

Profile and Outcomes of Children with Acute Glomerulonephritis in Northwestern Nigeria

Olayinka Rasheed Ibrahim¹ , Olajide Aladesua² , Michael Abel Alao³ , Abdurrazzaq Alege² 

¹University of Ilorin Teaching Hospital, Department of Paediatrics, Ilorin, Nigeria

²Federal Teaching Hospital, Department of Paediatrics, Katsina, Nigeria

³University College Hospital & University of Ibadan, Department of Paediatrics, Ibadan, Nigeria

ORCID ID: O.R.I. 0000-0002-2621-6593; O.A. 0000-0001-7034-0789; M.A.A. 0000-0003-0109-4435; A.A. 0000-0003-3648-5479

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ABSTRACT

Objective: Studies on acute glomerulonephritis (AGN) in Nigeria described the epidemiological profile without an in-depth analysis of variables associated with outcomes. Herein, we describe the profile and factors associated with hospitalization outcomes (discharge or death) among childhood AGNs at a health facility in northwestern Nigeria.

Material and Methods: This prospective cross-sectional study was conducted between 1st January 2018 and 31st December 2019 at a tertiary health facility in northwestern Nigeria. The diagnosis of AGN was based on a clinical diagnosis. We also obtained relevant history, clinical, and laboratory features.

Results: Thirty-five children were admitted with AGN during the study period. The mean age was 7.7 ± 3.3 years. Most were aged 5 to 10 years (23; 65.7%), male (60.0%), and from a lower socio-economic class (77.2%). The annual incidence of AGN was 11 cases per 1000 children. The most common clinical presentations were generalized body swelling (100.0%), reduced urine output (85.7%), and hypertension (74.3%). The medians (interquartile range) of urea and creatinine were 10.0 (4.50 to 23.90) mmol/L and 85 (67.60 to 204.00) μ mol/L, respectively. Among the clinical features, only fever was associated with outcomes, while serum urea and creatinine levels were significantly higher among non-survivors, $p < 0.05$. We recorded four deaths (case fatality rate of 11.4%), two each from congestive cardiac failure and hypertensive encephalopathy.

Conclusion: This study shows a high incidence of childhood AGN and mortality in Katsina, northwestern Nigeria. Fever was associated with outcomes, while serum creatinine and urea levels were elevated among non-survivors.

Keywords: Child, Acute Glomerulonephritis, Outcomes, Nigeria

INTRODUCTION

Acute glomerulonephritis (AGN) is a non-suppurative inflammatory kidney disease characterized by a decline in renal functions, hypertension, hematuria, variable degree of proteinuria, and edema (1). While AGN can be caused by a variety of pathogens (viral, bacterial, and protozoal), it is most commonly caused by post-streptococcal infection (Streptococcus group A -hemolytic); thus, the term "acute post-streptococcal glomerulonephritis" is used interchangeably in some publications (1,2).

Acute glomerulonephritis constitutes a significant burden among kidney diseases, with an estimated incidence of 722,244 and more than 10,000 deaths in 2019 (GBD 2019) (3). Children bear the greater burden of AGN, with a peak incidence at 10 to 14 years old (3)(3). Furthermore, about 95% of AGN occurs in developing countries, including Nigeria, which is attributable

to the high prevalence of risk factors such as poor hygiene, overcrowding, and low socio-economic factors (4).

Acute glomerulonephritis (AGN) is one of the common childhood renal diseases in Nigeria, with a decline from the annual incidence of about 50 cases per year in the early 80s to less than 10 cases per year in some recent studies (5,6). Besides, there are variations in the reported burden of AGN across the country due to possible environmental factors, genetic predispositions, and study methods such as retrospective vs. prospective. For example, a recent study in Abuja (north-central Nigeria)(7) reported an annual incidence of 3.25 cases (13 cases over four years), whereas, in Zamfara (northwestern Nigeria)(6), the annual incidence was 9.6 cases (24 cases over 2.5 years); in Ibadan (southwestern Nigeria)(8), the annual incidence was 8.5, while in Port Harcourt (south-south Nigeria),(9) it was as high as 15 cases per year. Though

