

Varied Presentations of Acute Glomerulonephritis in Children

Single centre experience from a developing country

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العروض المختلفة لالتهاب كُبيبات الكلى الحاد عند الأطفال تجربة مركز منفرد في دولة نامية

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المخلص: الهدف: هدفت هذه الدراسة الاستباقية التي أجريت في مستشفى مانيبال التعليمي في بخارى لتوثيق العروض السريرية المختلفة لالتهاب كُبيبات الكلى الحاد عند الأطفال . ومقارنة ذلك مع المتغيرات البيولوجية المتوفرة في نيبال الغربية. **الطريقة:** المتغيرات السريرية والتجريبية للأطفال الذين يعانون من الوذمة والبيلة الدموية العيانية والمجهرية. **النتائج:** خلال سبع سنوات (2000-2007) تم تشخيص 92 طفلا بالتهاب كُبيبات الكلى الحاد . التحليلات السريرية والتجريبية كانت زاخرة بالأحداث. **الخلاصة:** الدراسة الحالية سلطت الضوء على العروض المختلفة لالتهاب كُبيبات الكلى الحاد . وبينت أن العروض والمضاعفات اللانمطية أكثر انتشارا من العروض الكلاسيكية في المنطقة الغربية من النيبال. **مفتاح الكلمات:** مرض الكلية . التهاب كُبيبات الكلى . حاد . التهاب المجاري البولية . نيبال.

ABSTRACT: Objectives: The objective of this prospective study, carried out at Manipal Teaching Hospital, Pokhara, was to document the various clinical presentations of children with acute glomerulonephritis and compare them with the available biological parameters in Western Nepal. **Methods:** Clinical and laboratory parameters of children with oedema and microscopic/macrosopic haematuria. **Results:** For seven years (2000-2007), 92 cases of children were clinically diagnosed with acute glomerulonephritis (AGN). Other clinical and laboratory analyses were also eventful. **Conclusion:** The present study highlights the varied presentations of AGN, atypical presentations or complications of glomerulonephritis being more common than the classical presentation in the Western Region of Nepal.

Key words: Renal disease; Glomerulonephritis, acute; Urinary tract infection; Nepal.

GLOMERULONEPHRITIS (GN) IS THE TERM generally reserved for the variety of renal diseases in which inflammation of the glomerulus, manifested by proliferation of cellular elements, is secondary to an immunologic mechanism.¹ Most incidents of AGN appear to be associated with a postinfectious state with known aetiological agents like bacteria, parasite, virus. Amongst the GN secondary to bacterial infections, post-streptococcal GN is the most frequent and usually presents with typical clinical findings;² however, the scenario in this study was different. Out of 92 cases of acute glomerulonephritis, only 33 cases presented with typical clinical

features of GN; the remaining 59 had atypical clinical presentations. Atypical postinfectious glomerulonephritis (PIGN) may mimic a great variety of glomerular diseases.^{3,4}

METHODS

This prospective study was conducted between September 2000 and March 2007 at the Department of Pediatrics, Manipal Teaching Hospital, Pokhara, Nepal. The case collection was from September 2000 to February 2005 and follow-up was continued until March 2007. Ninety-two children of all age groups presenting either with oedema (facial puffiness and/or

Table 1: Age and Sex distribution of patients at presentation

Sex	Age				Acute Glomerulonephritis (AGN) (n = 92)
	<1yr	>1-5yr	>5-10yr	>10yr	
Male = 57 (61.95 %)	0	3	21	33	
Female = 35 (38.04%)	0	1	12	22	
Total	0	4	33	55	92

pedal oedema) and haematuria (microscopic or frank and/or cola coloured urine) were considered for this study. Borderline cases, those with urinary stones and with hypercholesterolemia suggestive of nephrotic syndrome, (4+ proteinuria with high cholesterol level requiring treatment with prednisolone) were excluded from the study. Both outpatients as well as hospitalized patients were enrolled for the study. Consent of the patients was taken and the parents or guardians received information about the study and follow-ups. A detailed history was taken and a clinical examination performed, followed by relevant available investigations. The investigations included urine routine and microscopic examination, urine culture and sensitivity, renal function tests, antistreptolysin O (ASO) titres and ultrasound of the abdomen. Facilities for doing serum complement levels, electron microscopy and immunofluorescence studies for renal biopsy were not available in this centre. These cases were followed up for two years.

