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**Original Research Article**

# Clinical picture of acute post-streptococcal glomerulonephritis in children at Ruteng hospital

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## ABSTRACT

**Background:** Acute post-streptococcal glomerulonephritis (PSGN) is the main cause of acute nephritis in children, globally reaches more than 470,000 cases per year, 97% of which occur in developing countries. Sublinical cases are 4 times more common than symptomatic, so reports on the incidence of acute PSGN are very limited.
**Methods:** This study used a descriptive retrospective method from medical records at RSUD Ruteng from January to June 2023. Data were analyzed using the statistical package for the social sciences (SSPS) 22 program.
**Results:** Results of the study were obtained as 37 pediatric patients with acute PSGN. The patients age ranged 4-17 years with an average 9 years, 51.4% women and 48.6% men. Most cases occur after respiratory tract infections (75.7%). Symptoms of edema and hypertension (89.2% stage I and 10.8% stage II) was found in all patients and become the reason why patients come. Patients experienced macroscopic hematuria 16.2%. The laboratory test showed 100% microscopic hematuria, proteinuria in 72.1% and ASTO titer increased by more than 200 IU in all patients. Eleven patients with complications, acute renal failure (24.3%), hypertension encephalopathy (5.4%) and 1 patient with pulmonary edema. The average length of stay is 8 days (3-22 days).
**Conclusions:** The incidence of acute PSGN at RSUD Ruteng within 6 months is quite high. Acute PSGN in children causes severe complicationsand longer treatment. The prevention is needed to care about the importance of clean and healthy living behavior.

**Keywords:** Glomerulonephritis, Streptococcus, ASTO, Acute kidney injury

## INTRODUCTION

Acute post-streptococcal glomerulonephritis (PSGN) is a kidney disease that occurs due to an inflammatory processes and immune system mediation, so it becomes the main cause of acute nephritis in children. Acute PSGN is characterized by the proliferation of cellular elements (nephritogenic type M) resulting from immunological mechanisms post-skin infection or upper respiratory tract infections (pharyngitis and tonsillitis) caused by group A beta-hemolytic streptococcal infection.[1]

Global reports of the incidence of acute PSGN reach more than 470,000 cases per year, 97% of which occur in developing countries, due to poor sanitation, population density and socioeconomic status. In general, manifestations of acute PSGN appear 1-2 weeks after upper respiratory tract infections (tonsillitis and pharyngitis) and 3-6 weeks after streptococcal infections of the skin.[2]

Acute PSGN mostly occurs in children aged 3-12 years and very rarely found under 3 years. Most children with acute PSGN come to health facilities with clinical swelling, hypertension, hematuria, and even asotemia. The majority of acute PSGN cases are asymptomatic, so recording the number of cases is only limited to symptomatic children.[3]

Although the clinical manifestations of acute PSGN are very typical, in daily practice, differences in clinical symptoms, laboratory findings and complications are often encountered. For this reason, through this study, we will discuss the clinical features, laboratory findings, and complications in acute PSGN patients in health facilities with limited supporting examinations.

## METHODS

This study used a retrospective method by recording the medical records of pediatric patients with acute PSGN who were treated at RSUD Ruteng, Manggarai Regency, East Nusa Tenggara Province from January to June 2023. Data were obtained from hard copy records with no ethical approval. All patients admitted with a diagnosis of acute PSGN with or without complications during that period were included in the study. Meanwhile, patients who do not have the acute PSGN criteria and acute PSGN patients with incomplete data will be excluded.

There were a total of 37 pediatric patients diagnosed with acute PSGN within 6 months. Based on the consensus of acute PSGN IDAI in 2012, diagnosis was established when clinical features were found, at least three of the symptoms: edema, hypertension, proteinuria, hematuria, and oliguria, accompanied by a positive ASTO titer. Children with a history of chronic kidney disease, hemolytic uremic syndrome, anaphylactic purpura, and lupus nephritis were not included in this study. There are recorded history and symptoms that point to sore throat or previous skin infections.

Variables assessed in this study included patient characteristics, source of infection, clinical symptoms, laboratory findings, complications, and length of stay. The characteristics of the patient were including age, gender and the source of previous infection, whether it was an upper respiratory tract infection or skin infection. The clinical symptoms observed are edema, hypertension and macroscopic hematuria. The classification of hypertension based on the Guideline for Childhood Hypertension (American Academy of Paediatrics) is distinguished by stage I: ≥percentile 95 to <percentile 95+12 and stage II: ≥percentile 95+12. The laboratory examinations observed were urinalysis to see levels of proteinuria and microscopic hematuria, as well as ASTO titer examination. Data obtained using the statistical package for the social sciences (SPSS) 22 application, then analyzed and described descriptively in the form of narration and tables.

