

A²DS² Score to Predict the Risk of Stroke-Associated Pneumonia in Acute Stroke: An Indian Perspective

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Abstract

Background Stroke-associated pneumonia (SAP) is an important cause of poststroke morbidity and mortality. Several clinical risk scores predict the risk of SAP. In this study, we used the A²DS² score (age, atrial fibrillation, dysphagia, sex, and stroke severity) to assess the risk of SAP in patients admitted with acute stroke.

Methods A high (5–10) and a low (0–4) A²DS² score was assigned to patients with acute stroke admitted to the neurology ward. Univariate binary logistic regression analysis was performed to find the strength of association of SAP and A²DS² score.

Results There were 250 patients with acute stroke of which 46 developed SAP. Forty-four patients developed SAP in high score as against 2 in low-score group (odds ratio [OR] = 0.03, 95% confidence interval [CI] = 0.01–0.15, *p* = 0.0001). A²DS² score >5 had sensitivity of 82.6% and specificity of 65.1% to predict SAP. The mean A²DS² score in patients with pneumonia was 7.02 ± 1.40 compared to 4.75 ± 1.92 in patients without pneumonia (*p* = 0.0001).

Conclusions A²DS² score has a high sensitivity of 82% in predicting the risk of SAP and is a useful tool to monitor patients after acute stroke. A²DS² score can help in timely detection and prevention of SAP and reduction in caregiver's burden.

Keywords

- ▶ A²DS² score
- ▶ stroke
- ▶ stroke-associated pneumonia

Introduction

Stroke is a main cause of death and disability globally with increased burden on caregivers, especially in developing countries. In the acute stage, stroke patients are prone to chest infections, cardiac dysfunction, and urinary tract infections that have grave consequences over stroke outcome. These complications occur in one-third of stroke patients and are a major cause of death in acute and subacute stage of stroke and also prolong the hospitalization.^{1,2} These medical complications have an additional negative effect on post-stroke functional outcome and impair with active and passive rehabilitation strategies.²

Stroke-associated pneumonia (SAP) is a predominant cause of poststroke morbidity and mortality.^{1,3,4} The incidence of SAP is variable, ranging from 2.3 to 28% in various studies, depending on the type and level of medical

and nursing care, the use of nasogastric feeding, and judicious use of empirical antibiotics.^{5–8} SAP independently increases mortality (2- to 6-fold) and length of hospitalization and is a marker for poor outcome in survivors.^{9–13} Dysphagia/aspiration, age, and stroke severity are important clinical risk factors seen to be associated with SAP, and several clinical risk scores have been developed to predict the risk of SAP. Few such scores used in clinical practice are pneumonia score in Korea,¹⁴ integer-based pneumonia risk score in the United Kingdom,¹⁵ and the acute ischemic stroke-associated pneumonia score (AIS-APS) in China.¹⁶ A rather simple and effective score is the A²DS² score (age, atrial fibrillation [AF], dysphagia, sex, and stroke severity) using the National Institutes of Health Stroke Scale [NIHSS] score). This score was developed from the Berlin Stroke Registry cohort and subsequently validated using German stroke registry.¹⁷



No reliable scoring system is currently available in routine clinical practice or clinical trials in Indian patients. Thus, in this study, we assessed the risk of SAP in patients with acute stroke using the A²DS² score.

Materials and Methods

This study was done in the Department of Neurology at Dr. Ram Manohar Lohia Institute of Medical Sciences, a tertiary care referral institute in the capital city of Uttar Pradesh, India. This was a prospective study, and patients were enrolled from the ward and intensive care unit of neurology.

Inclusion Criteria

Patients, older than 18 years with acute stroke of <7 days' duration, both ischemic and hemorrhagic, were included in the study.

Exclusion Criteria

All patients with a clinical or radiological suggestion of primary respiratory pathology at presentation, those with a retroviral positive status, associated comorbidities such as chronic renal or liver failure, congestive heart failure, and malignancies were excluded from the study. A written informed consent was obtained from the patient's relatives before the recruitment.

Evaluation

A detailed history was taken, and once a clinical diagnosis of acute stroke was established, an urgent brain imaging was done to confirm the diagnosis. At the point of entry, a Glasgow Coma Scale score and NIHSS were done and recorded. A note was made of the demographic and risk factors in the patients (age, sex, habits such as smoking, alcohol, or any other addictions, history of hypertension, diabetes mellitus, dyslipidemia, and cardiac pathologies such as valvular or coronary heart disease, prior strokes, or transient ischemic attacks).

