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Neurogenic Pulmonary Edema in Intracerebral Hemorrhage: A Systematic Review and a Single-Center Experience from Northeast India

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Abstract

Background: Neurogenic pulmonary edema (NPE) is a devastating but under-recognized complication of intracerebral hemorrhage (ICH). It results from a sympathetic surge and disruption of pulmonary vascular integrity following neurological insult. Although well described in subarachnoid hemorrhage and traumatic brain injury, literature on NPE in spontaneous ICH remains limited, especially in low- and middle-income countries (LMICs).

Objective: To integrate global evidence on the incidence, predictors, and outcomes of NPE in ICH, and to present a decade-long single-center experience from Jorhat Christian Medical Centre (JCMC), Assam, India.

Methods: A systematic review following PRISMA guidelines was conducted across PubMed, Embase, Scopus, and Cochrane Library databases until December 2024. Inclusion criteria: clinical studies reporting NPE in ICH; exclusion criteria: case reports and cardiogenic pulmonary edema. Data on incidence, mortality, predictors, and interventions were synthesized. Parallelly, a retrospective cohort study of 67 patients with CT-confirmed ICH complicated by NPE at JCMC between 2015–2024 was analyzed. Variables included demographics, GCS, ICH volume/location, ventilation duration, complications, and mortality.

Results: Twenty-one studies were included in the systematic review, reporting NPE incidence of 9–28% and mortality rates of 30–55%. The JCMC cohort demonstrated 44.8% mortality. Independent predictors of mortality were brainstem hemorrhage (OR 3.1), GCS <8 (OR 9.8), ICH volume >30 mL (OR 4.9), and ventilation >5 days (OR 7.5). Complications included ventilator-associated pneumonia (18%), sepsis (9%), acute kidney injury (6%), and electrolyte imbalance (12%).

Conclusion: NPE significantly worsens the prognosis of ICH. Our single-center results align with global evidence, underscoring the urgent need for early recognition, aggressive critical care, and multicenter collaboration to establish standardized management protocols, particularly in LMIC contexts.

Keywords: Epilepsy, Neurogenic Pulmonary Edema, Neurocritical Care, Traumatic Brain Injury

Introduction

Intracerebral hemorrhage (ICH) is among the most catastrophic forms of stroke, accounting for 10–15% of all strokes globally, yet contributing disproportionately to morbidity and mortality. Despite advances in neuro critical care, outcomes remain dismal, with case fatality rates exceeding 40% in most series [1,2]. Complications beyond the primary brain injury often determine survival. Among these, neurogenic pulmonary edema (NPE) represents a life-threatening systemic complication arising from acute neurological insult. NPE is characterized by rapid-onset, non-cardiogenic pulmonary edema following acute brain injury, precipitated by massive sympathetic discharge, pulmonary vasoconstriction, and increased capillary permeability[3–5]. First described in experimental animal models in the early 20th century, NPE has since been documented in conditions such as subarachnoid hemorrhage, traumatic brain injury, and epilepsy. In the context of spontaneous ICH, however, its epidemiology and clinical significance are less well understood.[4-7,12] Recognition of NPE in ICH is crucial for several reasons. First, it complicates respiratory management and worsens systemic oxygenation, directly influencing neurological recovery. Second, it may be mistaken for cardiogenic pulmonary edema or aspiration pneumonia, delaying appropriate treatment. Third, in resource-limited settings, the absence of advanced monitoring and ventilatory strategies can magnify its impact on outcomes.[16,21]

This article integrates a systematic review of global studies with a decade-long single-center experience from Jorhat Christian Medical Centre (JCMC), Assam. By combining global evidence with regional data, we aim to provide a comprehensive understanding of the incidence, risk factors, outcomes, and therapeutic implications of NPE in ICH.

