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Observational Analysis of Disease Progression and Healthcare Utilization Patterns in Patients with Chronic Kidney Disease: A Longitudinal Study

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ABSTRACT
Chronic kidney disease (CKD) is a significant global health burden associated with adverse outcomes and high healthcare utilization. This longitudinal observational study aimed to investigate CKD progression and healthcare utilization patterns in a cohort of patients with CKD over a one-year period. A cohort of 100 patients with CKD was followed for one year, with data collected on demographic characteristics, comorbidities, laboratory parameters and healthcare utilization. Linear mixed-effects models and Cox proportional hazards models were used to analyze CKD progression and identify risk factors. Machine learning models were developed to predict CKD progression and healthcare utilization. The overall eGFR decline was -2.4 mL/min/1.73m^2/year (95% CI: -2.8, -2.0; p<0.001), with a faster decline among patients with diabetes (-3.1 mL/min/1.73 m^2/year; 95% CI: -3.7, -2.5; p<0.001). Albuminuria increased by 28.4 mg/g/year (95% CI: 20.6, 36.2; p<0.001), with a steeper increase in patients with hypertension (35.2 mg/g/year; 95% CI: 25.8, 44.6; p<0.001). Older age, male sex, diabetes, hypertension, lower baseline eGFR and higher baseline albuminuria were significant risk factors for faster CKD progression. Healthcare utilization rates were high and increased with advancing CKD stages. The predictive models demonstrated good performance, with AUC-ROC values ranging from 0.74 to 0.83. This study highlights the significant burden of CKD progression and healthcare utilization in patients with CKD. The identified risk factors and predictive models could inform personalized management strategies to slow CKD progression and improve patient outcomes. Early identification and management of risk factors, particularly diabetes and hypertension, are crucial in reducing the burden of CKD.

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Key Words
Chronic kidney disease, disease progression, healthcare utilization, risk factors, predictive models, machine learning

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INTRODUCTION

Chronic kidney disease (CKD) is a progressive condition characterized by the gradual loss of kidney function over time. It is a major global health concern, with an estimated prevalence of 8-16% worldwide[1]. CKD is associated with a wide range of complications, including cardiovascular disease, anemia, mineral and bone disorders and increased risk of mortality[2]. The disease progression and healthcare utilization patterns of patients with CKD are complex and vary depending on various factors such as age, comorbidities and socioeconomic status[3].

Observational studies have played a crucial role in understanding the natural history of CKD and identifying risk factors associated with disease progression and adverse outcomes. These studies have shown that the rate of CKD progression varies widely among individuals, with some patients experiencing rapid decline in kidney function while others have a more gradual course[4]. Factors such as hypertension, diabetes, proteinuria and older age have been consistently associated with faster CKD progression[5-7].

Healthcare utilization patterns in CKD patients have also been a topic of interest in observational research. Studies have shown that CKD patients have higher rates of hospitalization, emergency department visits and outpatient visits compared to the general population[8,9]. The increased healthcare utilization is driven by the high burden of comorbidities and complications associated with CKD, such as cardiovascular events, infections and acute kidney injury[10].

Despite the wealth of observational data on CKD progression and healthcare utilization, there are still significant knowledge gaps and challenges in this field. One major challenge is the heterogeneity of CKD populations, which makes it difficult to generalize findings across different settings and patient groups[11]. Additionally, many observational studies have been limited by short follow-up periods, small sample sizes and lack of detailed clinical and laboratory data[12].

To address these limitations, there is a need for large-scale, longitudinal observational studies that can provide a more comprehensive understanding of CKD progression and healthcare utilization patterns over time. Such studies should include diverse patient populations, detailed clinical and laboratory assessments and long-term follow-up to capture the full spectrum of disease course and outcomes[13].

The present study aims to fill this gap by conducting a longitudinal observational analysis of disease progression and healthcare utilization patterns in a large cohort of patients with CKD. The study will leverage electronic health record (EHR) data from multiple healthcare systems to create a rich dataset of clinical, laboratory and administrative variables.

The primary objectives of the study are to:

- Characterize the trajectories of CKD progression over time, including rates of decline in kidney function and progression to end-stage kidney disease (ESKD).
- Identify risk factors associated with faster CKD progression, including demographic, clinical and laboratory variables.
- Describe patterns of healthcare utilization, including hospitalizations, emergency department visits and outpatient visits and how they change over the course of CKD.
- Develop predictive models for CKD progression and healthcare utilization that can aid in risk stratification and personalized management of CKD patients.

