

# Epidemiological and Evolving aspects of Nephrotic Syndrome in Children Aged 0-15 Years in Tanguiéta District Hospital (Benin)

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## Abstract

**Introduction:** Childhood Nephrotic Syndrome is the most common glomerular impairment seen in nephrology and its progression affects the African child unfavorably.

**Objectives:** Study the epidemiological and evolving aspects of Nephrotic Syndrome (NS) in children aged 0-15 years in Tanguiéta District Hospital from January 2013 to December 2016.

**Methods:** It was a retrospective study conducted from January 2013 to December 2016 on 39 NS patients in Tanguiéta District Hospital. Socio-demographic, biological, clinical and evolving data were collected.

**Outcome:** The prevalence of NS was 0.78% with an incidence of 13 cases per annum. Sex-ratio was 1.5. The mean age of the children was  $8.2 \pm 3.3$  years. Nephrotic Syndrome recorded 71.28%. The progression of the disease affected 70% of the patients unfavorably with: 45% steroid resistance, 25% relapse, 20% IRC, 10% steroid dependence and a case-fatality rate of 10.25%. The unfavorable progression was closely related to the delayed wait time before admission and regular intake of herbal tea.

**Conclusion:** This study reveals the seriousness of Childhood Nephrotic Syndrome in Tanguiéta District Hospital which is especially characterized by unfavorable progression. There is need to raise awareness among the parents to have their children consulted at an early stage of life, in order to mitigate the risk of unfavorable progression of this medical condition through herbal teas.

**Keywords:** Epidemiological aspects; Nephrotic syndrome; Children; Tanguiéta

## Introduction

Idiopathic Nephrotic Syndrome (INS) is the most common childhood glomerular nephropathy [1]. Its global average incidence varies between 2-7 cases per 100,000 children for a prevalence of 16 cases for 10,000 children [2]. Nephrotic syndrome has several etiologies. In Sub-Saharan Africa, traditional causes described in the West, several infectious, viral and parasitic agents were involved in the etiology [3]. There could be several complications during NS, such as infections, thromboembolic events, metabolic disorders, kidney injury and malnutrition. The African Child Nephrotic Syndrome is a distinct issue. In addition to histological variants, the response to steroids may vary depending on the geographical location and ethnicity. In the literature, 95% of NS with minor glomerular injury are steroid sensitive, nonetheless 75% cause relapse [4]. Despite the incidence of this renal dysfunction in children and its complications, no study has ever focused on this issue in the North-West of Benin. That is the rationale behind initiating this research work for the

purpose of studying the epidemiological and developmental aspects of Childhood Nephrotic Syndrome (CNS) in Tanguiéta District Hospital from January 2013 to December 2016.

## Patients and Methods

The study was conducted in Tanguiéta District Hospital on account of its great attendance. This health center has the features of an international regional center, given its border position in-between three countries. In the Region of Atacora, this hospital is the most equipped and the only one providing varied and specialized services. Childhood kidney disease treatment is subsidized. It was a retrospective, descriptive and analytical study conducted from 1<sup>st</sup> January 2013 to 31<sup>st</sup> December 2016. The study population included all children aged 0-15 years of age admitted for consultation in the Department of Pediatrics, diagnosed for NS on the basis of 24 h-proteinuria above 50 mg/kg associated with hypo proteinemia <60 g/L, hypo albuminemia <30 g/l [5] and having clinical records

with the minimum paraclinical examinations results. Children with 24 h-proteinuria below 50 mg/kg or whose medical records are either incomplete or unusable were excluded from the study. Idiopathic NS was concluded when the etiological investigation of sickle cell disease, lupus, diabetes, HIV and HBV all proved negative [6]. Steroid sensitivity was defined by negative 24 hr urine protein test after four weeks of oral treatment with 2 mg/kg/day prednisone, or after 3 bolus methylprednisolone dose of 1 g/1.73 m<sup>2</sup> of body surface area per bolus. Steroid resistance was defined by failure of the patient to maintain remission eight days after methylprednisolone infusions. Steroid dependence was defined by a relapse during decreased steroid therapy or less than three months after therapy. The survey was wholly conducted. The dependent variable was the progression of NS. It is a binary variable coded as favorable or unfavorable. The patients were treated with corticoid in compliance with the protocol proposed by the Society of Pediatric Nephrology (SPN) [6]. The independent variables included socio-demographic and clinical factors. Data collection tool was a questionnaire integrating all the variables described. Data entry and analysis were conducted using Epi info version 7. The average values are highlighted with their standard deviation and ratios/frequencies and their confidence interval. Pearson Chi<sup>2</sup> test (when theoretical number >5) was used to compare prevalence according to the procedures. The average values were compared through Student's *t*-test. The gap is statistically significant for a *p*-value below 0.05. The results are highlighted as absolute value, relative frequency or average values + standard deviation.

## Outcomes

### Incidence of admission for nephrotic syndrome

During the study period, 52 children had NS. This disease accounts for 0.79% of pediatric admissions. The incidence of NS was estimated at 13 cases per annum. Out of the 52 patients admitted, the medical records of 39 were usable. The rate of medical records usability was 75.00% in our series.

