications during the follow-up period was generally lower in the early initiation group compared to the delayed group, though the differences did not achieve statistical significance. Retinopathy was observed in 4.17% of the early group versus 10.42% of the delayed group (p = 0.24). Nephropathy was less

frequent in the early group (2.08% vs. 8.33%, p = 0.17). Neuropathy occurred in 4.17% of patients in the early initiation group compared to 12.50% in the delayed initiation group (p = 0.14). Macrovascular complications, including ischemic heart disease (2.08% vs. 6.25%, p = 0.31) and cerebrovascular events (0.00% vs. 4.17%, p = 0.15), were also less frequent in the early initiation group. Although not statistically significant, the trend consistently favored early initiation of insulin therapy in reducing diabetes-related complications.

Table 1: Baseline Demographic and Clinical Characteristics of Patients

Parameter	Early Initiation (n=48)	Delayed Initiation (n=48)	p-value
Age (years, mean ± SD)	51.23 ± 8.45	52.18 ± 9.12	0.64
Male sex (%)	28 (58.33%)	26 (54.17%)	0.69
BMI (kg/m², mean ± SD)	27.56 ± 3.12	28.04 ± 3.28	0.48
Family history of diabetes (%)	19 (39.58%)	21 (43.75%)	0.68
Systolic BP (mmHg, mean ± SD)	132.46 ± 12.15	134.27 ± 11.83	0.45
Diastolic BP (mmHg, mean ± SD)	83.72 ± 8.41	84.63 ± 7.92	0.61

Table 2: Baseline Biochemical Parameters

Parameter	Early Initiation (n=48)	Delayed Initiation (n=48)	p-value
FPG (mg/dL, mean ± SD)	176.38 ± 32.24	178.92 ± 34.18	0.72
PPG (mg/dL, mean ± SD)	251.46 ± 44.32	254.18 ± 42.87	0.68
HbA1c (%)	8.92 ± 1.12	8.87 ± 1.15	0.81
Total cholesterol (mg/dL)	201.34 ± 28.63	204.76 ± 30.12	0.57
LDL-C (mg/dL)	128.46 ± 22.18	130.21 ± 23.64	0.68
HDL-C (mg/dL)	42.15 ± 6.74	41.62 ± 7.02	0.65
Triglycerides (mg/dL)	165.27 ± 37.45	168.42 ± 36.18	0.58

Table 3: Glycemic Control at Follow-Up (6 months)

Parameter	Early Initiation (n=48)	Delayed Initiation (n=48)	p-value
FPG (mg/dL, mean ± SD)	118.54 ± 18.62	134.78 ± 20.41	0.001
PPG (mg/dL, mean ± SD)	162.43 ± 28.17	181.64 ± 30.22	0.002
HbA1c (%)	6.82 ± 0.72	7.34 ± 0.85	0.004
Patients achieving HbA1c <7% (%)	34 (70.83%)	23 (47.92%)	0.02

Table 4: Hypoglycemia and Weight Changes

Parameter	Early Initiation (n=48)	Delayed Initiation (n=48)	p-value
Hypoglycemic episodes (%)	6 (12.50%)	3 (6.25%)	0.30
Mean weight change (kg, ±SD)	+1.24 ± 1.82	+0.72 ± 1.65	0.19

Table 5: Diabetes-Related Complications during Follow-Up

Complication	Early Initiation (n=48)	Delayed Initiation (n=48)	p-value
Retinopathy (%)	2 (4.17%)	5 (10.42%)	0.24
Nephropathy (%)	1 (2.08%)	4 (8.33%)	0.17
Neuropathy (%)	2 (4.17%)	6 (12.50%)	0.14
Ischemic heart disease (%)	1 (2.08%)	3 (6.25%)	0.31
Cerebrovascular events (%)	0 (0.00%)	2 (4.17%)	0.15

DISCUSSION

In our cohort, baseline demographics and clinical measures were well balanced between groups (mean age 51.23 ± 8.45 vs. 52.18 ± 9.12 years; BMI 27.56 ± 3.12 vs. 28.04 ± 3.28 kg/m²; all p > 0.05), reflecting the profile of middle-aged, overweight adults typically enrolled in landmark T2DM cohorts. For instance, the UKPDS enrolled newly diagnosed patients with a median age ≈54 years and overweight phenotype, establishing a benchmark population to which our baseline appears broadly comparable.[8]

Our similar baseline glycemic indices between groups (FPG 176.38 ± 32.24 vs. 178.92 ± 34.18 mg/dL; PPG 251.46 ± 44.32 vs. 254.18 ± 42.87 mg/dL; HbA1c 8.92 ± 1.12 vs. 8.87 ± 1.15%; all p > 0.05) parallel the hyperglycemic ranges used for randomization in classic trials (e.g., UKPDS inclusion FPG 6.1–15.0 mmol/L ≈ 110–270 mg/dL), supporting internal validity for subsequent between-group comparisons.[9]

Early insulin initiation produced significantly better glycemic control in our study—FPG 118.54 ± 18.62 vs. 134.78 ± 20.41 mg/dL (p = 0.001), PPG 162.43 ± 28.17 vs. 181.64 ± 30.22 mg/dL (p = 0.002), and HbA1c 6.82 ± 0.72 vs. 7.34 ± 0.85% (p = 0.004)—consistent with randomized evidence that early intensive insulin normalizes glucose rapidly and improves β-cell function versus oral agents (e.g., time to target ≈4–6 days and 1-year remission 44.9–51.1% with insulin vs. 26.7% with OADs).[10]

