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Benign Nephroangiosclerosis: Diagnostic Criteria of Bamako, Mali

Seydou Sy[1,2*], Magara Samake[3,4], Aboubacar Sidiki Fofana[3,4], Djénéba Maîga[1,4], Sidi Fomba[1], Atabieme Kodio[1], Djibril Sy[2,5], Hamadoun Yattara[1,2], Modi Sidibe[1,4], Alkaya Toure[1,4], Moustapha Tangara[1,4], Saharé Fongoro[1,4]

[1]Nephrology and Hemodialysis Department, University Teaching Hospital of Point-G, Bamako, Mali
[2]Faculty of Medicine and Odontostomatology, University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali
[3]Nephrology Unit, Fousseyni Daou Hospital in Kayes, Kayes, Mali
[4]National Center for Scientific and Technological Research (CNRST), Bamako, Mali
[5]Department of Internal Medicine, University Teaching Hospital of Point-G, Bamako, Mali
Email: *seydousy2002@yahoo.fr

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Abstract

Introduction: Long-standing and inadequately controlled high blood pressure (HBP) can cause a chronic kidney disease called benign nephroangiosclerosis (BNAS). Objective: To determine the frequency of BNS using clinical and paraclinical criteria adapted to our practice setting, where renal biopsy was not routinely performed. These criteria will now serve as diagnostic criteria for benign nephroangiosclerosis. **Methodology:** Retrospective descriptive study from January 1, 2021, to December 31, 2022, focusing on patients hospitalized in the nephrology and hemodialysis department of the Point G University Hospital during that period. Our criteria for defining BNS were: chronic kidney disease (CKD) at the stage of chronic renal failure (CRF) (defined as an eGFR < 60 ml/min/1.73 m^2 for more than 3 months) resulting from untreated or poorly treated hypertension for at least 3 years, associated with minimal proteinuria ≤ 1g/24h with normal urinary sediment, harmoniously reduced kidney size, hypertensive retinopathy, and/or left ventricular hypertrophy. **Results:** Among 1511 patients, 139 met our criteria, representing a frequency of 9.2%. The sex ratio was 1.27. The average age was 43.45 ± 13.47 years. Symptoms included vomiting (81.3%). CKD was in the end-stage in 92.80% of cases. Grade III hypertension was present in 51.62%. Proteinuria was minimal in 90.52%. Urinary sediment was normal in 52.5%. LVH was present in 73.72% on ECG. Hypertensive retinopathy was present in 67% of cases. The kidneys were atrophied in 88.72% of cases. Antihypertensive drugs were used in 95.7% of cases. Patients underwent hemodialysis in 93.53% of cases. The mortality rate was 15.1%. **Conclusion:** This study shows that be-

nign nephroangiosclerosis is common in hospitals. These clinical and paraclinical criteria will enable rapid diagnosis in the absence of other potential causes of CKD. It affects young, highly active individuals, which is why national community programmes must be developed in Africa, particularly in Mali, for a broad campaign of prevention, early detection, and effective and appropriate management of hypertension in order to effectively and significantly reduce this high incidence of chronic kidney disease.

Keywords

Benign Nephroangiosclerosis, CKD/CRF, Dialysis, Mali

1. Introduction

High blood pressure (HBP) is accompanied by widespread changes in blood vessels, particularly in the kidneys [1]. Indeed, long-standing and poorly controlled HBP can cause chronic hypertensive kidney disease known as benign nephroangiosclerosis (BNAS) [2]. This condition results in slowly progressive renal failure, which can progress to end-stage renal disease.

Hypertensive vascular nephropathies account for nearly 15% of cases of chronic renal failure (CRF) in developing countries [3] [4].

The incidence of end-stage renal failure (ESRF) related to hypertension is estimated to be 1 in 2200 hypertensive patients in the United States and closer to 1 in 6000 hypertensive patients in Europe. In new dialysis patients, hypertension is one of the main causes of ESRD. NASB is the leading cause of dialysis in France and is responsible for more than 20% of dialysis cases in the United States. It is a growing cause of dialysis worldwide [5] [6].