## RESULTS

This study showed that 37 pediatric patients with clinical symptoms and laboratory diagnosed with acute PSGN criteria had been analyzed. Patients in this study were between 4-17 years old with an average age 9 years old. This disease occurs more often in women (51.4%) than men (48.6%). In this study, the majority of acute GNAPS cases occurred after upper respiratory tract infections (75.7%) rather than skin infections (24.3%) (Table 1).

**Table 1: Baseline characteristics of children hospitalized with PSGN.**

| Baseline characteristics | All children (N=37) (%) |
|---|---|
| **Median age, year (range)** | 9 (4-17) |
| **Sex** | |
| Male | 18 (48.6) |
| Female | 19 (51.4) |
| **Preceding infection** | |
| Skin sores | 9 (24.3) |
| Sore throat | 28 (75.7) |

Clinical symptoms of edema and hypertension were found in all patients (100%) with varying degrees of severity, while dark or tea-like colored urine was found in a small percentage of patients (16.2%). The majority of patients had stage II hypertension (89.2%), while stage I hypertension (10.8%) (Table 2).

**Table 2: Clinical characteristics at presentation.**

| Clinical characteristics | All children (N=37) (%) |
|---|---|
| **Oedema** | 37 (100) |
| **Hematuria** | 6 (16.2) |
| **Hypertension** | |
| Stage I | 4 (10.8) |
| Stage II | 33 (89.2) |

The laboratory showed hematuria was found in urine examination of all patients, with results of +1 in 9 patients (24.3%), +2 in 8 patients (21.6%), and +3 in 20 patients (54.1%). Other laboratory findings, namely proteinuria, were +1 in 3 patients (8.1%), +2 in 15 patients (40.5%), +3 in 8 patients (21.6%) while 11 patients (29.7%) showed negative results. From blood tests, positive ASTO levels (>200) were obtained in all patients according to acute PSGN criteria with 8 patients (21.6%) having a two-fold increase ASTO titers (400 IU) (Table 3).

**Table 3: Laboratory characteristics at presentation.**

| Laboratory characteristics | All children (N=37) (%) |
|---|---|
| **Proteinuria** | |
| Negative | 11 (29.7) |
| ++ | 18 (48.6) |
| +++ | 8 (21.6) |
| **Hematuria** | 37 (100) |
| **Elevated ASTO** | |
| >200 IU | 29 (78.4) |
| >400 IU | 8 (21.6) |

Eleven patient (29.7%) experienced complications due to acute PSGN. Complications found include acute renal failure (ARF), hypertensive encephalopathy and

pulmonary edema. In this study, it was found that 11 out of 37 children (29.7%) experienced complications due to acute PSGN. Complications found include acute renal failure (ARF), hypertensive encephalopathy and pulmonary edema. Acute renal failure was found in 9 children (24.3%), ARF was confirmed by calculating EGFR with the Schwartz method. In 2 patients (5.4%) with hypertensive encephalopathy there were vomiting, loss of consciousness and seizures associated with increased blood pressure. Symptoms of encephalopathy show improvement after hypertension is treated. There was also 1 patient (2.7%) who had complication of pulmonary edema with symptoms of shortness of breath and assessed by chest X-ray. Patients are treated for an average of 8 days, depending on their condition and whether there are complications. The shortest length of stay is 3 days and the longest is 22 days (Table 4).

**Table 4: Complication and length of stay at presentation.**

| Complication characteristics | All children (N=37) (%) |
|---|---|
| **Complication** | 11 (29.7) |
| **Acute kidney injury** | 9 (24.3) |
| **Hypertensive encephalopathy** | 2 (5.4) |
| **Pulmonary edema** | 1 (2.7) |
| **Length of stay - day (range)** | 8 (3-22) |

## DISCUSSION

Acute post-streptococcal glomerulonephritis is a disease that occurs due to infection by nephritrogenic strains of group A beta hemolytic streptococcus that has not been resolved previously. Acute PSGN is the main cause of acute nephritis in children worldwide and has a high prevalence in developing countries.[1] Acute PSGN is one of the most frequent complications of unresolved streptococcal infections (throat or skin infection) besides rheumatic fever. The relationship between infection and glomerulonephritis in acute PSGN is clear but the pathogenesis and factors involved in acute damage and disease progression are not fully known yet.