Investigations

After admission, routine blood investigations were done including a complete hemogram, tests for liver and renal functions, blood sugars, serum sodium, and potassium. An electrocardiogram was done in all patients and two-dimensional echocardiography in patients suspected with a cardioembolic source of stroke. A chest X-ray was done in all patients, and those having a respiratory pathology at presentation were excluded.

Dysphagia Screening

Dysphagia screening was done using the 3-ounce water swallow test.¹⁸ Ryle's tube was inserted, and enteral nutrition was given in all patients screened positive for dysphagia.

A²DS² Scoring

A²DS² scoring system was used, and a score was assigned to all patients. The patients were arbitrarily divided into two groups. The Group A comprised patients with a score of 0 to 4 and Group B with a score of 5 to 10 (► **Table 1**).

Table 1 A²DS² score

Clinical variables	Points assigned
Age >75 y	1
Atrial fibrillation	1
Dysphagia	2
Male sex	1
Stroke severity	
NIHSS 0–4	0
5–15	3
>16	5

Abbreviation: NIHSS, National Institutes of Health Stroke Scale.

Treatment and Follow-Up

All patients were managed as per standard stroke management guidelines. All patients were followed daily up to discharge for any signs and symptoms of pneumonia such as fever, cough with or without expectoration, chest pain, dyspnea, altered mentation, basal crepitations, and desaturation as seen on monitor. Those with a suggestion of pneumonia were evaluated with a repeat X-ray chest and sputum examination. The diagnosis of pneumonia was made as per the Centers for Disease Control and Prevention (CDC) criteria for hospital-acquired pneumonia.¹⁹ All patients with pneumonia were aggressively managed with antibiotics according to susceptibility testing and supportive care. Empirical therapy was given till the cultures were awaited in accordance with the American Thoracic Society/Infectious Disease Society of America guidelines 2016.²⁰

Statistical Analysis

The results are presented in frequencies, percentages, and mean ± standard deviation. Univariate binary logistic regression analysis was performed to find the strength of association of incidence of pneumonia with various factors. The factors seen to be associated significantly with SAP were then tested on multivariate regression analysis. Multivariate logistic regression analysis was done for those comorbidities that were found statistically significant on univariate logistic regression with the incidence of pneumonia. The Unpaired *t* test was used to compare continuous variables. The odds ratio (OR) with its 95% confidence interval (CI) was calculated. The positive predictive value (PPV) and negative predictive value (NPV) were calculated. *p* < 0.05 was considered statistically significant. All the analysis was performed on SPSS 16.0 version (SPSS Inc., Chicago, Illinois, United States). Ethics approval for the study was obtained from the institutional ethics committee.

Results

A total of 250 patients of acute stroke (ischemic and hemorrhagic) were seen within 7 days of onset of ictus between March 2016 and August 2017 (141 men and 109 women). The age ranged from 30 to 93 years. Forty-six patients (18.4%) developed SAP in our study cohort. On age breakup, it was

seen that maximum number of patients fell in the age group of 51 to 60 years (28.8%) followed by 61 to 70 years (28.4%). The incidence of pneumonia in the age group of 41 to 50 years was 22.9%, 51 to 60 years was 15.3%, 61 to 70 years was 19.7%, >70 years was 22%, and <40 years was 5.6% (►Table 2). The incidence was about five times in the fifth decade compared with patients <40 years although it did not reach a statistically significant level (OR = 5.05, 95% CI = 0.60–42.36). The incidence of SAP was high among women (20.2%) as compared with men (17%), although again a statistically significant association could not be established (OR = 0.81, 95% CI = 0.42–1.54). Of 148 patients, 29 (19.6%) patients with ischemic stroke, and of 102 patients, 17 (16.67%) hemorrhagic stroke patients developed SAP without any significant association ($p = 0.55$). Likewise, lesion location in both ischemic and hemorrhagic strokes had no significant association with the development of SAP.

