High cerebrospinal fluid pressure measured at first lumbar puncture and mortality in acute infectious encephalitis

SYSTEMATIC REVIEW

ORIGINAL ARTICLE BY

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ABSTRACT

OBJECTIVE

To identify the association between increased intracranial pressure and mortality in patients with acute encephalitis.

METHODS

We conducted a retrospective cohort study using the database from Khon Kaen Hospital, Thailand from January 2011 to May 2017 with preliminary diagnosis as acute infectious encephalitis undergoing lumbar puncture with measured open pressure. Mortality was our primary outcome.

RESULTS

From 291 patients with acute infectious encephalitis. From Cox regression model analysis, we found no significant association between high open pressure (more than or equal 27 cmH_2O) and mortality (hazard ratio (HR), 1.34; 95% confidence interval (CI), 0.79 to 2.28). Also, by using Kaplan-Meier survival analysis, there was no significant association between high open pressure and mortality (P=0.263). However, the incidence density of mortality significantly increased 1.02 times in each year of patient age (HR, 1.02; 95% CI, 1.01 to 1.04), and a subgroup analysis of various cut-point showed incidence density of mortality significantly increased 2.18 times in patients with open pressure more than or equal to 20 cmH2O (HR, 2.18; 95% CI, 1.29 to 3.70).

CONCLUSION

High cerebrospinal fluid open pressure was not associated with mortality of patients with acute infectious encephalitis.

INTRODUCTION

Encephalitis has its worldwide annual incidence of 0.07 to 12.6 cases per 100,000 population.[1] There were 3,777 cases of acute encephalitis per year in Thailand between 1993 to 1998.[2] The condition can increase intracranial pressure (ICP).[3,4] Consequently, this might affect the treatment outcomes. In patients with head injuries, we found that ICP more than 20 millimeters of mercury (mmHg) increased the mortality rate of the patient from 17% to 47%.[5] Moreover, the mortality rate increases 3.12 times per every 10 mmHg higher from the average ICP of 20 mmHg.[6] For patients with acute encephalitis, very few studies have defined the effects of ICP on mortality; a prospective cohort study in the US; 1988 in ten patients with acute viral encephalitis showed that six patients with ICP higher than 20 mmHg, five of whom died and four patients with ICP lower than 20 mm. Hg, all survived.[7] A later cohort study in Vietnam; in 2002 with 91 patients with acute viral encephalitis showed the same result that patients with increased ICP more than 25 cmH_2O had 8.69 times higher mortality rate.[8] However; the results of the two previous studies did not show a precise relationship between ICP and mortality in acute viral encephalitis patients because of their small sample sizes. We aimed to conduct a study with a larger sample size to ascertain the relationship between high ICP and the mortality of the patient with acute viral encephalitis as well as acute infectious encephalitis.

METHODS

STUDY DESIGN

We conducted a retrospective cohort study by reviewing medical records using the database of Khon Kaen Hospital, Thailand between January 2011 and May 2017. We used the recorded data to identify open pressure measured at first lumbar puncture (LP) and mortality as our primary outcome of the present study to ascertain the relationship between ICP and mortality. Khon Kaen Hospital is one of the largest tertiary health care facilities in Thailand that has more than 65,000 in-patients admitted annually between 2009 and 2016 and more than 650,000 outpatients visits between 2009 to 2016.[9]

PATIENTS

The medical records of the patients with the first visit of preliminary diagnosis of acute infectious encephalitis with ICD10 code including G04 and A80 to A89 and undergoing lumbar puncture (LP) were verified and reviewed. We excluded the medical records of the patients without data regarding open pressure after the first LP.

EXPOSURE

High open pressure defined as cerebrospinal fluid (CSF) open pressure more than or equal to 27 cmH_2O from the first LP was identified as the exposure of the current study collected by reviewing the medical record of the patients.

OUTCOMES

The primary outcome was the mortality of patients identified by reviewing the medical records and searching the database of Civil registration where appropriate. The secondary outcomes were neurological complications of the patients in the admission; classified into four groups (i) severe impairment defined as patients with quadriparesis i.e., gross flaccid paralysis of all limbs and trunk in one patient, (ii) moderate impairment defined as patients develop seizure and status epilepticus

