

## Abstract

**Background:** Ischemic stroke is the first cause of death in women and the third in men, in Thailand. Treatments depend on the time of the onset and available penumbra imaging assessment, to best preserve the brain functions. And besides weakness, disability in stroke patients, dysphagia is also common. Dysphagia is a factor to develop pneumonia as well. Both disease complications and other infections during admission can prolong the length of stay.

**Objective:** To find the incidence and associated factors of pneumonia in ischemic stroke patients in Rajavithi stroke unit

**Methods:** This epidemiological study was conducted based on a retrospective cohort of ischemic stroke patients, admitted to Rajavithi stroke unit from September 1<sup>st</sup>, 2019 to August 31<sup>st</sup>, 2020. Ischemic stroke severity was given with NIHSS (National Institutes of Health Stroke Scale) by the first neurologist who exposed the patient. Pneumonia was diagnosed by the Modified CDC criteria.

**Results:** From 149 patients, there are 19 (12.8%) patients with dysphagia, and 8 patients (5.4%) with pneumonia during the admission. From the demographic data, 60 patients have diabetes mellitus as a comorbid. We found the relationship between dysphagia and diabetes mellitus with pneumonia, with the statistically significant p-value at 0.022 and 0.018 respectively.

**Conclusion:** The associated factor with pneumonia is diabetes mellitus. The disease-related factor is dysphagia without clinical severity related. Dysphagia and diabetes mellitus should be evaluated and properly managed for pneumonia prevention or decrease severity. This study does not provide enough data on clinically related factors to find more relationships with pneumonia.

**Keywords:** Stroke associated pneumonia, Dysphagia, Ischemic stroke, Respiratory tract infections

# Incidence of Pneumonia and Associated Factors in Ischemic Stroke Patient Admitted in Rajavithi Stroke Unit

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## Introduction

Ischemic stroke is one of the common diseases, the first cause of death in women and the third in men, in Thailand. The disease also extends the period of hospital stay to 2.75 times, as recorded from 1997. 10% of the patients with ischemic stroke die and 50-60% leaves the hospital with a disability. In this high medical innovation era, the patients are still confounded to the 4.5 hours golden period counting from the first symptoms to hospital arrival. To preserve the penumbra, the thrombolytic agent will be given or mechanical thrombectomy will be performed as indicated. Somehow some patients do not respond to the specific treatment or arrived at a hospital later than the golden period, which may result in a higher tendency of disability. Despite the weakness, the most common disability, dysphagia, also has affected their quality of life.

Arnold et al. finds, patient with dysphagia has an average of NIHSS at  $9.8 \pm 7.02$  which is a risk factor of stroke associated pneumonia and aspirated pneumonia. Patient with ischemic stroke also has a comorbid underlying disease such as hypertension, diabetes mellitus, dyslipidemia, etc. Smoking also increases the severity of pneumonia, which increases the length of hospital stay, mortality, and disability.

It is known that developing pneumonia in the first week of stroke is multifactorial and dysphagia is also one. Dysphagia presented in 58.5% of the admissions, in the study of Emily et al. respiratory infections developed in 17% of the patients with dysphagia.<sup>1</sup> As the speaks of dysphagia, it is frequently found in the patients with a moderate to severe National Institutes of Health Stroke Scale (NIHSS). Because dysarthria can score 1-2 points in NIHSS, and dysphagia may be involved in dysarthria. The NIHSS can score from 0 to 5 points (NIHSS 0-4 = 0, 5-15=3,  $\geq 16=5$ ).

Other than NIHSS, the A2DS2 score was presented as a predictor for stroke-associated pneumonia. The A2DS2 score includes age, atrial fibrillation, dysphagia, sex, and NIHSS. The research from Sarah et al shows that the proportion of pneumonia and A2DS2 score is varied between 0.3% in patients with a score of 0 points with 39.4% in patients with a score of 10 points.<sup>2</sup>

Therefore it is expected that the more severe of the disease, by NIHSS or A2DS2 score, the more incidence of pneumonia. It also aims to find the relationships of stroke associated pneumonia and other associated variables in patients admitted in Rajavithi stroke unit. With the expectation that by knowing or be able to predict the incidence of pneumonia. We could prevent or decrease pneumonia incidence and may reduce the length of hospital stay and disability.

