



Risk factors associated with in-hospital mortality following intracerebral hemorrhage

¹Dr. Sarita Jalodiya, ²Dr. Mohan Bhandare, ³Dr. Pankaj Kumar Jain.

⁴Dr. Arun Kumar Pargi

¹Senior Consultant, Medicine, Khandwa, M.P. India

²Senior Consultant, Medicine, Udgir, Maharashtra, India

³Assistant Professor, Department of Medicine, N.S.C. Government Medical College, Khandwa, M.P, India

⁴Assistant Professor, Department of Surgery, N.S.C. Government Medical College, Khandwa, M.P, India

Corresponding Author:

Dr. Arun Kumar Pargi

ABSTRACT

Background: Intracerebral hemorrhage (ICH) is the most severe subtype of stroke. Non-traumatic ICH occurs due to bleeding from a vascular source directly into the brain substance. Its mortality rate is high, and most survivors experience significant disability.

Aims & objectives: To assess primary patient risk factors associated with mortality following ICH.

Materials & Methods: We performed a prospective study carried out in the department of medicine in a tertiary care hospital, central India. All patients admitted with a non-traumatic ICH were included. Detailed clinical history, general and systemic examination was done. All relevant investigation was done and ICH was confirmed by CT/MRI brain.

Results: A total of 200 patients diagnosed with intracerebral hemorrhage, 133 (66.5%) were male and 67 (33.5%) were female. 54% of subjects were between 60 to 80 years of age. The overall mortality rate among ICH patients admitted to the hospital was 46.7%. Hypertension, smoking, alcohol habit, diabetes and dyslipidemia were the common factors associated with mortality in ICH. Factors significantly associated with in-hospital mortality were Glasgow Coma Scale (GCS) score (≤ 8), and midline shift.

Conclusion: Higher rate of mortality was observed during the first two weeks of hospitalization following ICH. Neuroimaging features along with GCS score can help the clinicians in developing their prognosis.

INTRODUCTION:

Intracerebral hemorrhage (ICH) is the subtype of stroke, usually caused by rupture of small penetrating arteries secondary to hypertensive changes or other vascular abnormalities [1-2]. Stroke is the third leading cause of death in developed countries, after heart disease and

cancer, and it is also a leading cause of disability in adults [3]. ICH remains the most devastating form of stroke. Within 1 month of injury, 40% of patients with ICH die, and by 1 year, this number increases to 54% [4]. Young stroke patients have a greater socioeconomic burden and an excess of mortality across all age groups of patients [5]. Many risk factors associated with the ICH such as hypertension, diabetes mellitus, apolipoprotein allele E2 or E4, obesity, frequent use of alcohol and cigarette smoking, through hypertension is the most prevalent risk factor in ICH patients [6-7]. The outcome of ICH is variable, depending on hematoma volume, location, extension to ventricles, and other factors.⁶ However, compared to ischemic stroke, ICH leads to higher mortality and more severe disability [8]. Use of anticoagulation reversal agents, early access to critical care, and development of dedicated inpatient stroke units have all contributed to lower rates of in-hospital mortality following spontaneous ICH [9-10]. Patients who were survived a first-time ICH, leading to a growing population of ICH survivors. The long-term causes of death in the ICH survivor population are unclear. Survivors of ICH are at risk for subsequent ischemic stroke, as those with atrial fibrillation (AF) are often not restarted on anticoagulation therapy.¹² Survivors also remain at risk for recurrent hemorrhage, a complication that is estimated to occur in about 2%–7% of patients [11-12].

Aims & objectives: The aim of the current study was to determine the mortality rate and to evaluate the influence of various factors on the mortality of patients with intracerebral hemorrhage (ICH).

MATERIAL AND METHODS:

This was a prospective study conducted in the Department of Medicine, G.R. Medical College & Group of Hospitals, Gwalior, central India, over a period of 3 years (2016-2018). All patients whom diagnosed as intracerebral hemorrhage confirmed by CT scan/MRI admitted in the our hospital during the study period were enrolled in the study

Inclusion Criteria:

- Age ranged from 18 to 75 years
- Cases of ICH diagnosed by CT scan/MRI.
- Who are willing to participate in the study

Exclusion Criteria:

- Aged <18 or >75 years
- ICH secondary to head trauma, brain tumour, subarachnoid hemorrhage.
- Patients who are not willing to give consent

Detailed clinical history was taken with special reference to risk factors and comorbid condition. The collected data were patient age, gender, socio-economic status, duration of hospitalization, etiopathogenesis, risk factors clinical manifestations, laboratory data and imaging at admission. Detailed general and systemic examination especially neurological examination was done.

All the selected patients were subjected to routine blood investigations like CBC, RBS, RFT, LFT, lipid profile. Mortality of all admitted patients was assist during course of hospitalization.