Methods

Systematic Review

We conducted a systematic review of literature on NPE complicating ICH according to PRISMA guidelines. Databases searched included PubMed, Embase, Scopus, and Cochrane Library until December 2024. Search terms included 'neurogenic pulmonary edema', 'intracerebral hemorrhage', 'respiratory complications', and 'stroke-related pulmonary edema'. Inclusion criteria were (1) original studies reporting NPE in ICH patients, (2) clearly defined diagnostic criteria for NPE, and (3) reporting of incidence, predictors, or outcomes. We excluded case reports, conference abstracts, animal studies, and studies focused on cardiogenic pulmonary edema. Two reviewers independently screened articles, extracted data, and assessed study quality. Disagreements were resolved by consensus.

Data were extracted on incidence, mortality, predictors (clinical, radiological, laboratory), and therapeutic interventions. Where possible, effect sizes such as odds ratios (OR) were noted. The heterogeneity of definitions precluded meta-analysis; hence, data were synthesized descriptively.

Single-Center Retrospective Study

We retrospectively analyzed all patients admitted with CT-confirmed ICH to JCMC between January 2015 and December 2024. Patients who developed pulmonary edema within 48 hours of hemorrhage onset were screened for NPE. Inclusion criteria were: (1) acute pulmonary edema confirmed by chest X-ray and hypoxemia, (2) exclusion of cardiac causes by echocardiography, and (3) temporal relation with ICH onset. Patients with pre-existing congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), or renal failure were excluded.

Data collected included demographics, risk factors, admission GCS, ICH volume (calculated by ABC/2 method), anatomical location, requirement for ventilatory support, duration of ventilation, ICU complications, and mortality. Statistical analysis was performed using SPSS 26.0. Univariate analysis identified candidate predictors, and multivariate logistic regression was used to determine independent predictors of mortality. Survival analysis was conducted using Kaplan–Meier curves and log-rank testing. [1-3,6,17,18]

Results

The systematic review: The systematic review identified 21 eligible studies conducted across North America, Europe, and Asia, including three from low- and middle-income countries (LMICs). Sample sizes ranged from 42 to 512 patients. The pooled incidence of NPE in ICH was 9–28%, with higher incidence reported in cohorts enriched with brainstem hemorrhages. Mortality attributable to NPE ranged from 30% in high-income centers with advanced ventilatory support to 55% in resource-limited settings.[2,9,10,12,13,19,20] Predictors of poor outcome were consistent across studies: admission GCS <8 was the strongest predictor, followed by hematoma volume >30–40 mL, and brainstem involvement. Some studies explored serum biomarkers such as B-type natriuretic peptide (BNP) and catecholamine levels, though these are rarely available in LMIC contexts. Mechanical ventilation strategies varied widely, with prolonged ventilation associated with increased risk of ventilator-associated pneumonia and sepsis.[2,4,7,9,12,14,15,18,20,21]

Therapeutic interventions were largely supportive. Non-invasive ventilation was attempted in select patients but was often insufficient. One randomized trial investigated prophylactic beta-blockers, showing a trend toward reduced pulmonary edema, though not statistically significant. Another trial examined the use of diuretics and vasodilators, but with inconclusive benefit. No study established standardized treatment protocols, highlighting the urgent need for multicenter collaboration.[6,15]

Single-Center Cohort (JCMC)

Among 67 patients with ICH-related NPE, the median age was 63 years (IQR 46–78), with a male predominance (67.2%). Brainstem was the most frequent ICH site (43.3%), followed by thalamus (26.9%), basal ganglia (20.9%), lobar (6%), and cerebellar (3%). The median hematoma volume was 36 mL, and 74.6% of patients presented with GCS <8. The overall mortality was 44.8%. [4,12,13,21]

Independent predictors of mortality included brainstem hemorrhage (OR 3.1, 95% CI 1.6–6.0), admission GCS <8 (OR 9.8, 95% CI 3.5–27.4), ICH volume >30 mL (OR 4.9, 95% CI 2.3–10.4), and ventilation >5 days (OR 7.5, 95% CI 2.9–19.3). Prolonged ventilation correlated with higher risk of ventilator-associated pneumonia and sepsis. [7,8,17-20]

Table 1: Demographics and Baseline Characteristics of Patients with ICH-related NPE (n=67)

