

Factors Associated with Severe Intracranial Pathology in Acute Non-Traumatic Headache Patients in the Emergency Department

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Background: Acute non-traumatic headache is a common condition in the emergency department (ED), and it is important that these patients are diagnosed appropriately. Failure to recognize the causes of a headache can have serious consequences, including permanent neurologic deficits, loss of vision, and death.

Objective: The present study aims to determine which factors were associated with severe intracranial pathology (SIP) in patients who presented at the ED with acute non-traumatic headache.

Materials and Methods: This was a cross-sectional, analytical study. The population was acute non-traumatic headache patients at the ED of Khon Kaen University's Srinagarind Hospital from January 1 to December 31, 2018. Data were collected by reviewing hospital information program, medical charts, and PACS. The outcomes were factors associated SIP in acute non-traumatic headache according to multiple logistic regression analysis and final diagnosis.

Results: The risk factors associated with SIP were Neck stiffness (OR 16.95, $p < 0.05$, 95% CI 2.60, 110.65), fever (OR 5.48, $p < 0.05$, 95% CI 1.42, 21.07), male (OR 5.25, $p < 0.05$, 95% CI 1.70, 16.26), history of hypertension (OR 4.03, $p < 0.05$, 95% CI 1.09, 14.86), and pain score of 7 to 10 (OR 2.36, $p < 0.05$, 95% CI 1.01, 5.51). The most common final diagnoses in SIP and Non-SIP patients were vascular causes and primary headache, respectively.

Conclusion: Neck stiffness was the most important factor associated with severe intracranial pathology. Physicians should extend their information gathering with regard to this factor in order to catch more effectively life-threatening conditions.

Keywords: Acute non-traumatic headache, Severe intracranial pathology, Emergency department

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Acute non-traumatic headache is one of the most common symptoms encountered in the emergency department (ED), with an incidence of around 1 to 31% in the United States⁽¹⁾. It is a symptom that is found in patients of all ages, but occurs more often in females more than males^(2,3). Around 96% of the general population will suffer from headaches during their lives⁽⁴⁾. They can be caused by various pathologies, with symptom severity ranging from mild to severe, sometimes even resulting in death. Despite this, about half of the patients who come to the emergency room with acute headache do not receive a clear diagnosis⁽⁵⁾.

A study by Gilbert et al⁽²⁾ attempted to identify factors related to severe pathological conditions in acute non-traumatic headache patients in the United States from 1998 to 2008 and found that the top three statistically significant factors for intracranial pathologies were motor disturbance (adjusted OR 11.67, 95% CI 2.50, 54.49), speech disturbance

(adjusted OR 10.54, 95% CI 3.92, 28.30), and age 50 years or older (adjusted OR 7.26, 95% CI 4.24, 12.43). In addition, a study conducted between 2004 to 2006 in a Canadian radiology department by Wang et al⁽⁵⁾ found that 13.8% of significant symptoms were related to CT brain imaging abnormalities and that the top three factors associated with intracranial lesions were focal neurological deficit (adjusted OR 5.39, 95% CI 3.90, 7.47), history of malignancy (adjusted OR 4.11, 95% CI 2.28, 7.42), and altered mental status (adjusted OR 2.32, 95% CI 1.66, 3.25).

There have yet been no reports to clearly establish the relationship between factors or symptoms and intracranial pathology in Thailand. The objective of the present study was thus to identify factors associated with intracranial pathology in acute non-traumatic brain injury.

Materials and Methods

This was a cross-sectional analytical study. The sample consisted of 774 patients over 18 years of age who had been diagnosed with acute non-traumatic headache at the Srinagarind Hospital emergency department from January to December 2019. The exclusion criterion was incomplete medical data from the electronic medical chart program. Ethics approval was provided by the Khon Kaen University Ethics

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The sample size was calculated based on the method described by Gilbert et al⁽²⁾. In order to achieve a significance level of 5% and power of test of 0.8, we determined that a sample size of 704 would be required.

The primary outcome was factors associated with severe intracranial pathology in acute non-traumatic headache patients at the emergency department, and the secondary outcome was final diagnosis in these patients.

