

Original Research Article

Adult nephrotic syndrome in the Niger delta sub region: a single centre study at the university of Port Harcourt teaching hospital

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Received: 03 November 2019

Revised: 12 January 2020

Accepted: 24 January 2020

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ABSTRACT

Background: Adult nephrotic syndrome is a common cause of chronic kidney disease globally and in Sub-Saharan Africa. In Nigeria there are only few studies on adult nephrotic syndrome, mostly from the south-western Nigeria and rarely from the Niger delta sub-region of Nigeria. This study aims at contributing to the National data on adult nephrotic syndrome, from the perspective of the Niger delta sub-region.

Methods: Retrospective analysis of five-year clinical data (January 2007 to December 2011) of adult nephrotic syndrome patients in the University of Port Harcourt teaching hospital was conducted.

Results: Forty-four patients, representing 1% of medical admissions and 7.3% of adult renal cases were seen during the period, with mean age of 27.7 ± 8.5 years. There were 32 males (72.7%). Mean duration of illness was 25.3 ± 30.3 months. Peak age group was the 20-29 year age group, accounting for 52.3% of cases. Hypertension was seen in 45.5%. Mean e-GFR was 73.5 ± 33.8 ml/min/1.73m² with CKD 1-3 constituting 93.2% of cases. Mean 24-hour urinary protein excretion was 13.6 ± 8.4 grams/day. Protein excretion >10grams/day was observed in 65.8% of the patients. Mean total serum protein, albumin and total cholesterol were 51.4 ± 11.7 g/dl, 22.5 ± 9.9 g/dl and 8.1 ± 3.0 mmol/L, respectively. Anemia was common (68%) and histology showed MCGN (52.6%), MCD (21.1%), membranous (15.8%) and FSGS (10.5%). Though response to therapy was generally poor, immunosuppressive therapy showed better outcomes.

Conclusions: The prevalence and pattern of adult nephrotic syndrome in the Niger delta sub-region is similar to that in other parts of Nigeria. It is predominantly a disease of young adult males with high prevalence of hypertension, and poor histologic categories.

Keywords: Adult nephrotic syndrome, Niger delta, Nigeria

INTRODUCTION

Nephrotic syndrome, defined on the tripod of generalized body swelling (anasarca), heavy proteinuria of >3.5 g/24-hours, with consequent hypoalbuminemia, and hyperlipidemia is among the most common diagnostic groups of renal disease that manifest before the age of 25 years which together encompass >70% of early-onset CKD.¹

The nephrotic syndrome is caused by either primary glomerular diseases (genetic or acquired) as well as a sundry of other secondary causes ranging from infective/inflammatory, autoimmune, toxic and malignant disorders.

In Nigeria as in most other sub-Saharan African countries, most of the reported studies of Nephrotic syndrome are mostly in children with a relative paucity of

data on nephrotic syndrome in adults.²⁻⁴ The few available data of adult nephrotic syndrome in Nigeria are from single center hospital based clinical studies, carried out mostly from the south western part of Nigeria.⁵⁻⁷ The actual incidence and prevalence of adult nephrotic syndrome in the country remain conjectural.

This study seeks to contribute to the data base on adult nephrotic syndrome in Nigeria, from the perspective of the Niger-delta geographical sub-region of Nigeria.

Aims and objectives of the study was to establish a baseline data on the epidemiological, clinical characteristics and therapeutic outcomes of adult nephrotic syndrome in the University of Port Harcourt teaching hospital and to contribute to the national data on adult nephrotic syndrome in Nigeria.

METHODS

The study is a retrospective analysis of data of cases of adult nephrotic syndrome seen in the renal unit of the University of Port Harcourt teaching hospital (UPTH) between January 2007 and December 2011, a period of five years.

The renal unit of the department of medicine, the UPTH is the foremost and organized renal unit in the Niger delta geographic sub-region. The UPTH renal clinic serves as referral center for all states in the Niger delta including adjoining states of Imo and Abia states.⁸ The total adult population of the Niger delta states is about 31 million people.⁹

The case notes of all patients attending the renal clinic, and those admitted into the medical wards of the hospital, who satisfy the diagnostic criteria for Nephrotic syndrome and who were aged 15 years and above (during the period under study) were retrieved and data analyzed. To ensure a more efficient retrieval from the medical records department, case notes of all patients with the admission diagnosis of “nephrotic syndrome”, “nephritis”, “acute glomerulonephritis”, “chronic glomerulonephritis”, “acute renal failure”, “chronic renal failure”, “anaemic heart failure”, “Generalized oedema”, and “congestive cardiac failure” were retrieved for preliminary evaluation and selection. Subsequently, only clinical case notes of adult patients which satisfied the criteria for the diagnosis of nephrotic syndrome were analyzed.¹⁰