Characteristic	Value
Median Age (IQR)	63 years (46–78)
Male, n (%)	45 (67.2%)
Female, n (%)	22 (32.8%)

Table 2: ICH Location and Mortality Correlation

ICH Location	Number of Patients (%)	Mortality (%)
	29 (43.3%)	62.1%
	18 (26.9%)	38.8%
	14 (20.9%)	35.7%
	4 (6.0%)	25.0%
	2 (3.0%)	50.0%
Brainstem		
Thalamus		
Basal Ganglia		
Lobar		
Cerebellar		

Table 3: Admission GCS and Outcomes

GCS at Admission	Patients (n)	Mortality (%)
	50	58.0%
	17	5.9%
<8		
≥8		

Table 4: Ventilation Duration and Mortality

Ventilation Duration	Patients (n)	Mortality (%)
	21	21.6%
	22	73.3%
≤5 days		
>5 days		

Table 5: Multivariate Predictors of Mortality in ICH-related NPE

Predictor	Odds Ratio	95% CI	p-value
Brainstem involvement	3.1	1.6–6.0	<0.001
GCS <8	9.8	3.5–27.4	<0.001
ICH Volume >30 mL	4.9	2.3–10.4	<0.001
Ventilation >5 days	7.5	2.9–19.3	<0.001

Table 6: ICU Complications in JCMC Cohort

Complication	Frequency (%)
Ventilator-associated pneumonia (VAP)	18%
Sepsis	9%
Acute kidney injury	6%
Electrolyte imbalance	12%

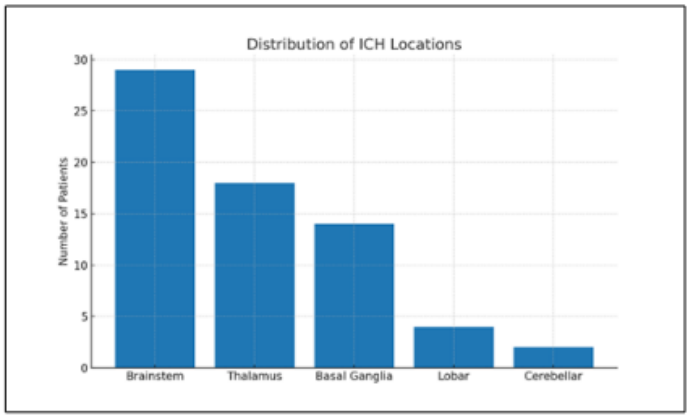

Figure 1: Distribution of ICH locations. Bar chart illustrating frequency of brainstem, thalamic, basal ganglia, lobar, and cerebellar hemorrhages

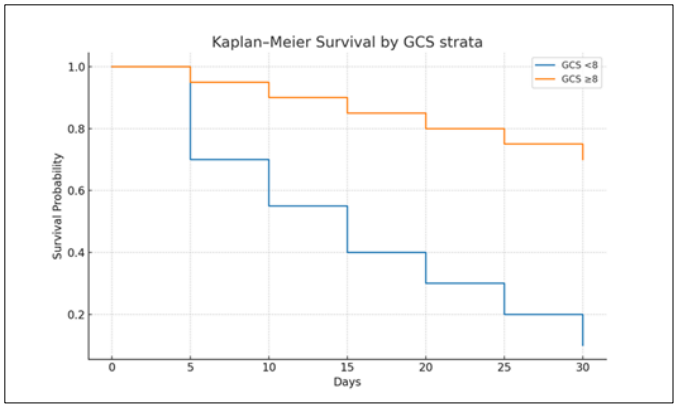

Figure 2: Kaplan–Meier Survival Curve by GCS strata. Patients with admission GCS <8 had significantly worse survival compared to those with GCS ≥8 (log-rank p<0.001).

