OUTCOME OF CHILDREN WITH ACUTE POST STREPTOCOCCAL GLOMERULONEPHRITIS IN TIKUR ANBESSA SPECIALIZED TEACHING HOSPITAL Addis Ababa, Ethiopia.

Lamesginew Mossie MD*. Damte Shimelis MD*.

Abstract

Back Ground*: post streptococcal glomerulonephritis is one of the commonest causes of glomerular disease in developing countries. It is also one of the commonest causes of morbidity and in few cases mortality if proper identification and supportive treatment is not delivered.*

Objective: *the objective of this study is to look into the outcome and identify the predictors of outcomes of patients with post streptococcal glomerulonephritis in a tertiary care hospital***.**

Materials and methods*: Retrospective analysis of admissions of post streptococcal glomerulonephritis was conducted at Tikur Anbessa Specialized Teaching Hospital in Addis Ababa over eight year's period from 2003 to 2010. Data was collected from patient records.*
The record of each patient was examined for the following information: age, sex, and address sociodemographic characteristics, predictors of outcome and complications of APSGN.

Results: *there were 68 children with APSGN enrolled during the study period. 40 (58.8%) were males and 28 (41.2%) were females. The common age group of presentation was between 6 and 10years (30/68, 44.1%) followed by 3 and 5years (21/68, 30.9%). The age range was between 2.5-14years with a mean age of 7.5years.Two patients had unusual age of presentation one at 2years and 6 months and the other at 2yrs and 11months. 44 (64.7%) had sore throat or skin infection before presentation while 24(35.3%) did not give any history of infection before presentation.*
Fifty two (76.5%) patients were from Addis Ababa and 14 patients presented from Oromia region around Addis Ababa while 2 patients came from remote areas
Thirty two (47.1%) patients had follow up at the renal clinic for a duration,of 6 months - 1 year while the remaining were followed for less than 6 months and were released from follow up when they were stabilized.

Conclusion: *There was no significant association between age, sex, renal dysfunction and severity of hypertension to the outcome of patients and .there was no complication observed during the follow up period.*

***Department of pediatrics and child health , AAU

Introduction

Acute post streptococcal glomerulonephritis (APSGN) is a disease characterized by the sudden appearance of edema, hematuria, proteinuria, hypertension and acute renal dysfunction. APSGN results from infection of the throat or the skin by nephritogenic streptococci. (1, 2)

Post streptococcal glomerulonephritis is most common in children aged 5–12 years and uncommon before the age of 3 years. The typical patient develops an acute nephritic syndrome 1–2 weeks after an antecedent streptococcal pharyngitis or 3–6 weeks after a streptococcal pyoderma. (3)
Scarlet fever was first associated with the occurrence of acute glomerulonephritis in the late 1800s and early 1900s, and shortly thereafter acute glomerulonephritis was commonly associated with a previous streptococcal infection. Most cases of acute glomerulonephritis seen today are associated with a group A streptococcal infection and are not usually associated with scarlet fever. (4)
APSGN usually occurs as sporadic cases, but epidemic outbreaks have taken place in communities with densely populated dwellings that have poor hygienic conditions with a high incidence of malnutrition, anemia and intestinal parasites. A strong seasonal variation is noted; sporadic APSGN following upper respiratory infection, pharyngitis, and tonsillitis is more common in winter and spring in temperate areas , where as skin infections are commonly found to precede APSGN in the more tropical and subtropical areas, with a peak incidence during summer and autumn. (5)

Unlike rheumatic fever, the outbreaks of acute glomerulonephritis have continued to decline and may be due to changes in the streptococci or the host. Regions of the world which still exhibit a high incidence of post streptococcal acute glomerulonephritis include Africa, the Caribbean, South America, New Zealand, and Kuwait(6)

Acute post streptococcal glomerulonephritis occurs primarily in children and young adults, with males affected twice as often as females, and individuals over 40 can also be subjected to the disease. The epidemiology of acute post streptococcal glomerulonephritis is related to its presence in southern and temperate climates, where pyoderma-associated glomerulonephritis demonstrated peak occurrence in the summer, while rheumatic fever peaked in the autumn and winter months of the year. In northern climates, acute glomerulonephritis is associated with throat infection. However, frequently the same organism infecting the skin in impetigo will also infect the throat. In general, skin infection precedes that of the throat. Past epidemics in the United States have been community associated, with the most notable outbreaks in the Red Lake Indian Reservation in Minnesota in 1953 and 1966. Other factors such as crowding, poor hygiene, and poverty are also associated with outbreaks of acute glomerulonephritis. (3)

