

Low Glasgow Coma Scale Score as a Risk Factor of Death in Children with Acute Encephalitis Syndrome

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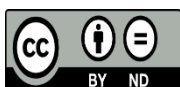


Keywords:

GCS, acute encephalitis syndrome, children, outcome

ABSTRACT

Acute encephalitis syndrome (AES) is a global health problem. Globally, the incidence found in 10.5 per 100.000. In a study in India, the most common age for AES cases was 1 to 7 years. Children with AES have a tendency to experience bad outcomes both disability and even death. In AES, diffuse brain edema occurs which causes disturbance of consciousness. The Glasgow Coma Scale (GCS) is the instrument of choice for assessing a person's level of consciousness and is widely associated with children's outcomes with AES especially in health care center with limited resources. This cross-sectional study, subjects were children treated with AES that were treated in Sanglah hospital in January 2018 to December 2019. *Chi-square* test was performed to assess categorical data. Followed by logistic regression multivariate analysis with backward method. A total of 142 subjects were analysed for their GCS score and the outcomes in this study. The results of multivariate analysis showed GCS values were associated with outcomes of children with AES [OR = 2.756, 95% CI 1.201 to 6.323, *P* 0.017]. Seizure status have a statistically significant relationship with the outcomes of children with AES [OR = 0.332, 95% CI 0.142 to 0.773, *P* 0.011]. Low GCS score is a risk factor of death in children with AES.



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1. Introduction

Acute encephalitis syndrome (AES) is defined as the acute onset of fever and change in mental status (including symptoms such as confusion, disorientation, coma or inability to talk) and/or new onset seizures (excluding simple febrile seizures) and/or acute flaccid paralysis in a person of any age at any time of the year [1]. Most AES cases were viral encephalitis where Japanese Encephalitis (JE) accounts for approximately one-quarter of cases [2]. Globally, incidence of AES in children were found 10.5 per 100.000 whereas. In Asia incidence were found 15 per 100.000 [3]. Incidence of AES in Bali, Indonesia in 2001 to 2003 were found 8.2 per 100.000 [4]. However in 2015, incidence of AES in Bali were found to be 1.2 per 100.000 [5]. *Acute encephalitis syndrome* were reported tend to have poor outcome. It affects over 50,000 people annually, leading to 8-30% mortality and 50-60% disability, with children bearing the brunt of the disease burden [2]. In Bali, Indonesia 36% children with AES had permanent disability on follow-up

[5]. Risk factors of outcome become important to be investigate due to high burden of morbidity and mortality among children with AES especially in the area with limited resources. In AES, there is diffuse brain damage that affecting patient' level of consciousness. Refractory seizure, Glasgow coma scale (GCS) <8, bradycardia, shock and severe anaemia were predictors of child mortality with AES [6]. Other study stated that low GCS score, focal weakness and status epilepticus were independent predictors of poor outcome in AES [7]. *Glasgow coma scale* is the instrument of choice for assessing one's level of consciousness since it is easy to use and had sensitivity of 79-97% and specificity 84-97%. Based on the high burden of the disease, knowing risk factors of bad outcome become important. In this study, we report the GCS as one of risk factor to death in AES children since GCS is a simple approach that can be use in healthcare centre with limited resources.

2. Methods

This is a cross-sectional retrospective study of pediatric patients that treated as AES in Sanglah hospital during January 2018 to December 2019. Inclusion criteria included children with AES in the range of age 1 month old to 18-year-old. Exclusion criteria were those with malignancy, autoimmune disease, human immunodeficiency virus (HIV) infection that has been diagnosed and stated in medical record and those with insufficient data of medical records. A total of 151 children of AES were treated in Sanglah hospital during period of research, 9 children were excluded due to lack of data. Therefore 142 subjects reviewed in this study. Subject characteristics with categorical scale showed in frequency and percentage. Chi-square test were used to analyzed correlation of non-parametric nominal dichotomy data and followed by logistic regression multivariate analysis with backward method. Statically significant were when p-value < 0.05. All analysis was conducted using IBM SPSS version 23. This study was approved by the Ethics Committee of Research and Development Faculty of Medicine Udayana University/ Sanglah hospital.

3. Results

3.1 Subject characteristics

The youngest subject was 1 month old and the eldest was 17-year-old. Ratio between male and female was 1.2:1. Level of consciousness assessed using GCS at the time subject admitted to the hospital. Most subjects (64.1%) had GCS score >8 where 35.9% had GCS ≤ 8. Subjects characteristics were shown in Table 1.