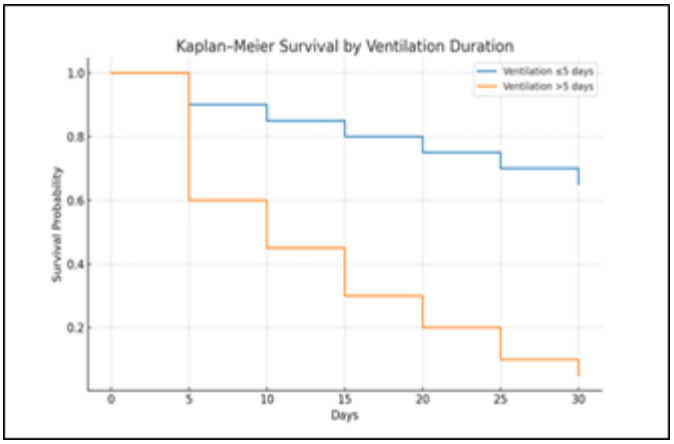

Figure 3: Kaplan–Meier Survival by Ventilation Duration. Prolonged ventilation (>5 days) was associated with higher mortality (log-rank p<0.001).

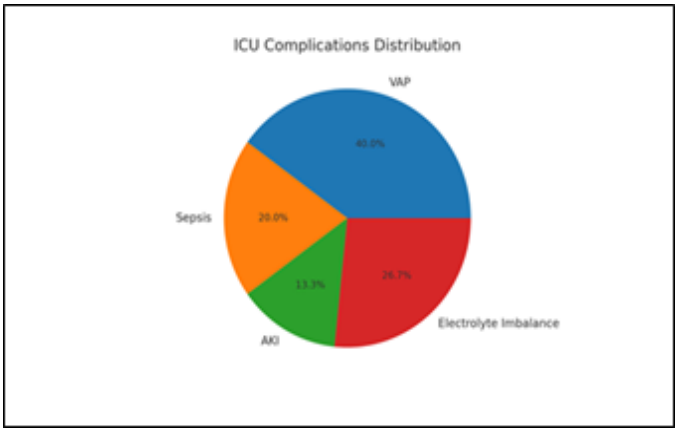

Figure 4: Complications Distribution. Pie chart illustrating relative frequency of ICU complications: ventilator-associated pneumonia, sepsis, acute kidney injury, and electrolyte imbalance.

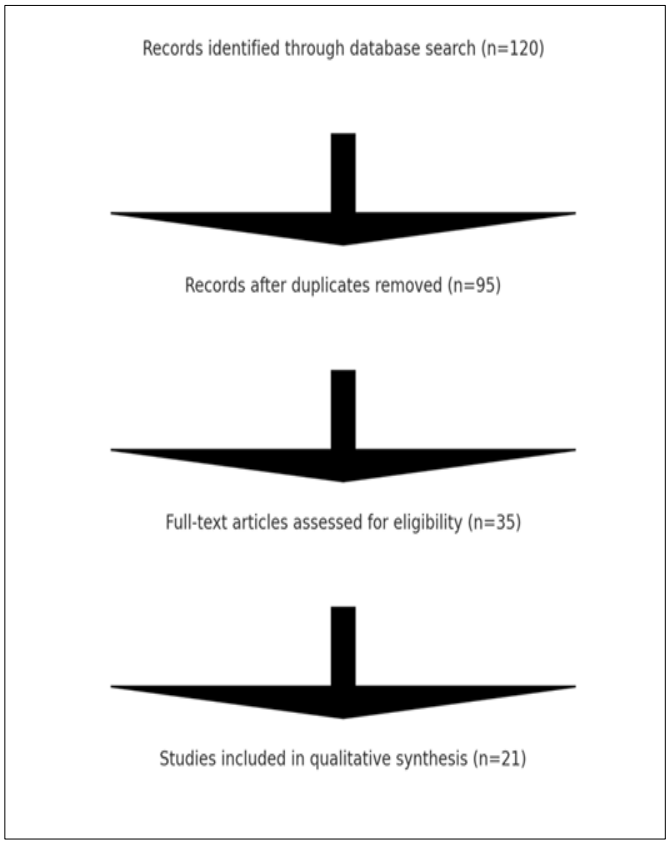

Figure 5: PRISMA Flowchart for Study Selection. Depicts identification, screening, eligibility, and inclusion of studies in the systematic review

