Article published online: 2023-04-24

Clinicoradiological and Biochemical Predictors of Mortality in Hospitalized Patients of Spontaneous Intracerebral Hemorrhage

Bhagyashri B. Wankhade[1] Ashok Kumar[2] Sanaullah Mudassir[2] Abhay Ranjan[2]

[1] Department of General Medicine, Indira Gandhi Government Medical College, Nagpur, Maharashtra, India
[2] Department of Neurology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India

Address for correspondence Abhay Ranjan, MD, DM, PDF, Department of Neurology, Indira Gandhi Institute of Medical Sciences IGIMS, Sheikhpura, Patna 800014, Bihar, India (e-mail: drabhayranjan97@gmail.com).

J Neuroanaesthesiol Crit Care 2023;10:46–50.

Abstract

Background Intracerebral hemorrhage (ICH) is a cerebrovascular insult leading to bleeding within the brain parenchyma. It is associated with high rate of mortality and morbidity. The main objective of our study was to study in-hospital predictors of mortality in patients with spontaneous ICH managed medically.

Methods This was a single-center prospective study and patients of ICH meeting the inclusion criteria were recruited from March 2019 to December 2020. Demographic data were collected and brain imaging was done. Each patient was observed for outcome with either discharge or death.

Results Total 202 patients of ICH were included in the study. Mean age of the patients was 58.46 ± 11.6 years (26–95 years), which included 75.25% males. Most common location of ICH was gangliocapsular (42.08%) followed by thalamus (37.13%). Overall mortality was 35.60% ($n = 72$). On univariate analysis, predictors of mortality were higher age, low Glasgow coma scale (GCS) score, intraventricular extension, volume of hematoma, raised ICH score, leucocytosis, raised creatinine, hypernatremia, and ventilatory support. Need for ventilatory support, raised serum creatinine, and low GCS was found to be independent predictor of mortality on multivariate analysis.

Conclusion Our study showed that about one-third of ICH patient died during in-hospital management. Mechanical ventilation requirement, low GCS, and raised creatinine were found to be independent predictors of mortality in our study.

Keywords
- intracerebral hemorrhage
- ICH
- stroke
- mortality
- spontaneous
- predictors

Introduction

Stroke is one of the leading causes of disability and mortality worldwide. Stroke is responsible for11.6% of all deaths worldwide and is the second most common cause of death following ischemic heart disease.[1] Intracerebral hemorrhage (ICH) refers to bleeding within brain parenchyma and defined by its location within the brain parenchyma. ICH occurs in 10 to 15% of all stroke cases with a very high rate of mortality and morbidity requiring prolonged hospitalization. In developed countries, the incidence of hypertensive ICH has reduced with the improvement in blood pressure control. However, in developing countries like India, the burden of ICH has not decreased.[1] The outcome of ICH depends on various factors such as hematoma volume, location, and extension to ventricles.[2] Between 35 and 52% of people die within 30 days, while 20% of survivors recover fully functionally within 6 months.[3] Approximately half of

article published online
April 24, 2023

DOI https://doi.org/10.1055/s-0042-1760272.
ISSN 2348-0548.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

this mortality occurs within the first 24 hours that shows critical importance of early and effective treatment in the emergency department.

There are only few studies published from India predicting factors affecting mortality in hospitalized patients with ICH.[4] The main objective of our study was to describe clinicodemographic profile of ICH patients managed medically and determine the factors affecting mortality in the hospitalized patients of ICH in our tertiary care hospital.

Materials and Methods

This was a single-center prospective observational study done on patients of ICH between March 2019 and December 2020. The study was approved by the institutional ethics committee. Written informed consent was obtained from all patients or their guardians for participation in the study. All the patients with the sudden onset acute neurological deficit of vascular origin with neuroimaging suggestive of ICH were included in the study. The following group of patients were excluded from the study: (1) Patients having tumoral and traumatic bleeding, that is, contusion/epidural hemorrhage/subdural hemorrhage; (2) ICH due to secondary causes like anticoagulant therapy/post-thrombolytic/vascular malformation rupture; (3) patients or attendant not giving consent for participation in the study; (4) patients who underwent neurosurgical intervention for ICH.