### Characteristics of the children in consultation

The mean age of CNS was 8.21 ± 3.3 years (2 and 15 years as extreme values). The majority of children affected with the disease were in the 5-10 years age group (53.12%). There were 24 males (61.54%) out of the 39 children, representing a sex-ratio of 1.60. Most of the patients (41.66%) were living over 50 km from the District Hospital. Table 1 below highlights the distribution of patients according to socio-demographic variables.

**Table 1:** Distribution of CNS in the Tanguieta District Hospital Department of Pediatrics from 2013 to 2016, according to socio-demographic variables (n=39).

	Size of the population	Incidence (%)
<b>Age (years)</b>		
[0-5]	7	15.79
[5-10]	19	50.00
[10-15]	13	34.21
<b>Sex</b>		
Male	24	61.54
Female	15	38.46
<b>Place of residence (km)</b>		
<5	5	12.82
[5-50]	18	46.15
≥ 50	16	41.03

## Clinical data

The major reasons for admission included: lower-limb edema related to kidney disease in 33 subjects (89.74%), ascites in 13 (28.21%) and oliguria in eight children (20.51%). The median wait time prior to admission was 90 days (1 and 721 days as extreme values, with an interquartile range from 21 to 157.5 days). The 1<sup>st</sup> and 3<sup>rd</sup> quartile was respectively 21 days and 157.5 days. Most of the patients (46.15%) reported to the hospital between 60 to 364 days after the onset of the first signs or symptoms. Out of the 39 patients admitted, 20 (51.28%) were herbal tea-takers. Typical NS and mixed or atypical NS was respectively recorded in 28 patients (71.80%) and 11 patients (28.20%). Idiopathic NS accounted for 71.80% of all cases, whilst secondary NS represented 28.20%.

## Therapeutic characteristics

The average duration of CNS was 84 ± 59.48 days with 3 and 251 days as extreme values. Thirty one (79.49%) and five (12.82%) patients were subject to steroid therapy and immunosuppressive therapy, respectively. The average duration of disease-modifying therapy with steroid was 66.03 ± 39.51 days (14 and 152 days as extreme values). Out of the 31 patients under steroids, 21 patients were non-adherent to medical treatment (53.84%) as recorded. Three reasons accounted for non-adherence, namely: voluntary withdrawal of nine patients representing 42.86%, drugs stock-out for six patients (28.57%) and non-compliance with diet and hygiene instructions by six patients

**Table 2:** Distribution of CNS in the Tanguieta District Hospital Department of Pediatrics from 2013 to 2016, according to clinical and therapeutic variables (n=39).

	Size of the population	Incidence (%)
<b>Reasons for admission</b>		
Lower-limb edema	35	89.74
Ascites	11	28.21
Oliguria	8	20.51
Diarrhea	7	17.95
Fever	5	12.82
Abdominal pain	4	10.26
<b>Median wait time prior to admission (days)</b>		
<7	3	6.45
7-14	5	12.90
15-29	4	9.67
30-59	2	3.22
60-364	18	46.15
≥ 365	7	16.12
<b>Regular intake of herbal tea</b>		
Yes	20	51.28
No	19	48.72
<b>Type of nephrotic syndrome</b>		
Typical	28	71.79
Atypical or mixed	11	28.21
<b>Nephrotic syndrome etiological category</b>		
Idiopathic	31	79.49
Secondary	8	20.51
<b>Treatment methods</b>		
Steroid therapy	31	79.49
Steroids+immunosuppressive therapy	05	12.82

(28.57%). Table 2 highlights the distribution of patients according to clinical and therapeutic variables (n=39).

### Nephrotic syndrome progression with steroid therapy

The progression of NS was favorable in nine patients (30.00%) and unfavorable in 21 patients (70.00%). Among patients with unfavorable development, 11 (44.00%) were steroid resistance, five (20.00%) steroid dependent, other five (20.00%) experienced delayed NS relapses and four (16.00%) had chronic kidney disease. The disease-related complications were anemia in three cases (7.69%), infections in two cases (5.12%), acute pulmonary edema in two cases (5.12%) and four cases (10.25%) of acute kidney injury. Four cases (10.26%) of death were recorded.

### Identifying factors associated with the progression of nephrotic syndrome

The progression of NS was statistically associated with the median wait time prior to patients admission ( $p=0.005$ ), the regular and excessive intake of herbal tea ( $p=0.002$ ) and the effect of herbal tea intake on the duration of steroid therapy ( $p=0.014$ ).

The median wait time prior to admission recorded in patients with favorable progression was 78 days against 98 days in patients with unfavorable progression of the disease.

Out of 20 children who regularly and excessively took herbal tea (80.00%), 16 experienced favorable progression against nine out of 19 (47.37%) who were not herbal tea-takers ( $p=0.002$ ).

The average duration of disease-modifying therapy with steroid was 80.44 days in the herbal tea-takers population, while it was 46.07 days in those who were not herbal tea-takers ( $p=0.014$ ). Table 3 highlights the correlation between unfavorable progression of NS and associated factors.