RESULTS

Of the 92 children, 57 (61.95%) were male and 35 (38.05%) were female. All were diagnosed to have acute glomerulonephritis (AGN). The male: female ratio was 1.6:1. Eighty-eight children (95.7%) were above 5 years (school going age group); only four (4.3%) of the children were under 5 years (preschool age group) [Table 1]. The classical presentation of AGN was seen only in 33 (35.9%) cases, while 59 (64.1%) presented with atypical findings or complications [Figure 1]. The pattern of atypical presentations/complications were hypertensive encephalopathy (n = 11, 18.6%); nephrotic onset (n = 10, 16.9%); urinary tract infection (UTI) (n = 10, 16.9%); joint pains and rash (n = 2, 3.3%); heart failure (HF) (n = 6, 10.1%); combined HF and UTI (n = 3, 5.1%); rapid deterioration or progression (n = 5,

8.5%); acute renal failure (n = 4, 6.7 %); combined cardiac and renal failure (n = 1, 1.69 %), associated with rheumatic fever (n = 3, 5.1%); epistaxis (n = 2, 3.3%); malena (n = 1, 1.69%); associated with enteric fever and UTI (n = 1, 1.69 %) [Table 2].

Clinically, all (100%) children had facial puffiness and/or pedal oedema and macroscopic haematuria (frank and/or cola coloured urine). Other main clinical features were hypertension (n = 80, 86.9%), fever (n = 60, 65.2%), headache (n = 58, 63.0%) and oliguria (n = 50, 54.3%) followed by pyodermas, vomiting, burning micturition, painful abdomen, sore throat, altered sensorium, convulsions and shortness of breath. Some rare clinical features were also noted cough (n = 14, 15.2%), systolic murmur (n = 7, 7.6%), joint pains and rash (n = 2, 2.1 %), hepatomegaly (n = 3, 3.2 %), diarrhoea (n = 3, 3.2 %), epistaxis (n = 2, 2.1 %), malena (n = 1, 1.0 %) [Table 3].

Table 4 shows the results of the investigations into urea, creatinine and albumin levels in these patients. ASO titres were found to be positive in only 50% of

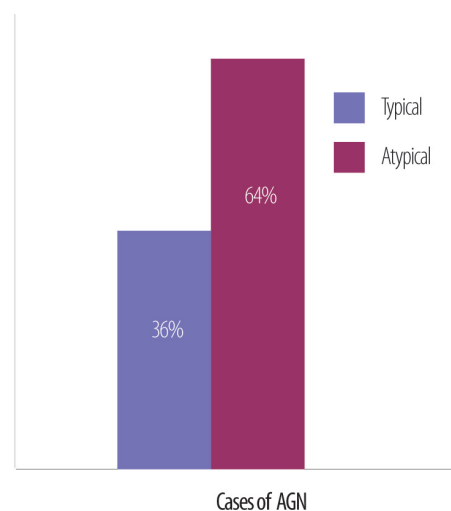


Figure 1: Clinical Presentation

Table 2: Pattern of atypical presentations/complications of acute glomerulonephritis (AGN)

AGN cases (n = 59)	Number	Percentage
AGN with hypertensive encephalopathy	11	18.6%
AGN with nephrotic picture	10	16.9 %
AGN with urinary tract infection (UTI)	10	16.9 %
AGN with heart failure	6	10.1%
AGN with rapid progressive GN	5	8.5%
AGN with acute renal failure	4	6.7 %
AGN with rheumatic fever	3	5 %
AGN with heart failure + UTI	3	5 %
AGN with joint pains and rash	2	3.3 %
AGN with epistaxis	2	3.3 %
AGN with malena	1	1.69%
AGN with heart failure and acute renal failure	1	1.69 %
AGN with enteric fever and urinary tract infection	1	1.69 %
Total	59	100%

the cases. An ultrasonography (USG) of the kidney, ureters and bladder revealed Grade I renal parenchymal changes (RPC) in 48%; Grade II RPC, mild renal dysfunction (MRD) in 24%; Grade III RPC in 6.5% and normal in 22% cases [Figure 2]. All the three renal biopsies showed crescentic glomerulonephritis.

