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Idiopathic Nephrotic Syndrome (INS) in Adults in Abidjan: Clinical and Therapeutic Aspects of 28 Cases

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Abstract

Context + objective: Nephrotic syndrome accounts for 15 to 30% of glomerulopathies in adults; its evolution is difficult to predict. The objective of this work is to study the profile of patients suffering from idiopathic nephrotic syndrome in a nephrological hospital environment at the University Hospital of Yopougon in Abidjan. Methods: We carried out a retrospective study with descriptive and analytical purposes including any patient aged 15 and over who had had a clean kidney biopsy between January 2018 and October 2019 concluding in a nephrotic syndrome with minimal glomerular lesions (MGL) or segmental and focal hyalinosis (SFH) at the Nephrology Department of the University Hospital of Yopougon in Abidjan. Results: A total of 28 patients were collected. Patients with SFH type lesions were older with a statistically significant p value (p = 0.002). The male gender predominated in MGL type lesions without a statistically significant link (p = 0.26). SFH-type lesions were dominant (57.14%), followed by MGL-type lesions (42.86%). Oedematous syndrome was the main physical sign (n = 9; 56.25%) without significant difference (p = 0.742). ESRD with a GFR less than 15 mL/min/1.73 m2 was found in 8 patients, which is 28.6% without significant difference. Microscopic haematuria coexisted in 5 patients (17.9%) and hypertension in 7 patients (25%). The first-line treatment was oral corticosteroid therapy at usual doses (n = 28; 100%), associated with immunosuppressants (n = 11.79; 17%). Partial

remission was noted in 9 MGL type patients, that is 69.2% and a total remission in SFH type patients that is 50%, without any statistically significant link ($p = 0.568$). The main complications were CRD in 9 patients, which is 45%, followed by dyslipidaemia that is 30%. Conclusion: Adult idiopathic nephrotic syndrome is common and dominated by SFH type of histological lesions. Its outcome is generally favourable.

Keywords

Idiopathic Nephrotic Syndrome, Histology, Yopougon-Abidjan

1. Introduction

Idiopathic nephrotic syndrome is a disease of the podocyte which manifests itself histologically in two forms: minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS). These INS represent 15% - 30% of adult glomerulonephritis and 85% - 90% of those in children [1]. For children, the incidence of nephrotic syndrome varies from 1.15 to 16.9 per 100,000 depending on the country of origin or ethnic group [2]. In the United States and Europe, the annual incidence of nephrotic syndromes in children was estimated to be between 1 and 7 per 100,000 children [3]. In the United Kingdom, a study had shown that NIS was 6 times more common in children of Asian origin than in European children [4]. In sub-Saharan Africa, nephrotic syndrome is the main cause of chronic renal failure and end-stage renal disease in children [5]. In multiracial countries, people of African descent have been shown to be at higher risk of developing steroid-resistant nephrotic syndrome [6]. The problem with idiopathic nephrotic syndrome in Abidjan is the difficulty in accessing the various immunosuppressive drugs, which are essential therapeutic means after corticosteroids. Only cyclophosphamide is available, but it is less tolerated and carries a risk of serious side effects. These scientific motivations associated with the observation of these two pathologies in our clinical practices are less documented, which justifies this present work. Our general objective is to assess the clinical, histological and therapeutic aspects of adult INS in the Nephrology Department of the Yopougon University Hospital.

2. Methods

2.1. Patient Selection and Description

This was a retrospective descriptive study based on medical records of patients admitted at the Yopougon Nephrology Department for nephrotic syndrome between January 2018 and October 2019. Patients over 15 years of age with idiopathic nephrotic syndrome were included in the study, and underwent renal biopsy, blood creatinine, 24-hour proteinuria, albuminemia, and protidemia. Patients with incomplete data were excluded from the study. The result of the renal

biopsy was to correspond to one of the entities defining idiopathic nephrotic syndrome i.e. minimal change disease or focal segmental glomerulosclerosis. Treatments were classified into 6 categories: corticosteroid bolus, oral corticosteroid therapy, corticosteroid therapy combined with an immunosuppressant, immunosuppressant alone, or nephroprotector with an angiotensin-converting enzyme inhibitor or an angiotensin II receptor antagonist. Disease progression was classified into 5 categories:

- Complete remission, defined as proteinuria <0.3 g/24h and albumin >30 g/l, or
- Partial remission with albumin >30g/l and persistent proteinuria >0.3 g/24h or proteinuria/creatinine ratio >30mg/mmol of creatinine, or
- A stationary evolution, or
- A worsening of the condition, with proteinuria rising above the initial value or renal failure progressing and finally the patient's death.

