



## Risk Factors and Functional Outcomes of Delirium in Acute Stroke: A Prospective Observational Study

Dr Lavanya D<sup>1</sup>, Dr Maria Annita Tellcott Solomon<sup>2</sup>, Dr Sivabackiya Chithiravelu<sup>3</sup>, Dr Parimala Elangovan<sup>4</sup>

<sup>1</sup>Assistant Professor cum Clinical Psychologist, Department of Psychiatry, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Chengalpattu, Tamil Nadu

<sup>2</sup>Assistant Professor, Department of Psychiatry, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Chengalpattu, Tamil Nadu

<sup>3</sup>Assistant Professor, Department of Psychiatry, SRM Medical College Hospital and Research Centre, SRMIST, Chengalpattu, Tamil Nadu

<sup>4</sup>General Physician, Stanley Medical College and Hospital, Chennai, Tamil Nadu (Corresponding author)

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### KEYWORDS

Delirium, Stroke, Mortality, Barthel Index, India

### ABSTRACT:

**Background:** Stroke often results in complex neurological deficits, and the incidence of delirium among stroke patients can significantly impact clinical outcomes.

**Objective:** To determine the risk factors associated with the development of delirium among patients presenting with acute stroke and to assess the outcomes (mortality and functional outcomes assessed using Barthel index) at 1 month.

**Methods:** This was a prospective observational study conducted in the Intensive care and Stroke Units, Department of Neurology in a tertiary teaching healthcare facility in India between January 2023 and June 2024.

**Results:** The incidence of delirium among acute stroke patients was 21.0%. Patients with delirium were significantly older (mean age 67.3 years) compared to those without (57.4 years,  $p < 0.001$ ). Gender, hypertension, diabetes, smoking, and previous stroke or transient ischemic attack were not significantly associated with delirium. However, delirium patients had a higher prevalence of cardiac disease (47.6%,  $p = 0.064$ ). Neurologically, delirium was significantly linked with lower Glasgow Coma Scale (GCS) scores ( $p < 0.001$ ) and higher National Institutes of Health Stroke Scale (NIHSS) scores ( $p < 0.001$ ). Stroke types also differed; ischemic stroke was more common in non-delirium patients (73.4%), while intracerebral haemorrhage and right hemisphere strokes were more common in those with delirium ( $p = 0.006$  and  $p = 0.018$ , respectively). Cardio-embolic strokes were more frequent in delirium patients (50.0%), while large-artery atherosclerosis (LAA) and small-artery occlusion (SAO) were more common in non-delirium patients. Delirium was associated with poorer functional outcomes, reflected by lower Barthel Index scores at one month ( $p < 0.001$ ), and higher mortality (28.6% versus 6.3%,  $p = 0.004$ ).

**Conclusion:** Delirium was significantly correlated with worse neurological status, poorer functional recovery, and increased mortality among stroke patients.

### Introduction

Delirium is a common neuropsychiatric condition characterized by acute onset, fluctuating course, and

disturbances in attention and cognition.(1) It has garnered increasing attention in the medical community, particularly in the context of acute illnesses such as stroke. Stroke, a leading cause of morbidity and mortality



worldwide, often results in complex neurological deficits, and the incidence of delirium among stroke patients can significantly impact clinical outcomes.(2) Research indicates that the incidence of delirium in stroke patients ranges from 10% to 30%, with variability depending on the stroke subtype and severity.(3-5) The development of delirium has been associated with poor prognosis, including higher mortality rates and worse functional recovery.(6-8) Several risk factors contribute to the onset of delirium in stroke patients, including older age, severity of stroke, pre-existing cognitive impairment, and metabolic disturbances.(9)

The pathophysiology of delirium in stroke patients is complex and multifactorial. It may involve neuroinflammation, metabolic imbalances, and disruption of neurotransmitter systems.(10) For instance, ischemic damage can lead to the release of inflammatory cytokines, which may exacerbate cognitive decline and promote delirium.(11) Furthermore, the lateralization of stroke plays a significant role in the development of delirium, as right hemisphere strokes have been associated with a higher risk of cognitive impairment and behavioural disturbances.(12, 13)

