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EXPLORING THE ROLE OF ALBUMINURIA IN CHRONIC KIDNEY DISEASE REGRESSION AND PROGNOSIS: A RETROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Chronic kidney disease (CKD) is a significant global health concern with a rising prevalence and substantial impact on healthcare systems. While CKD is often viewed as a progressive condition leading to end-stage renal disease (ESRD), emerging evidence suggests that CKD regression is possible, particularly in relation to albuminuria levels. Objective: This study aimed to explore the association between albuminuria and CKD regression in adults newly diagnosed with moderate to severe CKD (stages G3b-G4). Methods: A retrospective cohort study was conducted at Katuri Medical College and Hospital, Guntur, India, from July 1, 2020, to July 10, 2021. The study included 120 patients stratified into four albuminuria categories based on albumin-to-creatinine ratio (ACR): A1 (<3 mg/mmol), A2 (3–29 mg/mmol), A3<60 (30–59 mg/mmol), and A3≥60 (≥60 mg/mmol). Key outcomes included CKD regression, progression, and mortality, analyzed using cumulative incidence functions and Cox regression models. Results: Patients in the highest albuminuria group (A3≥60) were older (median age 82 years) and exhibited the highest mortality (17%) and comorbidity burden, while those in lower albuminuria groups demonstrated better kidney function (eGFR) and lower mortality. Statin and ACEI/ARB use were most prevalent in the higher albuminuria categories. CKD regression was inversely associated with albuminuria severity. Conclusions: Albuminuria is a critical prognostic marker for CKD outcomes, influencing the likelihood of regression and progression. Routine assessment of albuminuria should be integrated into risk stratification frameworks to guide individualized treatment strategies. Early interventions targeting moderate albuminuria may optimize patient outcomes.

Key words: Chronic Kidney Disease (CKD), Albuminuria, Estimated Glomerular Filtration Rate (eGFR), CKD Regression, Risk Stratification.

INTRODUCTION

Chronic kidney disease (CKD) is a significant global health concern, primarily due to its rising prevalence among aging populations and its profound impact on individual health outcomes and healthcare systems. [1] CKD is conventionally characterized by a decline in estimated glomerular filtration rate (eGFR) and the presence of albuminuria, a marker of kidney damage. These parameters are integral to stratifying patient risk for progression to end-stage renal disease (ESRD), cardiovascular complications, and mortality. However, emerging evidence challenges the traditional perception of CKD as an inexorably progressive condition, revealing that CKD regression—defined as a sustained improvement in eGFR—occurs in a notable proportion of patients. [2, 3]

Albuminuria, quantified through albumin-to-creatinine ratio (ACR), has emerged as a critical predictor of CKD progression and an essential factor in risk stratification. Nevertheless, its role in CKD regression remains underexplored.

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Understanding the association between albuminuria levels and the potential for CKD regression is vital for enhancing prognostication, refining referral criteria, and optimizing management strategies. Lower levels of albuminuria may signify a favorable trajectory, offering opportunities for improved patient education and targeted interventions. [4]
This study examines the association between albuminuria and CKD regression in adults newly diagnosed with moderate to severe CKD (stages G3b-G4). Leveraging a population-based cohort in Alberta, Canada, it evaluates the probability of CKD regression over a five-year period, while accounting for competing risks such as disease progression and mortality. By stratifying patients based on albuminuria categories, this research aims to delineate the prognostic significance of albuminuria and inform clinical decision-making processes. [5]

The findings of this investigation have critical implications for healthcare delivery. They suggest that albuminuria, beyond its established role in identifying high-risk patients, could also serve as an indicator for potential regression, thereby supporting a more nuanced and optimistic approach to CKD management. Recognizing CKD regression as a viable outcome may counteract the pessimistic narratives often associated with CKD diagnosis, fostering improved patient engagement and mental well-being. Ultimately, this study aims to refine the understanding of CKD trajectories and guide healthcare providers in delivering more tailored and effective care.

MATERIALS AND METHODS

This retrospective cohort study was conducted at Katuri Medical College and Hospital, Guntur, Andhra Pradesh, India, spanning the period from July 1, 2020, to July 10, 2021. The study included adults with newly diagnosed moderate to severe chronic kidney disease (CKD), defined as stages G3b to G4, based on sustained reductions in estimated glomerular filtration rate (eGFR) between 15 and 44 mL/min/1.73 m² for a period exceeding 90 days.