Table 1. Subject characteristics

	N = 142	Survivors (N=108)	Death (N=34)
Age(month), n (%)			
< 60 month	97 (68,3)	77 (71,3)	20 (58,8)
≥60 month	45 (31,7)	31 (28,7)	14 (41,2)
Gender, n(%)			
Male	79 (55,6)	57 (52,8)	22 (64,7)
Female	63 (44,4)	51 (47,2)	12 (35,3)
Seizure, n (%)			
Yes	100 (70,4)	82 (75,9)	18 (52,9)
No	42 (29,6)	26 (24,1)	16 (47,1)
Residence, n (%)			
Urban	54 (38)	37 (34,3)	17 (50)
Rural	88 (62)	71 (65,7)	17 (50)
Payment method, n (%)			
Self-fund	45 (31,7)	28 (25,9)	17 (50)
National health insurance	97 (68,3)	80 (74,1)	17 (50)
Agent, n (%)			
JE	6 (4,2)	4 (3,7)	2 (5,9)

3.2 Case Distribution

The highest incidence was found in December both in 2018 as well as in 2019. There were 15 cases in December 2018 and 13 cases found in December 2019. The lowest incidence found in January both in 2018 and 2019. Graphic shown in Figure 1.

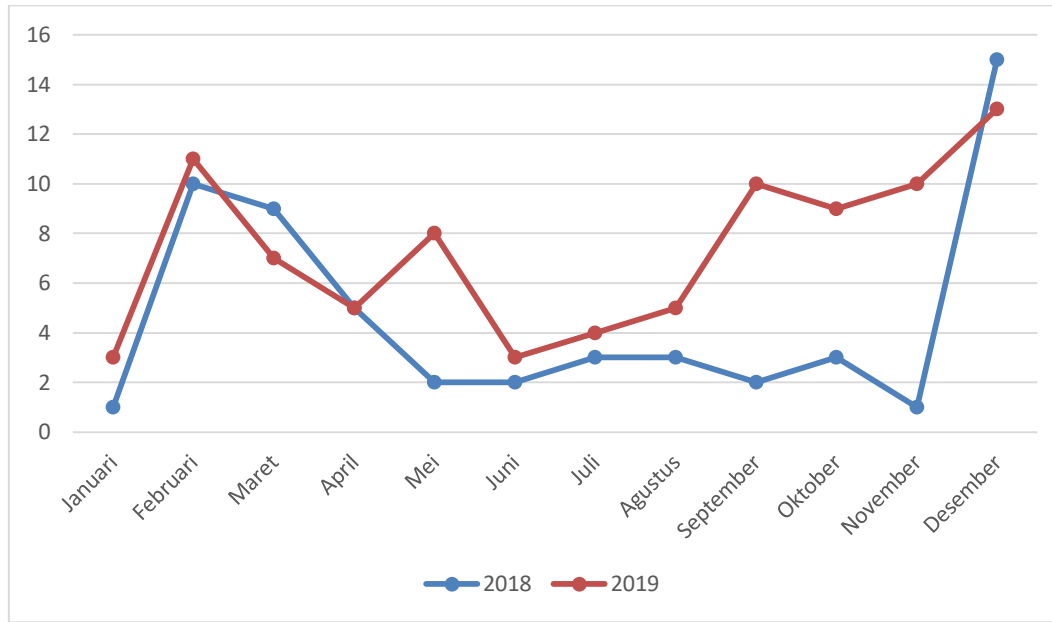


Figure 1. AES distribution between 2018 and 2019.

3.3 Analysis of the GCS Score between Groups of Survivors and Death

Outcomes were compared between subjects with GCS ≤ 8 and GCS >8 , as well as those with and without seizure on admission. The results were statically significant, as show in Table 2.