Despite the recognized significance of delirium in stroke patients, there remains a paucity of studies focusing on its risk factors and outcomes, particularly in diverse populations. Understanding the relationships between stroke characteristics – such as type, laterality, and severity – and the incidence of delirium is crucial for developing targeted prevention and treatment strategies. Against this background, the aim of the present study was to determine the risk factors associated with the development of delirium among patients presenting with acute stroke to a tertiary healthcare facility and to assess the outcomes (mortality and functional outcomes assessed using Barthel index) at 1 month.

## Materials and Methods

This was a prospective observational study conducted in the Intensive care and Stroke Units, Department of Neurology in a tertiary teaching healthcare facility in India between January 2023 and June 2024. The participants (and their attenders) were given the Participant Information Sheet (PIS) in their native language, and its contents were verbally explained to ensure their understanding and satisfaction. Enrolment

into the study proceeded upon receipt of written informed consent. The minimum required sample size was computed to be 100 patients presenting with acute stroke – divided into two groups – Group A, stroke patients with delirium and Group B, stroke patients without delirium. We used nonprobability sampling technique – complete enumeration of patients. Patients more than or equal to 30 years of age, presenting with acute stroke including cerebral infarction, intracerebral haemorrhage and subarachnoid haemorrhage were enrolled in the present study. However, patients with transient ischemic attacks, history of severe head trauma, cerebral venous sinus thrombosis, brain tumours, history of psychosis, severe dementia prior to the onset of stroke, history of anticholinergic medication intake before stroke, and aphasia; comatose patients; and patients with hepatic impairment, renal impairment, or respiratory failure were excluded.

A detailed medical history was obtained, with special attention to past medical history provided by the patients or their relatives. This was done to identify the presence of any risk factors such as hypertension (HTN), diabetes mellitus (DM), smoking, cardiac diseases, and other factors like previous transient ischemic attacks or ischemic strokes. A complete general examination was performed, along with a thorough neurological examination. All patients in the study were subjected to a full neurological assessment, which included the Mini Mental State Examination (MMSE) and the National Institutes of Health Stroke Scale (NIHSS).(14, 15) The initial stroke severity was assessed using the NIHSS within the first 24 hours of stroke onset at admission. The subtypes of ischemic stroke were classified according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria.(16) These included large-artery arteriosclerosis, small-artery occlusion, cardio-embolism, undetermined aetiology, and other undetermined aetiologies. Additionally, clinical ischemic stroke syndromes were determined by applying the Oxfordshire Community Stroke Project criteria, which classified strokes into total anterior circulation infarction (TACI), partial anterior circulation infarction (PACI), lacunar infarction (LACI), and posterior circulation infarction (POCI).(17) Screening for delirium was conducted within three days after the stroke based on the Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> Edition (DSM-IV) criteria.(18) Routine laboratory



investigations were conducted at admission, and brain imaging (either computed tomography or MRI) was performed. Follow-up assessments were conducted one month later, with repeat brain CT scans, clinical evaluations using the NIHSS, and functional assessments using the Barthel Index to evaluate the patient's outcomes and mortality.

**Statistical analysis:** The data obtained was manually entered into Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) v23. All the categorical variables were summarised using frequencies and percentages. Continuous variables were summarized using mean (standard deviation) (based on the results of data normality, tested using Kolmogorov–Smirnov test and the Shapiro–Wilk test). To test for statistical significance, Chi square test (for categorical variables) and independent “t” test (for continuous variables) was used. Statistical significance was considered at p value less than 0.05.

