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Renal Biopsy in Sub-Saharan Africa

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Abstract

Background: Renal biopsy (RB) is a significant advance in the management of kidney disease. In sub-Saharan Africa, few studies were conducted. The objective of our work was to evaluate the indications of RB, to determine the epidemiological and histological characteristics of nephropathies diagnosed in sub-Saharan Africa.

Materials and Methods: We conducted a retrospective and descriptive study on RBs examined between January 2015 and December 2019, at the Pathological Anatomy and Cytology Departments of Cocody-Abidjan and Bouaké Teaching Hospitals. RBs came from four African countries (Côte d'Ivoire, Togo, Guinea-Conakry and Burkina Faso). Optical microscopy and/or direct immunofluorescence techniques were used. Included in this study were RBs containing epidemiological, clinical, biological and anatomic pathological data (optical microscopy and/or direct immunofluorescence). The parameters studied were: indication of RB, epidemiological and clinical profile, proteinuria and histology.

Results: Over the study period, we collected 179 RBs, or 35.8 RBs/year. The mean age of patients was 32.9 13.8 years (extremes of 11 and 70 years). The sex ratio (M/F) was 1.03. Nephrotic syndrome was the main indication (64.2%, n=115) followed by persistent acute kidney disease (7.8%, n=14), rapidly progressive glomerulonephritis (7.3%, n=13), nephrotic syndrome with chronic kidney disease (6.1%, n=11), isolated chronic kidney disease (5.6%, n=10) and other indications (8.9, n=16). Glomerular nephropathy (GN) was observed in 97.8% (n=175) and tubulointerstitial disease (TID) in 2.2% (n=4). Focal segmental glomerulosclerosis (FSGS) (34.6%, n=62), nephrotangiosclerosis (10.6%, n=19), extramembranous GN (10%, n=18), post-infectious GN (8.9%, n=16), lupus GN (7.3%, n=13) were the main nephropathies.

Conclusion: The Renal biopsy is a crucial gesture for the diagnosis of nephropathy. Focal segmental glomerulosclerosis is the main nosology. The establishment of a kidney registry would allow a better knowledge and management of kidney pathologies in sub-Saharan Africa.

Keywords: Kidney • Indication • Biopsy • Histology • Sub-Saharan Africa

Introduction

Introduced by Iverson and Brun in 1951, the renal biopsy (RB) underwent several modifications by Kark R, et al. [1]. This is an act frequently performed during the exploration of kidney disease. The technical improvements made in recent years made this gesture increasingly reliable and safe [2]. It can be used to characterize kidney disease, guide treatment, and assess short-, medium- and long-term renal prognosis. Performed on native kidneys or transplanted kidneys (grafts), it requires a rigorous procedure in order to avoid sometimes fatal complications [3]. Renal biopsy (RB) is a common practice in Western, Asian, North African and South African countries [1-6]. In sub-Saharan African countries, and particularly in French-speaking countries, it is rarely practised [5,7]. In Côte d'Ivoire, the first data on renal biopsies date back to the work of Diallo AD, et al. [8]. Biopsies were systematically sent to France for confirmation of microscopic diagnosis [8]. This practice has gradually intensified since the establishment of the Nephropathhology Unit of the Cocody and Bouaké Teaching Hospital in 2015 and 2019, which has led to collaboration between Côte d'Ivoire and the Francophone countries of the West African region, to improve the management of kidney disease. In carrying out this work, we set ourselves the objective of studying the indications of RBs and of describing the epidemiological, clinical, pathological and anatomic pathological characteristics of nephropathies diagnosed in sub-Saharan Africa in order to compare them with data from the literature.