Group A beta-hemolytic Streptococcus (GAS) is the most common infectious agent responsible for acute glomerulonephritis in children. Over 470,000 cases of APSGN occur annually, leading to approximately 5000 deaths; 97% of these cases occur in less developed countries (8). A decline in the incidence of acute post streptococcal glomerulonephritis in developed and developing countries have been reported over the last 2-3 decades. As many as 50% of cases may be subclinical; thus, the true incidence of the disease is unknown. Nevertheless, acute post streptococcal glomerulonephritis continues to have a wide distribution as indicated by reports of the disease from all over the world. Because a high percentage of persons affected with acute post streptococcal glomerulonephritis have mild disease and are asymptomatic (estimates of the ratio of asymptomatic to symptomatic patients vary from 2:1-3:1), the actual incidence of the disease is not known. (4)

Post-streptococcal complications are known to be common among Ethiopian children. Little is known, however, about the epidemiology of beta haemolytic streptococci in Ethiopia. The monthly carrier rate of group A beta-haemolytic streptococci in Ethiopia varied from 7.5-39%, average being 17 %. (7)

Though recent studies were not conducted in our set up, it is not hard to imagine that acute glomerulonephritis continues to be a significant cause of morbidity, as can clearly be seen in our day to day clinical practices.

The objective of this study aims to look in to the natural history and some of the predictors of outcome of patients with APSGN at Tikur Anbessa Specialized Teaching Hospital department of Pediatrics and Child health.

Tikur Anbessa Hospital is a tertiary referral teaching hospital with a bed capacity of about 500. Department of Pediatrics and Child Health has a bed capacity of 150. It trains both under and post graduate students and gives service to all referred pediatric patients. Children with different renal and urologic problems are given care in the department and followed at the renal clinic.

Materials and Methods

Records of all children <15 years of age with the clinical diagnosis of APSGN and who were on regular follow up at the renal clinic in the study period were reviewed. The presence of three or more of the following manifestations such as a sudden onset of hematuria, hypertension (systolic and diastolic blood pressure above the 95th percentile for age, height and gender), acute renal dysfunction manifested by a serum creatinine above the age adjusted range; facial edema, oliguria and fast recovery within the hospitalization period with supportive therapy were the inclusion criteria in this study.

Children with evidence of pre-existing renal disease, whose proteinuria and hematuria and acute renal dysfunction were considered secondary to other causes than APSGN with a protracted course in the hospital like lupus nephritis, IgA nephropathy, or Henoch-Schonlein purpura and renal dysfunction secondary to other systemic diseases were excluded.

There were 68 patients under follow up with the same diagnosis in the study period and data was collected from chart review of patients using questionnaire that comprises the following variables: age at diagnosis and current age, sex, complaint at presentation like hematuria, body swelling, and history of sore throat and/or skin infection. Laboratory results like renal function test, ASO titre, urine analysis results were collected and analysed.

The collected data were checked for completeness by principal investigator and entered to SPSS 16.0 and analysed.

The study was approved by Addis Ababa University, College of Health Sciences Institutional Review Board. A written legal permission regarding the study was obtained from the department of Pediatrics and Child health Research and Publication committee prior to the study.

RESULTS

During the study period records of 68 children with APSGN were enrolled in accordance to the inclusion criteria. The common age group of presentation was between 6 and 10years 30/68 (44.1%) followed by 3 and 5 years 21/68(30.9%). The age range was between 2.5-14years with a mean age of 7.5years.Two patients presented at 2years and 6 months and 2years and 11months respectively. Forty patients (58.8%) were males and 28 patients (41.2%) were females. Fifty two (76.5%) patients

were from Addis Ababa and 14 patients presented from Oromia region around Addis such as Woliso, Sululta, Alemgena, etc. the other 2 patients came from remote areas from Addis (Table1).

Thirty two (47.1%) patients had follow up from 6 months up to 1 year and the common reason identified for short duration of follow up was that patients were discharged from renal clinic once they were stabilized (Table1).

The most common chief complaints at presentation were body swelling 53/68 (77.9%) and hematuria 5/68 (7.4%). Twenty six(38.2%) and 18(26.5%) children respectively presented with history of sore throat and skin lesion prior to presentation to hospital (Fig.1).Of those who gave history of any of the infections, only 22.7% of patients were treated with antibiotics in their nearby health institutions (Table2).

