

Original Research Article

Pharmacy

Effect of Pharmacist Intervention on Electrolyte Homeostasis in Patients with Type 2 Diabetes Mellitus: A Longitudinal Controlled Study

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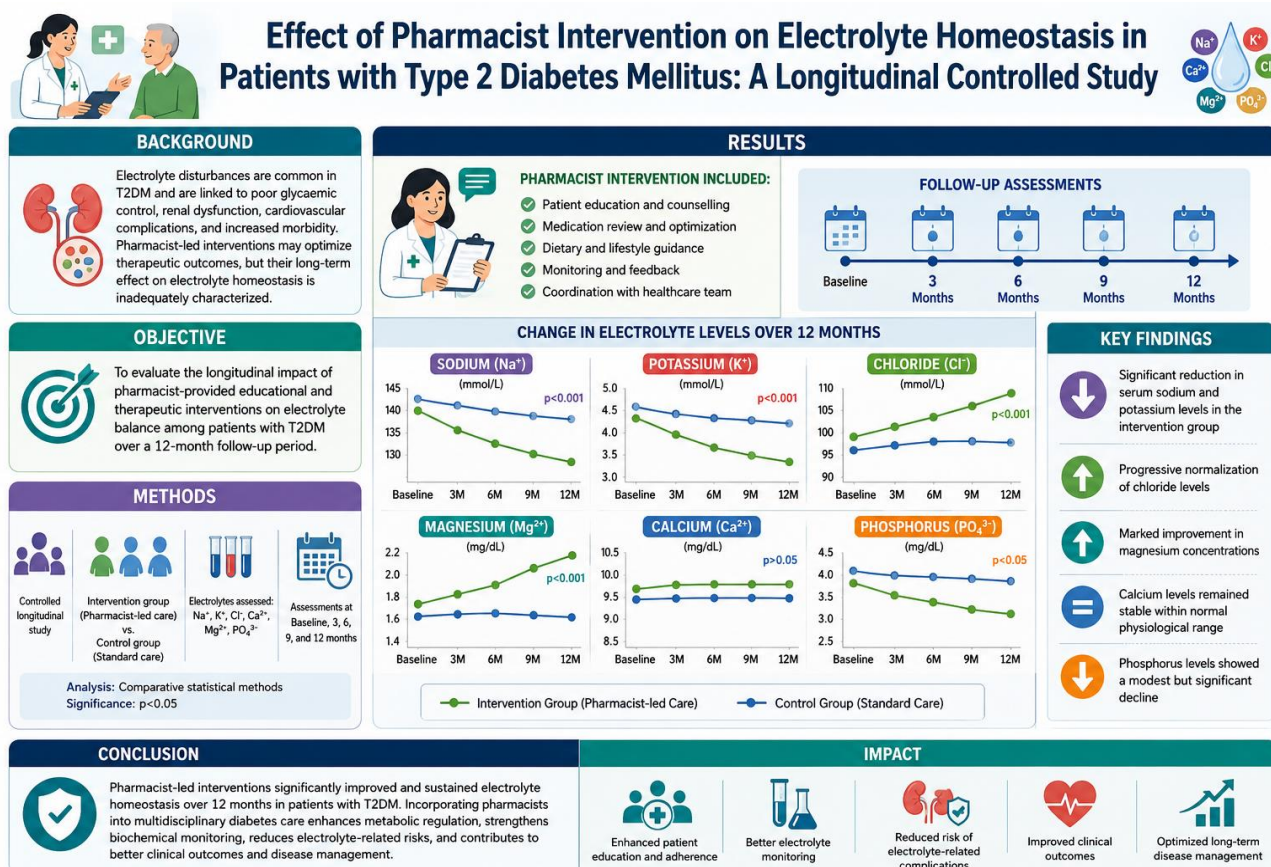
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Abstract