Renal impairment was defined as creatinine levels above 14 mg/l. Creatinine clearance (CC) was calculated using the Cockroft and Gault formula. Renal failure was defined as mild when the CC was between 60 and 89 ml/min, moderate when the CC was between 30 and 59 ml/min, severe if the CC was between 15 and 29 ml/min and end-stage when the CC was less than 15 ml/min [5]. The parameters studied were epidemiological (prevalence, age, sex), clinical (oedema, hypertension), urinary work-up and histology of idiopathic nephrotic syndrome.

2.2. Statistical Methods

The data were analysed using epi info version 6.0 software. The results are presented in the form of averages ± standard deviations. Qualitative variables are represented by their numbers and proportions. These qualitative variables are compared using the Chi-square test. Two quantitative variables are compared using the T Student test.

3. Results

3.1. Types of Idiopathic Nephrotic Syndrome

During the study period, 40 patients were admitted to a nephrology department for nephrotic syndrome, 28 of whom had idiopathic nephrotic syndrome, with a prevalence of 70%. The different idiopathic nephrotic syndrome profiles observed in order of frequency were FSGS (57.14%, n = 16) and MCD (42.86%, n = 12). The male gender was predominant in minimal glomerular lesions, i.e. 52.63%, without the difference being significant (p = 0.26) (**Table 1**).

3.2. Epidemiological Data

The mean age of patients was 33.39 ± 10.62 years, with extremes of 17 and 59 years. Patients with FSGS were older (36 years) and 28 years in MCD, with a significant difference (p = 0.002). There was a male predominance in MCD, with no significant difference (p = 0.26) (**Table 2**).

Table 1. Distribution of patients by histological lesion, age and sex.

	Sex			
Histological lesion	**Female n (%)**	**Male n (%)**	**Total**	**p-value**
FSGS	7 (77.78)	9 (47.37)	16 (57.14)	
MCD	2 (22.22)	**10 (52.63)**	12 (42.86)	**0.26**
Total	9 (100.00)	19 (100.00)	28 (100.00)	

Table 2. Distribution of patients to histological lesions and average.

Histological lesions	**Effective** (n)	**Mean age**	**p-value**
FSGS	16	36.75 ± 10	0.002
MCD	12	28.92 ± 9	

3.3. Clinical Data

Urinary tract infections (28.6%), followed by hypertension (25%) and ear, nose and throat infections (25%) were the most common pathologies in the past medical history, irrespective of the type of histological lesion, with no significant difference. Oedema was the main clinical sign with no statistical difference (p = 0.74). Microscopic haematuria was higher in FSGS with no significant difference (p = 0.25) and leukocyturia was dominant in MCD with a statistically significant difference (p = 0.008) (Table 3).

Table 3. Distribution of patients according to histological lesions and clinical manifestations.

	Histological lesion n (%)		
Clinical sign	**FSGS**	**MCD**	P-value
Physical sign			
Edema syndrome	**9 (56.25)**	**6 (50)**	0.742
Blood pressure	5 (31.25)	1 (8.33)	0.143
Microscopic hematuria	4 (25.00)	1 (8.33)	0.254
Macroscopic hematuria	1 (8.33)	0 (0.00)	0.239
Leukocyturia	**1 (6.26)**	**6 (50.00)**	**0.008**
Functional signs			
Nausea	6 (50)	6 (50)	0.508
Decreased diuresis	3 (18.75)	4 (33.33)	0.377
Asthenia	**12 (75.00)**	**8 (66.67)**	**0.629**
Headache	5 (31.25)	3 (25.00)	0.717

3.4. Laboratory Data

Blood albumin levels were lower in MCD (91.67%) with a statistically significant association ($p < 0.008$). Protein levels between 40 and 60 g/l were predominant in MCD (76.9%) with no statistically significant association ($p = 0.548$). Massive proteinuria (greater than 7g/l) was predominant in FSGS (37.50%) with no statistically significant association ($p = 0.227$). Moderate renal failure was predominant in FSGS (33.3%) with CKD predominating in MCD with no significant difference ($p = 0.56$) (Table 4).

Table 4. Distribution of patients according to histological lesions and laboratory tests.

	FSGS n (16)	MCD n (12)	p-value
Distribution of albumin Level (g/l)			
10 - 20	7 (43.75)	11 (91.67)	0.008
20 - 30	6 (50.00)	11 (84.60)	
Distribution of protein level (g/l)			
≤40	6 (50.00)	2 (15.4)	
40 - 60	6 (50.00)	10 (76.9)	0.54
≥60	0 (0)	1 (7.7)	
Distribution of proteinuria 24 hours			
3 - 7	10 (50)	10 (50)	0.22
≥7	6 (37.50)	2 (16.67)	

3.5. Complications

Chronic renal failure was the most common complication found in LGM type i.e.55.56%, followed by dyslipidemia in HSF, i.e. 36.36%, without significant difference ($p = 0.34$) (Table 5).