Corresponding Author: Olayinka Rasheed Ibrahim E-mail: ibroplus@gmail.com

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the disease has a good clinical outcome, a varying mortality rate has also been observed, ranging from 1.4% to 9.7% depending on the cohort studied (9,10). Despite the well-described epidemiology of AGN across the six geopolitical zones, most studies did not thoroughly analyze the factors associated with poor outcomes. Identifying these factors may provide an opportunity for patients who may require and benefit from focused intervention. Therefore, we hypothesized that the incidence of AGN in Katsina, one of the states in northwest Nigeria, differed from the rest of the country and that there were factors associated with poor hospitalization outcomes. Hence, we aimed to describe the epidemiological profile and factors associated with poor hospitalization outcomes (defined as discharge or death) among children diagnosed with AGN at a tertiary health facility in Katsina, northwestern Nigeria.

MATERIAL AND METHODS

Study design and setting

This prospective cross-sectional study was conducted at the Federal Teaching Hospital in Katsina, Nigeria, between 1st January 2018 and 31st December 2019. Federal Teaching Hospital Katsina (FTHK) is a 700-bed tertiary health facility that receives referrals from the state, parts of adjoining states (Kano, Kaduna, and Zamfara), and the Niger Republic. The hospital's pediatric department served as the study's location and ran a nephrology clinic with an average of three to five cases per week under the supervision of a consultant nephrologist.

Study participants

Children under 14 who were diagnosed with acute glomerulonephritis based on a clinical history of dark urine, hypertension, hematuria, proteinuria, and edema lasting less than or equal to 14 days participated in this study (11). Children with chronic kidney disease (based on history and laboratory findings), such as nephrotic syndrome and chronic glomerulonephritis, were excluded.

Sample size

This study included all children managed during the two-year study period who met the inclusion criteria.

Data collection

A pretested semi-structured questionnaire was used to collect relevant information on socio-demographics, prior history of sore throat, and skin rashes. The socio-demographic classification of the children was based on Oyedepi's social classification (12). The classification was derived from the sum of the parents' educational levels and occupations on a scale of 1 to 5. All the children had a detailed physical examination, including blood pressure measurement with an appropriate cuff, and other findings at admission were also noted. All of the patients also had laboratory investigations, including complete blood counts, an anti-streptolysin assay (ASO titer), urinalysis, urine microscopy, culture and sensitivity, electrolytes, urea, creatinine, and blood culture where indicated. The urea and creatinine were repeated based on the findings at admission. Two patients received dialysis due to increased serum creatinine (one each for peritoneal dialysis and hemodialysis).

Definitions

Acute glomerulonephritis: This was defined as a child admitted with a history of the passage of dark-colored urine, a reduction in urine output, hypertension, and findings of hematuria and proteinuria with varying degrees of renal impairment within two weeks (11).

Hypertension: Blood pressure measurement greater than the 95th percentile for age and sex (13).

Acute kidney injury (AKI): Based on the 2012 Disease Improving Global Outcomes.

(KDIGO) definition of AKI (rise in serum creatinine of more than 0.3mg/dl within 48 hours or a rise of 1.5 times the baseline within seven days (14).

Outcome variables: The primary outcomes of this study were the hospitalization outcomes and associated factors among children admitted with acute glomerulonephritis. Also, the secondary outcomes included the clinical and epidemiological profiles of the children admitted with AGN.

Statistical analysis

The data were entered and analyzed with SPSS version 25. The age was summarized as the mean with standard deviations, while the serum creatinine and urea were summarized as the median with an interquartile range (not normally distributed). Also, clinical features were summarized as frequencies and percentages. A chi-square was used to compare discrete variables (between survived and those who died). The Mann-Whitney U test was used to compare the continuous variables (serum urea and creatinine) that were not normally distributed. Clinical and laboratory parameters with p values less than 0.2 on bivariate analysis, along with those reported in the literature (serum urea and creatinine) to be associated with outcomes, age, and sex, were entered into a binary logistic regression to identify factors that may be associated with poor hospitalization outcomes. The binary logistic regression results were reported as adjusted odds ratios with 95% confidence intervals. A p-value less than 0.05 was set as the level of statistical significance.

Ethical considerations and approval

This study was conducted according to Helinski's declaration. Informed consent was obtained from the parents and caregivers of the recruited children. This study was approved by the federal teaching hospital Katsina's ethical review committee (FMCNHREC/REG/003/082016).

