Research Article

Prognostic Factors in Predicting Primary Brainstem Hemorrhage Patients: An Experience in Indonesia's Rural Hospital

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ABSTRACT

Background: Primary brainstem hemorrhage is a rare type of hemorrhagic stroke with a very high reported mortality rate in Indonesia. **Aim:** This study aims to demonstrate the mortality rate of cases in one of Indonesia's rural hospitals. To help reduce the mortality rate, the prognostic factors of several cases were studied. These steps are needed to be able to predict the prognosis of primary brainstem hemorrhage patients and to give a better explanation to the family of the patients. **Methods**: A cross-sectional study was undertaken with collecting medical and radiological records from January 2018 to August 2020. A total sampling technique was done, and 340 patients were diagnosed with hemorrhagic stroke during that period. Only ten patients met the inclusion criteria and were included as the study samples. Statistical analysis using SPSS 22 and the Spearman correlation test adjusted for each variable. **Results:** Low prevalence of primary brainstem hemorrhage (7%). There were correlation between GCS score, brainstem hemorrhage location, and length of stay with the patient's prognosis. **Conclusion**: Understanding these prognostic factors would reduce the prevalence of this primary brainstem hemorrhage and to ease the process of explaining the patients' condition to the family.

Key words: Brainstem, Factor, Intracerebral hemorrhage, Primary, Prognosis

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INTRODUCTION

Spontaneous intracerebral hemorrhage (ICH) is a collection of blood in the brain parenchyma or ventricle that is caused by non-traumatic incidence.[1] ICH can be classified into lobar and deep ICH. Lobar ICH includes cortical-subcortical areas, whereas deep ICH includes basal ganglia, internal capsule, cerebellum, and brainstem.[2]

Brainstem hemorrhage refers to bleeding that happens in the pons, pontomedullary junction, pontomesencephalic junction, midbrain, and medulla oblongata.[3] The prevalence of this kind of stroke is 5–10% [7]with its main risk factor is hypertension[4-6]

Brainstem hemorrhage correlates with poor outcomes.[8] In the previous study, the mortality rate reached 57,5%. [9] Other studies said that the mortality rate of brainstem hemorrhage was 56% and 60–90%.[10,11] The outcome of brainstem hemorrhage is variable, ranging from early death to long-term survival without neurological deficit, depending on clinical severity and radiological appearance.[12,13]

Higher mortality rate, varied management of brainstem hemorrhage, unestablished risk factors, lack of markers[9] to predict the outcome of brainstem hemorrhage, and lack of studies on prognosis of brainstem hemorrhage in Indonesia were the background of this study. Another reason for the background of the study was the still ineffective multi strategic management with poor outcomes.[14] This study will widen the reference of the evidence-based medicine of brainstem hemorrhage in Indonesia.

METHODS

Patients

Data gathered from a patient's medical record from January 2018 to August 2020 at Cileungsi District Hospital. Cileungsi is an outskirt area of Jakarta (capital city of Indonesia) that is located about 50 km from Jakarta. However, the majority of the patients live in the rural area with difficult access to health facilities.

Of 340 patients with hemorrhagic stroke, 23 patients were diagnosed with brainstem hemorrhage. We excluded etiology such as a tumor, arteriovenous malformation, and cavernoma were excluded. Next, the location of the hemorrhage should be in braistem. Patients with anticoagulant consumption were also excluded. Patients with hemorrhagic stroke in whom the involvement of the brainstem was an extension of the hemorrhagic stroke from other brain areas were also excluded.

The independent variables were age, sex, level of consciousness which assessed with Glasgow Coma Scale score, systolic blood pressure, diastolic blood pressure, hemorrhage volume, brainstem location, white blood cell count, blood glucose level, extension to the ventricle, hydrocephalus, insertion of extraventricular drainage, and length of stay. Based on CT Scan appearance, the location of hemorrhage was notified in pons, or midbrain or pons and midbrain or pons and medulla oblongata or pons, midbrain, and medulla oblongata.