The theory of complex immune deposits in the kidneys is the main theory for mechanism of acute PSGN. This involves deposits of streptococcal antigen, formation of immune complexes or deposits of antigen-antibody complex at glomerulus. In addition, other factors related to host and streptococcus are interrelated with the immune complex and affect the progression of the disease. Some products of streptococcus are nephritogenic, and affect clinical findings in patients with acute PSGN. Deposits of immune complexes in the kidneys trigger local inflammation (through complement activation), podocyte damage, proliferation and proteinuria.

Acute PSGN occurs after infection, with a latent period between 1-8 weeks. Upper respiratory tract infections (pharyngitis and tonsillitis) before acute PSGN are more often found in areas with cold climates, while skin infections or bacterial infections in scabies are found in areas with warm climates. Acute PSGN preceded by ARI is associated with Beta Hemolytic Streptococcus A strains 12, 4 and 1, while those preceded by skin infections are associated with strains 49,42,2,57. Based on recent studies, acute PSGN can occur 1-2 weeks after ARI with a risk of 5% and 3-6 weeks after skin infection with a risk of 25% of total infection cases, but overall only 2% cause clear clinical symptoms.[5] This study showed that of the 37 cases of acute PSGN that occurred at RSUD Ruteng, 28 cases (75.7%) started from upper respiratory tract infections while 9 cases (24.3%) started with skin infections.

The worldwide incidence of acute PSGN is estimated at 472,000 cases, of which more than 95% of cases occur in developing countries. The risk of acute PSGN increases in children 5-12 years old and elderly over 60 years old with incidence rates varying from 9.5 to 28.6 per 100,000 population.[1,6] Clinically, acute PSGN has two fold more symptoms in men than women, however subclinically, the incidence rate is approximately the same.[7] Australian studies report an average acute PSGN age distribution between 6-11 years old with a median of 7 years. Acute PSGN patients in this study were in range of 4-17 years old with a median age of 8 years old. The incidence ratio in men and women is 1.04:1.[8] In contrast to this study, it was found that acute PSGN occurred more often in women with 19 cases (51.4%) compared to men with 18 cases (48.6%).

Acute PSGN can be asymptomatic (subclinical) but with findings of microscopic hematuria and decreased serum complement, or clinical with symptoms of acute nephritis or nephrotic syndrome. A study shows, the incidence of subclinical acute PSGN is 4 times more frequent than symptomatic cases.

The diagnosis of acute PSGN is based on clinical and laboratory findings. Specific clinical symptoms include, hematuria, edema, hypertension and oliguria, as well as other additional symptoms.[7] The most frequent symptom in patients is swelling, especially in the periorbital and face. Hematuria (both visible and microscopic) is another prominent symptom where the urine color appears tea-like or reddish. Hypertension also often occurs due to increased water volume in the body and sodium retention in the kidneys. Other symptoms that may arise such as oliguria, fatigue, decreased appetite and sometimes low back pain. In severe cases, some patients may show symptoms of acute renal failure such as decreased urine volume and uremic symptoms.[6] Clinical symptoms of edema were found in all patients in the study, especially in the facial area. In contrast to hematuria or dark or tea-colored urine, it was only found in 6 cases (16.2%). Hypertension is also a symptom found in all patients (100%) with different levels of severity. The majority of patients experience

stage II hypertension; 33 cases (89.2%), while the remaining 8 cases were stage I hypertension. A retrospective cohort study in Australia showed that of 96 patients the most common clinical symptoms were hematuria (93.8%), hypertension (90.6%), and edema (68.8%).[2]

In establishing the diagnosis of acute PSGN, a thorough evaluation is required including clinical symptoms, laboratory examinations and serological tests. Urine examination can reveal microscopic hematuria, RBC casts and proteinuria. Blood tests may show increased creatinine levels, decreased serum complement (C3) levels and increased antistreptolysin O (ATSO) titers as signs of previous streptococcal infection. Kidney biopsy is rarely needed for diagnosis but may be considered in atypical or severe cases to confirm the diagnosis and evaluate kidney damage further.[6] Urinalysis examination in all patients (100%) showed hematuria, while proteinuria was found in 26 patients (70.3%). ASTO levels (titer >200) as a marker of previous streptococcal infection were also found in all patients, with 8 patients (21.6%) experiencing 2 times increase in ASTO titer (400 IU). A study in Bangladesh showed that 80.2% of urinalysis found positive proteinuria. Hematuria was found in 92.3% of patients, hematuria affected the length of stay and 6% of cases is persisted until the patient was discharged.[9] ASTO titers were recorded to increase by 42.9% in a study in Pakistan. Increase of ASTO titers helps in confirming previous streptococcal infections, but is not necessarily positive in skin infections because there is fatty tissue that functions as a barrier.[10]

