# Risk Factors of Rehospitalization in Chronic Kidney Disease Patients: An Observational Study

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**ABSTRACT**

**Objective:** The objective of the study was to determine the factors associated with early rehospitalization among patients with chronic kidney disease.

**Methods:** This was a case-control study conducted at the Department of Nephrology, The Kidney Centre, Postgraduate Training Institute, Karachi, Pakistan. Each group (rehospitalization and no rehospitalization) had 63 subjects. The subjects were deemed eligible if they were known cases of chronic kidney disease, above 30 years of age, either gender, cases with rehospitalization within 30 days of discharge from the hospital, and controls with no rehospitalization within 30 days of discharge from the hospital. Odds ratio was calculated to observe the strength of association between factors and rehospitalization.

**Results:** A total of 126 patients were enrolled. The mean age of patients in cases and controls was $69.5 \pm 6.7$ and $62.0 \pm 9.6$ years, respectively. Diabetes mellitus and heart failure were more common in the cases cohort in comparison with controls (69.8% vs. 34.9% and 50.8% vs. 7.9%, respectively). Among cases, mean serum hemoglobin and albumin levels were statistically lower in contrast to controls ($10.0 \pm 0.8$ vs. $12.2 \pm 1.0$ g/dL, $P < .0001$ and $3.0 \pm 0.6$ versus $3.9 \pm 0.5$ mg/dL, respectively, $P < .0001$). Serum creatinine level was significantly higher in cases than in controls ($2.8 \pm 0.4$ vs. $1.7 \pm 0.3$ mg/dL, respectively, $P < .0001$). The multivariate association of comorbidities with rehospitalization of chronic kidney disease patients was studied and found significant for diabetes mellitus (OR 7.07, CI 2.73-18.29, $P < .0001$) and heart failure (odds ratio 18.72, CI 5.72-61.25, $P < .0001$).

**Conclusion:** The study showed that serum hemoglobin and albumin were significantly lower in rehospitalized cases. Furthermore, diabetes mellitus and heart failure were observed as significant risk factors for early rehospitalization.

**Keywords:** Chronic kidney disease, complications, early rehospitalization, Pakistan

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## INTRODUCTION

Chronic kidney disease (CKD) is one of the most common and burgeoning diseases worldwide, contributing to significantly high morbidity and mortality. In fact, it has been reported that CKD patients are prone to frequent hospitalization owing to the long-standing nature of disease and are at risk of high mortality in comparison with the general population. Moreover, the death rate for CKD is globally diverse due to regional and even countrywide dialysis practices, clinical and demographic features of patients, and underlying cardiovascular comorbidities.[1]

Despite comparatively low mortality in the Asian region than in America and European nations, patients with CKD, across the globe, bear the burden of high mortality than the general populace.[1] In contrast to patients without any kidney disease, CKD patients have a high

propensity for hospital admission and succeeding frequent readmissions. According to one report from the United States, approximately one-fifth (19%) of CKD patients are rehospitalized within 1 month of discharge.[2]

Readmission to the hospital poses a significant emotional burden to patients and their caregivers. Several international studies have reported higher rehospitalization among CKD patients with complications like hypertension, dyslipidemia, heart failure, and diabetes. Diabetes mellitus was significantly higher among rehospitalized CKD patients as compared to non-rehospitalized patients.[3]

Pakistan is heavily burdened with CKD.[4-6] A thorough literature search revealed that studies determining the leading factors for rehospitalization among CKD patients are scarce in our region. For a nation, like Pakistan, with fluctuating economy and financial uncertainties, it is important that the associated risk factors should be determined. Moreover, the available data show conflicting results.[3,7] Therefore, the present study may help to resolve the controversy and thereby decision could be taken to label certain factors as possibly associative.

## METHODS
***Study Settings:*** The study was conducted in the Department of Nephrology, The Kidney Centre, Postgraduate Training Institute, Karachi.