Materials and Methods

This was a retrospective and descriptive study carried out in the Pathological Anatomy and Cytology Departments of Cocody (Abidjan) and Bouaké Teaching Hospitals. The study period was five years (January 2015 to December 2019), RBs came from the Nephrology departments of the Yopougon and Treichville Teaching Hospitals in Abidjan and Bouaké, the Nephopediatrics department of the Yopougon Teaching Hospital (Abidjan), private clinics in Abidjan (Danga-Cocody Clinic, International Polyclinic Sainte Anne Marie) and services of Nephrology of the Sylvanus Olympio Teaching Hospital in Togo, of the Donka Hospital (Guinea-Conakry), of the Nura Clinic

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(Burkina Faso). The samples were taken after ultrasound identification with needles of variable caliber, ranging from 16 to 18 Gauge depending on the morphology of the patient. Two samples were systematically taken in each patient.

The first fragment intended for the study in optical microscopy, was fixed in Alcohol Formol Acetic Acid (AFA) and underwent the technique of conventional histopathology (a paraffin inclusion, a 3 to 5 micrometer section with a microtome, Masson's trichrome staining, Schiff's periodic acid, eosin haematoxylin and Jones' silvering). Depending on the diagnostic orientation, special colorations were made (Congo red, Perls, Ziehl Neelsen etc.).

The second sample, intended for the direct immunofluorescence study, was wrapped in a non-woven compress soaked in physiological serum and immediately sent to the Pathological Anatomy and Cytology Department within 4 hours for freezing. Michel's liquid was used as a fixator for samples taken from countries in the sub-region. After rinsing, the biopsy fragments were frozen in cryostat at -30°C for a few minutes and 3 to 5 micrometer slices were performed. The ribbons were spread on Super-Frost or desylannized blades. The polyclonal antibodies of Dako were used for direct immunofluorescence. These were immunoglobulin antibodies (IgA, IgM, IgG), complement fractions (C3, C1q), light chains (Kappa, Lambda) and albumin. The slides were read under a fluorescence microscope in a darkroom by two dedicated pathologists.

All samples were accompanied by an analysis bulletin containing information on epidemiological data, personal history (medical, surgical, gynecologic-obstetric, and lifestyle), clinical and biological data, biopsy indications, previous biopsy information, and possibly diagnostic assumptions. This study was conducted in accordance with national and international good clinical practice and guidelines for medical research. The confidentiality of the data collected was scrupulously respected. Data capture and analysis was carried out using Epi info 7.2.2.6 software. Quantitative variables were expressed as mean with standard deviation and extreme values.

The parameters studied were: frequency, age, gender, occupation, history, indication of RB, proteinuria, and pathological aspects (glomerular elementary lesions, tubulointerstitial, vascular, deposits of extra and endomembrane immune complexes). Correlations between histological diagnoses and epidemiological parameters and indications of renal biopsy were also investigated.

Results

Epidemiological characteristics

We received 203 RBs over the study period, 179 of which met the inclusion criteria. Other non-contributory biopsies were RBs of medullary topography (7 cases), RBs with fixation defects (5 cases) and a biopsy addressed without biological assessment. Three patients had received a recovery, and were counted only once in our collection. Of the 179 biopsies included, 12 were performed in 2015, 50 in 2016, 56 in 2017, 27 in 2018 and 34 in 2019. Withdrawals came from Côte d'Ivoire (79.9%, n=143), Togo (8.4%, n=15), Burkina Faso (7.8%, n=14) and Guinea-Conakry (3.9%, n=7). The average age of patients at the time of diagnosis was 32.9 13.7 years with extremes of 11 and 70 years. The vast majority of patients were between the ages of 18 and 59 (82.1%, n=23). Children and adolescents represented 12.8% (n=23) of the study population (0-17 years). Subjects aged 60 years and older accounted for 5.1% of cases (n=9). We noted 50.8% (n=91) of men and 49.2% (n=88) of women, a sex ratio (M/F) of 1.03. Students and pupils accounted for 33.5% (n=60) of patients followed by civil servants (17.9%, n=32), unemployed (17.3%, n=31), patients in the informal sector (15.6%, n=28), the private sector (10.1%, n=18) and patients in the agricultural sector (5.6%, n=10). The most common medical histories were relapsing oedemato-ascitic and/or ascitic syndromes in 27.4% (n=49), hypertension in 25.7% (n=46), HIV infection in 20.1% (n=36), self-medication and/or traditherapy in 10% (n=18) patients and viral hepatitis B infection in 5% (n=9).

