The profile of acute glomerulonephritis among Indonesian children

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ABSTRACT

Background Acute glomerulonephritis (AGN) is a form of glomerulonephritis characterized by sudden and explosive onset of glomerular injury symptom. It usually occurs after recent infection by group A beta-hemolytic streptococcus. AGN among Indonesian children seems to be less frequently reported than that among other countries.

Objective To determine the current profile of AGN among Indonesian children hospitalized in eleven teaching centers.

Methods This was a descriptive, cross-sectional study, based on a review of the standard medical records of 509 children with AGN hospitalized in 11 teaching centers in Indonesia over a five-year period (1997-2002). Data extracted from the medical records consisted of history of illness, clinical and laboratory findings, and chest X-rays.

Results Age of the patients at the onset of AGN ranged from 2.5 to 15 years, with peak age of 8.5 years. The majority (76.4%) was above 6 years old with male predominance (58.3%). About 68.9% and 82% of the patients came from low socioeconomic and low educational status families. Antecedent upper respiratory infections were observed in 45.8% cases and pyoderma in 31.6%. The disease seemed to be more commonly elicited by streptococcal infection than by other infections, as proved by an elevated anti-streptolisin O (ASO) titer (66.6%) and decreased C3 concentrations (60.4%). The frequent clinical features included periorbital edema (76.3%), hypertension (61.8%), and gross hematuria (53.6%). The most prevalent laboratory findings were microhematuria (99.3%), proteinuria (98.5%), and raised erythrocyte sedimentation rate (85.3%). The initial chest X-rays showed pleural effusion (81.6%) and cardiomegaly (80.2%), whereas echocardiogram documented pericardial effusion (81.6%). Acute pulmonary edema (11.5%), hypertensive encephalopathy (9.2%), and acute renal failure (10.5%) were frequent complications noted in our study.

Conclusion Despite no adequate data on throat or skin cultures, AGN among Indonesian children seems mostly to be poststreptococcal AGN as proved by the elevated ASO titer and decrease in serum C3 concentration [Pediatr Indones 2005;45:264-269].

Keywords: acute glomerulonephritis, poststreptococcal glomerulonephritis, Indonesian children

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Methods

This was a descriptive, cross-sectional study, based on a review of the standard medical records of all children hospitalized in eleven teaching centers with a diagnosis of AGN between January 1997 and January 2002. All children with AGN hospitalized at the centers over the five-year period were included in the study. Prior approval was obtained from the Ethical Committee of Wahidin Sudirohusodo Hospital, Makassar. The contributors of the data were the NWG of the Indonesian Society of Pediatricians in 11 teaching centers including Andalas University (Unand), Padang; Sriwijaya University (Unsri), Palembang; University of Sumatera Utara (USU), Medan; University of Indonesia (UI), Jakarta; Diponegoro University (Undip), Semarang; Gajah Mada University (UGM), Yogyakarta; Padjadjaran University (Unpad), Bandung; Airlangga University (Unair), Surabaya; Udayana University (Udayana), Bali; Hasanuddin University (Unhas), Makassar, and Sam Ratulangi University (Unsrat), Manado.

Data from the standard medical records of all patients, including of history of illness, clinical and laboratory findings, and chest X-rays were obtained. Echocardiography was performed on admission and after resolution of the clinical manifestations, by the Hasanuddin University teaching center to investigate the cause of cardiomegaly documented on the chest films. The diagnosis of PSAGN was established based on the following clinical and laboratory criteria: edema, hypertension, gross hematuria, and/or microhematuria with or without red blood cell casts in the urinary sediment, recent history of group A beta-hemolytic streptococcal infection demonstrated by an elevated anti-streptolysin O (ASO) titer, and low serum C3 concentration.1,2,4,5 Patients who did not fulfill the above mentioned criteria were diagnosed as having NPSAGN. Hypertension was defined as systolic and/or diastolic blood pressure values exceeding the 95th percentile for age and sex.6 Microhematuria was considered present if the red blood cell count was greater than 5 cells/high power field in centrifugated urine shown by light microscopy. Missing data was defined as no data documented in the standard medical records. Patients with complete standard medical records were further reviewed in this study.

Results

The number of subjects enrolled in this study was 509, consisting of 58.3% boys and 41.7% girls, with boy to girl ratio of 1.4:1. Age at the onset of AGN ranged from 2.5 to 15 years, with the peak age of 8.5 years. The majority was above 6 years at onset of AGN (76.4%) (Table 1). About 68.9% of the patients came from low socioeconomic status families and 82% from low educational status families (Table 3).