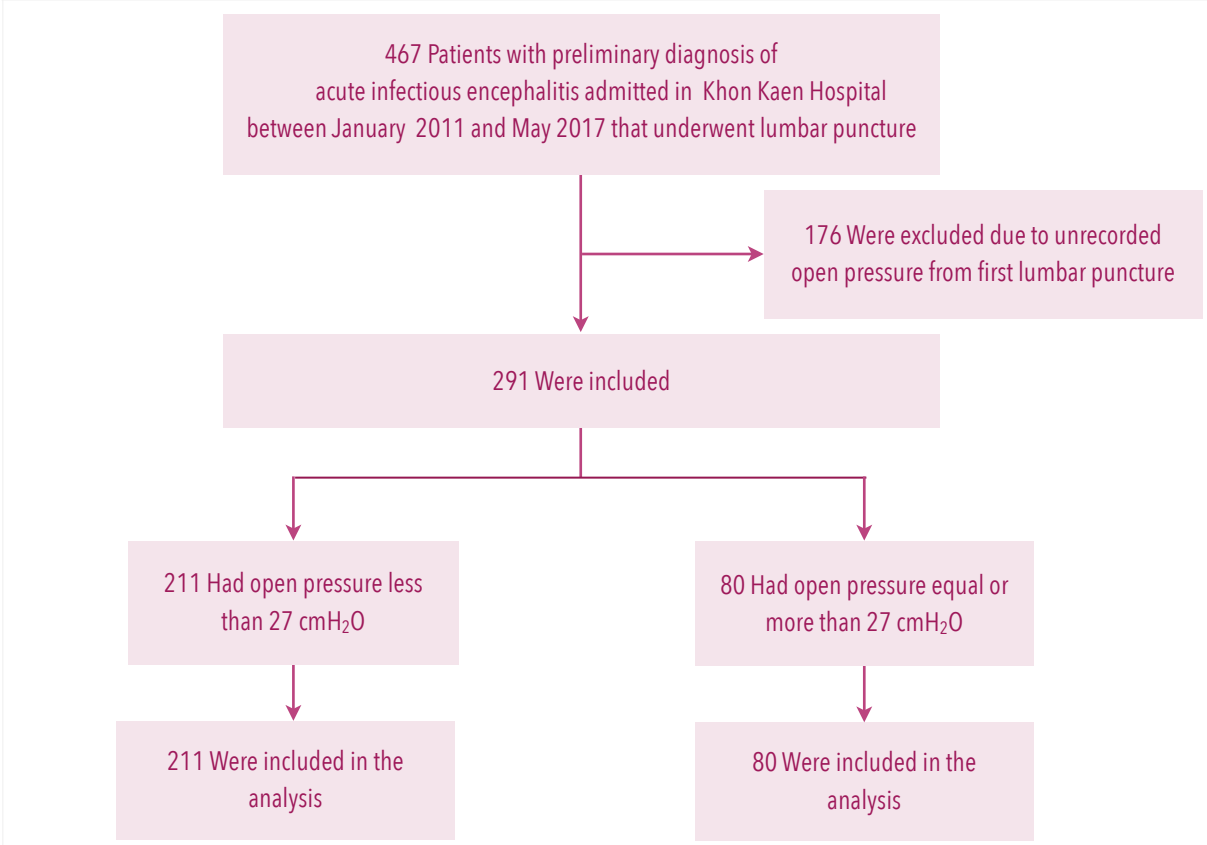

Figure 1. The patients flow in the analysis

after admission or paraparesis i.e., weakness of lower limb of the body defined as motor power between grade two and three according to medical research council scale or hemiparesis i.e., weakness on one side of the body defined as motor power between grade two and three according to medical research council scale or diplegia i.e., gross flaccid paralysis of two limbs defined as motor power grade zero or grade one according to medical research council scale or monoplegia i.e., gross flaccid paralysis of one limb defined as motor power grade zero or grade one according to medical research council scale that reduce functional score lower than three, (iii) mild impairment defined as patients with diparesis i.e., weakness on two limb of the body defined as motor power between grade two and three according to medical research council scale or monoparesis i.e., weakness on one limb of the body defined as motor power between grade two and three according to medical research council scale or other neurological deficit that functional score greater than or equal to three, and (iv) patients who fully recovery. The other secondary outcomes were cardiac arrest i.e., having the evidence of cardiopulmonary resuscitation (CPR) in medical records, admission to the intensive care unit (ICU), developing of nosocomial infection i.e., an infection that occurred after 48 hours after admission ,and use of a mechanical ventilator, length of ICU stay in days, length of hospital stay in days.

