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Original Research Article

Clinical profile and outcome of acute nephritic syndrome in children from a tertiary care centre in south India: a descriptive study

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ABSTRACT

Background: Acute nephritic syndrome (ANS) is major cause of morbidity in developing countries. This study is an attempt to evaluate the clinical characteristics, complications and outcome of acute nephritic syndrome.
Methods: This hospital based descriptive study was conducted at a tertiary care hospital in Kerala, South India. 103 children with ANS were analysed. Detailed clinical examination and relevant laboratory investigations were done. These children were followed up for 1 year.
Results: Out of 103 patients studied 64% were male and 36% were female. The peak age group was 6 to 8 years. Skin infection was the most common predisposing condition (68.9%). Hypertension was present in 60.1% of patients. 26.2% of patients developed complications. Of these Acute renal failures was the most commonly encountered complication (18.4%). Proteinuria (87.4%) and microscopic hematuria (80.6%) were the most consistent features. 82.5 % patients had low C3 at the time of diagnosis. Majority of patients with low C3 level had positive ASO titre. ($p = 0.014$). At 3month follow up C3 became normal in 95.2% of patients. At 3 months' majority of patients with normal C3 had incomplete recovery. ($p = 0.010$). At the end of 12m, microscopic heamaturia was present in 4 patients, persistent hypertension in 2 patients, 11 patients had proteinuria. These patients are kept under long term follow up.
Conclusions: Complications and morbidity is significantly high during the acute phase in ANS. This study highlights the need for long term follow up of these patients.

Keywords: Acute glomerulonephritis, Acute post streptococcal glomerulonephritis, Complement C3

INTRODUCTION

Diseases involving the renal glomeruli are encountered frequently in clinical practice and are the most common causes of end stage renal disease worldwide. Some do not cause progressive renal failure but are important causes of morbidity and considerable medical expense.

Acute glomerulonephritis is defined as those glomerular diseases that may present with an acute nephritic syndrome(ANS).[1] Acute post streptococcal glomerulonephritis (APSGN) is a classic example of the ANS characterised by sudden onset of gross hematuria, oedema, hypertension, and renal insufficiency. 97% of APSGN occur in less developed countries.[2]

(APSGN) predominantly affects children between the ages of 2 and 10 years, with a slight predominance of males.[3] It is an acute, reversible disease characterized by spontaneous recovery in the vast majority of patients. Typically, gross hematuria and edema develop 7 days to 12 weeks after the streptococcal infection.[1,3] Spontaneous

resolution of the clinical manifestations is generally rapid: diuresis usually ensues within one to two weeks, and the serum creatinine concentration returns to base line within four weeks. The rate at which urinary abnormalities disappear is more variable. Hematuria usually resolves within 6 months, but mild proteinuria is present in 15 percent of patients after 3 years and in 2 percent of patients after10 years.[3]

The long-term prognosis of patients with (APSGN) has been a subject of controversy. Although most patients eventually have a complete recovery, hypertension, recurrent or persistent proteinuria, and chronic renal insufficiency develop in some. The reported incidence of chronic renal insufficiency ranges from 0 to 20 percent. It has been suggested that misdiagnosis, racial differences in the risk of progression of renal disease, and differences in the natural history of sporadic and epidemic glomerulonephritis may account for these discrepancies.[3]

ANS is a common cause of admission to the Paediatric wards in South India. There are only a few studies on the clinical profile and follow up of these patients. The analysis of the outcome is important for a better awareness of the long-term prognosis. This study is an attempt to identify the various clinical manifestations of acute nephritic syndrome and to analyse the course and outcome during one year follow up period.