Between 2012 and 2014 in Nigeria, in a study conducted by OMOTOZO B on 208 hypertensive patients from outpatient clinics at Obafemi Awolowo University Teaching Hospital Complex (OAUTHC) Ile-Ife, 125 (60%) met the diagnostic criteria for NAS [7].

In Senegal, at the A. Le Dantec University Hospital in Dakar, in a retrospective study covering the period from 2012 to 2016, the hospital prevalence of benign NAS was 10.43% [8].

In Mali, hypertension is the leading cause of haemodialysis. Most patients are young and consult at the stage of end-stage renal failure, which prompted us to propose these clinical and paraclinical criteria for use in similar clinical contexts. The aim of this study was to describe the epidemiological, clinical, therapeutic and evolutionary aspects of BNAS.

2. Methodology

This was a retrospective descriptive study covering the period from January 1, 2021, to December 31, 2022. It focused on patients hospitalized in the nephrology

and hemodialysis department of the Point G University Hospital during that period.

Our criteria for defining NASB were: chronic kidney disease (CKD) at the stage of CRF (defined as an eGFR < 60 ml/min/1.73m^2 for more than 3 months) resulting from untreated or poorly treated hypertension lasting at least 3 years, associated with minimal proteinuria ≤ 1g/24h with normal urinary sediment, harmoniously reduced kidney size, and hypertensive retinopathy and/or left ventricular hypertrophy.

A pre-established individual survey form was used to collect patient data from hospital and outpatient records.

The variables were initially recorded on survey forms and then entered into an epidemiological analysis tool, SPSS version 22.0. The results were expressed as averages with extreme values for quantitative variables and as proportions for qualitative variables. For text and graphic processing, Microsoft Office 2016 Word and Excel software and various tests (Chi-square, continuity correction, Fisher's exact test) were used as appropriate to search for correlations between qualitative variables with a significance threshold set at 5%.

The variables studied were socio-demographic characteristics (age, sex, residence, ethnicity, nationality), clinical characteristics (reasons for consultation, hemodynamic parameters, symptoms, general signs, physical signs), paraclinical characteristics (creatinine, azotemia, uric acid, blood count, urine culture, 24-hour proteinuria, ECG, cardiac ultrasound, fundus examination, blood ionogram, calcium-phosphorus balance, renal ultrasound), therapeutic variables, and variables related to progression.

The confidentiality of the files was respected. The results of this work were used for scientific purposes only.

Operational definitions:

Chronic kidney disease: This is defined as the existence for more than three months of:

- Renal failure defined by a glomerular filtration rate (GFR) < 60 ml/min/1.73m^2 (see Table 1);
- And/or a morphological or histological renal abnormality, provided that it is clinically significant;

Table 1. Stages of chronic kidney disease based on GFR.

Stages	Description	DFG (ml/min/1.73m^2)
1	Chronic kidney disease with normal kidney function	≥90
2	Chronic kidney disease with mild kidney failure	60 - 89
3A	Mild to moderate kidney failure	45 - 59
3B	Moderate to severe kidney failure	30 - 44
4	Severe kidney failure	15 - 29
5	End-stage kidney failure	<15

- And/or an abnormality in blood or urine composition secondary to renal impairment.

Criteria for defining benign nephroangiosclerosis (BNAS)

BBNS is defined as CKD at the stage of CRF (defined as an eGFR < 60 ml/min/1.73m^2 for at least 3 months) resulting from untreated or poorly treated hypertension that has been present for at least three (03) years, associated with:

- minimal proteinuria ≤ 1 g/24h;
- normal urinary sediment;
- harmoniously reduced kidney size;
- hypertensive retinopathy;
- and/or left ventricular hypertrophy.

The threshold value of 3 years or more for a history of hypertension was chosen because we found that most patients consulting already had markers of renal and extra-renal damage associated with hypertension. This threshold was also mentioned in Lemrabott's study in Dakar [8].