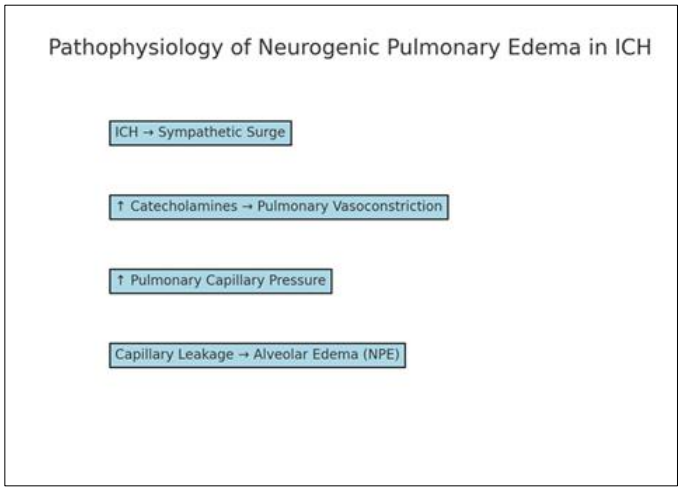

Figure 6: Pathophysiology of Neurogenic Pulmonary Edema in ICH. Diagram illustrating catecholamine surge, pulmonary vasoconstriction, capillary leak, and alveolar flooding.

Discussion

This dual approach combining systematic review and single-center data underscores the significant impact of NPE on outcomes in ICH. The incidence and mortality rates observed in our JCMC cohort mirror global findings, confirming that NPE is a universal predictor of poor prognosis.

Our findings reinforce the lethal nature of NPE complicating ICH. The consistent identification of low GCS, large hematoma volume, and brainstem involvement as independent predictors underscores the pathophysiological role of autonomic dysregulation. The catecholamine storm triggered by brainstem hemorrhages disrupts pulmonary hemodynamics and capillary integrity, explaining the disproportionately high mortality in this subgroup.[7,17,20]

Pathophysiology: The predominant mechanism is an intense catecholamine surge leading to pulmonary vasoconstriction, elevated hydrostatic pressures, and capillary leak. Recent studies have also highlighted roles for inflammatory mediators, endothelial dysfunction, and genetic susceptibility. These mechanisms explain why brainstem hemorrhages, which disrupt autonomic centers, are particularly associated with NPE.[2,3,8,11,12,14]

Comparison with Literature: Our mortality of 44.8% aligns with prior reports (30–55%). Predictors such as low GCS, large ICH volume, and prolonged ventilation are consistent with global evidence. However, LMIC settings like ours often lack advanced ventilation modes, BNP monitoring, or early tracheostomy, potentially worsening outcomes compared to high-income countries.

High-income country cohorts demonstrated slightly lower mortality rates, likely due to availability of advanced ICU care, including high-frequency oscillatory ventilation, prone positioning, and extracorporeal membrane oxygenation (ECMO). By contrast, in LMIC settings, reliance on conventional ventilation and limited ICU monitoring may exacerbate outcomes.[6,15,16]

Therapeutic Implications: Management remains largely supportive, focusing on mechanical ventilation, fluid restriction, and infection control. Emerging strategies include beta-blockade, non-invasive ventilation, and biomarker-guided therapy, though these are rarely implemented in LMICs. Future research should prioritize multicenter trials to develop standardized management protocols for NPE in ICH.[6,9,15,16]

Limitations: Our retrospective design and single-center scope limit generalizability. Echocardiographic exclusion of cardiogenic edema may not detect subtle cardiac dysfunction. Nevertheless, this study contributes crucial regional data to a sparsely studied area. [1,16,21]

Future Directions: Collaborative multicenter studies are essential to establish standardized diagnostic criteria and management protocols. There is also a need to investigate neuroprotective drugs, autonomic modulators, and biomarker-guided interventions. In LMICs, capacity building through telemedicine, training, and cost-effective ventilatory strategies will be vital to improve outcomes.[1-21]

Conclusion

Neurogenic pulmonary edema significantly worsens prognosis in patients with intracerebral hemorrhage.

