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Predictors of Stroke-associated Pneumonia after the First Episode of Acute Ischaemic Stroke

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ABSTRACT

Objectives: Pneumonia is one of the most common complications of stroke with significant impact on patients' outcome. The aim of this study is to look for the predictors of stroke-associated pneumonia (SAP) and its 30-day mortality and to analyse the survival of ischaemic stroke patients with pneumonia. **Methodology:** This is a prospective observational study, involving all acute first time ischaemic stroke patients admitted to a tertiary hospital that fulfilled the inclusion and exclusion criteria over a 6-month period. Demographic data were obtained on admission. Patients were reassessed for SAP, on day 5 and day 30. Assessment was done using the National Institutes of Health Stroke Scale (NIHSS) score, Barthel index and modified Rankin scale (MRS). All patients with pneumonia were assessed with the pneumonia severity index (PSI) for SAP. **Results:** One hundred and twenty patients were enrolled consecutively within the 6-month study period. 15.8% developed SAP. Independent predictors of SAP were clinical dysphagia (OR 76.32; 95%CI 4.46 to 1307.05), random blood glucose (RBS) on admission (OR 1.34; 95%CI 1.06 to 1.68) and NIHSS score on admission (OR 1.15; 95%CI 1.02 to 1.30). Independent predictors for 30-day mortality were NIHSS score on day 5 (OR 1.20; 95%CI 1.08 to 1.33) and occurrence of pneumonia (OR 14.90; 95% CI 3.34 to 66.42). There was a significant difference in mean survival between SAP and non-SAP patients. **Conclusions:** Clinical dysphagia, RBS on admission and NIHSS score on admission were independent predictors of SAP. NIHSS score on day 5 and pneumonia were independent predictors of 30-day mortality. SAP patients had shorter survival time compared to non-SAP patients.

Keywords: **Ischaemic stroke, stroke-associated pneumonia, pneumonia score index**

INTRODUCTION

Stroke is a major problem which significantly affects mortality and morbidity. Pneumonia is a known complication in patients with ischaemic stroke, usually acquired within the first 7 days. The incidence reported was in the range of 6.9% to 13.6% and is higher in intensive care units at 21% [1-4]. It is important to recognise the predictors of the development of pneumonia, given that the 30-day stroke mortality from stroke related pneumonias is increased by threefold with much poorer outcome [2,3].

There are several types of pneumonia that can occur in stroke patients such as hospital-acquired pneumonia (HAP), community-acquired pneumonia (CAP), aspiration pneumonia and ventilator-associated pneumonia (VAP). However there is no specific criterion for each type of pneumonia and different studies used different criteria, although there is not much difference between them. In our study, we specifically looked at stroke-associated pneumonia (SAP), which has its own defined criteria [5].

Several predictors of pneumonias have been recognized, including severe disability, large middle cerebral artery (MCA) infarct and poor Glasgow coma score (GCS), which independently predict the development of early infection such as urinary tract infection in stroke patients.[6]

Several studies have looked at predictors of aspiration pneumonia or nosocomial pneumonia specifically, and a few predictors have been recognized such as oropharyngeal dysphagia, posterior circulation stroke, mechanical ventilation and serum albumin [7-9].

Oropharyngeal dysphagia is a commonly documented morbidity after stroke and has been associated with increased risk of pulmonary complications and mortality. Patients tend to have higher risk of developing pneumonia due to multiple factors such as impaired swallowing physiology related to loss of control of mastication, pharyngeal peristalsis, alterations in upper airway sensitivity, glottic injury, and laryngeal muscular dysfunction.[5]

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There are two conflicting reports with regards to the location of the infarct as predictors of pneumonia. In the study by Hamidon BB *et al*., large MCA infarcts were predictors of pneumonia whereas in the study by Hilker *et al*., the posterior circulation was the main location [4-6].

In our study, we aimed to determine the predictors of stroke-associated pneumonia (SAP) and the 30-day mortality in patients with the first episode of acute ischaemic stroke and to analyse the survival of stroke patients with pneumonia in a tertiary hospital.

METHODOLOGY

This was a prospective observational study done over six months, involving all first episode acute ischaemic stroke patients who were admitted to a tertiary hospital. The study proposal was reviewed and approved by the relevant Research and Ethics Committee.