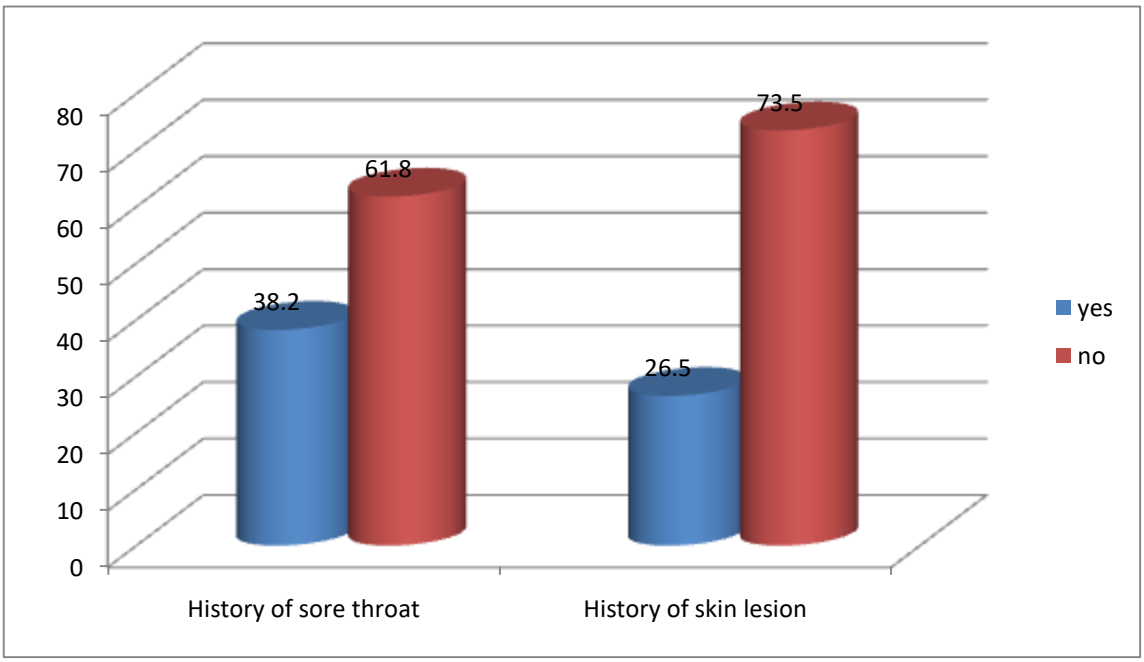

Fig 1.History of infection prior to presentation (percentage) of children with APSGN at Tikur Anbessa Specialized Teaching Hospital; January 2003 to December 2010.

Fifty eight (85.3%) patients had systolic and /or diastolic hypertension in reference to their age, gender and height during presentation to hospital. Of these, 44 patients (64.7%) had severe hypertension (Fig2).

All patients were treated with furosemide either oral or parenteral. But only 14 patients (20.6%) mandated additional antihypertensive drugs such as Nifedipine, Hydralazine or Methyldopa (Table 4).