The data for analysis include the demographic data, clinical history and important physical signs and biophysical measurement at first presentation such as weight, height, and blood pressures were also obtained. The details of urine examinations such as dipstick urinalysis as well as 24-hour urinary protein excretion were included. Haematologic parameters were also included. The biochemical parameters include plasma concentrations of urea, creatinine, electrolytes, uric acid,

total proteins, albumin, calcium and phosphate and fasting plasma lipids.

Also studied were the kidney ultrasound scan reports as well as the kidney biopsy reports for patients who had renal biopsy done. The estimated glomerular filtration rate (e-GFR) was calculated using the Cockcroft and Gault equation.¹¹ Subsequently, patients were grouped into CKD stages in accordance with the NKF/KDOQI classification.¹² Definition of hypertension and the grading of severity of hypertension were in accordance with JNC7-guidelines.¹³

The treatment of the patients were grouped into three categories as follows: diuretic group for those who were treated with diet and diuretics only, Steroid treatment group for those treated with prednisolone in addition to diet and diuretics and the immunosuppressive treatment group for those treated with immunosuppressive agents.

Therapeutic response was assessed only in those patients who were still attending clinic six months from date of entry and evidence of at least three consecutive months of therapy. The response to therapy were categorized as complete remission, partial remission or non-remission. Therapeutic response was assessed after a minimum of 12 weeks of commencement of therapy. Complete clinical remission was defined as the reduction of 24-hour urinary protein to less than 1g/day, loss of oedema and the normalization of serum albumin and total cholesterol levels. Partial remission is the improvement in the above parameters but less than full remission status. Nonresponse is the failure to achieve even partial remission.¹⁰ Progression of CKD was assessed by the doubling of serum creatinine level from baseline at six months.

The overall patient outcomes were categorized into those living and attending clinic from the time of entry, those who are no longer attending clinic, and those who died in hospital.

Data management

Data was analyzed with Epi-info (version 2000) statistical packages for analysis of biomedical data. Continuous variables are presented as mean±standard deviation and categorical variables as percentages. Student-t and Chi-square tests were used for comparisons as appropriate, while Pearson’s correlation test was used to analyze relationship between variables. Significant level was set at $p < 0.05$.

RESULTS

Data of 44 patients aged between 15 and 59 years who satisfied the criteria for diagnosis of nephrotic syndrome were analysed. They constituted approximately 1% of medical admissions and 7.3% of renal disorders seen during the period.

They comprise 32 males (72.7%) and 12 females, with a male to female ratio of 2.7:1 and a mean age of 27.7±8.5 years. The age and sex distribution of the patients are outlined in (Table 1). The peak age of occurrence is in the age group 20-29years, constituting 53.4% of the patients. None of the patients was above 60 years of age.

Table 1: Age and sex distribution.

Age group (Years)	M	F	Total	Percentage
<20	3	2	5	11.5
20-29*	18	5	23	52.3
30-39	6	2	8	18.2
40-49	4	1	5	11.4
50-59	1	2	3	6.8
60	0	0	0	00.0
Total	32	12	44	100.0

The duration of illness was between one month and 8 years, with a mean duration of illness of 25.2±30.3months. While 54.5% of the patients had been ill for less than one year, about 9.1 percent of the patients had nephrotic syndrome for over five years. Their unadjusted mean body mass index (BMI) was 26.9±5.9 (12.8-44.80) kg/m² with 18 (40.9%) overweight and 9 (20.5%) being obese, respectively.

The mean systolic and diastolic blood pressures (SBP) at presentation were 129.6±12.8 (100-160mmHg) and 86.6±10.4(70-120) mmHg, respectively. Twelve (28.6%) had grade 1 and none had grade 2 systolic hypertension, while nineteen patients (43.2%) and 4 (9.0%), respectively had grades 1 and 2 diastolic hypertension in accordance with JNC-712 criteria. Overall hypertension was seen in 20(45.5%) of the patients.

The mean estimated glomerular filtration rate (e-GFR) was 73.6±33.8mls/min/1.73m², with a chronic kidney disease stage distribution of: stage -1: 15 (34.1%), stage-2: 14 (31.8%), stage -3: 12(27.3%) and stage- 4: 3 (6.8%), respectively. None of the patients was in end stage kidney failure.