DATA COLLECTION

The other variables collected in the present study included age, sex, the present of altered mental

Table 1. Characteristics of patients

Characteristics	Systemic Corticosteroid (N = 211)	Non Systemic Corticosteroid (N = 80)	P Value
Age -yr			0.02
Median	54.9	44.8	
Interquartile range	27.1–67.9	25.9–57.5	
Male sex–no. (%)	114 (54.0)	51 (63.7)	0.14
Altered mental status–no. (%)	184 (87.2)	68 (85.0)	0.62
New onset of seizure–no. (%)	64 (30.3)	20 (25.0)	0.37
New onset of Status epilepticus–no. (%)	21 (10.0)	8 (10.0)	0.99
History of seizure–no. (%)	14 (6.6)	3 (3.8)	0.42
Comorbidities–no. (%)			
Diabetes mellitus	51 (24.4)	8 (10.0)	0.01
Hypertension	53 (25.4)	13 (16.3)	0.10
HIV infection	11 (5.3)	4 (5.0)	1.00
Tuberculosis infection	8 (3.8)	2 (2.5)	0.73
Gouty arthritis	8 (3.8)	2 (2.5)	0.73
Cirrhosis	2 (1.0)	4 (5.0)	0.05
Vital sign			
Body temperature-degree celsius			0.13
Median	37.5	37.9	
Interquartile range	36.8–38.4	37.0--38.5	
Pulse rate-beat per minute			0.34
Median	99	100	
Interquartile range	84–112	90-116	
Systolic blood pressure-mmHg			0.90
Median	128	126	
Interquartile range	115–149	115–154	
Diastolic blood pressure-mmHg			0.04
Median	74	79	
Interquartile range	66–85	68.5–90.8	

Table 1. (continued)

Characteristics	Systemic Corticosteroid (N=211)	Non Systemic Corticosteroid (N=80)	P Value
Cranial nerve defects–no. (%)	18 (8.7)	5 (6.5)	0.55
Positive upper motor neuron sign–no. (%)	32 (15.7)	10 (13.3)	0.63
Focal neurological deficit–no. (%)			
Quadriparesis–no. (%)	27 (13.8)	10 (13.0)	0.86
Hemiparesis–no. (%)	12 (6.1)	2 (2.6)	0.36
Paraparesis–no. (%)	5 (2.6)	0	0.33
Glasgow coma scale			0.07
Median	11	10	
Interquartile range	8–14	7.5–13	
On mechanical ventilation on admission–no (%)	62 (29.4)	30 (37.5)	0.18
Thrombocytopenia–no. (%)	18 (9.2)	9 (12.7)	0.41
Serum sodium level–mmol/dl			0.57
Median	136	135.5	
Interquartile range	132–140	131–139	

status, new onset of a seizure, new onset of status epilepticus, history of seizure, comorbidities i.e. history of diabetes mellitus, hypertension, human immunodeficiency virus (HIV) infection, Mycobacterium tuberculosis (TB) infection, gouty arthritis, cirrhosis. Also, a body temperature, pulse rate, systolic blood pressure, diastolic blood pressure, the presence of cranial nerve defects, quadriparesis, hemiparesis, paraparesis, positive upper motor neuron sign, Glasgow coma scale, on mechanical ventilation on admission, thrombocytopenia, and serum sodium were collected. Furthermore, the CSF profile of the patient and the treatment that patients receive after admission included CSF close pressure, CSF leukocyte count, CSF protein level, glucose CSF: blood ratio, CSF polymorphonuclear leukocyte (PMN) proportion, CSF lymphocyte proportion, administration of systemic corticosteroid, mannitol, antibiotic in the various group i.e. penicillin group, cephalosporin group, macrolide group, fluoroquinolone group, aminoglycoside group,

Table 2. Cerebrospinal fluid profile of acute infectious encephalitis patients in first lumbar puncture

Cerebrospinal fluid profile	Low open pressure (N=211)	High open pressure (N=80)	P Value
Closed pressure–cmH_2O*			<0.001
Median	14	26	
Interquartile range	10-18	22.5-30	
Leukocyte count-cells/μL			<0.001
Median	39.3	195	
Interquartile range	0-405	30-2,110	
Protein level-mg/dL			0.06
Median	91	139	
Interquartile range	43.3–279.9	52.7–378.6	
Glucose CSF:blood ratio <0.5–no. (%)	95 (53.1)	48 (68.6)	0.03
PMN proportion–no. (%)			<0.001
Median	20	90	
Interquartile range	0–90	17–96	
Lymphocyte cell proportion–no. (%)			0.27
Median	6.5	7	
Interquartile range	0–35.3	3–40	

* Closed pressure measured from first LP.

metronidazole, polymyxin group, glycopeptide group, lincosamide group, tetracycline group, carbapenem group were also collected. In addition to this, the data on the length of antibiotic use and acyclovir treatment were also collected in the present study.