The Kirkendall classification was used for this retinopathy:

- Stage I: severe diffuse arterial narrowing.
- Stage II: in addition, presence of retinal hemorrhages, dry exudates, and cotton wool spots.
- Stage III: in addition, presence of papilledema.

3. Results

Of 1511 patients, 139 met our criteria, representing a frequency of 9.2%. Males accounted for 56.1% of cases, with a sex ratio of 1.27. The reason for consultation was impaired renal function in all patients. The average age was 43.45 ± 13.475 years, ranging from 18 to 84 years. Uremic syndrome was characterized by vomiting (81.3%), asthenia (53.9%), and anorexia (49.6%) (see **Table 2**). Functional signs included headaches (71.2%), dizziness (59.7%), and oliguria (46.8%). At admission, hypertension was present in 82.02% of cases. It was systolic-diastolic in 82.46% and grade III in 51.62% (see **Table 3**). CKD was in the terminal stage in 92.80% of cases (**Figure 1**). The mean creatinine level was 1392.04 ± 697.205 µmol/L, with extremes of 170 and 3399 µmol/L. The mean proteinuria was 0.64 ± 0.647 g/24h, and minimal in 90.52% of cases. Diuresis was preserved in 70 patients, or 50.4% of cases. Hemoglobin levels were 6–8 g/dL in 54.7% of cases, with a mean of 7.56/dL and extremes of 3 and 13 g/dL. The kidneys were reduced in size (88.72%), poorly differentiated (87.96%), and hyperechoic (60.15%).

HVG was present in 40.14% of patients undergoing cardiac ultrasound and in 73.72% of patients undergoing ECG.

Hypertensive retinopathy was present in 47.1% of patients. It was stage 2 according to Kirkendhal in 44.66% of cases (**Figure 2**).

Hemodialysis patients accounted for 93.53% of cases. Antihypertensive drugs were used in 95.7% of cases. Calcium channel blockers were used in 87.8% of patients, followed by loop diuretics in 53.2% (see **Table 4**).

Complications of CRF included anemia (94.16%), metabolic acidosis (37.41%), OAP (25.18%), and hyperkalemia (25.17%) (see Table 5).

The outcome was marked by the death of 21 patients (15.2%). The causes of death are shown in Figure 3.

Table 2. Distribution according to symptoms of uremic syndrome.

Symptoms	Number (n = 139)	Percentage (%)
Vomiting	113	81.3
Asthenia	75	53.9
Anorexia	69	49.6
Insomnia	22	15.8
Nausea	21	15.1
Tremor	18	12.9
Epistaxis	9	6.5
Uremic Péricarditis	6	4.3
Muscle crampe nucturia	5	3.6
Daytime sleepiness	3	2.2
Confusion	2	1.4
Pruritus	2	1.4
Coma	1	0.7

Table 3. Distribution of patients according to hypertension grade.

Grade of hypertension	Number (n = 124)	Percentage (%)
High normal BP	10	8.06
Grade I	28	22.58
Grade II	22	17.74
Grade III	64	51.62
Total	**124**	**100**