RESULTS

General characteristics

Thirty-five cases of acute glomerulonephritis (AGN) were admitted between 1st January 2018 and 31st December 2019. The mean age was 7.7 ± 3.3 years (range from 1.5 to 13 years). Most of the children were aged 5 to 10 years (23; 65.7%), with a dominance of males (60.0%), and most children (77.2%) were from a lower socio-economic class (Table 1).

Table 1: General characteristics of the children with acute glomerulonephritis.

Variables	Frequency n=35	Percent (100.0)
Age group (years)		
Less than five	6	17.1
5 to 10	23	65.8
Greater than 10	6	17.1
Sex		
Male	21	60.0
Female	14	40.0
Socio-economic class		
Upper	2	5.7
Middle	6	17.1
Lower	27	77.2
Mothers' educational level		
No formal education	22	62.9
Primary	7	20.0
Secondary	4	11.4
Tertiary	2	5.7

Incidence of AGN

Of the 3177 children (1511 in 2018 and 1666 in 2019) admitted during the study period, 35 cases were diagnosed as AGN, giving an incidence rate of 11 cases per 1000 children per year and an annual rate of 17.5 cases per year.

Clinical and laboratory profiles of the children with AGN.

The most common clinical presentation was generalized body swelling (n=35; 100.0%), followed by reduced urine output (85.7%) and hypertension (74.3%). History of sore throat and skin rashes were present in 22.9% and 37.1% of the participants, respectively. Urea and creatinine had medians with interquartile ranges of 10.0 (4.50 to 23.90) mmol/L (reference range 2.0 to 6.8 mmol/L) and 85 (67.60 to 204.00) mol/L (reference range 18 to 88 mol/L), respectively. Furthermore, the clinical features were comparable in those who died and those who were discharged, except for fever. The blood pressure at admission and the point of outcomes were also comparable between the survivors and nonsurvivors. Out of the 35 children, 28 (80.0%) had acute kidney injury (AKI), and most were in stage 1 (n = 14; 40.0%), as shown in Table 2a. At the point of outcomes, serum urea and creatinine were significantly higher among the nonsurvivors (Table 2b). Also, 13 (37.1%) had congestive cardiac failure at presentation, out of which two died, with a percentage case fatality of 15.4%. Similarly, 11 (31.4%) patients also had hypertensive encephalopathy, with two deaths (18.2%), as shown in Table 2b.

Outcomes

Four of the 35 children died, with a case fatality rate of 11.4% (95% CI 3.2 to 26.7). The median (IQR) duration of hospitalization was 7 (4–10) days. The median length of stay in those who were discharged was 7 (4 to 9.5) days, and in

those who died, it was 9 (4.5 to 13.5 days), p=0.603 (Table 2). Binary logistic regression showed that age, sex, fever, serum urea, and creatinine (at baseline) were not predictive of poor outcomes (death), as shown in Table 3. Two of the four deaths recorded during hospitalization were caused by hypertensive encephalopathy, while the other two were caused by congestive cardiac failure (Table 4).

Based on the pharmacological intervention, all the children with AGN received an appropriate dose of frusemide. In addition, other anti-hypertensives were added based on blood pressure levels and the presence of features of hypertensive encephalopathy (Figure 1). The children also received appropriate fluid therapy and antibiotics where indicated.

DISCUSSION

Acute glomerulonephritis is a common childhood kidney disease in Nigeria, with a variable incidence reported in previous studies (6–9). This study shows a high annual incidence of 17.5 cases. Though less than the incidence observed in Nigeria in the 80s (5) and early 90s (10), it was higher than the recent studies in Abuja (7), Zamfara (6), Ibadan (8), and Australia (15). The differences in the findings in this study compared with the recent studies may be because this is a prospective study compared to some of the previous retrospective studies (Abuja, Zamfara, and Australia). It is also a possible reflection of the differences in the social indices between our study site and others. This study took place in northwestern Nigeria, which has a high poverty level and poor childhood health indices compared with most geopolitical zones in Nigeria (16). The study's findings imply that AGN is still more prevalent in some parts of the country, requiring proactive steps to reduce risk factors.

