Original Article

Prognosis of Acute Post-streptococcal Glomerulonephritis in Sudanese Children

EL-Tigani M. A. Ali1, Amal M. T. A. Babiker2, Somayya EL-Assad3 and Mohamed B. Abdelrahim1

1. Department of Pediatrics and Child Health, Faculty of Medicine, University of Khartoum, Khartoum, Sudan
2. Department of Pediatrics, Soba University Hospital, Khartoum, Sudan
3. Omdurman Children Hospital, Khartoum, Sudan

Abstract

Introduction: Acute post streptococcal glomerulonephritis (APSGN) is a form of acute nephritic syndrome characterized by edema, hematuria, proteinuria, and hypertension. The immediate prognosis of acute post-streptococcal glomerulonephritis in children is usually excellent, however, the long-term prognosis has been a subject of debate.

Methods: This is a retrospective and prospective cohort study of Sudanese children with APSGN followed in a tertiary care hospital between 2006 and 2010. Patients who presented for follow-up 1-5 years after initial diagnosis were assessed for proteinuria, hematuria, urinary albumin to creatinine ratio (ACR), hypertension and glomerular filtration rate (GFR).

Results: Data of 69 children (46 males, 66.7%) was analyzed. At presentation, 29% had severe acute disease requiring dialysis. On discharge, 60 children (87%) recovered their renal function, seven children (10.1%) showed no recovery and two children (2.9%) died. Forty out of 69 children presented to follow-up 1-3 years after initial diagnosis. Thirty-four of these children (83%) had normal blood pressure and GFR while six children (15%) progressed to chronic kidney disease (CKD); three of whom died. Among children with normal GFR, eight (23.5%) had microalbuminuria plus hematuria and four (11.7%) had hematuria. Persistence of proteinuria and/or hematuria was universal among the 14 children with normal GFR who continued follow-up more than three years after initial presentation.

Conclusion: APSGN in this group of Sudanese children had a less favorable prognosis. This reflects the tertiary care set-up of this study. Persistence of hematuria and/or proteinuria was common on follow-up.

Key words: Children; Chronic kidney disease; Post-streptococcal Glomerulonephritis; Prognosis; Sudan

The authors declared no conflict of interest

Introduction

Acute post-streptococcal glomerulonephritis (APSGN) is a form of acute nephritic syndrome characterized by edema, hematuria, proteinuria, and hypertension [1, 2]. It occurs predominantly in males and is known to follow infection of the throat or skin by group-A Beta hemolytic streptococci [3]. The clinical course is usually benign, but severe acute renal failure (ARF) with crescent formation does occur [4]. APSGN commonly presents with dark urine and facial edema. Hypertension occurs in 60-70% of cases [5]. The immediate prognosis of APSGN in children is known to be excellent but the long-term prognosis has been the subject of many studies [6]. Follow up of children with APSGN for 10-20 years has shown that about 20% of the patients have urinary abnormalities on urine analysis, with less than 1% having permanent renal failure [7]. In hospitalized children, few patients with initial severe disease have persistent or progressive renal failure.

Methods

This is a retrospective and prospective hospital based study conducted at Soba University Hospital, a tertiary care hospital with a specialized pediatric renal unit receiving patients from all parts of the country. Records of all children diagnosed as having APSGN between 2006 and 2010 were reviewed. The diagnosis of APSGN was based on the presence of two or more of the following criteria [8]:

1. Macroscopic or microscopic hematuria (10 red blood cells/HPF or hematuria ≥ 2++ using urine dipstick).
2. Facial, limb or generalized edema,
Table 1: Age distribution of the study group (n=69)

<table>
<thead>
<tr>
<th>Age group (in years)</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5</td>
<td>7</td>
<td>10.0%</td>
</tr>
<tr>
<td>5 – 10</td>
<td>41</td>
<td>59.5%</td>
</tr>
<tr>
<td>≥10</td>
<td>21</td>
<td>30.5%</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Table 2: Clinical and laboratory findings of APSGN at presentation

