

Readmissions to a Nephrology Service in Abidjan: Prevalence and Risk Factors

Sery Patrick Diopoh, Serge Didier Konan^{*}, Kolo Claude Ouattara, Marie Dominique Kouadio, Donafologo Drissa Yeo, Kouame Hubert Yao

Department of Medicine and Medical Specialities, University Félix Houphouët-Boigny, Abidjan, Côte d'Ivoire Email: *sergedidier.konan@gmail.com, serydiopoh@gmail.com, mcsdashing@yahoo.fr, mariedomi.md@gmail.com, idrisyehau@gmail.com, yaohubert@yahoo.fr

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Abstract

Background: Readmission of patients with kidney disease is a reality in our practice setting. Objectives: To assess the prevalence of readmission and identify factors associated with readmission and death of readmitted patients. Materials and Methods: This was a retrospective study conducted from the 1st of October 2017 to the 31st of December 2019 in the nephrology department of Treichville Teaching Hospital. Results: During the study period, 1142 patients were admitted, of whom 154 patients were readmitted, representing a prevalence of 13.48%. The mean age of the patients was 42.31 [15; 77 years] and the sex ratio was 1.35 in favour of men. The unemployed were the most represented (24.78%). The average time between hospitalisations was 28.23 ± 21.83 days [3; 123 days]. Patients were readmitted within 30 days of discharge in 65.48% of cases, between 30 and 60 days in 23.90% and after 60 days in 10.62%. The uremic syndrome was the main reason for readmission (68, 14%). The causes of readmission were dominated by dialysis failure (82.30%), followed by complications of vascular access, notably dialysis catheter infection (10.60%). Mortality was 30.97%. Obstructive nephropathy (p = (0.029) and hypocalcaemia (p = 0.030) were associated with the risk of hospital mortality. Severe anaemia was associated with early readmission (p = 0.047)and hypertension with the risk of non-early readmission. Conclusion: The prevalence of readmission at hospitals is high. The causes are dominated by dialysis failure and dialysis catheter infection. Hence, there is an interest in improving accessibility to dialysis for patients and raising awareness on prevention and management of risk factors of chronic kidney disease.

Keywords

Hospital Readmissions, Kidney Disease, Hemodialysis, Catheter

1. Introduction

Hospital readmission is broadly defined as an episode in which a patient discharged from one hospital is readmitted to another hospital within a specified time interval. The initial hospitalization is called a "baseline admission" and the subsequent hospitalization is called a "readmission" [1]. Different timeframes of hospitalization are used, the most common of which are hospital readmissions at 30 days (HR30), 90 days (HR 90) and one year after the initial hospitalization. Readmissions can be planned, *i.e.* scheduled during or shortly after the index hospitalization. However, they are most often unplanned and, therefore, represent a significant problem for health systems.

Hospital readmissions are encountered in both medical and surgical services with high frequencies of 21.1% and 15.6%, respectively, for HR30 according to Kripalani and Theobald in the USA [2]. They are associated with poor patient quality of life and high hospital costs, with approximately \$17.4 billion in annual Medicare expenditures alone, with 19.6% of patients being readmitted within 30 days of discharge and 34% when looking at 90-day hospitalizations [2]-[4]. In Canada, one in 11 patients is readmitted within 30 days of discharge, with an estimated annual expenditure of \$2.1 billion [5].

Factors such as age and chronic disease tend to increase hospital readmissions. For example, patients with chronic kidney disease, especially those with end-stage renal disease undergoing iterative hemodialysis, face a higher readmission rate compared to the general population and exceptionally high hospitalization costs [6]. In 2013, 34.9% of hemodialysis patients in Canada were readmitted within 30 days of discharge according to MATHEW [4], and 70.1% of these readmissions were preventable [7]-[9].

In sub-Saharan Africa, the situation may seem more critical due to poverty, inadequate technical facilities, poor health structures and the increasing frequency of chronic diseases. However, very little work has been done on hospital readmissions of patients with kidney disease.

The present study aims to describe the profile of readmitted patients and to identify the risk factors for readmission to the nephrology setting in our practice context.

2. Materials and Method

2.1. Materials

Our study took place during the period from 1 October 2017 to 31 December 2019 in the Nephrology-Internal Medicine D department of Treichville's Teaching Hospital. This service is composed of a consultation unit; a unit for the care of people living with HIV, a day hospital unit and a conventional hospitalization unit.

This is a retrospective analytical study carried out over a period of two (02) years.

The study population consisted of all patients who were initially hospitalized

in the nephrology department of Treichville's Teaching Hospital and then discharged and having been re-hospitalized at least once during the study period.

Patients discharged against medical advice during the first hospitalization and those whose medical records were incomplete for the parameters sought were not included.

2.2. Methods

Variables

The present investigation focused on the medical records of readmitted patients. We referred to the daily staff register to select readmitted patients and search for their records in the archives.

For each included patient the following data on the first and last hospitalization were collected using a standardized survey form:

- Socio-demographic data (age, gender, profession)
- Co-morbidities (diabetes, arterial hypertension, HIV infection, nephropathy, progressive cancer, CRF, other...)
- Clinical data (blood pressure, PAO, vomiting, disturbance of consciousness, presence of oedema, others...)
- Laboratory data (creatinemia, urea, blood glucose, blood calcium, hemoglobin, platelets, mean blood volume, HIV serology, etc.)
- Radiological data (renal ultrasound; other...)
- Hospitalization data (mode of entry, length of stay, number of hospitalizations, reason for hospitalization, treatment received, others...)

For the last hospitalization: the reason for hospitalization; the mode of entry; the length of stay; the diagnosis adopted; the treatment received, the evolutionary data...

2.3. Operational Definition of Terms

Hospital readmission was defined as an episode in which a patient who had been discharged from our department is re-admitted to our department or to the internal medicine department of Treichville University Hospital within a specified time frame. Different hospitalization delays are used, the most frequent of which are hospital readmissions at thirty days (HR₃₀), at 90 days (HR₉₀) and at one year after the first hospitalization [1].

Chronic kidney disease (CKD) was defined and classified into 5 stages according to the KDIGO recommendations [10]. Our reference formula was the simplified Modification in Diet of Renal Disease (MDRD) formula. CKD stage 5 was defined by A drop in eGFR below 15 ml/min/m² of body surface area, which may be associated with renal atrophy persisting for more than three months. [11] [12].