Management in acute PSGN patients is only supportive because this disease is self-limiting. Children with diagnosed acute PSGN and showing clinical symptoms such as hypertension, generalized edema, or decreased renal function, should be treated for blood pressure monitoring and renal function monitoring. Treatment of acute PSGN patients includes fluid restriction, antihypertensive administration, diuretics, and renal replacement therapy (hemodialysis), if needed.[3]

The use of antibiotics in group A beta hemolytic infections did not show significant results on the incidence of acute PSGN. Giving antibiotics will only prevent the spread of infection, but will not prevent the progression of the disease to acute PSGN. Prophylactic antibiotics in acute PSGN cases also did not show significant results.

Thiazide diuretics are the first line of antihypertensive options in cases of acute PSGN. Loop diuretics are also recommended, especially in patients with problems (eGFR <30 ml/min per 1.73 $m^2$) and significant edema. Diuretics are often used in combination with vasodilators such as the calcium channel blocker (CCB) to overcome the problem of hypervolemia due to water and sodium restrictions. Short acting Nifedipine is a safe CCB choice in children, especially in treating emergency hypertension in the acute phase. Several studies show that the use of angiotensin-converting enzyme (ACE) inhibitors provides better blood pressure control effects compared to diuretics. However, ACE inhibitors are not recommended in the acute phase.[3,5]

In addition to antihypertension, fluid and salt restriction also plays an important role for management of acute PSGN. Patients with clinical generalized edema are recommended to follow a low-salt diet of 1-2 mEq/kg per day. The recommended fluid restriction is 2/3 of the total fluid intake, while monitoring input and output fluids, vital signs, and serum electrolytes. Some patients show clinical dsypnea due to cardiogenic pulmonary edema. This condition is caused by decreased renal function in acute PSGN patients, thus showing symptoms of acute respiratory distress syndrome. Management focuses on providing adequate oxygen such as non-invasive positive pressure ventilation. In this study, the therapy given to the majority of patients included furosemide, antihypertension such as captopril and nifedipine as well as fluid and salt restriction. Administration of nifedipine and furosemide showed significant results in reducing hypervolemia and controlling hypertension.

Steroids in acute PSGN cases is still controversial. Some patients with impaired kidney function and pulmonary edema have shown significant clinical improvement, although the mechanism of action is still unclear. The latest consensus recommends the use of steroids in patients who are proven to have kidney damage up to 30% through biopsy results.[11] Dialysis recommended in pediatric patients with severe renal disorders due to hypervolemia and electrolyte imbalances such as hyperkalemia or acidosis. Renal replacement therapy (RRT) is indicated for patients with fluid overload of more than 20% of body weight, or more than 10% and not responding to diuretics.[3]

Complications may occur in acute phase of PSGN. Complications that arise include emergency hypertension, congestive heart failure, pulmonary edema, to hypertension crisis which induces encephalopathy and retinopathy. Cerebral complications were reported in 30-35% of patients with acute PSGN and 12.3% of acute PSGN patients experienced congestive heart failure. Meanwhile, 21.5% of acute PSGN patients with emergency hypertension were recorded and required intravenous nitroprusside infusion in the ICU.[12.3]

In this study, the most common complication was acute renal failure which are 9 children (24.3%). In addition, 2 patients (5.4%) with hypertension encephalopathy and 1 patient (2.7%) with clinical pulmonary edema.

***Limitations***

The limitations in this study may occur because the study was conducted retrospectively so that the data obtained only depends on recording medical records. Recording of medical records for inpatients at RSUD Ruteng is still done manually.

## CONCLUSION

Acute glomerulonephritis in pediatric patients in this study showed clinical features and laboratory findings that were in accordance with the diagnosis criteria. The characteristics found for each variable assessed in this study showed varying results. This difference depends on the patients who come and are treated at the hospital during that period. Management of acute PSGN requires cooperation from various parties to treat previous infections and early detection of acute PSGN in order to get early treatment and prevent more severe complications.

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