The subjects were recruited based on predetermined inclusion and exclusion criteria, after obtaining written informed consent. The inclusion criteria included all first episode acute ischaemic stroke patients admitted to the tertiary hospital, with both clinical as well as radiological evidence. The exclusion criteria included patients with hemorrhagic stroke, patients with severe active pulmonary diseases such as lung malignancy, chronic obstructive pulmonary disease and bronchiectasis, patients with pneumonia or other infections, in the recent 3 months prior to the acute stroke, patients who refused to give written informed consent, patients who died within 5 days of admission without any evidence of pneumonia and patients with recurrent stroke.

Demographic data obtained were age at diagnosis, gender, and types of stroke. Stroke subtype was based on the Oxfordshire Community Stroke Project Subtype Classification (OCSP)– Total Anterior Circulation Infarct (TACI), Partial Anterior Circulation Infarct (PACI), Lacunar Infarct (LAI) and Posterior Circulation Infarct (POCI). Other variables included blood pressure on admission (taking the average of the first two readings), random blood glucose on admission, feeding (defined as any oral intake of food or fluids of any amount after the onset of symptoms), clinical dysphagia (defined as the presence of cough or choking immediately or within 1 minute of ingestion of calibrated volumes of water (5, 10, and 15 mL presented in duplicate), assessment of severity of stroke on admission, on day-5 of admission and day-30 of stroke, based on the Glasgow coma score(GCS), modified Rankin scale (MRS), and NIHSS Score and Barthel index (BI), assessment of severity of pneumonia based on the pneumonia score index (PSI) for stroke and finally the 30-day outcome (looking at the incidence of death within 30 days of the onset of stroke).

Definition of Pneumonia

Stroke-Associated Pneumonia (SAP) was diagnosed according to the Centers for Disease Control and Prevention (CDC) criteria [5]. This was defined as pneumonia occurring within the first 5 days of hospitalization based on:

1. Clinical evidence: (a) lung auscultation and percussion, (b) presence of fever of ≥37.7ºC under axillary area, (c) purulent tracheal secretion
2. Microbiological evidence: (a) tracheal specimens, (b) blood cultures
3. Radiological evidence:(a) chest x-ray findings

Statistical Analysis

Statistical analyses were performed by using the Statistical Package for the Social Sciences (SPSS version 15.0, IL, Chicago) for Windows. Univariate analyses were performed on the demographical characteristics, types of stroke, severity of stroke, functional disability of patients and the outcomes for both pneumonia and 30-day mortality. These were followed by multivariate analysis and logistic regression to look for independent predictors for pneumonia and 30-day mortality. The Kaplan Meier survival analysis was used for the calculation of survival rate. Any p values of less than 0.05 were considered statistically significant.

RESULTS

During the 6-month study period, a total of 120 patients were enrolled in the study. Sixty six (55.0%) were women. Nineteen (15.8%) patients had SAP. Of the 120 patients, 18 (15.0%) died within 30 days of the onset of stroke and 102 (85.0%) survived. The demographical data on admission are summarised in Table 1. On Day-5 and Day-30, all surviving patients were assessed for the functional disability (Table 2).

Among the variables entered into the univariate analysis the following were found to predict SAP in ischaemic stroke patients: age, TACI, LACI, clinical dysphagia, random blood glucose on admission, GCS on admission and NIHSS on admission. Logistic regression analysis showed clinical dysphagia (p=0.003), random blood sugar on admission (p=0.013) and NIHSS on admission (p=0.022) to be significant independent predictors for the development of SAP (Table 2).

For the 30-day mortality, univariate analysis found the following to predict mortality: age, TACI, LACI, clinical

Table 1. Baseline characteristics

Demographic Data	mean + SD
Age at the onset in years	59.3 + 13.4
Blood Pressure on Admission	
- Systolic Blood Pressure	175 + 31.1
- Diastolic Blood Pressure	97.6 + 17.4
Stroke type	
- TACI	19 (15.8)
- PACI	22 (18.3)
- LACI	75 (62.5)
- POCI	4 (3.3)
Dysphagia	
- No dysphagia	84 (70.0)
- Dysphagia	36 (30.0)
Feeding prior admission	
- No feeding	74 (61.7)
- Feeding	46 (38.3)
Pneumonia	
- No pneumonia	101 (84.2)
- Pneumonia	19 (15.8)
30 days Outcome	
- Alive	102 (85.0)
- Death	18 (15.0)