STATISTICAL ANALYSIS

We compared the characteristics of the medical records of the included patients at the time of admission that could be potentially confounded to our primary and secondary outcomes. We divided the patients into two groups, a high open pressure

Table 3. Treatment that patients received after admission

Treatment	Low open pressure (N=211)	High open pressure (N=80)	P Value
Therapy of cerebral edema–no. (%)			
None	139 (65.9)	48 (60.0)	0.35
Systemic corticosteroid	62 (29.4)	28 (35.0)	0.36
Mannitol	23 (10.9)	9 (11.3)	0.93
Antibiotic use–no. (%)	203 (96.2)	79 (98.8)	0.45
Penicillin group	99 (46.9)	42 (52.5)	0.40
Cephalosporin group	186 (88.2)	74 (92.5)	0.28
Macrolide group	19 (9.0)	4 (5.0)	0.26
Fluoroquinolone group	9 (4.3)	2 (2.5)	0.73
Aminoglycoside group	3 (1.4)	0	0.56
Metronidazole	11 (5.2)	7 (8.8)	0.28
Polymyxin group	17 (8.1)	8 (10.0)	0.60
Glycopeptide group	39 (18.5)	15 (18.8)	0.96
Lincosamide group	18 (8.5)	10 (12.5)	0.31
Tetracycline group	15 (7.1)	8 (10.0)	0.41
Carbapenem group	60 (28.4)	26 (32.5)	0.50
Length of antibiotic use–day			0.50
Median	9	7	
Interquartile range	4-14	3-14	
Acyclovir treatment–no. (%)	83 (39.3)	25 (31.3)	0.20

group i.e., open pressure exceeds 27 cmH_2O, and a lower open pressure group i.e., open pressure does not exceed 27 cmH_2O. We used descriptive statistics to summarize the characteristics of the patients in each group; using numbers with percentages for the categorical variables, using

Table 4. Outcomes of the treatment

Outcome	Low open pressure (N=211)	High open pressure (N=80)	Relative risk (95% CI)	Mean difference (95% CI)
Primary outcome				
Death–no. (%)	71 (33.6)	33 (41.3)	1.23 (0.89–1.69)	
Secondary outcome				
Cardiac arrest–no. (%)	24 (11.4)	15 (18.8)	1.65 (0.91–2.98)	
Neurological complication–no. (%)				
Severe impairment	2 (0.9)	0		
Moderate impairment	48 (22.7)	16 (20.0)	0.88 (0.53–1.46)	
Mild impairment	1 (0.5)	1 (1.3)	2.64 (0.17–41.67)	
Fully recovery	160 (75.8)	63 (78.8)	1.04 (0.91–1.19)	
ICU admission–no. (%)	27 (12.8)	19 (23.8)	1.86 (1.10–3.15)	
Developing of nosocomial infection–no. (%)	61 (28.9)	31 (38.8)	1.34 (0.95–1.90)	
Using of mechanical ventilation–no. (%)	118 (55.9)	55 (68.8)	1.23 (1.02–1.49)	
Length of the ICU stay–day				–4.22 (–17.53–9.09)
Median	5.9	5.4		
Interquartile range	3.9–12.8	2.5–10.6		
Length of Hospital stay–day				–1.07 (–4.30–2.17)
Median	6	6		
Interquartile range	3.0–12.9	3.4–10.7		

mean together with standard deviation (SD) for the normally distributed continuous variables, median with interquartile range (IQR) for non-normally distributed continuous variables. For inferential statistics, we use either Pearson's chi-squared test, Fisher's exact test, or Mann-Whitney U test which appropriate to compare the characteristic of the patients in the two groups. Also, we used relative risk (RR), crude odds ratio (COR) to compare the outcomes between the two groups. To identify the factors that might influence our primary outcome, we used binary logistic regression analysis and Cox proportional hazard regression together with an adjusted odds ratio (AOR) and hazard ratio (HR) with their 95% confidence intervals (95% CI), respectively. We also used a Kaplan-Meier plot to

demonstrate time against cumulative survival within 30 days of admission between the two groups.

RESULTS

CHARACTERISTIC OF PATIENTS

Between January 2011 and May 2017, 467 patients who were preliminarily diagnosed with acute infectious encephalitis admitted in Khon Kaen Hospital and underwent lumbar puncture. One hundred and seventy-six patients with no open pressure records were excluded. Finally, a total of 291 patients were included in the analyses, 211 patients who had the open pressure less than 27-centimeter water (cmH_2O) as the low open pressure group and 80 patients who had the open pressure equal or more than 27 cmH_2O as high open pressure group (Figure 1).