METHODS

This hospital based prospective study was conducted at a tertiary care hospital in South India, after obtaining approval from institute ethics committee. Patients admitted with ANS in paediatric medicine wards were studied. The objectives were to study the various clinical manifestations and complications and to identify those children who needed long term follow up. All children less than 12 years of age with acute nephritic syndrome who presented in the department of paediatrics during 1 year were included in this study. Those children more than 12 years, those diagnosed as nephrotic syndrome within 2 weeks of hospitalisation were excluded. ANS is characterised by hematuria, proteinuria,oliguria, hypertension, edema, RBC casts in urine and circulatory congestion.[1] Oliguria is defined as urine volume less than 1ml/kg/hr. Edema is puffiness of face , bilateral pitting pedal edema and abdominal wall edema. Macroscopic hematuria is defined as visible pink or brown colored urine owing to the presence of red blood cells confirmed by microscopic examination. Microscopic hematuria is defined as more than 5 RBC's per high power field in the sediment of 10 ml of centrifuged freshly voided urine sample. Hypertension is defined as average systolic BP /or diastolic BP that is ≥95th percentile for gender, age and height on ≥3 occasions.[4] Abnormal proteinuria is defined as 4-40mg/ m^2/hr and Nephrotic range is defined as more than 40 mg/m^2/hr.[2] Patients admitted with ANS in the paediatric wards were included in the study after the initial clinical and laboratory evaluation. Those patients who fulfilled the inclusion criteria were interviewed by the invigilator. Detailed clinical examination was done and relevant laboratory investigations were done.

Anti-streptolysin O titre (ASO titre) was measured by latex agglutination. ASO titre more than 200IU/ml was considered as evidence for recent streptococcal infection.[5] Serum complement 3 (C3) levels were measured by immunoturbidimetric method. APSGN was diagnosed based on the following criteria. Features of acute nephritic syndrome and evidence of recent streptococcal infection (recent pyoderma or pharyngitis with positive ASO titre or throat swab positive for group A streptococcus) and low serum C3 with normalisation of C3 on 12 week follow up. Patients who were discharged were advised follow up for any evidence of residual renal injury at the end of 3 months. Incomplete recovery was defined as one or more of the following features at the end of 3 months a) Edema b) Proteinuria c) Hematuria d) Hypertension e) Abnormal renal functions f) Low C3. All patients who had incomplete recovery were kept under long term follow up.

Data analysis was done using SPSS software and the results obtained are shown in the form of frequencies along with percentages. Diagrams and charts were drawn wherever necessary to supplement the most salient findings.

RESULTS

Out of 103 patients studied 64% were male and 36% were female (Figure 1).

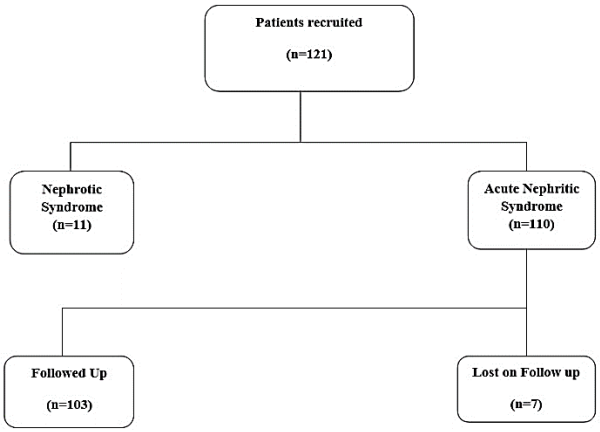

Figure 1: Flow chart depicting enrolment of patients for the study.

The peak age group was 6-8 years. Skin infection was the most common predisposing condition (68.9%) (Figure 2). Sore throat was less frequent in children below six years (Figure 3). Latent period of sore throat was 8 to14 days in majority of cases (41%). Latent period of skin infection was 15 to 21 days in majority of cases (39%).

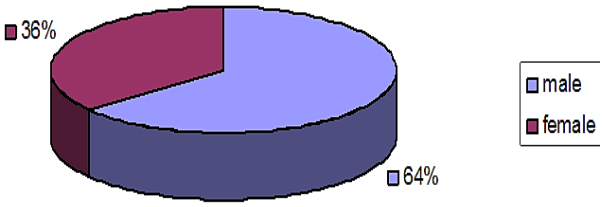

Figure 2: Sex distribution of children with acute nephritic syndrome (n = 103).

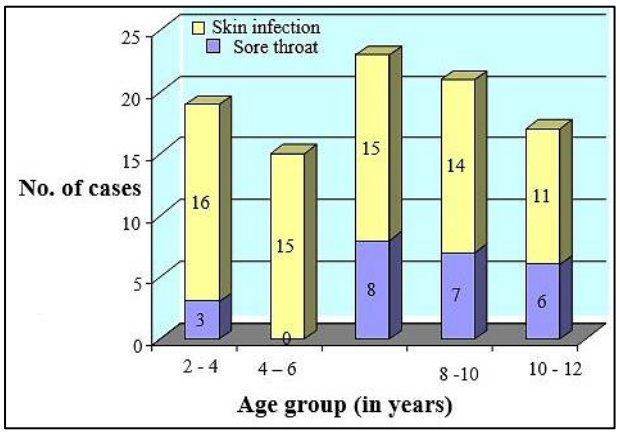

Figure 3: Age distribution of patients with sore throat and skin infection (n = 95).