## Subjects and Methods

### 1. Data collections

Data were randomly collected in even numbers, from 304 ischemic stroke patients admitted in Rajavithi stroke unit, from the September 1<sup>st</sup>, 2019 to August 31<sup>st</sup>, 2020. Therefore, with the inclusion and exclusion criteria, there were 149 patients to be involved.

### 2. Investigated factors

**Demographic data:** gender, age, underlying diseases, and a risk factor of atherosclerosis which is smoking.

**Stroke associated data:** NIHSS, the onset of disease, dysphagia, and A2DS2 score at the arrival.

**Specific treatment:** thrombolytic agents, in patients who arrived at the hospital in the golden period and had no contraindications for the treatment.

### 3. Study population

It retrospectively analyzed 149 patients with the diagnosis of ischemic stroke by a neurologist and admitted them for more than 3 days in Rajavithi stroke unit from September 1<sup>st</sup>, 2019 to August 31<sup>st</sup>, 2020. This study excluded the patients who were intubated at the Emergency Department, history of the previous stroke with a current nasogastric tube feeding, an underlying of asthma, a chronic lung disease which is undergoing treatment, or died during the admission.

Demographic data from 149 ischemic stroke patients, age ranged from 26 to 91 years old, where the mean age is 60.15 ( $\pm$ 13.86) years old. There were 71 females (47.7%) and 78 males (52.3%). Hypertension was the most common comorbidity in this study, presented in 96 patients which are 64.4%. Followed by diabetes mellitus, 62 patients counted as 41.6%. For the first-hand smoker, there were 21 patients which are 14.1%.

The onset of ischemic stroke ranged from 3 minutes to 10 days, where the mean is 18.32 ( $\pm$ 32.42) hours. The NIHSS during the arrival ranged from 0 to 23, where the mean is 5.75 ( $\pm$ 4.72) score.

19 patients (12.8%) had dysphagia and required oromotor rehabilitation. For the A2DS2 score of 10, ranging from 0 to 9, mean 2.65 ( $\pm$ 2.25).

Patients who arrived in the golden period, within 4.5 hours of onset, were indicated for thrombolytic agents. Without contraindications, there were 19 patients (12.8%) who received Alteplase as the specific treatment. 130 patients received the standard treatment for acute ischemic stroke included antiplatelet, intravenous hydration, and rehabilitation and swallowing evaluations.

### 4. Diagnosis of stroke-associated pneumonia<sup>3</sup>

Stroke-associated pneumonia (SAP) is diagnosed by the Modified Centers for Disease Control and Prevention (CDC) criteria, (Table 1):

#### Probable SAP:

All CDC criteria are met, but initial CXR and serial/repeat CXR nonconfirmatory (or not undertaken), and no alternative diagnosis or explanation

#### Definite SAP:

All CDC criteria are met, including diagnosis CXR changes (on the least one)

**Table 1** Recommended diagnostic criteria for definite and probable SAP in patients not receiving mechanical ventilation based on the CDC criteria

