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Pathological and Etiological Aspects of Nephrotic Syndrome at the Niamey General Reference Hospital

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Abstract

Introduction: Studies have been conducted on nephrotic syndrome in Niger. The study aimed to determine the histological and etiological aspects of nephrotic syndrome. **Patients and Method:** This was a retrospective study from February 1st, 2018 to January 31st, 2024. All patients with nephrotic syndrome who underwent renal biopsy were included. Samples were analyzed at the anatomy-cytology pathology laboratory of the Faculty of Medicine in Dakar (Senegal). The variables studied included clinical, biological, histological and etiological characteristics. Data were analyzed using Excel 2013 and Epi-info 7.2.0 software. **Results:** The study included 119 patients with nephrotic syndrome. Prevalence of nephrotic syndrome was 11.24%. The male-to-female ratio was 2.25:1. The mean age at diagnosis was between 34.5 ± 18.84 years. Edema was the reason for admission in 40.34% of cases. The nephrotic syndrome was impure in 63.86% of cases. Nine histological lesions were identified. Focal and segmental glomerulosclerosis (40.09%), minimal change disease (23.53%), membranous nephropathy (13.45%), diabetic nephropathy (10.92%), membranous proliferative glomerulonephritis (3.36%), acute glomerulonephritis (3.36%), glomerular thrombotic microangiopathy (2.52%), non-IgA mesengial proliferative glomerulonephritis (1.68%) and amyloidosis (0.84%). Nephrotic syndrome was primary in 57.98% of cases. Secondary etiologies were dominated by diabetes (11.76%), followed by hepatitis B virus (9.24%), lupus, lymphoma, malaria, syphilis, cryoglobulinemia, sickle cell disease and HIV. **Conclusion**: Future studies should investigate the causes of glomerulopathy secondary to chronic tubulointerstitial lesions.

Keywords

Nephrotic Syndrome, Anatomopathology, Niamey General Reference Hospital

1. Introduction

Nephrotic syndrome indicates the presence of glomerular nephropathy. It is characterized by proteinuria exceeding 3 g/24h in adults or 50 mg/kg/d in children, serum albumin below 30 g/L and serum protein below 60 g/L [1] or proteinuria-creatinuria ratio on fresh urine exceeding 200 mg/mmol associated with hypoalbuminemia below 30 g/L in children [2]. When associated with hypertension and/or renal failure and/or microscopic hematuria, it is classified impure; otherwise, it is considered pure. Nephrotic syndrome accounts for 90% of glomerular disease cases in children and 20% in adults [3]. Renal biopsy is mandatory for diagnosing glomerular nephropathy. Offering histological diagnostic, therapeutic and prognostic insights for managing nephrotic syndrome [4]. Renal biopsy is common practice in Western, Asian, North African and South African countries [5] but it is uncommon in French-speaking sub-Saharan Africa [6] [7]. The study of renal biopsies carried out in this region has completely altered diagnostic reasoning and consequently the therapeutic management of patients [8]. In Niger, studies have been conducted on nephrotic syndrome [1] [9]; however, they did not consider the histological aspect. Therefore, we undertook this study to contribute to a better understanding of the histopathological and etiological aspects of nephrotic syndrome by analyzing our six years of experience at the Niamey General Reference Hospital.

2. Patients and Method

The study was conducted at the Nephrology-Dialysis department of Niamey General Reference Hospital from February 1st, 2018 to January 31st, 2024. It was a descriptive and retrospective study. The target population included all patients admitted (consultation and hospitalization) with nephrotic syndrome. The inclusion criteria comprised all confirmed cases of nephrotic syndrome who underwent renal biopsy in adults and children. Patients who had a diagnosis of nephrotic syndrome but did not undergo renal biopsy were excluded.

Nephrotic syndrome was diagnosed based on biological criteria, characterized by proteinuria exceeding 3 g/24h with hypoprotidemia below 60 g/L and hypoalbuminemia below 30 g/L in adults, or proteinuria/creatinuria ratio exceeding 200 mg/mmol associated with hypoalbuminemia below 30 g/L in children.