Table 2a: Comparison of clinical and laboratory features between survivors and nonsurvivors

Variables	Frequency (%)	Discharged	Death	p*
Body swelling	35 (100.0)	31 (88.6)	4 (11.4)	-
Decreased urine	30 (85.7)	26 (86.7)	4 (13.3)	0.612
Dark colored urine	26 (74.3)	23 (88.5)	3 (11.5)	1.000
Hypertension	26 (74.3)	23 (88.5)	3 (11.5)	1.000
Fever	20 (57.1)	20 (100.0)	0 (0.0)	0.026
ASO titer elevated	18 (51.4)	16 (88.9)	2 (11.1)	1.000
Tachycardia	17 (48.6)	15 (88.2)	2 (11.8)	1.000
Past history of skin rash	13 (37.1)	12 (92.3)	1 (7.7)	1.000
Cough	9 (25.7)	8 (88.9)	1 (11.1)	1.000
Difficulty with breathing	9 (25.7)	7 (77.8)	2 (22.2)	0.553
Past history of sore throat	8 (22.9)	7 (87.5)	1 (12.5)	1.000
Convulsion	8 (22.9)	7 (87.5)	1 (12.5)	1.000
SBP (admission) mmHg	134.86 (30.9)	135.48 (32.3)	130.00 (18.3)	0.744
DBP (admission) mmHg	84.40 (25.1)	84.52 (26.5)	83.50 (12.5)	0.941
SBP (hospitalization**) mmHg	106.54 (17.6)	105.45 (17.2)	115.00 (20.8)	0.315
DBP (hospitalization**) mmHg	70.37 (14.2)	69.77 (14.4)	75.00 (12.91)	0.494
LOH (days)	7	7	9	0.603 ^U
Median (IQR)	(4-10)	(4 to 9.5)	(4.5 to 13.5)	
KDIGO-No AKI (%)	7 (20.0)	7	0	0.562 ^f
AKI (%)	28 (80.0)	24	4	
stage 0	7 (20.0)	7	0	0.373 ^f
stage 1	14 (40.0)	13	1	
stage 2	5 (14.3)	4	1	
stage 3	9 (25.7)	7	2	

ASO-Antistreptolysin O titers; LOH-Length of hospitalization; P value derived from Fischer’s exact test; IQR-Interquartile range; U-Mann-Whitney U test. **values at discharge or death, SBP-systolic blood pressure, DBP-diastolic blood pressure Admission SBP Vs. Hospitalization SBP p=0.004; Admission DBP Vs. Hospitalization DBP, p< 0.001. AKI-acute kidney injury, KDIGO- Disease Improving Global Outcomes.

The socio-demographics of peak age at 5 to 10 years, more males, and more cases in the lower socio-economic class in this study are in keeping with previous studies (8,10,15). While the reasons for more male cases remain unclear, it has been partly attributed to a higher rate of physical activities that increased exposure to β-hemolytic group A Streptococcus (17,18). Similarly, low socio-economic status has been linked to more prevalent poor living conditions and likely unsanitary environments, which promote streptococcal infection and the subsequent increased development of post-streptococcal glomerulonephritis (19). Furthermore, more cases in children aged 5 to 10 indicate a high streptococcal infection and carriers in this age group (3). These findings call for targeted intervention in this age and socio-economic group, such as health education, and prompt and adequate treatment of skin and throat infections.

Our study also showed that clinical features were comparable between those who survived and those who died, except for fever. A similar study in Indonesia shows that most clinical parameters except the level of consciousness were similar between those who survived and those who died (17). In

contrast, most Nigerian studies (6,8,10) did not compare clinical features between those who died and those who were discharged, limiting further comparison. This study also showed that the laboratory parameters (urea and creatinine) were significantly higher among the nonsurvivors compared with those who were discharged. Our observation is in keeping with the study in Indonesia (17), where serum urea and creatinine were elevated in those who died.

The duration of hospitalization was also comparable between those who died and those who were discharged home, according to this study. Most studies on childhood AGN in Nigeria analyzed the total length of hospitalization without distinguishing between those who died and those who were discharged, which limits our comparison (6,8,10). Though the sample size is small, this study shows that the duration of hospitalization may not contribute to outcomes in children with AGN in our environment and suggests the need to look for other factors that may influence the outcomes.

