# Stroke-associated pneumonia: microbiological data and outcome

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## ABSTRACT

Introduction: Pneumonia is a common complication after acute stroke. It affects the outcome adversely. However, data regarding microbiology of stroke-associated pneumonia and its effect on outcome is scarce.

Methods: Stroke-associated pneumonia was identified through chart review of all ICD-9 identified adult stroke patients admitted to our hospital over a period of four years (1998-2001). The demographical, laboratory, radiological, microbiological data and outcome of patients with stroke-associated pneumonia were recorded and analysed.

**Results:** 443 patients with stroke were admitted over the four-year period and 102 (23 percent) had stroke-associated pneumonia. Their ages range from 28 to 100 (mean 64+/-14) years. 69 (68 percent) were men. Median length of stay was nine days compared to four days for all stroke patients. 68 (67 percent) patients manifested pneumonia within 48 hours and 34 (33 percent) after 48 hours of admission. Yield of tracheal aspirate cultures was 38 percent and that of chest radiographs was 25 percent. Pseudomonas aeruginosa and Staphylococcus aureus were the most common organisms (12 percent each) followed by Streptococcus pneumoniae and Klebsiella pneumoniae (4 percent each). Patients with infiltrates on chest radiographs were more likely to have positive tracheal aspirate cultures (p-value is 0.003). 35 patients (34 percent) expired during hospital stay. Positive chest radiographs and tracheal aspirates were independent predictors of prolonged hospital stay (p-value is less than 0.005).

<u>Conclusion</u>: Pneumonia is a common medical complication of stroke. It is associated with a high mortality and prolongs the hospital stay. The yield of chest radiographs and tracheal aspirates is low. However, these are independent predictors of prolonged hospital stay. *Pseudomonas aeruginosa* and *Staphylococcus aureus* are most common organisms in stroke-associated pneumonia.

Keywords: cerebrovascular accident, pneumonia, Pseudomonas aeruginosa, Staphylococcus aureus, stroke

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### INTRODUCTION

Pneumonia is a common medical complication after acute stroke which complicates the course in 7-22% of the stroke patients<sup>(1-7)</sup>. It accounts for 10% of stroke-related deaths<sup>(3)</sup>, and significantly increases the mortality<sup>(3,5-7)</sup>. It also prolongs hospital stay by two-fold<sup>(5)</sup>.

Data regarding the microbiology of strokeassociated pneumonia (SAP) and its effect on outcome is scarce<sup>(5)</sup>. The objectives of this study were to assess outcome of patients with SAP, and the relation of radiological and microbiological data to the outcome.

## METHODS

All adult (aged 14 years and above) patients admitted to our hospital, over a period of four years (1998-2001), with acute stroke, were identified through ICD-9 coding system of the hospital medical records. Patients who developed pneumonia were then identified by chart review of the stroke patients. The demographical, laboratory, radiological, microbiological data and acute outcome at discharge (mortality and length of hospital stay) of patients with SAP were recorded and analysed. Patients who had prior (before the index event) residual neurological deficits, history of dysphagia before the index stroke and those who required mechanical ventilation during the hospital stay, were excluded. Patients who had other identifiable source of infection before development of the pneumonia and those who had fever before stroke onset, were also excluded.

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Organism	*Group I	†Group II
Pseudomonas aeruginosa	9 (13%)	3 (9%)
Staphylococcus aureus	8 (12%)	4 (12%)
Streptococcus pneumonae	3 (4%)	I (3%)
Acinetobacter	( %)	3 (9%)
Enteroccoci coli	( %)	I (3%)
Klebsiella pneumonae	0	4 (12%)
Others	0	I (3%)
No growth	46 (68%)	17 (50%)
Total	68	34

\* Pneumonia manifested clinically within 48 hours of admission,

† Pneumonia manifested clinically after 48 hours of admission.

Table II. Comparison of group I and group II patients	Table II. C	omparison	of group	I and group I	l patients.
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Variable	Group I (n= 68)	Group II (n=34)	p-value
Mean age (in years)	62±14	67±12	0.087
*Gender (M:F)	46:22	23:11	0.55
†Stroke type (I vs H)	39:29	19:15	0.88
Positive TA cultures	22 (32%)	17 (50%)	0.086
Infiltrates on chest radiographs	19 (28%)	6 (18%)	0.24
Mortality	25 (37%)	10 (29%)	0.45

\* M: male; F: female; †I: ischaemic stroke; H: haemorrhagic stroke.

Table III. Comparison between those who died and survivors.