### Discussion

Our study is the first ever conducted in the northern region of Benin. It explored the epidemiological and evolving aspects of CNS in Tanguieta District Hospital. It will serve as a database for or other studies.

### Comment on the results and comparison with those of other authors

**Incidence of nephrotic syndrome:** The rate of CNS in Tanguieta District Hospital was 0.79% with an incidence of 13 cases per annum.

Our result is similar to 0.80% recorded by Moyon G, et al., in Congo Brazzaville [7]. This frequency is higher than that of 0.02 to 0.04%

reported in developed countries (United States, China and the United Kingdom) but lower than that of 2.00% found by Gbadoé AD, et al., in Nigeria and Uganda [8].

The children mean age was  $8.21 \pm$  years of age. In our series, 50.00% of the children were in the 5-10 years of age. Our result was also comparable with  $7.11 \pm 3.14$  years recorded in Senegal by Keita [9]. On the other hand, the mean age in Europe, Asia and America is approximately 5 years [8]. Recourse to care in modern health facilities is delayed, and this may account for high mean age despite earlier onset of the disease. Our study revealed that the male sex was mostly affected by this medical condition (61.64%) with a sex ratio of 1.60. This male predominance with a sex ratio of 1.85 was recorded by Keita Y, et al., in Senegal [9]. The majority of children came from regions located over 50 km away from Tanguieta Health District. This could be explained by the fact that kidney disorders treatments are subsidized in this hospital.

Clinically, edematous syndrome related to kidney disease was recorded among 89.74% of the patients. Safaei A, et al., recorded the presence of edematous syndrome in 95% of patients and Kéita Y, et al., reported 100% in their series [9,10]. This observation of an edematous syndrome related to kidney disease could explain the pathophysiology of the disease which involves a drop of colloid osmotic pressure. However, the development of an edematous syndrome into anasarca could be associated with the delayed treatment.

Most patients were seen between 60 and 363 days following the onset of the first signs. Gbadoe AD, et al., reported this same delayed consultation [8].

In our series, typical NS represented 71.28% and atypical or mixed NS 28.20%. These results are relatively close to those of Keita who reported 72.50% of typical SN [10]. These results corroborate the high incidence of typical NS in the literature.

**Progression of the disease:** Favorable progression is concluded on the basis of negative 24 hr urine protein test. In our series, the progression of NS was favorable in 32.43 % of cases and unfavorable in 67.57%. These values are significantly lower than those recorded by other authors. 77% and 84% favorable progression based on steroid sensitivity was respectively reported by Kéita Y, et al., in Senegal and Adonis-Koffy LY, et al., in Côte d'Ivoire [9,11]. This may stem from the fact that health professionals were not able to diagnose NS early. Not all health facilities are provided with the equipment required for conducting biological diagnosis of NS. More so, the treatment provided in peripheral health facilities was rather symptomatic instead of etiopathogenic. Furthermore, in our series idiopathic and secondary NS cases were studied. Thus, this important unfavorable progression

**Table 3:** Highlights the correlation between unfavorable progression of NS and associated factors.

	Total (N)	Unfavorable progression of SN*	RP [IC 95%]	p
		Size (n)	Prevalence (%)	
<b>Median wait time prior to admission <math>\geq</math> 98 days</b>				
Yes**	39	15	38.46	1
No	39	24	61.53	0.62 [0.10-4,54]
<b>Regular and excessive intake of herbal tea</b>				
Yes**	39	20	51.28	1
No	39	19	48.72	1.05 [0,41-2,55]
<b>Poor adherence to steroid therapy</b>				
Yes**	39	28	71.43	1
No	39	11	28.57	2.50 [1,15-4,42]

\*NS: Nephrotic Syndrome; \*\*Referral method

involves the patient's renal and vital functional prognosis because proteinuria is known as a predictor of cardiovascular mortality [12].

**In the factors associated with unfavorable progression:** The median wait time prior to admission was estimated at 98 days and above paved the way for unfavorable progression of the disease. The children were not self-reliant, so unable to report to the hospital early. Their admission to the hospital is upon the decision of the parents who first resorted to self-medication. Moreover, most of the parents did not want to go to the referral hospital directly, unless upon complications.

The progression was unfavorable for 80.00% of the patients who regularly and excessively took herbal tea. More so, the effect of herbal tea on the duration of steroid therapy was 80.44 days in patients with regular intake and only 46.07 days for others. The populations with excessive intake of herbal tea have no knowledge of either the tea composition or renal pharmacology. Most herbal teas contain heavy metals which are not excreted by the kidneys. Similarly, the herbal tea preparation is not understood by consumers, thereby exposing them to appalling consequences.

### Conclusion

Nephrotic syndrome is common in Tanguiéta District Hospital with an incidence of 13 cases per annum for 1000 children. The progression of the disease is basically unfavorable in children. This unfavorable progression stems from the delayed admission to the hospital and unreasonably excessive intake of herbal tea. Therefore, there is urgent need to raise awareness among the population on all aspects of this medical condition and the factors associated with an unfavorable progression, so that they could go for early consultation upon the onset of the first signs or symptoms to avoid complications.

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