Graphical Abstract

Background: Electrolyte disturbances are frequently encountered in patients with Type 2 Diabetes Mellitus (T2DM) and are closely associated with poor glycaemic regulation, renal dysfunction, cardiovascular complications, and increased morbidity. Pharmacist-led interventions have emerged as a valuable strategy for optimizing therapeutic outcomes; however, their influence on long-term electrolyte homeostasis remains inadequately characterized. **Objective:** To evaluate the longitudinal impact of pharmacist-provided educational and therapeutic interventions on electrolyte balance among patients with T2DM over a 12-month follow-up period. **Methods:** A controlled longitudinal study was conducted involving patients with T2DM allocated to either an interventional group receiving structured pharmacist-led care or a control group receiving standard management. Serial assessments of serum sodium, potassium, chloride, calcium, magnesium, and phosphorus were performed at baseline and at 3-, 6-, 9-, and 12-month intervals. Temporal changes in electrolyte parameters were analyzed using comparative statistical methods, with significance established at $p < 0.05$. **Results:** Participants receiving pharmacist intervention demonstrated substantial and sustained improvements in electrolyte regulation throughout the study period. Significant reductions in serum sodium and potassium concentrations were observed in the interventional cohort, accompanied by progressive normalization of chloride levels ($p < 0.001$). Magnesium concentrations increased markedly from baseline, indicating enhanced metabolic and cellular electrolyte equilibrium. Calcium levels remained physiologically stable, whereas phosphorus concentrations exhibited a modest but significant decline over time. In contrast, the control group displayed comparatively limited or inconsistent electrolyte modulation across follow-up assessments. The magnitude and consistency of change were significantly greater among intervention recipients, suggesting superior maintenance of electrolyte homeostasis. **Conclusion:** Pharmacist-led interventions exerted a pronounced positive effect on long-term electrolyte stability in patients with T2DM. Integrating clinical pharmacists into multidisciplinary diabetes care may facilitate improved metabolic regulation, enhance biochemical monitoring, and mitigate the risk of electrolyte-related complications, ultimately contributing to better clinical outcomes and disease management.

Keywords: Type 2 Diabetes Mellitus; Pharmacist-Led Intervention; Electrolyte Homeostasis; Pharmaceutical Care; Electrolyte Imbalance; Longitudinal Study.

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INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from insulin resistance and progressive β -cell dysfunction. The global burden of T2DM continues to rise, contributing substantially to cardiovascular disease, nephropathy, neuropathy, retinopathy, and premature mortality. Despite advances in pharmacotherapy, metabolic derangements associated with diabetes remain a significant clinical challenge. [1]

Electrolyte homeostasis is essential for maintaining cellular function, neuromuscular activity, acid-base balance, and cardiovascular stability. Patients with T2DM frequently experience disturbances in serum electrolytes, including sodium, potassium, chloride, calcium, magnesium, and phosphorus. These abnormalities arise from multiple mechanisms such as osmotic diuresis, hyperglycaemia-induced fluid shifts, insulin-mediated electrolyte redistribution, renal dysfunction, and the use of antidiabetic medications. [2,3] Electrolyte imbalances have been associated with poor glycaemic control, increased hospitalization rates, cardiovascular complications, and adverse clinical outcomes in diabetic populations.[2]

Among the various electrolyte abnormalities observed in T2DM, alterations in potassium and magnesium levels are of particular concern due to their influence on insulin secretion, insulin sensitivity, cardiac conduction, and vascular function. Similarly, disturbances in sodium, chloride, calcium, and phosphorus may reflect underlying metabolic dysregulation and contribute to disease progression.

[3,4] Therefore, routine monitoring and appropriate correction of electrolyte abnormalities constitute an important component of comprehensive diabetes management.

Clinical pharmacists have increasingly become integral members of multidisciplinary diabetes care teams. Through medication review, patient education, therapeutic monitoring, lifestyle counselling, adherence enhancement, and early identification of medication-related problems, pharmacist-led interventions have demonstrated significant improvements in glycaemic control and overall clinical outcomes among patients with T2DM. [5,6] However, evidence evaluating the longitudinal impact of pharmacist interventions on electrolyte homeostasis remains limited.

Given the clinical significance of electrolyte disturbances in diabetes and the expanding role of pharmaceutical care, the present study was undertaken to assess the effect of pharmacist-led interventions on electrolyte homeostasis among patients with T2DM over a 12-month follow-up period. The study aimed to evaluate temporal changes in serum sodium, potassium, chloride, calcium, magnesium, and phosphorus concentrations and to determine whether structured pharmacist involvement could contribute to improved biochemical stability and metabolic outcomes.