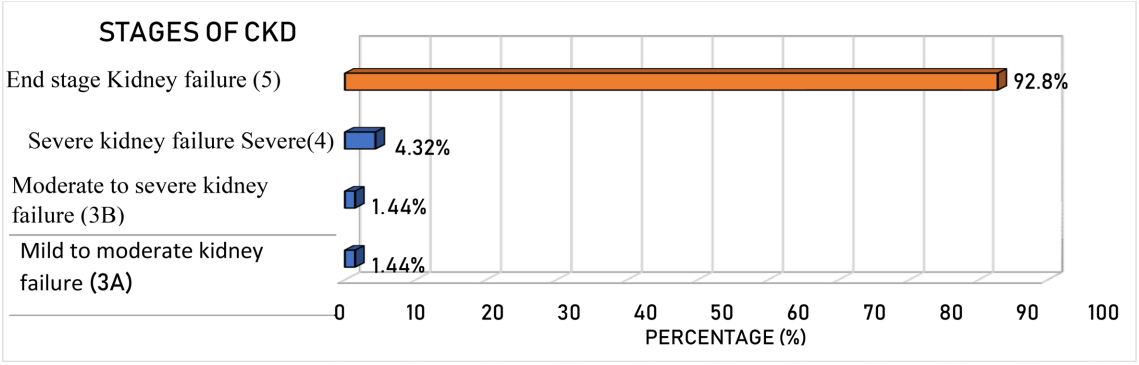

Figure 1. Distribution of patients according to stage of CKD.

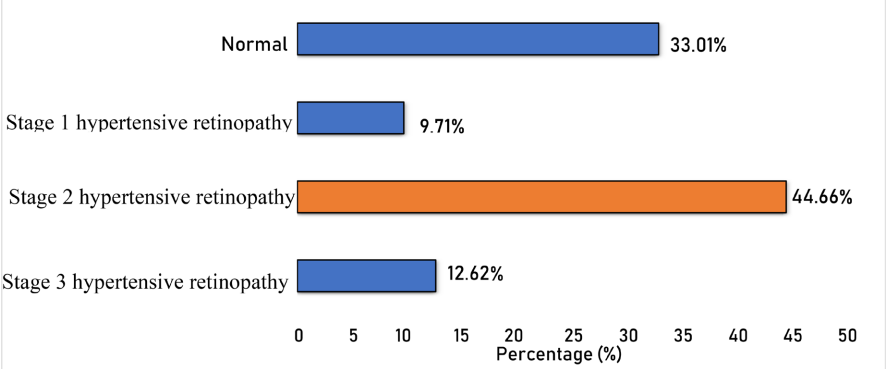

Figure 2. Distribution of patients according to fundus examination.

Table 4. Distribution of patients according to the type of antihypertensive drug used.

Antihypertensive drugs	Number (n = 139)	Percentage (%)
Calcium channel blockers	122	87.8
Loop diuretics	74	53.2
Central antihypertensive drugs	63	45.3
ACE inhibitors	29	20.9
Beta blockers	15	10.8
ARBs	7	5

Table 5. Distribution according to complications of CRF.

Complications		Workforce	Percentage (%)
Haematological	Anemia	125	94.96
Cardiovascular	left ventricular hypertrophy	120	87.59 56.83
	Uncontrolled hypertension	79	44.6
	heart failure	62	25.18
	acute pulmonary oedema	35	5.76
	Uremic pericarditis	8	
Electrolyte imbalances	Hyponatremia	105	75.53
	Hyperkaliemia	35	25.17
	hypokalemia	6	4.31
	Hypernatraemia	2	1.43
Calcium and phosphorus disorders	Hyperphosphataemia PTH	100	71.94
	high	96	69.06
	Vitamin D deficiency	52	37.41
	Hypocalcaemia	50	35.97
Metabolic	Metabolic acidosis	52	37.41
	Malnutrition	35	25.18

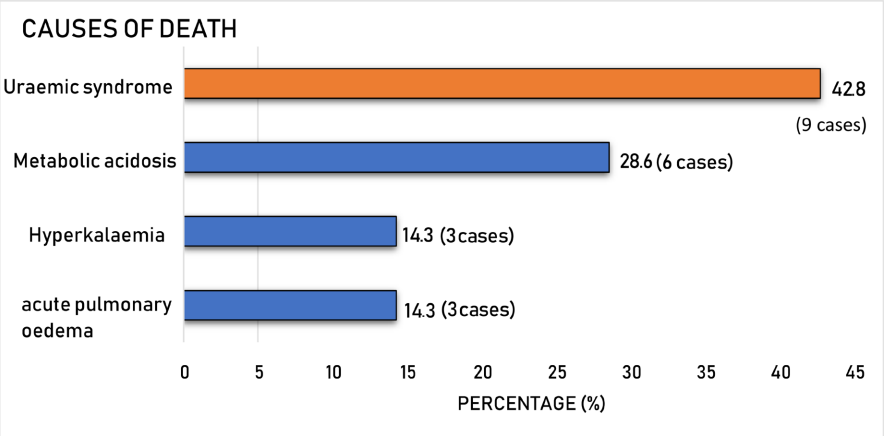

Figure 3. Distribution by cause of death.