At least 1 of the followings:
1. Fever ( $> 38^{\circ}\text{C}$ ) with no other recognized cause
2. Leukopenia ( $< 4000 \text{ WBC/mm}^3$ ) or leukocytosis ( $> 12000 \text{ WBC/mm}^3$ )
3. For adults $\geq 70$ years old, altered mental status with no other recognized cause
And at least 2 of the followings:
1. New onset of purulent sputum, or change in character of sputum over a 24 hours period, or increased respiratory secretions, or increased suctioning requirements
2. New onset or worsening cough, or dyspnea, or tachypnea (respiratory rate $> 25/\text{min}$ )
3. Rales, crackles, or bronchial breath sounds
4. Worsening gas exchange (eg, $\text{O}_2$ desaturation [eg, $\text{Pa}_{\text{O}_2}/\text{FiO}_2 \leq 240$ ], increased oxygen requirements*)
And $\geq 2$ serial chest radiographs with at least 1 of the followings:
New or progressive and persistent infiltrate, consolidation, or cavitation
Note: In patients without underlying pulmonary or cardiac disease, 1 definitive chest radiograph is acceptable
Probable SAP: all CDC criteria are met, BUT initial CXR and serial/repeat CXR nonconfirmatory (or not undertaken), and no alternative diagnosis or explanation.
Definite SAP: ALL CDC criteria met, including diagnostic CXR changes (on at least one). CDC indicated Centers for Disease Control and Prevention; CXR, Chest x-ray; $\text{FiO}_2$ , fraction of inspired oxygen; $\text{Pa}_{\text{O}_2}$ , partial pressure oxygen; SAP, Stroke-associated pneumonia; and WBC, white blood cell.
*Category of increased ventilator demand removed.
†CDC recommendation is for repeat CXR at days $2\pm 7$ if initial CXR negative.

## 5. Statistical analysis

The correlation metric was used to investigate on the assumption of all of the variables. Therefore, the multiple hierarchical regressions with the remove technique were used to analyze the cause-effect relationships between the independent variables and the dependent variables. The independent variables in this study were demographic data, disease and treatment, and A2DS2 scoring. The dependent variables were the incidence of stroke-associated-pneumonia and length of hospital stay.

## Results

### Incidence of disease (Table 2)

Among randomly collected 149 patients were admitted to Rajavithi stroke unit from September 1<sup>st</sup>, 2019 to August 31<sup>st</sup>, 2020. The severity of ischemic

stroke at the arrival, NIHSS score, had been classified into 3 groups as in A2DS2 scoring. There are 0-4, 5-15, and  $\geq 16$  scores which are 76 (51.1%), 63 (42.3%), and 10 (6.7%) patients respectively. By the bedside swallowing examination and assigned for oromotor rehabilitation by a physician, there were 19 (12.8%) patients with dysphagia. Then there were 8 patients (5.4%) who were diagnosed and treated with pneumonia. There was one patient (0.7%) who was treated for 3 episodes of pneumonia, 2 patients (1.4%) had 2 episodes of pneumonia, and 5 patients (3.4%) with an episode of pneumonia. For the length of hospital stay, there were 36 (24.2%) patients who stayed longer than 7 days of the acute ischemic stroke period. And, 113 (75.8%) patients stayed in the hospital for less than 7 days.

Table 2 Data of the Patients on arrival

Characteristics	Number of patients (149)	Percentage
<b>Sex</b>		
Male	78	52.35
Female	71	47.65
<b>Underlying diseases</b>		
Hypertension	96	64.43
Diabetes mellitus	60	40.27
Atrial fibrillation	12	8.05
<b>Smoking</b>	21	14.09
<b>NIHSS</b>		
0-4 points	76	51.01
5-15 points	63	42.28
$\geq 16$ points	10	6.71
<b>Dysphagia</b>	19	12.75
<b>Length of hospital stay</b>		
$\leq 7$ days	113	75.84
$> 7$ days	36	24.16

The data were analyzed with the multiple regression methods, to find any relationship between all of the variables. By the correlation

metrics, the result showed only NIHSS and A2DS2 score has 0.829 ( $>0.8$ ) correlation coefficient. (Table 3)