Our study also shows a high fatality rate of 11.4%. This mortality rate is higher than in Calabar (20) (5%), in Niger Delta (21) (5%),

Table 2b: Comparison of clinical and laboratory features between survivors and nonsurvivors

Variables	Frequency n (%)	Discharged 31	Death 4	p*
Urinalysis-Proteinuria				
(1+)	13 (37.1)	10	3	0.378 ^f
(2+)	19 (54.3)	18	1	
(3+)	3 (8.6)	3	0	
Urinalysis-Proteinuria				
none	13 (37.1)	12	1	1.000 ^f
(1+)	15 (42.9)	13	2	
(2+)	7 (20.0)	6	1	
Urea-median (IQR) (Admission) mmol/L	10.00 (4.50 to 23.90)	9.8 (4.50 to 23.68)	15.00 (8.30 to 21.60)	0.641 ^u
Urea-median (IQR) (hospitalization**) mmol/L	5.60 (4.00 to 12.75)	5.20 (4.00 to 8.98)	15.50 (14.50 to 18.50)	0.009 ^u
Creatinine- median IQR (Admission) µmol/L	85.00 (67.60 to 85.00)	77.00 (61.15 to 195.00)	159.8 (106.50 to 250.80)	0.223 ^u
Creatinine- median IQR (hospitalization**) µmol/L	76.00 (44.00 to 116.50)	66.00 (43.25 to 104.75)	150.00 (113.00 to 260.00)	0.034 ^u
eGFR- median IQR (Admission) per 1.73m2	51.11 (20.76 to 69.76)	54.53 (24.26 to 73.19)	27.47 (17.79 to 45.05)	0.213 ^u
eGFR- median IQR (hospitalization**) per 1.73m2	55.12 (28.61 to 102.60)	68.30 (35.36 to 103.31)	27.73 (17.31 to 39.98)	0.055 ^u
Congestive cardiac failure	13 (37.1)	11 (84.6)	2 (15.4)	0.618 ^f
Hypertensive encephalopathy	11 (31.4%)	9 (81.8)	2 (18.2)	0.575 ^f

**values at discharge or death; eGFR-estimated glomerular filtration rate; P value derived from Fischer's exact test; IQR-Interquartile range; U-Mann-Whitney U test. Admission Urea Vs hospitalization urea, p=0.002; Admission serum creatinine Vs hospitalization serum creatinine, p=0.001; Admission eGFR Vs hospitalization eGFR, p<0.001

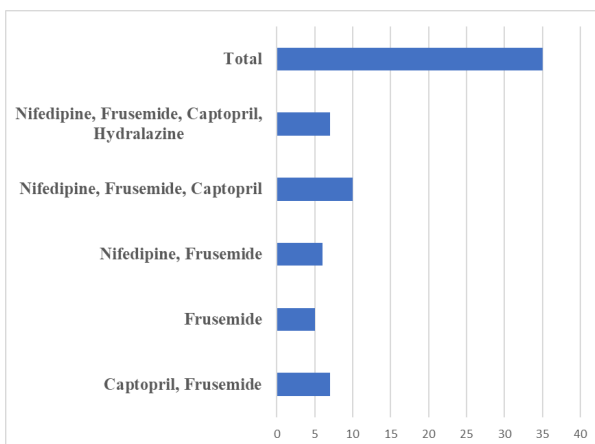


Figure 1: Summary of the pharmacological intervention for children with acute glomerulonephritis.

in Ibadan (8) (4.3%), and in Port Harcourt (9) (9.7%). However, the mortality rate is slightly less than 12.2% in Sokoto (6), the same geopolitical zone as the current study site. This study's high mortality rate in children with AGN may be due to delays in presentation, which are common among the low socio-economic class in northern Nigeria, with subsequent late interventions and poorer outcomes (22). It is also a source of concern,

especially compared with other parts of the country, and calls for a proactive step, including advocacy for early presentation with subsequent intervention and improved outcomes. On multivariable analysis, age, sex, and laboratory parameters (urea and creatinine) were not predictive of a poor outcome (death). This observation is similar to the findings in Ethiopia(23), where age, sex, and abnormalities in urea and creatinine levels were not associated with outcomes. In contrast, a study in Indonesia (17) showed that only serum creatinine levels were associated with poor outcomes. The inability to identify factors that are predictive of a poor outcome on multivariable analysis (binary logistic regression) in this study may be due to our small sample size (n = 35), suggesting the need for a larger sample size and, preferably, a multi-center study across the country.