The dependent variable was the outcome at discharge and at three months after discharge which was determined using modified Rankin Score (mRS). For the purpose of data analysis, mRS is divided into two

groups, which are mRS 0, 1, 2 defined as good outcome and mRS 4, 5, 6 defined as poor outcome.

Statistical analysis

We used Chi Square, Fisher's exact, Kolmogorov-smirnov, and Spearman correlation tests to assess relationship between each of independent variables and dependent variable. Analyis data was utilized using SPSS software. There were two radiology assistants that were double blinded to the study to identify the location of brainstem hemorrhage based on CT scan appearance.

Ethical declaration

This study was approved by Universitas Pembangunan Nasional Veteran Jakarta Number 2767/IX/2020/KEPK.

RESULTS

From January 2018–August 2020, 340 hemorrhagic stroke patients were admitted to Cileungsi District Hospital. Among hemorrhagic stroke patients, 23 patients were diagnosed with brainstem hemorrhage, but only 10 patients fulfilled the inclusion criteria. Table 1 shows characteristics of brainstem hemorrhage patients.

Of 10 brainstem hemorrhage patients, 6 (6%) were male and 4 (4%) were female with the mean age 47,40±11,45 years. The mean systolic and diastolic blood pressure on admission was 206,40±38,59 mmHg and 116,90±19,18 mmHg. The mean Glasgow coma scale on admission was 6,90±3,66. Laboratory findings, which include blood glucose level and white blood cell count was obtained from 10 patients with the mean blood glucose level was 158,70±39,705 and the mean white blood cell count was 16630±6963,72.

Table 1: The characteristics of brainstem hemorrhage's patients.

Characteristics	Value
Sex, n (%)	
Male	6 (6)
Female	4 (4)
Age, years	47,40 ± 11,45
Systolic blood pressure, mmHg	206,40 ± 38,59
Diastolic blood pressure, mmHg	116,90 ± 19,18
Glasgow Coma Scale	6,90 ± 3,66
Blood glucose level, mg/dL	158,70 ± 39,705
White blood cell count, μL	16630 ± 6963,72
Location, n (%)	
Pons	3 (3)
Midbrain	0
Pons and midbrain	7 (7)
Pons and medulla oblongata	0
Pons, midbrain, and medulla oblongata	0
Volume, cc	621,20 ± 6963,72
Intraventricular hemorrhage, n (%)	
(+)	3 (3)
(-)	7 (7)
Hydrocephalus, n (%)	
(+)	6 (6)
(-)	4 (4)
Extraventricular drainage, n (%)	
(+)	1 (1)
(-)	9 (9)
Length of stay, days	2,50 ± 3,808
Outcome at discharge, n (%)	
Good (mRS 0– 3)	2 (2)
Poor (mRS 4–6)	8 (8)

Hemorrhage occurred in different anatomical locations of the brainstem. 7 (7%) of patients occurred in the pons and midbrain, the remaining 3 (3%) occurred in the pons. The mean hemorrhage volume was 621,20±6963,72. CT finding pointed that intraventricular hemorrhage occurred in 3 (3%) patients and hydrocephalus occurred in 6 (6%) patients. 9 (9%) patients didn't undergo extraventricular drainage.

The mean length of stay was 2,50±3,808 days. The outcomes assessed at discharge were good in 2 (2%) patients and poor in 8 (8%) patients.

The correlation between characteristics and the outcomes were shown in table 2. It emphasizes that Glasgow coma scale (p=0,005) with the correlation coefficient 0,807, location of hemorrhage (p=0,016) with the correlation coefficient 0,764, and length of stay (p=0,035) with the correlation coefficient -0,667 were correlated with the outcomes.

