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Original Research Article

Evaluating HbA1c reduction with protocol-driven drug therapy in early type 2 diabetes: a prospective analysis

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ABSTRACT

Background: Effective blood sugar control is critical to preventing complications in type 2 diabetes. While intensive drug therapy can improve glycemic outcomes, the long-term benefit of starting with aggressive regimens tailored to disease severity remains under investigation.
Methods: This study categorized patients with type 2 diabetes into three groups based on initial HbA1c levels: Group 1 (mild, 7–9%), Group 2 (moderate, 9–11%), and Group 3 (severe, >11%). Treatment was escalated accordingly: triple therapy for Group 1, quadruple therapy for Group 2, and quintuple therapy for Group 3. The medication regimen included pioglitazone, metformin, dapagliflozin, teneligliptin, and gliclazide. HbA1c levels were tracked to assess glycemic improvement and therapy simplification over time.
Results: All groups achieved significant reductions in HbA1c. Group 1 saw a 24.4% reduction, Group 2 a 29.0% reduction, and Group 3 a 51.7% reduction ($p=0.001$). Notably, many patients in Group 3 were able to simplify their medication regimens during follow-up, transitioning from five drugs to fewer agents while maintaining glycemic control ($p<0.05$).
Conclusions: Tailored intensive therapy based on initial glycemic severity leads to significant HbA1c improvement. Starting with robust combination therapy and later reducing drug burden may be an effective, sustainable strategy in managing type 2 diabetes.

Keywords: Type 2 diabetes mellitus, HbA1c, Glycemic control, Treatment intensification, Drug tapering, Antidiabetic therapy

INTRODUCTION

Diabetes is the health concern of the twenty-first century, with the fastest pace of increase. It is predicted that Diabetes is about to affect 783 million people by 2045, with middle and low-income countries (LMICs) accounting for 94% of this growth.[1] Obesity and age are the primary causes of type 2 diabetes, which is the most prevalent form in 90% of cases.[1] Glycated hemoglobin (HbA1c), which shows average blood glucose levels over two to three months, is an essential biomarker in the diagnosis and treatment of diabetes.[2] The American Diabetes Association (ADA) and the World Health Organization suggest it as a target for glycemic management and as a diagnostic tool.[3] A decrease in HbA1c is associated with a decreased risk of complications from diabetes, making it a crucial indicator for long-term glycemic control.[4] Because of their combined advantages in glycemic management and GLP-1 receptor agonists cardiovascular protection, and SGLT2 inhibitors are recommended as effective pharmacological treatments in the amended ADA 2025 guidelines.[5] Clinical

decision-making requires a comprehensive review of HbA1c-lowering medicines due to the rising prevalence of diabetes and changing treatment paradigms. When the HbA1c is below 5.7%, it indicates good glucose control and a low risk of developing diabetes.[6] A higher risk of diabetes and lifestyle modifications are indicated by the prediabetic range, which falls between 5.7% and 6.4%.[7] 6.5% or above is the diabetic range, which denotes diabetes and necessitates ongoing care and medical attention.[8] Acceptance of treatment and daily self-management are necessary to meet glycemic goals.[9] Failing to do so could result in early death and poor clinical outcomes.[10] During the follow-up period, the UKPDS study showed that the percentage of patients who maintained glycated hemoglobin A1c (HbA1c) levels <7% by monotherapy decreased annually, indicating that the monotherapy may not be able to effectively control hyperglycemia for a longer period.[11] As a result, more and more physicians are using medication combination therapy.[12] Drug combination therapy is a medical approach in which two or more medications are administered at the same time in an effort to have a more noticeable therapeutic impact than would be possible with just one medication. Drug combination therapy has a complex mechanism of action that includes antagonizing resistance, complementing effects, and synergistic effects, among other things.[13] Early interventions is essential to halting the evolution of type 2 diabetes, particularly in achieving optimal HbA1c levels. While current therapeutic techniques usually depend on physician discretion and tailored regimens, protocol-driven pharmacological therapy offers a structured, evidence-based alternative that may enhance treatment efficacy and standardize care. Despite its potential, there is a lack of prospective evidence regarding the outcomes of these protocolized treatments, particularly in recently diagnosed patients. This study aims to evaluate the reduction in HbA1c achieved in patients with early-stage type 2 diabetes by protocol-driven pharmaceutical therapy in order to provide information for bettering initial treatment options.