## Results

The results of the present study showed that the incidence of delirium among patients with acute stroke was 21.0%. The mean age of those with delirium was significantly higher at 67.3 years (SD 8.1) compared to 57.4 years (SD 9.5) for those without delirium, with a statistically significant p-value of <0.001. Gender distribution showed no significant difference, as 47.6% of patients with delirium were male, compared to 55.7% of those without (p=0.509). Regarding comorbidities, 81.0% of delirium patients had hypertension compared to 69.6% in those without delirium (p=0.304). Diabetes was present in 33.3% of patients with delirium and 41.8% in the non-delirium group (p=0.483). Smoking was slightly more common in patients without delirium (39.2%) than in those with delirium (28.6%), but this difference was not statistically significant (p=0.368). Previous stroke and transient ischemic attack (TIA) were also not significantly different between the groups (p=0.461 and p=0.717, respectively). Cardiac disease was more prevalent in the delirium group (47.6%) compared to the non-delirium group (26.6%), approaching significance with a p-value of 0.064.

Neurologically, patients with delirium were more likely to have a Glasgow Coma Scale (GCS) score below 12 (66.7%) compared to 11.4% in the non-delirium group,

with a highly significant p-value of <0.001. Similarly, National Institutes of Health Stroke Scale (NIHSS) scores showed significant differences, with none of the delirium patients having an NIHSS score below 5, compared to 16.5% of non-delirium patients. Patients with delirium were more likely to have higher NIHSS scores, with 47.6% scoring between 21 and 42, compared to only 2.5% in the non-delirium group (p<0.001). These findings indicate significant associations between delirium and both lower GCS and higher NIHSS scores.

The distribution of stroke types differed significantly between those with and without delirium (p=0.006). Among the patients with delirium, 47.6% had ischemic stroke, 47.6% had intracerebral haemorrhage, and 4.8% had subarachnoid haemorrhage. In contrast, 73.4% of patients without delirium had ischemic stroke, 15.2% had intracerebral haemorrhage, and 11.4% had subarachnoid haemorrhage. When examining the infarction subtypes among ischemic stroke patients (N=68), 30.0% of patients with delirium had large-artery atherosclerosis (LAA), compared to 43.1% in the non-delirium group (p=0.261). Small-artery occlusion (SAO) was present in 20.0% of delirium patients and 27.6% of non-delirium patients. Cardio-embolic stroke was more common in delirium patients (50.0%) compared to non-delirium patients (15.5%). None of the delirium patients had strokes of undetermined or other determined aetiology, whereas 10.3% and 3.4% of non-delirium patients, respectively, had these aetiologies.

The Oxfordshire classification among ischemic stroke patients revealed that total anterior circulation infarction (TACI) was significantly more common in delirium patients (60.0%) compared to non-delirium patients (8.6%) with a p-value of <0.001. Partial anterior circulation infarction (PACI) was observed in 10.0% of delirium patients and 48.3% of non-delirium patients, while lacunar infarction (LACI) was absent in delirium patients but present in 27.6% of non-delirium patients. Posterior circulation infarction (POCI) occurred in 30.0% of delirium patients and 15.5% of non-delirium patients.

Laterality of stroke also showed a significant association with delirium (p=0.018). Right hemisphere strokes were much more common in patients with delirium (71.4%) compared to those without (35.4%). Left hemisphere strokes occurred in only 9.5% of delirium patients but in



35.4% of non-delirium patients. Brainstem or cerebellar strokes were relatively similar between the groups, with 14.3% in the delirium group and 13.9% in the non-delirium group. Strokes without clear laterality were less common in delirium patients (4.8%) compared to non-delirium patients (15.2%).

In this study of 100 acute stroke patients, mortality was significantly higher in those who developed delirium, with 28.6% mortality in the delirium group compared to 6.3% in those without delirium ( $p=0.004$ ). Overall, 11% of the patients died. Functional outcomes, assessed using the Barthel Index at 1 month, were also significantly worse in patients with delirium. The mean Barthel Index score for the delirium group was 7.3 (SD 3.9), while patients without delirium had a mean score of 13.6 (SD 4.7), with a statistically significant difference ( $p<0.001$ ). The overall mean Barthel Index score for the entire cohort was 10.5 (SD 4.3), indicating poorer functional outcomes among those who developed delirium.