Table 3 Data correlations

	Gender	Age	Smoking	DM	HT	AF	DLP	Stroke	Onset	Pneumonia	NIHSS	Dysphagia	A2DS2 score	Length of Stay
Gender	1	.223**	-.232**	0.067	0.091	0.014	0.104	-0.016	0.075	0.010	0.056	0.038	-0.115	0.145
Age		1	-.175*	0.109	.357**	.177*	.308**	.174*	0.059	0.044	0.003	0.114	0.134	0.089
Smoking			1	0.010	-0.142	0.122	-.233**	-0.020	-0.114	-0.087	-0.020	0.019	-0.014	-0.101
DM				1	.400**	-0.100	.218**	0.059	.183*	0.145	-0.057	0.085	0.016	0.013
HT					1	0.014	.263**	0.113	0.105	-0.027	-0.105	0.032	-0.016	-0.056
AF						1	.171*	0.094	-0.102	-0.063	0.147	0.109	.300**	0.006
DLP							1	.164*	0.114	-0.107	-0.062	0.000	0.035	-0.080
Stroke								1	.201*	0.028	0.055	0.080	0.029	0.061
Onset									1	-0.033	0.025	-0.024	0.033	-0.053
Pneumonia										1	.220**	.400**	.225**	.572*
NIHSS											1	.460*	.829**	.306**
Dysphagia												1	.536**	.463**
A2DS2 score													1	.333*
Length of Stay														1

\*\*Correlation is significant at the 0.01 level (2-tailed)

\*Correlation is significant at the 0.05 level (2-tailed)

#### Relationships of disease severity, A2DS2 scoring, specific treatment, and length of hospital stay with pneumonia (Table 4)

The R square test of the independent variable of disease severity; NIHSS, the onset of disease, dysphagia, A2DS2 score at the arrival, specific treatment and length of hospital stay, and pneumonia was statistically significant at p-value < 0.05 level (F = 11.606). With the multiple regression methods, only dysphagia and length of stay were statistically significant with p-value of 0.022 and < 0.001, respectively.

#### Relationships of demographic variables and smoking with pneumonia (Table 4)

The R square test of every independent variable; demographic data and smoking were statistically significant at p-value < 0.05 level (F = 6.682). Other than dysphagia and the length of hospital stay, diabetes mellitus was also significant with the p-value at 0.018.

Table 4 Results of the multiple regression, pneumonia as the dependent variable

	Sig. (p-value < 0.05)
<b>Disease associated factors</b>	
Onset of ischemic stroke	0.710
NIHSS	0.590
Dysphagia	0.022
A2DS2 score	0.323
Length of hospital stay	0.000
<b>Demographic data and smoking</b>	
Sex	0.123
Age	0.402
Hypertension	0.548
Diabetes Mellitus	0.018
Atrial fibrillation	0.609
Dyslipidemia	0.242
<b>Smoking</b>	<b>0.173</b>

#### Relationships of disease severity, A2DS2 scoring, and pneumonia with the length of hospital stay (Table 5)

The R square test of independent variables of disease severity; NIHSS, the onset of disease, dysphagia, A2DS2 score at the arrival, specific treatment and pneumonia, and length of hospital

stay was significant at p-value < 0.05 level (F = 14.215). With the multiple regression methods, dysphagia and pneumonia had their significant results. For dysphagia, the p-value was < 0.01 and the p-value for pneumonia is 0.014.

**Table 5** Results of the multiple regression, length of hospital stay as the dependent variable

	Sig. (p-value < 0.05)
<b>Disease associated factors</b>	
Onset of ischemic stroke	0.355
NIHSS	0.863
Dysphagia	0.014
A2DS2 score	0.321
Pneumonia	0.000