METHODS

Study population

This prospective study analyzed computerized outpatient department (OPD) records of 343 newly diagnosed type 2 diabetes mellitus patients from clinics at SL Raheja Hospital, Mahim, Mumbai, and Lilavati Hospital, Mumbai.

Table 1: Demographic data of study population.

Parameter	All patients (n=343)
Mean age (years)	54.6±10.2
Sex ratio (M:F)	~1.3:1
Mean BMI (kg/m²)	27.8±3.6
Age range (years)	30–80

Study design

This retrospective observational study analyzed computerized outpatient records of newly diagnosed type 2 diabetes mellitus (T2DM) patients from January to October 2021.

Participants

Inclusion criteria included adults aged 30–80 years with T2DM diagnosed within the past 6 months. Exclusion criteria were pregnancy, gestational diabetes, insulin use, hospitalization, eGFR <45, type 1 diabetes, and age <30 or >80 years.

Grouping and intervention

Patients were categorized based on baseline HbA1c: group 1 (HbA1c 7–9%)- triple therapy (Metformin, Pioglitazone and Dapagliflozin, group 2 (HbA1c 9–11%)- quadruple therapy (group 1 and Teneligliptin), group 3 (HbA1c >11%)- quintuple therapy (group 2 and Gliclazide)

Data collection and follow-up

Baseline and follow-up data (at 3rd, 6th, and 9th months) included demographics, BMI, FBS, PPBS, and HbA1c. Estimated HbA1c was calculated via a clinic software based on FBS and PPBS, which also suggested treatment regimens using an algorithm.

Statistical analysis

Data analysis was conducted utilizing Microsoft Excel and SPSS version 17. Descriptive statistics and the Student's t-test were utilized. A p value of 0.05 or lower was deemed statistically significant.

RESULTS

Among the 343 participants, the mean age was 54.6±10.2 years, with a male-to-female ratio of approximately 1.3:1. The average BMI was 27.8±3.6 kg/m², indicating that the majority of patients were overweight or mildly obese.

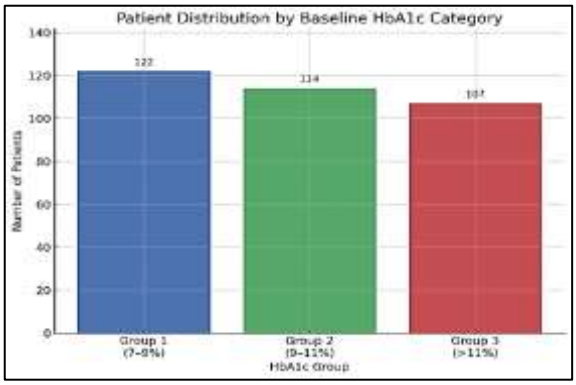

Figure 1: Patient distribution.

Over a six-month period, changes in mean HbA1c levels were used to measure group 1's glycemic response to treatment. The mean HbA1c level at baseline was 7.22% ±0.54, which indicates that blood glucose levels are moderately increased and need to be treated. There was significant decrease in HbA1c after three months of treatment. The average HbA1c dropped to 6.00% ±1.45, which was 16.9% lower than the baseline reading and an absolute drop of 1.22 percentage points. With a p value of 0.004, this improvement was statistically significant, demonstrating the treatment's effectiveness in enhancing short-term glycemic control. Over the next three months, the glycemic status improvement was not only maintained but also improved. At the 6-month follow-up, the mean HbA1c was 5.46% ±0.93, a further decline. This was a 24.4% loss, or an overall decrease of 1.76 percentage points from baseline, and it was also highly significant (p=0.001). These results show that patients in group 1 had a steady, increasing, and statistically significant improvement in their glycemic control. The group's HbA1c showed a consistent lower trend over the course of six months, indicating that the treatment plan was successful and long-lasting.

Table 2: Effect of treatment duration on HbA1c levels over 6 months in group 1.

Duration	Mean HbA1c (±SD)	Mean difference from baseline	% reduction from baseline	P value	Significance
Baseline	7.22±0.54	-	-	-	-
After 3 months	6.00±1.45	-1.32±1.53	16.90	0.004	Significant
After 6 months	5.46±0.93	-1.98±0.75	24.40	0.001	Significant

Table 3: Effect of treatment duration on HbA1c levels over 6 months in group 2.