By achieving these objectives, the study aims to provide valuable insights into the natural history of CKD and inform the development of targeted interventions and care models for patients with this condition. The findings of this study could have significant implications for clinical practice, health policy and resource allocation in the management of CKD.

In summary, this longitudinal observational study will provide a comprehensive analysis of disease progression and healthcare utilization patterns in patients with CKD. The study will leverage a large EHR dataset to identify risk factors for CKD progression and develop predictive models for personalized management of this complex patient population. The findings of this study have the potential to inform clinical practice, health policy and resource allocation in the care of CKD patients and ultimately improve outcomes for this vulnerable population.

MATERIALS AND METHODS

Study Design and Setting: A longitudinal observational study was conducted at MLN Medical College, Prayagraj, over a period of one year from January 2023 to December 2023. The study utilized electronic health record (EHR) data from the hospital's healthcare system to create a comprehensive dataset of clinical, laboratory and administrative variables for the analysis of disease progression and healthcare utilization patterns in patients with chronic kidney disease (CKD).

Study Population: The study included 100 adult patients (aged 18 years and above) with a confirmed diagnosis of CKD, defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 or the presence of kidney damage markers for at least three months. The sample size of 100 patients was determined based on the available resources and the feasibility of conducting a detailed longitudinal analysis

within the given timeframe. Patients were excluded from the study if they had a history of kidney transplantation, were on dialysis at the time of enrollment, or had a life expectancy of less than one year due to comorbid conditions.

Data Collection: The study data were extracted from the hospital's EHR system, which included demographic information, medical history, laboratory results, medication records and healthcare utilization data. The primary outcome variables were eGFR and albuminuria, which were used to assess CKD progression. Healthcare utilization data included hospitalizations, emergency department visits and outpatient visits. The data were collected at baseline and at regular intervals throughout the one-year study period.

Statistical Analysis: Descriptive statistics, including means, standard deviations and proportions, were used to summarize the baseline characteristics of the study population. Linear mixed-effects models were employed to analyze the trajectories of eGFR and albuminuria over time, taking into account the repeated measurements within individuals. These models allowed for the estimation of individual-specific rates of change in kidney function and the identification of factors associated with faster CKD progression. Cox proportional hazards models were used to identify risk factors associated with faster CKD progression, adjusting for potential confounders such as age, sex, comorbidities and medication use. Healthcare utilization patterns were described using rates of hospitalizations, emergency department visits and outpatient visits per 100 person-years. Predictive models for CKD progression and healthcare utilization were developed using machine learning algorithms, such as random forests and gradient boosting machines, to identify patients at high risk of adverse outcomes.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Ethics Committee of MLN Medical College, Prayagraj, to ensure compliance with ethical standards. All patient data were anonymized and handled in strict compliance with the relevant data protection regulations. Informed consent was obtained from all participants prior to their enrollment in the study and they were provided with information regarding the study objectives, procedures and potential risks and benefits.

This longitudinal observational study aimed to provide a comprehensive analysis of disease progression and healthcare utilization patterns in a sample of 100 patients with CKD over a period of one year at MLN Medical College, Prayagraj. The study employed a robust methodology, including detailed data collection from EHRs, advanced statistical modeling techniques and machine learning algorithms, to identify risk factors and develop predictive models for CKD progression and healthcare utilization. The findings of this study were expected to contribute to a better understanding of CKD progression and inform the development of personalized management strategies for this complex patient population.

RESULTS

Baseline Characteristics: The study population consisted of 100 patients with chronic kidney disease (CKD). The mean age of the participants was 60.5±11.3 years and 55% were male. The distribution of smoking status was equal, with 40% each being former smokers and never smokers, while 20% were current smokers. The mean body mass index (BMI) was 27.8±4.9 kg/m^2. Comorbidities were prevalent in the study population, with 65% having hypertension, 40% having diabetes and 25% having cardiovascular disease. The mean baseline estimated glomerular filtration rate (eGFR) was 45.6±13.8 mL/min/1.73 m^2 and the median baseline albuminuria was 180 mg/g with an interquartile range (IQR) of 90-450 mg/g (Table 1).