4. Discussion

During the study period, 1511 patients were admitted to the nephrology and hemodialysis department of Point G University Hospital. Of these, 139 met our inclusion criteria, representing a frequency of 9.2%. This result was similar to those observed by Robles NR *et al.* in a study conducted in the nephrology department of the Infanta Cristina Hospital in Spain [9] and by Lemrabott A *et al.* in a study conducted at the A. Le Dantec University Hospital in Dakar, Senegal [8], which found frequencies of 9.4% and 10.43%, respectively. However, it was much lower than that found by Omotoso BA in his study conducted in outpatient clinics at the Obafemi Awolowo University Teaching Hospital Complex (OAUTHC) in Ile-Ife, Nigeria [7], where the frequency was 60%, as this was the frequency of patients diagnosed with BNAS among hypertensive patients and not among all patients hospitalized in the outpatient clinics at the university hospital complex where the study was conducted. All of the above frequencies were determined on the basis of a diagnosis of BNAS based on clinical criteria. However, in the same study conducted by Omotoso BA [7], out of 37 subjects with an adequate biopsy sample, 26 (70.27%) actually had the morphological characteristics of NASB. Similarly, in an earlier study conducted by Pietro Zucchelli and Alessandro Zuccalà [10] [11], out of 136 patients diagnosed with NASB on clinical grounds, a thorough diagnostic evaluation including a renal biopsy revealed true BNAS in 44.1% of patients. Furthermore, in one of the prospective studies [12] [13] involving 58 patients meeting the selection criteria for clinical hypertensive nephrosclerosis, true hypertensive nephrosclerosis was confirmed in 46%.

These data demonstrate the low specificity of NAS diagnosis based on clinical criteria. However, although this condition is defined by histological lesions of the renal arteries, arterioles, and interstitium that occur as a result of long-term essential hypertension, it is rarely diagnosed on the basis of a renal biopsy [14].

In our study, males predominated, accounting for 56.1% of cases, with a sex ratio of 1.27. This predominance of BNAS in males was also found in studies by Robles NR *et al.* [5] and Lemrabott A *et al.* [8], where the sex ratios were 1.33 and

1.07, respectively. However, Omotoso BA [7] found a female predominance in his study, with a sex ratio of 0.42.

The average age of patients in our study sample was 43.45 ± 13.47 years, with extremes of 18 and 84 years. Patients in the 30-44 age group accounted for 38.1% of cases. In the studies conducted by Lemrabott A *et al.* [8], Robles NR *et al.* [9], and Omotoso B [7], the mean ages were 56.95 ± 13.23 years, 66.6 ± 12.1 years, and 57.0 ± 5.32 years, respectively.

The main reason for consultation was increased serum creatinine associated with Dieulafoy's neurosensory signs, found in 80.6% of patients in our sample. In the study by Lemrabott A *et al.* [8], impaired renal function was the most common reason for consultation (84.32% of patients). This high proportion of increased serum creatinine as a reason for consultation could be explained by the fact that almost all patients in our study were referred for elevated serum creatinine. The high prevalence of Dieulafoy's neurosensory signs among the reasons for hospitalization can be explained by the fact that the patients in our sample, all of whom had had hypertension for at least three years, generally consulted their physician when clinical manifestations of hypertension appeared, with renal function impairment already present.

