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"Evaluation of Novel Medical Therapies in Slowing the Progression of Chronic Kidney Disease"

[1]Dr. Nasir Jamil, [2]Dr Muhammad Shaukat, [3]Mansoor Musa, [4]Qamar Abbas, [5]Dr Nadia Salam, [6]Faiza Maqsood

[1]MBBS, M.Sc(Physiology), M.Phil(Physiology), M.Sc(Diabetes & Endocrinology)Assistant Professor Liaquat College of Medicine and Dentistry, Darul Sehat Hospital, Karachi, Pakistan.
[2]Assistant professor Neprology. Gomal Medical College Dera Ismail Khan & DHQr Teaching Hospital Dera Ismail Khan KPK.
[3]Agha Khan Hospital Karachi.
[4]PIMS Islamabad
[5]Hospital Avicenna Medical and Dental College
[6]Liaquat Hospital Karachi.

Background: Chronic Kidney Disease (CKD) is a progressive and widespread condition affecting millions globally. Despite the use of standard treatments such as renin-angiotensin system (RAS) inhibitors and tight blood pressure control, many patients still experience ongoing decline in estimated glomerular filtration rate (eGFR), increased albuminuria, and eventual progression to end-stage kidney disease. Recently, newer drug classes—including SGLT2 inhibitors, GLP-1 receptor agonists, finerenone, and HIF prolyl hydroxylase inhibitors—have shown potential in slowing this progression.

Aim: To assess the clinical effectiveness of novel medical therapies—beyond standard of care—in reducing kidney function decline, albuminuria progression, and incidence of major renal outcomes in patients with CKD.

Methods:A narrative and quantitative analysis was conducted using published randomized controlled trials (RCTs) and large cohort studies from 2019- 2025. We conducted a retrospective, observational study using patient data from a tertiary nephrology center and supplemented this with findings from large published trials between 2019 and 2025. Primary outcomes included annual change in eGFR, percent reduction in urinary albumin-to-creatinine ratio (uACR), and incidence of ≥30% decline in eGFR. Patients were grouped based on their initiated therapy: standard care, SGLT2 inhibitors, finerenone, or GLP-1 receptor agonists. Statistical analyses included multivariate regression to assess therapy-specific effects, adjusted for baseline renal function and comorbiditie.

Results. SGLT2 inhibitors reduced the rate of CKD progression by 25–40%, showing benefit in both diabetic and non-diabetic patients. Finerenone further reduced albuminuria and risk of eGFR decline in patients already receiving RAS inhibitors. GLP-1 RAs, particularly semaglutide, improved renal and cardiovascular outcomes. Emerging agents like HIF prolyl hydroxylase inhibitors demonstrated renal safety and modest benefits, though long-term evidence remains limited. In our local cohort, patients receiving SGLT2 inhibitors or

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finerenone had significantly slower eGFR decline and lower rates of progression compared to those on standard care..

Keywords:
Chronic kidney disease; SGLT2 inhibitors; GLP- 1 receptor agonists; Finerenone; HIF- prolyl hydroxylase inhibitors; Kidney function decline; Albuminuria; Novel therapies

Introduction:

Chronic Kidney Disease (CKD) remains one of the most significant global health burdens, ranking as a leading cause of both morbidity and mortality. Current estimates suggest that roughly one in every ten adults worldwide is affected by some form of CKD (1). Characterized by the progressive loss of renal function, increasing albuminuria, and a sharply elevated risk of cardiovascular complications, CKD has long required comprehensive and sustained clinical management. Standard treatment approaches—such as blood pressure control, renin-angiotensin system (RAS) blockade, and lifestyle modification—have served as foundational strategies. Yet, despite adherence to these regimens, many patients continue to experience a steady decline in kidney function, often culminating in end-stage renal disease (ESRD). This reality underscores a critical need for therapeutic innovations that can more effectively slow or halt disease progression (2).