Values in parentheses are percentage

Table 2. Multivariate Analysis of Stroke Associated Pneumonia Predictors

Characteristic	Pneumonia	No Pneumonia	Odds Ratio	95% CI	p
Clinical Dysphagia	18	1	76.3	4.45-1307.04	0.003
Random Blood Glucose (mmol/L)	9.9 (5.1)	7.677 (3.8)	1.3	1.06-1.68	0.013
NIHSS on Admission	17.1 (6.4)	7.29 (5.5)	1.1	1.020-1.29	0.022

Table 3. Multivariate Analysis of 30 Days Outcome Predictors

Characteristic	Death	Alive	Odds Ratio	95% C	p
NIHSS on Day 5	17.7 (7.11)	6.52 (5.05)	1.19	1.07-1.33	0.001
Pneumonia	13	6	14.89	3.34-66.4	<0.001

dysphagia, pneumonia, GCS on admission, NIHSS on admission, and MRS and Barthel index on day 5. All these parameters were entered into the logistic regression analysis and it was found that pneumonia ($p<0.001$) and NIHSS on day 5 ($p=0.001$) were the independent predictors for 30-day mortality (Table 3).

There was a statistically significant difference in survival between the SAP group (mean 19.3 days) and non-SAP group (mean 98 days) using the Kaplan Meier survival analysis ($p<0.05$). (Figure 1)

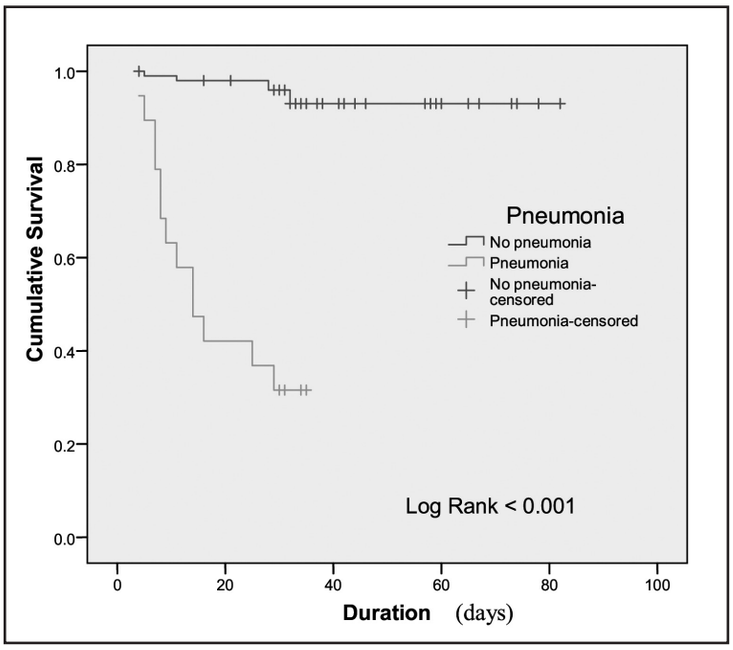

Figure 1. Survival Plot for Pneumonia groups

DISCUSSION

Post stroke infection is one of the most common complications that can occur in stroke patients and it usually occurs within the few days after the acute stroke; the most common infections being urinary tract infection and pneumonia. These infections occur in 25–65% patients with acute stroke and can lead to deterioration of the patient and will affect the survival of the patients [11].

In our study, we concentrated on first time acute ischaemic stroke patients who were identified and classified according to the Oxfordshire Community Stroke Project classification. We found the incidence of stroke-associated pneumonia in first time acute stroke patients in our hospital to be higher than other studies done both locally as well as worldwide, at 15.8% [3, 6, 11, 22]. This could be attributed to various factors. In particular, feeding by family members or traditional healers prior to admission could have led to detrimental effects on the patients with clinical dysphagia, an independent predictor for the development of pneumonia. However neither admission delay nor feeding prior to admission predicted the occurrence of pneumonia in our study. We wonder whether the common practice of traditional medication before modern medicine has any role to play here. Unfortunately we did not look into that aspect.

In patients with acute stroke, dysphagia occurs in 55%. Forty percent of patients who had stroke will have aspiration as evidenced by videofluoroscopic swallow study (VFS) [13]. Some studies have broadened the definition of dysphagia and reported a higher rate of dysphagia with instrumental testing of up to 64% to 78%. A literature review has shown that there is a 3-fold increase in pneumonia risk among stroke patients with dysphagia [14].