The summary of the laboratory parameters of the patients at presentation are shown in (Table 2). Dyslipidaemia was common with total cholesterol levels ≥5.2mmol/l observed in 38(86.4%) patients, triglyceride levels ≥1.7mmol/l in 23 (52.3%) and high-density lipoprotein levels ≤1.1mmol/l observed in 25 (56.8%), respectively. For most patients, proteinuria was heavy with a mean 24-hour urinary protein excretion of 13.6±8.4g (4.1-34.7). Over two-thirds (88.5 %) of the patients had 24-hour urine protein excretion of more than 5g, and of these 27 (65.8%) patients had 24-hour urine protein excretion of more than 10g/day.

The mean bipolar lengths of right and left kidneys of the patients by ultrasound scan were within normal limits, 11.1±1.2 (9.1-13.2) cm and 11.1±1.3 (9.5-14.0) cm,

respectively. Poor cortico-medullary differentiation was reported in only 2 (4.5%) patients. No significant abnormalities of the pelvi-calyceal systems were reported.

Table 2: Baseline laboratory parameters.

Parameter	Range	Mean±SD
Haemoglobin (g/dl)	6.7-13.4	10.0±2.0
Haematocrit (%)	20-40	30.8±6.1
Sodium (mmol/l)	111-155	134.8±8.0
Potassium(mmo/l)	2.9-5.5	4.1±0.7
Bicarbonate(mmol/l)	13.5-39	21.8±5.9
Urea(mmol/l)	2.2 -43.8	11.1±10.7
Creatinine(umol/l)	60-1340.0	243.8±263.0
Total protein(g/dl)	34-84	51.4±11.7
Albumin(g/dl)	3.6-47	22.5±9.9
Total Cholesterol (mmol/l)	3.3 -16.5	8.1±3.0
Triglycerides (mmol/l)	0.9-4.6	2.3±0.9
HDL*(mmol/l)	0.2-3.1	0.93±0.6
24-hr urine protein (g)	4.1- 34.7	13.6±8.4

*HDL - High density lipoprotein

Only one patient (2.2%) was positive for the human acquired immunodeficiency virus (HIV) infection- presumably a case of HIVAN, while none of the patients was positive for hepatitis B or C virus infections.

The light microscopic histology reports of renal biopsies in 19(43.2%) patients who had renal biopsy done were as follows: Mesangiocapillary glomerulonephritis (MCGN) 10(52.6%), Minimal change disease (MCD) 4(21.1%), Membranous nephropathy (MN) 3(15.8%) and Focal segmental glomerulosclerosis (FSGS) 2(10.5%), respectively.

Correlation analysis

Body mass index (BMI) showed negative correlations with e-GFR (r= -0.4) but positive correlation with 24-hour urine protein excretion (r =+0.3). Systolic blood pressures showed weak positive correlation with 24-hour urine protein excretion (r=+0.01), while diastolic blood pressure showed negative correlation with 24-hour urine protein excretion (r= -0.06). The mean duration of illness showed positive correlations with 24-hour urine protein excretion (r= +0.09) and mean e-GFR (r =+0.5), respectively.

Therapeutic modalities

Ten patients (22.7%) were treated with diet and loop diuretics only (diuretic group), 18 patients (40.9%) received prednisolone in addition to diuretics (steroid group), while the remaining 16 patients (36.4%) had additional immunosuppressive agents, mainly azathioprine (immunosuppressive group). All the patients were on statins, angiotensin converting enzyme inhibitors

(ACEI) or angiotensin receptor blockers (ARB) were also administered to all patients for the control of proteinuria and hypertension. Other antihypertensive agents were added as indicated.

Response to treatment

Response to therapy was evaluated only in patients who were still attending clinic for a minimum of six months after presentation and consistently on therapy for at least three consecutive months (12 weeks). Twenty-five (56.8%) of the 44 patients satisfied this condition. The choice of therapy was initially empirical, based on clinical judgment, but later modified according to clinical response and histology, when available.

Of the twenty-five cases, 6 (24.0%) belonged to the diuretic's treatment group, another 6 (24.0%) in the steroid treatment group, while 13 (52%) were of the immunosuppressive therapy group. The response rates according to the treatment categories are shown in (Table 3). On the whole a total of eight patients (32.0%) across treatment groups achieved complete clinical remission as defined, 11 (44%) had partial remission while, 6 (24.0%) did not show response to treatment.¹⁰ Further analysis of the response rate according to treatment groups (Table 3) showed that the immunosuppressive group had a higher remission rate compared to the other groups but the differences were not statistically significant ($p>0.5$). Due to the relatively small numbers and dropouts from follow-up, analysis of the therapeutic outcomes according to histologic types was not possible.