Total hypercalcemia was defined as a plasma concentration greater than 103 mg/l and ionised hypercalcemia as a concentration greater than 52 mg/l.

Total hypocalcemia was defined as a plasma concentration below 88 mg/l, and

ionised hypocalcemia as a concentration below 45 mg/l [13].

Anemia was defined as a hemoglobin level below 12 g/dl. It was said to be severe when the hemoglobin level was below 8 g/dl, moderate between 8 and 10 g/dl and mild between 10 and 12 g/dl.

The indications for emergency hemodialysis were:

- Persistent anuria for 48 hours
- Plasma urea level greater than 2 g/l
- Hyperkalemia greater than 6 mEq/l
- Metabolic acidosis
- PAO resistant to high dose diuretic therapy
- Uremic encephalopathy

Uremic syndrome was defined as all signs related to the retention of nitrogenous waste or uremic toxins.

Blood pressure was measured according to the World Health Organization (WHO) [14] using an electronic blood pressure monitor on the right arm with the participants in a sitting position, after at least five minutes of rest. Blood pressure measurements were taken twice and their mean was used in all analyses.

Hypertension was defined by the finding of blood pressure figures \geq 140 mmHg for systolic and/or \geq 90 mmHg for diastolic or in people on antihypertensive medication with normal blood pressure [14].

Ethical issues

This study obtained the agreement of the local ethics committee of our hospital and the agreement of the Head of Department. Confidentiality was respected by assigning an anonymity number to the patients' data.

Statistical analysis

The data were entered into an Excel database and then analyzed using EPI INFO software version 7.1.

We first performed a descriptive analysis. The quantitative variables were described with the means \pm standard deviation when their distribution was normal or, in the opposite case, with the medians and percentiles.

In univariate analysis, the proportions of qualitative variables were compared between the patients' clinical parameters and the occurrence of readmission or death by a chi-square test or a Fisher exact test. The relative quantitative variables were transformed into categorical variables according to pathological norms. Variables with p < 0.05 were included in a logistic regression model. The association between the variable and the different parameters was assessed by the odds ratio (OR). The threshold of p < 0.05 was considered significant.

3. Results

We collected 1142 patients hospitalized during the study period. During this period 154 patients were readmitted, a prevalence of 13.48%. We excluded 41 patients for incomplete records such as epidemiologic, administrative and medical information about the patient.

Our study therefore involved 113 patients (Figure 1).

Readmission was verified based on the patient's ID and whether he or she had already been hospitalized and discharged from the department at least once.

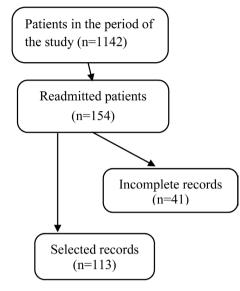


Figure 1. Flow chart.

We included 65 male patients (57.52%), a sex ratio of 1.35. The average age of our patients was 42.31 ± 13.62 years, with extremes of 15 and 77 years. The most affected age group was 35 - 45 years (33.62%). The majority of our patients were unemployed (24.78%) or worked in the informal sector as traders or artisans in 17.78% and 14.16% of cases respectively. Housewives represented 11.5% of patients.

The patients were known to be hypertensive in 63.72% of cases, HIV-infected in 15.04% and diabetic in 11.50%.

The average time to readmission was 28.23 ± 21.83 with extremes of 3 and 123 days and this readmission was early in 65.48%. The average length of stay was 11.41 \pm 8.36 with extremes of 1 and 45 days for the last hospitalization. Patients were admitted for the second time in 88.49% of cases (**Table 1**).

The main reason for readmission was uremic syndrome (68.14%).

The main clinical signs at the last hospitalization were hypertensive crisis (83.19%), conjunctival pallor (97.35%), and acute pulmonary oedema (38.94%).

Kidney disease was stage 5 in 95.6% of the cases at the last hospitalization. The hemoglobin level was below 8g/dl in 82.3% of cases at the time of the last hospitalization. Anemia was normocytic normochromic in 63.39% and microcytic hypochromic in 36.61% of the cases at the time of the last hospitalization. Thrombocytopenia was observed in 43.36% of cases at the time of the last hospitalization.

The diagnosis chosen was dialysis failure 82.30% followed by dialysis catheter infection 10.6%. Prior to readmission 97.35% of patients were treated with iterative dialysis, while 2.65% had stabilised renal function.

Variables	Total (n = 113)	Percentage
Gender		
Male	65	57.52%
Female	48	42.48%
Age (years)		
<35	33	29.20%
35 - 65	73	64.60%
≥65	7	6.20%
Occupation		
Unemployed	28	24.78%
Tradesmen	20	17.78%
Craftsmen	16	14.16%
Housewives	13	11.50%
Others	36	31.78%
Comorbidities		
HBP	72	63.72%
HIV	17	15%
Diabetes	13	11.50%
Nephropathy	9	7.96%
Active cancer	2	1.70%
Heart disease	1	0.88%
CKD Stage		
Stage 3	4	3.52%
Stage 4	1	0.88%
Stage 5	108	95.60%
Reason for admission		
Uremic syndrome	77	38.18%
Fever on catheter	11	9.73%
Disturbance of consciousness	10	8.85%
Dyspnea	9	7.96%
Clinical signs		
Pallor	110	97.35%
HBP flare	94	83.19%
Oedema	59	52.52%
PAO	44	38.94%
Fever	34	30.09%

Table 1. General characteristics of readmitted patients.

Dehydratation	33	29.20%
Neurological disorders	28	24.78%
Readmission time		
<30 days	74	65.48%
30 - 60 days	27	23.90%
>60 days	12	10.62%
Number of readmission		
2	100	88.49%
3	12	10.61%
4	1	0.88%
Length of stay		
<7 days	38	33.62%
7 - 15 days	42	37.16%
15 - 30 days	27	23.89%
>30 days	6	5.30%
Dialysis before admission		
Iterative dialysis	110	97.35%
Stabilization	3	2.65%
Hemoglobin level (g/ dL)		
<8	93	82.30%
8 - 10	17	15.04%
10 - 12	3	2.65%
Diagnosis chosen		
Dialysis failure	93	82.30%
Catheter infection	12	10.60%
DVT	5	4.42%
Catheter bleeding	3	2.65%
Treatment received		
Dialysis	106	93.61%
Blood transfusion	103	91.15%
Antihypertensive	84	74.34%
Antibiotic therapy	70	61.85%
Antiproteinuric	16	14.16%
Anticoagulant	15	13.27%
Evolution		
Deaths	35	31%
Iterative dialysis	78	69%

The main treatments received were dialysis (93.61%) of cases, blood transfusion (91.15%), antihypertensive (74.34%) and antibiotic therapy (61.85%).