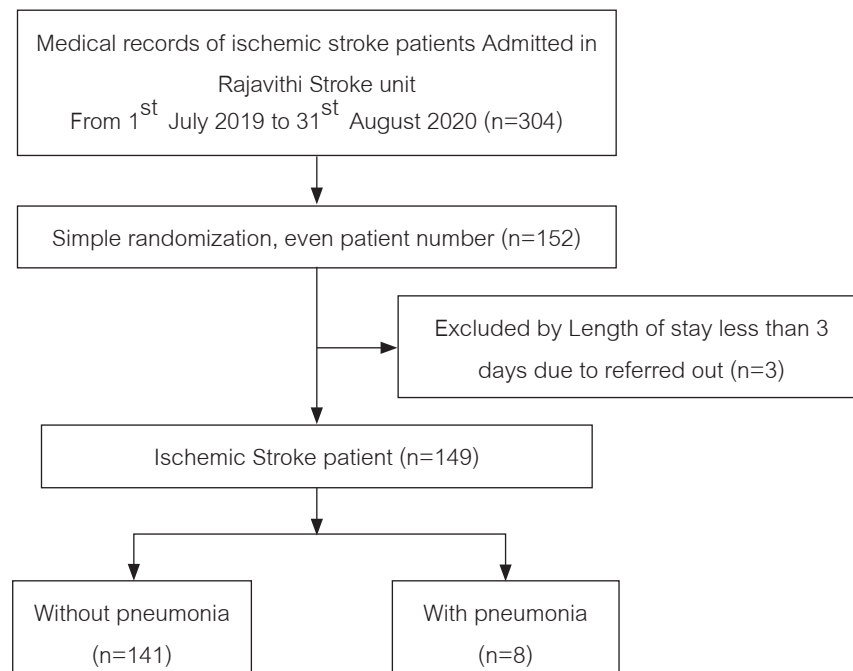
**Relationships of demographic variables and smoking with the length of hospital stay**

The R square test of every independent variable; demographic data and smoking and length of hospital stay were not statistically significant (F = 1.312).

**Discussion**

As the studies reviewed about stroke-associated pneumonia, the incidence had a range of 4.1% - 56.6%<sup>4</sup> and costs more in a visit. Furthermore, the disease severity, the NIHSS as an indicator, the higher score, the more incidence of respiratory tract infection, and disability. Most of the patient with high NIHSS usually had dysphagia. Therefore, it increases the length of hospital stay for 4.4±2.8 more days compared to those without dysphagia.<sup>5</sup>

As patients are unlikely to present with just one problem of ischemic stroke. They usually present with multiple comorbidities, therefore we think the multiple regression methods could suit well in this study. Also, the coexist underlying, metabolic diseases is the risk factor of ischemic stroke.



**Figure 1** Study flow diagram

In this study, the ischemic stroke patient in Rajavithi stroke unit had an incidence of pneumonia at 5.4% which was a small numbers compared to the previous studies. From the independent variables that had been studied, diabetes mellitus, dysphagia and length of hospital stay have a relationship with pneumonia significantly. Normally, the higher NIHSS, the more possibility that a patient would have dysphagia, but a patient with dysphagia may not have a high NIHSS. The A2DS2 score with NIHSS as one of the scoring factors also has no correlations with pneumonia incidence. The patient who has pneumonia also shows a relationship between a longer period of hospital stay because of the treatment. Diagnosis of pneumonia, antibiotics are required for at least 4-7 days, intravenous. The relationship is significant due to the treatment guidelines.

Moreover, for the patient with dysphagia and pneumonia, the result is a vice versa with dysphagia in common, to have a longer length of stay. Despite dysphagia and the length of hospital stay, it is shown diabetes mellitus significantly has a relationship with pneumonia. It supports the result of Rubo et al.<sup>6</sup> Because diabetes mellitus has its known complication of microvascular, macrovascular, and immune dysfunctions. Suzane et al. stated that some microorganisms become more virulent in a high glucose environment. And another mechanism which can lead to the increased prevalence of infections in diabetic patient is an increase adherence of microorganisms to diabetic compared to nondiabetic cells.<sup>7</sup> Thus, one of those complications or other factors about diabetes mellitus is the risk of pneumonia in patients who presented with other diseases, should be further studied.

Unfortunately, we did not study other factors such as an ability to move, daily basis status, the modified ranking scale, etc. which can also be associated with pneumonia. And from the hypothesis that the higher NIHSS or the more severe of the ischemic stroke may increase the incidence of pneumonia. It turns out that they were neither related in this study, nor the length of hospital stays.

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