We observed 70.83% in the early-insulin group versus 47.92% with delayed initiation attaining HbA1c < 7% (p = 0.02). Real-world cohorts of insulin initiators typically report lower short-term target attainment: in a national Chinese registry of >12,000 BI initiators, 39.9% achieved HbA1c < 7% at 6 months overall, rising to 47.9% when metformin

was continued—figures that bracket our delayed-group result and sit below our early-insulin outcome, underscoring the advantage of timely insulin start.[11]

Non-severe hypoglycemia occurred in 12.50% with early insulin versus 6.25% with delayed therapy (p = 0.30) in our data. Large trials using basal analogs report low absolute severe hypoglycemia rates yet a modest increase with insulin exposure; in ORIGIN (n=12,537), severe hypoglycemia was 1.00 vs. 0.31 per 100 person-years for glargine versus standard care over ≈6 years, highlighting that while insulin improves glycemia, vigilance for hypoglycemia remains essential.[12]

Weight gain in our cohort was modest (+1.24 ± 1.82 vs. +0.72 ± 1.65 kg; p = 0.19). Narrative syntheses indicate that insulin-treated T2DM often experience small-to-moderate weight increases, typically in the 1–3% range, influenced by insulin type and titration practices—aligning with our findings and suggesting contemporary regimens can temper weight accrual.[13]

Although our short follow-up showed only non-significant trends favoring early insulin for microvascular/macrovascular events (e.g., retinopathy 4.17% vs. 10.42%; nephropathy 2.08% vs. 8.33%), long-term evidence supports a "legacy effect" whereby earlier tight control yields durable microvascular benefits. Post-trial UKPDS follow-up demonstrated persistent risk reductions for any diabetes-related endpoint and microvascular disease a decade after randomized intensive control, reinforcing the potential downstream impact of the superior glycemia we observed at 6 months.[14]

Our between-group differences mirror the broader problem of therapeutic inertia: delaying insulin for years is common and clinically costly. Modeling based on UK practice estimated insulin initiation is often deferred by ≈8 years, with each patient losing >7 months of life expectancy on average compared with timely initiation—consistent with our observation that earlier initiation achieved better HbA1c and directional reductions in complications.[15]

CONCLUSION

Early initiation of insulin therapy in newly diagnosed type 2 diabetes patients was associated with significantly better glycemic control, higher achievement of HbA1c targets, and a favorable trend toward fewer diabetes-related complications compared to delayed initiation. Although early insulin use showed a slightly higher, non-significant risk of hypoglycemia and modest weight gain, its overall benefits outweighed these concerns. These findings support timely initiation of insulin as a strategy to improve metabolic outcomes and potentially reduce long-term complications in type 2 diabetes management.

REFERENCES

1. World Health Organization. Diabetes – fact sheet. 2024. Available from: https://www.who.int/news-room/fact-sheets/detail/diabetes
2. International Diabetes Federation. IDF Diabetes Atlas (global data & statistics). 2024–2025 portal. Available from: https://diabetesatlas.org/
3. Davies MJ, et al. Management of hyperglycemia in type 2 diabetes, 2022: ADA/EASD consensus report. Diabetes Care. 2022;45(11):2753-2786. Available from: https://diabetesjournals.org/care/article/45/11/2753/147671/
4. American Diabetes Association. Summary of Revisions: Standards of Care in Diabetes—2024. Diabetes Care. 2024;47(Suppl 1):S5-S14. Available from: https://diabetesjournals.org/care/article/47/Supplement_1/S5/153943/
5. ACCORD Study Group (Gerstein HC, et al.). Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008;358:2545-2559. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa0802743
6. ADVANCE Collaborative Group (Patel A, et al.). Intensive blood glucose control and vascular outcomes in type 2 diabetes. N Engl J Med. 2008;358:2560-2572. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa0802987
7. Khunti S, et al. Therapeutic inertia in type 2 diabetes: prevalence, causes, consequences and methods to overcome inertia. Ther Adv Endocrinol Metab. 2019;10:1-11. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6502982/
8. UKPDS Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in type 2 diabetes. Lancet. 1998;352(9131):837-53. https://pubmed.ncbi.nlm.nih.gov/9742976/
9. UKPDS Group. Intensive blood-glucose control with sulphonylureas or insulin… (trial entry criteria and outcomes). Lancet. 1998;352(9131):837-53. https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(98)07019-6.pdf
10. Weng J, et al. Effect of intensive insulin therapy on β-cell function in newly diagnosed T2DM: randomized trial. Lancet. 2008;371:1753-60. https://pubmed.ncbi.nlm.nih.gov/18502299/
11. Zhang P, et al. Effectiveness and safety of basal insulin with vs. without metformin in a national cohort (China). BMC Endocr Disord. 2022;22:26. https://bmcendocrdisord.biomedcentral.com/articles/10.1186/s12902-021-00892-6
12. ORIGIN Investigators (Gerstein HC, et al.). Basal insulin glargine and cardiovascular/other outcomes in dysglycemia. N Engl J Med. 2012;367:319-28. https://pubmed.ncbi.nlm.nih.gov/22686416/
13. McFarlane SI, et al. Insulin therapy and type 2 diabetes (review of efficacy/weight). Postgrad Med. 2009;121(3):7-15. https://pmc.ncbi.nlm.nih.gov/articles/PMC8673427/
14. Holman RR, et al. 10-year follow-up of intensive glucose control in type 2 diabetes (UKPDS legacy). N Engl J Med. 2008;359:1577-89. https://www.nejm.org/doi/full/10.1056/NEJMoa0806470
15. Goodall G, et al. Consequences of delaying insulin initiation in UK T2DM. BMC Endocr Disord. 2009;9:19. https://bmcendocrdisord.biomedcentral.com/articles/10.1186/1472-6823-9-19.