Presence of edema was recorded in all the patients. Hypertension was present in 60.1% of patients. Hypertension was more common in children aged 6 to 10 years. 26.2% of patients developed complications (Table 1).

Table 1: Percentage of complications in acute nephritic syndrome (n = 103).

	No. of cases	%
Hypertensive encephalopathy	3	2.9
Congestive Heart Failure	5	4.9
Acute Renal Failure	19	18.4

Of these acute renal failures was the most commonly encountered complication (18.4%). Proteinuria (87.4%) and microscopic hematuria (80.6%) were the most consistent features. Nephrotic range proteinuria was present in 9.7% patients. 82.5 % patients had low C3 at the time of diagnosis (Table 2).

Table 2. Acute nephritic syndrome and C3 level (n = 103).

C3	No. of cases	%
Normal	18	17.5
Low	85	82.5

Table 3. Comparison of ASO titre with C3 level (n = 58).

		ASO		p-value
		Positive	Negative	
C3	Normal	3	11	0.014
	Low	26	18	

Majority of patients with low C3 level had positive ASO titre. This was found to be statistically significant (p= 0.014) (Table 3). At the end of 3 months 4 patients had persistent hypertension and 15 patients had microscopic hematuria. Renal functions were normal in all patients. At 3 months C3 became normal in 95.2% of patients. 5 patients were having low C3 at the end of 3 months (Table 4). These patients were followed up. At 3 months' majority of patient with normal C3 had incomplete recovery and this was found to be statistically significant (p=0.014) (Table 5). At the end of 12 months, microscopic hematuria was present in 4 patients, persistent hypertension in 2 patients; 11 patients had proteinuria (Table 6).

Table 4: Outcome of disease (n = 103).

Outcome	3 months	6 months	9 months	12 months
Complete recovery	50 (48.5%)	63 (61.1%)	72 (69.9%)	81 (78.6%)
Incomplete recovery	48 (46.6%)	35 (34%)	26 (25.2%)	17 (16.5%)
Nephrotic	4(3.9%)	0	0	0
Expired	1 (1%)	0	0	0

Table 5: C3 and outcome at 3 months (n = 103).

		3 months			
		Complete recovery	Incomplete recovery	Nephrotic	Expired
C3	Normal	5	10	3	0
	Low	43	40	1	1
p - value		0.010			

Table 6: Persistence of clinical and laboratory abnormalities on follow up.

		3 months	6 months	9 months	12 months
Edema		6	0	0	0
Hypertension		4	1	1	2
Proteinuria	≤ 1+	19	16	15	11
	> 1+	4	0	0	0
Microscopic hematuria		15	9	7	4
Macroscopic hematuria		0	0	0	0
Abnormal renal functions		0	0	0	0
Low C3		5	2	1	1

DISCUSSION

121 patients under the age of 12 years with ANS hospitalised in paediatric wards were enrolled for the study. Of this, 11 patients were diagnosed as nephrotic syndrome within two weeks of hospitalization and 7 patients were lost on follow up. After applying exclusion criteria, total of 103 patients were taken up for analysis. Most of the published data are on post streptococcal glomerulonephritis, which is the most common cause for acute nephritic syndrome.

In Tejani et al. study, acute glomerulonephritis affects children between ages of 2-10 years.[6] Less than 5 % of the patients were under 2 years of age. In a recent study from South India (2015), the mean age was 6.8 years with 78.5% of subjects being above 5-year-old.[5] The immature immune response in very young children has been attributed as the cause for rarity of APSGN in this age group.[7,8] In the present study the age group ranged from 2 to 12 years and the peak age group was 6 to 8 years i.e. the school going age.