DISCUSSIONS

Brainstem hemorrhage is a rare type of stroke hemorrhage. In our cases, among 340 patients with hemorrhagic stroke, the prevalence of brainstem hemorrhage was only 7%. In the previous study, the prevalence of brainstem hemorrhage was 4,6%. [5] Other studies that focused on pontine hemorrhage pointed-out that the prevalence was 11,5% among 881 patients with pontine hemorrhage and 10% among intracerebral hemorrhage patients.[15,16]

Although rarely encountered, the mortality rate of brainstem hemorrhage was very high. The mortality rate in our study was 60%. This result was in line with other studies that looked at the mortality rate of brainstem hemorrhage and almost have the same results.[9,10,11] The reason of higher mortality rate of those cases was the damage in the brainstem that depressed consciousness level and, damage the cardiovascular system, as well respiratory system.[17,18]

In our study, most of the patients were male. According to a previous study, the male patient had a higher risk of brainstem hemorrhage.[5,9,19] Regarding age, this study pointed that the mean age was 47,40±11,45. According to Dinsdale, pontine hemorrhage occurred from 40–60 years old.[20] Older age was also determined as a risk factor in brainstem hemorrhage and related to poor outcomes.[5,19]

The mean systolic and diastolic blood pressure on admission was 206,40±38,59 and 116,90±19,18. This result was in accordance to study, by Dziewas et al, that demonstrated that systolic blood pressure >180mmHg, correlated with poor outcome.[21] Another study that emphasized pontine hemorrhage also showed that systolic blood pressure >160 mmHg was significantly related to pontine hemorrhage related-death, whereas diastolic blood pressure >100 mmHg was marginally related with pontine hemorrhage-related death.[10] These findings were also consistent with a previous study which explained that hypertension was the risk factor of brainstem hemorrhage.[4,6]

The majority of patients who were admitted to the hospital had GCS 3–8 and the mean GCS was 6,90±3,66. Coma on admission occurred due to rapid destruction of the brainstem, specifically ascending reticular activating system in the upper third of the pontine tegmentum that caused by hemorrhage and the effects of acute hydrocephalus.[22] Our study found a correlation between low GCS and poor outcomes at discharge. Several authors have reported that lower GCS correlated with poor outcomes.[5,9,10,22,23]

High blood glucose level on admission was found in our study with the mean blood glucose level was 158,70±39,705. Hyperglycemia is determined as the risk factor for predicting the functional outcomes in brainstem hemorrhage. Fan et al also reported that increased blood glucose levels related to the poor outcome 90 days after diagnosed with brainstem hemorrhage.[14] According to an animal study, which conducted by Song et al, intracerebral hemorrhage followed by hyperglycemia can cause brain edema and cell death.[24]

Table 2: Correlation of characteristics and the outcome at discharge in patients with brainstem hemorrhage.

Characteristics	Total (n=10)	Outcome		p-value	Correlation coefficient (r)
		Good (n=2)	Poor (n=8)		
Sex				0,356	0,327
Male	6	2	5		
Female	4	0	3		
Age, years	47,40 ± 11,45			0,900	-0,046
<40	2	0	2		
40–49	3	1	2		
50–59	4	1	3		
60–69	0	0	0		
≥70	1	0	1		
Systolic blood pressure, mmHg	206,40 ± 38,59			0,489	-0,248
<120	0	0	0		
120–129	1	0	1		
130–139	0	0	0		
≥140	1	0	1		
≥180	8	2	6		
Diastolic blood pressure, mmHg	116,90 ± 19,18			0,691	-0,144
≤60	0	0	0		
<80	1	0	1		
80–89	0	0	0		
≥90	5	1	4		
≥120	4	1	3		
Glasgow Coma Scale	6,90 ± 3,66			0,005	0,807
13–15	1	1	0		
9–12	2	1	1		
3–8	7	0	7		
Blood glucose level, mg/dL	158,70 ± 39,705			0,779	0,102
<150	4	1	3		
≥150	6	1	5		
White blood cell count	16630 ± 6963,72			0,645	-0,167
Normal	1	0	1		
Leukocytosis	9	2	7		
Location				0,010	0,764
Pons	3	2	1		
Midbrain	0	0	0		
Pons and midbrain	7	0	7		
Pons and medulla oblongata	0	0	0		
Pons, midbrain and medulla oblongata	0	0	0		
Volume, cc	621,20 ± 6963,72			0,221	0,425
<5	2	1	1		
5–10	5	1	4		
10–15	3	0	3		
Intraventricular hemorrhage				0,356	-0,327
(+)	3	0	3		
(-)	7	2	5		
Hydrocephalus				0,060	-0,612
(+)	6	0	6		