## Discussion

The present study aimed to identify risk factors associated with the development of delirium in patients presenting with acute stroke and to assess mortality and functional outcomes at one-month post-stroke. The incidence of delirium in our cohort was 21.0%, aligning with previous studies that report delirium incidence in stroke patients ranging from 10% to 30% (Fleischmann et al., 2023; Nydahl et al., 2017). (19, 20) This prevalence underscores the significant impact of delirium on the acute stroke population and highlights the necessity for vigilant monitoring and early intervention strategies. A key finding was the significantly higher mean age in patients with delirium (67.3 years) compared to those without (57.4 years). Advanced age is a well-documented risk factor for delirium, likely due to age-related neurodegenerative changes and increased vulnerability to physiological stressors (Inouye et al., 2014). (2) Interestingly, gender distribution did not significantly differ between the groups, which is consistent with some studies that find no gender predilection for delirium in stroke patients (Girard et al., 2008). (21)

Regarding comorbidities, hypertension (HTN) and diabetes mellitus (DM) were prevalent in both groups, though their association with delirium was not statistically significant. While hypertension has been

linked to increased stroke severity and poorer outcomes, its direct association with delirium remains inconclusive. Similarly, diabetes mellitus, a known risk factor for stroke, did not show a significant correlation with delirium in our study, which aligns with mixed findings in existing literature (Dostovic et al., 2016; Fleischmann et al., 2023). (19, 22) Smoking status also did not significantly differ between the groups. Although smoking is a modifiable risk factor for stroke, its relationship with delirium is less clear and may be influenced by other confounding variables (Ferro et al., 2002). (23) The prevalence of cardiac disease approached statistical significance, suggesting a potential trend that warrants further investigation. Cardiac diseases, particularly atrial fibrillation, are associated with cardio-embolic strokes, which may predispose patients to more severe neurological deficits and subsequent delirium (Girard et al., 2008). (21)

Neurological assessments revealed that patients with delirium had significantly lower GCS scores and higher NIHSS scores. Lower GCS scores indicate reduced consciousness, which is a strong predictor of delirium (Roberson et al., 2021). (24) Similarly, higher NIHSS scores, reflecting greater stroke severity, were significantly associated with delirium. This association is consistent with studies demonstrating that more severe neurological impairment increases the risk of delirium due to factors such as increased inflammation, greater metabolic demands, and more extensive brain injury (Cunningham, 2011). (25) The distribution of stroke types significantly differed between patients with and without delirium. A higher proportion of intracerebral haemorrhage and subarachnoid haemorrhage was observed in the delirium group compared to the non-delirium group. Haemorrhagic strokes are often associated with more acute and severe neurological deficits, which may contribute to the development of delirium (Gjestad et al., 2024). (26) Moreover, among ischemic stroke subtypes, cardio-embolic strokes were more prevalent in the delirium group. Cardio-embolic strokes typically result in larger and more severe infarcts, increasing the risk of cognitive disturbances and delirium (Dahl et al., 2010). (27)

The Oxfordshire classification system revealed that patients with delirium were significantly more likely to have total anterior circulation infarction compared to



those without delirium. Specifically, 60.0% of delirium patients had TACI, while only 8.6% of non-delirium patients had this type of stroke, a difference that was highly statistically significant ( $p < 0.001$ ). TACI strokes, which involve both cortical and subcortical regions supplied by the anterior circulation, are often associated with more extensive brain damage and greater neurological deficits (Yang et al., 2016).(28) The larger infarct size and the involvement of critical areas such as the frontal lobes, which are implicated in cognition and behaviour, may explain the higher incidence of delirium in this group (Etherton et al., 2018).(29) In contrast, partial anterior circulation infarctions and lacunar infarctions, which are smaller and typically cause less severe deficits, were more common in the non-delirium group. These findings are consistent with previous studies showing that larger strokes, particularly those involving the anterior circulation, are more likely to precipitate delirium (Rhee et al., 2022).(30)