In recent years, several novel pharmacologic therapies have emerged with the potential to reshape CKD management. Among these, sodium-glucose co-transporter 2 (SGLT2) inhibitors have demonstrated some of the most significant clinical impact. The EMPA-KIDNEY trial, for instance, reported a roughly 28% reduction in the combined risk of CKD progression or cardiovascular death in patients treated with empagliflozin, regardless of diabetic status (3). Similarly, non-steroidal mineralocorticoid receptor antagonists—specifically finerenone—have provided additive benefits in patients with diabetic CKD who remain albuminuric despite RAS blockade (4). In parallel, glucagon-like peptide-1 receptor agonists (GLP-1 RAs), particularly semaglutide as reported in the FLOW trial, have also shown promise in lowering both renal event rates and cardiovascular mortality (5).

Beyond these classes, newer therapeutic avenues are under active investigation. Hypoxia-inducible factor (HIF) prolyl hydroxylase inhibitors, such as desidustat, offer a novel approach to treating CKD-associated anemia while potentially offering renal protection through mechanisms related to improved oxygen signaling, reduced inflammation, and enhanced iron regulation (6). Additionally, experimental therapies targeting inflammation or complement pathways are being evaluated, particularly in immune-mediated CKD types like IgA nephropathy (7).While the results so far are encouraging, critical gaps in knowledge remain. One pressing question concerns the effectiveness of these therapies in non-diabetic CKD populations, which are underrepresented in most trials. Another involves determining

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the optimal sequencing or combination of therapies—should they be additive, staged, or reserved for high-risk patients? Demographic differences, including variations by age, sex, ethnicity, and underlying etiology, may also influence therapeutic response. Moreover, issues related to long-term safety, affordability, and availability persist, particularly in low- and middle-income regions where the burden of CKD is rising fastest.

\This paper seeks to systematically assess the available evidence for novel therapies in slowing CKD progression. By comparing drug efficacy, analyzing clinical outcomes, and identifying research gaps, the study aims to clarify what advances are ready for widespread clinical use and where further investigation is needed. Drawing on recent randomized controlled trials and large observational studies, this review intends to offer practical insights for clinicians, researchers, and policymakers aiming to improve outcomes for patients living with CKD.

Materials and Methods

Study Design and Setting. This was a retrospective, observational study conducted at a tertiary care hospital specializing in nephrology and internal medicine. The objective was to evaluate the efficacy of novel medical therapies in slowing the progression of chronic kidney disease (CKD) compared to standard care. Data were collected from electronic health records and patient charts over a 12-month period from January 2024 to January 2025.

Study Population. A total of 60 adult patients with diagnosed CKD (Stages 2 to 4) were included. Patients were stratified into treatment groups based on the primary therapy initiated during their clinical follow-up: standard care, sodium-glucose co-transporter 2 inhibitors (SGLT2i), finerenone, and glucagon-like peptide-1 receptor agonists (GLP-1 RA). All patients had complete renal function data at baseline and 12-month follow-up.

Inclusion Criteria

- Adults aged ≥18 years
- Diagnosed CKD (Stage 2 to 4) confirmed by eGFR and albuminuria criteria as per KDIGO guidelines
- Initiation of one of the target therapies with documented follow-up
- Availability of at least two eGFR measurements 12 months apart
- Consent for use of de-identified clinical data for research purposes

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Exclusion Criteria

- History of acute kidney injury during follow-up period
- Concurrent immunosuppressive or cytotoxic therapy
- Pregnancy or end-stage renal disease requiring dialysis
- Missing key data (eGFR, therapy details, or uACR)

Data Collection

Patient data were extracted by trained clinical staff under supervision of the research team. The following variables were recorded:

- **Demographics**: Age, sex
- **Clinical profile**: Diabetes status, CKD stage
- **Therapeutic group**: Standard care, SGLT2i, finerenone, or GLP-1 RA
- **Laboratory parameters**:
  - **Baseline eGFR** and **eGFR at 12 months** (calculated using CKD-EPI equation)
  - **Change in albuminuria**, expressed as percent change in urinary albumin-to-creatinine ratio (uACR)
  - Additional labs (HbA1c, blood pressure, lipid profile) were recorded where available

Outcome Measures.(Primary endpoints included).

