International Journal of Research and Review
Vol. 9; Issue: 4; April 2022
Website: www.ijrrjournal.com
Research Article *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Hematologic Indicators and Its Association with Outcomes of Status Epilepticus Patients in Sanglah General Hospital, Denpasar, Bali

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DOI: https://doi.org/10.52403/ijrr.20220433

ABSTRACT

Background: Hematologic parameter had been considered as simple prognostic markers for status epilepticus. Hematologic profile might be related to outcomes. This research was aimed to address status epilepticus cases in Sanglah General Hospital and to analyze the relationship between hematologic profiles and the outcomes of status epilepticus patient.

Method: This research used cross sectional design. We resumed status epilepticus cases in Sanglah General Hospital, Bali, Indonesia, from 2019 to 2020. With consecutive sampling, we obtained data from medical records. Statistic tests were done with software.

Results: One hundred and eight patients with status epilepticus, 58 males and 50 females aged 18 to 95 years old were involved. Fifty-five had focal and 53 general seizures. Fifty-one (47.2%) survived and 57 (52.8%) did not. Intensive care was given to 34 (31.5%) patients. Factors that had relationship with outcome were comorbidity ($p<0.01$), renal failure ($p=0.05$), pneumonia ($p<0.01$), sepsis ($P<0.01$), intensive care ($p=0.01$), length of stay ($p<0.01$), and platelet count ($p<0.01$). Neutrophil to Lymphocyte Ratio did not have relationship with the outcome ($p=3.22$). In additional analysis with numeric variable, there were suggestions that Neutrophil to Lymphocyte Ratio and Hemoglobin might have weak correlation with length of stay ($p<0.05$).

Conclusion: Future studies with better designs should be conducted to really address the real relationship between hematologic profile and outcome in status epilepticus patients.

Keywords: hematologic profile, status epilepticus, outcome

INTRODUCTION

Status epilepticus according to International League Against Epilepsy 2017 is defined as seizure lasting 5 minutes or more for general seizure and 10 minutes or more for focal seizure, or repeated seizures without recovery of consciousness between. The incidence varies from 9.9 to 41 per 100.000 lives. The mortality of status epilepticus might reach 50% and most of them were difficult to manage.[1] Status epilepticus could be followed by neurological sequel such as secondary epilepsy, cognitive decline, behavioral symptoms, and neurological deficits.[2] The outcomes were influenced by a lot of factors, such as age, gender, etiology, duration of seizure, type of seizure, consciousness, and complications.[3] In a systematic review, status epilepticus could be caused by cryptogenic cause, febrile seizure, central nervous system infection, cerebrovascular diseases, metabolic abnormalities, hypoxia, alcoholism, trauma, and tumor.[2]

Status epilepticus causes acute complications such as respiratory failure and hypoxia, acid base disturbance, glucose metabolism failure, infection and inflammatory response, thermal dysregulation, heart failure, rhabdomyolysis, renal impairment, physical

trauma, and gastrointestinal distress. Most cases need intensive care with tight monitoring. Management of status epilepticus requires seizure control with anticonvulsant, etiology therapy, and complication prevention.[4]

Several studies had tried to find relationship between status epilepticus and inflammatory response. Status epilepticus was pro-inflammatory and was found to be related to inflammatory laboratory markers such as C-reactive protein, albumin, and granulocytes. The inflammation took place due to interactions between neurons, microglia, and endothelium.[4] Laboratory markers of inflammation were not always feasible to obtain, hence clinicians need simpler approaches. Several studies had been conducted and showed that systemic inflammation is related to status epilepticus. A few simple markers had also been studied as outcome predictors for status epilepticus. Some of them were hematocrit, platelet, leucocyte, differential count, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR). In literatures, PLR and NLR were known as inflammatory indicators which found to influence prognosis.[5]

Based on above, this research was done to give a brief description and analysis of relationships between several hematologic and laboratory indicators and outcomes of status epilepticus in Sanglah General Hospital Denpasar.

MATERIALS AND METHODS

was a cross sectional study which collected data of status epilepticus due to various etiologies from patients in Sanglah General Hospital Denpasar, Bali, Indonesia, since January 2019 until December 2020. The inclusion criteria were age 18 and above and diagnosed as status epilepticus according to ILAE 2017. The exclusion criteria were pregnancy and lack of necessary data.

A number of 108 subjects were included with consecutive sampling. The data we collected were among others gender, age, etiology, type of seizure, comorbidities, intensive care, length of stay, outcome, blood glucose, hematology profiles, and NLR. The data were collected from medical records and information system.