The characteristics between the low open pressure group and high open pressure group were different in terms of (i) age of patients (median 54.9 years in the lower group vs. 44.8 years in the higher group, P=0.02), (ii) patients with diabetes mellitus (24.4% vs. 10%; P=0.01), (iii) Diastolic blood pressure (median 74-millimeter mercury [mmHg] vs. 79 mmHg; P=0.04). There was no significant difference between the two groups in other characteristics (Table 1).

CSF profile between the two groups were significantly different in most of parameters except lymphocyte cell proportion was relatively similar; (i) closed pressure from first LP (median 14.0 cmH_2O. vs. 26.0 cmH_2O; P<0.001), (ii) leukocyte count from CSF (median 39.3 cell per microliter [cell/µL] vs. 195.0 cell/µL, P=<0.001), (iii) glucose CSF:blood ratio<0.5% (53.1% vs. 68.6%; P=0.03), (iv) PMN proportion from CSF (median 20 vs. 90; P<0.001) (Table 2). Treatments that patients received after admission between the two groups were all relatively similar (Table 3).

STUDY OUTCOMES

There was no significant difference in mortality rates between the high open pressure group and the low open pressure group (41.3% in high open pressure group vs. 33.6% in low open pressure group; RR, 1.23; 95% CI, 0.89 to 1.69). Also, other outcomes were relatively similar between the two groups. However, there was a significant difference in an increased risk of ICU admission 1.86 times (23.8% vs. 12.8%; RR, 1.86; 95% CI, 1.10 to 3.15) and increased risk of using mechanical ventilation 1.23 times in the high open pressure group (68.8% vs. 55.9%; RR, 1.23; 95% CI, 1.02 to 1.49) (Table 4).

FACTORS DETERMINE OUTCOME

From the crude analysis of the odds ratio; there was a small but significant increase in mortality rate every year older (COR, 1.03; 95% CI, 1.02 to 1.04) and every milligrams higher level of CSF protein (COR, 1.002; 95% CI, 1.001 to 1.003). Moreover, mortality rate significantly increase in patient with diabetes mellitus (COR, 2.43; 95% CI, 1.36 to 4.35), hypertension (COR, 3.30; 95% CI, 1.87 to 5.82), on mechanical ventilation on admission (COR, 2.12; 95% CI, 1.28 to 3.53), systemic corticosteroid use times (COR, 1.71; 95% CI, 1.03 to 2.85) and thrombocytopenia (COR, 2.58; 95% CI, 1.15 to 5.78). However, mortality rate decrease with higher Glasgow coma scale (GCS) (COR, 0.88; 95% CI, 0.82 to 0.95) and antiviral treatment (COR, 0.46; 95% CI, 0.27 to 0.78). On the contrary, high open pressure and other factors were not significantly associated with the mortality rate (Table 5).

From binary logistic regression model analysis; there was a significant increase in mortality rate in patients with high open pressure (AOR, 3.58; 95% CI, 1.10 to 11.68), systemic corticosteroid use (AOR, 3.15; 95% CI, 1.16 to 8.52), higher age (AOR, 1.04; 95% CI, 1.01 to 1.08), higher body temperature (AOR, 1.63; 95% CI, 1.02 to 2.60) and a higher level of CSF protein

Table 5. Multivariable analysis of factors associated with mortality in acute infectious encephalitis patient