Systematic tests performed included:

- Blood: azotemia, creatininemia, proten, albumin, hemogram, platelets, prothrombin rate/normalized ratio index (INR), activated partial thromboplastin time (APTT).
- Urine: albustix (urine dipstick: albuminuria, hematuria, leukocyturia, nitrituria, glycosuria, pH, specific gravity, urobilinogen, bilirubin), 24-hour proteinuria, urine culture.
- Imaging: renal ultrasound.

Renal biopsy was performed in the absence of contraindications and after ultrasound localization. Two fragments were fixed in acetic acid-formaldehyde-alcohol

(AFA) fixative tube. Samples were analyzed at the pathology and cytology laboratory of the Faculty of Medicine and Pharmacy of Cheikh Anta Diop University in Dakar, Senegal.

Data collection was done through a documentary review of hospitalization, consultation, renal biopsy registers, patient records and renal biopsy result. Hospital administration approval and informed consent from all patients were obtained. An informed consent form was signed by all patients before renal biopsy was performed. Anonymity was maintened during data processing and presentation of results. The variables studied were patient sociodemographic characteristics, admission reasons (consultation and hospitalization), clinical, biological, histological and etiological characteristics. The analytical study was made to explore differences in histological and etiological patterns between gender, age and clinical presentations. Data analysis was performed using Excel 2013 and Epi-info 7.2.0. Results were presented as tables and figures, showing frequencies for qualitative variables and mean, standard deviation, maximum and minimum for quantitative variables. A p-value < 0.05 was considered significant.

3. Results

The study included 119 patients with nephrotic syndrome. They included 82 men (68.91%) and 37 women (31.09%). The male-to-female ratio was 2.21:1. Mean age at diagnosis 34.5 ± 18.84 years; aged range from 3 to 84 years. Eleven patients were under 12 years of age. Admission reasons are presented in Table 1. Edema was the main reason in 48 cases (40.34%), associated with renal failure in 12 cases (10.08%). Nephrotic syndrome was impure in 76 patients (63.86%) and pure in 43 (36.13%). The 11 patients under 12 years were biopsied for impure nephrotic syndrome in 7 cases and steroid-resistant pure nephrotic syndrome in 4 cases (36.36%). Mean proteinuria was 4.5 ± 2.25 g/24h; mean serum albumin and protein were 19.07 ± 6.18 g/L and 46.91 ± 8.16 g/L respectively. Mean serum creatinine was 119.93 ± 80.99 µmol/L (extremes 8.76 to 1633 µmol/L) and 61 patients (51.26%) had no renal failure. Six patients (5.04%) had complications: right pelvic limb thrombophlebitis documented in 2 cases, pulmonary embolism

Table 1. Distribution of patients by reason for admission.

Reasons for admission	Workforce	Percentages
Œdema	48	40.34
Renal failure	32	26.89
Nephrotic syndrome	13	10.92
Renal failure + Œdema	12	10.08
Hypertension + renal failure	7	5.88
Hypertension + discovery of massive proteinuria	7	5.88
TOTAL	**119**	**100.00**

documented in 1 case, suspected cerebral sinus thrombosis in 1 case (in a 16-year-old child) resolved with anticoagulant treatment, orchitis in 1 case and pyelonephritis caused by *Escherichia coli* treated with imipenem in 1 case. Three patients had complications within the first 24 hours after the kidney biopsy: macroscopic hematuria in 1 case and pain intensity 6/10 in 2 cases.

Table 2 shows demographic, and clinical features in different histopathological groups and comparative results of our patients. Focal and segmental glomerulosclerosis (FSGS) was the most common in 48 cases (40.34%), followed by minimal change disease (MCD) in 28 cases (23.53%) and membranous glomerulonephritis (MGN) in 16 cases (13.45%). Other histopathological lesions were diabetic nephropathy (DN), Membranous proliferative glomerulonephritis (MPGN), glomerular thrombotic microangiopathy (glomerular TMA), mesengial proliferative (MP) and glomerular amyloidosis.

Table 2. Demographic, clinical features in different histopathological groups and comparative results.