Mortality was 31%, and in 69% of cases our patients were on iterative dialysis. In univariate analysis, we looked for risk factors for death and factors associated with the risk of early readmission. Thus, creatinine levels were on average higher in the deceased group compared to the non deceased group with a statistically significant difference (p = 0.049). Similarly, hemoglobin levels were on average higher in the deceased group compared to the non deceased group with a statistically significant difference (p = 0.037). In addition, the proportion of patients with hypocalcemia was statistically significantly higher in the deceased group (p = 0.03). The same was true for the proportion of patients with obstructive nephropathy (p = 0.029) (Table 2).

Table 2	. Risk	factors	for	death	in	readmitted	patients.
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	1			
Factors	Deceased $(n = 35)$	Not deceased $(n = 78)$	Value P	OR (IC 95%)
Gender				
Female	34.29% (12/35)	46.15% (36/78)	0.2	0.6 (0.2 - 1.4)
Male	65.71% (23/35)	53.85% (42/78)		
Age				
15 - 25	5.71% (2/35)	7.79% (6/78)	0.7	0.7 (0.1 - 3.8)
25 - 35	17.14% (6/35)	24.36% (19/78)	0.9	0.9 (0.1 - 6)
35 - 45	25.71% (9/35)	38.46% (30/78)	0.9	0.9 (0.1 - 5.2)
45 - 55	20% (7/35)	16.67% (13/78)	0.6	1.6 (0.2 - 10)
55 - 65	20% (7/35)	7.69% (6/78)	0.2	3.5 (0.5 - 24)
65 and plus	11.43% (4/35)	5.13% (4/78)	0.3	3 (0.3 - 25)
Comorbidities				
HBP	68.57% (24/35)	61.54% (48/78)	0.4	0.7 (0.3 - 1.7)
Diabetes	14.29% (5/35)	10.26% (8/78)	0.5	0.68 (0.2 - 2.2)
Cancer	2.86% (1/35)	3.85% (3/78)	0.8	1.3 (0.13 - 13)
Nephropathy	11.43 (11/35)	6.41% (5/78)	0.36	0.5 (0.1 - 2.1)
HIV/AIDS	11.43 (4/35)	16.67% (13/78)	0.47	1.5 (0.47 - 5.1)
Heart disease	0	1.28% (1/78)	1	
Readmissions				
2	85.71% (30/35)	89.74% (70/78)	0.5	0.68
3	11.42% (4/35)	10.25% (8/78)	1	1.12
4	2.85% (1/35)	0	0.3	
Time				
<30 days	74.28% (26/35)	61.53% (48/78)	0.1	1.8
time \geq 30 days	25.71% (9/35)	38.46% (30/78)		
Clinical signs				

HBP flare	88.57% (31/35)	80.77% (63/78)	0.3	0.5 (0.1 - 1.7)
Conjunctival pallor	97.14% (34/35)	97.44% (76/78)	0.9	1.11 (0.09 - 12
РАО	51.43% (18/35)	33.33% (26/78)	0.6	0.4 (0.2 - 1.06)
Edema	54.29% (19/35)	51.28% (40/78)	0.7	0.8 (0.4 - 1.9)
Neurological disorder	22.86% (8/35)	25.64% (20/78)	0.75	1.1 (0.4 - 2.9)
Dehydration	29.49% (10/35)	29.49% (23/78)	0.9	1.04 (0.4 - 2.5)
Digestive disorder	17.14% (6/35)	6.41% (5 - 78)	0.07	0.3 (0.09 - 1.6)
Large painful leg	2.85% (1 - 35)	2.65% (3 - 78)	0.52	7.2 (0.7 - 72)
Digestive bleedings	33.33% (2 - 35)	50.00% (1 - 78)	0.17	4.6 (0.4 - 53)
Pulmonary condensation Syndrome	2.85% (1 - 35)			
Creatinine				
levels Mean (mg/L)	213.0194	180.91	0.149	
Hb level Mean (g/dL)	6.1	6.7	0.037	
Calcemia (mg/L)				
Hypocalcemia	85.71% (30/35)	51.28% (40/78)	0.03	1.5 (2.1 - 10)
Normal calcemia	11.42% (4/35)	41% (32/78)	0.98	2.33 (0.17 - 0.2
Hypercalcemia	2.85% (1 - 35)	7.7% (6/78)	0.6	0.44 (2.4 - 4.1)
CKD				
CRF	2.86% (1 - 35)	6.41% (5/78)	0.43	2.32 (0.2 - 20.7
ESRD	97.14% (34/35)	93.59% (73/78)	0.43	0.4 (0.04 - 3.8)
Kidney damage				
Glomerular	51.43% (18/35)	50% (39/78)	0.88	0.9 (0.1 - 2.1)
Vascular	44.12% (15/35)	48.72% (38/78)	0.65	1.2 (0.5 - 2.7)
Interstitial	8.57% (3/35)	5.13 (4/78)	0.48	0.57 (0.1 - 0.27
Etiology				
НВР	48.57% (17/35)	60.26% (47/78)	0.24	1.6 (0.7 - 3.5)
Diabetes	34.29% (12/35)	19.23% (15/78)	0.08	0.45 (0.18 - 1.1
HIV/AIDS	11.43% (4/35)	16.67% (13/78)	0.47	1.55 (0.4 - 5.1)
Cancer	2.86% (1/35)	2.56% (2/78)	1	0.9 (0.1 - 10.2)
Obstruction	11.76% (4/35)	1.28% (1/78)	0.029	10 (1.11 - 100
Treatment				
Dialysis	100% (35/35)	91.02% (71/78)	0.09	2.3 (2.6 - 8.5)
Transfusion	88.57% (31/35)	92.30% (72/78)	0.7	1.55 (1.23 - 3.5
Anti HBP	77.14% (27/35)	73.07% (57/78)	0.6	0.8 (5.12 - 10)
Antibiotic	68.57% (24/35)	58.97% (46/78)	0.3	0.6 (2.8 - 14)
Antiproteinuric	8.57% (03/35)	16.66% (13/78)	0.3	2.13 (12.1 - 25
Anticoagulant	17.14% (06/35)	11.53% (09/78)	0.4	0.6 (4.6 - 10.1)

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We also compared patients with early readmission to those with non-early readmission. The proportion of patients with a hemoglobin level ≤ 8 g/dl was statistically higher in the early readmission group (p = 0.047). The proportion of patients with comorbid hypertension was statistically lower in the early readmission group (Table 3). Thus, hemoglobin level ≤ 8 g/dl appears to be a factor associated with early readmission and hypertension is a factor for non-early readmission.