Clinical and biological data

Indications for RB were nephrotic syndrome (64.2%, n=115), persistent acute kidney disease (AKD) (7.8%, n=14), rapidly progressive glomerulonephritis (RPGN) (7.3%, n=13), chronic kidney disease (CKD) (6.1%, n=11) and isolated CKD (5.6%, n=10) and other indications (8.9, n=16) (Table 1). The protein assay was performed in all patients. The mean proteinuria at diagnosis was 4.6 g/24H (extremes of 0.45 and 21.6g/24H). In our collection, the transparietal or percutaneous RB technique represented 96.1% (n=172). The transparietal technique associated with the transvenous were 2.8% (n=5) and the isolated transvenous was 1.1% (n=2). Hemorrhagic complications were observed after RNB. There were 3 cases of macroscopic hematuria and one case of pancreatic involvement with resolute peritoneal hemorrhage after hospitalization. No cases of death were recorded.

Anatomopathological aspects

In histology, the average core length was 10.1 +/- 2.9 mm (extreme 04 mm and 20 mm). The topography of the tissue fragments examined was cortico-medullary (86% of cases, n=154), cortical (11.2% of cases, n=20) and cortico-medullo-cortical (2.8% of cases, n=5). The average number of glomeruli per core was 20.8 15.8 (03 and 105 extremes). The number of permeable glomeruli per core was 16.9 11.4 (extremes of 03 and 66 glomeruli). The direct immunofluorescence (DIF) study was conducted in 85.5% (n=153) of patients. Among DIF-unconfirmed kidney disease, we had 11 cases of FSGS, 3 cases of Nephroangiosclerosis, 3 cases of extramembranous GN, 3 cases of tubulointerstitial nephritis, 3 cases of RPGN, 2 cases of amyloidosis and 1 case of Extracapillary Glomerulonephritis (ECGN)

Nephropathy was diagnosed as Focal segmental glomerulosclerosis (FSGS) (34.6%, n=62), nephroangiosclerosis (10.6%, n=19), extramembranous GN (10%, n=18), post-infectious GN (8.9%, n=16), lupus GN (7.3%, n=13), Membranoproliferative Glomerulonephritis (5%, n=9) and other nephropathies (17.9, n=32) (Figure 1). The distribution of histological types by gender is reported in Table 2. The most common nephropathy in

Table 1. Distribution of RNB indications.

Indications	Number	Percentage
Nephrotic Syndrome	115	64.2%
Acute Kidney Disease (AKD)	14	7.8%
RPGN	13	7.3%
Nephrotic Syndrome + CKD	11	6.1%
Chronic Kidney Disease (CKD)	10	5.6%
Nephrotic Syndrome + AKD	5	2.8%
Nephrotic Syndrome + Haematuria	5	2.8%
Nephritic Syndrome	4	2.2%
AKD + RPGN	1	0.6%
Nephritis Syndrome + AKD	1	0.6%
Total	179	100%

Note: AKD: Acute kidney disease; CKD: Chronic kidney disease; RPGN: Rapidly progressive

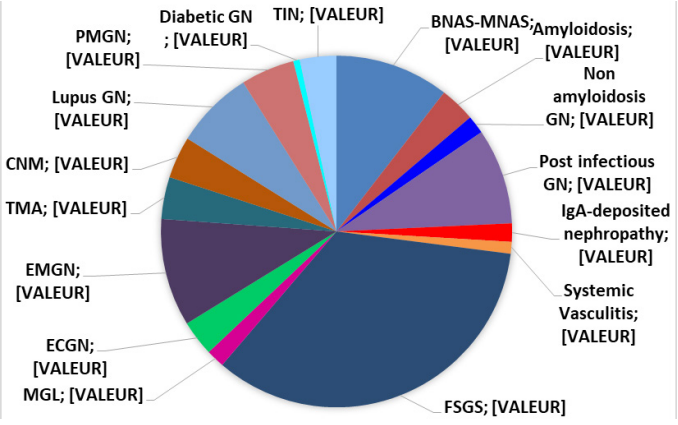

Figure 1. Distribution of nephropathies.