The possibility of aspiration pneumonia was believed to be high in patients who were fed prior to admission. Previous literature quoted that aspiration occurred in two thirds of dysphagic patients [15]. The risk of developing pneumonia following aspiration is said to be 20 times higher [16]. The risk of pneumonia in aspirators varies between studies suggesting the possibility of other influencing factors in the development of pneumonia in this group. This was supported by Langmore *et al*. who found dysphagia to be an important risk but generally not sufficient to cause pneumonia unless other risk factors were present as well [17]. In our study we did not find that oral feeding after acute stroke, predicted the development of pneumonia. Perhaps this was due to the fact that only 41.3% of the 46 patients who were orally fed had clinical dysphagia, thus lowering the risk for developing aspiration pneumonia. Out of the 19 patients who developed pneumonia, only 10 patients were actually fed prior to admission.

Another independent predictor for the development of pneumonia that we found in our study was random blood glucose on admission. The risk of developing pneumonia was found to increase in patients with a higher random blood glucose on admission. This is possibly due to poor glycaemic control predisposing stroke patients to infection although this postulation needs to be studied further. Patients with stroke are known to have hyperglycaemia (blood glucose level >200 mg/dL) during the first 24 hours after stroke, which independently predicted expansion of the volume of ischemic stroke and poor neurological outcomes. The persistent hyperglycaemia is thought to be associated with infarct expansion and worsened functional outcome [18].

In our study only the NIHSS score on admission independently predicted pneumonia compared to other assessment methods. This finding is similar to other studies that showed the relationship of NIHSS score with the occurrence of pneumonia [3, 19, 20].

There are many factors contributing to the mortality and morbidity of stroke outcome within 30 days. We focused on the mortality within 30 days and several predictors were identified. Our study showed a 15% mortality after 30 days follow-up which is higher compared to other studies that looked at 30-day mortality [21, 25].

Univariate analysis showed that age, clinical dysphagia, pneumonia, stroke subtypes and worsening functional disability were also predictors of 30-day mortality. Although increasing age has been shown to predict mortality, it was not an independent predictor for the development of pneumonia as this ageing group would have multiple premorbid conditions.

Clinical dysphagia which was found to be a predictor for developing pneumonia, was also one of the independent predictors of 30-day mortality in this study. The mortality rate over 30 days in the SAP group in our study was 68.4%, which is higher compared to others. One population-based study found that respiratory infections accounted for 22% of deaths during the first month, and 26% of deaths during the first year after ischaemic stroke.[22] Hamidon *et al.* found that not only pneumonia but any early infection can increase the mortality of stroke patients.[6] A few other studies have also shown that post stroke infections are the leading cause of death in stroke patients [23-24].

Many previous studies have shown the importance of the NIHSS in predicting the outcome of patients, whether it was measured during admission or upon discharge [25-26] Even though there are methodological differences between studies, as in our case where we assessed NIHSS scores on admission as well as on day 5, the final results regarding NIHSS seemed similar.

Survival analysis showed a marked difference in the survival of patients with SAP and without SAP. The mortality rate was higher in the first 30 days in patients with SAP, with mean survival of 19 days compared to 78 days in patients without SAP. From this study, the risk of mortality was 14 times higher in patients with pneumonia compared to the severity of stroke based on the NIHSS on day 5; therefore respiratory infections remain the strongest influence on the survival of stroke patients regardless of its severity.

CONCLUSIONS AND CLINICAL IMPLICATIONS

Clinical dysphagia, random blood glucose on admission and NIHSS score on admission were independent predictors of SAP. NIHSS score on day 5 and pneumonia independently predict its 30-day mortality. SAP patients were also found to have shorter survival time compared to non-SAP patients. Perhaps by identifying dysphagia and high random blood glucose and early intervention such as Ryle's tube insertion and controlling blood sugar, we will be able to reduce the incidence of pneumonia in stroke patients in hospitals. Aggressive treatment of pneumonia may help reduce the mortality rate but this needs further studies.

REFERENCES

[1] Weimar C, Roth MP, Zillessen G, *et al.* Complications following acute ischemic stroke. Eur J Neurol 2002; 48: 133-40.

[2] Katzan IL, Cebul RD, Husak SH, *et al.* The effect of pneumonia on mortality among patients hospitalized for acute stroke. Neurology 2003; 60: 620-5.

[3] Aslanyan S, Weir CJ, Diener HC, *et al.* Pneumonia and urinary tract infection after acute ischaemic stroke: A tertiary analysis of the GAIN International trial. Eur J Neurol 2004; 1: 49-53.