DISCUSSION

The global burden of severe Group A streptococcal disease is concentrated largely in developing countries including Nepal. Group A streptococcal diseases are more common in children than in adults with diseases ranging from pharyngitis and impetigo to invasive infections and the post-streptococcal sequelae: acute rheumatic fever and acute post-streptococcal glomerulonephritis.³ Acute post-streptococcal glomerulonephritis is the commonest cause of AGN in this country which usually exhibits milder symptoms or signs like haematuria, mild oedema, oliguria and hypertension which has a simple clinical course and an excellent prognosis. On the other hand, atypical presentations may mimic a great variety of glomerular disease, have a worse prognosis and need better diagnosis and care. Glomerular disease with atypical presentations will include mild mesangial and/or en-

Table 3: Signs and Symptoms of patients at presentation

Signs and symptoms	Number (n=92)	percentage
Hypertension	80	86.9%
Fever	60	65.2%
Headache	58	63%
Oliguria	50	54.3%
Pyoderma	42	45.6 %
Vomiting	33	35.8 %
Burning urine	32	34.7 %
Pain abdomen	31	33.6 %
Sore throat	28	30.4 %
Altered sensorium	21	22.8 %
Convulsions	21	22.8 %
Shortness of breath	18	19.5%
Cough	14	15.2 %
Systolic murmur	7	7.6 %
Hepatomegaly	3	3.2 %
Diarrhoea	3	3.2 %
Joint pain with rash	2	2.1 %
Epistaxis	2	2.1 %
Malena	1	1.0 %

docapillary glomerulonephritis (GN); focal segmental glomerulosclerosis (FSGS) with diffuse IgM mesangial deposits; rapidly progressive or crescentic GN with C3 hump-like deposits or with microabscesses; focal mesangiocapillary GN superimposed on endocapillary pattern; membranous GN with diffuse exudative changes and postinfectious glomerulonephritis with anti-glomerular basement membrane (anti-GBM) linear deposits.⁴ Some other study states that mesangial proliferative GN is the commonest histopathological lesion forming 66% of all primary GN. Minimal lesion, focal global sclerosis and focal segmental glomerulosclerosis accounted for 7% each. Membranous GN was uncommon (3%), while mesangiocapillary GN, diffuse endocapillary GN and crescentic GN were even rarer.⁵ In this study, we tried to ascertain age incidence, sex ratio, common clinical presentations and available biochemical parameters of primary glomerulonephritis. Out of 92 children, there were 59 atypical findings of AGN. Those with positive ASO titres were treated as poststreptococcal glomerulonephritis cases. The others were given the benefit of the doubt and treated for the same. Lack of facilities for investigations and financial constraints in a developing country did not permit us to proceed with further workups. Hence the confirmatory diagnosis could not be made in these cases. Like other studies, this study also showed a preponderance of males (61.95%) as

Table 4: Biochemical parameters of the patients

Parameters	Number	Percentage
Urea : Normal range 0.535-14.28mmol/L (15-40mg/dl)		
<14.28mmol/L (< 40mg/dl)	40	43.5%
14.63-17.85mmol/L (41-50mg/dl)	22	24%
18.20-35.70mmol/L (51-100mg/dl)	20	22%
>35.70mmol/L (>100mg/dl)	9	10%
Creatinine : Normal range 53.04-132.6µmol/L (0.6-1.5mg/dl)		
<132.6µmol/L (<1.5mg/dl)	54	59%
141.44-142µmol/L (1.6-5mg/dl)	23	25%
>142µmol/L (5 mg/dl)	15	16%
Albumin : Normal range 3.5-5gm/dl		
<25gm/L (2.5 g /dl)	16	17.4%
26-30gm/L (2.6 -3.0g/dl)	38	41%
31-35gm/L (3.1 - 3.5 g/dl)	18	19.6%
>35gm/L (3.5g/dl)	20	22%