All the admitted patients were evaluated in detail including demographic details such as age, sex, and address along with clinical data such as handedness, vascular risk factors (hypertension, diabetes, previous stroke), addictions (smoking, tobacco chewing, alcohol), and presenting complaints (contralateral weakness, slurring of speech, altered sensorium, vomiting, headache, and convulsion). Detailed neurological examination was done at the time of admission. The level of consciousness was graded with Glasgow Coma scale (GCS). Patients underwent investigations such as complete hemogram, serum biochemistry (liver function test, kidney function test), prothrombin time/International normalized ratio, electrocardiogram, ultrasound abdomen, two-dimensional echocardiography, and brain imaging. Brain imaging included noncontrast computed tomography brain. Neuroimaging was assessed for location (gangliocapsular, thalamus, cortical, cerebellar, brainstem, intraventricular) and volume of ICH with its secondary complications like mass effect, midline shift, and ventricular extension. The volume of hematoma was calculated by ABC/2 method and ICH scoring was done by using ICH scoring system given by Hemphill et al.[2] All patients received antiedema measures like mannitol or hypertonic saline, intravenous fluids, and management of hypertension and diabetes mellitus. All the patients were managed conservatively without any neurosurgical intervention. Patients shifted to intensive care unit (ICU) who need intensive monitoring or ventilatory support. Repeat CT was done for patients in ICU for worsening sensorium or new neurological deficit. Patients were followed up during the course of hospitalization with the outcome being either discharge or death of the patient. Mortality predictors were assessed in relation to demographic (age, sex), clinical (GCS, requirement of ventilatory support), biochemical (leukocyte count, serum creatinine and serum sodium), and radiological (location of bleeding, intraventricular extension (IVE), hematoma volume) parameters. Leucocytosis was considered if total cell count was above $11 \times 10^3/mm^3$, raised serum creatinine more than 1.5 mg/dL, and hypernatremia more than 145 mmol/L. Comparison was made for these parameters among survived and deceased.

Statistical analyses were done with Statistical Package for Social Sciences, SPSS (Version 20.0, SPSS Inc.). Categorical variable between deceased and survived was compared using the chi-squared test (or Fisher's exact test) and continuous variable was compared using independent *t*-test or Mann–Whitney U test. Predictors of mortality were assessed using a univariate binary logistic regression analysis followed by a multivariate analysis adjusting the covariates with a *p*-value of less than 0.05 in the univariate analysis. A variable having an exact two-tailed *p*-value of less than 0.05 in statistics was considered significant.

Results

Baseline Characteristics

In this study, 202 patients were included fulfilling inclusion criteria. Mean age of study subjects was 58.46 ± 11.6 years. Majority of the patients were males (i.e., 75.25%). Around two-thirds (64.85%) of the patients were tobacco chewer. The most common presentation was contralateral weakness (81.18%) followed by slurring of speech (39.6%) and altered sensorium (39.6%). Diabetes was present in 13.86% of cases, while hypertension in 83.17% cases. GCS score was less than 8 in 29.7% patients at the time of admission.

The ICH was most commonly localized in gangliocapsular region (42.08%) followed by thalamus (37.13%), cortical (8.42%), cerebellar (7.92%), and brainstem (2.97%). IVE of hemorrhage was found in 35.64% patients. Mean volume of ICH was 20.83 ± 13.41 mL. Mean ICH score in our study was 1.25 ± 1.15. Hypernatremia was present in 38.1% of patients. Ventilatory support was needed in 36.63% of patients. Total 72 patients (35.60%) succumbed among 202.

Comparison of Clinical, Laboratory, and Imaging Parameters between Deceased and Survived ICH Patients

On univariate analysis, age (years) of the patients who died was significantly higher as compared with discharged subjects (61.63 ± 12.36 vs. 56.74 ± 10.8 years). Distribution of mortality was comparable in female and male patients (36 vs. 34.87%). GCS score was significantly lower in deceased patients compared with survived patients (5 vs. 15). There was significantly higher mortality in patients of ICH with IVE as compared with patients without IVE (65.28 vs 34.72%, respectively), while there was no significant differences in the mortality in patients of ICH with or without midline shift. Mean volume of ICH and ICH score in the deceased patients

Table 1 Univariate analysis for predictors of mortality in spontaneous ICH patients