Table 3. Factors associated with readmission.

Factors	Time < 30 days	Time \geq 30 days	Value P	OR (IC 95%)
Occupation				
Administration	8.11% (6/74)	10.26% (4/39)	0.7	0.72 (0.2 - 2.9)
Healthcare workers	00% (0/74)	5.13% (2/39)	0.1	
Craftsmen	13.51% (10/74)	15.38% (6/39)	0.78	0.85 (0.3 - 2.5)
Tradesmen	16.22% (12/74)	20.51% (8/39)	0.56	0.75 (0.27 - 2.02)
Pupil-students	9.46% (7/74)	7.69% (3/39)	0.75	1.25 (0.3 - 5.1)
Teachers	00% (0/74)	2.56% (1/39)	0.2	
Housewives	12.16% (9/74)	10.26% (4/39)	0.76	1.21 (0.3 - 4.2)
Retired	12.16% (9/74)	5.13% (2/39)	0.2	2.5 (0.5 - 12.4)
Unemployed	27.03% (20/74)	20.31% (8/39)	0.44	1.4 (0.5 - 3.6)
Others	1.35% (1/74)	2.56% (1/39)	0.6	0.5 (0.03 - 8.5)
Comorbidities				
HBP	56.76% (42/74)	76.92% (30/39)	0.034	2.5 (2.5 - 6.09)
Diabetes	10.81% (8/74)	15.82% (5/39)	0.7	1.2 (0.3 - 3.9)
Cancer	9.46% (7/74)	5.13% (2/39)	0.4	0.5 (0.1 - 2.6)
Nephropathy	17.57% (13/74)	10.26% (4/39)	0.3	0.5 (0.1 - 1.7)
HIV/AIDS	2.70% (2/74)	5.13% (2/39)	0.4	1.9 (0.2 - 14.3)
Heart disease	1.35% (1/74)		1	
Clearance Mean (mL/mn)	4.6593	4.6729	0.9	
Hb level				
<8	94.5% (70/74)	58.9% (23/39)	0.047	3 (1.17 - 2.05)
8 - 10	4.05% (3/74)	35.89% (14/39)	0.9	1.04 (0.25 - 5.1)
10 - 12	1.35% (1/74)	5.12% (2/39)	0.5	
CKD				
CRF	5.41% (4/74)	5.13% (2/39)	0.3	0.9 (0.3 - 5.4)
ESRD	94.59 (70/74)	94.87% (37/39)	0.9	1.5 (0.1 - 6.04)
Renal injury				
Glomerular damage	50% (37/74)	51.28% (29/39)	0.9	1.05 (0.4 - 2.2)

Continued				
Vascular damage	46.58% (34/74)	48.72 (19/39)	0.92	1.08 (0.5 - 2.3)
Interstitial damage	5.41% (4/74)	7.69% (3/39)	0.6	1.4 (0.3 - 6.8)
Etiology				
HBP	51.35% (38/74)	66.67% (26/39)	0.11	1.9 (0.8 - 4.2)
Diabetes	28.38% (21/74)	15.38% (6/39)	0.12	0.4 (0.1 - 1.2)
HIV/AIDS	17.57% (13/74)	10.26% (4/39)	0.3	3.9 (0.3 - 44.9)
Cancer	1.35% (1/74)	5.13% (2/39)	0.2	0.4 (0.05 - 4.3)
Urinary tract obstruction	5.41% (4/74)	2.63% (1/39)	0.5	0.7 (0.01 - 6.7)
Treatment				
Dialysis	94.59% (70/74)	92.30% (36/39)	1	0.9 (2.1 - 5.1)
Transfusion	93.24% (69/74)	84.61% (33/39)	0.9	1.33 (0.45 - 8)
Anti HBP	59.45% (44/74)	51.28% (20/39)	0.4	0.7 (1.4 - 85)
Antibiotic	27.02% (20/74)	43.58% (17/39)	0.1	1.76 (0.7 - 20)
Antiproteinuric	13.51% (10/74)	15.38% (6/39)	0.8	1.15 (0.12 - 7)
Anticoagulant	4.05% (03/74)	30.76 (12/39)	0.2	2.25 (0.6 - 25)
Evolution				
Iterative dialysis	95.95% (71/74)	100% (39/39)	0.5	
Stabilization	4.5% (3/74)			

4. Discussion

The risk of hospital readmission is high in patients with chronic kidney disease. In our study, the overall prevalence was 13.48% and the prevalence of readmissions within 30 days of hospital discharge (HR30) was 65.5%. The frequency of HR30 readmissions is significantly higher than that observed in the West. In a study of readmission of patients with end-stage renal disease on hemodialysis, the HR30 prevalence was 35.2% according to Mathew and Rosen in the USA with a hospitalization rate of 1.73 per patient year, and 19% in the general population [4] [8]. According to Jencks and Williams, the highest rates of HR30 readmission are found in patients with heart failure at 26.9% and recent vascular surgery at 23.9% [3].

The sex ratio of 1.35 in our study confirms the excess male morbidity observed in the nephrology department already reported by other authors, notably Sakandé in Burkina Faso who reported that 55.2% of these patients were men [15]. According to Pouteil-Noble and Villar [16], this male predominance could be explained by the higher frequency of renal disease in men and the more rapid progression of these diseases towards CKD. In the West, the unfavourable influence of the male gender on hospital readmission was established both in the general population and in patients with renal disease [8] [17] [18]. Readmission can occur at any age. In our series, our patients were young adults with a mean age of 42.31 and extremes of 15 and 77 years. In addition, 6.19% of the patients were 65 years or older. This contrasts with Western data where the mean age of patients readmitted for renal disease is over 65 years according to Jencks in the USA and 74 years according to Sood in Canada [3] [19]. In our work, the shorter life expectancy in Africa but also the late diagnosis of renal disease at the stage of complications whose management remains very costly would explain this observation to a large extent.