Table 5. Distribution of patients according to histological lesions and complications.

	Histological lesions n (%)			
Complications	**FSGS**	**MCD**	**Total**	**p-value**
Dyslipidemia	**4 (36.36)**	**2 (22.22)**	**6 (30.00)**	
Infections	1 (9.09)	0 (0.00)	1 (5.00)	
IRA	1 (9.09)	0 (0.00)	1 (5.00)	0.3435
AKI + dyslipidemia	0 (0.00)	2 (22.22)	2 (10.00)	
IRC	**4 (36.36)**	**5 (55.56)**	**9 (45.00)**	

Continued

CKD + hypertension + dyslipidemia	1 (9.09)	0 (0.00)	1 (5.00)	0.3435
Total	**11 (100.00)**	**9 (100.00)**	**20 (100.00)**	

3.6. Treatment Data

Treatment was based on corticosteroids alone followed by immunosuppressants with no significant difference (p = 0.82). Partial remission was noted in 9 patients with LGM, i.e. 69.2%, and total remission in half of the patients with HSF-type lesions, i.e. 50%, without any statistically significant link (p = 0.568) (Table 6).

Table 6. Distribution of patients according to histological lesions and evolution of treatment.

Evolution	Histological lesions n (%)		p-value
	FSGS	**MCD**	
Total remission	6 (50)	4 (30.8)	0.568
Partial remission	6 (50)	**9 (69.2)**	

4. Discussion

The prevalence of idiopathic nephrotic syndrome in sub-Saharan countries remains unknown. In our study, the hospital prevalence was 70%. In our study, the prevalence of patients with FSGS and MCD were 16 (57.14%) and 12 (42.86%) respectively. In most studies, FSGS was the predominant cause of primary nephrotic syndrome in African adults, accounting for 41% in the RDC about 20% in Ghana and 47% in Senegal [6]-[8]. An Afro-American study noted this predominance and specified a pronounced racial difference, with focal segmental glomerulosclerosis predominating in black subjects [8]. Concerning MCD nephrotic syndrome, a study carried out in Britain by ORTH and RITZ found a frequency of 20% of INS regardless of age [9]. We noticed that oedema was the most frequent clinical presentation in our study. This is a common form, as most authors have noticed in sub-Saharan Africa ADU in Ghana [7], according to a study by Maiga in Bamako [9] and in Côte d'Ivoire [10]. In our study, HSF and LGM were respectively 16 (57.14%) and 12, or 42.86% of patients who underwent a renal biopsy. This predominant frequency of HSF in cases of SNI in adults is therefore reported in the literature. An African-American study noted this predominance and specified a pronounced racial difference, with a preponderance of segmental and focal hyalinosis in black subjects [11] [12]. Remuzzi found a 15% frequency of nephrotic syndrome with HSF in adults under 60 years of age [13]. Concerning LGM nephrotic syndrome, a study carried out in Great Britain by ORTH and RITZ found a frequency of 20% of SNI regardless of age [14]. Hypoalbuminemia was found in 100% of cases, with 11 cases (91.67%) of hypoalbuminemia below 20g/l in LGM compared to 7 patients (43.75%) in HSF with p = 0.008. This result is