Comorbidities and Stroke-Associated Pneumonia

The incidence of pneumonia was significantly higher among patients where AF was detected (OR = 4.71, 95% CI = 1.79–12.40, $p = 0.001$). Hypertensions, diabetes, prior ischemic heart disease, dyslipidemia, prior smoking, or alcohol abuse was not significantly associated with SAP risk (►Table 3). One hundred and nine (43%) patients had dysphagia as detected on bedside oral swallowing test. The incidence of pneumonia was significantly higher in the presence of dysphagia (OR = 29.97, 95% CI = 8.96–100.16, $p = 0.0001$) (►Table 4). Multivariate logistic regression model using pneumonia as a dependent variable and dysphagia and AF as independent variables was constructed. This model revealed significantly higher incidence of pneumonia in patients with dysphagia (OR = 28.30, 95% CI = 8.43–95.04) and in patients where AF was detected (OR = 3.52, 95% CI = 1.11–11.14).

A²DS² Score and Stroke-Associated Pneumonia

A²DS² score was obtained in all admitted patients. A total of 115 (46%) patients had a low A²DS² score (Group A), whereas 135 (54%) patients had a high A²DS² score (Group B). In high-score group, 44 patients developed pneumonia compared with 2 patients with a low A²DS² score (OR = 0.03, 95% CI = 0.01–0.15, $p = 0.0001$) (►Table 5). A²DS² score >5 had sensitivity of 82.6% and specificity of 65.1% to predict pneumonia after stroke (►Table 6). The mean A²DS² score

in patients with pneumonia was 7.02 ± 1.40 , while it was 4.75 ± 1.92 in patients without pneumonia ($p = 0.0001$).

Discussion

Various studies have shown that in patients with stroke, the medical complications are also responsible for post-stroke functional status and ultimately to morbidity and mortality.^{2,5} The incidence of SAP is most frequent during the first week after stroke and particularly within the first 3 days in 10% of hospitalized patients.⁷ This number can be as high as 40% in high-risk patients.¹³ Because of the development of stroke units, aggressive attention to high-risk patients, and dedicated medical and paramedical teams, significant trends toward reduction of this complication have been observed.⁸

SAP occurred in 46 of 250 patients (18%) in our study. SAP is commonly associated with risk factors such as age, dysphagia, stroke severity, and location and conscious level at the onset of ictus. Numerous baseline factors such as age, dysphagia, severity of stroke, low conscious level, type, and location of stroke have greater impact on the development of SAP.¹² Kemmling et al noted SAP to be more frequent in strokes localized to the right hemispheric peri-insular region.²¹ In our study, there was no correlation between lesion location and SAP. Based on these risk factors, several clinical scores have been derived to help identify patients at high risk of SAP as discussed earlier. High-risk group patients can be closely monitored, and timely institution of appropriate care can thus provide for a better functional recovery from stroke.^{13–16,22} A need for an easy-to-apply valid score is the need of the hour. Helmy et al compared A²DS² score, the AIS-APS, and the preventive antibacterial therapy in AIS score in predicting SAP. Of the 26 patients, who developed pneumonia among the 70 patients included in the study, authors found that the area under receiver operating characteristic curve, a marker for predicting outcome, was significantly higher in A²DS² score as compared to the other two scores. They concluded that A²DS² is a valid and easy-to-use tool with the best performance in predicting SAP.²³ Thus, we used the A²DS² score in our patients of stroke as a marker to predict the occurrence of SAP. To the best of our knowledge, no such study has been conducted in Indian patients till date.

Table 2 Age breakup of patients and stroke-associated pneumonia ($n = 250$)

Age, y	Number of patients	With pneumonia ($n = 46$), n (%)	Without pneumonia ($n = 204$), n (%)	OR (95% CI)	p -Value
<40	18	1 (5.6)	17 (94.4)	1.00 (reference)	
41–50	48	11 (22.9)	37 (77.1)	5.05 (0.60–42.36)	0.13
51–60	72	11 (15.3)	61 (84.7)	3.06 (0.36–35.45)	0.30
61–70	71	14 (19.7)	57 (80.3)	4.17 (0.51–34.09)	0.18
>70	41	9 (22.0)	32 (78.0)	4.78 (0.55–40.96)	0.15
Total	250	46 (18.4)	204 (81.6)		

Abbreviations: CI, confidence interval; OR, odds ratio.