Statistical Methods

The collected data were presented in frequency and central tendencies according to variable types. All variables were tested for normality using Kolmogorov-Smirnov. The normally distributed data would be used in comparative parametric test (Chi Square and Unpaired T-test) for nominal variables and correlative test (Pearson) for numeric variables. If the distribution were abnormal, data would be used in comparative non parametric test (Mann-Whitney) for nominal variables and correlative test (Spearman) for numeric variables. The significance of result was determined by p value ($p<0.05$).

The sampling technique was carried out by consecutive non-random sampling method, that is, all subjects who came and met the eligibility criteria were included in the study until the required number of samples was met.

RESULTS

From this research, 108 subjects (58 males and 50 females) with status epilepticus aged from 18 to 95 years old were collected. The seizure types were focal (n=55) and general (n=53). Fifty-one subjects survived and the rest did not. Among them, 34 (31.5%) needed intensive treatment. The length of stays were approximately 2 to 37 days. Description of data was presented in Table 1.

Normality tests showed that Hemoglobin and age were normally distributed. Data about leucocyte, platelet, NLR, glucose, and length of stay were not normally distributed. Transformation of data was not feasible so that non parametric tests were used for those abnormally distributed variables. Table 2 showed comparative results from each variable with outcomes.

Table 1: Characteristics of status epilepticus subjects

Characteristics	Number (%)	Mean (Min-Max)
Gender		
Male	58 (53.7)	
Female	50 (46.3)	
Age		49.9 (18-95)
Etiology		
Stroke	33 (30.6)	
Tumor	12 (11.1)	
Trauma	2 (1.9)	
Metabolic	33 (30.6)	
Infection	20 (18.5)	
Idiopathic	8 (7.4)	
Seizure Type		
Focal aware	3 (2.8)	
Focal impaired awareness	15 (13.9)	
Focal to bilateral	27 (25)	
General	63 (58.3)	
Comorbidity		
Present	79 (73.1)	
None	29 (26.9)	
Type of Comorbidities		
Diabetes	22 (20.4)	
Hypertension	43 (39.8)	
Renal failure	42 (38.9)	
Pneumonia	30 (27.8)	
Cardiovascular	32 (29.6)	
Sepsis	36 (33.3)	
Malignancy	6 (5.6)	
Intensive Care		
Yes	34 (31.5)	
No	74 (68.5)	
Outcomes		
Survival	51 (47.2)	
Death	57 (52.8)	
Length of Stay (LOS)		8.8 (1-37) days
Hemoglobin		12.3 (5.2-17.2) g/dl
Leucocytes		16.5 (1.7-79.2) thousands/m3
Platelet		265 (30-1040) thousands/m3
NLR		14.9 (27-148.2)
Blood glucose		163 (41-854) mg/dl

*LOS= *Length of Stay*.

Table 2: Comparative Analysis of Each Variables to Outcome

Variables	Outcome		P value	Statistic tests used
	Survival (n=51)	Death (n=57)		
Gender				
Male	27 (52.9%)	31 (54.4%)	0.881	*Chi-Square*
Female	24 (47.1%)	26 (45.6%)		
Age	49.8 (18-95)	50.0 (18-78)	0.212	Unpaired t test
Comorbidity				
Present	28 (54.9%)	51 (89.5%)	<0.01	*Chi-Square*
None	23 (45.1%)	6 (10.5%)		
Type of comorbidity				
Diabetes	13 (25.5%)	9 (15.8%)	0.211	*Chi-Square*
Hypertension	18 (35.3%)	25 (43.9%)	0.364	
Renal failure	15 (29.4%)	27 (47.4%)	0.050*	
Pneumonia	4 (7.8%)	26 (45.6%)	<0.01	
Cardiovascular	14 (27.5%)	18 (31.6%)	0.639	
Sepsis	4 (7.8%)	32 (56.1%)	<0.01	
Malignancy	2 (3.9%)	4 (7.0%)	0.483	
Intensive Care				
Yes	8 (15.8%)	26 (45.6%)	<0.01	*Chi-Square*
No	43 (84.3%)	31 (54.4%)		
LOS	10 (2-37) hari	6 (1-25) hari	<0.01	Unpaired t test
Hemoglobin	12.3 (5.7-16.3)	12.2 (5.7-17.2)	0.106	Unpaired t test
Leucocytes				
Mean	16.8	16.2	0.202	*Mann-Whitney*
Median (Range)	17.8(4.8-38.8)	13.4 (1.7-79.1)		
Platelet				
Mean	282.1	249.8	<0.01	*Mann-Whitney*
Median (Range)	280.7(30-510.9)	219.5(37.8-1040)		

Table no.2 continued....				
NLR				
Mean	12.0	17.6	0.322	*Mann-Whitney*
Median (Range)	7.84(1.1-55.0)	10.9(0.3-148.3)		
Blood glucose				
Mean	178.9	149.3	0.169	*Mann-Whitney*
Median (Range)	140 (69-854)	137 (41-399)		

NLR=*Neutrophyl to Lymphocyte Ratio*, LOS= *Length of Stay*, p significance <0.05*

Comparative analysis showed that comorbidities, renal failure, pneumonia, sepsis, intensive care, length of stay, and platelet count were significantly associated with outcomes. Meanwhile, table 3 presented correlation test among numeric variables and length of stay using Spearman.

