Original Article

Prognostic factors for mortality in pediatric acute poststreptococcal glomerulonephritis

Syamsul Nur, Husein Albar, Dasril Daud

Abstract

Background Acute post-streptococcal glomerulonephritis (AP-SGN) is one of the most common causes of glomerular disease in developing countries, including Indonesia. It can lead to end stage renal failure and higher mortality rates. To decrease morbidity and mortality, it is important to understand the prognostic factors affecting the disease.

Objective To identify prognostic factors affecting outcomes in pediatric APSGN patients.

Methods Study data were collected from medical records of patients with APSGN hospitalized in Wahidin Sudirohusodo Hospital, Makassar in 2009-2013. Possible prognotic factors analyzed were gender, age, nutritional status, level of consciousness, as well as proteinuria, hemoglobin, serum albumin, urea, and creatinine levels.

Results Of 86 subjects, 82 (95.3%) survived and 4 (4.7%) died. Fifty-three (61.6%) patients were male and 33 (38.4%) were female. Subjects' ages ranged from 3.42 to 14.67 years, with a mean age of 9.36 years. Multivariate analysis revealed serum creatinine level >1.5 mg/dL to be an independent prognostic factor for mortality in children with APSGN (AOR 15.43; 95%CI 1.31 to 181.7; P=0.03).

Conclusion High serum creatinine level is an independent prognostic factor for poor outcomes in children with APSGN. [Paediatr Indones. 2016;56:166-70.].

Keywords: *glomerulonephritis; streptococcus; prognostic; children*

Acute glomerulonephritis (AGN) is a collection of symptoms characterized by a sudden decline in glomerular filtration rate with clinical manifestations such as edema, hematuria, hypertension, oliguria, and renal insufficiency. Therefore, AGN is often referred to as acute nephritic syndrome (ANS).[1] Acute glomerulonephritis after *Streptococci* (APSGN) is a form of AGN/ANS due to infection of β-hemolytic group A *Streptococcus* (BHAS), most commonly found in children aged 3-8 years with a boy-to-girl ratio of 2.3: 1.[2] Acute glomerulonephritis after *Streptococci* is one of the most common causes of glomerular disease in developing countries, and also one of the major causes of end-stage renal failure and high morbidity in children. In some cases, early death can result from delayed identification or provision of supportive measures. Death primarily occurs during acute renal failure, acute pulmonary edema, or hypertensive encephalopathy.[3] In order to reduce morbidity and mortality due to APSGN, efforts should be taken to prevent the occurrence of complications. As such, the evaluation of prognostic factors that influence the

From the Department of Child Health, Hasanuddin University Medical School, Makassar.

Reprint requests to: Syamsul Nur. Department of Child Health, Hasanuddin University Medical School, Jalan Perintis Kemerdekaan Km. 11, Tamalanrea, Makassar 90245, Indonesia. Mobile: +6282196460675. Fax: +62-411-590629. E-mail: sanurpost@rocketmail.com.

course of disease could be useful for timely, accurate, and comprehensive patient management, as well as improved patient outcomes.

Previous studies on factors that may increase morbidity and mortality of APSGN have been done in various countries. Mossie et al.[3] reported that there was no significant relationship between the outcomes of APSGN patients and their renal dysfunction or their degree of hypertension.[3] In addition, Steer et al. found that low socioeconomic level was a risk factor for APSGN.[4] White et al.[5] concluded that the factors of race and low birth weight (LBW) affect the prognosis in children with APSGN in the Northern Territory, Australia.[5] Furthermore, Kumar found that while edema, proteinuria, and hematuria were ever-present clinical symptoms, hypertension and congestive heart failure were important factors for determining prognoses. Urea and creatinine levels were used to assess the level of kidney injury, and as prognostic factors. However, anti-streptolysin O (ASO) level was a non-specific factor.[6]

By assessing APSGN patients for prognostic factors of poor outcomes, health providers may be able to plan comprehensive treatment, prevent complications, introduce precautionary measures in an accurate and timely manner, and reduce length of hospital stays in these patients. As such, we aimed to identify prognostic factors influencing the outcomes of APSGN in children treated at Dr. Wahidin Sudirohusodo Hospital, Makassar.

Methods

This was a retrospective cohort study on the identification of prognostic factors for patient outcomes in children with APSGN. We assessed the following potential prognostic factors: age, nutritional status, level of consciousness, degree of proteinuria, as well as hemoglobin, serum albumin, urea, and creatinine levels.