MATERIALS AND METHODS

Study Design

A prospective, longitudinal, controlled interventional study was conducted over a period of 12 months to evaluate the effect of pharmacist-led

interventions on electrolyte homeostasis among patients diagnosed with Type 2 Diabetes Mellitus (T2DM).

Study Setting

The study was carried out in the Department of General Medicine and Endocrinology of a tertiary care teaching hospital. Eligible patients attending outpatient and inpatient services were screened and recruited according to predefined inclusion and exclusion criteria.

Study Population

Adult patients with a confirmed diagnosis of T2DM receiving antidiabetic therapy were enrolled in the study. Participants were followed prospectively for a period of 12 months.

Sample Size and Group Allocation

A total of 400 eligible patients were included in the study. Participants were randomly allocated into two equal groups:

- Interventional Group (n = 200)
- Control Group (n = 200)

Inclusion Criteria

- Patients aged 18 years and above.
- Diagnosed with Type 2 Diabetes Mellitus.
- Receiving one or more antidiabetic medications.
- Willing to provide written informed consent and participate throughout the study period.

Exclusion Criteria

- Patients with Type 1 Diabetes Mellitus or gestational diabetes.
- Critically ill or terminally ill patients.
- Patients with severe hepatic disease or end-stage renal disease.
- Patients with cognitive impairment affecting participation.
- Patients unwilling to provide informed consent.

Pharmacist Intervention

Patients assigned to the interventional group received structured pharmacist-led educational and clinical interventions at baseline and each follow-up visit. The intervention included individualized medication counselling, education regarding diabetes-related complications, adherence reinforcement, dietary recommendations for electrolyte balance, hydration counselling, self-monitoring guidance, identification and prevention of drug-related electrolyte disturbances, and lifestyle modification support. Educational leaflets and follow-up counselling sessions were provided regularly.

Control Group

Patients in the control group received routine medical care and standard physician-directed management without structured pharmacist intervention.

Follow-Up Schedule

Participants in both groups were evaluated at baseline, 3 months, 6 months, 9 months, and 12 months. During each follow-up visit, electrolyte parameters and glycaemic indices were reassessed, and clinical progress was documented.

Outcome Measures

Primary Outcome

- To evaluate longitudinal changes in serum electrolyte concentrations, including sodium, potassium, chloride, calcium, magnesium, and phosphorus, following pharmacist intervention.

Secondary Outcomes

- To compare electrolyte homeostasis between interventional and control groups at each follow-up period.
- To assess temporal trends in electrolyte parameters over 12 months.
- To determine the effectiveness of pharmacist-led education in preventing electrolyte abnormalities among patients with T2DM.

Statistical Analysis

All collected data were entered into Microsoft Excel and subsequently analyzed using Statistical Package for the Social Sciences (SPSS) version 32.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were employed to summarize demographic, clinical, and laboratory characteristics of the study population. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as frequencies and percentages.

The normality of continuous data distribution was assessed using the Shapiro–Wilk test. Baseline comparisons between the interventional and control groups were performed using the Independent Samples t-test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate.

Longitudinal changes in electrolyte parameters, including serum sodium, potassium, chloride, calcium, magnesium, and phosphorus, were evaluated using Repeated Measures Analysis of Variance (RM-ANOVA). Where significant differences were identified, Bonferroni post-hoc analysis was applied to determine pairwise comparisons between follow-up time points. Intergroup differences at each assessment interval were examined using the Independent Samples t-test.

Changes from baseline (Δ values) were calculated for each electrolyte parameter to assess the magnitude of variation over the study period. Corresponding 95% confidence intervals (95% CI) were computed to estimate the precision of observed effects.

All statistical tests were two-tailed, and a p-value <0.05 was considered statistically significant. Statistical significance was categorized as p <0.05 (), p <0.01 (), and p <0.001 () for interpretation of results. The findings were presented using tables and graphical representations to facilitate comparison of electrolyte

trends between the interventional and control groups over the 12-month follow-up period.