mens were (73.7%, n=14), extramembranous glomerulonephritis (61.1%, n=11) and post-infectious glomerulonephritis (62.5%, n=10). In women, it was Focal segmental glomerulosclerosis (56.5%, n=35) and lupus nephropathy (100%, n=13) exclusively. We analysed the distribution of histological types according to age groups (Table 3). In children and adolescents (0-17 years), FSGS (39.1%, n=9), post-infectious GN (21.7%, n=5) and ECGN (13%, n=3) were predominant. In contrast, predominant nephropathy in adults was FSGS (36.1%, n=53), nephroangiosclerosis (12.9%, n=19) and extramembranous GN (11.6%, n=17). Analysis of histological types based on biopsy indications showed that nephrotic syndrome was the main indication of lupus nephropathy (92.3%, n=12), extramembranous GN (77.8%, n=14), SFH (69.3%, n=43), post-infectious GN (62.5, n=10) and Benign and Malignant Nephroangioslerosis (BMNA) (36.8%, n=7). Persistent AKI was found in tubulointerstitial nephritis (50%, n=2), FSGS (12.9%, n=8) and BMNA (10.5%, n=2). In addition, RPGN was observed in 66.7% (n=4) of extracapillary GN, 26.3% (n=5) BMNA, 14.3% (n=1) TMA and 7.7% (n=1) lupus kidney disease. Nephritic syndrome was only observed in post-infectious GN (Figure 2).

Discussion

In the French-speaking countries of sub-Saharan Africa, the practice of kidney biopsy, which is essential for the diagnostic confirmation of kidney disease and the treatment of patients, is uncommon [7,9]. This region, made up of countries with limited resources, shares the French language in one of Africa's most important economic exchanges [10]. We carried out this preliminary study, the purpose of which was to provide an epidemiological description of kidney diseases diagnosed by biopsies from four countries: Côte d'Ivoire, Burkina Faso, Guinea-Conakry and Togo, over a period of five years (January 2015 to December 2019). The samples were transported by land or air transport connecting the various capitals of the region (Table 4).

Many biases and limitations were observed during the course of this work. Indeed, many patients could not be biopsied for economic reasons on the one hand (impoverishment of populations and the lack of financial subsidy for the biological and immunological assessment and the sometimes high cost of

Table 2. Distribution of histological types according to gender.

Histological types	Total	Male		Female	
		Number	%	Number	%
Focal Segmental Glomerulosclerosis	62	27	29.7	35	39.8
Nas Benign/Malignant	19	14	15.4	5	14.8
G Extramembranous	18	11	12.1	7	7.9
Post Infectious Gn	16	10	11	6	6.8
Lupus Gn	13	-	-	13	14.8
Membranoproliferative Gn	9	4	4.4	5	5.7
Thrombotic Microangiopathy	7	5	5.5	2	2.3
Myeloma Cylinders N	7	4	4.4	3	3.4
Extracapillary Gn	6	4	4.4	2	2.3
Amyloidosis	6	2	2.2	4	4.6
Tubulointerstitial Nephritis	4	1	1.1	3	3.4
Non Amyloid Gn	3	3	3.3	-	-
Minimal Glomerular Lesion	3	2	2.2	1	1.1
Iga N	3	2	2.2	1	1.1
Systemic Vasculitis	2	2	2.2	-	-
Diabetic N	1	-	-	1	1.1
Total	179	91	100	88	100

Note: Gn = Glomerular Nephropathy; N = Nephropathy

Table 3. Distribution of histological types according to age groups.