<table>
<thead>
<tr>
<th>Clinical finding</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematuria</td>
<td>69</td>
<td>100%</td>
</tr>
<tr>
<td>Edema</td>
<td>69</td>
<td>100%</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>58</td>
<td>84%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>41</td>
<td>59%</td>
</tr>
<tr>
<td>Oliguria with high creatinine</td>
<td>29</td>
<td>42%</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 3: APSGN outcome on discharge of studied children (n=69)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovery of renal function</td>
<td>60</td>
<td>87.0%</td>
</tr>
<tr>
<td>No recovery</td>
<td>7</td>
<td>10.1%</td>
</tr>
<tr>
<td>Death</td>
<td>2</td>
<td>02.5%</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>100%</td>
</tr>
</tbody>
</table>

3. Hypertension, more than 95th percentile for age and gender.

4. Evidence of antecedent streptococcal infection, elevated or rising anti-streptolysin O antibody (ASO) titer.

Serum C3 level was available for few patients. Indications for renal biopsy were development of severe ARF, nephrotic syndrome, and insufficient evidence of antecedent streptococcal infection [4]. Patients with incomplete records were excluded. Demographic data, symptoms and signs at presentation, anthropometric measurements and investigations (urinalysis, ASO titre, blood urea and creatinine, histopathology reports) were all recorded. On follow up, patients were assessed for weight, height, blood pressure, and for proteinuria, hematuria, urinary albumin to creatinine ratio (ACR), and glomerular filtration rate (GFR). Proteinuria was tested by dipstick using morning urine sample after the first void. The results were recorded as negative, trace, 1+ (30 mg/dL), 2+ (100 mg/dL), 3+ (300 mg/dL) and 4+ (2000 mg/dL) [9]. Hematuria was defined as ≥5 RBCs/HPF [10, 12]. The main outcome measure used was albumin to creatinine ratio (ACR) determined in spot urine (morning sample), which is a sensitive early marker of renal damage [17]. The results of ACR were categorized as normal (<1.1 mg/mmol), suspicious (1.1-3.3 mg/mmol), microalbuminuria (5-33 mg/mmol), or overt albuminuria (≥34 mg/mmol). Serum creatinine was measured and GFR was estimated using the Schwartz formula. Estimated GFR in mL/min/1.73m² = K × Pcr where K is constant (0.45 in infants and 0.55 in children and adolescent), L is height in cm, and Pcr is plasma creatinine in mg/dL [12]. CKD was defined as GFR <60 mL/min/1.73m² for ≥3 months with or without kidney damage [14]. CKD stages were defined according to the National Kidney Disease Outcome Quality Initiative guidelines [15].

Blood pressure values and definitions were based on the Fourth Task Force Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescence [16].

Data analysis was done using statistical package for social science (SPSS) version 18. Descriptive statistics used comprised mean, standard deviation (SD) and percentages.

Results

Data of 69 patients with APSGN were analyzed. The mean age at time of presentation was 9±4.6 years (range 2-16 years). The majority of patients were aged 5-10 years (Table 1). Patients were predominantly males (66.7%).

Clinical and laboratory findings of children at presentation with APSGN are outlined in Table 2. On admission to hospital 20/69 patients (29%) had severe acute disease requiring dialysis. Their mean serum creatinine was 8.2±3.31 (range 3.6-15.3) mg/dL and mean GFR was 103±49 (range 4.2-19) mL/min/1.73m². On discharge, 60/69 patients (87%) had normal blood pressure and normal renal function with a mean serum creatinine of 0.7 ± 0.19 (range 0.4-1.7) mg/dL and mean GFR of 110.6±29 (62-168) mL/min/1.73m². Of the remaining 9 patients, two (2.9%) died in the acute stage and seven (10.1%) showed no recovery after three months and progressed to CKD (Table 3). In these nine patients initial renal biopsy showed severe crescents in five patients and diffuse proliferative GN in four. Serology for lupus and hepatitis B and C was negative in all of them.
Table 4: APSGN outcome of studied children after 1-5 years follow up (n=40)

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal GFR and BP</td>
<td>34</td>
<td>85%</td>
</tr>
<tr>
<td>Microalbuminuria+ hematuria</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Hematuria</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease (CKD)</td>
<td>6</td>
<td>15%</td>
</tr>
<tr>
<td>ESRF</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>100%</td>
</tr>
</tbody>
</table>

APSGN: acute post-streptococcal glomerulonephritis; GFR: glomerular filtration rate; BP: blood pressure (p<0.05).