Table 3 Comorbidities and stroke-associated pneumonia

Comorbidity	Number of patients	With pneumonia (n = 46), n (%)	Without pneumonia (n = 204), n (%)	OR (95% CI)	p-Value
Hypertension					
Yes	161	32 (19.9)	129 (80.1)	1.32 (0.66–2.64)	0.41
No	89	14 (15.7)	75 (84.3)	1.00 (reference)	
Diabetes					
Yes	81	15 (18.5)	66 (81.5)	1.01 (0.51–2.00)	0.97
No	169	31 (18.3)	138 (81.7)	1.00 (reference)	
Dyslipidemia					
Yes	10	4 (40.0)	6 (60.0)	3.14 (0.85–11.62)	0.07
No	240	42 (17.5)	198 (82.5)	1.00 (reference)	
IHD					
Yes	23	6 (26.1)	17 (73.9)	1.65 (0.61–4.44)	0.31
No	227	40 (17.6)	187 (82.4)	1.00 (reference)	
New/old AF					
Yes	19	9 (47.4)	10 (52.6)	4.71 (1.79–12.40)	0.001 ^a
No	231	37 (16.0)	194 (84.0)	1.00 (reference)	
Alcohol					
Yes	87	19 (21.8)	19 (78.2)	1.40 (0.73–2.71)	0.30
No	163	27 (16.6)	27 (83.4)	1.00 (reference)	
Smoking					
Yes	80	14 (17.5)	66 (82.5)	0.91 (0.45–1.83)	0.80
No	170	32 (18.8)	138 (81.2)	1.00 (reference)	
Previous stroke					
Yes	26	5 (19.2)	21 (80.8)	1.06 (0.37–2.98)	0.90
No	224	41 (18.3)	183 (81.7)	1.00 (reference)	

Abbreviations: AF, atrial fibrillation; CI, confidence interval; IHD, ischemic heart disease; OR, odds ratio.

^ap < 0.05.

Table 4 Stroke-associated pneumonia and dysphagia

Dysphagia	Number of patients	With pneumonia (n = 46), n (%)	Without pneumonia (n = 204), n (%)	OR (95% CI)	p-Value
Present	109	43 (39.4)	66 (60.6)	29.97 (8.96–100.16)	0.0001 ^a
Absent	141	3 (2.1)	138 (97.9)	1.00 (reference)	

Abbreviations: CI, confidence interval; OR, odds ratio.

^ap < 0.05.

In our study, mean A²DS² score was 7.02 ± 1.40 in patients with SAP and it was 4.75 ± 1.92 in stroke patients who did not develop SAP (p = 0.0001). Out of 46, 44 patients with SAP (96%) were in high A²DS² score (5–10) and only 2 patients were in low A²DS² score (0–4) (► **Table 4**). The incidence of pneumonia was 97% significantly (p = 0.0001) lower among A²DS² score of 0–4 than those with a score of 5 to 10 (OR = 0.03, 95% CI = 0.01–0.15). Zhang et al

also showed that higher A²DS² score was associated with higher risk of SAP (OR = 9.68, 95% CI = 6.12–15.30).²⁴ Li et al investigated 1,279 stroke patients and 308 patients developed SAP. On using the A²DS² tool, the incidence of SAP was 3.7% in patients with score 0, 22.7% in patients with scores 1 to 9, and up to 71.7% in patients with scores ≥10 with significant difference in incidence of SAP in these three groups.²⁵ The value of A²DS² score >5 to predict SAP

Table 5 A²DS² score and stroke-associated pneumonia

A ² DS ²	Number of patients	With pneumonia, n (%)	Without pneumonia, n (%)	OR (95% CI)	p-Value
0–4	115	2 (1.7)	113 (98.3)	0.03 (0.01–0.15)	0.0001 ^a
5–10	135	44 (32.6)	91 (67.4)	1.00 (reference)	

Abbreviations: CI, confidence interval; OR, odds ratio.

^ap < 0.05

Table 6 Sensitivity and specificity of score A²DS² to predict stroke-associated pneumonia

A ² DS ²	With pneumonia (n = 46), n (%)	Without pneumonia (n = 204), n (%)	Total, n (%)
≥5	38 (15.2)	70 (28.0)	108 (43.2)
≤5	8 (3.2)	134 (53.6)	142 (56.8)
Total	46 (18.4)	204 (81.6)	250 (100.0)
Predictive value of A ² DS ² score >5 (95% CI)			
Sensitivity	82.6 (71.7–93.6)		
Specificity	65.7 (59.2–72.2)		
PPV	35.2 (26.2–44.2)		
NPV	94.4		