Additionally, posterior circulation infarction was more prevalent among patients with delirium (30.0%) compared to those without delirium (15.5%), although the difference was not statistically significant. Posterior circulation strokes affect the brainstem, thalamus, and occipital lobes, regions that are crucial for arousal and consciousness (Go, 2015; Mehndiratta et al., 2012).(31, 32) Delirium in this context may result from impaired reticular activating system function, which regulates attention and wakefulness. This study also found a significant association between the laterality of the stroke and the development of delirium. Right hemisphere strokes were much more common in patients with delirium (71.4%) compared to those without (35.4%), while left hemisphere strokes were less frequent in the delirium group (9.5% vs. 35.4%,  $p = 0.018$ ). The right hemisphere is known to play a crucial role in visuospatial processing, attention, and awareness, and damage to this hemisphere may predispose patients to delirium by disrupting these cognitive functions. Right-sided strokes have been associated with a higher risk of cognitive impairment and delirium in multiple studies (Ott et al., 2023),(33) likely due to their impact on attentional networks. In contrast, left hemisphere strokes, which are more commonly associated with language deficits, may have less of a direct impact on the cognitive domains that are critical for the development of delirium.

The study's findings also indicate that delirium is associated with significantly higher mortality in stroke patients. Mortality in the delirium group was 28.6%, compared to 6.3% in the non-delirium group ( $p = 0.004$ ). Delirium has been consistently associated with higher mortality rates in acute stroke patients, likely due to the exacerbation of underlying physiological stress, increased risk of complications such as infections and falls, and the detrimental effects of delirium on overall brain function (Inouye et al., 2014).(2) Delirium may also be an indicator of more severe strokes, which independently increase the risk of mortality. Functional outcomes, as measured by the Barthel Index, were significantly worse in patients with delirium. The mean Barthel Index score at one month was 7.3 in the delirium group, compared to 13.6 in the non-delirium group, with a statistically significant difference ( $p < 0.001$ ). These findings are consistent with the literature, which shows that delirium is associated with poorer functional recovery following stroke (Fialho Silva et al., 2021; Klimiec-Moskal et al., 2022; Shi et al., 2012).(34-36) Delirium can lead to prolonged hospital stays, delayed rehabilitation, and a higher likelihood of long-term dependency (Girard et al., 2008).(21) The Barthel Index measures basic activities of daily living, and a lower score indicates greater disability. In the context of stroke, delirium may hinder the recovery of motor and cognitive functions, further reducing a patient's ability to regain independence.

As with any observational study, certain limitations must be acknowledged. The use of nonprobability sampling may limit the generalizability of our findings, as the study was conducted at a single tertiary care facility in India. Additionally, the study did not account for potential confounding variables such as pre-existing cognitive impairment or medication use, which may have influenced the development of delirium.

## Conclusion

The present study demonstrates that delirium is a significant complication among patients with acute stroke, particularly in those with right hemisphere involvement, total anterior circulation infarctions, and more severe strokes as indicated by higher NIHSS scores. Delirium was found to be associated with significantly higher mortality and poorer functional outcomes, as measured by the Barthel Index at one



month. These findings emphasize the need for early identification of high-risk patients, particularly those with larger or more severe strokes, and the implementation of targeted strategies to prevent delirium. Improving delirium management may not only enhance patient recovery but also reduce mortality rates and long-term disability.

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**Table 1: Sociodemographic and clinical characteristics of acute stroke patients with and without delirium**

		Delirium			P value
		Present N = 21	Absent N = 79	Total N = 100	
		n (%)	n (%)	n (%)	
Age (in years) <i>Mean (SD)</i>		67.3 (8.1)	57.4 (9.5)	62.4 (8.8)	<0.001*
Gender	Male	10 (47.6)	44 (55.7)	54 (54.0)	0.509