***Study Duration:*** The study duration was 7 months from October 2018 to April 2019.

***Study Design:*** This was a case-control study.

***Sample Size:*** It was calculated on the following parameters: (1) Dyslipidemia in early rehospitalization group was 13.6%,[7] (2) dyslipidemia in no early rehospitalization group was 34.9%,[7] (3) power of the test 80%, and (4) significance level 5%. The final sample size for each group (rehospitalization and no rehospitalization) was 63 subjects, with a total sample size of 126 CKD patients for the study.

***Sampling Technique:*** Non-probability consecutive sampling was used for the study.

***Eligibility Criteria:*** The subjects were deemed eligible if they are (1) known cases of CKD, (2) above 30 years of age, (3) of

### MAIN POINTS

- Serum hemoglobin and albumin were significantly lower in rehospitalized cases.
- No association between gender and dyslipidemia and risk of early rehospitalization was onserved.
- Diabetes mellitus and heart failure were significantly associated with risk of early rehospitalization.

either gender, (4) cases with rehospitalization within 30 days of discharge from the hospital, and (5) controls with no rehospitalization within 30 days of discharge from the hospital. Non-consenting patients, patients with CKD stages G2 and G5 and with associated diseases like liver cirrhosis and chronic obstructive pulmonary disease were excluded.

### Data Collection Procedure
This study was conducted after getting approval from the (REU) of College of Physician and Surgeon of Pakistan. Eligible patients who met the inclusion criteria were enrolled in the study. Before enrolment, the pros and cons of the study were explained. Signed informed consent was also taken from all patients. Subjects were labeled as cases on rehospitalization within 30 days of discharge from the hospital and controls with no rehospitalization within 30 days of discharge from the hospital and attending outpatient department for scheduled follow-up. Information regarding age, gender, weight (measured on a bathroom scale and recorded nearest to 0.1 kg, measured without shoes and in light clothes), height (measured on stadiometer without shoes and hat/cap in cm and later converted to meters by dividing cm by 100), body mass index (BMI, weight in kg/height in m$^2$), and all leading factors like diabetes, hypertension, heart failure, and dyslipidemia were noted for both cases and controls. Serum hemoglobin, albumin, and creatinine levels were also noted at the time of rehospitalization, and at the same time, the data were collected from the no rehospitalization group. All information was entered in a predesigned proforma.

### Statistical Analysis
Data were analyzed by using the Statistical Package for the Social Sciences version 21.0 (IBM SPSS Corp.; Armonk, NY, USA). Mean and standard deviation was calculated for age, weight, height, BMI, serum hemoglobin, albumin, and creatinine levels. Frequency and percentages were calculated for gender and leading factors like diabetes, hypertension, heart failure, and dyslipidemia. Comparison was done to see the association of related factors with early and no rehospitalization by applying binary logistic regression analysis. *P* value <.05 was taken as statistically significant. Odds ratio was calculated to observe the strength of association between factors and rehospitalization. Serum hemoglobin, albumin, and creatinine levels were compared between rehospitalization and no rehospitalization groups by applying unpaired *t*-test. Effect modifiers like age, gender, residence (rural/urban), and BMI were addressed through stratification. Post-stratification chi-square test was applied at a significance level of 0.05.

### RESULTS
A total of 126 patients of either gender with age more than 30 years meeting inclusion criteria of study were included in the study to determine the factors associated with early rehospitalization among patients with CKD. In both study groups, group A (case group—early rehospitalization) and group B (control