Characteristics	Total (n=10)	Outcome		p-value	Correlation coefficient (r)
		Good (n=2)	Poor (n=8)		
(-)	4	2	2		
Extraventricular drainage				0,645	-0,167
(+)	1	0	1		
(-)	9	2	7		
Length of stay, days	2,50 ± 3,808			0,035	-0,667
< 7	9	1	8		
≥ 7	1	1	0		

Our study also found a high white blood cell count on admission. The mean white blood cell count was 16630 ± 6963,72. Some authors reported that higher white blood cell count in patients with intracerebral hemorrhage is related to poor outcomes such as a decrease of consciousness, hemorrhage expansion, and intraventricular hemorrhage. [25,26] However, leukocytosis was not the main factor for predicting the poor outcome in intracerebral hemorrhage patients, other factors were detrimental such as age, initial bleeding volume, and Glasgow coma scale scores on admission.[27].

Regarding the anatomical location of the brainstem, in this study hemorrhage occurred in the pons and midbrain in the majority of patients. Our study also showed that there was a correlation between hemorrhage that occurred in the pons and the midbrain and the poor outcome. Several authors reported that the expansion of hemorrhage beyond the pons was associated with a poor outcome.[10,28]

The majority of patients studied by Wijdicks and Louis also had a hemorrhage in the pons and midbrain.[28] Tao et al in their study of factors that influence the functional outcome in pontine hemorrhage patients undergoing surgery, also stated that the expansion to the rostrocaudal especially the midbrain was an independent factor that can predict the functional outcome within 3 months.[29]

Radiological findings such as hemorrhage volume were associated with the poor outcome in the previous study.[9,22] This study showed no correlation between hemorrhage volume and the outcomes. Extension to the ventricle rarely occurred in our study. Hydrocephalus occurred in most of the patients. Several studies found that acute hydrocephalus was associated with the survival outcome. [9,22] In the present study, the majority of patients didn't undergo extraventricular drainage even when hydrocephalus occurred in most patients. It happened because most of the patient's family didn't approve.

Length of stay (LOS) is defined as the time that the patient used to receive medical treatment in a hospital. According to Amiman, LOS in hemorrhagic stroke patients is longer than ischemic stroke.[30] However, in the present study, the mean LOS was 2,50±3,808 days and correlated with the poor outcomes. That was because the majority of patients who came was already in a terminal condition, thus patients died a few hours or 1 day after coming to the hospital.

Characteristics that were not correlated with the outcome of brainstem hemorrhage patients in this study were not fully referenced in clinical practice. The small sample size and the lack of sample variance in each characteristic group cause the possibility of a bias in this study.

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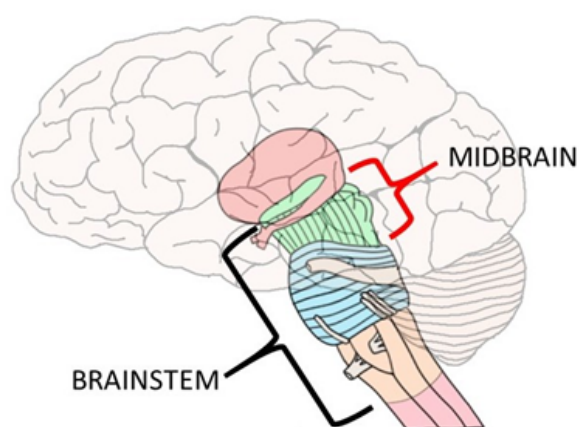
GRAPHICAL ABSTRACT

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This study aims to demonstrate the mortality rate of cases in a center in Indonesia's rural hospitals. To help reduce the mortality rate, the prognostic factors of several cases were studied.

Low prevalence of primary brainstem hemorrhage (7%). There were correlation between GCS score, brainstem hemorrhage location, and length of stay with the patient's prognosis