Table 3: Therapeutic outcomes.

Therapeutic group(n=25)	Complete remission	Partial remission	Non-remission	Total
Diuretics alone (conservative group)	1	2	3	6
Diuretics +Prednisolone (steroid group)	1	2	1	4
Diuretics+Prednisolone+Azathioprine (immunosuppressive group)	6	7	2	15
Total (%)	8(32)	11(44)	6(24)	25(100)

Progression to chronic kidney disease

Progression of disease as evidenced by the doubling of serum creatinine level or more, after six months of treatment was observed in 11 (44.0%) of the 25 patients. At the time of study none of the patients had progressed to end stage renal disease (ESRD).

End point outcomes

As at the time of study, 23 (52.3%) of the 44 patients were still attending clinic, 17 (38.6%) were no longer attending, while 4 (9.0%) died in the hospital. Of the four dead, 3 (90%) died from complications of intractable ascites such as peritonitis and cardiac decompensation. One patient (10%) died of suspected pulmonary embolism.

DISCUSSION

The results from this study show that nephrotic syndrome is a relatively common renal disorder in adults in the University of Port Harcourt teaching hospital, occurring at an average frequency of 11 cases per year. It was responsible for 7.3% of all renal cases (in and out-patients) seen in renal unit during the period under study, and 1.0% of medical admissions.

An earlier study of nephrotic syndrome in children in UPTH by Anochie et al, reported 28 cases seen over a period of 15 years (1989-2004) giving an annual frequency of about 2 cases per year suggesting a much lower frequency of nephrotic syndrome in children than in adults, in the same hospital.¹⁴ This is however, was not supported by the study of Olowu et al, in Ile-Ife (South-West, Nigeria), who reported 78 cases in children over a period of 9 years giving an annual frequency of 8.6 cases per year, which is close to the observation.¹⁵

In the adult population in other centers in Nigeria, Adeniyi et al, in Illorin (North-West, Nigeria) reported 108 cases seen during a period of 6 years giving an annual frequency of 18 cases/year. Similarly, Adekoya et al, in Ilorin, studied 50 cases of adult nephrotic syndrome seen during a period of 3 years giving an annual case frequency of 16.6 cases/year.^{5,6} Arije et al, in Ibadan (South-West, Nigeria), reported 9 cases of adult nephrotic syndrome in one year accounting for 4.43% of renal admissions.⁷

From the foregoing available Nigerian statistics, nephrotic syndrome in adults in Nigeria occurs at an average annual frequency ranging from 9 to 25 cases per year (an average of 15.7 cases per year) and an average medical admission rate of about 4.4%.

Earlier studies, in the mid-1980s, from other Sub-Saharan Africa countries, such as Uganda, Senegal, Zimbabwe, reported medical admission prevalence of nephrotic syndrome ranging from 0.7 to 4.0 percent. These reports were however, mainly on children.³

The mean age of the patients and those of previous Nigerian studies (Table 4) indicate that nephrotic

syndrome in the adult population is predominantly a disease of the adolescent and young adults. Over 70 percent of our patients were less than 40 years of age, with the peak age group in the 20-29-year age group. None of the patients was over 60 years old. Similarly, the mean age from other centers in Nigeria (Table 4) ranged from 25.2 to 29.7 years.

Table 4: Summary of some nephrotic syndrome studies in Nigeria.

Parameters	Study centers				
	IUTH (Illorin)	ABUTH (Zaria)	OAUTH (Ile-Ife)	UPTH (Port Harcourt)	*UPTH (Port Harcourt)
Authors	Adeniyi et al ⁵	Kwaifa et al ²¹	Olowu et al ¹⁵	Anochie et al ¹⁴	Emem-Chioma and Wokoma
Year of study	2007	2010	2009	2005	2010
Period under study (yrs)	6	Not stated	9	15	4
Study population	Adults (>15-55yrs)	Adults (12-55yrs)	Children	Children (1-14 yrs)	Adults (15 yrs-54yrs)
Study sample size(N)	(108)	(20)	(78)	(28)	(44)
Mean age(yrs)	25.2	29.7	7.1	Not stated	27.7
Sex ratio	1.5:1	1.8:1	1.7:1	1.1:1	2.7:1
Mean 24hr-urine protein(gm/day))	Not stated	Not stated	Not stated	2.5	13.5
Mean plasma total protein (g/dl)	-	-	-	17.3	51.4
Mean plasma albumin(g/dl)	17.7	-	-	-	22.5
Mean total cholesterol	-	-	-	8.7	8.1
Mean HDL	-	-	-	-	0.9
Histologic pattern (%)					
MCD	2.7	40.0	18.5	No biopsies reported	21.1
FSGS	25.0	20.0	25.9		10.5
MPGN	38.9	10.0	44.4		52.6
MN	33.3	30.0	7.4		15.8