The socio-professional groups most affected in our series were the unemployed (24.78%) followed by traders (17.70%) and craftsmen (14.16%). In the majority of cases, these were patients with low socio-economic status and a precarious financial situation. The low socio-economic status of patients observed in our study confirms data from African studies [20]-[22]. Similarly, in the West, according to Mathew and al., patients living in low-income postal codes, particularly the unemployed, were at high risk of hospital readmission [4] [8] [23]. The low socio-economic level poses a problem of overall management of hospital readmission that is extremely costly, especially for hemodialysis patients [3] [7].

The comorbidities observed in our study were dominated by high blood pressure in 63.72% of cases followed by HIV/AIDS infection (15%) and diabetes 11.5%. These rates are significantly lower than the Flythe rates found in hospitals at the University of North Carolina in renal readmitted patients, which are 75% for hypertension and 35% for diabetes, respectively [24]. These comorbidities are also reported by most western series [4] [25] [26], and complications such as heart failure, stroke, myocardial infarction are true readmission factors [27].

In almost all cases (86.73%), patients were admitted via the medical emergency department with impaired renal function as the main reason for admission (84.07%). However, uraemic syndrome was the main reason for readmission (68.14%).

The clinical manifestations observed in our study were polymorphic as in most reviews of readmission of patients with chronic kidney disease [4] [19] [24] [25], and are almost identical during the different episodes of readmission. This is not the case in the Western series, due to the early management of patients in a dialysis-transplant programm in the West [21] as soon as creatinine clearance is less than 10 ml/min and also due to the effective existence of medical insurance especially for patients with chronic kidney disease [3] [25] [28].

The main clinical manifestations observed in our study are cutaneous-mucosal pallor related to anemia in 91.15% of cases and high blood pressure (86.73%), which is the main cardiovascular and respiratory manifestation in our series. High blood pressure is widespread in the population of hemodialysis patients as described by most western series with a high rate of hospital readmission related to its many complications [18] [25] [27]. Furthermore, edema was noted in 55.75% of cases, and acute lung edema in 24.78% of cases compared to 14% ac-

cording to Plantinga in the United States [29]. Other signs such as dehydration 24.78%, neurological manifestations 16.81%, fever 14.16%, and digestive manifestations (12.36%) were observed. The high frequency of these signs observed in our study would be largely related to insufficient supplementation treatment. Interventions to reduce readmissions related to these signs could have a substantial impact on readmissions as a whole.

In our study, more than 9 out of 10 patients had an ESRD according to the MDRD equation and only 5% had a stage 4 CRF. These are patients whose survival is strongly linked to treatment by renal supplementation with its risk cortege of re-occurrence hospitalization associated with dialysis and its complications [30]-[32].

Anemia was observed in all patients. It was mainly normochromic normocytic in 56% and severe in 65% of cases. The same observation was made in France but with a lower prevalence of anemia [33]. The high frequency is partly related to the high cost of recombinant erythropoietin in the management of anemia in our hemodialysis patients, unlike in the West where the availability of cheaper EPO has considerably reduced readmissions [34]-[36].

Thrombocytopenia was noted in 43.36% of cases during readmission and hypocalcemia in 69.02% of cases. This hypocalcemia results from the inability of the kidney to hydroxylate 25-hydroxyl D3, which is the active form of vitamin D. Vitamin D deficiency, which leads to decreased intestinal absorption of calcium, may explain the observed hypocalcemia [37]. According to POWE, post-hospital vitamin D intake reduces readmissions in ESRD patients by 4.5% [34].

The cause of readmission was different from the reason for the baseline hospitalization in the majority of patients. Our patients were readmitted for dialysis failure (82.30%) followed by vascular access complications including dialysis catheter infection (10.60%) and deep vein thrombosis (4.42%). In the West, cardiovascular causes remain the leading cause of readmission of patients with end-stage renal disease and account for 40% of deaths [38]. According to Wetmore *et al.*, they are dominated by congestive heart failure (35%) followed by arrhythmias (11%) and acute coronary syndromes (9%) [39] [40]. According to Doshi [25] in the United States, among MEDICARE patients undergoing iterative hemodialysis, the causes of readmission are dominated by infections, vascular access complications and sepsis [36] [41] [42]. The inaccessibility of dialysis for the majority of our patients, due to its high cost and the insufficient number of dialysis machines in our health structures, would be the main cause of readmission in our work.

Treatment in our study was mainly symptomatic. It consisted of treatment of anemia, hypertension, correction of biological abnormalities and dialysis. The treatment of anemia involved blood transfusion and the prescription of erythropoietin. Transfusion of packed red blood cells still plays an important role in the treatment of anemia in Africa in relation to the severity of chronic renal failure at the time of diagnosis. It represented 71% for Ouattara [43], 73% for Ah-

med [44]. In our study, 91.15% of the patients had received a transfusion of packed red blood cells. The prescription of erythropoietin was rare, as in African series, unlike in the West, due to its prohibitive cost [22].

The treatment of hypertension involved therapeutic classes recommended in the literature, namely diuretics, conversion enzyme inhibitors and calcium channel blockers. According to Honkonen, the class and quantity of antihypertensive drugs does not affect the readmission rate [45] as it did in our work.

In Africa, very few ESRD patients benefit from replacement therapy. In our study, 82.30% of patients were readmitted for dialysis failure. The lack of dialysis facilities described in most African studies is the main reason [21] [22].

In the West, in addition to symptomatic treatment, the emphasis is on communication and coordination between hospitals and dialysis centers for better exchange of patient data according to Wingard and al. An additional monthly visit by the nephrologist and the use of palliative care consultation can reduce hospital readmissions [46]-[50].