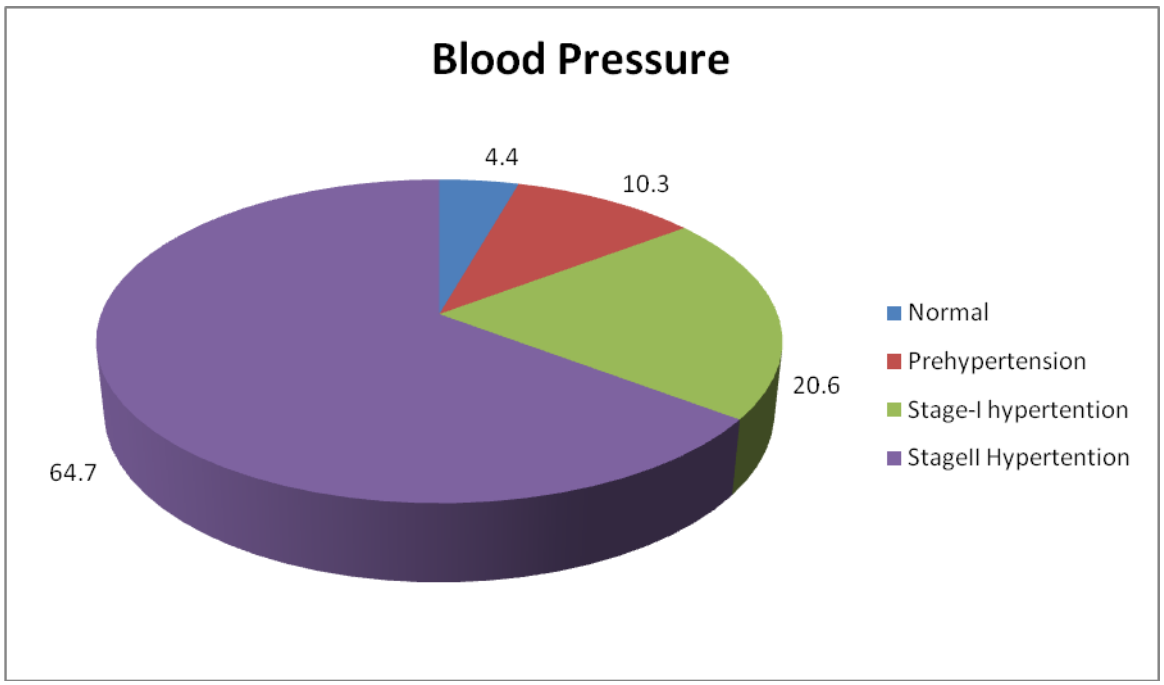

Fig.2.Children with PSAGN and their blood pressure recordings at Tikur Anbessa Specialized Teaching Hospital January 2003 to December 2010.

All children had facial puffiness and/ or peripheral edema. Sixty (88.2%) patients had no edema on their 2nd week chart records and the remaining improved between 2 weeks and 6weeks. Fourteen patients had respiratory signs such as flaring of alae nasi, intercostal and/or subcostal retraction and creptation on auscultation of the chest (Table2).

All patients had microscopic hematuria but only 52.9% had RBC casts in their urinalysis. Hematuria was cleared between 6 weeks and 1year in 57.4% of patients and early before 6wks in 41.2% of patients. Only 1 patient was found to have persisted microscopic hematuria more than a year.

Of all patients, 59 (86.8%) had nephritic range proteinuria and the rest had nephrotic range at presentation (Table3)

The serum creatinine level results were categorized based on severity of derangement for acute kidney injury and the upper limit was taken 0.7mg/dl for the study age group (14). The mean serum creatinine was 1.5mg/dl (range 0.5-9.7mg/dl).Fifty three patients (77.9%) had deranged renal function test with serum creatinine ranging from 0.8 to 9.7mg/dL (Fig.3). ASO titer was done only for 39 patients of which 15(38.5%) were positive (Table 3).