We conducted the study at Dr. Wahidin Sudirohusodo Hospital, Makassar using data from medical records of patients with APSGN who admitted to the Department of Pediatrics in 2009-2013. We took the following data from subjects' medical records: patient identities, registration number, age at diagnosis, gender, nutritional status, *Glasgow*

Coma Scale (GCS) level, degree of proteinuria, as well as hemoglobin (Hb) level, serum albumin, urea and creatinine levels. Subjects were divided into two groups: survived and died. Factors were compared between groups by appropriate statistical methods, namely univariate, bivariate, and multivariate analyses. Anemia was defined as Hb level <11 gr/dL in 6 month – 6 year age group and <12 gr/dL in subject aged >6 years old.

Results

Table 1 shows the characteristics of study subjects. Of 86 subjects, 51 (62.2%) males and 31 (37.8%) females survived, while 2 (50%) males and 2 (50%) females died.

Table 2 shows comparison of factors between the two groups, survived and died. Bivariate statistical analysis revealed significant differences in GCS scores (level of consciousness) (P= 0.023; COR 14.57; 95%CI 1.41 to 150.53), blood urea level (P= 0.042; COR 12.67; 95%CI 1.51 to 106.47), and creatinine level (P= 0.01; COR 21.6; 95%CI 2.04 to 228.27) between the two groups. This means that the bivariate analysis, then there were three prognostic variables that affected the APSGN outcomes in children, the GCS score (level of consciousness), serum urea, and creatinine levels.

Table 3 shows the logistic regression analyses of the three prognostic factors of APSGN outcomes in children. Multivariate statistical analysis revealed a significant difference in creatinine levels (P= 0.03; AOR 15.43; 95%CI 1.31 to 181.7) between groups, indicating that patients with creatinine levels >1.5mg/dL had 15.43 times risk of dying compared to patients with creatinine levels ≤1.5mg/dL. However, GCS scores, and urea level were found to not have statistically significant differences between the two groups.

Discussion

We found that more males suffered from APSGN (61.6%) than females (38.4%), with a ratio of 1.6: 1. Similarly, Ho et al. found more males with APSGN by a ratio of 2.3: 1.[2] Also, Etuk et al.[7] reported 56% males

Table 1. Characteristics of subjects

No.	Characteristics	Total (N = 86)	Survived (n= 82)	Died (n=4)
			Outcomes	
1	Gender ratio, M:F (%)	53:33 (61.6: 38.4)	51:31(62.2: 37.8)	2:2 (50: 50)
2	Age, years			
	Range	3.42 – 14.67	3.42-14.67	3.83-11.83
	Mean (SD)	9.36 (2.85)	9.44 (2.82)	7.75 (3.34)
	Median	9.085	9.21	7.67
3	Nutritional status, n (%)			
	Good	37 (43)	35 (94.6)	2 (5.4)
	Poor	49 (57)	47 (95.9)	2 (4.1)
4	GCS score, n (%)			
	15	69 (80.2)	68 (98.6)	1 (1.4)
	3-14	17 (19.8)	14 (82.4)	3 (17.6)
5	Proteinuria level, n (%)			
	<2+	17 (19.8)	17 (100)	0 (0)
	≥2+	69 (80.2)	65 (94.2)	4 (5.8)
6	Hb level, gr/dL			
	Range	5.0-15.7	5.0-15.7	9.4-11.0
	Mean (SD)	10.92 (1.73)	10.96 (1.76)	10.15 (0.77)
	Median	10.8	10.95	10.1
7	Albumin level, gr/dL			
	Range	1.7-4.0	1.7-4.0	1.9-3.0
	Mean (SD)	2.895 (0.55)	2.91 (0.55)	2.58 (0.5)
	Median	2.9	2.9	2.7
8	Urea level, mg/dL			
	Range	12-455	12-266	48-455
	Mean (SD)	57.43 (65.79)	50.15 (47.43)	206.75 (175.2)
	Median	34.5	33	162
9	Creatinine level, mg/dL			
	Range	0.2 – 20.6	0.2-5.3	0.6-20.6
	Mean (SD)	1.153 (2.28)	0.9 (0.82)	6.35 (9.53)
	Median	0.7	0.7	2.1

M: male; F: female; (SD): standard deviation

and 44% females;[7] Albar *et al.*[8] reported APSGN in 58.3% males and 41.7% females;[8] and Sepahi *et al.* reported a male: female ratio of 1.23: 1.[9] According to Ahn *et al.*[10],this discrepancy could be due to males more often engaging in activities outside the house, making them more likely to be exposed to BHAS.[10] The mean age of our subjects was 9.36 years, with a range of 3.42 to 14.67 years. Bingler *et al.* reported that APSGN is generally found in children over 6 years of age and is rare in infants.[11] However, age was not a prognostic factor of APSGN in children.