Statistical Analysis: All the data analysis was performed using SPSS version 20 software. Numerical data were expressed as mean \pm standard deviation. P value < 0.05 was considered significant

RESULTS

In present study, out of 200 patients, 53 (26.5%) had expired

Figure 1: Mortality incidence after ICH

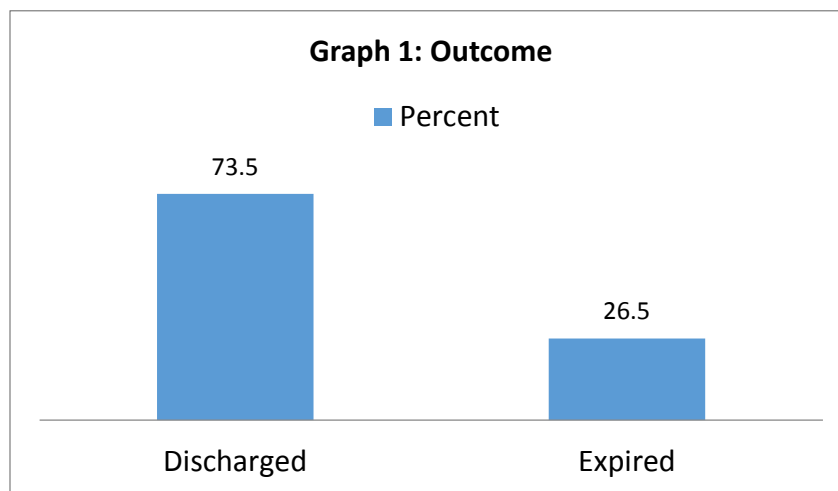


Table 1: Comparing the socio-demographic variables with ICH outcome

Socio-demographic variables		ICH outcomes		Total	P value
		Discharged	Expired		
Age of patient (in years)	18-40	14	6	20	0.877
	41-60	48	15	63	
	61-80	76	26	108	
	>80	9	6	15	
Total		147	53	200	
Gender	Male	95	38	133	0.350
	Female	52	15	67	
GCS score	<8	68	47	115	<0.001
	9-12	46	1	47	

	13-15	86	5	91	
--	-------	----	---	----	--

Table 2: Comparing mortality with the risk factors

Risk factors	No of patients	Mortality	P value
Smoking	57	19	0.003
HTN	38	38	
Diabetes	23	6	
Alcohol	43	10	
H/o CAD	25	8	
Hypercholesteromia	20	6	

Mortality was highest among the patients who had hypertension (100%) followed by smokers (33.33%) and patients who had alcohol addiction (23.25%) (p=0.003).

Table 3: Comparing mortality with TLC

		Frequency	Mortality rate	P value
Total Leukocyte Count	<4000	9	6 (33.33%)	<0.001
	4000-11000	145	22 (15.17%)	
	>11000	46	25 (54.34%)	
B. Urea	Normal (<45mg/dl)	154	24 (15.58%)	<0.001
	Raised (>45mg/dl)	46	29 (63.04%)	
Serum Creatinine	Normal (<1.4mg/dl)	172	35 (20.34%)	<0.001
	Raised (>1.4mg/dl)	28	18 (64.28%)	
RBS	Normal (<200 mg/dl)	186	46 (24.73)	0.039
	Raised (>200 mg/dl)	14	7 (50%)	

Patients with higher TLC (>11000) had highest mortality (54.34%)(p<0.001). Patients with raised blood urea had significantly higher mortality (63.04%) compared to patients with normal blood urea (p<0.001) similarly patients with raised serum creatinine level had significantly higher mortality prevalence (64.28%) compared to patients with Normal creatinine levels.

Table 4: Comparing SITE OF LESION with mortality

Site of lesion	Frequency	Percent	Mortality	p value
Thalamic or basal ganglia	149	74.5	41(25.51%)	0.558
Lobar	40	20	10 (25%)	
Brainstem	6	3	2 (33.3%)	

Cerebellum	5	2.5	0 (0)	
Total	200	100%		

Majority of the patients had lesion at thalamic or basal ganglia (74.5%) and out of that 25.51% had mortality similarly out of 20% patients who had lesion at lobar, 25% had mortality and out of 3% patients who had brainstem lesion, 33.33% had mortality. Comparison was insignificant ($p=0.558$)

Table 5: Comparing IVH extension / midline shift with mortality

IVH extension / midline shift	Frequency	Percent	Mortality	P value
Yes	58	29	44 (75.86%)	0.002
No	142	71	14 (9.85%)	

Mortality was higher among the patients who had IVH extension / midline shift, out of 29% patients of IVH extension / midline shift, 75.86% had mortality ($p=0.002$).

DISCUSSION

The leading causes of death in ICH survivors were infection, recurrent intracranial hemorrhage, respiratory failure, cardiac disease, and ischemic stroke. Death in patients with AF was significantly more likely to be due to ischemic stroke or cardiac disease, and less likely to be caused by recurrent intracranial hemorrhage [13]

The incidence of ICH increases with advanced age, in agreement to that in present study the incidence of mortality was higher in old age group ICH patients, similar finding also reported by Jolink et al [14], Sang Joon et al [15] and Nilesh kumar et al [16].

Current study determined the mortality rate of intracerebral haemorrhage patients were more in male than female, but not significant statistically ($p>0.05$), our results are comparable with study conducted by Sia SF et al [17] and Broderick J et al [18].