Factor	Odds ratio (95% confidence interval)		Hazard ratio (95% confidence interval)
	Crude analysis	Adjusted analysis	
High open pressure	1.38 (0.82–2.35)	3.58 (1.10–11.68)	1.53 (0.91–2.57)
Age–yr	1.03 (1.02–1.04)	1.04 (1.01–1.08)	1.02 (1.01–1.04)
Male sex	0.55 (0.34–0.89)	0.40 (0.15–1.06)	0.52 (0.33–0.84)
Altered mental status	1.13 (0.55–2.31)	0.43 (0.09–2.00)	0.59 (0.29–1.22)
New onset of seizure	0.50 (0.28–0.88)	0.83 (0.23–2.94)	0.60 (0.32–1.11)
History of seizure	0.37 (0.10–1.31)	0.06 (0.001–5.58)	0.57 (0.13–2.52)
Diabetes mellitus	2.43 (1.36–4.35)	0.79 (0.21–2.90)	
Hypertension	3.30 (1.87–5.82)	2.05 (0.58–7.19)	
Body temperature–degree celsius	1.05 (0.85–1.30)	1.63 (1.02–2.60)	1.06 (0.85–1.31)
Pulse rate–beat per minute	1.003 (0.99–1.01)	1.02 (0.99–1.05)	1.00 (0.99–1.02)
Systolic blood pressure–mmHg	1.01 (1.00–1.02)	0.99 (0.97–1.02)	1.00 (0.99–1.01)
Diastolic blood pressure–mmHg	1.01 (1.00–1.03)	1.02 (0.98–1.07)	1.01 (0.99–1.03)
Glasgow coma scale	0.88 (0.82–0.95)	0.94 (0.76–1.16)	0.93 (0.84–1.03)
On mechanical ventilation on admission	2.12 (1.28–3.53)	0.47 (0.10–2.16)	1.50 (0.76–2.95)
Administration of corticosteroid	1.71 (1.03–2.85)	3.15 (1.16–8.52)	1.09 (0.67–1.78)
Acyclovir treatment use	0.46 (0.27–0.78)	0.71 (0.20–2.54)	1.07 (0.61–1.85)
CSF Leukocyte count–cells/μL	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)
CSF Protein level–mg/dL	1.002 (1.001–1.003)	1.004 (1.001–1.006)	1.001 (1.001–1.002)
CSF PMN proportion–%	1.01 (1.00–1.01)	0.99 (0.97–1.002)	
CSF Lymphocyte cell proportion–%	0.99 (0.98–1.00)	0.998 (0.98–1.01)	
CSF Thrombocytopenia	2.58 (1.15–5.78)	1.55 (0.36–6.72)	
Serum sodium level–mmol/dl	0.98 (0.95–1.01)	0.97 (0.92–1.02)	0.97 (0.95–1.00)

Table 6. Subgroup analysis of various cut-off point of open pressure

Cutpoint of open pressure (cmH_2O)	High open pressure patients	Death	Hazard ratio (95% confidence interval)
>20	150	65 (43.3)	2.18 (1.29–3.70)
>25	97	40 (41.2)	1.46 (0.88–2.43)
>30	63	27 (42.9)	1.64 (0.92–2.92)
>35	37	14 (37.8)	1.26 (0.59–2.70)
>40	21	9 (42.9)	1.40 (0.56–3.50)

(AOR, 1.004; 95% CI, 1.001 to 1.006). However, no other factors were significantly associated with the mortality rate (Table 5).

From Cox proportional hazard regression model analysis using the length of hospital stay within 30 days, the incidence density of mortality significantly increased 1.02 times in each year of patient age (HR, 1.02; 95% CI, 1.01 to 1.04) and slightly increased 1.001 times per milligram of CSF protein higher (HR, 1.001; 95% CI, 1.001 to 1.002). On the other hand, the incidence density of mortality decreased 0.52 times in male patients (HR, 1.02; 95% CI, 0.33 to 0.84). Nevertheless, high open pressure was not significantly associated with mortality congruently with the Kaplan-Meier plot (Figure 2). Also, other investigated factors were found not be significantly associated with mortality (Table 5).

SUBGROUP ANALYSIS

From Cox proportional hazard regression model analysis using various cutpoint of open pressure, the incidence density of mortality significantly increased 2.18 times in patients with open pressure more than or equal to 20 cmH_2O (HR, 2.18; 95% CI, 1.29 to 3.70). The results of other cutpoints of open pressure were similar between the two groups (Table 6).

DISCUSSION

MAIN FINDINGS

In this retrospective cohort study based on 291 patients with acute infectious encephalitis, we found no significant difference in mortality rate between those with or without high open pressure. Also, after additional adjustment still no significant association between high open pressure and incidence density of mortality. However, the incidence density of mortality rate significantly increases when the definition of high open pressure group change to CSF open pressure more than or equal to 20 cmH_2O.

COMPARISON WITH OTHER STUDIES

To our knowledge, there were two studies have defined the effects of ICP on mortality in patients with acute encephalitis.[7, 8] However, our findings contrast with the previous two studies.[7, 8] The first study in ten patients showed that four patients with an ICP less than 20 mmHg survived, whereas five of six patients with ICP higher than 20 mmHg died ($P<0.05$). But because of the small sample size, there were no inferential statistics to generalize the outcome to the population.[7] The second study found that patients with CSF open pressure greater than or equal to 25 cmH_2O had significant 8.69