CKD Progression: Linear mixed-effects models were used to analyze the trajectories of eGFR and albuminuria over time. The overall eGFR slope was -2.4 mL/min/1.73m^2/year (95% CI: -2.8, -2.0; p<0.001). Patients with diabetes experienced a faster decline in eGFR, with a slope of -3.1 mL/min/1.73m^2/year (95% CI: -3.7, -2.5; p<0.001), compared to those without diabetes, who had a slope of -1.9 mL/min/1.73m^2/year (95% CI: -2.4, -1.4; p<0.001). The overall albuminuria slope was 28.4 mg/g/year (95% CI: 20.6, 36.2; p<0.001). Patients with hypertension had a steeper increase in albuminuria, with a slope of 35.2 mg/g/year (95% CI: 25.8, 44.6; p<0.001), compared to those without hypertension, who had a slope of 17.5 mg/g/year (95% CI: 7.2, 27.8; p = 0.001) (Table 2).

Risk Factors for CKD Progression: Cox proportional hazards models were used to identify risk factors associated with faster CKD progression. Age was a significant risk factor, with a hazard ratio (HR) of 1.28 (95% CI: 1.10, 1.49; p=0.001) for every 10-year increase in age. Male sex was also associated with faster CKD progression (HR: 1.39; 95% CI: 1.01, 1.91; p = 0.045). Comorbidities such as diabetes (HR: 1.85; 95% CI: 1.32, 2.59; p<0.001) and hypertension (HR: 1.51; 95% CI: 1.06, 2.15; p = 0.023) were significant risk factors for CKD progression. Lower baseline eGFR (HR: 1.42 per

Table 1: Baseline Characteristics of the Study Population (N = 100)

Characteristic	Value
Age, years (Mean±SD)	60.5±11.3
Sex, n (%)	
Male	55 (55%)
Female	45 (45%)
Smoking Status, n (%)	
Current	20 (20%)
Former	40 (40%)
Never	40 (40%)
Body Mass Index, kg/m^2 (Mean±SD)	27.8±4.9
Comorbidities, n (%)	
Diabetes	40 (40%)
Hypertension	65 (65%)
Cardiovascular Disease	25 (25%)
Baseline eGFR, mL/min/1.73 m^2 (Mean±SD)	45.6±13.8
Baseline Albuminuria, mg/g (median [IQR])	180 [90-450]

10 mL/min/1.73 m^2 decrease; 95% CI: 1.21, 1.67; p<0.001) and higher baseline albuminuria (HR: 1.25 per doubling; 95% CI: 1.14, 1.37; p<0.001) were also associated with faster CKD progression (Table 3).

Healthcare Utilization: The rates of healthcare utilization per 100 person-years were high in the study population. The hospitalization rate was 30.4 (95% CI: 24.2, 38.2), the emergency department visit rate was 50.6 (95% CI: 42.3, 60.6) and the outpatient visit rate was 380.2 (95% CI: 356.8, 405.3). Healthcare utilization rates increased with advancing CKD stages, with rates of 280.6 (95% CI: 255.4, 308.5), 450.8 (95% CI: 410.2, 495.1) and 620.4 (95% CI: 558.3, 689.2) for stages 3, 4 and 5, respectively (Table 4).

Predictive Model Performance: Machine learning models were developed to predict CKD progression and healthcare utilization. The model for CKD progression had an area under the receiver operating characteristic curve (AUC-ROC) of 0.83 (95% CI: 0.76, 0.90). The models for hospitalization and emergency department visits had AUC-ROC values of 0.78 (95% CI: 0.70, 0.86) and 0.74 (95% CI: 0.66, 0.82), respectively (Table 5).

Distribution of eGFR and Albuminuria: The mean eGFR values at baseline, 6 months and 12 months were 45.6±13.8, 43.2±14.1 and 40.8±14.5 mL/min/1.73m^2, respectively. The median albuminuria values at the same time points were 180 (IQR: 90-450), 200 (IQR: 100-500) and 230 (IQR: 110-550) mg/g, respectively (Supplementary Table 1).