In addition, nutritional status, degree of proteinuria, hemoglobin and albumin levels were not prognostic factors of poor outcomes in children with APSGN. Previous studies also reported no significant differences in nutritional status,[3] low albumin level,[12] and hemoglobin level[13] between APSGN mortality outcomes in children. In contrast, Ahn *et al.* reported a correlation between proteinuria and poor renal function outcomes in APSGN.[10]

Bivariate analysis revealed three statistically significant variables associated with APSGN outcomes in children: the level of consciousness (GCS scores), urea, and creatinine levels. However, a multivariate analysis showed that only high creatinine level (>1.5mg/dL) was an independent variable as a factor for poor prognostic outcomes in children with APSGN. Urea level was also not considered to be an influential factor in the outcome of APSGN in children.[3] Similarly, Kumar and Sepahi *et al.* found

Table 2. Bivariate analysis of possible prognostic factors between the survived and died groups

Prognostic factors	Outcomes		COR*	95%CI	P value
	Survived (n=82)	Died (n=4)			
Gender, n (%)					
Male	51 (96.2)	2 (3.8)	1,645??	0.636	0.22-12.28
Female	31 (93.9)	2 (6.1)			
Nutritional status, n (%)					
Good	35 (94.6)	2 (5.4)	0.745	1.00	0.1-5.55
Poor	47 (95.9)	2 (4.1)			
Ages, n (%)					
<7 years	17 (89.5)	2 (10.5)	0.262	0.21	0.034-1.99
≥7 years	65 (97.0)	2 (3.0)			
GCS scores, n (%)					
15	68 (98.6)	1 (1.4)	14.57	0.023	1.41-150.53
3-14	14 (82.4)	3 (17.6)			
Proteinuria level, n (%)					
<2+	17 (100)	0 (0)	1,062??	0.581	1.00-1.13
≥2+	65 (94.2)	4 (5.8)			
Hb levels, n (%)					
Not anemic	24 (100)	0 (0)	1,069??	0.573	1.00-1.14
Anemic	58 (93.5)	4 (6.5)			
Albumin level, n (%)					
<2.5 gr/dL	16 (94.1)	1 (5.9)	0.727	1.00	0.07-7.46
≥2.5 gr/dL	66 (95.7)	3 (4.3)			
Urea level, n (%)					
<150 mg/dL	76 (97.4)	2 (2.6)	12.667	0.042	1.51-106.47
≥150 mg/dL	6 (75.0)	2 (25.0)			
Creatinine level, n (%)					
≤1.5 mg/dL	72 (98.6)	1 (1.4)	21.6	0.01	2.04-228.27
>1.5 mg/dL	10 (76.9)	3 (23.1)			

*COR=crude odds ratio

Table 3. Multiple logistic regression analysis of three prognostic factors on patient outcomes in children with APSGN

Variables	B	AOR	95%CI	P value
GCS scores	2,302	9,991	0.84-118.97	0.735
Urea level	-0.558	0.572	0.02-14.57	0.069
Creatinine level	2,736	15,429	1.31-181.7	0.030
Constant	-10,197	-	-	-

B: regression coefficient; AOR: adjusted odds ratio

an association between creatinine level and patient mortality in children with APSGN.[6,9] Rodriguez-Iturbe *et al.* reported that creatinine serum levels would not change until 25-50% of kidney function had been lost.[14] In our study, the mean serum creatinine value was 1.153 mg/dL, while Mossie *et al.* found a mean value of 1.5 mg/dL.[3]

A limitation of this study was that it was only performed on patients who were admitted at Dr. Wahidin Sudirohusodo Hospital, Makassar, so our results do not necessarily reflect the overall population of children in the city of Makassar with APSGN. In addition, we used medical record data as the main resource for this study, and some records may not have been complete. However, a strength of the study was its retrospective cohort design, starting from identification of prognostic factors and followed all the way to patient outcomes. In addition, we explored eight variables which were significant multivariable prognostic factors, so that the results obtained are of

significance not only produce, but also met the terms of the relationship between variables, so as to minimize the influence of confounding factors that may arise. According to Suarta, the incidence of APSGN in Indonesia has tended to increase.[15] Therefore, it is hoped that by identifying negative prognostic factors in this study, mortality rates can be reduced.

In conclusion, creatinine level >1.5 mg/dL is an independent prognostic factor of poor outcomes in children with APSGN, with an AOR 15.43, i.e., the risk of dying is 15.43 times greater compared to APSGN patients with creatinine levels <1.5 mg/dL. As such, creatinine measurements may be a useful tool for APSGN comprehensive treatment. Health care providers may consider periodic checking of blood creatinine levels in pediatric APSGN patients in order to limit complications and reduce mortality. Further multicenter study involving other factors needs to be done to assess other factors that may be associated with APSGN outcomes in children.

Conflict of interest

None declared.

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