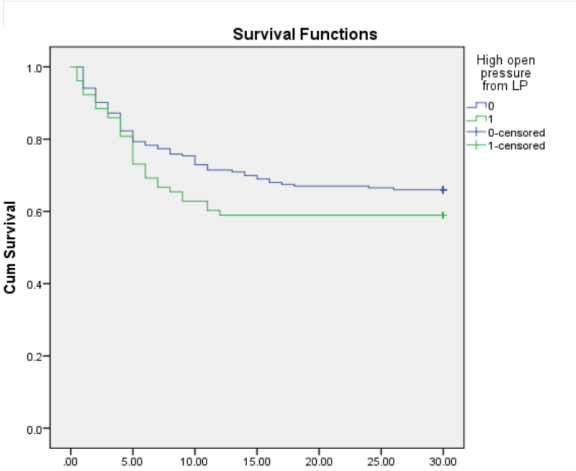

Figure 2. Kaplan-Meier comparing mortality in 30 days versus high open pressure record at first LP.

times higher mortality rate than those who were not. From our perspective, the difference in findings was because of the difference in the median age of patients in our study and the previous study. The median age of the patient in the previous study was 8 to 9 years old. However, in our study, the median age of patients was 54 years old in patients with CSF open pressure greater than or equal to 27 cmH_2O, and the median age of 44 years old in the other group. The difference in the median age of the patients in the two groups has the potential to affect the mortality rate in the two groups. Owing to the increase in age of patients also increases the mortality rate of patients with infectious disease.[26-28]

STRENGTHS AND LIMITATIONS OF STUDY

The strength of our study was the size of the database that we used. This is one of the world's largest databases of patients with encephalitis at the current period.

The limitations of the current study; first, the database that we used was from the medical records of the tertiary care unit that is a referral center. However, some of the patients may undergo LP from the primary or secondary care unit before. Thus; the open pressure we collected may not be the precise one to show the relationship between increased ICP and mortality. Second, there were many missing data in our medical records. As a result, it increased missing bias. Third, the methods of measurement ICP are varied because we were not able to standardize the method of measurement. Fourth, the difference of age in the two groups between the low open pressure group and high open pressure group.

CONCLUSION AND IMPLICATIONS

Our study showed that there was no relationship between high open pressure and mortality rate. However, our study still has the limitation in aspects of missing data and unstandardized measurement of open pressure resulting in missing bias and uncertain open pressure. Thus, further studies with adequate data and more accurate open pressure are required.

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REFERENCES

[1].Granerod J, Tam CC, Crowcroft NS, Davies NWS, Borchert M, Thomas SL. Challenge of the unknown. A systematic review of acute encephalitis in non-outbreak situations. Neurology. 2010 Sep 7;75(10):924–32.

[2].Henrich TJ, Hutchaleelaha S, Jiwariyavej V, Barbazan P, Nitatpattana N, Yoksan S, et al. Geographic dynamics of viral encephalitis in Thailand. Microbes Infect. 2003 Jun;5(7):603–11.

[3].Rebaud P, Berthier JC, Hartemann E, Floret D. Intracranial pressure in childhood central nervous system infections. Intensive Care Med. 1988;14(5):522–5.

[4].Marton, R., et al. "Acute herpes simplex encephalitis: clinical assessment and prognostic data." Acta neurologica scandinavica 93.2–3 (1996): 149-155

[5].Balestreri M, Czosnyka M, Hutchinson P, Steiner LA, Hiler M, Smielewski P, et al. Impact of intracranial pressure and cerebral perfusion pressure on severe disability and mortality after head injury. Neurocrit Care. 2006;4(1):8–13.

[6].Badri S, Chen J, Barber J, Temkin NR, Dikmen SS, Chesnut RM, et al. Mortality and long-term functional outcome associated with intracranial pressure after traumatic brain injury. Intensive Care Med. 2012 Nov;38(11):1800–9.

[7].Barnett GH, Ropper AH, Romeo J. Intracranial pressure and outcome in adult encephalitis. J Neurosurg. 1988 Apr;68(4):585–8.

[8].Solomon T, Dung NM, Kneen R, Thao LTT, Gainsborough M, Nisalak A, et al. Seizures and raised intracranial pressure in Vietnamese patients with Japanese encephalitis. Brain J Neurol. 2002 May;125(Pt5):1084–93.

[9]. Kkh.go.th. (2017). banner. [online] Available at: http://www.kkh.go.th/main.php [Accessed 25 Jun. 2017].

[10].Sonneville R, Mariotte E, Neuville M, Minaud S, Magalhaes E, Ruckly S, et al. Early-onset status epilepticus in patients with acute encephalitis. Medicine (Baltimore) [Internet]. 2016 Jul 29 [cited 2017 Jun 17];95(30).

[11].Modi S, Mahajan A, Dharaiya D, Varelas P, Mitsias P. Burden of herpes simplex virus encephalitis in the United States. J Neurol. 2017 Jun;264(6):1204–8.