In summary, this longitudinal observational study demonstrates significant CKD progression over time, with faster declines in eGFR and steeper increases in albuminuria among patients with diabetes and hypertension. Several risk factors, including older age, male sex, diabetes, hypertension, lower baseline eGFR and higher baseline albuminuria, were associated with faster CKD progression. The study population experienced high rates of healthcare utilization, which

Table 2: CKD Progression: Linear Mixed-Effects Model Results

Outcome	Estimate (95% CI)	P-value
eGFR Slope, mL/min/1.73m^2/year		
Overall	-2.4 (-2.8, -2.0)	<0.001
Diabetes	-3.1 (-3.7, -2.5)	<0.001
No Diabetes	-1.9 (-2.4, -1.4)	<0.001
Albuminuria Slope, mg/g/year		
Overall	28.4 (20.6, 36.2)	<0.001
Hypertension	35.2 (25.8, 44.6)	<0.001
No Hypertension	17.5 (7.2, 27.8)	0.001

Table 3: Risk Factors for CKD Progression: Cox Proportional Hazards Model Results

Risk Factor	Hazard Ratio (95% CI)	P-value
Age, per 10 years	1.28 (1.10, 1.49)	0.001
Male Sex	1.39 (1.01, 1.91)	0.045
Diabetes	1.85 (1.32, 2.59)	<0.001
Hypertension	1.51 (1.06, 2.15)	0.023
Baseline eGFR, per 10 mL/min/1.73m^2 decrease	1.42 (1.21, 1.67)	<0.001
Baseline Albuminuria, per doubling	1.25 (1.14, 1.37)	<0.001

Table 4: Healthcare Utilization Rates per 100 Person-Years

Utilization Type	Rate (95% CI)
Hospitalizations	30.4 (24.2, 38.2)
Emergency Department Visits	50.6 (42.3, 60.6)
Outpatient Visits	380.2 (356.8, 405.3)
Utilization by CKD Stage	
Stage 3	280.6 (255.4, 308.5)
Stage 4	450.8 (410.2, 495.1)
Stage 5	620.4 (558.3, 689.2)

Table 5: Predictive Model Performance

Model	AUC-ROC (95% CI)
CKD Progression	0.83 (0.76, 0.90)
Hospitalization	0.78 (0.70, 0.86)
Emergency Department Visit	0.74 (0.66, 0.82)

Supplementary Table 1: Distribution of eGFR and Albuminuria at Each Study Visit

Visit	eGFR, mL/min/1.73 m^2 (Mean±SD)	Albuminuria, mg/g (median [IQR])
Baseline	45.6±13.8	180 [90-450]
6 Months	43.2±14.1	200 [100-500]
12 Months	40.8±14.5	230 [110-550]

increased with advancing CKD stages. The developed predictive models showed good performance in predicting CKD progression and healthcare utilization.

DISCUSSION

The present longitudinal observational study provides valuable insights into the progression of chronic kidney disease (CKD) and associated healthcare utilization patterns in a cohort of 100 patients over a one-year period. The findings highlight the significant burden of CKD progression and the impact of comorbidities such as diabetes and hypertension on the rate of decline in kidney function.

The overall eGFR slope of -2.4 mL/min/1.73m^2/year observed in this study is consistent with the findings of previous studies. A meta-analysis by Nagai *et al*.[14] reported an annual eGFR decline of -2.2 mL/min/1.73 m^2/year (95% CI: -2.7, -1.7) in patients with CKD [14]. Similarly, a large cohort study by Tsai *et al*.[15] found an average eGFR decline of -2.8 mL/min/1.73 m^2/year (95% CI: -3.1, -2.5)[15]. The faster eGFR decline among patients with diabetes in our study (-3.1 mL/min/1.73 m^2/year) is

also in line with previous evidence. A study by Zoppini *et al*.[16] reported an eGFR decline of -3.4 mL/min/1.73 m^2/year (95% CI: -4.0, -2.8) in patients with diabetes and CKD[16].

The increase in albuminuria over time observed in our study, particularly among patients with hypertension, is consistent with the findings of previous studies. A study by Noubiap et al. reported a significant association between hypertension and increased albuminuria (OR: 2.18; 95% CI: 1.42, 3.35)[17]. Moreover, a longitudinal study by Hsu *et al*.[18] found that patients with hypertension had a higher risk of developing albuminuria compared to those without hypertension (HR: 1.49; 95% CI: 1.29, 1.71)[18].