**Table 1.** Descriptive Statistics of Study Participants (n = 126)

| Variables | Cases (n = 63) | Controls (n = 63) |
|---|---|---|
| Age (years, mean ± SD) | 69.5 ± 6.7 | 62.0 ± 9.6 |
| Gender (n, %) | | |
|    Male | 40 (63.5) | 37 (58.7) |
|    Female | 23 (36.5) | 26 (41.3) |
| BMI (kg/m², mean ± SD) | 24.5 ± 4.3 | 23.0 ± 4.8 |
| Diabetes mellitus (n, %) | 44 (69.8) | 22 (34.9) |
| Heart failure (n, %) | 32 (50.8) | 5 (7.9) |
| Dyslipidemia (n, %) | 11 (17.5) | 37 (30.2) |
| Serum hemoglobin (g/dL, mean ± SD) | 10.0 ± 0.8 | 12.2 ± 1.0 |
| Serum albumin (mg/dL, mean ± SD) | 3.0 ± 0.6 | 3.9 ± 0.5 |
| Serum creatinine (mg/dL, mean ± SD) | 2.8 ± 0.4 | 1.7 ± 0.3 |

SD, standard deviation.

**Table 2.** Comparison of Mean Serum Hemoglobin, Albumin, and Creatinine Levels of Study Participants (n = 126)

| Variables | Cases (n = 63) | Controls (n = 63) | P |
|---|---|---|---|
| Serum hemoglobin (g/dL, mean ± SD) | 10.0 ± 0.8 | 12.2 ± 1.0 | **<.0001*** |
| Serum albumin (mg/dL, mean ± SD) | 3.0 ± 0.6 | 3.9 ± 0.5 | **<.0001*** |
| Serum creatinine (mg/dL, mean ± SD) | 2.8 ± 0.4 | 1.7 ± 0.3 | **<.0001*** |

Unpaired *t*-test was applied.
***Significant at .05 level.

group—no early rehospitalization), 63 patients were included. In group A, males were 63.5%, while in group B, there were 58.7% males. The demographic and clinical characteristics of the study participants are presented in Table 1.

The mean age of patients in cases and controls was 69.5 ± 6.7 and 62.0 ± 9.6 years, respectively. The mean weight and height of patients in cases were 66.4 ± 10.9 kg and 165.1 ± 6.7 cm, respectively *(data not shown)*. In controls, the mean weight and height of patients were 62.3 ± 11.8 kg and 165.0 ± 6.3 cm, respectively *(data not shown)*. Diabetes mellitus and heart failure were more common in cases cohort in comparison with controls (69.8% vs. 34.9% and 50.8% vs. 7.9%, respectively).
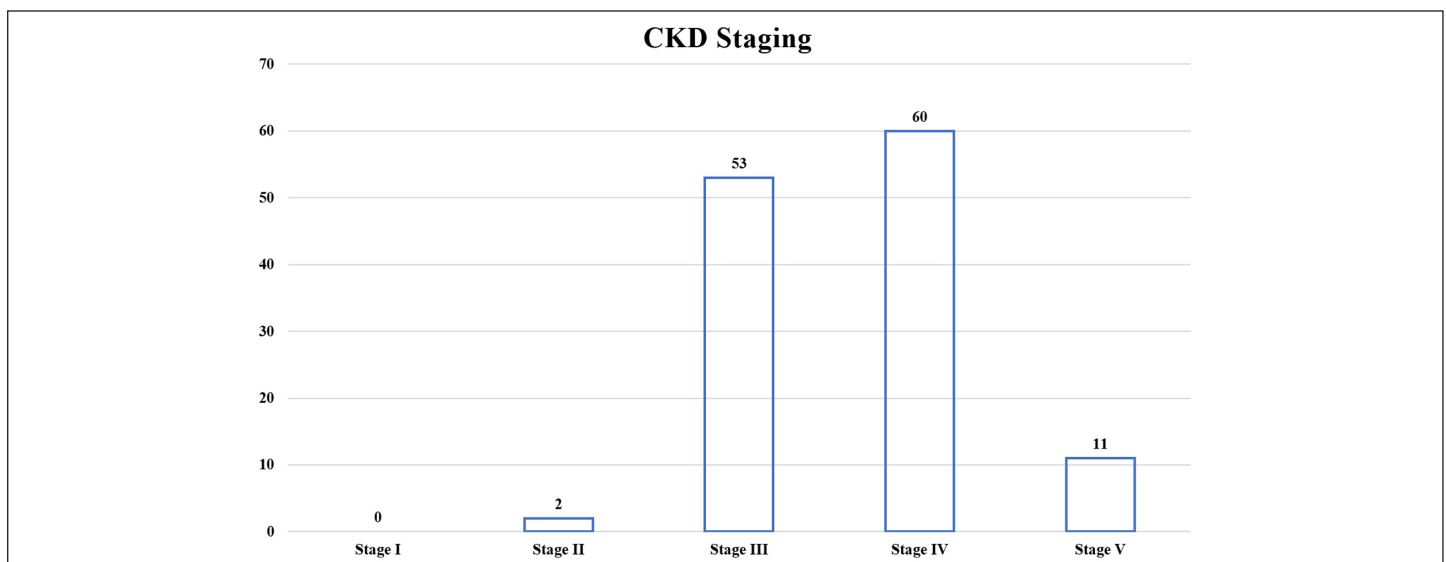
The mean BMI of cases and controls was 24.5 ± 4.3 and 23.0 ± 4.8 kg/m², respectively (Table 1). The mean estimated glomerular filtration rate (eGFR) value was 30.34 mL/min/1.73 m². The CKD staging was performed by CKD-EPI creatinine and has been shown in Figure 1.