In our study, the in-hospital mortality rate was 30.97%. Nine out of ten patients who died had ESRD on chronic hemodialysis. In Canada, according to Sood, the death rate was 7.5% and 22% in patients over 65 years of age with ESRD [19]. The high mortality rate noted in our study is linked to poverty and comorbidities, particularly heart disease, and to the inadequacy of the technical facilities in our health structures. In the West, patients with CKD have a shorter length of stay in hospital, averaging 4 days, and a longer average time to readmission [36] [39]. In our study, the average length of stay was 15.89 ± 11.5 days with extremes of 3 and 61 days. Hypocalcemia was associated with mortality risk (p = 0.030) as was obstructive nephropathy (p = 0.029), probably related to the cause of obstruction dominated by pelvic cancers.

Finally, severe anemia (Tx hemoglobin < 8 g/dl) was associated with the risk of early readmission (p = 0.037) and among the comorbidities, hypertension was associated with the risk of non-early readmission (p = 0.034) due to the fact that the blood pressure figures remained high and were linked to poor compliance with the treatment, the accessibility of antihypertensive treatment which often includes three or even four or five drugs.

Elsewhere, we did not find an association between the different factors studied (reason for admission, occupation, age, sex, clinical signs, stages of CKD, treatment) and the death of patients as well as readmissions.

Our work has some limitations: the absence of some information due to the retrospective nature of the work has influenced our comments. Indeed, it was impossible to specify the complete imaging data and the nature of self-medication.

5. Conclusions

The prevalence of readmission in our study was high (13, 48%). Readmitted patients were young adults, male, with low socio-economic status. The main causes of readmission were insufficient dialysis and complications of vascular access, including infection. Access to dialysis outside of hospitalization is not easy in our context. In fact, the cost of dialysis is enormous compared to the SMIG. Patients who are no longer hospitalized can no longer have regular dialysis, which leads to their return to hospitalization in the context of severe uremia. High blood pressure was a factor for non-early readmission. Hemoglobin level below 8 g/dl was a factor in early readmission.

Mortality was high (30, 97%). Complications of CKD such as hypocalcemia and anemia were associated with the risk of death. These results reveal the value of accessibility for all ESRD patients to dialysis while waiting for kidney transplantation and the search for strategies to reduce the risk of readmissions of patients with chronic kidney disease.

Declarations

Ethics Approval and Consent to Participate

This study was authorized by the National Research Ethics Committee [CNER] in Côte d'Ivoire.

Both attested to the ethical nature of the study and gave their consent to its conduct.

All the experiments carried out during our study and the information collected were done in strict compliance with current guidelines and regulations (Declaration of Helsinki).

Participation in this study was entirely free and voluntary. Participants were free to accept or refuse to participate in our study. Those who accepted were also free, at any time, to end their participation, and, on simple verbal notice without giving an explanation.

Informed Consent Was Obtained from All Subjects

The study was conducted in compliance with ethics and medical deontology, human dignity.

The participants were submitted to a confidential questionnaire, and in order to preserve their anonymity a unique number was assigned to them.

Participation in the study was not subject to financial compensation for the participants

Availability of Data and Materials

The physical data of the study including the recordings of the interviews will be kept by kidney department of the teaching hospital of Treichville. For the duration of the study, the information concerning the study has been stored in a restricted and closed room.

The data of this study are available on request to Pr. YAO KOUAME HUBERT whose contact details are available in the chapter relating to the contact details of the authors.

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Authors' Contributions

KONAN Serge Didier wrote this article, conducted the study and entered the data. DIOPOH Sery Patrick carried out the statistical analysis of the data. YAO Kouamé Hubert directed this work from the protocol to the final draft and coordinated the study and publication of this article. KONAN Serge Didier submitted the article online and adapted it to the journal's recommendations. OUATTARA Kolo Claude, KOUADIO Marie Dominque, YEO Donafologo Drissa followed the patients in the Department of Nephrology-Internal Medicine D, Teaching Hospital of Treichville. All the authors contributed to the writing and proofreading of this work.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- Woodside, M. (1684) York Clinic: A Note on Readmissions. *Guy's Hospital Gazette*, 67, 48-50.
- [2] Kripalani, S., Theobald, C.N., Anctil, B. and Vasilevskis, E.E. (2014) Reducing Hospital Readmission Rates: Current Strategies and Future Directions. *Annual Review* of Medicine, 65, 471-485. <u>https://doi.org/10.1146/annurev-med-022613-090415</u>
- [3] Jencks, S.F., Williams, M.V. and Coleman, E.A. (2009) Rehospitalizations among Patients in the Medicare Fee-for-Service Program. *New England Journal of Medicine*, **360**, 1418-1428. <u>https://doi.org/10.1056/nejmsa0803563</u>
- [4] Mathew, A.T., Strippoli, G.F.M., Ruospo, M. and Fishbane, S. (2015) Reducing Hospital Readmissions in Patients with End-Stage Kidney Disease. *Kidney International*, 88, 1250-1260. <u>https://doi.org/10.1038/ki.2015.307</u>
- [5] Harel, Z., Wald, R., McArthur, E., Chertow, G.M., Harel, S., Gruneir, A., et al. (2015) Rehospitalizations and Emergency Department Visits after Hospital Discharge in Patients Receiving Maintenance Hemodialysis. *Journal of the American Society of Nephrology*, 26, 3141-3150. <u>https://doi.org/10.1681/asn.2014060614</u>
- [6] Kshirsagar, A.V., Hogan, S.L., Mandelkehr, L. and Falk, R.J. (2000) Length of Stay and Costs for Hospitalized Hemodialysis Patients. *Journal of the American Society* of Nephrology, 11, 1526-1533. <u>https://doi.org/10.1681/asn.v1181526</u>
- [7] Medicare (2020) Hospital Readmissions Reduction Program.
- [8] Mathew, A.T., Rosen, L., Pekmezaris, R., Kozikowski, A., Ross, D.W., McGinn, T., *et al.* (2018) Potentially Avoidable Readmissions in United States Hemodialysis Pa-

tients. *Kidney International Reports*, **3**, 343-355. https://doi.org/10.1016/j.ekir.2017.10.014