Variable	Died (n= 35)	Survived (n= 67)	p-value
Mean age (in years)	60±13	66±14	0.069
Gender (M:F)	25:10	44:23	I
Stroke type (I vs H)	15:20	43:24	0.39
Positive TA cultures	12 (34%)	27 (40%)	0.55
Infiltrates on chest radiographs	8 (23%)	17 (25%)	0.77
*Onset (GI vs GII)	25:10	43:24	0.45

\*GI: Group I, onset within 48 hours of admission; G II: Group II, onset after 48 hours of admission; TA: tracheal aspirate; I: ischaemic stroke; H: haemorrhagic stroke.

Acute stroke was defined by stroke that presented at the hospital within 72 hours of stroke onset. Stroke was defined as rapidly-evolving focal or global loss of cerebral function, with symptoms leading to death or lasting more than 24 hours due to a vascular aetiology<sup>(8)</sup>. The diagnosis of pneumonia was made according to CDC (Center for Disease Control) criteria<sup>(9)</sup>, based on abnormal chest examination, fever (temperature  $\geq 37.8^{\circ}$ C), purulent sputum, infiltrates on chest radiographs and growth of microorganism on tracheal aspirate culture. All of our patients with pneumonia had abnormal chest examination, fever (temperature  $\geq 37.8^{\circ}$ C), and purulent sputum.

102 patients met the criteria for SAP and were divided into two groups, consisting of group I: patients who developed fever within 48 hours, and group II: those who developed fever after 48 hours of admission. The reason for dividing these patients was based on the assumption that pneumonia which developed early in the course is community-acquired, while that developed late in the course is usually hospital-acquired<sup>(10)</sup>. Chest radiographs were done in all the patients at the time of admission. Tracheal cultures and repeat chest radiographs were performed in all patients with suspicion of aspiration pneumonia. Brain imaging, either computed tomography (CT) or magnetic resonance (MR) imaging, was performed in all patients to differentiate the stroke subtypes.

Death or discharge from the hospital was the primary end point. The outcome was defined as unfavourable if the patient expired during hospital stay and favourable if the patient survived. The data was analysed using Statistical Package for Social Sciences (SPSS) version 10.0 (Chicago, IL, USA). The continuous data is presented in means  $\pm$  standard deviation or median, as appropriate. Chi-square test was used to assess the association between outcome and qualitative variables. while association between the outcome and quantitative variables was assessed by Mann-Whitney U test (if the variable was not normally distributed) and Student's t-test (if distribution was normal).

#### RESULTS

443 patients were admitted with stroke during the study period. Their mean age was 58 ( $\pm$ 10) years and median length of hospital stay (LOS) was four days. 102 (23%) patients met the inclusion criteria for SAP. Their ages ranged from 28 to 100 (mean 64 $\pm$ 14) years. 69 (68%) were men and 33 (32%) were women. 44 (43%) suffered haemorrhagic stroke and 58 (57%) ischaemic stroke. Median LOS of patients with SAP was nine days. SAP manifested within 48 hours of hospital admission (group I) in sixty eight (67%) patients and after 48 hours of admission (group II) in 34 (33%) patients.

Infiltrates on chest radiographs were found only in 25 (25%) patients. 39 (38%) patients had

positive cultures of tracheal aspirates. *Pseudomonas aeruginosa* and *Staphylococcus aureus* were most common organisms, followed by *Streptococcus pneumonia* and *Klebsiella pneumoniae* (Table I). Yield of the cultures was significantly greater in patients with infiltrates on chest radiographs i.e. 64% (16/25 patients) as compared to those without infiltrates on chest radiographs (23/77; 30%) (p=0.003). Combined yield of the cultures and chest radiographs was 47%.

Patients in group II tended to be older as compared to patients in group I, and there was also a trend of greater yield of tracheal aspirate in group II. However, this difference failed to reach statistical significance (Table II). Gender distribution, stroke subtype, frequency of infiltrates on chest radiographs and outcome were comparable in the two groups (Table II). There were some differences in the organisms isolated between two groups but the most common organisms overall were *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Table I).

35 (34%) patients died during the hospital stay. Mortality was not affected by age, gender, stroke subtypes, onset latency (time lag between admission and manifestation of pneumonia), findings of chest radiograph or tracheal aspirate cultures (Table III). Mean LOS in patients with infiltrates on chest radiographs versus those who did not have the infiltrates was 17 versus ten days (p=0.004), while that in patients with positive tracheal aspirate cultures versus those with the negative cultures was 17 versus eight days (p=<0.001). It was also greater in patients who had both abnormalities as compared to those with both tests negative i.e. 15 versus eight days (p=<0.001). Multivariate analysis revealed that positive tracheal aspirate cultures and infiltrates on chest radiographs were independent predictors of prolonged hospital stay, with odd ratios of 15 (95% CI: 9-21) and 8 (95% CI: 4-13), respectively.