Table 3: Corelation of hematologic profile to length of stay

Variable	Correlation Coefficient	Strength	Direction	P value
Hemoglobin	-0.23	Weak	Negative	0.019*
Leucocyte	0.18	Weak	Positive	0.061
Platelet	0.042	Weak	Positive	0.666
NLR	0.25	Weak	Positive	0.010*
Blood glucose	0.08	Weak	Positive	0.409

From correlation analysis, Hemoglobin and NLR were found to be weakly correlated with length of stay. p significance <0.05*

DISCUSSION

Several inflammatory markers had been associated with status epilepticus prognosis and outcomes, such as Procalcitonin, C-reactive protein, albumin, uric acid, and cytokines. Unfortunately, those markers were not always feasible to obtain. Simpler markers such as hematology profile could be used to mark inflammation process that surely takes place in status epilepticus.[1] Other circumstances such as age, complications, and comorbidities also influence the outcome. Among others are respiratory failure and hypoxia, acid base disturbance, glucose plasma abnormality, infection and inflammatory response, thermal dysregulation, cardiovascular dysfunction (cardiomyopathy and heart failure), rhabdomyolysis, renal impairment, and physical trauma. [3] The need of intensive care also took part in worse outcome.[4]

Status epilepticus was related to systemic inflammation, blood brain barrier disruption, and neuron hyperexcitability. In previous literature, leucocyte had important rule in seizure process. Patients with epilepsy had higher leucocyte count in brain, especially neutrophil. In the same moment, lymphocyte was found to be decreased in acute seizure. That suggested that Neutrophil to Lymphocyte Ratio (NLR) could be a good marker of ongoing inflammatory process that took place in the presence of seizure and status epilepticus. Several studies revealed that leucocytes, platelet, neutrophil, lymphocyte, NLR, and PLR in status epilepticus were greater than normal control group.[5]

Gunes et al (2020) in their study revealed that NLR value is related to systemic inflammation in status epilepticus. Other inflammatory marker such as leucocyte and neutrophil count also increased in status epilepticus.[6] Ozdemir et al (2016) also revealed that NLR value were increased in acute phase of status epilepticus. It was said that this inflammatory process could predict diagnosis, prognosis, and therapy.[7]

Outcome indicators which were regularly used in status epilepticus were mortality and length of stay. In a study conducted by Ogun et al (2019), several factors were found to be associated with status epilepticus outcome, among others were length of stay, blood glucose, C-reactive protein, NLR, and leucocyte count. Platelet and hemoglobin had not been found to have association.[8]

In this study, we found that presence of comorbidity, renal failure, pneumonia, sepsis, intensive care, length of stay, and platelet count had association with

mortality. NLR was found not associated with the outcomes/mortality. On the other hand, NLR and hemoglobin level were found to have weak correlation with length of stay.

This was a pilot study to reveal the possible relationships between hematologic profile with status epilepticus outcome in general circumstances. This study was limited because of the sample size and design could not control the influencing variables. The limitation could interfere with data analysis. We hope that this study could be followed by better design and variable controls that address specific issues.

CONCLUSION

In conclusions, the study found that comorbidity, renal failure, pneumonia, sepsis, intensive care, length of stay, and platelet count had significant association with outcome/mortality in status epilepticus cases in Sanglah General Hospital, Denpasar, Bali, Indonesia. There were weak correlations between NLR and hemoglobin level and length of stay. More specific study designs are needed to address each association more specifically.

Informed Consent and Patient Details

The authors declare that this research does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers.

Acknowledgement: None

Conflict of Interest: There are no conflicts of interest to declare by any of the authors of this study.

Source of Funding: This work did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics Committee Approval: This study has obtained ethical clearance issued by the Research Ethic Commission of Faculty of Medicine, Udayana University, Sanglah General Hospital, Denpasar.

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How to cite this article: Skolastika Savitri, I Wayan Widyantara. Hematologic indicators and its association with outcomes of status epilepticus patients in Sanglah General Hospital, Denpasar, Bali. *International Journal of Research and Review*. 2022; 9(4): 277-281. DOI: *https://doi.org/10.52403/ijrr.20220433*

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