Abbreviations: CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

had sensitivity of 82.6% and specificity of 65.1% (► **Table 6**). A high (NPV, 94.4) compared with a PPV of 35.2 compares with the previous study done by Helmy et al,²³ thereby suggesting a good prediction for no development of SAP in stroke patients with lower score. An important observation was a much higher incidence of SAP (18.4%) in our study as compared with the Berlin study by Hoffmann et al (7.2%) and Chinese study by Zhang et al (7.3%).^{17,24} This is mostly attributable to the lack of infrastructure and supporting staff in managing critical care patients. The concept of stroke units with a multidisciplinary approach is the ideal setting in managing patients with acute stroke. Cochrane database showed that specialized stroke unit care as compared with the nursing care administered in the general wards not only prevented the early complications but also improved the overall functional outcome in patients of acute stroke.²⁶ Higher age and male sex have been associated with high incidence of SAP as per prior studies.^{24,27} On the contrary, we found that SAP was seen maximally in patients not only in the sixth and seventh decades but also in the fifth decade. Furthermore, our study had a nonsignificant incline toward female sex getting more SAP than males. We cannot explain these observations at this point of time, and the same might require a larger cohort to arrive at any definite conclusions. In our study, we observed a significantly high incidence of SAP in the presence of AF, both newly detected and old. None of the other comorbidities analyzed had any significant association with SAP. AF is an established independent risk factor in medical complications associated with stroke. Irregular cardiac activity and hemodynamic changes in AF cause decreased cardiac output and pulmonary congestion. With respiratory functions already compromised in

stroke patients, there occur alveoli flooding and reduced microbial clearance that favors the occurrence of pneumonia.²⁸ Dysphagia was significantly associated with SAP in the current study. Swallowing requires a coordination of muscles of the oral cavity and larynx. Dysphagia can be assessed on bedside examination by different variables such as evaluating cough reflexes, voice change after oral feeds, difficulty in chewing, and presence of dysphonia. Tests that can be done to evaluate for dysphagia include timed test, Burke dysphagia screening test, and 3-oz water swallowing test. However, fiber optic endoscopic evaluation and videofluoroscopic swallowing study are the gold standards to confirm dysphagia.²⁹ We used 3-oz water swallow test to screen and score patients for dysphagia. The patient swallowed 3 oz of water uninterrupted, and abnormality was defined by coughing during swallowing or 1 minute after completion. The presence of a wet/hoarse voice quality after swallowing also was scored as abnormal.¹⁸ We could not get a videofluoroscopic assessment in this group of patients to establish swallowing abnormalities. Dysphagia was seen to increase the odds for aspiration pneumonia by 13 times as studied by Abubakar and Jamoh.³⁰ Patients with dysphagia are known to experience silent aspiration and pooling of endotracheal secretions that are a harbinger to the development of respiratory tract infections that prolong hospital stay and morbidity. A low NIHSS was associated with lower risk of SAP. NIHSS >15 had a sensitivity of 82.6% and specificity of 68.1% for predicting the development of SAP. This is quite obvious as patients with a high NIHSS are the ones with large territorial infarcts/hemorrhages, have a poor sensorium, and hence more prone to developing aspiration and SAP. As earlier stated, this is a prospective hospital-based

study, and to the best of our knowledge, the first is in the Indian subcontinent. The incidence of SAP in our cohort was higher, probably emphasizing the need of stroke units with appropriate infrastructure and well-trained staff.

Finally, SAP has multifactorial causes, and each needs to be targeted through a multidisciplinary approach. Hand washing is included as a part of CDC guidelines for the prevention of nosocomial pneumonia at least since 1985, and its importance cannot be undermined. Patients should be kept nil per oral on admission till swallowing is checked. Swallowing assessment by simple bedside tests in the absence of invasive techniques significantly decreases the risk of SAP. Nasogastric tube feeding or a percutaneous gastrostomy is used if swallowing is compromised although these do not eliminate the occurrence of aspiration. Early mobilization is recommended, if possible for the prevention of aspiration.^{31,32}

Conclusions

A²DS² score has a sensitivity of 82% in predicting the risk of SAP after acute stroke. In the Indian context, A²DS² score might be a valid tool to predict the development of SAP. Patients with a higher score should be monitored in stroke units with good chest physiotherapy and prophylactic antibiotics. Timely detection and prevention of SAP will reduce the hospital stay and long-term morbidity in patients with stroke.

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Conflict of Interest

None declared.

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