	Female	11 (52.4)	35 (44.3)	46 (46.0)	
Hypertension	Present	17 (81.0)	55 (69.6)	72 (72.0)	0.304
	Absent	4 (19.0)	24 (30.4)	28 (28.0)	
Diabetes	Present	7 (33.3)	33 (41.8)	40 (40.0)	0.483
	Absent	14 (66.7)	46 (58.2)	60 (60.0)	
Smoking	Present	6 (28.6)	31 (39.2)	37 (37.0)	0.368
	Absent	15 (71.4)	48 (60.8)	63 (63.0)	
Previous stroke	Present	3 (14.3)	17 (21.5)	20 (20.0)	0.461
	Absent	18 (85.7)	62 (78.5)	80 (80.0)	
TIA	Present	3 (14.3)	9 (11.4)	12 (12.0)	0.717
	Absent	18 (85.7)	70 (88.6)	88 (88.0)	
Cardiac disease	Present	10 (47.6)	21 (26.6)	31 (31.0)	0.064
	Absent	11 (52.4)	58 (73.4)	69 (69.0)	
GCS	≤12	14 (66.7)	9 (11.4)	23 (23.0)	<0.001*
	>12	7 (33.3)	70 (88.6)	77 (77.0)	
NIHSS	<5	0 (0.0)	13 (16.5)	13 (13.0)	<0.001*
	5 to 15	3 (14.3)	52 (65.8)	55 (55.0)	
	16 to 20	8 (38.1)	12 (15.2)	20 (20.0)	
	21 to 42	10 (47.6)	2 (2.5)	12 (12.0)	

\*Statistically significant at  $p < 0.05$   
SD, Standard deviation; TIA, Transient ischemic attack; GCS, Glasgow coma scale; NIHSS, National Institutes of Health Stroke Scale

Table 2: Stroke characteristics of acute stroke patients with and without delirium

		Delirium			P value
		Present N = 21	Absent N = 79	Total N = 100	
		n (%)	n (%)	n (%)	
Type of stroke	Ischemic	10 (47.6)	58 (73.4)	68 (68.0)	0.006*
	Intracerebral haemorrhage	10 (47.6)	12 (15.2)	22 (22.0)	
	Subarachnoid haemorrhage	1 (4.8)	9 (11.4)	10 (10.0)	
Infarction subtypes (among ischemic stroke patients, N = 68, 10 had delirium and 58 did not)	LAA	3 (30.0)	25 (43.1)	28 (28.0)	0.261
	SAO	2 (20.0)	16 (27.6)	18 (18.0)	
	Cardio-embolic	5 (50.0)	9 (15.5)	14 (14.0)	
	Undetermined aetiology	0 (0.0)	6 (10.3)	6 (6.0)	
	Other determined aetiology	0 (0.0)	2 (3.4)	2 (2.0)	
Oxfordshire classification (among ischemic stroke patients, N = 68, 10 had delirium and 58 did not)	TACI	6 (60.0)	5 (8.6)	11 (11.0)	<0.001*
	PACI	1 (10.0)	28 (48.3)	29 (29.0)	
	LACI	0 (0.0)	16 (27.6)	16 (16.0)	
	POCI	3 (30.0)	9 (15.5)	12 (12.0)	
Laterality of stroke	Right hemisphere	15 (71.4)	28 (35.4)	43 (43.0)	0.018*
	Left hemisphere	2 (9.5)	28 (35.4)	30 (30.0)	
	Brainstem-cerebellum	3 (14.3)	11 (13.9)	14 (14.0)	



	No laterality	1 (4.8)	12 (15.2)	13 (13.0)	
*Statistically significant at p<0.05 LAA, Large-artery atherosclerosis; SAO, Small-artery occlusion; TACI, Total anterior circulation infarction; PACI, Partial anterior circulation infarction; LACI, Lacunar infarction; POCI, Posterior circulation infarction					

**Table 3: Outcomes of acute stroke patients with and without delirium**

		Delirium			P value
		Present N = 21	Absent N = 79	Total N = 100	
		n (%)	n (%)	n (%)	
Mortality	Yes	6 (28.6)	5 (6.3)	11 (11.0)	0.004*
	No	15 (71.4)	74 (93.7)	89 (89.0)	
Barthel index Mean (SD)		7.3 (3.9)	13.6 (4.7)	10.5 (4.3)	<0.001*
*Statistically significant at p<0.05 SD, Standard deviation					