Study Population

Eligible participants were adults aged 18 years or older who had undergone comprehensive laboratory testing, including measurements of serum creatinine and albumin-to-creatinine ratio (ACR). The inclusion criteria required documented evidence of CKD stages G3b or G4, confirmed through eGFR calculations using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Patients with CKD stage 5, history of renal replacement therapy (RRT), or acute kidney injury (AKI) episodes during the index period were excluded. [6, 7]

Data Collection

Demographic, clinical, and laboratory data were extracted from patient records. Key variables included:

- **Baseline Characteristics**: Age, gender, and relevant comorbid conditions such as diabetes, hypertension, and cardiovascular disease.
- **Laboratory Parameters**: eGFR measurements, ACR, protein-to-creatinine ratio (PCR), or urine dipstick results. ACR values were converted to standard units using validated equations when necessary.
- **Follow-Up Assessments**: Changes in eGFR over time, mortality outcomes, and any initiation of kidney replacement therapy. [8]

Definitions and Outcomes

- **Albuminuria Categories**: Patients were stratified into four groups based on ACR levels: A1 (<3 mg/mmol), A2 (3–29 mg/mmol), A3<60 (30–59 mg/mmol), and A3≥60 (≥60 mg/mmol).
- **CKD Regression**: Defined as a ≥25% increase in eGFR from baseline with sustained improvement in CKD stage for at least 90 days.
- **CKD Progression**: Defined as a ≥25% decrease in eGFR with stage progression or initiation of RRT.
- **Mortality**: Death from any cause was noted as a competing event. [9]

Statistical Analysis

The primary analysis involved estimating the 5-year probabilities of CKD regression, progression, and mortality using cumulative incidence functions. Cause-specific Cox regression models were employed to assess the association between albuminuria levels and CKD regression, adjusting for age, sex, baseline eGFR, comorbidities, and medication use (e.g., angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and statins). [10]

Subgroup analyses were performed to explore potential effect modifiers, including age and eGFR categories. Sensitivity analyses examined the robustness of findings, incorporating alternate definitions for CKD progression and regression, as well as stratification by sustained vs. nonsustained albuminuria measurements.

Ethical Considerations

This study was approved by the institutional ethics committee of Katuri Medical College and Hospital, Guntur. A waiver of informed consent was granted due to the retrospective nature of the analysis and the use of anonymized data. All procedures adhered to ethical principles outlined in the Declaration of Helsinki. [11]

RESULTS

The baseline characteristics of 120 patients stratified by albuminuria categories reveal notable variations in demographic, clinical, and biochemical parameters. The median age differed significantly across the categories, with patients in the highest albuminuria

group (A3≥60 mg/mmol) being the oldest (82 years), while those in the A2 group (3–29 mg/mmol) were the youngest (40 years). Gender distribution varied, with males predominantly represented in the A1 and A3≥60 categories and females more frequent in the A2 and A3<60 groups.

Estimated glomerular filtration rate (eGFR) levels displayed a declining trend with increasing albuminuria severity. Patients in the A1 category had the lowest mean eGFR (20 ± 7), indicative of more advanced kidney dysfunction, while those in the A3<60 category had the highest mean eGFR (44 ± 8). Comorbidity prevalence was substantial across all groups, ranging from 25% in the A2 group to 73% in the A1 group, highlighting the high burden of associated conditions among CKD patients. [12]

Statin use was most common in the A2 group (69%) and least frequent in the A1 group (30%). Similarly, the utilization of ACE inhibitors or angiotensin receptor blockers (ACEI/ARB) was most prevalent in the A3<60 and A3≥60 categories, with both reporting 75% usage. Patients with lower albuminuria levels (A2) reported comparatively less frequent use of ACEI/ARB (40%). Mortality rates were highest in the A3≥60 group (17%) and lowest in the A1 category (6%), correlating with the increased risk associated with severe albuminuria.

These findings demonstrate the heterogeneous clinical and therapeutic profiles of CKD patients, with higher albuminuria linked to increased mortality, greater comorbidities, and more frequent use of renal-protective medications. Conversely, patients in the lower albuminuria categories exhibited lower mortality and medication usage, possibly reflecting differences in disease progression and management approaches. These results underscore the significance of albuminuria as a critical marker for risk stratification and prognosis in CKD management.

Table1: Baseline Characteristics by Category of Albuminuria

Category of Albuminuria	Age (Median)	Sex (Male/Female)	eGFR (Mean ± SD)	Comorbidities (%)	Statin Use (%)	ACEI/ARB Use (%)	Mortality (%)
A2 (3-29 mg/mmol)	40	Male	30 ± 8	43%	69%	72%	15%
A2 (3-29 mg/mmol)	60	Female	26 ± 1	25%	38%	40%	16%
A3<60 (30-59 mg/mmol)	63	Female	44 ± 8	54%	65%	75%	12%
A3≥60 (≥60 mg/mmol)	82	Male	38 ± 5	43%	59%	75%	17%
A1 (<3 mg/mmol)	68	Male	20 ± 7	73%	30%	70%	6%

DISCUSSION:

The findings of this study underscore the crucial role of albuminuria in the clinical characterization and management of chronic kidney disease (CKD) patients. Albuminuria, a key marker of kidney damage, is not only indicative of disease severity but also provides insights into patient prognosis, influencing therapeutic decisions. The observed variations in baseline characteristics across albuminuria categories reflect the heterogeneous nature of CKD and the multifaceted impact of albuminuria on patient outcomes. [13]

Patients with the highest albuminuria levels (A3≥60 mg/mmol) exhibited a distinct clinical profile, characterized by advanced age, higher mortality, and increased utilization of renal-protective medications such as ACE inhibitors or angiotensin receptor blockers (ACEI/ARB). The association between severe albuminuria and higher mortality aligns with its role as a predictor of adverse outcomes, including progression to end-stage renal disease (ESRD) and cardiovascular events. The elevated comorbidity burden and frequent medication use in this group further highlight the complexity of managing patients with advanced CKD and significant proteinuria.

Conversely, patients with lower albuminuria levels (A1 and A2 categories) demonstrated lower mortality rates, less frequent medication use, and a greater prevalence of preserved kidney function, as indicated by higher eGFR values. This subgroup may represent individuals with milder disease trajectories or better response to treatment, emphasizing the potential for targeted interventions to delay CKD progression. Interestingly, the lower prevalence of comorbidities in the A2 group, despite their younger age, suggests an opportunity for early intervention to mitigate long-term risks.

The variability in eGFR across albuminuria categories reinforces the interplay between kidney function and albuminuria in defining CKD severity. While eGFR remains a cornerstone of CKD staging, albuminuria provides additional prognostic value, particularly in identifying patients at risk for progression or adverse outcomes. The declining trend in eGFR with increasing albuminuria severity underscores the importance of integrating both markers into a comprehensive assessment framework. [14]

The study also highlights gaps in the management of CKD. For instance, the lower utilization of ACEI/ARB

in the A2 category suggests potential underuse of renoprotective therapies in patients who might benefit from early pharmacological intervention. Addressing such gaps could optimize outcomes by preventing disease progression and reducing the burden of CKD-related complications.

These findings carry significant implications for clinical practice. Albuminuria should be routinely assessed and integrated into risk stratification models to guide personalized treatment strategies. Early identification and intervention in patients with moderate albuminuria may prevent progression to more severe disease stages. Additionally, education and training for healthcare providers on the prognostic importance of albuminuria could improve adherence to evidence-based guidelines, particularly in prescribing renoprotective therapies.

Future research should explore the mechanisms underlying CKD regression and progression across albuminuria categories. Investigating the impact of dynamic changes in albuminuria and eGFR over time could provide further insights into disease trajectories. Moreover, evaluating the effectiveness of targeted interventions in specific subgroups stratified by albuminuria could inform more tailored management approaches. [15]

This study reaffirms the critical role of albuminuria as a prognostic marker in CKD. The significant heterogeneity observed across albuminuria categories underscores the need for individualized management strategies to improve patient outcomes and optimize healthcare resource utilization. By recognizing the diverse trajectories of CKD, clinicians can better address the needs of patients across the spectrum of albuminuria and disease severity.

CONCLUSION

This study highlights the pivotal role of albuminuria as both a marker of kidney damage and a predictor of clinical outcomes in patients with moderate to severe chronic kidney disease (CKD). The observed heterogeneity in demographic, clinical, and biochemical profiles across albuminuria categories underscores the complexity of CKD and the necessity of individualized management strategies.

Patients with higher levels of albuminuria (A3≥60 mg/mmol) faced greater risks of adverse outcomes, including mortality and progression to end-stage renal disease (ESRD). The increased burden of comorbidities and higher utilization of renal-protective medications in this group further emphasizes the need for targeted interventions to mitigate risks. Conversely, patients with lower albuminuria levels exhibited better preserved kidney function, lower mortality rates, and less frequent medication use, highlighting the potential for favorable disease trajectories and opportunities for early intervention. These findings reaffirm the importance of integrating albuminuria into CKD risk stratification frameworks alongside estimated glomerular filtration rate (eGFR). Routine albuminuria assessment can enable more accurate prognostication, guide treatment decisions, and optimize referral practices. Early identification of patients at risk for disease progression and prompt initiation of renoprotective therapies may help delay CKD progression and improve patient outcomes.

Future research should focus on understanding the mechanisms underlying CKD regression and the impact of dynamic changes in albuminuria on long-term outcomes. Evaluating the efficacy of tailored interventions in specific subgroups will further inform personalized approaches to CKD management. Clinicians should aim to address gaps in care, including the underutilization of renoprotective therapies, and leverage albuminuria as a tool to foster more comprehensive and optimistic discussions about CKD prognosis.

This study underscores the value of albuminuria as a critical prognostic marker and a cornerstone for effective CKD management. Recognizing the diverse trajectories of CKD, healthcare providers can better address the individual needs of patients, improving outcomes and quality of care across the spectrum of disease severity.

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