Among cases, mean serum hemoglobin and albumin levels were statistically lower in contrast to controls (10.0 ± 0.8 vs. 12.2 ± 1.0 g/dL, *P* < .0001 and 3.0 ± 0.6 vs. 3.9 ± 0.5 mg/dL, respectively, *P* < .0001). Serum creatinine level was significantly higher in cases than in controls (2.8 ± 0.4 vs. 1.7 ± 0.3 mg/dL, respectively, *P* < .0001) (Table 2).

The association of gender and comorbidities with rehospitalization of CKD patients was studied and found that diabetes mellitus (OR 4.31, CI 2.04-9.10, *P* < .0001) and heart failure (OR 11.97, CI 4.23-33.82, *P* < .0001) were significantly associated. No significant association was found for gender (OR 1.22, CI 0.59-2.50, *P* = .584) and dyslipidemia (OR 0.49, CI 0.21-1.13, *P* = .094). On multivariate analysis, diabetes mellitus (OR 7.07, CI 2.73-18.29, *P* < .0001) and heart failure (OR 18.72, CI 5.72-61.25, *P* < .0001) showed significant association with risk of

**Figure 1.** CKD stage by CKD-EPI creatinine. CKD, chronic kidney disease.

**Table 3.** Univariate and Multivariate Logistic Regression of Association of Demographic and Clinical Characteristics with Rehospitalization of CKD Patients (n = 126)

| Variables | Univariate Analysis | | Multivariate Analysis | |
|---|---|---|---|---|
| | OR (95% CI) | *P* value | OR (95% CI) | *P* |
| **Gender** | | | | |
| Female | Reference | | - | |
| Male | 1.22 (0.59-2.50) | 0.584 | - | - |
| **Diabetes mellitus** | | | | |
| No | Reference | | Reference | |
| Yes | **4.31 (2.04-9.10)** | **<0.0001** | **7.07 (2.73-18.29)** | **<.0001** |
| **Heart failure** | | | | |
| No | Reference | | Reference | |
| Yes | **11.97 (4.23-33.82)** | **<0.0001** | **18.72 (5.72-61.25)** | **<.0001** |
| **Dyslipidemia** | | | | |
| No | Reference | | - | |
| Yes | 0.490 (0.21-1.13) | 0.098 | - | - |

OR, odds ratio.
***Significant at .05 level.

rehospitalization. Univariate and multivariate results of associations are presented in Table 3.