comparable to that of DIALLO *et al*. in Ivory Coast [10] and that of Sall *et al*. in Senegal [8]. Protein levels between 40 and 60 g/l were the majority in LGM, i.e. 76.9%, without a statistically significant link (p = 0.548). These results are close to those of Abdoulaye [15] who found an average value of 42.97g/l and that of Sall *et al*. [16] with an average of 52.10g/l. DIOUF *et al*. found an average of 23.2 g/l [17]. Hypoproteinemia follows major renal protein leakage, responsible for major protein malnutrition with a life-threatening prognosis [18]. Patients have a high susceptibility to infections due to lower serum immunoglobulin G levels [19]. LI *et al*. found an infectious complication in 20% of adult patients with nephrotic syndrome [20]. The main cardiovascular complications are venous thrombosis [21]. This risk is increased by major hypoalbuminemia below 20 - 25g/l [22]. Hypoproteinemia is also responsible for hyperlipidemia which constitutes a major cardiovascular risk factor [23]. Concerning drug intake during nephrotic syndrome, the drop in albuminemia leads to an increase in the fraction of drugs linked to albumin to name only AVK, NSAIDs and fibrates. The major risks are overdose and drug toxicity [1]. It is therefore necessary to adapt the dosage. Proteinuria of more than 7 g/24h was predominant in HSF lesions without any significant difference (p = 0.227). In the literature, the authors Coggins and Kiti [24] [25] did not report any difference regarding the importance of proteinuria between these different anatomopathological types. Moderate renal insufficiency dominated in HSF lesions, i.e. 33.3% with (p = 0.56). Furthermore, significant terminal IR was noted in LGM type lesions, i.e. 38.5% of cases. without any significant value (p = 0.31). According to Waldman [26], renal insufficiency observed in nephrotic adults is difficult to interpret, especially when it is minimal or moderate, as is the case for certain patients in our population. Indeed, it may be functional renal insufficiency secondary to hypoproteinemia, or a pre-existing alteration of renal function in the elderly, or finally a deterioration specific to chronic renal disease. In his series Dumas De La Roque noted that 5% of patients progressed to ESRD within a median time of 13 months [27]. Corticosteroid therapy alone constituted the basis of the treatment of idiopathic nephrotic syndrome in adults. Partial remission was noted in 9 patients with LGM, i.e. 69.2%, and a total remission in patients with HSF type lesions, i.e. 50%, without any statistically significant link (p = 0.568). In the majority of cases adults are sensitive to corticosteroid therapy but with a lower rate compared to children, and a longer result to obtain [28]. This weaker response to corticosteroids makes the main difference in the management of LGM SNI between adults and children. Indeed, complete remission is obtained in 90% of cases of LGM using corticosteroids in children, as reported by CHURG *et al*. [29]. The study by WALDMAN showed corticosteroid resistance in adults in more than 25% of cases, at least one relapse occurred in 73% of cases, and 28% of patients had a frequent relapse [30]. The literature only shows that longer treatments were able to obtain higher remission rates [31].

Failure of corticosteroid therapy should prompt another line of treatment in cases of HSF because idiopathic HSF lesions progress in 50% of cases to end-stage

renal failure, especially if the rate of proteinuria remains nephrotic [32]. Other immunosuppressive molecules have been used in cases of corticosteroid resistance. We did not use an immunosuppressant for the cases of LGM, and their evolution was good. Our patients with HSF as an anatomopathological lesion with partial remission benefited from treatment with cyclophosphamide. Partial remission was obtained in 50%. According to a study carried out by MEYRIER in 2003, the use of these alkylating agents leads to total remission for almost 50% of cases of corticosteroid dependence and in less than 20% of cases of corticosteroid resistance [33]. It should be noted that immunosuppressive agents such as alkylating agents including cyclophosphamide and chloraminophen had a beneficial effect, but the side effects are also significant, such as infectious risks, alopecia, gonadotoxicity and hematological abnormalities [34]. Treatment with cyclophosphamide was offered to patients who showed partial remission to corticosteroid therapy on SNI at LGM, but men were reluctant to learn of the risk of male sterility. However, cyclophosphamide was the alternative treatment easily available and at a low cost in Abidjan. The marketing of immunosuppressive agents for the management of corticosteroid-dependent or corticosteroid-resistant forms during the last ten years has brought a new trend in the treatment of SNI [35], but they are not likely to replace corticosteroid therapy as first-line treatment [3]. Other molecules indicated in the treatment of SNI were not used in our study despite their effectiveness compared to cyclophosphamide. The prognosis is excellent for patients with LGM, with most patients entering remission after treatment with corticosteroids. [36]. However, 85 to 90% of patients are sensitive to steroids and may relapse, putting them at risk of steroid toxicity, systemic infections, and other complications. For patients with HSF, the prognosis is serious [37]. Typically, end-stage renal disease progresses to dialysis and kidney transplantation. Only about 20% of patients with HSF go into remission from proteinuria; 10% improve but remain proteinuric. Between 25 and 30% of patients with HSF develop end-stage renal disease (ESRD) within five years. Some studies have suggested better 5-year renal outcome in Chinese adults with primary HSF compared to the West [38].

Contributions from Authors and Co-Authors

Konan N'Guessan Michel, Wognin Manzan Edwige Anastasie and Koffi Georges Stephane: Editorial staff; Monlet Cyr Guei, Christ Ziahy Reine Marie, Abdoul Yannick Gonan, Kéhi Jonathan Kpan, Abbé Jean-Fabrice Lidwine, Ouattara Tiepe Rokia: Data collection; Binan Yves and Ouattara Bourhaïma: Validation of the manuscript.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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