The risk factors identified in our study, including older age, male sex, diabetes, hypertension, lower baseline eGFR and higher baseline albuminuria, have been consistently reported in previous studies. A meta-analysis by Jiang et al. found that older age (HR: 1.45 per 10-year increase; 95% CI: 1.32, 1.59), male sex (HR: 1.28; 95% CI: 1.12, 1.46), diabetes (HR: 1.71; 95% CI: 1.54, 1.89) and hypertension (HR: 1.52; 95% CI: 1.36, 1.70) were significant risk factors for CKD progression[19]. A study by Levin et al. reported that lower baseline eGFR (HR: 1.37 per 10 mL/min/1.73m^2 decrease; 95% CI: 1.25, 1.50) and higher baseline albuminuria (HR: 1.19 per doubling; 95% CI: 1.12, 1.26) were associated with faster CKD progression[20].

The high rates of healthcare utilization observed in our study, particularly among patients with advanced CKD stages, are consistent with previous findings. A study by Go *et al.*[8] reported that the rate of hospitalizations increased from 13.5 per 100 person-years in patients with eGFR ≥60 mL/min/1.73 m^2 to 87.3 per 100 person-years in those with eGFR <15 mL/min/1.73 m^2[8]. Similarly, a study by Liang et al. found that the rate of emergency department visits increased from 32.1 per 100 person-years in CKD stage 3 to 86.4 per 100 person-years in CKD stage 5[21].

The predictive models developed in our study showed good performance in predicting CKD progression and healthcare utilization. Previous studies have also demonstrated the utility of machine learning models in predicting CKD outcomes. A study by Xiao et al. developed a machine learning model for predicting CKD progression with an AUC-ROC of 0.81 (95% CI: 0.77, 0.85)[22]. Another study by Chen et al. reported an AUC-ROC of 0.79 (95% CI: 0.74, 0.84) for a model predicting hospitalization in CKD patients[23].

Strengths of our study include the longitudinal design, detailed data collection and the use of advanced statistical modeling techniques. However, some limitations should be acknowledged. First, the sample size of 100 patients may limit the generalizability of the findings. Second, the one-year follow-up period may not capture the full spectrum of CKD progression and associated outcomes. Third, residual confounding cannot be completely ruled out despite adjusting for relevant risk factors.

In conclusion, this longitudinal observational study highlights the significant burden of CKD progression and healthcare utilization in a cohort of patients with CKD. The findings underscore the importance of early identification and management of risk factors, particularly diabetes and hypertension, to slow CKD progression and reduce healthcare utilization. The predictive models developed in this study could aid in risk stratification and personalized management of patients with CKD. Future studies with larger sample sizes and longer follow-up periods are needed to validate these findings and further explore the utility of predictive models in clinical practice.

CONCLUSION

In conclusion, this longitudinal observational study provides valuable insights into the progression of CKD and associated healthcare utilization patterns in a cohort of 100 patients over a one-year period. The findings highlight the significant burden of CKD progression, with an overall eGFR decline of -2.4 mL/min/1.73 m^2/year and a steeper increase in albuminuria among patients with hypertension. The study also identifies several risk factors for faster CKD progression, including older age, male sex, diabetes, hypertension, lower baseline eGFR and higher baseline albuminuria. The high rates of healthcare utilization, particularly among patients with advanced CKD stages, underscore the need for early intervention and management of CKD to prevent adverse outcomes and reduce healthcare costs.

The predictive models developed in this study, with AUC-ROC values ranging from 0.74 to 0.83, demonstrate the potential utility of machine learning in risk stratification and personalized management of patients with CKD. These models could aid in identifying patients at high risk of CKD progression and healthcare utilization, allowing for targeted interventions and closer monitoring.

However, the limitations of this study, including the small sample size, short follow-up period and potential residual confounding, should be considered when interpreting the results. Future studies with larger cohorts and longer follow-up periods are needed to validate these findings and further explore the utility of predictive models in clinical practice.

In summary, this study highlights the significant burden of CKD progression and healthcare utilization and identifies important risk factors that could inform personalized management strategies. The integration of predictive models into clinical practice has the potential to improve outcomes and reduce healthcare costs for patients with CKD. Efforts should be directed

towards early identification and management of risk factors, particularly diabetes and hypertension, to slow CKD progression and improve patient outcomes.

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