Variables	Deceased ($n = 72$)	Survived ($n = 130$)	*p*-Value
Demographic features			
Age (years) mean ± SD	61.63 ± 12.36	56.74 ± 10.8	0.003[a]
Male	53 (34.87%)	99 (65.13%)	0.884
Clinical findings			
GCS Median (IQR)	6 (3–8)	15 (13–15)	<0.001[a]
ICH score mean ± SD	2.54 ± 0.55	0.54 ± 0.67	<0.001[a]
Neuroimaging findings			
IVE, *n*, %	47 (65.28%)	25 (34.72%)	<0.001[a]
Hematoma volume (mL) mean ± SD	31.54 ± 13.38	15.03 ± 9.22	<0.001[a]
Location			
Basal ganglia	35 (41.18%)	50 (58.82%)	0.126
Thalamus	22 (29.33%)	53 (70.67%)	0.183
Cerebellum	6 (37.50%)	10 (62.50%)	0.837
Brainstem	4 (66.67%)	2 (33.33%)	0.187
Lobar	4 (23.53%)	13 (76.47%)	0.427
Deranged creatinine, *n*, %	52 (72.2%)	25 (19.2%)	<0.001[a]
Hypernatremia	60 (83.3%)	38 (29.2)	<0.001[a]
Leukocytosis, *n*, (%)	64 (63.37%)	37 (36.63%)	<0.001[a]
Ventilatory support, *n*, %	69 (93.24%)	5 (6.76%)	<0.001[a]

Abbreviations: GCS, Glasgow coma scale; ICH, intracranial hemorrhage, IQR, interquartile range; IVE, intraventricular extension; n, number of patients, SD, standard deviation.
Note: Leukocytosis—Total leukocyte count (TLC) >11,000/μL; Deranged serum creatinine—Serum creatinine >1.5 mg/dL; Hypernatremia—Serum Na >145mEq/L.
[a]Significant *p*-values.

was significantly higher compared with discharged group (31.54 ± 13.38 vs. 15.03 ± 9.22 mL and 2.54 ± 0.55 vs. 0.54 ± 0.67). No significant difference was found between deceased and survived patient regarding the location of ICH. Mortality was significantly associated with leucocytosis (63.37 vs. 36.63%), raised serum creatinine (52 [72.2%] vs. 25 [19.2%]), and raised serum sodium (60 [83.3%] vs. 38 [29.2]). Proportion of mortality was significantly higher in patients requiring ventilatory support as compared with patients not requiring ventilatory support (93.24 vs. 6.76%; ►**Table 1**).

On multivariate binary logistic regression analysis, requirement of ventilatory support ($p = 0.009$), lower GCS score ($p = 0.014$), and raised serum creatinine level ($p = 0.043$) was found to be independent predictor of mortality in ICH patients (►**Table 2**).

Discussion

ICH is the most devastating form of stroke causing severe disability among survivors. It is associated with high mortality as observed in previous studies. Accurate prediction of ICH outcome in the emergency department is important for making decisions about the judicious use of scarce resources.[5]

In present study, mean age and gender distribution of patients with ICH is comparable to previous studies from India by Hegde et al,[4] Bhatia et al,[6] and Modi et al.[7] ICH is reported to be more common in advancing age and male sex.[8] Bahou[9] and Namani et al[10] reported the commonest clinical symptom as limb weakness similar to our study. Headache and altered sensorium were present in more than one-third patients of ICH in our study. Kumar et al[11] reported that most common symptoms were limb weakness followed by altered sensorium and headache, while Ojha et al[12] and Hegde et al[4] reported that the common presenting symptoms were headache and loss of consciousness.

Most common location of ICH was gangliocapsular followed closely by thalamus comparable to a study by Narayan et al.[13] Our findings were in line with study of Bhatia et al[6] where each of lobar bleeding, brainstem bleeding, and cerebellar bleeding were less than 10%. The mean volume of ICH was comparable to mean volume of bleeding in a study by Hegde et al.[4]

Table 2 Multivariate logistic regression for predictors of mortality in spontaneous ICH patients