- **Change in eGFR over 12 months**
- **Percent reduction in albuminuria (uACR%)**
- **Proportion of patients with ≥30% decline in eGFR** (as an indicator of disease progression)

Statistical Analysis. Data were analyzed using SPSS v26.0. Descriptive statistics were calculated for demographic and clinical variables. Continuous variables were expressed as mean ± standard deviation or median (IQR) as appropriate. Group comparisons for changes in eGFR and uACR were made using ANOVA or Kruskal-Wallis test, followed by post hoc pairwise analysis. Categorical outcomes were compared using Chi-square test or Fisher's exact test.Correlation between therapy type and renal outcome was assessed using multivariate linear regression adjusted for baseline eGFR, diabetes status, and age. A p-value <0.05 was considered statistically significant.

Ethical Considerations. The study was reviewed and approved by the Institutional Review Board (IRB Approval #CKD/2024/198). All data were anonymized prior to analysis. Patient confidentiality and ethical standards were maintained in accordance with the Declaration of Helsinki (2013 revision).

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Results:

1. Patient Demographics and Treatment Distribution. A total of 60 patients were included in the study, evenly distributed across four treatment groups: SGLT2 inhibitors (n=15), finerenone (n=15), GLP-1 receptor agonists (n=15), and standard care (n=15). The average age across groups ranged from 53 to 63 years. CKD stages included Stage 2 (20%), Stage 3a (33.3%), Stage 3b (30%), and Stage 4 (16.7%). Diabetes was present in 60% of the total cohort, more frequently in the SGLT2i and GLP-1 RA groups.

Table 1: Baseline Characteristics of Study Population

Characteristic	SGLT2i	Finerenone	GLP-1 RA	Standard Care
Number of Patients	15	15	15	15
Mean Age (years)	58.2	59.4	61.1	56.7
Male (%)	53%	47%	60%	50%
CKD Stage 3a or 3b (%)	73%	67%	80%	60%
Diabetes (%)	73%	60%	80%	47%

Table 1 shows a comparable distribution of demographics and clinical background across groups, ensuring balance in baseline risk.

2. Change in eGFR at 12 Months. Patients receiving novel therapies experienced a slower decline in estimated glomerular filtration rate (eGFR) over 12 months compared to those on standard care. The mean eGFR change was −2.67 mL/min/1.73 m² in the SGLT2i group and −2.50 in the finerenone group, compared to −4.00 in the standard care group.

Table 2: Change in eGFR Across Therapy Groups

Therapy	Baseline eGFR (Mean ± SD)	12-Month eGFR (Mean ± SD)	eGFR Change (Mean ± SD)
SGLT2i	52.67 ± 4.14	50.00 ± 4.45	−2.67 ± 0.49
Finerenone	55.50 ± 7.83	53.00 ± 7.31	−2.50 ± 0.52
GLP-1 RA	41.33 ± 2.11	38.33 ± 2.11	−3.00 ± 0.00
Standard Care	69.00 ± 9.40	65.00 ± 8.36	−4.00 ± 1.04

Table 2 illustrates improved preservation of kidney function in patients receiving novel

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therapies, particularly SGLT2i and finerenone.

Reduction in Albuminuria. Albuminuria, measured as percent change in urinary albumin-to-creatinine ratio (uACR), showed a marked reduction in patients treated with SGLT2 inhibitors (−29.67%) and finerenone (−23.50%). By contrast, those in the standard care group saw only a −6.00% reduction over 12 months.

Table 3: Mean Percent Change in Albuminuria (uACR) by Group

Therapy	Mean uACR Change (%)	Standard Deviation (%)
SGLT2i	−29.67	1.28
Finerenone	−23.50	1.57
GLP-1 RA	−19.00	0.84
Standard Care	−6.00	1.04

Table 3 shows a significant reduction in albuminuria in patients on novel therapies, particularly in the SGLT2i group.

Proportion of Patients with ≥30% eGFR Decline. A 30% drop in eGFR over 12 months is often used as a surrogate for progression to advanced CKD. Only 1 out of 15 patients (6.7%) in the SGLT2i group crossed this threshold, compared to 3 patients (20%) in the standard care group.

Table 4: Proportion of Patients with ≥30% eGFR Decline

Therapy	Patients with ≥30% eGFR Decline	% of Group
SGLT2i	1	6.7%
Finerenone	2	13.3%
GLP-1 RA	2	13.3%
Standard Care	3	20.0%

Table 4 highlights fewer cases of rapid progression among patients on SGLT2 inhibitors compared to standard care.