[12].Whitley RJ, Soong SJ, Dolin R, Galasso GJ, Ch'ien LT, Alford CA. Adenine arabinoside therapy of biopsy-proved herpes simplex encephalitis. National Institute of Allergy and Infectious Diseases collaborative antiviral study. N Engl J Med. 1977 Aug 11;297(6):289–94.

[13].Whitley RJ, Soong SJ, Linneman C, Liu C, Pazin G, Alford CA. Herpes simplex encephalitis. Clinical Assessment. JAMA. 1982 Jan 15;247(3):317–20.

[14].Raschilas F, Wolff M, Delatour F, Chaffaut C, De Broucker T, Chevret S, et al. Outcome of and prognostic factors for herpes simplex encephalitis in adult patients: results of a multicenter study. Clin Infect Dis Off Publ Infect Dis Soc Am. 2002 Aug 1;35(3):254–60.

[15].Van Allen MW. Aids to the Examination of the Peripheral Nervous System. Arch Neurol. 1977;34(1):61. doi:10.1001/archneur.1977.00500130081027

[16].Poissy J, Champenois K, Dewilde A, Melliez H, Georges H, Senneville E, et al. Impact of Herpes simplex virus load and red blood cells in cerebrospinal fluid upon herpes simplex meningo-encephalitis outcome. BMC Infect Dis. 2012 Dec 18;12:356.

[17].Thakur KT, Motta M, Asemota AO, Kirsch HL, Benavides DR, Schneider EB, et al. Predictors of outcome in acute encephalitis. Neurology. 2013 Aug 27;81(9):793–800.

[18].Canalese J, Gimson AE, Davis C, Mellon PJ, Davis M, Williams R. Controlled trial of dexamethasone and mannitol for the cerebral oedema of fulminant hepatic failure. Gut. 1982 Jul;23(7):625–9.

[19].von Berenberg P, Unterberg A, Schneider GH, Lanksch WR. Treatment of traumatic brain edema by multiple doses of mannitol. Acta Neurochir Suppl (Wien). 1994;60:531–3.

[20].Gobiet W, Bock WJ, Liesegang J, Grote W. Treatment of Acute Cerebral Edema with High Dose of Dexamethasone. In: Intracranial Pressure III [Internet]. Springer, Berlin, Heidelberg; 1976 [cited 2017 Jun 17]. p. 231–5.

[21].McGrath N, Anderson NE, Croxson MC, Powell KF. Herpes simplex encephalitis treated with acyclovir: diagnosis and long term outcome. J Neurol Neurosurg Psychiatry. 1997 Sep;63(3):321–6.

[22].Misra UK, Kalita J. Seizures in encephalitis: Predictors and outcome. Seizure. 2009 Oct;18(8):583–7.

[23].Paternostro-Sluga T, Grim-Stieger M, Posch M, Schuhfried O, Vacariu G, Mittermaier C, et al. Reliability and validity of the Medical Research Council (MRC) scale and a modified scale for testing muscle strength in patients with radial palsy. J Rehabil Med. 2008 Aug;40(8):665–71.

[24].Kleyweg RP, van der Meché FG, Schmitz PI. Interobserver agreement in the assessment of muscle strength and functional abilities in Guillain-Barré syndrome. Muscle Nerve. 1991 Nov;14(11):1103–9.

[25].Whitley RJ, Soong SJ, Hirsch MS, Karchmer AW, Dolin R, Galasso G, et al. Herpes simplex encephalitis: vidarabine therapy and diagnostic problems. N Engl J Med. 1981 Feb 5;304(6):313–8.

[26]. Dimopoulos G, Koulenti D, Blot S, Sakr Y, Anzueto A, Spies C, Violán JS, Kett D, Armaganidis A, Martin C, Vincent JL. Critically ill elderly adults with infection: analysis of the extended prevalence of infection in intensive care study. Journal of the American Geriatrics Society. 2013 Dec 1;61(12):2065-71.

[27]. Hak E, Bont J, Hoes AW, Verheij TJ. Prognostic factors for serious morbidity and mortality from community-acquired lower respiratory tract infections among the elderly in primary care. Family practice. 2005 Apr 1;22(4):375-80.

[28]. Reunes S, Rombaut V, Vogelaers D, Brusselaers NE, Lizy CH, Cankurtaran M, Labeau S, Petrovic M, Blot S. Risk factors and mortality for nosocomial bloodstream infections in elderly patients. European journal of internal medicine. 2011 Oct 31;22(5):e39-44.