	FSGS (n = 48)	MCD (n = 28)	MGN (n = 16)	DN (n = 13)	MPGN (n = 4)	AGN (n = 4)	Glomerular TMA (n = 3)	MGN (n = 2)	Amyloidosis (n = 1)
Gender									
F	13	7	6	6	1	1	2	1	0
M	35	21	10	7	3	3	1	1	1
p valu	0.22	0.22	0.27	0.11	0.42	0.42	0.12	0.31	0.34
Age (years)									
Mean age ± SD	33.59 ± 17.07	27.19 ± 17.49	31.57 ± 12.57	51.33 ± 7.93	33 ± 22.94	24 ± 9.93	46 ± 8.71	35.5 ± 20.5	84
Clinical features									
Micro hematuria	19	8	3	5	3	2	0	2	1
Edema alone	36	25	14	9	1	2	2	1	1
Hypertension alone	11	2	0	3	1	0	0	1	0
Edema/ hypertemsion	0	1	1	1	1	4	1	0	0
Edema and prurigo	0	0	1	0	0	0	0	0	0
Pleurisy	0	0	0	0	1	0	0	0	0
Proteinuria (g/24h)	4.76 ± 2.25	3.97 ± 1.71	4.76 ± 2.25	4.66 ± 2.17	6.21 ± 3.49	3.79 ± 1.5	3.42 ± 1.22	3.15 ± 1.21	3.6
Albumin (g/L)	18.35 ± 6.51	17.88 ± 6.36	18.59 ± 4.37	24.07 ± 3.52	18.35 ± 6.51	24.97 ± 5.16	23 ± 6.34	19.55 ± 0.63	20.6
Protein (g/L)	46.51 ± 8.91	46.37 ± 8.07	45.97 ± 6.05	52.38 ± 5.02	48.30 ± 10.27	50.22 ± 3.05	47.5 ± 4.76	42.45 ± 5.02	46.2

Etiological distribution in different histopathological groups is listed in Table 3. Nephrotic syndrome was primary in 69 cases (57.98%). Secondary etiologies were dominated by diabetes in 14 cases (11.76%), followed by hepatitis B virus (HBV) in 11 cases (9.24%). Diabetis was the cause of glomerular thrombotic microangiopathy (TMA) in 1 case and diabetic nephropathy (DN) in 13 cases. HBV has been identified as a cause of focal and segmental glomerulosclerosis,

minimal change disease and membranous proliferative glomerulonephritis (MPGN). Focal and segmental glomerulosclerosis secondary to tubulointerstitial nephritis was found in 7 cases. The 4 cases of acute glomerulonephritis were secondary to severe malaria. Lymphoma was the cause of MCD and MPGN. Syphilis, HIV, cryoglobulinemia, systemic lupus erythematosus, sickle cell and non-steroidal anti-inflammatory drugs (NSAIDs) were other etiologies.

Table 3. Distribution of etiology of nephrotic syndrome in different histopathological groups.

	FSGS (n = 48)	MCD (n = 28)	MGN (n = 16)	DN (n = 13)	MPGN (n = 4)	AGN (n = 4)	Glomerular TMA (n = 3)	MGN (n = 2)	Amyloidosis (n = 1)
Primitive (n = 69)	**30**	23	13	0	1	0	1	0	1
Diabete (n = 14)	0	0	0	13	0	0	1	0	0
Hepatitis B virus (n = 11)	7	2	0	0	2	0	0	0	0
CTIN (n = 7)	7	0	0	0	0	0	0	0	0
Lupus (n = 4)	**0**	0	3	0	0	0		1	0
Lymphoma (n = 2)	0	1	0	0	1	0	0	0	0
Syphilis (n = 2)	**1**	1	0	0	0	0	0	0	0
Malaria (n = 4)	0	0	0	0	0	4	0	0	0
Sikle cell disease (n = 2)	2	0	0	0	0	0	0	0	0
Cryoglobuminemia (n = 2)	0	0	0	0	0	0	1	1	0
NSAIDS (n = 1)	0	1	0	0	0	0	0	0	0
HIV (n = 1)	1	0	0	0	0	0	0	0	0

CTIN: chronic tubulointerstitial nephritis; NSAIDS: non-steroidal anti-inflammatory drugs; HIV: human immunodeficience virus

4. Discussion

This descriptive and retrospective study of nephrotic syndrome included both adults and children. It determined the histological lesions and specify the etiologies of nephrotic syndrome at the Niamey General Reference Hospital, the first in Niger to perform renal biopsy. This study has some limitations. Indeed, the monocentric nature of the study means that the results obtained cannot be generalized. Many patients could not be biopsied for financial reasons, and not all nephrologists in the country perform renal biopsy.