compared to females (38.05%) with the ratio 1.6:1. The reasons for this male predominance are not known.¹ As in other studies,⁶ most children were above 10 yrs (57.9%). Hypertensive encephalopathy was found in 18.6%, a much higher percentage compared to 5% & 4.3 % in other studies.^{7, 5} In these patients, hypertension is usually difficult to control and accompanied by signs of central nervous system dysfunction such as headaches, vomiting, depressed sensorium, confusion, visual disturbances, aphasia, memory loss, coma, and convulsions. All these features were also noted in our study. Twelve of the cases, which presented as nephrotic onset, had anasarca with proteinuria >40 mg/m²/hr. All of them (100%) had haematuria and hypertension; their features resolved with symptomatic treatment and did not require steroids. The incidence of nephrotic features was higher in other studies, 61.7%, 66%, 29% and 34.48% respectively as compared to ours which was only 13%.^{5, 8-10} Seventeen percent had associated UTI which is quite frequently seen. AGN complicated by UTI was also observed in 20% cases in a study in Nigeria.¹¹ Rapidly progressive glomerulonephritis (RPGN) is a disease of the kidney that results in a rapid decrease in the glomerular filtration rate of at least 50% over a short period, from a few days to 3 months and is irreversible.¹² This was observed in 8.5 % in our study. The frequency is estimated at 1-2 cases per 100,000 persons internationally. The main pathologic finding is fibrinoid necrosis (>90% of biopsy specimens); extensive crescent formation is present in at least 50% of glomeruli.¹² As biopsy was not done in our cases we could not confirm the

cases by pathological findings, hence the observed fre-

quency was higher. Heart failure (HF) and acute renal failure (ARF) were the sole systemic complications in 7/29 and 2/29 in AGN patients respectively, noted by Olowa WA in Nigeria.¹⁰ Heart failure was seen in 3% cases in another study,¹³ whereas in our study 10% presented with shortness of breath, cough, hepatomegaly. Acute renal failure is defined as abrupt or rapid decline in renal filtration function. The condition is often transient and usually completely reversible.¹⁴ Acute renal failure was present in 56 (76%) in one study and dialysis required in 14, but this presentation was much less in our study and only 4 required dialysis.⁹ We also observed some rare features like rheumatic fever (5%), epistaxis in 2 patients, melena in one. Literature on these presentations was not available. A few double systemic complications were also noted: AGN with enteric fever with UTI (1.69%), AGN with HF and ARF (1.69%). Three patients had double systemic complications in another study: one with hypertensive encephalopathy (HTE) with HF, and two with acute renal failure (ARF) with HF.¹⁰ The development of clinical nephritis (i.e. haematuria and/or oedema) either during or within 2-5 days after the onset of a respiratory tract infection is atypical and suggests the possibility of some other form of GN.¹⁵ In our study, nephritis developed following respiratory infection in 15% cases. Hypertension was the commonest mode of presentation (87%) in a study by Corpa, Soares V. The prevalence of arterial hypertension was 62.7%¹⁶ and it was 50% and 86.7% respectively in another study.^{17, 8} The pathogenesis of the hypertension is unknown; howev-

Table 5: Follow-up of patients

	Classical presentation (n = 33)		Atypical or complicated presentation (n = 59)	
Follow-up				
Yes	33 (100%)	n = 33	28 (30.4%)	n = 59
No	0 (0%)		31 (52.5%)	
- Complete resolution	33 (100%)	n = 33	12 (42.85%)	n = 28
- With impaired renal function	0 (0%)		9 (32.14%)	
- End stage renal disease on haemodialysis at higher centre	0 (0%)		5 (17.85%)	
- Mortality	0 (0%)		2 (7%)	

er, it is probably multifactorial and related only in part to extracellular fluid (ECF) volume expansion. Haematuria and proteinuria was present in 41% in one study⁵ and in 48.8% in another study.⁸ According to some investigators, oedema is found in approximately 85% of patients.¹⁵ Oedema usually appears abruptly and the degree of oedema varies markedly and depends on a number of factors, including the severity of glomerular involvement, the fluid intake, and the degree of hypoalbuminaemia. In our study also the degree of oedema was variable. Gross haematuria occurs at onset in 30-50% of children with poststreptococcal glomerulonephritis (PSGN) who require hospitalisation.¹⁸ The cardinal features are associated with various degrees of malaise, lethargy, anorexia, fever, abdominal pain and headache. Observant parents may also note oliguria. All these features were observed in this study. Almost characteristic by their absence are arthralgia, arthritis, carditis, hepatic involvement, and gastrointestinal bleeding,^{19, 17} but in this study these findings were also noted. Systolic murmur was observed in 7.6% of the cases, hepatomegaly in 3%, diarrhoea in 3% and joint pain with rash in 2%. In this study, pyoderma and sore throat were the preceding cause of GN in 46% and 30 % of cases respectively. This indicates the possibility of post streptococcal origin; however, in the remaining 24% cases there was no preceding pyoderma or sore throat. Other postinfectious causes that have been reported are: *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Rickettsia rickettsiae*, *Mycoplasma species*, *Meningococcus species*, *Leptospira species*. Also, viral illnesses have preceded the onset of typical AGN; among the most common are the varicella zoster virus, cytomeg-