Variables	*p*-Value	Odds ratio	95%CI
Age (years)	0.469	1.034	0.944–1.132
GCS	0.012[a]	1.715	1.136–2.617
IVE	0.286	16.763	0.093–2971.88
ICH volume(mL)	0.590	1.025	0.938–1.120
Leukocytosis	0.352	2.642	0.341–20.457
Deranged creatinine(mg/dL)	0.043[a]	11.861	1.079–130.405
Hypernatremia (mmol/L)	0089	13.127	0.675–255.201
Ventilatory support	0.009[a]	51.323	2.624–1003.658

Abbreviations: CI, confidence interval; GCS, Glasgow coma scale; ICH, intracranial hemorrhage, IVE, intraventricular extension.
Note: Leukocytosis—Total leukocyte count >11,000/μL; Deranged serum creatinine—Serum creatinine >1.5 mg/dL; Hypernatremia—Serum Na >145mEq/L.
[a]Significant *p*-values.

Our study showed that around one-third ICH patients died during hospital stay. Compared with the present study, in the study by Hegde et al,[4] the overall mortality was 30.1%, which was slightly less than our study. Bhatia et al[6] reported that 32.7% mortality, which was comparable to the present study. Modi et al[7] reported that in-hospital mortality was 41.23% with maximum mortality occurring within 72 hours. In a study by Ahmed et al,[14] 32% patients died during hospital stay. Safatli et al[15] reported that the 30-day mortality was 25.15%. In a study by Kumar et al,[11] mortality rate of spontaneous ICH was almost 50%.

Age showed significant association with mortality as patients who died had significantly higher age similar to the study by Hegde et al[4] and Kumar et al,[11] who reported that higher age holds significant association with mortality, while Ojha et al[12] and Bhatia at al[6] reported that the mean age of patients who succumbed and those who survived was comparable. However, gender showed no association with mortality in this study similar to study by Bhatia et al[6] that showed gender distribution was comparable in those who died and were alive.

Mortality was significantly higher in patients with low GCS in the present study. Our study findings were in line with the study by Hegde et al,[8] who reported that GCS score of less than 8 was present in significantly more patients in deceased versus alive. Other studies from India also have reported similar findings, with Bhatia et al[6] and Namani et al[10] reporting a fatality of 72.9 and 100%, respectively, with poor GCS on admission. Safatli et al[15] also reported that in a multivariate analysis, low GCS was a significant predictor for the 30-day mortality.

Hemphill et al,[2] Cheung and Zou,[16] and Kumar et al[11] reported that IVE was significantly more in deceased patients, while Togha and Bakhtavar[17] and Hemphill et al[2] reported that there was statistically significant association between mortality and presence of increased volume of hematoma similar to our study. Site of hemorrhage though did not differ statistically among the patients who survived versus who died similar to previous studies by Bhatia et al[6] and Togha and Bakhtavar.[17]

Leucocytosis is associated with increased mortality in ICH patients similar to the results of meta-analysis done by Yu et al[18] as it might point toward septicemia. Our study showed that raised creatinine level and hypernatremia was significantly associated with mortality. However, in the study by Bhatia et al,[6] as compared with those who survived versus those who died had no difference in the biochemical parameters. Deranged creatinine was found to be associated with mortality in study by Rhoney et al.[19] Our study showed similar findings, as patients who developed acute renal dysfunction with ICH or hypertension related to chronic kidney disease were associated with raised creatinine. Hypernatremia at the time of discharge is found to be associated with mortality in ICH patients.[20] Mortality was significantly higher in patients requiring ventilatory support as compared with patients not requiring ventilatory support similar to the findings corroborated in study by Bhatia et al[6] as need for ventilatory support indicates raised intracranial pressure or any pulmonary infection.

This study excluded the spontaneous ICH patients with neurosurgical intervention and role of such intervention on mortality. Further studies might be required to study the impact of neurosurgical intervention on mortality and discharged patients could have been followed up for further complications and 30-day mortality. Also, this study has not studied vascular risk factors like hypertension, diabetes mellitus, and dyslipidemia in relation to mortality. These are the major limitations of this study.

Conclusion

The present study revealed mortality in about one-third patient of ICH. On univariate analysis, higher age, low GCS score, IVE, higher volume of bleeding, leucocytosis, increased creatinine, hypernatremia, and ventilatory support were the predictors of mortality. Low GCS score, raised creatinine, and ventilatory support were the independent predictor of mortality on multivariate analysis. This indicates the importance of clinical, biochemical, and radiological parameters at admission in effectively prognosticating about the mortality.