RESULTS

Table 1: Longitudinal Changes in Sodium Levels Between Interventional and Control Groups Over 12 Months

Time Point	Group	Mean $\pm$ SD	Change from Baseline (Δ)	95% Confidence Interval	p-value
Baseline	Interventional Group	141.225 $\pm$ 2.365	–	140.938 to 141.512	–
	Control Group	139.680 $\pm$ 1.715	–	139.393 to 139.967	–
3 Months	Interventional Group	140.225 $\pm$ 2.365	–1.000	139.935 to 140.515	<0.001***
	Control Group	140.095 $\pm$ 1.764	0.415	139.805 to 140.385	0.534 NS
6 Months	Interventional Group	139.725 $\pm$ 1.982	–1.500	139.469 to 139.981	<0.001***
	Control Group	139.620 $\pm$ 1.685	–0.060	139.364 to 139.876	0.568 NS
9 Months	Interventional Group	139.725 $\pm$ 1.453	–1.500	139.500 to 139.950	0.012*
	Control Group	140.135 $\pm$ 1.770	–0.455	139.910 to 140.360	<0.001***
12 Months	Interventional Group	139.225 $\pm$ 1.398	–2.000	139.007 to 139.443	0.016*
	Control Group	139.605 $\pm$ 1.722	–0.075	139.387 to 139.823	<0.001***

Table 2: Longitudinal Changes in Serum Potassium Levels Between Interventional and Control Groups Over 12 Months

Time Point	Group	Mean $\pm$ SD	Change from Baseline (Δ)	95% Confidence Interval	p-value
Baseline	Interventional Group	6.662 $\pm$ 0.484	–	6.587 to 6.737	–
	Control Group	6.405 $\pm$ 0.594	–	6.330 to 6.480	–
3 Months	Interventional Group	6.294 $\pm$ 0.440	–0.369	6.220 to 6.368	<0.001***
	Control Group	6.394 $\pm$ 0.606	–0.011	6.320 to 6.468	0.058 NS
6 Months	Interventional Group	5.913 $\pm$ 0.418	–0.750	5.843 to 5.983	<0.001***
	Control Group	6.341 $\pm$ 0.566	–0.064	6.271 to 6.411	NS
9 Months	Interventional Group	5.543 $\pm$ 0.384	–1.120	5.476 to 5.610	<0.001***
	Control Group	6.342 $\pm$ 0.561	–0.063	6.275 to 6.409	NS
12 Months	Interventional Group	5.177 $\pm$ 0.354	–1.485	5.112 to 5.242	<0.001***
	Control Group	6.333 $\pm$ 0.562	–0.073	6.267 to 6.399	NS

Table 3: Longitudinal Changes in Chloride Levels (Chlo) Over 12 Months Between Interventional and Control Groups

Time Point	Group	Mean $\pm$ SD	Change from Baseline (Δ)	95% Confidence Interval	p-value
Baseline	Interventional Group	99.575 $\pm$ 1.836	–	99.297 to 99.853	–
	Control Group	100.455 $\pm$ 2.147	–	100.177 to 100.733	–
3 Months	Interventional Group	100.575 $\pm$ 1.836	1	100.302 to 100.848	<0.001***
	Control Group	100.415 $\pm$ 2.089	–0.040	100.142 to 100.688	0.416 (NS)
6 Months	Interventional Group	101.575 $\pm$ 1.836	2	101.276 to 101.874	<0.001***
	Control Group	100.935 $\pm$ 2.429	0.48	100.636 to 101.234	0.003**
9 Months	Interventional Group	102.475 $\pm$ 1.837	2.9	102.174 to 102.776	<0.001***
	Control Group	100.920 $\pm$ 2.446	0.465	100.619 to 101.221	NS
12 Months	Interventional Group	103.455 $\pm$ 1.804	3.88	103.177 to 103.733	<0.001***
	Control Group	100.445 $\pm$ 2.177	–0.010	100.167 to 100.723	NS

Table 4: Longitudinal Changes in Calcium Levels (Cal) Over 12 Months Between Interventional and Control Groups

Time Point	Group	Mean $\pm$ SD (mg/dL)	Δ from Baseline	p-value vs Baseline
Baseline	Interventional	9.45 $\pm$ 0.41	–	–
	Control	9.04 $\pm$ 0.30	–	–
3 Months	Interventional	9.42 $\pm$ 0.38	–0.03	0.123
	Control	9.14 $\pm$ 0.30	0.1	<0.001 **
6 Months	Interventional	9.44 $\pm$ 0.41	–0.01	0.384
	Control	9.24 $\pm$ 0.30	0.2	<0.001 **
9 Months	Interventional	9.44 $\pm$ 0.39	–0.01	0.319