The most common complications in this study were hypertensive encephalopathy (31% of cases) and congestive cardiac failure (37% of cases), both of which were associated with deaths. Though less frequent as a cause of death, congestive cardiac failure, which usually results from salt and water retention with hypertension, has also been reported in a few studies (10,24). The observation of hypertensive encephalopathy as a cause of death in this study is also in keeping with the previous studies, where rapidly elevated high blood pressure is associated with a fatal outcome (10,20,24). This further calls for close monitoring

Table 3: Binary logistic regression of factors that are associated with death.

Variable	sub-category	B	SE	Adjusted OR	95% C1	p
Age (years)	< 5	0.068	0.119	1.070	0.847, 1.352	0.569
Sex	Female	-0.102	0.091	0.903	0.755, 1.079	0.960
Fever	Present	-0.094	0.091	0.910	0.761, 1.088	0.301
Urea	> 2.5	-0.006	0.111	0.994	0.799, 1.237	0.960
Creatinine	> 1.5	-0.089	0.095	0.910	0.761, 1.088	0.350

B-Beta coefficient; SE-Standard error of beta coefficient. OR-odds ratio; CI-confidence interval.

Table 4: Summary of deaths

Variables	Patient 1	Patient 2	Patient 3	Patient 4
Age	6	12	3	13
Sex	Female	Male	Male	Female
Complaints	Body swelling, dark color urine, oliguria	body swelling, oliguria	body swelling, dark color urine, oliguria, past history of skin rash	Convulsion, body swelling, dark color urine, cough, oliguria, past history of sore throat
SBP mmHg	140	110	120	150
DBP mmHg	70	80	84	100
Hypertension	Stage 2	No hypertension	Stage 2	stage 2
Urinalysis (admission)	protein (1+) hematuria (+)	protein (1+) hematuria (+)	protein (1+) hematuria (3+)	protein (2+) hematuria (2+)
ASO titer	Not elevated	Elevated	Elevated	Not elevated
Admission Urea -mmol/L	4.6	12.00	18.00	25.20
Hospitalization** Urea-mmol/L	15.0	14.0	21.00	16.00
Admission Cr µmol/L	75	138	181.60	320.00
Hospitalization** Cr µmol/L	106.0	120	180	340.00
Admission eGFR /1.73m2	53.06	37.04	17.89	17.68
Hospitalization** eGFR /1.73m2	37.46	37.46	42.50	18.01
KDIGO AKI stage	1	2	3	3
LOH	4	13	14	5
Treatment	Nifedipine, Frusemide	Frusemide, Captopril	Nifedipine, Frusemide, Captopril	Nifedipine, Frusemide, Captopril
Cause of death	Hypertensive encephalopathy	Congestive cardiac failure	Congestive cardiac failure	Hypertensive encephalopathy

SBP-systolic blood pressure, DBP-diastolic blood pressure; ASO-Antistreptolysin O titers; Cr-serum creatinine value; eGFR-estimated glomerular filtration rate; **values at death; KDIGO- Disease Improving Global Outcomes; AKI-acute kidney injury; LOH-length of hospitalization.

of blood pressure in children with AGN and appropriate early intervention where the need arises.

Limitations of the study

Though our study is a prospective cohort, there are some limitations. Our sample size is small (n = 35). Due to limited resources, we could not prospectively follow up with the patients after discharge. Renal biopsy and complement C3 were also not done due to non-availability during this study.

CONCLUSION

This study shows a high incidence of childhood AGN and mortality rate in Katsina, northwestern Nigeria. Among the clinical features of AGN, only fever was associated with outcomes, while both serum creatinine and urea were elevated among the nonsurvivors. We recommend a proactive approach to reduce the burden and improve the outcomes of childhood AGN in the northwestern part of Nigeria.

Ethics Committee Approval: This study was approved by the federal teaching hospital Katsina's ethical review committee (FMCNHREC/REG/003/082016).

Informed Consent: Informed consent was obtained from the parents and caregivers of the recruited children.

Peer Review: Externally peer-reviewed.

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