In the present study, the M: F ratio was 1.8:1. According to Rodriguez Iturbe, males more frequently have clinical nephritis and females are more likely to have subclinical disease.[9] In their study the M: F ratio reported was 2:1. In Gunashekaran et al. study, the M: F ratio was 1.16:1.[5]

In the present study 92.2% cases had history of either pharyngitis or skin infection in the recent past. The antecedent event was skin infection in 68.9% of cases and sore throat in 23.3% cases. Sore throat was less frequent in children below 6 years. Nissenson et al. study reports that patients with skin lesions tend to be younger than those with pharyngitis.[10] In this study the overall risk of skin infection with type 49 strain was seen to be approximately 25%, the risk was higher in children younger than 6.5 years of age i.e. 43%. In older children, it was 5%. In the present study skin lesions were the most common predisposing condition in all age groups.

In the study by Nissenson et al. latent periods reported were 1 to 3weeks in pharyngitis and 3 to 6 weeks in skin infection.[10] In the present study the latent period was slightly shorter. The latent period of sore throat to the onset of nephritis was 1 to 2 weeks in 41% of cases and that for skin infection was 2 to 3 weeks in 39% of cases.

In the present study, more than 75% presented with all the cardinal features of acute nephritic syndrome viz. edema, hematuria, oliguria, and hypertension. Edema was recorded in all patients at the time of diagnosis; hematuria was present in 80.6% of patients, oliguria in 74.8% of patients, and hypertension in 60.2% of patients.

At the time of diagnosis rash was present in 2 patients. Investigations including ANA were done in these patients. No specific aetiology could be recognized. Pneumonia was present in 2 patients on evaluation, suggesting a different aetiology.

In Gunashekaran et al. study, 4.6% of children with PSGN developed hypertensive encephalopathy and Congestive cardiac failure developed in 12.3%.[5] In our study only 2.9% developed hypertensive encephalopathy and Congestive cardiac failure was present in 4.9%.

In the present study 18.4% of patients had acute renal failure and one patient expired at the onset due to acute renal failure and congestive cardiac failure. In Rajajee et al study 13.3% had ARF.[11] In Becquet et al study, 43.7%, Sarkissian et al 1%, Wong et al 18%.[12-14] In Gunashekaran et al. Study 23.5% had ARF.[5] Most of the studies show that a significant percentage have the complication of ARF.

Shroff et al. study, 88% of children with acute glomerulonephritis had low C3 levels.[15] In Becquet et al study low C3 was 90%, Sarkissian et al 95%, Wong et al 61.5%, Gunashekaran et al. 100%.[12-14,5] In the present study, at the time of presentation 82.5% of patients had low levels of serum C3 suggesting post infectious glomerulonephritis. Normal C3 at the time of onset of disease was present in 17.5% of patients. Majority of patients with normal C3 at onset had incomplete recovery at 3 month follow up, and this was found to be statistically significant (p= 0.010).

In the present study ASO titre was elevated only in 50% cases of acute glomerulonephritis. ASO titre does not increase in all patients with streptococcal infection and

the absence of a high titre does not exclude a streptococcal infection. This is especially true in patients with skin infection. In majority of cases the antecedent event was skin infection. Other tests like anti-DNAse B.[16] are required in these cases to rule out streptococcal aetiology which was not available in our setting. In the present study majority of patients with low C3 level had positive ASO titre and this was found to be statistically significant (p= 0.014).

Regarding outcome evaluation, as per the operational definitions, recovery was incomplete at 3 months in 48 patients (46.6%). Proteinuria was the predominant abnormality, which was detected in 23 patients, and 15 patients had microscopic hematuria, and 5 patients had low C3 levels.

However, at the end of 12 months, microscopic hematuria was present in 4 patients, and persistent hypertension in 2 patients. They are kept under follow up and renal biopsy is required for further evaluation. At the end of 12 months, 11 patients had proteinuria, but it was trace in 10 patients and one patient had 1+ proteinuria.

According to Cameron et al., C3 concentrations are depressed early in the course of the disease, and in most cases, return to normal in six to eight weeks.[17] In the present study C3 became normal in 95.2% of patients at 3months. Low C3 was present in 2 patients at 6 months, and it became normal at the end of 9 months in one patient and at 15 months in the other. These children are under regular follow up and both are showing normal growth, blood pressure and renal function now.

CONCLUSION

Acute nephritic syndrome is common is South India. It is the cause of considerable morbidity and occasional mortality. These patients need inpatient care and continuous monitoring. Sudden decrease in C3 followed by normalisation in 6 to 8 weeks is of diagnostic importance. Serial measurements of C3 during follow up and finding of persistently low C3 helps the clinician to recognise patients who need long term follow up.

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

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