According to the history of illness, we found that AGN was more frequently preceded by an upper respiratory tract infection (URTI) (45.8%) than...
by pyoderma (32.6%) (Table 1). The disease seemed to be more commonly elicited by streptococcal infection (PSAGN) than by other infections (NPSAGN), as proved by an elevated ASO titer (66.6%) and decreased C3 concentrations (60.4%) (Table 2). The frequently observed clinical presentations were periorbital edema (76.3%), hypertension (61.8%), gross hematuria (53.6%), and oliguria (23.9%) (Table 2).

Table 2 shows the abnormalities of laboratory findings in our cases. The majority of patients had proteinuria (98.5%), and microhematuria (99.3%) while the remaining of the patients had elevated erythrocyte sedimentation rate (ESR) (85.3%), anemia (61.0%) as shown by hemoglobin levels ≤10 g/dl, red blood cell (RBC) casts on urinary sediments (44.3%), azotemia (10.5%) consisting of elevated serum urea and creatinine, mild hypercholesterolemia (5.7%), and mild hypoproteinemia (4.7%), respectively.

Chest X-ray examinations revealed the presence of cardiomegaly and pleural effusion in 80.2% and 81.6% of cases, respectively, and echocardiography demonstrated pericardial effusion in 81.6%. Acute pulmonary edema (11.5%) was the most common complication observed besides hypertensive encephalopathy (9.2%) and acute renal failure (10.5%) (Table 3). As shown in Table 3, all patients recovered within 7-14 days with the majority of patients (73.5%) recovered within 12 days.

### Discussion

This study seems to be one of the large published series of AGN cases to date. Several studies indicated that AGN was more commonly encountered in children older than 6 years. More boys than girls were affected; other studies have reported a ratio of 2:1, 3:2, and 3:1. A study in Benin city noted the peak incidence at 3 years for both sexes, with female predominance. Meanwhile, a report from Armenia showed that the majority of patients was boys in the age group 4-9 years. Our study showed that most patients with AGN were older than 6 years with a boy to girl ratio of 1.4:1. Our subjects were of lower socioeconomic status than those in the study in Benin city.

In the present study antecedent URTI was observed in 45.8% of cases and pyoderma in 32.6% of cases. The disease seems to be more commonly caused by streptococcal infections (PSAGN) than by other agents (PSAGN). Elevated ASO titer (66.6%) and decreased C3 concentrations (60.4%) were objective evidence of recent streptococcal infection prior to AGN in our cases. Puri et al. and Manhas et al. reported pyoderma as the most common antecedent infection (67.5% and 60%). Others reported a significant rise in ASO titer (70-80%) following pharyngitis-related AGN and a decreased serum C3 concentration (80-96%). In the cases we reviewed, measurement of ASO titers and C3 concentrations were done only on admission and were not repeated.

| Teaching centers | MH (%) | PTR (%) | NRP (%) | RBCc (%) | RESR (%) | LHB (%) | AZA (%) | HASO (%) | LSC3 (%) |
|------------------|--------|---------|---------|----------|----------|--------|---------|----------|----------|
| Unand            | 100.0  | 100.0   | 25.0    | 25.0     | 100.0    | 25.0   | 50.0    | 100.0    | 100.0    |
| USU              | 84.0   | 69.6    | 6.5     | 45.0     | 68.3     | 70.4   | 20.4    | 54.1     | 57.7     |
| Unsri            | 87.0   | 99.7    | 2.3     | 16.7     | 71.1     | 59.6   | 10.6    | 93.6     | 51.1     |
| UI               | 90.8   | 89.7    | 4.3     | 16.9     | 96.0     | 77.9   | 9.1     | 42.3     | 52.1     |
| Unpad            | 94.4   | 84.7    | 4.3     | 4.3      | 66.7     | 82.4   | 3.4     | 40.4     | 40.4     |
| UGM              | 96.0   | 84.9    | 4.5     | 42.3     | 96.0     | 41.7   | 9.1     | 76.3     | 90.6     |
| Unair            | 100.0  | 100.0   | 4.3     | 40.8     | 80.0     | 54.0   | 16.1    | 79.2     | 80.6     |
| Udayana          | 100.0  | 79.3    | 0.0     | 16.8     | 50.0     | 69.2   | 23.8    | 58.6     | 58.6     |
| Unhas            | 95.7   | 87.8    | 6.0     | 60.9     | 68.0     | 51.0   | 14.8    | 98.0     | 91.8     |
| Unsri            | 96.5   | 99.7    | 2.2     | 42.7     | 78.6     | 52.4   | 18.2    | 50.9     | 50.9     |
| Total            | 99.3   | 98.5    | 6.0     | 44.3     | 85.3     | 61.0   | 19.1    | 66.6     | 60.4     |