Time Point	Group	Mean $\pm$ SD (mg/dL)	Δ from Baseline	p-value vs Baseline
12 Months	Control	9.34 $\pm$ 0.30	0.3	<0.001 **
	Interventional	9.44 $\pm$ 0.39	-0.01	1.000 (NS)
	Control	9.44 $\pm$ 0.30	0.4	<0.001 **

Table 5: Longitudinal Changes in Magnesium Levels (mg/dL) Across Time Points in Interventional and Control Groups

Time Point	Group	Mean $\pm$ SD	Change from Baseline (Δ)	95% Confidence Interval	p-value
Baseline	Interventional	1.804 $\pm$ 0.070	–	1.796 to 1.811	–
	Control	1.788 $\pm$ 0.034	–	1.780 to 1.796	<0.001 ***
3 Months	Interventional	1.903 $\pm$ 0.070	0.099	1.895 to 1.912	<0.001 ***
	Control	1.835 $\pm$ 0.044	0.047	1.826 to 1.843	<0.001 ***
6 Months	Interventional	2.004 $\pm$ 0.070	0.2	1.995 to 2.012	<0.001 ***
	Control	1.881 $\pm$ 0.058	0.093	1.872 to 1.890	<0.001 ***
9 Months	Interventional	2.104 $\pm$ 0.070	0.3	2.093 to 2.114	<0.001 ***
	Control	1.927 $\pm$ 0.074	0.139	1.917 to 1.937	<0.001 ***
12 Months	Interventional	2.203 $\pm$ 0.070	0.399	2.192 to 2.215	<0.001 ***
	Control	1.974 $\pm$ 0.091	0.186	1.962 to 1.985	<0.001 ***

Table 6: Longitudinal Changes in Phosphorus Levels (mg/dL) Across Time Points in Interventional and Control Groups

Time Point	Group	Mean $\pm$ SD	Change from Baseline (Δ)	95% Confidence Interval	p-value
Baseline	Interventional	4.123 $\pm$ 0.058	–	4.115 to 4.131	–
	Control	4.123 $\pm$ 0.058	–	4.115 to 4.131	–
3 Months	Interventional	4.059 $\pm$ 0.055	-0.064	4.051 to 4.067	<0.001 ***
	Control	4.059 $\pm$ 0.054	-0.064	4.051 to 4.066	<0.001 ***
6 Months	Interventional	3.997 $\pm$ 0.053	-0.126	3.990 to 4.004	<0.001 ***
	Control	3.996 $\pm$ 0.053	-0.126	3.989 to 4.004	<0.001 ***
9 Months	Interventional	3.937 $\pm$ 0.053	-0.186	3.929 to 3.944	<0.001 ***
	Control	3.937 $\pm$ 0.052	-0.186	3.929 to 3.944	<0.001 ***
12 Months	Interventional	3.876 $\pm$ 0.052	-0.247	3.867 to 3.885	<0.001 ***
	Control	3.871 $\pm$ 0.081	-0.252	3.862 to 3.881	<0.001 ***

DISCUSSION

The present longitudinal controlled study evaluated the impact of pharmacist-led intervention on electrolyte homeostasis among patients with Type 2 Diabetes Mellitus (T2DM) over a 12-month follow-up period. The findings demonstrated that structured pharmacist involvement was associated with significant improvements in electrolyte regulation, particularly with respect to serum potassium, chloride, and magnesium concentrations, compared with standard care. These results underscore the important role of clinical pharmacists in optimizing metabolic control and preventing biochemical abnormalities frequently encountered in patients with diabetes.

Electrolyte disturbances are highly prevalent among individuals with T2DM due to hyperglycaemia-induced osmotic diuresis, altered renal handling of electrolytes, insulin deficiency or resistance, and the effects of concomitant pharmacotherapy.[7] Previous studies have established that dysregulation of sodium and potassium homeostasis contributes to increased cardiovascular morbidity, impaired glycaemic control, and adverse clinical outcomes in diabetic populations.[8] In the present study, a progressive normalization of serum sodium levels was observed in the interventional group throughout the follow-up period, whereas only minimal fluctuations were detected in the control group.

These findings suggest that pharmacist-led counselling regarding medication adherence, hydration practices, dietary management, and regular monitoring may contribute to improved sodium balance.