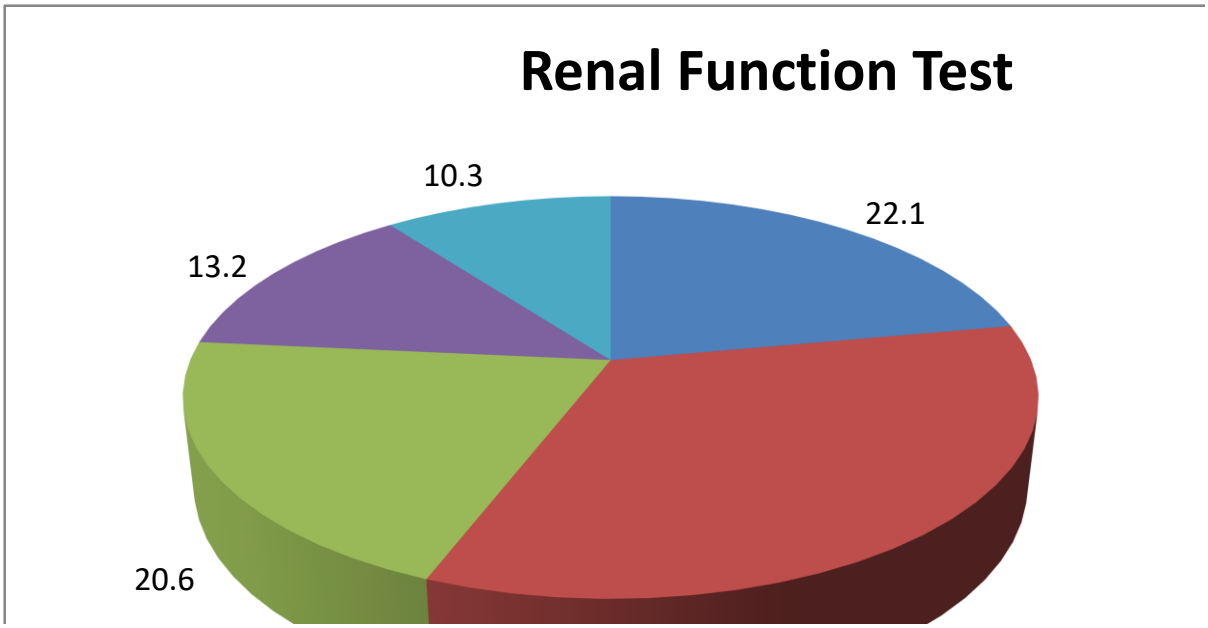

Fig.3.Serum creatinine level of children with APSGN at TASTH, January 2003 to December 2010.

Fifty four patients (79.4%) stayed admitted in hospital for 1 week or less and 6 patients (8.8%) were managed as outpatient (Table4). Five patients were admitted with severe manifestations such as seizure and/or encephalopathy for which phenytoin was prescribed apart from antibiotics and anti hypertensives and 3 patients were diagnosed to have congestive heart failure at admission. But after management of their acute illness, none of them were found to have cardiac lesion clinically and/or using echocardiography. All patients were treated with antibiotics, the common drugs being Crystalline Penicillin and Amoxicillin.

All children recovered from the disease and no child had recurrence of proteinuria or abnormal blood pressure once corrected. All patients had normal serum creatinine during subsequent follow up. All children were followed for a minimum of 6 months on a monthly basis before they were declared free. Children with hematuria and or proteinuria were followed until their problem gets subsided.

Statistical test was done for any association but there was no significant association between age, sex, serum creatinine level and severity of hypertension. In this study there was also no association between prior antibiotic treatment and severity of manifestation.

Discussion

The burden of PSAGN is known to be high in developing countries the prevalence being common in children <15 years and more common in males than females. This study included children below 15 years and the result showed male predominance which accounted 58.8% of children(M:F=1.4:1).This is comparable to the study done in French children by Odile et al which showed 54% male predominance (8). In the study done at Tikur Anbessa Hospital by W.Tewodrros and L.Muhe, etal the male: female ratio of streptococcal infection was1.9:1 which was also comparable to this study (7). The common age at presentation was between 6 and 10 years (range 2.5-14years) followed by 3 and 5years (30.9%) with mean age of 7.5years. In French children, the mean age was 6.7 years. In a 16 year period study in Sydney, Australia the mean age was 8.1years (range 2.6-14.1years).This also indicates a

similarity to the age of children affected with PSGN (8, 10).

In contrast to the study done in French children (8), in which fever was the commonest reason for consultation 30/50 (60%), the most common complaint in our review was body swelling (77.9%) and fever was the main complaint in only 3 patients (4.4%) This might be due to overlooking of fever in our situation. In this study 44/68 (64.7 %) of children had had sore throat or skin lesion before presentation and only 10 (22.7%) were treated with antibiotics.

History of infection was high in our study as compared to the study done in Scotland in which 'Sore throat/inflamed throat' was identified as a prodrome in 39 (49 %) of their cases. This might be because our study included history of both throat and skin infections in contrast to the study in Scotland by which the authors only reported physical sign of acute throat infection at the time of presentation(9).

Fifty eight (85.3%) of our patients had arterial hypertension in reference to their age, gender and height. Of these, 44 patients had severe hypertension. All patients were treated with furosemide either oral or parenteral. But 20.6% of patients mandated additional antihypertensive drugs such as Nifedipine, Hydralazine or Methyldopa. Furosemide is prescribed in our setup not only for blood pressure control but also for treatment of edema. But in French Polynesia children, any type of hypertension was found in 64% of children and a diuretic therapy (furosemide) had been prescribed for 33/50 children (66%) and a second anti-hypertensive treatment (nicardipine) had been given to 17/50 (34%) of children (8).