The mean age of our patients was 34 years. This is comparable to the mean age reported in France [3] and in sub-Saharan Africa [8]. It is higher than the ages reported by Diouf et al [10], Hassimi *et al.* [1] and Bah *et al.* [4] who reported mean ages of 28, 27 and 26 respectively. The male predominance found in this study has been reported by several African authors [1] [4] [10] and is constant according to Bah *et al.* Edema which was the main reason for the admission of our patients was reported in the first study conducted at National Hospital of Lamordé in Niger [1]. Late consultation of patients when edema is

well constituted and extensive would be the reason. The long delay in medical consultation could be explained by cultural beliefs, poverty and ignorance in Niger. Impure nephrotic syndrome was predominant in the study conducted by Hassimi *et al.* contrary to the literature [1]. This suggests that impure nephrotic syndrome is more frequent in Niger.

Thromboembolic and infectious complications in our patients, with 5.04% and 0.84% respectively. It is well known that patients with nephrotic syndrome have thromboembolic and infectious complications. Nephrotic syndrome can be complicated by bacterial infections, hypovolemia with collapse and renal failure, venous or arterial thrombosis and malnutrition [11]. According to Arjun Khanna [12], patients with nephrotic syndrome have an increased risk for thrombotic events such as deep veinous thrombosis, renal vein thrombosis and pulmonary embolism.

Optimization of the percutaneous renal biopsy technique, particularly real-time ultrasound guidance and automatic gun technique has made this procedure safe and free of major complications. However, there is always a risk of complications. Macroscopic hematuria was observed in 0.8% of patients, and pain of intensity 6/10 in 1.68%. These complications resolved spontaneously during post-kidney biopsy monitoring.

Glomerulonephritis is characterized based on histological lesions. Renal biopsy remains gold standard providing diagnostic and prognostic information forming the basis of current therapy [13]. Focal and segmental glomerulosclerosis followed by minimal change disease were the most frequent lesions, as reported in some studies [3] [4] [14] [15]. Focal and segmental Glomerulosclerosis (40.09%) was the most frequent histological lesion in our study. This was reported on a larger scale (47%) by Diouf *et al.* in Senegal [10] and Rahbar [15]. These results are higher than the prevalences of 26.1% reported across Africa and 34.6% in sub-Saharan Africa [8] while it is significantly lower (18.7%) in North Africa [16]. This suggests that focal and segmental glomerulosclerosis is more common in black individuals. Minimal change disease was found in 23.53% of our patients. It is comparable to African data (22.4% across the continent and 19% in West Africa) but lower than the 29.7% prevalence reported in North Africa [16] indicating minimal change disease might be more common in white individuals. Membranous nephropathy was 13.45% in our series. This is higher than reported in West Africa (5.9%) [16] and in sub-Saharan Africa (10%) [8] but lower than the 19.1% in East Africa [16]. Diabetic nephropathy was 10.92%, significantly lower than the 33% reported by Diallo *et al.* [17]. Membranoproliferative glomerulonephritis was found in 3.6% of cases in our study, comparable to the prevalence reported in West Africa. [16]. Acute glomerulonephritis was reported in 3.6%, compared to 2.6% in Africa. [16]. We found 0.84% of renal amyloidosis, while Diallo *et al.* [17] reported amyloidosis in 15% of cases. The histological lesions found in the 4 children biopsied for steroid-resistant nephrotic syndrome were a histological form of minimal change disease with diffuse mesangial sclerosis in 2.52% and focal and segmental glomerulosclerosis

in 0.84%.