alovirus, and the Epstein-Barr virus.²⁰ In the analysis of laboratory parameters, it was noted that impairment of urea was seen in 56% and impairment of creatinine in 41%. Renal impairment observed in other studies was 33.3%⁸ and 5.5% respectively.^{8, 21, 19} Low albumin levels of >35gm/L were observed in 78% of cases (25gm/L in 17.4%; 26-30gm/L in 41%; 31-35gm/L in 19.6%) and normal levels of >35gm/L in 22%. In the majority (60.6%) of cases it was between 2.6 - 3.5 g/dl. The reason why many patients had albumin levels slightly on the low side can be explained by the fact that these children were malnourished, which is again a common problem of this country. A rise in the titer of ASO is observed in only 50% of patients.^{22, 20} In our study too, ASO was positive in 50% of cases. Ultrasound of the kidney, ureters and bladder was normal in 22% cases. Forty-eight percent of patients with RPC had RPC Grade I (RPC), 24% had Grade II, and 6.5% had Grade III. RPC Grade I is echogenicity of kidney the same as the liver, RPC Grade II is echogenicity of the kidney more than the liver. RPC Grade III means that renal fat sinus and renal parenchyma cannot be differentiated with accentuated/ATT - corticomedullary differentiation.^{23, 21}

The follow-up of this study was not good as just over half the patients (52.5%) did not return for follow-up. Maybe the referral to a higher level centre was the reason for this. Among those who came for follow-up, the ones with classical presentation AGN had complete resolution of the disease. Complete resolution was also observed in 42.85% cases that had atypical or complicated presentations. This means many may still have fallen into postinfectious forms, which are very common in our environment. Of these, 32.14%

had impaired renal function and 17.85% had gone into end stage renal disease and were on haemodialysis at a higher level centre. There was 7% mortality [Table 5].

The enlisted cases were provisionally assumed to be of poststreptococcal origin and were treated likewise since PSGN is the commonest cause in a developing country like ours. However, these cases, especially the ones which were ASO negative, needed better diagnostic and confirmatory support such as complement C3, C4 levels and immunofluorescence for the biopsy specimens. These investigations were unfortunately unavailable at our setup and elsewhere in the city. Many investigations were also limited due to financial constraints of the patients. As optimum workup was required, we referred many of the cases to higher level centres. Some of these cases were subsequently lost to follow-up.

CONCLUSION

We conclude that AGN is common in children of the Western region of Nepal and that an unusual atypical presentation is frequent. Better outcomes can be achieved with more detailed laboratory and diagnostic methods which are limited at present. Renal biopsy in these cases is mandatory and helpful, especially in allowing rational use of corticosteroids and other immunosuppressive drugs. Financial constraints are a major contributing factor in a developing country like Nepal. Nevertheless as PSGN is the commonest cause of GN in our country, it is justified to give the benefit of treatment to these patients before considering other causes. Symptomatic treatments and careful supportive care will allow the majority of children to recover from post streptococcal AGN.

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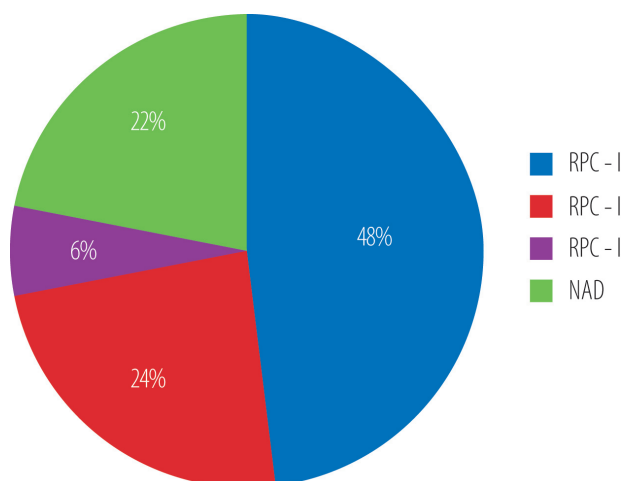


Figure 2: Results of ultrasonogram of kidney ureters and bladder region

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