TC: teaching centers, MH: microhematuria, PTR: proteinuria, NRP: nephrotic range proteinuria, AZA: azotemia, RBCc: red blood cell casts, RESR: raised erythrocyte sedimentation rate, LHB: low hemoglobin level, HASO: high anti-streptolysin O titer, LSC3: low serum C3 level

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during hospitalization, resulting in figures different from those in other studies. The frequently observed clinical presentations in our patients included periorbital edema (76.3%), hypertension (61.8%), gross hematuria (53.6%), and oliguria (23.9%). These data relatively agreed with those from previous reports. Ibadin and Abiodun\textsuperscript{11} reported edema in 93.7% of their patients, Manhas et al\textsuperscript{13} in 83.4%, and Lewy\textsuperscript{7} in 66.7%. Gross hematuria occurred in 30-70% of children with AGN and microhematuria was present in almost all children with AGN.\textsuperscript{1,4,7,8,16,17} Hematuria and proteinuria of varying degrees occurred in all children with AGN in Ibadin and Abiodun’s study,\textsuperscript{11} but hypertension and oligouria were observed only in 82.5% and 47.6% of children, respectively, which is higher than the figures in our study. Hypertension reported by Rubin\textsuperscript{16} (60-70%) was similar to the present study and oliguria\textsuperscript{1,16} was much lower (5-10%) than that observed in our patients. The incidence of hypertensive encephalopathy observed in our study (6%) is similar to previous study (5-10%).

Lewy\textsuperscript{7} observed azotemia in a higher proportion of subjects than we did. RBC casts were found in a much lower proportion of our patients (44.3%) than that observed by Travis and Kalian\textsuperscript{1} (60-85%). The proportion of elevated ESR in our cases was higher than that reported by Manhas et al\textsuperscript{13} (19.8%), but slightly lower than Puri et al\textsuperscript{15} (95%). Anemia as indicated by hemoglobin levels <10 g/dl was reported by Puri et al\textsuperscript{14} (44%) and Manhas et al\textsuperscript{13} (27.1%) in lower proportions of patients than in the present observations (61%). Reduction in Hb and hematocrit is believed to be due to hemodilution as well as hematuria. Hypoproteinemia is also in part due to the dilutional effect of intravascular volume expansion.\textsuperscript{1,17}