- [9] Donzé, J., Aujesky, D., Williams, D. and Schnipper, J.L. (2013) Potentially Avoidable 30-Day Hospital Readmissions in Medical Patients: Derivation and Validation of a Prediction Model. *JAMA Internal Medicine*, **173**, 632-638. <u>https://doi.org/10.1001/jamainternmed.2013.3023</u>
- [10] Akinsola, W., Odesanmi, W.O., Ogunniyi, J.O. and Lapido, G.O.A. (1989) Diseases Causing Chronic Rénal Failure in Nigérians, a Prospective Study of 100 Cases. *African Journal of Medicine and Medical Sciences*, **18**, 131-137.
- [11] Levey, A.S., Stevens, L.A., Schmid, C.H., Zhang, Y., Castro, A.F., Feldman, H.I., *et al.* (2009) A New Equation to Estimate Glomerular Filtration Rate. *Annals of Internal Medicine*, **150**, 604-613. https://doi.org/10.7326/0003-4819-150-9-200905050-00006
- [12] (2013) Classification en différents stades de l'insuffisance rénale: Y a-til un intéret? Pourquoi? <u>https://www.realites-cardiologiques.com/wp-content/uploads/sites/2/2013/12/10.pdf</u>
- [13] "Physiologie Rénale et Troubles Hydro-Electrolytiques" Janvier 2022. https://cuen.fr/spip.php?article169
- [14] World Health Organization (1999) International Society of Hypertension Guidelines for the management of hypertension. Guidelines Sub-Committee of the World Health Organization. *Clinical and Experimental Hypertension*, **21**, 1009-1060.
- [15] Sakandé, J., Sawadogo, M., Nacoulma, E.W.C., Sidikath, E.S., Kabré, E., Sawadogo, S., *et al.* (2006) Profil biologique de l'insuffisance rénale chronique au CHN-YO (Burkina Faso). *Annales de Biologie Clinique*, **43**, 3-8.
- [16] Pouteil-Noble, C. and Villar, E. (2001) Epidémiologie et étiologie de l'insuffisance rénale chronique. *La Revue du praticien*, **51**, 365-371.
- Shipton, S. (1996) Risk Factors Associated with Multiple Hospital Readmissions. Home Care Provider, 1, 83-85. https://doi.org/10.1016/s1084-628x(96)90234-8
- [18] Vest, J.R., Gamm, L.D., Oxford, B.A., Gonzalez, M.I. and Slawson, K.M. (2010) Determinants of Preventable Readmissions in the United States: A Systematic Review. *Implementation Science*, 5, 88-91. <u>https://doi.org/10.1186/1748-5908-5-88</u>
- [19] Sood, M.M., Roberts, D., Komenda, P., Bueti, J., Reslerova, M., Mojica, J., et al. (2011) End-stage Renal Disease Status and Critical Illness in the Elderly. Clinical Journal of the American Society of Nephrology, 6, 613-619. https://doi.org/10.2215/cjn.01160210
- [20] Benja, R.A., Eliane, M.I., Mihary, D.O., Evanirina, R.A. and Willy, F.R. (2009) Une étude rétrospective sur l'insuffisance rénale chronique dans le service de Médecine interne et de Néphrologie au CHU de Antananarivo à Madagascar. *Médecine d'Afrique Noire*, 23, 408-411.
- [21] Diallo, A.D., Niamkey, E.K. and Béda, B.Y. (1997) L'insuffisance rénale chronique en Côte d'ivoire: Étude de 800 cas hospitaliers. *Bulletin de la Societe de Pathologie Exotique*, 90, 346-348.
- [22] Hubert, Y.K., Serge-Didier, K., Sindou, S., Patrick, D.S. and Demba, D.A. (2018) Prevalence and Risk Factors of Chronic Kidney Disease in an Internal Medicine Department in Cote d'Ivoire: An Analytic Study. *Saudi Journal of Kidney Diseases and Transplantation*, **29**, 153-159.
- [23] Philbin, E.F., Dec, G.W., Jenkins, P.L. and DiSalvo, T.G. (2001) Socioeconomic Sta-

tus as an Independent Risk Factor for Hospital Readmission for Heart Failure. *The American Journal of Cardiology*, **87**, 1367-1371. https://doi.org/10.1016/s0002-9149(01)01554-5

- [24] Flythe, J.E., Katsanos, S.L., Hu, Y., Kshirsagar, A.V., Falk, R.J. and Moore, C.R. (2016) Predictors of 30-Day Hospital Readmission among Maintenance Hemodialysis Patients: A Hospital's Perspective. *Clinical Journal of the American Society of Nephrology*, **11**, 1005-1014. <u>https://doi.org/10.2215/cjn.11611115</u>
- [25] Doshi, S. and Swish, J.B. (2021) Strategies to Reduce Rehospitalization in Patients with CKD and Kidney Failure. *Clinical Journal of the American Society of Nephrology*, 16, 328-334.
- [26] Chan, L., Chauhan, K., Poojary, P., Saha, A., Hammer, E., Vassalotti, J.A., et al. (2017) National Estimates of 30-Day Unplanned Readmissions of Patients on Maintenance Hemodialysis. *Clinical Journal of the American Society of Nephrology*, **12**, 1652-1662. <u>https://doi.org/10.2215/cjn.02600317</u>
- [27] Donze, J., Lipsitz, S., Bates, D.W. and Schnipper, J.L. (2013) Causes and Patterns of Readmissions in Patients with Common Comorbidities: Retrospective Cohort Study. *BMJ*, 347, f7171. <u>https://doi.org/10.1136/bmj.f7171</u>
- [28] Gruneir, A., Dhalla, I.A., van Walraven, C., et al. (2011) Unplanned Readmissions after Hospital Discharge among Patients Identified as Being at High Risk for Readmission Using a Validated Predictive Algorithm. Open Medicine, 5, e104-e111.
- [29] Plantinga, L.C., King, L.M., Masud, T., Shafi, T., Burkart, J.M., Lea, J.P., et al. (2017) Burden and Correlates of Readmissions Related to Pulmonary Edema in US Hemodialysis Patients: A Cohort Study. Nephrology Dialysis Transplantation, 33, 1215-1223. https://doi.org/10.1093/ndt/gfx335
- [30] Daratha, K.B., Short, R.A., Corbett, C.F., Ring, M.E., Alicic, R., Choka, R., et al. (2012) Risks of Subsequent Hospitalization and Death in Patients with Kidney Disease. Clinical Journal of the American Society of Nephrology, 7, 409-416. https://doi.org/10.2215/cjn.05070511
- [31] Perl, J., McArthur, E., Bell, C., Garg, A.X., Bargman, J.M., Chan, C.T., Harel, S., Li, L. and Jain, A.K. (2017) Modalité de dialyse et réadmission après la sortie de l'hôpital: Une étude de cohorte basée sur la population. *American Journal of Kidney Diseases*, **70**, 11-20.
- [32] Sood, M.M., Miller, L., Komenda, P., Reslerova, M., Bueti, J., Santhianathan, C., et al. (2011) Long-Term Outcomes of End-Stage Renal Disease Patients Admitted to the ICU. Nephrology Dialysis Transplantation, 26, 2965-2970. https://doi.org/10.1093/ndt/gfq835
- [33] Dardim, K., Fernandes, J., Panes, A., Beisel, J., Schmidt, A., Wolfram, J., et al. (2023) Incidence, Prevalence, and Treatment of Anemia of Non-Dialysis-Dependent Chronic Kidney Disease: A Retrospective Database Study in France. PLOS ONE, 18, e0287859. https://doi.org/10.1371/journal.pone.0287859
- [34] Powe, N.R., Griffiths, R.I., Watson, A.J., Anderson, G.F., de Lissovoy, G., Greer, J.W., et al. (1994) Effect of Recombinant Erythropoietin on Hospital Admissions, Readmissions, Length of Stay, and Costs of Dialysis Patients. *Journal of the Ameri*can Society of Nephrology, 4, 1455-1465. https://doi.org/10.1681/asn.v471455
- [35] Chan, K.E., Lazarus, J.M., Wingard, R.L. and Hakim, R.M. (2009) Association between Repeat Hospitalization and Early Intervention in Dialysis Patients Following Hospital Discharge. *Kidney International*, **76**, 331-341. <u>https://doi.org/10.1038/ki.2009.199</u>
- [36] Hansen, L.O., Young, R.S., Hinami, K., Leung, A. and Williams, M.V. (2011) Inter-