Table 2. Bivariate Analysis Result

	Median (N = 142)		RP	CI 95%	P*
	Survivors (N=108)	Death (N=34)			
Seizure					
Yes, n (%)	82 (82)	18 (18)	0,473	0,268-0,835	0,010
No, n (%)	26 (61,9)	16 (38,1)			
GCS					
≤ 8 , n (%)	33 (64,7)	18 (35,3)	2,007	1,124-3,584	0,018
>8 , n (%)	75 (82,4)	16 (17,6)			

RP, Risk Prevalence; CI, Confidence Interval, *chi-square test

Multivariate analysis was performed using logistic regression. The result was shown on Table 3. Seizure on admission had a OR of 0.364 (CI 95%), while subjects with GCS ≤ 8 had OR 2.504 (CI 95%)

Table 3. Logistic Regression Multivariate Analysis Result

	B	S.E.	OR	CI 95%		P
				Min	Mak	
Seizure on admission	-1,011	0,420	0,364	0,160	0,828	0,016
GCS \leq 8	0,918	0,412	2,504	1,117	5,612	0,026

SE, standard error; OR, odd ratio

4. Discussion

In this study, subjects age ranges from 1 month to 17 years with median of 2-year-old. A total of 68.3% were children less than 60 months old. More male than female (1.2:1). Similar result found in India where 33 subjects were male and 28 subjects were female within 2007-2008 [8]. Other study supporting this finding found that male to female ratio was 1.5 :1. The higher incidence in males is caused by more outdoor male activity than females so that the risk of being bitten by vector mosquitoes that play a role in JE transmission is greater [9]. In this study, more cases were come from rural area which was 62% of subjects. Other study also found similar findings that incidence in rural area was higher in urban, 0.069 and 0.061 per day, respectively [10]. This might be related to the existence of rice field where vector and reservoir live.

Peak incidence of AES was found in December in both years. There were 15 cases in December 2018 and 13 cases in December 2019. Rainy season in Bali was started in November. However, in Uttar Pradesh, India the epicenter of AES, cases remain all year long with peak of incidence were in July to October. Incidence of AES related to seasons since vector which mostly mosquitos grow fast right after rainy season over [11].

In this study, GCS score found to have statistically significant correlation to death of AES children (OR 2.504, CI 95% 1.117 to 5.612, P 0.026). This result means that low GCS score was a risk factor of death in children with AES. Those whose GCS score \leq 8 had 2.504 times higher risk to death. A study held in America strengthen this finding. It stated that death in encephalitis had association with edema cerebri, status epilepticus and thrombocytopenia [12]. Other studies support this result where low GCS score with or without focal neurological deficits at initial have an independent association with mortality in children with AES [2]. In AES brain damage is diffuse so that it affects consciousness. The more diffuse brain damages the lower the level of consciousness. This condition has the potential to be life threatening or cause permanent damage to the brain. Other mechanism is the occurrence of edema in the brain. The brain is protected by a strong skull, when there is edema due to inflammation, the skull cannot be pressed by the brain, causing the brain to press in other directions including pressing on the brain stem, so that it will disrupt vital functions such as control of breathing and heart rate. This condition is actually reversible depending on the speed of intervention to the condition such as administration of anti-inflammatory drugs, hyperosmolar therapy, diuretic drugs (mannitol) and close monitoring of the intracranial pressure.

In this study, seizure on admission also show a statistically significant correlation to death in AES children (OR 0.364, CI 95% 0.160 to 0.828, P 0.016). Seizures had a statistically significant association with mortality in children with AES [OR=0.364, 95% CI 0.160 to 0.828, P 0.016]. Seizures were found to reduce the risk of death by 64% in children with AES. The Odds Ratio obtained shows a negative correlation. This is likely due to several things. A similar study found that patients who witnessed seizures on arrival at the hospital had a worse outcome [OR=4.50, 95% CI 1.94 to 10.52, P < 0.0001] although the study also stated that children with reduced consciousness were more likely to die when compared to children with seizures that stopped on their own [14% versus 0% with a P value of 0.003] [13]. Another study stated that seizures

in encephalitis were associated with morbidity but had no association with mortality. Limited resources in controlling for other possible confounders in the present study such as seizure duration, frequency, and pattern may also have contributed to these results [14]. However, further research need to be done to ensure this finding. Adjustment to other confounding factors that might contribute such as seizure duration, frequency and type of seizure need to be analyzed.

The weaknesses of this study were we are not able to fully control confounding factors such as causative agent that have not been able to be traced, duration of seizures at initial, other complaints at the onset of symptoms, other comorbid diseases, any usage of prehospital drugs, interventions during hospitalization, nutritional status, laboratory panels such as CSS analysis and blood panel. This is due to limited resources and this research is a retrospective study that fully rely on secondary data. This study also did not evaluate survivor outcome whether any neurological sequele exist or fully recovered.

5. Conclusions

Low GCS score is a risk factor of death in children with AES. Further research needed to analyze outcome of survivors with neurological sequele as well as long-term outcome of AES children.

Conflict of Interest

The authors declare that they have no competing interests.

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None

6. References

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