Histological types	Age groups						Total
	≤ 18 years		19 – 59 years		≥ 60 yeras		
	N	%	N	%	N	%	
FSGS	9	14.5	53	85.5	-	-	62
BMNAS	-	-	19	100	-	-	19
EMGN	1	5.6	17	94.4	-	-	18
PIGN	5	31.2	10	62.5	1	6.3	16
LGN	1	7.7	12	82.3	-	-	13
MPGN	1	11.1	7	77.8	1	11.1	9
TMA	-	-	7	100	-	-	7
CNM	1	14.4	3	42.8	3	42.8	7
ECGN	3	50	3	50	-	-	6
AL	-	-	4	66.7	2	33.3	6
TIN	-	-	3	75	1	25	4
NALGN	-	-	3	100	-	-	3
MGL	2	66.7	1	33.3	-	-	3
IgA N	-	-	3	75	1	25	4
SV	-	-	1	50	1	50	2
LN	-	-	1	100	-	-	1
Total	23	12.8	147	82.1	9	5.1	100

pathological analysis of biopsies). On the other hand, few nephrologists are trained in the practice of kidney biopsy in the French-speaking West African region. Despite this non-representative sampling of the population of the region, our study highlighted certain epidemiological, clinical and etiological features of inflammatory renal pathologies.

Over the study period, 179 kidney biopsies were collected that met the inclusion criteria of 35.8 cases/year. This incidence is lower than many authors in the African and Asian literature [4,11,12], but relatively higher than that of Mhamedi SA, et al. [4], in Morocco. The average age of patients at the time of performing renal biopsies varies according to the authors [2,4, 6,7,10-13]. Men were more represented in biopsy-proven kidney disease (50.8%), similar to observations in other regions [11,13,14]. Moreover, in Morocco, in the series of Mbarki H, et al. [13], a female predominance was reported in a cohort of renal biopsies whose sampling is more extensive. The presence of recurrent oedemato-ascitic syndrome and the existence of hypertension accounted for 16.8% and 5.8% respectively of the history. Mhamedi SA, et al. [4] in Morocco reported higher rates of High Blood Pressure in 36% of cases and a reduction in diuresis with OKI in 2% of cases. This difference between the populations could be explained by the small size of our sampling. HIV infection was found in 10.3% (n=36) of cases in our series. In South Africa, where the prevalence of the disease is higher, Okpechi IG, al. [6] found a frequency of 30% of cases. The association of renal pathologies with viral hepatitis B was weak in our work (3.1%). Elsewhere in Africa and Asia, higher rates were reported [6,15]. This may be related to the difficulties of performing biological and serological assessments in our region unlike other regions in Africa and Asia [6,7]. Biologically, the protein assay was performed in all patients in our study, as in Western and Asian countries where almost all patients benefit from the systematic protein assay [11,16]. Nephrotic syndrome was the most common mode of presentation of kidney disease and the main indication of RBs (64.2% of cases). This result is close to that of Mbarki SA, et al. [4], in Morocco who found a rate of 61% of cases, Okpechi IG, et al. [6] in South Africa who noted 58.6% of cases and other Western and Asian authors [11,17,18]. Persistent acute renal failure, the second indication of RBs in our series accounted for 7.8% of cases. A similar finding was made by Mhamedi in Morocco (14%) [4] and Senegal by Abou N, et al. [19] with 14% of cases. Other indications of RB, sometimes very varied, were reported in the literature [4,6]. Percutaneous biopsy is the main technique used as seen in the literature [4,10,18,19]. However, it remains a source of complications such as bleeding and often resolute abdominal viscera injury [1]. Halimi JM,et al. [20], reported a 5% risk of hemorrhage in a French cohort (2,765/52,138 percutaneous RBs) and a high risk of death. This result is lower than ours (2.2%). However, no cases of death were reported in our study despite the sometimes difficult conditions of implementation. The pathological examination confirmed the diagnosis of all the nephropathies. In the majority of cases, the immunofluorescence associated with the optical microscope study made it possible to affirm the diagnosis by highlighting specific antibody-antigen immune deposits. In other cases, the diagnosis was based on data from optical microscopy and after a multidisciplinary consultation between nephrologists and pathologists. This is the case of 11 cases of FSGS, 3 cases of nephroangiosclerosis, 3 cases of extramembranous GN, 3 cases of tubulointerstitial nephritis, 3 cases of MPGN, 2 cases of amyloidosis and 1 case of Extracapillary Glomerulonephritis (ECGN). We reported 97.7% glomerular nephropathy and 2.2% tubulo-interstitial nephritis during this work. High rates of glomerular nephropathy are consistently observed in the vast majority of series [11,14,19]. FSGS is the leading cause of nephrotic syndrome and the first kidney disease diagnosed on a kidney biopsy. This was also reported in Brazil, Saudi Arabia and India [18,21,22]. This would be linked firstly to the low rate of elderly people in this