Forty patients (28 males; 70%) presented to follow up 1-5 years after initial diagnosis (mean 2.7±2.4 years) including 12 children (30%) who had severe acute renal failure requiring dialysis at initial presentation. Assessment of outcome measures showed that 34 patients (85%) had normal blood pressure and normal GFR (mean 132±42 [94-165] mL/min/1.73m²) while six (15%) had progressed to CKD. All children who progressed to CKD had severe disease requiring dialysis at initial presentation. Among children with normal GFR urinary abnormalities were found in 12 patients (35.3%) microalbuminuria plus hematuria in eight cases (23.5%) and hematuria in four cases (11.8%). None of them had overt albuminuria (Table 4).

Hematuria and/or microalbuminuria were detected in all 14 patients with normal GFR who continued follow-up for more than 3 years after initial presentation.

Discussion

Data of 69 children with APSGN followed in our hospital was available for the study. The mean age at presentation was 9±6.6 years (range 2-15 years) and patients were predominantly males. These findings are consistent with other studies [1, 3, 17]. Clinical features at presentation were similar to findings reported in other studies [1-17-19]. However, our patients differed in showing high incidence (29%) of severe acute kidney injury (AKI) requiring dialysis at presentation. This could be explained by the fact that most of the APSGN cases seen at our unit were severe disease that required referral for tertiary care management.

Many studies reported excellent immediate prognosis for children with APSGN [6, 17]. However, other studies from Europe (Germany, Luxemburg, Austria) and India reported less favorable prognosis. Failure of recovery with progression to CKD and/or death occurred in 25%, 17% and 18% of these studies respectively [19-21]. In these studies, crescentic glomerulonephritis and nephrotic range proteinuria at presentation were significantly associated with progression to CKD. In our study, seven children (10.1%) showed no recovery of kidney function after three month, and two (2.9%) died. In more than half the patients with no recovery, biopsies showed crescentic GN. A similar association was reported in other studies [19-21].

The long term prognosis of APSGN was investigated in many studies. Initial reports suggested excellent prognosis but the periods of follow-up were relatively short. Results of subsequent studies were inconsistent in showing variable rates of urinary abnormalities (3.5% versus 60%) [22, 23]. Moreover, the long term prognosis in some populations may be influenced by the occurrence of other risk factors for CKD in the community [24]. Such observation were reported from Australian Aboriginal communities with high prevalence of low birth weight, diabetes, and metabolic syndrome [25]. Studies on the long term outcome of APSGN and its contribution to CKD had variable results. Reports from two Indian studies, Australia, and Venezuela showed high rates of urinary abnormalities and/or CKD on long term follow up [20, 21, 23, 24]. A large study from Australia reported albuminuria (any degree) in 22%, overt albuminuria in 6%, and hematuria in 10% [25]. The study from Venezuela reported overt proteinuria in 11.2% of cases [26]. Two Indian studies reported CKD in 19% and 14% of patients [20, 21]. Hypertension and urinary abnormalities were detected in 15% and 24% of cases respectively [20]. In contrast, studies from Europe and Trinidad reported low prevalence of persistent urinary abnormalities and CKD. In a study from Europe (Germany, Luxemburg, Austria), only three patients out of 137 developed CKD [19]. In the study from Trinidad, persistent urinary abnormalities and hypertension were detected in only 1.8% and 1.4% respectively [27]. In this study, hematuria and/or microalbuminuria were detected in all patients seen at 3-5 years (mean 3.8) follow up.

Limitations of this study include the relatively small number of patients with significant loss to follow up and the relatively short period of follow up. However, the study provided important baseline data on prognosis of childhood APSGN in Sudanese children. Further prospective studies would give the best evidence for link between the disease and risk of CKD.
Conclusion

APSGN in this group of Sudanese pediatric patients had less favorable immediate term prognosis. This may reflect the tertiary care set-up of the study. Persistence of proteinuria and or hematuria was universal among children with normal GFR who continued follow up three years after initial presentation.

References