### Table 3. Published Studies of Acute Glomerulonephritis in Children

| Clinical, laboratory, and x-ray findings | The present study 1997-2002 (509 patients) | Srinagar Kashmir\textsuperscript{13} 1976-1978 (350 patients) | Pondicherry India\textsuperscript{15} 1966-1973 (350 patients) | Iraq 1993-1997\textsuperscript{21} (47 patients) | Memphis USA\textsuperscript{19} 1979-1988 (95 patients) | Armenia\textsuperscript{12} 1992-1996 (474 patients) |
|----------------------------------------|------------------------------------------|-------------------------------------------------|-------------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|
| Age range/years                        | 2.5-15                                   | 2-14                                            | 3-8 (63%)                                       | 3 - 14                                   | 2 - 15                                   | 1 - 16                                   |
| The majority of age (years)            | >6 (76.4%)                               | >5-12 (98.3%)                                  | 3-8 (63%)                                       | 5-10 (70.2%)                             | 8.2                                      | >4-9 (62%)                               |
| The peak age (years)                   | 8.46                                     | 5-8                                            | >8 (28%)                                        | 8.2                                      | 8.2±3.6                                  | 7.5                                      |
| Boy:girl ratio                         | 1.39:1                                   | 1.94:1                                         | 1.44:1                                          | 2.35:1                                   | 2.27:1                                   | 1.88:1                                   |
| Low socioeconomic status               | 68.9%                                    | 66.9%                                          |                                                 |                                         |                                         |                                         |
| Low educational status                 | 82%                                      |                                                 |                                                 |                                         |                                         |                                         |
| Edema                                  | 76.3%                                    | 83.4%                                          | 100%                                            | 87%                                      | 82.10%                                   | 84%                                      |
| Gross hematuria                        | 53.6%                                    | 31.4%                                          | 55.6%                                           | 54.7%                                    | 93%                                      |                                         |
| Hypertension                           | 61.8%                                    | 69.1%                                          | 74.6%                                           | 73.7%                                    | 72%                                      |                                         |
| Oliguria                               | 23.9%                                    | 90%                                            | 85.7%                                           | 100%                                     |                                         |                                         |
| Hypertensive encephalopathy            | 9.2%                                     | 3.4%                                           |                                                 |                                         |                                         |                                         |
| Acute pulmonary edema                  | 11.5%                                    | 20%                                            | 31%                                             | 62.1%                                    | 51%                                      |                                         |
| Upper respiratory tract infection       | 45.8%                                    |                                                 |                                                 | 37.9%                                    | 13%                                      |                                         |
| Pyoderma                               | 31.6%                                    | 60%                                            | 67.5%                                           | 80%                                      |                                         |                                         |
| Microhematuria                         | 99.3%                                    | 98.5%                                          | 100%                                            |                                         |                                         |                                         |
| Red blood cell casts                   | 44.3%                                    | 37.1%                                          | 89.6%                                           |                                         |                                         |                                         |
| Proteinuria                            | 98.5%                                    | 99.4%                                          | 100%                                            |                                         |                                         |                                         |
| Nephrotic range proteinuria            | 6%                                       | 8.6%                                           | 9.9%                                            | 27.3%                                    |                                         |                                         |
| Elevated anti-streptolisin O           | 66.6%                                    |                                                 |                                                 | 33.3%                                    | 78.9%                                    |                                         |
| Low complement C₃                       | 60.4%                                    |                                                 |                                                 |                                         |                                         |                                         |
| Hemoglobin <10 g/dL                    | 61.0%                                    | 27.1%                                          | 100%                                            |                                         |                                         |                                         |
| Elevated ESR                           | 85.3%                                    | 19.8%                                          | 95%                                             |                                         |                                         |                                         |
| Azotemia                               | 10.5%                                    | 42.6%                                          | 65.1%                                           | 50%                                      |                                         |                                         |
| Hypoproteinemia                        | 4.7%                                     |                                                 |                                                 |                                         |                                         |                                         |
| Hypercholesterolemia                   | 5.7%                                     |                                                 |                                                 |                                         |                                         |                                         |
| Pleural effusion                       | 81.6%                                    | 0.3%                                           | 52%                                             |                                         |                                         |                                         |
| Cardiomegaly                           | 80.2%                                    | 19.4%                                          | 72%                                             |                                         |                                         |                                         |
| Pericardial effusion                   | 81.6%                                    |                                                 |                                                 |                                         |                                         |                                         |
| Average hospital stay (days)            | 12                                       | 7                                              | 7.9                                             |                                         |                                         |                                         |
The frequent complications of AGN in the present study including acute pulmonary edema (11.5%), hypertensive encephalopathy (9.2%), and acute renal failure (10.5%) were relatively consistent in proportion with observations by Ibadin and Abiodun (39.7%, 4.8% and 12.7%). Radiological abnormalities in our study (81.6%) seems to be consistent with that observed by Kirkpatrick et al (85.5%) and Puri et al (72%) but higher than by Manhas et al (19.4%). To investigate the cause of cardiomegaly, Unhas teaching center performed echocardiography. The initial chest films and echocardiograms (81.6%) demonstrated cardiomegaly and pericardial effusion, but after recovery the follow-up examinations showed that both had disappeared simultaneously. It means that cardiomegaly in our patients with AGN mainly resulted from pericardial effusion.

Table 3 shows the similarities and differences of observations between our study and other investigators. Patients with AGN have an expanded extracellular fluid volume secondary due to sodium and water retention leading to clinical manifestations of AGN and generalized circulatory congestion. Although circulatory congestion is similar to primary fluid overload, there is no evidence of abnormality in the heart and blood vessel. In other words, the generalized circulatory congestion is merely of renal origin. Complete recovery observed in our study ranged from 7 to 14 days with the majority of patients in 12 days; Iraqi patients mostly recovered within 2 weeks with average time of recovery 7.9 days while Kashmiri children 7 days. The different results observed in our study might be caused by the limitations of the study; we did not perform repeated examinations during hospitalization beside the difference in methodology, geography, and period of the study.

In conclusion, despite no adequate data on throat or skin cultures, AGN among Indonesian children seems mostly to be PSAGN as proved by the elevated ASO titer and decrease in C3 concentration.

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