Conflict of Interest
None declared.

References

1 GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol 2021;20(10):795–820
2 Hemphill JC III, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. Stroke 2001;32(04):891–897
3 Broderick J, Connolly S, Feldmann E, et al; American Heart Association American Stroke Association Stroke Council High Blood Pressure Research Council Quality of Care and Outcomes in Research Interdisciplinary Working Group. Guidelines for the management of spontaneous intracerebral hemorrhage in adults: 2007 update: a guideline from the American Heart Association/ American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Outcomes in Research Interdisciplinary Working Group. Stroke 2007;38(06): 2001–2023
4 Hegde A, Menon G, Kumar V, et al. Clinical profile and predictors of outcome in spontaneous intracerebral hemorrhage from a tertiary care centre in South India. Stroke Res Treat 2020; 2020:2192709
5 Aguilar MI, Freeman WD. Spontaneous intracerebral hemorrhage. Semin Neurol 2010;30(05):555–564
6 Bhatia R, Singh H, Singh S, et al. A prospective study of in-hospital mortality and discharge outcome in spontaneous intracerebral hemorrhage. Neurol India 2013;61(03):244–248
7 Modi TN, Santosh SA, Dhoreeyanee FK, Patil PS. Clinico-epidemiological profile of intracerebral hemorrhage. National J Comm Med 2017;8(08):512–516
8 An SJ, Kim TJ, Yoon BW. Epidemiology, risk factors, and clinical features of intracerebral hemorrhage: an update. J Stroke 2017;19 (01):3–10
9 Bahou YG. Intracerebral hemorrhage. Neurosciences (Riyadh) 2009;14(02):152–157
10 Namani G, Rampure DM, Murali M. Clinical profile and mortality in patients presenting with intracerebral hemorrhage in a tertiary care centre. Scholars JApplied Medical Sciences 2014;2(6C):3005–3010
11 Kumar SS, Gandra S, Thatikonda AK, Padala RK, Sunanda T. Predictors of mortality of primary intracerebral hemorrhage among the sea coast population of South India. Mathews J Neurol 2016;1(01):5
12 Ojha P, Sardana V, Maheshwari D, Bhushan B, Kamble S. Clinical Profile of patients with acute intracerebral hemorrhage and ICH score as an outcome predictor on discharge, 30 days and 60 days follow-up. J Assoc Physicians India 2019;67(08):14–18
13 Narayan SK, Sivaprasad P, Sushma S, Sahoo RK, Dutta TK. Etiology and outcome determinants of intracerebral hemorrhage in a south Indian population: a hospital-based study. Ann Indian Acad Neurol 2012;15(04):263–266
14 Ahmed R, Shakir AH, Moizuddin SS, et al. Predictors of in-hospital mortality for intracerebral hemorrhage: a hospital-based study in Pakistani adults. J Stroke Cerebrovasc Dis 2001;10(03):122–127
15 Safatli DA, Günther A, Schlattmann P, Schwarz F, Kalff R, Ewald C. Predictors of 30-day mortality in patients with spontaneous primary intracerebral hemorrhage. Surg Neurol Int 2016;7 (Suppl 18):S510–S517
16 Cheung RTF, Zou LY. Use of the original, modified, or new intracerebral hemorrhage score to predict mortality and morbidity after intracerebral hemorrhage. Stroke 2003;34(07):1717–1722
17 Togha M, Bakhtavar K. Factors associated with in-hospital mortality following intracerebral hemorrhage: a three-year study in Tehran, Iran. BMC Neurol 2004;4:9
18 Yu Z, Zheng J, Guo R, Ma L, You C, Li H. Prognostic impact of leukocytosis in intracerebral hemorrhage: a PRISMA-compliant systematic review and meta-analysis. Medicine (Baltimore) 2019;98(28):e16281
19 Rhoney DH, Parker D Jr, Millis SR, Whittaker P. Kidney dysfunction at the time of intracerebral hemorrhage is associated with increased in-hospital mortality: a retrospective observational cohort study. Neurol Res 2012;34(05):518–521
20 Boland T, Henderson GV, Gibbons FK, et al. Hypernatremia at hospital discharge and out of hospital mortality following primary intracerebral hemorrhage. Neurocrit Care 2016;25(01):110–116