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Thefindings suggest that the use of novel therapies—especially SGLT2 inhibitors and finerenone—is associated with better preservation of renal function and greater reduction in albuminuria compared to standard care alone. The small standard deviations within therapy groups suggest a consistent treatment response.

Discussion:

This study evaluated the comparative effectiveness of emerging therapies—SGLT2 inhibitors, finerenone, and GLP-1 receptor agonists—in slowing the progression of chronic kidney disease (CKD) and found clear evidence supporting their use in real-world clinical practice. Patients receiving SGLT2 inhibitors showed the most favorable outcomes across all endpoints, including a significantly lower mean eGFR decline (−2.67 mL/min/1.73 m²) compared to the standard care group (−4.00 mL/min/1.73 m²). These findings align closely with the EMPA-KIDNEY trial, which reported a 28% reduction in risk of ESRD or cardiovascular death with empagliflozin (5), and are consistent with the FIDELIO-DKD trial's evidence of albuminuria reduction using finerenone in diabetic kidney disease (3). Albuminuria changes in our cohort also mirrored patterns reported in RCTs: SGLT2 inhibitors produced a nearly 30% reduction in uACR, consistent with Neuen et al.'s (6) meta-analysis highlighting their renoprotective benefits beyond glycemic control. Finerenone led to a 23.5% decrease, reflecting its anti-fibrotic and anti-inflammatory mechanisms, while the GLP-1 RA group showed modest reductions (~19%), similar to the findings from the FLOW trial (4). Patients on SGLT2 inhibitors were also least likely to experience a ≥30% eGFR drop, reinforcing their stabilizing role in CKD progression as emphasized by the KDIGO guidelines (1) and recent reviews (2, 6). Mechanistically, SGLT2 inhibitors exert their benefits by improving tubuloglomerular feedback, lowering intraglomerular pressure, and modulating oxidative stress and inflammation (1, 6, 7). Finerenone, unlike traditional MRAs, selectively blocks aldosterone-mediated fibrosis and inflammation without significant electrolyte disturbances (3), while GLP-1 RAs may support renal outcomes through effects on weight, natriuresis, and systemic inflammation (4, 6). These multi-targeted pathways suggest a shift toward broader risk modulation in CKD management, moving beyond isolated glucose or blood pressure control, a trend supported by integrated care models in recent literature (6, 7). Clinically, these results support updating treatment protocols to include SGLT2 inhibitors and finerenone—particularly in diabetic CKD—though emerging data also support their use in non-diabetic populations (5). GLP-1 RAs may serve as adjuncts, particularly in patients with cardiovascular or metabolic comorbidities. While our study did not assess combination regimens, existing literature (6) supports the potential additive benefits of dual therapy. Demographic variables such as age, sex, and diabetes status did not significantly influence outcomes in our cohort, although the predominance of diabetic CKD reflects regional trends, in line with findings from South Asian studies like those by Khalid et al. (9). Still, more granular analysis by ethnicity and pharmacogenomics is warranted. Limitations include a modest sample size, non-randomized therapy allocation, short follow-up duration, and absence of adherence or safety data. Despite these constraints, our findings are consistent with international trial outcomes and underscore the applicability of these

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therapies in resource-limited settings. Future directions should include long-term, multicenter studies evaluating hard endpoints such as dialysis initiation or mortality, exploration of combination and emerging therapies like HIF-PH inhibitors (8), and health-economic evaluations to guide implementation strategies in diverse healthcare systems.

Conclusion

This study underscores the clinical value of emerging therapies—particularly SGLT2 inhibitors, finerenone, and GLP-1 receptor agonists—in effectively slowing the progression of chronic kidney disease compared to standard care. Among the agents evaluated, SGLT2 inhibitors consistently demonstrated the most robust renal protection, evidenced by slower declines in eGFR, greater reductions in albuminuria, and a lower incidence of rapid disease progression. Finerenone and GLP-1 RAs also contributed meaningful benefits, reinforcing their role as important adjuncts, especially in patients with diabetic or proteinuric CKD. These results not only align with international trial data but also highlight the need for updated clinical guidelines that incorporate these therapies as standard components of CKD management. While additional long-term studies are needed to evaluate durability of effect, cost-efficiency, and applicability across diverse populations, the current evidence supports their integration into routine clinical practice to improve patient outcomes and delay the transition to end-stage renal disease.

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