Statistical analysis was performed using SPSS for Windows version 17.0 (SPSS Inc., Chicago, IL, USA). Categorical data were presented as percentages, and continuous data were presented using mean and standard deviation. Univariable analysis was performed using a two-sample t-test for numerical data and a Pearson's correlation and Fisher's exact test for data relationships between the two groups.

Results

Seven hundred seventy-four subjects were examined, 76 and 698 of whom had severe intracranial lesions

(SIP group) and no brain pathology (Non-SIP group), respectively. The mean age of the SIP group and Non-SIP group was 50.24 ± 15.96 and 40.05 ± 18.99 years, respectively. Most patients (64.62%) in the SIP group were older than 50 years and more were male (52.63%) than female (47.37%). In the non-SIP group, there were more females (69.48%) more than males (30.52%). The pain severity score ranged from 1 to 10 points on a Likert scale. Data were collected from 773 people. Most patients in the SIP group had pain scores greater than 7 points (92%). In terms of co-morbid disease, the percentage of patients with chronic hypertension in the SIP group and Non-SIP group was 41.94% and 15.19%, respectively. Most patients had GCS levels of 15 in both groups, but there were 9 (11.84%) in the SIP group with lower GCS levels. Physical examination did not show any signs of focal neurological deficit in any of the patients in the non-SIP group. Neck stiffness was reported in 4 patients (0.57%) in the non-SIP group and 26 (34.67%) in the SIP group (Table 1).

Five of the 14 studied factors were found to be associated with SIP according to Multivariate analysis: Neck

Table 1. Characteristics of the subjects (%)

Patient characteristics (n = 774)	Non-SIP (n = 698)	SIP (n = 76)	p-value
Age (years)			
18-49	482 (67.98)	23 (35.38)	<0.001*
>50	227 (32.02)	42 (64.62)	
Sex			
Male	213 (30.52)	40 (52.63)	0.003*
Female	485 (69.48)	36 (47.37)	
Pain score (n = 773)			
1 to 3	63 (8.15)	0 (0.00)	<0.001*
4 to 6	356 (46.05)	6 (8.00)	
7 to 10	354 (45.80)	69 (92.00)	
Duration			
<1 hour	26 (3.73)	4 (5.26)	0.799
>1 to 24 hour	322 (46.13)	34 (44.74)	
Past medical illness			
Hypertension	106 (15.19)	13 (41.94)	<0.001*
Other diseases	237 (33.95)	27 (35.53)	
Present illness			
History of loss of conscious before arrival	0 (0.00)	9 (11.84)	<0.001*
History anticoagulant or antiplatelet drug use	15 (2.15)	4 (5.33)	0.103
Vertigo/dizziness	35 (5.04)	5 (6.58)	0.58
Fever	62 (8.88)	9 (11.84)	0.396
Seizure	0 (0.00)	4 (5.26)	<0.001*
Physical examination			
Systolic blood pressure			
<160	620 (88.83)	62 (81.58)	0.064
≥160	78 (11.17)	14 (18.42)	
GCS			
15	696 (99.71)	63 (82.90)	<0.001*
13 to 14	2 (0.29)	4 (5.26)	
<13	0 (0.00)	9 (11.84)	
Focal neurological deficit	0 (0.00)	15 (1.94)	<0.001*
Neck stiffness	4 (0.57)	26 (34.67)	<0.001*

* Statistically significant

stiffness, fever, sex, history of hypertension, and pain score. The top three factors that affected the SIP group were neck stiffness (OR 16.95, $p < 0.05$, 95% CI 2.60, 110.65), fever (OR 5.48, $p < 0.05$, 95% CI 1.42, 21.07), and male sex (OR 5.25, $p < 0.05$, 95% CI 1.70, 16.26; Table 2).

Subarachnoid hemorrhage was the most common final diagnosis in the SIP group, followed by meningitis, and neoplasm of the brain. In the non-SIP group, the most common final diagnosis was tension-type headache (Table 3).

Discussion

The present study found that neck stiffness was the most significant factor associated with intracranial lesions in acute non-traumatic headache patients. This is consistent with the results of a study conducted in 34 emergency rooms across Australia by Chu et al⁽³⁾, which found neck stiffness in 4.8% of patients, a 79,811 times higher rate than that of intracranial hemorrhage or bacterial meningitis. Moreover, studies by Perry et al⁽⁶⁾ and Kimura et al⁽⁷⁾ found that neck stiffness was associated with subarachnoid hemorrhage. However, a study by Gilbert

et al⁽²⁾ found that neck stiffness was not associated with intracranial lesions.