## DISCUSSION
Chronic kidney disease is a globally prevailing condition, and the numbers are increasing at high pace. Moreover, the count of end-stage kidney disease (ESKD) patients with failing kidneys and necessitating immediate and continuous dialysis has substantially heightened.[8] A handful of patients with no signs and symptoms of very early CKD has been reported in the literature,[9] and if unmanaged, these patients may go on to develop progressive kidney disease, culminating in ESKD, chronic dialysis, multiple comorbidities, transplantation, and eventually death. Chronic kidney disease has been demonstrated to be a key instigator of cardiovascular disease (CVD) morbidity. As such, it increases the risk of incidence of coronary heart disease and cerebrovascular accident in males and females, respectively.[10] From the financial and economic standpoint, CKD also escalates the burden on patients and country as a whole.[11] The hospitalization and rehospitalization associated with CKD significantly consume the resources that would otherwise be available for other patients.

Rehospitalization is common in CKD patients; however, it can be reduced. It has been categorically stated that nearly half of the rehospitalization can be avoided with apt interventions like appropriate early follow-up, devising volume managing approaches, giving optimal nutrition support, involving family members while developing a management plan, consulting palliative physicians for critically seriously ill CKD patients, planning goals of care in consultation with patients themselves, systematically introducing advance care support as outpatients, conceptualizing practices for patients with multiple chronic comorbidities like CVD, and rigorous treatment during the terminally ill stage.[12]

In the present study, we found that CKD patients with diabetes mellitus and heart failure were at increased risk of rehospitalization. Moreover, their serum albumin and hemoglobin levels were significantly low with high creatinine in comparison with controls. Metabolic syndrome like diabetes mellitus is one of the key risk factors associated with a decrease in kidney function. A study by Ninomiya et al[13] found that metabolic syndrome progression is directly associated with CKD progression. Diabetes mellitus also enhances the risk of infections associated with bacteria and therefore increases the risk of rehospitalization.[7] It means that if the lifestyle modifications are applied, then the eGFR can be improved which eventually will lead to reduced frequency of rehospitalization.

Kose et al[7] demonstrated that rehospitalization cohort has a significantly higher percentage (75%) of patients with diabetes mellitus in comparison to cohort with no rehospitalization.

Likewise, the frequency of heart failure was also high (55%) in the readmitted patients compared with the no readmission cohort. The plausible explanation of heart failure in rehospitalization cohort could be the compounding effect of renin-angiotensin aldosterone system, with elevation in blood pressure, fluid retention, and exacerbation of arteriosclerosis.[3] Literature suggests that the key risk factor for increasing burden of hospitalization in CKD is cardiovascular comorbidities, approximately one-fourth of the hospitalizations.[14,15] Furthermore, besides cardiovascular pathologies, infections are the key contributor (22% of hospitalizations),[14] and with low levels of albumin in rehospitalization cohort in the present study, this significantly increases the risk of high inflammation in such patients.[16] It is advisable that future actions should be concentrated at identifying underlying disease causes like cardiovascular and nutritional and managing them accordingly to reduce such rehospitalizations.

Our finding of significantly low albumin levels in rehospitalization cohort is also in agreement with the previous reports.[3,12] It is to be noted that reduced levels of albumin are linked with high systematic inflammation and malnutrition. This is very important as low albumin and resultant high inflammation will further potentiate the immunoinflammatory response within the body system. It provokes a vicious cycle of inflammation which definitely compromises and mandates vigilant management of such patients suffering

from multiple comorbidities. Therefore, while managing such patients, serum albumin cannot be ignored. It is a biomarker of nourishment in patients. Generally, serum albumin ≤3.5 g/dL suggests malnutrition.

## Limitations

The main limitation of our study was the small sample size. Other limitations of the present study include a single-center data and non-randomized study design. It was conducted in an urban setting; therefore, the results might not be generalizable to larger populations.

## CONCLUSION

The study showed that serum hemoglobin and albumin were significantly lower in rehospitalized cases. Furthermore, diabetes mellitus and heart failure were observed as significant risk factors for early rehospitalization. It is important to recognize and monitor all the factors associated with early rehospitalization as they may help in determining patient's prognosis. Also, measures should be taken to control modifiable factors like weight management and blood pressure in order to inhibit progression of CKD.

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