*Index study

Though the factors that predispose this age group to nephrotic syndrome are not well understood, their mean age however tend to be similar with the mean age group of adults with acute glomerulonephritis (AGN), suggesting possible shared aetiopathogenesis with AGN.³

Innate genetic predisposition, gene mutations with possible environmental interactions have been known to be implicated in primary glomerular disorders.^{16,17} This rather complex aetiopathogenesis of adult nephrotic syndrome pose challenges for prospect of preventive measures.

In this study as in all the previous Nigerian studies, there is a clear male predominance. Though this is consistent with the global pattern, the reason for the disparity is not

completely understood.³ The male gender dominance may further buttress the possibility of a genetic component to the aetiopathogenesis via a sex-linked recessive trait.

At first presentation the patients had risk factors for poor prognosis as evidenced by high rate of obesity of 20.5%, hypertension prevalence rate of 45.5%, heavy proteinuria, severe hypoalbuminemia and significant dyslipidaemia, which are all risk factors for cardiovascular and chronic kidney disease.^{18,19}

Similarly, the histologic pattern in the few patients that had histologic diagnosis showed high frequency of poor prognostic histologic variants dominated by mesangiocapillary GN and focal segmental

glomerulosclerosis with paucity of minimal change disease. This pattern is consistent with the histologic pattern of nephrotic syndrome in other parts of Nigeria, Sub-Saharan Africa and most tropical environments.^{5-7,20,21} This pattern is however, different from the histologic pattern of nephrotic syndrome in the temperate climates (Europe and North America) where MCD, steroid responsiveness and good prognosis are predominant.²²

Some of the reasons advanced for the differences in the histopathologic pattern of nephrotic syndrome between the temperate and Sub-Saharan African populations include, the dominance of MCD in the temperate regions, which is more of a primary glomerular disease whereas, in the tropical regions secondary underlying causes seem to dominate. These include immune response to streptococcal and other bacterial infections, some viral infections, parasitic infections such as malaria, filariasis, schistosomiasis and perhaps genetic factors.²³⁻²⁵ These causes of nephrotic syndrome are usually associated with poor histologic lesions such as FSGS and MPGN which respond poorly to steroid therapy.

The poor prognostic characteristics of the patients at presentation, characterized by massive proteinuria, anaemia, high prevalence of hypertension, low eGFR and the poor histologic categories, had the expected influence in the poor response to therapy of the patients. Only 8 (32.0%) of the 25 patients who attended clinic continuously for more than six months had complete remission. Nominally the patients who received immunosuppressive therapy seem to have better response rates compared with the other treatment groups, though not statistically significant.

This however, supports the fact that non-MCD histologic types predominate the pathology of Nephrotic syndrome in this population. Due to the small number and the low statistical power of the data it was difficult to compare the response rates according to the histologic types. Disease progression as evidenced by doubling of serum creatinine level at six months of treatment was high, have been observed in 44% of the twenty-five patients eligible for treatment analysis. This further buttress the poor prognostic outcomes of the patients.

Patient drop-out rate was also common. This may be due to deaths outside the hospital and search for alternative care, which is common practice in our population. Death in hospital was however relatively low probably due to the high drop-out rate.

The study suffers the limitations of a retrospective study and some operational challenges of studies in resource poor settings. The number of patients with histologic diagnosis were few and only light microscopy was possible for the biopsies. Facilities for immunofluorescence studies and electron microscopy were not available

CONCLUSION

Adult nephrotic syndrome is relatively common in the Niger delta geographical sub-region with epidemiologic and clinical characteristics similar to other parts of Nigeria. There is a strong male preponderance. Non-MCD histologic patterns dominate, characterized by high prevalence of risk factors for disease progression, poor steroid responsiveness, and poor prognosis.

More research is required especially with better biopsy rate to further characterize the condition in our population.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Chioma PC, Wokoma FS. Adult nephrotic syndrome in the Niger delta sub region: a single centre study at the university of Port Harcourt teaching hospital. *Int J Adv Med* 2020;7:439-45.