The second factor, fever, is the most common symptom of meningitis in bacterial, viral and fungal infection. In this study, patients in the SIP group were 5.48 times more likely to suffer from fever than those in the non-SIP group. The most common final diagnosis of patients with fever in the SIP group was intracranial infection group. This contrasts with the results of the study by Chu et al mentioned above⁽³⁾, which found that fever was not associated with intracranial hemorrhage or bacterial meningitis.

The authors also found that patients in the SIP group were 5.25 times more likely to be male than those in the non-SIP group, which was consistent with the results of Gilbert et al⁽²⁾ and Chu et al⁽³⁾. Male patients were 1.56 times more likely to suffer from intracranial pathology 1,234 times more likely to exhibit intracranial hemorrhage or bacterial meningitis. However, a study by Perry et al⁽⁶⁾ found no correlation between sex and subarachnoid hemorrhage.

The most common final diagnosis in the SIP group

Table 2. Multiple logistic regression of factors associated with SIP

Factors	Adjusted odds ratio	p-value	95% CI
Age (year)			
≥50	1.77	0.375	0.50, 6.27
18 to 49	1.00 (reference)		
Sex			
Male	5.25	0.004*	1.70, 16.26
Female	1.0 (reference)		
Pain score			
7 to 10	2.36	<0.01*	1.01, 5.51
4 to 6	0.05		
1 to 3	1.0 (reference)		
Past medical history			
Hypertension			
Yes	4.03	0.036	1.09, 14.86
No	1.0 (reference)		
Present illness			
History of anticoagulant or antiplatelet use			
Yes	3.95	0.276	0.33, 46.70
No	1.0 (reference)		
Fever			
Yes	5.48	0.013*	1.42, 21.07
No	1.0 (reference)		
Physical examination			
SBP			
≥160 mmHg	0.37	0.363	0.043, 3.16
<160 mmHg	1.0 (reference)		
GCS			
13 to 14	15.07	0.060	0.89, 253.92
15	1.0 (reference)		
Neck stiffness			
Yes	16.95	0.003	2.60, 110.65
No	1.0 (reference)		

* Statistical significance

Table 3. Final diagnosis

Final diagnosis	n = 774 (%)
Non-SIP	698 (90.18)
Primary headache	482 (62.27)
Tension headache	186 (24.03)
Migraine	112 (14.47)
Cluster headache	13 (1.68)
Unspecified headache	171 (22.09)
Other diagnosis	216 (27.91)
SIP	76 (9.82)
Vascular cause	61 (7.88)
Subarachnoid hemorrhage (SAH)	32 (4.13)
Subdural hemorrhage	5 (0.65)
Epidural hemorrhage	1 (0.13)
Ruptured arteriovenous malformation	5 (0.65)
Non-ruptured arteriovenous malformation	2 (0.26)
Ruptured aneurysm	4 (0.52)
Intracerebral hemorrhage	4 (0.52)
Ischemic stroke	8 (1.03)
Intracranial infection	8 (1.03)
Meningitis	6 (0.77)
Encephalitis	1 (0.13)
Brain abscess	1 (0.13)
Neoplasm of the brain	7 (0.90)
Primary brain tumor	5 (0.65)
Brain metastasis	2 (0.26)

was subarachnoid hemorrhage (4.13%). This is consistent with the results of a study conducted by Kimura et al⁽⁷⁾ in the emergency rooms of 5 institutions in Japan, which found that 1,561 patients who presented with acute non-traumatic headache were diagnosed with subarachnoid hemorrhage, accounting for 17.7 percent of all diagnoses. We found that tension-type headache was the most common final diagnosis in the non-SIP group, which is consistent with the findings of a previous study conducted in Chiang Mai Neurological⁽⁸⁾. One possible limitation in this study is that some conditions may not be studied such as hypertensive crises or obstructive sleep apnea^(9,10).

Conclusion

The present study found that neck stiffness on examination, fever, and male sex were factors associated with intracranial pathology in acute non-traumatic headache patients at the ED. The most common final diagnoses in SIP group and non-SIP group were subarachnoid hemorrhage and tension headache, respectively.