CRF was found in all of our patients. It was mild (1.4%), moderate (1.4%), severe (4.3%), and terminal (92.8%) with preserved diuresis in 50.4% of cases. Our study reveals the clinical paradox of term "benign nephroangiosclerosis", as nearly 93% of the studied cohort presented with severe end-stage renal failure. The manifestations associated with uremic syndrome were, in order of frequency: vomiting (81.3%), physical asthenia (54%), anorexia (49.6%), uremic frostbite (17.3%), nausea (15.1%), insomnia (15.8%), tremors (12.9%), epistaxis and/or hematemesis (6.47%), and muscle cramps (4.3%). Omotoso BA [7], in his study, found symptoms of nocturia (21.2%), polyuria (1%), facial swelling (3.8%), foamy urine (8.2%), anorexia, nausea, and daytime sleepiness in 2 (1%) of the study participants. The literature states that NAS is a remarkably discreet clinical disease and is completely asymptomatic for many years in most patients [15]. The high incidence of NASB symptoms in our study could be explained by the high frequency of end-stage renal disease (92.8%).

In our study, proteinuria was negative (5.26%), minimal (90.52%), moderate (1.05%), and massive (3.15%). Omotoso BA [7] found persistent proteinuria greater than 150 mg/24h in 84% of cases in his study.

The presence of moderate to severe proteinuria in some of our patients could be explained by the fact that in our sample, a significant proportion (34.35%) of patients had a positive urine culture, which would have increased the proteinuria value.

In our study, renal ultrasound showed a decrease in kidney size in 88.72% of our patients, poor corticomedullary differentiation in 87.96%, and hyperechogenicity in 60.15%. The literature indicates that radiologically or on ultrasound, the kidneys appear normal in size (at least initially) or slightly reduced, symmet-

rical, and with harmonious contours [15].

The fundus was normal in 33.01% of cases. Hypertensive retinopathy stage 1 was found in 9.71% of cases, stage 2 in 44.66% of cases, and stage 3 in 12.62% of cases. In the study by Lemrabott A *et al.* [11], stage II hypertensive retinopathy was also the most common, with a rate of 51.3%. Omotozo BA [7] found stage I, II, and III hypertensive retinopathy in 62.4%, 18%, and 3% of cases, respectively.

Hemodialysis was performed in 93.53% of our patients. This is due to the fact that a large number of patients had complications such as increased uremic syndrome, hyperkalemia, OAP, and metabolic acidosis.

The outcome was favorable in 55.4% of patients. Lemrabott A *et al.* [8] reported in their study that the outcome of renal function was favorable, with stabilization or improvement in GFR in 21.25% of patients. And in the study by Robles NR *et al.* [5], the estimated average survival was 194.0 ± 16.3 months and the actual average survival was 169.0 ± 18.0 months. Estimated survival was 96.0% after one year, 85.9% after five years of follow-up, and 81.6% after seven years of follow-up.

The mortality rate was 15.1% in our study. This mortality rate is likely to be underestimated given that we have no information on the outcome of the 15.82% of patients who were discharged against medical advice and also, among the 55.4% of patients discharged with a favorable outcome, a large number of them did not attend their follow-up appointments and were lost to follow-up.

5. Limitations of the Study

During our study, we encountered certain limitations, the main ones being unusable records, inadequate technical facilities in terms of treatment and the feasibility of certain medical analyses at the Point G University Hospital, and the low socio-economic status of patients, which limited treatment and comprehensive investigation of the pathology studied. It should also be noted that advanced CRF made the diagnosis of NASB ambiguous in a significant number of our patients who consulted late and in whom no renal biopsy was performed, and therefore other potential causes of CRF could not be definitively ruled out in patients with end-stage chronic kidney disease.

6. Conclusion

This study shows that benign nephroangiosclerosis is common in hospitals. These clinical and paraclinical criteria will enable rapid diagnosis in the absence of other potential causes of CKD. It affects young, highly active individuals, which is why national community programmes must be developed in Africa, particularly in Mali, for a large-scale campaign of prevention, early detection and effective, appropriate management of hypertension in order to effectively and significantly reduce this high incidence of chronic kidney disease.

Conflicts of Interest

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

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