A particularly notable finding was the significant reduction in serum potassium concentrations within the intervention cohort. Elevated potassium levels have been associated with insulin deficiency, diabetic nephropathy, and impaired renal excretion. [9] The observed improvement may be attributed to enhanced patient education regarding dietary potassium intake, optimization of pharmacotherapy, and improved glycaemic control facilitated by pharmacist intervention. Similar benefits of pharmacist-managed diabetes care have been reported by Aguiar *et al.*, who demonstrated significant improvements in metabolic parameters and therapeutic outcomes among patients receiving structured pharmaceutical care. [10]

Chloride concentrations exhibited a gradual increase toward physiological levels in the intervention group, whereas changes in the control group remained minimal and inconsistent. Chloride plays a crucial role in acid-base regulation and extracellular fluid balance. Alterations in chloride homeostasis may reflect underlying metabolic disturbances associated with chronic hyperglycaemia. [11] The improvement

observed in the intervention group suggests that comprehensive pharmaceutical care may indirectly contribute to restoration of electrolyte equilibrium through enhanced disease management.

Magnesium status has received increasing attention in diabetes research because hypomagnesaemia is frequently associated with insulin resistance, poor glycaemic control, endothelial dysfunction, and increased cardiovascular risk. [12] In the current study, magnesium concentrations increased significantly and consistently across all follow-up intervals in the interventional group. These findings are in agreement with previous investigations reporting that improved diabetes self-management and medication adherence can positively influence magnesium homeostasis. [13] The progressive rise in magnesium levels observed in the intervention arm may have contributed to improved metabolic stability and enhanced insulin sensitivity.

Serum calcium concentrations remained relatively stable throughout the study period in both groups. This finding is consistent with previous reports indicating that calcium homeostasis is generally maintained within a narrow physiological range despite metabolic disturbances associated with diabetes. [14] Although statistically significant increases were observed in the control group, these changes remained within normal clinical limits and were unlikely to possess major clinical significance.

A gradual decline in phosphorus concentrations was observed in both study groups over time. Similar findings have been reported in patients with diabetes, where alterations in phosphorus metabolism are influenced by glycaemic control, renal handling, and insulin-mediated cellular uptake. [15] However, the magnitude of phosphorus reduction was comparable between groups, suggesting that factors other than pharmacist intervention may have contributed to this observation.

The overall findings of this study support the growing body of evidence highlighting the clinical value of pharmacist-led interventions in chronic disease management. Previous systematic reviews have demonstrated that pharmacist involvement significantly improves medication adherence, glycaemic outcomes, patient education, and healthcare utilization among individuals with T2DM. [16,17] The present investigation extends these observations by demonstrating a favorable effect on long-term electrolyte homeostasis, an area that has received comparatively limited attention in the literature.

Several mechanisms may explain the observed benefits. Pharmacist-led interventions promote medication adherence, facilitate early detection of drug-related electrolyte disturbances, reinforce dietary recommendations, improve hydration practices, and

encourage regular laboratory monitoring. Collectively, these measures contribute to improved metabolic control and maintenance of physiological electrolyte balance. Consequently, integration of clinical pharmacists into multidisciplinary diabetes care teams may provide substantial benefits in reducing electrolyte-related complications and improving patient outcomes.

CONCLUSION

The present longitudinal controlled study demonstrated that pharmacist-led interventions significantly improved electrolyte homeostasis among patients with Type 2 Diabetes Mellitus over a 12-month follow-up period. Patients receiving structured pharmaceutical care exhibited favourable changes in serum sodium, potassium, chloride, and magnesium concentrations compared with those receiving standard care. Calcium levels remained stable, while phosphorus concentrations showed a modest decline in both groups. These findings highlight the pivotal role of clinical pharmacists in enhancing metabolic monitoring, promoting medication adherence, facilitating patient education, and preventing electrolyte-related complications. The incorporation of pharmacist-led services into routine diabetes management may contribute substantially to improved biochemical stability, optimized therapeutic outcomes, and enhanced quality of patient care.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this study.

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Ethical Approval

The study protocol was reviewed and approved by the Institutional Ethics Committee prior to commencement of the study. The research was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and Good Clinical Practice guidelines.

Informed Consent

Written informed consent was obtained from all participants before enrollment into the study. Participation was voluntary, and confidentiality of patient information was maintained throughout the study.

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