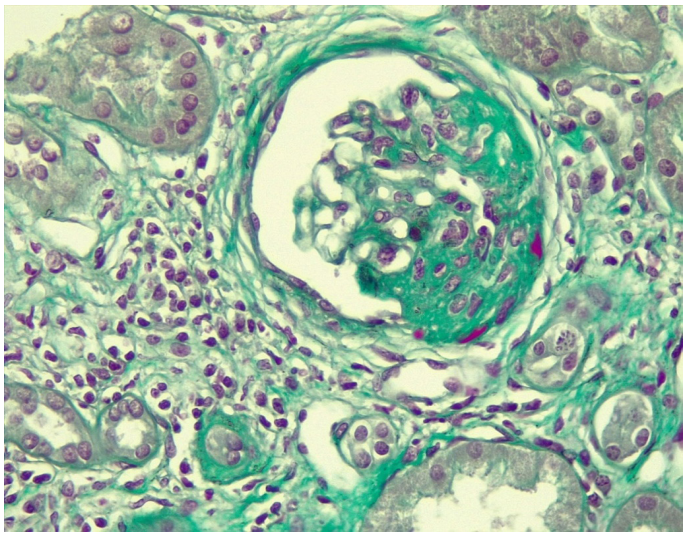

Figure 2. (Masson's Trichrome × 25): Focal segmental glomerulosclerosis lesion of collapsing type with retraction of the flocculus on the vascular pole and significant sclerosis (red circle) and a periglomerular interstitial monocytic infiltrate (red arrow).

Table 4. Distribution of histological types according to indications.

Histological types	Indications										
	NS	ARF	RPGN	NS+CKD	CKD	NS+ARF	NS+H	NST	RPGN+ARF	NST+ARF	Total
FSGS	43	8	1	4	4	2	-	-	-	-	62
BMNAS	7	2	5	4	1	-	-	-	-	-	19
EMGN	14	1	-	-		3	-	-	-	-	18
PIGN	10	-	-	-	1	-	1	4	-	-	16
LGN	12	-	1	-		-	-	-	-	-	13
PMGN	8	-	-	1		-	-	-	-	-	9
TMA	4	-	1	-		-	2	-	-	-	7
CNM	-	1	-	2	3	-	-	-	-	1	7
ECGN	2	-	4	-		-	-	-	-	-	6
AL	6	-	-	-		-	-	-	-	-	6
TIN	-	2	-	-	1	-	-	-	1	-	4
NALGN	3	-	-	-	-	-	-	-	-	-	3
MGL	3	-	-	-	-	-	-	-	-	-	3
IgA N	2	-	-	-	-	-	1	-	-	-	3
SV	-	-	1	-	-	-	1	-	-	-	2
LN	1	-	-	-	-	-	-	-	-	-	1
Total	115	14	13	11	10	5	5	4	1	1	179