The mean serum creatinine in our case series was 1.5 mg/dl (range 0.5-9.7mg/dl). Fifty three patients (77.9%) had deranged renal function test with serum creatinine ranging from 0.8 to 9.7mg/dL. This is comparable to the study done in Sydney, which showed 81.1% of the studied children had renal impairment (median peak creatinine, 1.08mg/dl, and range 0.44–10 mg/dl (10).This indicates that renal dysfunction is one of the commonest initial manifestation of patients with APSGN. In addition to renal failure 8 patients developed seizure and/or encephalopathy or heart failure; and the complications might be because of late presentation of patients. There was no significant association between age, sex, renal dysfunction and severity of hypertension. (Table 5). Severe hypertension, encephalopathy and congestive heart failure are common complications despite benign feature of APSGN.

Limitation of the study

The limitations to this study are those generally associated with retrospective studies, such as incomplete medical records.. There was no adequate information regarding socioeconomic status of parents and no phone numbers or full addresses to get patients for necessary information. Investigations such as C3 level, Anti-DNAse B titer determination are lacking in Ethiopia for confirming the diagnosis for patients with clinical evidences of APSGN.

Conclusion and Recommendation

Since Ethiopia is one of the developing countries and there is high risk of skin and respiratory infections, it is common to get large number of patients with streptococcal infections leading to non supportive complications such as APSGN and Rheumatic fever. Despite good outcome of the disease, it is better to follow patients for prolonged period. Accurate recording and chart keeping is the important part of patient management and should be encouraged. Prospective studies are recommended on this common problem.

Table 1.Demographic data of children with PSAGN at Tikur Anbessa Specialized teaching Hospital, Addis Ababa .January 2003 to December 2010.

Demography	**No**	**%**
Age (years)		
<3	2	2.9
3-5	21	30.9
6-10	30	44.1
11-15	15	22.1
Total	68	100
Sex		
Male	40	58.8
Female	28	41.2
Total	68	100
Address		
Addis Ababa	52	76.5
Oromia around Addis	14	20.6
Other places	2	2.9
Total	68	100
Duration of follow up		
6 month	20	29.4
6 mo-1 year	32	47.1
>1year	16	23.5

Table 2 clinical presentation of children with PSAGN at Tikur Anbessa Specialized Teaching Hospital, Addis Ababa. January 2003 to December 2010.

Variables	No	%
Use of antibiotics		
Yes	10	22.7(14.7)
No	34(58)	72.3(85.3)
Reason for presentation		
Body swelling	53	77.9
Hematuria	5	7.4
Decreased urine output	2	2.9
Shortness of breath	2	2.9
Body swelling and hematuria	1	1.5
Fever	3	4.4
Seizure	1	1.5
Abdominal pain	1	1.5
Total	68	100
Respiratory sign		
Yes	14	20.6
No	54	79.4
Total	68	100
Signs of CHF		
Yes	3	4.4
No	65	95.6
Total	68	100
Seizure/Encephalopathy		
Yes	5	7.4
No	63	92.6
Total	68	100
Persistence of edema(weeks)		
<2	60	88.2
2-6	8	11.8
Total	68	100

Table 3 Laboratory findings of children with PSAGN at Tikur Anbessa Specialized teaching Hospital, Addis Ababa. January 2003 to December 2010.

Variables	**No**	**%**
Microscopic Hematuria	68	100
RBC casts		
Yes	36	52.9
No	32	47.1
Total	68	100
Proteinuria		
Proteinuria of all kind	59	86.8
Nephrotic range	9	13.2
Total	68	100
Persistence of hematuria		
<6weeks	28	41.2
6weeks-1year	39	57.4
>1year	1	1.5
Total	68	100
ASO titer		
Positive	15	22.1
Negative	24	35.3
Not done/not documented	29	42.6
Total	68	100

Table 4. Management of children with PSAGN at Tikur Anbessa Specialized Teaching Hospital, Addis Ababa. January 2003 to December 2010

Variables	No	%
Duration of hospitalization		
≤1week	36	52.9
>1 week	26	38.2
Not admitted	6	8.8
Total	68	100
Medical Managements given		
Oral antibiotics	39	57.4
Parenteral antibiotics	29	42.6
Total	68	100
Diuretics /Antihypertensive		
Oral Furosemide	6	8.8
IV Furosemide	48	70.6
Furosemide and other antihypertensive drugs	14	20.6
Total	68	100

Table 5: Effect of Age, Sex and Renal Function test derangement on severity of Hypertension of Children with APSGN at Tikur Anbessa Specialized Teaching Hospital, Addis Ababa. January 2003 to December 2010.