Duration	Mean HbA1c (±SD)	Mean difference from baseline	% reduction from Baseline	P value	Significance
Baseline	9.09±0.61	-	-	-	-
After 3 months	6.35±1.07	-3.16±1.06	30.10%	0.001	Significant
After 6 months	6.45±0.83	-3.02±0.91	29.00%	0.001	Significant

The results in group 2 show that glycemic control improved significantly and statistically significantly during the six months after therapy started. Poor glycemic control and a significant risk of complications from diabetes were indicated by the mean HbA1c level at baseline, which was noticeably raised at 9.09% ±0.61. This degree of hyperglycemia called for a more intensive course of treatment. The mean HbA1c decreased quickly and significantly to 6.35% ±1.07 after three months of therapy, which was 30.1% lower than baseline (p=0.001). A strong response to the therapeutic approach is reflected in this steep drop throughout the first phase of treatment, indicating both high treatment efficacy and good patient adherence. According to clinical expectations, the bulk of glycemic improvement seems to have happened during this early phase, when the most noticeable alterations are usually produced by initial pharmacologic and lifestyle therapies. The average HbA1c at six months was 6.45% ±0.83, which was a 29.0% decrease from baseline (p=0.001). The majority of patients were able to maintain glycemic control throughout time, as evidenced by the small and non-statistically significant difference between this number and the three-month outcome.

With a mean of 12.92% ±2.54 at baseline, group 3 had the most significantly raised HbA1c readings, indicating poorly managed diabetes and a significant risk for both acute and long-term problems. The necessity and urgency of an aggressive therapeutic action are highlighted by this high baseline value. Within the first three months of starting medication, the group's glycemic control dramatically and statistically significantly improved. With a 52.2% decrease from baseline, the mean HbA1c fell precipitously to 6.17% ±1.38 (p=0.001). This remarkable improvement demonstrates the effectiveness of the treatment plan as well as the possibility of a quick metabolic recovery in patients with uncontrolled hyperglycemia who receive the right intensive therapy. At six months, the mean HbA1c was still under control at 6.24% ±1.61, which was 51.7% lower than the baseline (p=0.001). Despite being marginally greater than the three-month figure, the difference is insignificant and not statistically significant, suggesting that glycemic control has been maintained over time. Maintaining such a significant increase over six months is clinically significant since it improves patient quality of life and lowers the risk of long-term problems connected to diabetes.

Alongside notable gains in glycemic control, group 3's medication tapering profile shows a distinct and steady decrease in pharmacologic burden. Since all patients (100.0%) were receiving quintuple therapy at start, the elevated baseline mean HbA1c of 12.92% suggests that the most effective therapeutic intervention is required to address severe hyperglycemia. The change in treatment intensity at the first month of follow-up was statistically significant. While 65.7% of patients switched to quadruple therapy, the percentage of patients on quintuple therapy dropped precipitously to 26.4% (p<0.05). This early reduction demonstrates a quick clinical reaction that made it possible to safely scale back pharmacologic intervention.

Table 4: Effect of treatment duration on HbA1c levels over 6 months in group 3.

Duration	Mean HbA1c (±SD)	Mean difference from baseline	% reduction from baseline	P value	Significance
Baseline	12.92±2.54	-	-	-	-
After 3 months	6.17±1.38	-7.39±3.45	52.20	0.001	Significant
After 6 months	6.24±1.61	-7.02±3.05	51.70	0.001	Significant

Table 5: Tapering profile of medications in group 3 over time.

Therapy type	Baseline	1 month	3 months	6 months
	N (%)	N (%)	N (%)	N (%)
Quintuple	220 (100.0)	57 (26.4)	2 (0.9)	1 (0.5)
Quadruple	-	142 (65.7)	66 (30.6)	41 (19.0)
Triple	-	14 (6.5)	140 (64.8)	143 (66.2)
Dual	-	3 (1.4)	7 (3.2)	31 (14.4)
Monotherapy	-	-	1 (0.5)	-

A more noticeable tapering effect was seen at three months. Triple therapy was used to treat the majority of patients (64.8%), and at six months, 66.2% of patients were still receiving triple therapy. Concurrently, the percentage of patients kept on triple therapy dropped even lower to 19.0%, indicating continuous clinical stability that made treatment simplicity possible. The percentage of patients receiving dual therapy increased significantly over time, from 1.4% at one month to 14.4% at six months. None of the patients were still on monotherapy after six months, despite the fact that only 0.5% of them could be tapered to it by the third month.