Note: FSGS: Focal segmental glomerulosclerosis; BMNAS: Benign and malignant nephroangiosclerosis; EMG: Extramembranous glomerulonephritis; PIGN: Post-infectious glomerulonephritis; LN: Lupus nephropathy; MPGN: Membrano-proliferative glomerulonephritis; TMA: Thrombotic microangiopathy; CNM: Cylinder nephropathy myeloma; ECGN: Extracapillary glomerulonephritis; AL: Amyloidosis; TIN: Tubulointerstitial nephritis; NALGN: Non-amyloid glomerulonephritis; MGL: Minimal glomerular lesion; IgA N: IgA nephropathy; SV: Systemic vasculitis; LN: Lupus nephropathy

part of the world (sub-Saharan Africa) and secondarily to the pathologies of elderly people whose main causes are often hypertension, diabetes or other defects rarely requiring RB. Nephrotic syndrome was the primary indication for renal biopsy of lupus nephropathy (92.3%), extramembranous GN (77.8%), FSGS (69.3%) and post-infectious GN (62.5%) [6,16,23]. The high frequency of FSGS in our series is related to the APOL1 gene present in black populations [6]. In Western countries such as the USA, France, Italy and Australia [23-26], IgA-depositing nephropathy is the most common nephropathy whereas it is very rare in our study (1.7%). This high frequency of IgA-depositing nephropathy in the West is thought to be related to a high prevalence of genetic susceptibility and especially early detection of urinary abnormalities increasing the indications of kidney biopsies [15]. In children and adolescents, RB is not systematic in nephrotic syndrome. The 9 cases identified in our collection were carried out during an impure nephrotic syndrome. The main kidney diseases in these children and adolescents were FSGS, post-infectious GN and ECGN. Other authors cited a preponderance of MBG as the leading cause of nephrotic syndrome in children [13,18]. This difference could be explained by the lack of specialized infrastructure and the inherent difficulties in exploring children and adolescents suffering from impure nephrotic syndrome in our region. Adults represented a considerable proportion in our collection (82.1%) as is the case in other series [6,13,18]. Subjects aged 60 and over (5.1%) were biopsied in a lower proportion of our work. Persistent acute renal failure accounted for 7.8% of the indications in our work. It was observed in tubulo-interstitial nephritis in 50% of cases, in MBNA in 36.4% of cases and in FSGS in 12.9% of cases. The same findings were made in African series [6,19]. In addition, RPGN was observed during extracapillary GN, which is a diagnostic and therapeutic emergency. Nephritis syndrome was found during post-infectious GN [6,13]. The study of renal biopsies carried out in the French-speaking West African region completely changed the diagnostic reasoning and consequently the therapeutic management of patients. Our data underline the importance and value of systematically using RB in the management of kidney disease. Histological diagnosis is of great value in clinical nephrology and renal transplantation. It is used to guide the treatment of ECGN as a diagnostic and therapeutic emergency [4,13]. This study provided a general description of RB-proven kidney disease in the French-speaking West African region. However, these results should be interpreted with caution given the retrospective nature and small sampling of the series, in comparison with data from the literature. This study could be a first step towards a multicentre study that would compare the clinical and histological characteristics of kidney disease across West African countries, to determine the occurrence of certain kidney diseases and to guide epidemiological, diagnostic and therapeutic protocols.

Conclusion

The capacity of hemodialysis care in Ivory Coast has increased in recent years. Indeed, the policy of decentralization of hemodialysis services has allowed the opening of hemodialysis centers in the interior of the country, including the one that was the subject of our study. Our patients were mostly young adults with an average age of 41 years. Dialysis was initiated in our center in 85.9% of cases. The first session at the center was performed on a catheter in 81% of cases. Anemia was found in 90.6% of cases and its management by ESA was possible in 32.9%. Mortality was 26%. The more chronic kidney disease worsens, the more it requires continuous and simultaneous monitoring of various, sometimes divergent, parameters. This finding suggests that it justifies the development of a medical program to ensure continuity of care. This should include early identification of patients, an education program to help patients manage their chronic disease, and an evaluation of the quality of care. Finally, it should be noted that optimized management and renovation of pre-existing dialysis facilities is profitable for the patient and for the low-income population.

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Conflicts of Interest

The authors do not declare any conflicts of interest.

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