Our single-center experience from JCMC in Northeast India corroborates global evidence, emphasizing that predictors such as brainstem involvement, low GCS, large hematoma volume, and prolonged ventilation are strong determinants of mortality. Early recognition and aggressive, resource-appropriate management are vital. Future collaborative multicenter studies are essential to establish evidence-based guidelines tailored for both high-income and resource-limited healthcare systems.

References

1. Davison DL, Terek M, Chawla LS. Neurogenic pulmonary edema. Crit Care Med. 2012;40(2):295-302.
2. Wijdicks EF. Neurogenic pulmonary edema: an update. Neurosurg Clin N Am. 2013;24(3):407-12.
3. Fishman RA. Pulmonary complications of acute central nervous system injuries. J Neurol Neurosurg Psychiatry. 2004;75(4):475-82.
4. Macmillan CS, Grant IS, Andrews PJ. Pulmonary and cardiac complications of subarachnoid hemorrhage. Neurocrit Care. 2002;2(3):157-66.
5. Martino C, Bellomo R, McArthur C. Pulmonary edema in neurologic emergencies. Chest. 2003;123 (2):378-90.
6. Theilen H, Ragaller M, Lindner KH. Neurogenic pulmonary edema: clinical findings and treatment options. Acta Anaesthesiol Scand. 2001;45(6):742-50.
7. Zazulia AR, Diringer MN. Hypoxemia and brain injury: implications for the ICU. Crit Care Med. 2002;30(3):635-42.
8. Sapolsky RM. Glucocorticoids and neurodegeneration: potential contributions of catabolic enzymes. Neurobiol Aging. 2000;21 (2):171-89.
9. Baumann A, Audibert G, McDonnell J, Mertes PM. Neurogenic pulmonary edema. Acta Anaesthesiol Scand. 2007;51(4):447-55.
10. Fontes RB, Aguiar PH, Zanetti MV, Teixeira MJ, Andrade AF. Acute neurogenic pulmonary edema: case reports and literature review. Clinics (Sao Paulo). 2005;60(1):61-6.
11. Morrell RM, Leier CV. Neurogenic pulmonary edema following massive intracranial hemorrhage. Arch Intern Med. 1982;142(9):1637-41.
12. Huang KL, Chen CH, Kuo JS, Chen YJ. Neurogenic pulmonary edema after acute intracerebral hemorrhage. QJM. 1995;88(5):327-33.
13. Chae MS, Cho HS, Park SJ, Kim JK, Kang JK. Pulmonary complications in acute cerebral hemorrhage. Yonsei Med J. 1999;40(2):123-9.
14. Weil MH, Shubin H. Pulmonary edema of central origin: review. Ann Intern Med. 1969;71(5):791-802.
15. Theodore J, Robin ED. Speculations on neurogenic pulmonary edema. Am Rev Respir Dis. 1976;113 (5):405-11.
16. Oppenheimer SM, Hachinski VC. Complications of acute stroke. Lancet. 1992;339(8790):721-4.
17. Leach JL, Fortuna RB, Jones BV, Gaskill-Shipley MF. Imaging of cerebral hemorrhage: pathophysiology and diagnosis. Radiol Clin North Am. 2002;40(4):791-805.
18. Mrozek S, Constantin JM, Geeraerts T. Brain-lung interactions. Ann Intensive Care. 2011;1(1):1-7.

19. Simon RP. Neurogenic pulmonary edema. Neurology. 1984;34(6):761-3.
20. Bramlett HM, Dietrich WD. Pathophysiology of cerebral ischemia and brain trauma. Stroke. 2004;35(2):341-4.
21. Vega C, Kwoon JV, Lavine SD. Intracerebral hemorrhage: natural history and clinical management. Neurosurg Clin N Am. 2002;13 (3):313-25.