DISCUSSION

In this study, we demonstrate that prompt, algorithm-based initiation of antihyperglycemic therapy stratified by HbA1c level is a highly effective and practical approach for newly diagnosed T2DM patients, particularly in resource-limited settings. A key observation was that, despite severe baseline hyperglycemia in a majority of patients, substantial reductions in HbA1c were achieved within 3 months. By six months, most patients had safely transitioned from quintuple or quadruple therapy to triple or even dual therapy, reinforcing the feasibility of pharmacological de-intensification following early glycemic stabilization. These findings are consistent with emerging global treatment strategies emphasizing early, intensive glycemic control using combination therapies. Recent data show that combination regimens, particularly those including metformin, SGLT2 inhibitors, and DPP4 inhibitors, have become increasingly common over the past decade due to their complementary mechanisms and additive glycemic benefits 14. Fixed-dose triple therapies such as Qternmet XR and Trijardy XR represent regulatory support for this paradigm, demonstrating a shift toward tackling multiple pathophysiologic targets simultaneously in T2DM management. Our approach mirrors this philosophy by deploying multi-drug combinations based on severity at diagnosis, followed by rational tapering once glycemic control is achieved. Importantly, while many of the novel agents highlighted in the literature such as GLP1 receptor agonists (e.g., semaglutide, dulaglutide) and dual agonists like tirzepatide are reshaping pharmacotherapy in economically developed countries, they remain out of reach for many patients in low- and middle-income regions due to cost constraints.[15,16] In these contexts, metformin, sulfonylureas, and TZDs continue to play a central role. Our study underscores that meaningful glycemic control can still be achieved using algorithm-driven, readily available therapies often combining older generics with newer oral agents like DPP4 and SGLT2 inhibitors. The success of our de-intensification strategy also supports the growing body of evidence favoring personalized diabetes care, where treatment is adapted not only to disease severity but also to patient-specific factors such as adherence potential, cost, side-effect profile, and ease of administration.[17] Integrated care models that consider the patient's broader context medical history, social support, and motivation have been shown to improve outcomes and satisfaction, a principle we operationalized through structured follow-up and targeted step-down in therapy.[18] Furthermore, our findings resonate with the broader clinical imperative to simplify long-term diabetes management. The ability to step down from complex regimens to dual or monotherapy within six months not only reduces medication burden but may also improve long-term adherence, affordability, and quality of life. In doing so, our study adds real-world support to a growing literature advocating early intensification followed by simplification an approach that bridges innovation with practicality.

Limitations of the study

The study has certain limitations. Being a retrospective observational analysis, it is subject to inherent biases, including selection and reporting bias, which may affect the interpretation of results. Additionally, the use of estimated HbA1c values generated by clinic software,

instead of standardized laboratory measurements, may limit the precision of glycemic assessments. Furthermore, as the study population was derived from two tertiary care hospitals in Mumbai, the findings may not be generalizable to other regions or healthcare settings.

CONCLUSION

The results of this study unequivocally show that, even with different baseline HbA1c values, intense therapy interventions can result in notable and long-lasting improvements in glycemic control. Over a six-month period, mean HbA1c decreased statistically significantly in all three groups, which ranged from moderately to severely uncontrolled diabetes. However, the most notable improvements were seen in patients with the highest starting HbA1c values (group 3). By six months, individuals in group 1 with a moderately increased baseline HbA1c (7.22%) had reduced by 24.4%, demonstrating progressive and successful glycemic control. With a 30.1% reduction at three months and a 29.0% reduction at six months, group 2, which had a higher baseline of 9.09%, demonstrated a quicker first response, suggesting excellent early treatment efficacy and stable maintenance. With a HbA1c reduction of more than 52% at three and six months, group 3, which had the worst baseline glycemic control (mean HbA1c 12.92%), showed the most notable improvement. By six months, most patients had safely switched from full quintuple therapy at baseline to triple or even dual therapy, indicating that de-intensifying pharmacologic regimens after initial stabilization is feasible. All things considered, these findings highlight how successful prompt and customized treatment strategies are for managing diabetes. Glycemic control and sensible drug tapering are made possible by intensive early intervention, frequent follow-up, and dose modifications, which lessens the burden of long-term treatment. This approach is crucial for the long-term management of type 2 diabetes mellitus since it not only improves clinical outcomes but also patient adherence and quality of life.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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