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[4] Hilker R, Poetter C, Findeisen N, *et al.* Nosocomial pneumonia after acute stroke: Implications for neurological intensive care medicine. Stroke 2003; 34: 975-81.

[5] Garner JS, Jarvis WR, Emori TG, *et al.* CDC definitions for nosocomial infections. Am J Infect Control 1988; 16: 128-40.

[6] Hamidon BB, Raymond AA, Norlinah MI, *et al.* The predictors of early infection after an acute ischaemic stroke. Singapore Med J 2003; 44: 344-6.

[7] Sharma JC, Fletcher S, Vassallo M, *et al.* What influences outcome of stroke - pyrexia or dysphagia? Int J Clin Pract 2001; 55: 17-20.

[8] Sumer M, Ozdemir I, Erturk O. Progression in acute ischemic stroke: Frequency, risk factors and prognosis. J Clin Neurosci 2003; 10: 177-80.

[9] Dziedzic T, Pera J, Klimkowicz A, *et al*. Serum albumin level and nosocomial pneumonia in stroke patients. Eur J Neurol 2006; 13: 299-301.

[10] Aho K, Harmsen P, Hatano S, *et al*. Cerebrovascular disease in the community: Results of a WHO collaborative study. Bull World Health Organ 1980; 58: 113-30.

[11] Kwan J, Hand P. Infection after acute stroke is associated with poor short-term outcome. Acta Neurol Scand 2007; 115: 331-8.

[12] Ovbiagele B, Hills NK, Saver JL, *et al*. Frequency and determinants of pneumonia and urinary tract infection during stroke hospitalization. J Stroke Cerebrovasc Dis 2006; 15: 209-13.

[13] Daniels SK, Brailey K, Priestly DH, *et al.* Aspiration in patients with acute stroke. Arch Phys Med Rehabil 1998; 79: 14-9.

[14] Martino R, Foley N, Bhogal S, *et al*. Dysphagia after stroke: Incidence, diagnosis, and pulmonary complications. Stroke 2005; 36: 2756-63.

[15] Terre R, Mearin F. Oropharyngeal dysphagia after the acute phase of stroke: Predictors of aspiration. Neurogastroenterol Motil 2006; 18: 200-5.

[16] Teasell RW, McRae M, Marchuk Y, *et al*. Pneumonia associated with aspiration following stroke. Arch Phys Med Rehabil 1996; 77: 707-9.

[17] Langmore SE, Terpenning MS, Schork A, *et al*. Predictors of aspiration pneumonia: How important is dysphagia? Dysphagia 1998; 13: 69-81.

[18] Baird TA, Parsons MW, Phanh T, *et al*. Persistent poststroke hyperglycemia is independently associated with infarct expansion and worse clinical outcome. Stroke 2003; 34: 2208-14.

[19] Sellars C, Bowie L, Bagg J. Risk factors for chest infection in acute stroke: A prospective cohort study. Stroke 2007; 38: 2284-91.

[20] Upadya A, Thorevska N, Sena KN, *et al*. Predictors and consequences of pneumonia in critically ill patients with stroke. J Crit Care 2004; 19: 16-22.

[21] Saposnik G, Hill MD, O'Donnell M, *et al*; Registry of the Canadian Stroke Network for the Stroke Outcome Research Canada (SORCan) Working Group. Variables associated with 7-day, 30-day, and 1-year fatality after ischemic stroke. Stroke 2008; 39: 2318-24.

[22] Vernino S, Brown RD Jr, Sejvar JJ, *et al*. Cause-specific mortality after first cerebral infarction: A population-based study. Stroke 2003; 34: 1828-32.

[23] Henon H, Godefroy O, Leys D *et al*. Early predictors of death and disability after acute cerebral ischemic event. Stroke 1995; 26: 392-8.

[24] Viitanen M, Winblad B, Asplund K. Autopsy-verified causes of death after stroke. Acta Med Scand 1987; 222: 401-8.

[25] Chang KC, Tseng MC, Tan TY, *et al*. Predicting 3-month mortality among patients hospitalized for first-ever acute ischemic stroke. J Formos Med Assoc 2006; 105: 310-7.

[26] Adams HP Jr., Davis PH, Leira EC, *et al*. Baseline NIH Stroke Scale score strongly predicts outcome after stroke: A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). Neurology 1999; 53: 126-31.