	Blood pressure				Total	P-value
	Normal	Pre-HTN	Stage 1HTN	Stage 2 HTN		
Age (years)						
<3	0	1(1.5%)	0	1(1.5%)	2(2.9%)	
3-5	2(2.9%)	1(1.5%)	5(7.4%)	13(19.1%)	21(30.9%)	
6-10	0	4(5.9%)	6(8.8%)	20(29.4%)	30(44.1%)	0.573
11-15	1(1.5%)	1(1.5%)	3(4.4%)	10(14.7%)	15(22.1%)	
Total	3(4.4%)	7(10.3%)	14(20.6%)	44(64.7%)	68(100%)	
Sex			6(8.8%)	27(39.7%)	40(58.8%)	
Male	2(2.9%)	5(7.4%)	8(11.8%)	17(25%)	28(41.2%)	0.547
Female	1(1.5%)	2(2.9%)	14(20.6%)	44(64.7%)	68(100%)	
Total	3(4.4%)	7(10.3%)				
Serum Cr.						
<0.8	0	1(1.5%)	1(1.5%)	13(19.1%)	15(22.1%)	
0.8-1.0	1(1.5%)	2(2.9%)	5(7.4%)	15(22.1%)	23(33.8%)	
1.1-1.4	2(2.9%)	2(2.9%)	3(4.4%)	7(10.3%)	14(20.6%)	
1.5-2.0	0	1(1.5%)	3(4.4%)	5(7.4%)	9(13.2%)	0.689
>2.0	0	1(1.5%)	2(2.9%)	4(5.9%)	7(10.3%)	
Total	3(4.4%)	7(10.3%)	14(20.6%)	44(64.7%)	68(100%)	

References

1. Avner ED, Davis ID: Acute Poststreptococcal Glomerulonephritis. In: Behrman RE, Kliegman RM, Jenson HB. Nelson Textbook of Pediatrics. 17. Philadelphia: Elsevier Science; 2004:1740-1741.
2. Melania S and Karen K. An outbreak of acute post-streptococcal glomerulonephritis in remote Far North Queensland: Aust. J. Rural Health (2006) **14**, 160–163.
3. Clark G, White RHR, Glasgow EF, et al: Poststreptococcal glomerulonephritis in children: Clinic pathological correlations and long-term prognosis. Pediatr Nephrol: 1988; 2:381-388
4. Madeleine W. Pathogenesis of Group A Streptococcal Infections: Clinical Microbiology Reviews, July 2000, Vol. 13(3) : 489-490
5. Michael A., Demetrius E & Michael L. : Acute post-streptococcal glomerulonephritis in a 14-month-old boy: why is this uncommon? Pediatr. Nephrol (2007) 22:448–450
6. Wallings, H:, Acute Poststreptococcal glomerulo-nephritis in general practice: the contribution of infection to its onset and course. Epidemiol. Infect. (1996), 116, 193-201
7. Tewodros W, Muhe L. A one-year study of streptococcal infections and their complications among Ethiopian children. Epidemiol. Infect. (1992). 109;211-225
8. Odile B , Jérôme P & Hélène G etal: Acute post-streptococcal glomerulonephritis in children of French Polynesia: a 3-year retrospective study. Pediatr. Nephrol (2010) 25:275–280
9. J. L. Taylor and J. G. R. Howie, Antibiotics, sore throats and acute nephritis. Journal of the Royal College of General Practitioners, 1983, 33: 783-786.
10. Christopher C , Peter W and Andrew R . Post-streptococcal glomerulonephritis in Sydney: A 16-year retrospective review. Journal of Pediatrics and Child Health 43 (2007) :446–450
11. Afework M, Green-Abate C, Tafari N. Clinical profile of glomerular diseases in Ethiopian Children. Ethiop Med J 1980 V 18-19,
12. Meadow, S. R.. Poststreptococcal nephritis-a rare disease? Arch.Dis Child 1975:50, 379-381.
13. Kazuhide S, Yukihiko K and Hitoshi S: Girl with garland-pattern poststreptococcal acute glomerulonephritis presenting with renal failure and nephrotic syndrome. Patient Report. Pediatrics International (2007) 49, 115–117
14. Muhammad Si, Acute Kidney Injury. Current Diagnosis and Treatment, Nephrology and Hypertension, 2009:104.