Etiologies of nephrotic syndrome are primary or secondary [18]. While glomerulonephritis is characterized by histological lesions with primary and secondary forms, the renal biopsy does not always differentiate primary from secondary disease [13] necessitating an etiological investigation of nephrotic syndrome. In our series, nephrotic syndrome was primary in 57.98% and secondary in 42.02%. Idiopathic nephrotic syndrome can occur at any age and it was retained in front of a negative etiological assessment comprising a search for sickle cell, lupus, diabetes, human immunodeficiency virus (HIV) and hepatitis B virus (HBV) [19]. Focal and segmental glomerulosclerosis was the main primary lesion, and diabetes was the main secondary etiology of nephrotic syndrome in this study. Other patients testing positive for hepatitis B virus (HBV), syphilis, malaria and HIV were also identified as secondary etiologies as confirmed by Doumbia *et al.* that Parasitic (malaria) and bacterial infections were very frequent [19] in nephrotic syndrome. These confirm that, in addition to the classical causes described in the West, many infectious, viral and parasitic agents have been implicated in nephrotic syndrome etiology, especially in Black Africa [4]. Hepatitis B virus is a hepatotropic virus, but kidney disease may occur in 3-5% of patients with chronic HBV infection [20]. Three main forms of Glomerulonephritis have been described; the most common is membranous nephropathy, membranous proliferative glomerulonephritis and, more rarely, IgA nephropathy [21]. Cases of focal and segmental glomerulosclerosis have been described [20]. Studies [22] have suggested an association between plasmodium infection and the development of glomerulopathy, described mainly in the form of membranous proliferatve glomerulonephritis. Amoura *et al.* [22] reported 68.42% of collapsing focal and segmental glomerulosclerosis with negative HIV serology and minimal change disease due to malaria. Syphilis, non-steroidal anti-inflammatory drugs (NSAIDs), sickle cell disease, systemic lupus erythematosus, cryoglobinemia and lymphoma are recognized as glomerular involvement etiologies. Lupus glomerulonephritis was the second most reported secondary histological lesion by Diouf *et al.* [10] in 2001. Diallo *et al.* [17] reported cryoglobulinemia in 3% of cases. Hassimi *et al.* [1] reported sickle cell disease as the etiology of nephrotic syndrome in 3.07% in 2013. In our study we found 5.88% tubulointerstitial nephritis lesion as basic histological lesion although the indications for renal biopsy were impure nephrotic syndrome. Focal and segmental glomerulosclerosis lesions Secondary to these chronic tubulointerstitial lesions, explan the clinicobiological manifestations of nephrotic syndrome. No explanation was found for focal and segmental glomerulosclerosis lesions secondary to NTIC lesions in our study. Thus, Clovis *et al.* [23] in their work on diagnostic aspects of interstitial nephritis: an anatomo-clinical comparison of 24 cases, reported impure nephrotic syndrome in 16.66% and focal and segmental glomerulosclerosis lesions secondary to chronic tubulointerstitial lesions in 4.16%. According to Agnès [24] in addition to circulating factors, various lesions can cause

focal and segmental glomerulosclerosis lesions, which may even be secondary to severe, advanced primary tubulointerstitial disease, such as chronic obstruction or chronic pyelonephritis.

Histological diagnosis of kidney disease is of great value in clinical nephrology and renal transplantation. The results of this study underline the importance and value of establishing the indications for PBR in the management of patients.

5. Conclusions

The present study provided a diagnosis of renal diseases proven by renal biopsy in Niger. The histological lesions observed in nephrotic syndrome are diverse and dominated by segmental and focal glomerulosclerosis and minimal glomerular lesions. Diabetes has been the main secondary etiology. Infectious viral and parasitic etiologies were also found, as were segmental and focal glomerulosclerosis lesions secondary to chronic tubulointerstitial lesions. Future studies should investigate the causes of glomerulopathy secondary to chronic tubulointerstitial lesions.

This study could be a first step towards a national multicenter study that would enable the establishment of a national registry of kidney diseases in the country. Early detection of urinary anomalies in medical practice in Niger will increase the indications for renal biopsy. The lack of equipment and personnel for the processing and interpretation of renal biopsies is a major obstacle and must be resolved by opening nephropathology center in Niger.

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Conflicts of Interest

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

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