# DISCUSSION

Pneumonia is a common medical complication after acute stroke that complicates the course in 7-22% of the stroke patients<sup>(1-7)</sup>. During the study period, 443 patients were admitted with stroke and 102 (23%) developed pneumonia. This figure is probably underestimated as we excluded the patients who were either ventilated or had prior history of dysphagia. 68% of the patients in our study developed infection within 48 hours of admission. This figure is higher than that reported in the Western literature, i.e. 40-58%<sup>(3,4)</sup>.

Several factors have been incriminated in the development of SAP, with dysphagia and aspiration being most commonly mentioned<sup>(1,5,11-13)</sup>. Silent aspiration and large volume aspirations have been noted to carry the highest risk as compared to symptomatic aspirations and small volume aspirations<sup>(13)</sup>. Our patients did not undergo barium swallow or video-fluoroscopy, however, as most of them had dysphagia. Risk of SAP has been found to be greater in haemorrhagic strokes, compared to ischaemic ones(3,4). Although our study was not designed to determine predictors of strokeassociated pneumonia, the proportion of haemorrhagic strokes in our cohort was quite high, i.e. 57%. The frequency of haemorrhagic stroke has been reported to be 24% in our institution<sup>(14)</sup>.

The mean age of our patients was 64 years, six years more than the mean age of all the patients admitted to our centre with stroke during the study period. However, there are conflicting reports whether old age is a risk factor for SAP<sup>(4-6)</sup>. These observations are not directly related to our objectives, but these findings may provide basis for further studies.

We noted a low yield of tracheal aspirate cultures which revealed growth of micro-organisms in only 38 (37%) patients, only slightly higher in group II patients. However, this difference was not statistically significant (Table III). A similar yield has been reported earlier<sup>(5)</sup>. The yield of chest radiographs was even lower, i.e. only 25 (25%) patients had pulmonary infiltrates. This figure is much lower than that reported in the literature, i.e. 69%<sup>(5)</sup>. There is no clear reason for the observed difference. Time lag between symptom onset and obtaining chest radiographs, and number of chest radiographs performed in a given patient might be contributing factors. However, the prior investigators<sup>(5)</sup> have not addressed the issue and because of the retrospective nature of our study, we did not have sufficient data to address the issue. The patients with infiltrates on chests radiographs were more likely to have positive cultures, an observation consistent with the published literature<sup>(5)</sup>.

We divided our cohort into two groups (community-acquired and hospital-acquired), as microbiology and outcome between them may be different. Our assumption was that patients with onset of pneumonia within 48 hours of admission would have lower mortality rate, based on the published literature<sup>(15-17)</sup>. However, we noted that there was no significant difference in mortality between the two groups. *Streptococcus pneumoniae* and *Haemophilus influenzae* are the most common

causative organisms of community-acquired pneumonia<sup>(12,18)</sup> and *Staphylococcus aureus* and *Pseudomonas aeruginosa* are more likely to cause hospital-acquired pneumonia<sup>(10)</sup>. In our study, *Staphylococcus aureus* and *Pseudomonas aeruginosa* were the most common organisms in group I, while *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter* and *Klebsiella pneumonae* were most common organisms in group II (Table I).

We assume that the similar mortality rates in both groups may partly be explained by a relatively similar microbiological data between two groups, as the organisms (Staphylococcus aureus and Pseudomonas aeruginosa) are more virulent than S. pneumonae. However, why the microbiological results were similar between the two groups is unclear. One possible explanation for similar microbiological data is contamination of probes that were not immediately cultured. Another possibility is that organisms like Pseudomonas aeruginosa and Staphylococcus aureus may be more prevalent in our community; this is supported by a local study from our country which revealed that Staphylococcus aureus was the second most common pathogen, after Streptococcus pneumoniae, in communityacquired pneumonia<sup>(19)</sup>.

Although the positive cultures and infiltrates on chest radiographs did not affect the mortality rate among the cohort, hospital stay was significantly longer in patients who had positive tracheal aspirate cultures, infiltrates on chest radiographs, or both. SAP accounts for 10% of stroke-related deaths<sup>(3)</sup>, and has been reported to increase mortality rate by three-fold<sup>(3,5)</sup> and prolong the hospital stay by two-fold<sup>(5)</sup>. Median LOS of all stroke patients admitted to our hospital during the study period was four days while that of the patients who developed pneumonia (study population) was nine days. Our mortality rate was 34%, which is similar to that reported in literature<sup>(3)</sup>. However, the mortality rate was not affected by age, gender, stroke type, time of onset, and results of chest radiographs and cultures.

We conclude that SAP is associated with poor prognosis. It prolongs hospital stay and is also associated with high acute mortality (during initial hospital admission) in stroke patients. The yield of chest radiographs and tracheal aspirate is low; however, these are independent predictors of prolonged hospital stay. Microbiology of early (community-acquired pneumonia) and nosocomial pneumonia is almost similar; however, this requires confirmation in large scale prospective studies.

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