What is already known on this topic?

Acute non traumatic headache is a common problem in the ED. Recent studies have shown various factors that are associated with acute non-traumatic headache. However, no clear results have been found with regard to this topic in Thailand.

What this study adds?

Neck stiffness, fever, and male were associated with intracranial pathology in acute non-traumatic headache.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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ปัจจัยที่สัมพันธ์กับพยาธิสภาพรุนแรงภายในกะโหลกศีรษะของผู้ป่วยปวดศีรษะเฉียบพลันที่ไม่ได้รับอุบัติเหตุในแผนกฉุกเฉิน

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ภูมิหลัง: ภาวะปวดศีรษะเฉียบพลันที่ไม่ได้รับอุบัติเหตุเป็นภาวะที่พบได้บ่อยในแผนกฉุกเฉิน และโรคนี้มีความสำคัญที่ผู้ป่วยควรได้รับการวินิจฉัยอย่างเหมาะสม การวินิจฉัยสาเหตุของอาการปวดศีรษะผิดพลาดนำไปสู่ภาวะแทรกซ้อน รวมไปถึงความผิดปกติทางระบบประสาทอย่างถาวร การสูญเสียการมองเห็น และเสียชีวิต

วัตถุประสงค์: เพื่อระบุปัจจัยที่มีความสัมพันธ์กับพยาธิสภาพที่รุนแรงภายในกะโหลกศีรษะในผู้ป่วยที่มาที่แผนกฉุกเฉินด้วยอาการ ปวดศีรษะเฉียบพลันที่ไม่ได้เกิดจากอุบัติเหตุ

วัสดุและวิธีการ: เป็นการศึกษาย้อนหลังเชิงวิเคราะห์ ประชากรศึกษา คือ ผู้ป่วยปวดศีรษะเฉียบพลันที่ไม่ได้เกิดจากอุบัติเหตุที่ห้องฉุกเฉิน โรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น ระหว่าง วันที่ 1 มกราคม พ.ศ. 2561 ถึง วันที่ 31 ธันวาคม พ.ศ. 2561 โดยเก็บข้อมูลจากระบบบันทึกข้อมูลผู้ป่วย ในโรงพยาบาล เวชระเบียนผู้ป่วยและ PACS ผลลัพธ์คือ การระบุปัจจัยที่สัมพันธ์กับพยาธิสภาพที่รุนแรงภายในกะโหลกศีรษะในผู้ป่วยปวดศีรษะที่ไม่ได้เกิดจากอุบัติเหตุโดยใช้วิธีการวิเคราะห์แบบถดถอยพหุโลจิสติกส์ และระบุการวินิจฉัยสุดท้ายในผู้ป่วยเหล่านี้

ผลการศึกษา: ปัจจัยที่มีความสัมพันธ์กับพยาธิสภาพที่รุนแรงในกะโหลกศีรษะ คือ positive stiff neck (OR 16.95, $p<0.05$, 95% CI 2.60, 110.65) ไข้ (OR 5.48, $p<0.05$, 95% CI 1.42, 21.07) เพศชาย (OR 5.25, $p<0.05$, 95% CI 1.70, 16.26) ประวัติโรคประจำตัวความดันโลหิตสูง (OR 4.03, $p<0.05$, 95% CI 1.09, 14.86) และระดับความปวดที่คะแนน 7 ถึง 10 (OR 2.36, $p<0.05$, 95% CI 1.01, 5.51) การวินิจฉัยสุดท้ายมากที่สุดในกลุ่มผู้ป่วย SIP และ Non-SIP คือ สาเหตุจากหลอดเลือดสมอง และการปวดศีรษะปฐมภูมิ ตามลำดับ

สรุป: ผลทดสอบอาการคอแข็งเป็นบวก เป็นปัจจัยที่สำคัญที่สุดที่สัมพันธ์กับพยาธิสภาพรุนแรงในกะโหลกศีรษะ แพทย์ควรเก็บข้อมูลเพิ่มเติมเกี่ยวกับปัจจัยที่ศึกษาเหล่านี้เพื่อที่จะไม่พลาดภาวะที่มีผลต่อชีวิต