ventions to Reduce 30-Day Rehospitalization: A Systematic Review. *Annals of Internal Medicine*, **155**, 520-528. https://doi.org/10.7326/0003-4819-155-8-201110180-00008

- [37] Sizar, O., Khare, S., Goyal, A. and Givler, A. (2023) Vitamin D Deficiency. StatPearls [Internet]. StatPearls Publishing, Treasure Island (FL). http://www.ncbi.nlm.nih.gov/books/NBK532266/
- [38] USRDS (The United States Renal Data System) (1999) 1999 Annual Data Report. *American Journal of Kidney Diseases*, **34**, SI-S176.
- [39] Wetmore, J.B., Molony, J.T., Liu, J., Peng, Y., Herzog, C.A., Collins, A.J., et al. (2018) Readmissions Following a Hospitalization for Cardiovascular Events in Dialysis Patients: A Retrospective Cohort Study. *Journal of the American Heart Association*, 7, e007231. <u>https://doi.org/10.1161/jaha.117.007231</u>
- [40] Perkins, R.M., Rahman, A., Bucaloiu, I.D., Norfolk, E., DiFilippo, W., Hartle, J.E., et al. (2013) Readmission after Hospitalization for Heart Failure among Patients with Chronic Kidney Disease: A Prediction Model. *Clinical Nephrology*, 80, 433-440. https://doi.org/10.5414/cn107961
- [41] Laurin, L., Harrak, H., Elftouh, N., Ouimet, D., Vallée, M. and Lafrance, J. (2015) Outcomes of Infection-Related Hospitalization According to Dialysis Modality. *Clinical Journal of the American Society of Nephrology*, 10, 817-824. https://doi.org/10.2215/cjn.09210914
- [42] Jiang, H.J. and Wier, L.M. (2010) All-Causes Hospital Readmissions among Non-Elderly Medicaid Patients, 2017. <u>http://www.ncbi.nlm.nih.gov/books/NBK53601/</u>
- [43] Ouattara, B., Kra, O., Yao, H., Kadjo, K. and Niamkey, E.K. (2011) Particularités de l'insuffisance rénale chronique chez des patients adultes noirs hospitalisés dans le service de médecine interne du CHU de Treichville. *Néphrologie & Thérapeutique*, 7, 531-534. <u>https://doi.org/10.1016/j.nephro.2011.03.009</u>
- [44] Ahmed, M. (2006) Problématique de la prise en charge des insuffisants rénaux chroniques en dialyse à l'hôpital national du point G en 2005. Thèse de Medecine, University of Bamako.
- [45] Honkonen, M.N., McNeill, P., Jasensky, A. and Erstad, B.L. (2015) Readmissions Related to Antihypertensive Medications Used in Chronic Hemodialysis. *Renal Failure*, 38, 40-45. <u>https://doi.org/10.3109/0886022x.2015.1103655</u>
- [46] Erickson, K.F., Winkelmayer, W.C., Chertow, G.M. and Bhattacharya, J. (2014) Physician Visits and 30-Day Hospital Readmissions in Patients Receiving Hemodialysis. *Journal of the American Society of Nephrology*, 25, 2079-2087. <u>https://doi.org/10.1681/asn.2013080879</u>
- [47] Chettiar, A., Montez-Rath, M., Liu, S., Hall, Y.N., O'Hare, A.M. and Kurella Tamura, M. (2018) Association of Inpatient Palliative Care with Health Care Utilization and Postdischarge Outcomes among Medicare Beneficiaries with End Stage Kidney Disease. *Clinical Journal of the American Society of Nephrology*, **13**, 1180-1187. https://doi.org/10.2215/cin.00180118
- [48] Wingard, R.L., McDougall, K., Axley, B., Howard, A., O"Keefe, C., Armistead, N., et al. (2017) Right Trac[™] Post-Hospitalization Care Transitions Program to Reduce Readmissions for Hemodialysis Patients. American Journal of Nephrology, 45, 532-539. <u>https://doi.org/10.1159/000477325</u>
- [49] Jack, B.W. (2009) A Reengineered Hospital Discharge Program to Decrease Rehospitalization. *Annals of Internal Medicine*, **150**, 178-187.

https://doi.org/10.7326/0003-4819-150-3-200902030-00007

[50] Burke, R.E. and Coleman, E.A. (2013) Interventions to Decrease Hospital Readmissions: Keys for Cost-Effectiveness. *JAMA Internal Medicine*, **173**, 695-698. <u>https://doi.org/10.1001/jamainternmed.2013.171</u>