In our study Glasgow coma scale (GCS) was significantly associated with the mortality rate of ICH ($p<0.05$), concordance observation shown by M Togha et al [19] and Daniel et al [20].

Present study found mortality was highest among the patients who had hypertension (100%) followed by smokers and patients who had alcohol addiction, many factors like: hypertension, smoking, alcohol, diabetes, Hypercholesterolemia and h/o CAD were significantly associated with mortality ($p=0.003$), similar results obtained by Narayan et al [21], Zia E et al [22] and Martini SR et al [23].

In our study patients with raised TLC level (>11000), high blood urea, raised serum creatinine and raised blood sugar level ($>200\text{mg/dl}$) had significantly higher mortality rate ($p<0.05$), consistent finding reported by Chen et al [24] and V. Kasirajan et al [25].

Current study reported that mortality rate was highest in lesion at Brainstem, but site of the ICH not significantly associated with the mortality rate, accordance to the Flaherty ML et al [26] and Nilsson OG et al [27].

Mortality was significantly higher among the patients who had ICH extension or midline shift, ($p < 0.05$), in agreement to our study some other investigators reported the same results: Lindsey R. et al [28] and Arboix A. et al [29].

In present study, overall mortality rate of ICH was 26.5%, similar finding also reported by Zhang B. et al [30] and Morgan TC et al [31].

Known poor prognostic factors of ICH include large hematoma volume, hematoma expansion, intraventricular hemorrhage, infra-tentorial location, old age, contrast extravasation on CT scan (spot sign) and the use of anticoagulation. ICH Score, a simple clinical grading scale, may help stratify the risk; patients with high ICH score have a high mortality rate

CONCLUSIONS

We have concluded that higher mortality rate found in older age males. Hypertension and smoking was the predominant factors associated with the mortality in ICH. GCS score at the time of admission, volume of hematoma and midline shift could serve as independent prognostic factors for poor outcome and may help clinicians to assess prognoses more accurately.

Conflicts of interest: none

Source of funding: none

REFERENCES

1. Qureshi AI, Mendelow AD, Hanley DF. Intracerebral haemorrhage. *Lancet* 2009; 373:1632-1644.
2. Qureshi AI, Tuhim S, Broderick JP, Batjer HH, Hondo H, Hanley DF. Spontaneous intracerebral hemorrhage. *N Engl J Med* 2001; 344:1450-1460
3. Hemophil JC, Bonvich DC, Besmerits L: The ICH score- A simple reliable grading scale for intracerebral hemorrhage. *Stroke* 2001, 32:891-897.
4. Van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A, Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. *Lancet Neurol* 2010; 9:167–176.
5. Rutten-Jacobs LC, Arntz RM, Maaijwee NA, Schoonderwaldt HC, Dorresteijn LD, van Dijk EJ, et al. Long-term mortality after stroke among adults aged 18 to 50 years. *JAMA* 2013;309:1136–44
6. Woo D, Souerbeck LR, Kissela BM: Genetic and environmental risk factors for intracerebral hemorrhage. *Stroke* 2002, 33:1190-1195.
7. Hanel RA, Xavier AR, Mohammad Y: Outcome following intracerebral hemorrhage and subarachnoid hemorrhage. *Neurol Res* 2002, 24(1):58-62
8. Keep RF, Hua Y, Xi G. Intracerebral haemorrhage: mechanisms of injury and therapeutic targets. *Lancet Neurol* 2012; 11:720-731.

9. Parry- Jones AR, Sammut- Powell C, Paroutoglou K, et al. An intracerebral hemorrhage care bundle is associated with lower case fatality. *Ann Neurol* 2019;86:495–503.
10. Kuramatsu JB, Gerner ST, Schellinger PD, et al. Anticoagulant reversal, blood pressure levels, and anticoagulant resumption in patients with anticoagulation-related intracerebral hemorrhage. *JAMA* 2015;313:824–836
11. Claude HJ, Greenberg Steven M, Anderson Craig S, et al. Guidelines for the management of spontaneous intracerebral hemorrhage. *Stroke* 2015;46:2032–2060
12. Poon MTC, Fonville AF, Al-Shahi Salman R. Long-term prognosis after intracerebral haemorrhage: systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry* 2014; 85:660.
13. McCormick N, Bhole V, Lacaille D, Avina-Zubieta JA. Validity of diagnostic codes for acute stroke in administrative databases: a systematic review. *PLoS One* 2015;10: e0135834
14. Sang Joon An, Tae Jung Kim, Byung-Woo Yoon. Epidemiology, Risk Factors, and Clinical Features of Intracerebral Hemorrhage: An Update. *Journal of Stroke* 2017;19(1):3-10
15. Jolink WM, Klijn CJ, Brouwers PJ, Kappelle LJ, Vaartjes I. Time trends in incidence, case fatality, and mortality of intracerebral hemorrhage. *Neurology* 2015;85:1318-1324
16. Nilesh kumar M, Rajiv B Pandya, Chetan V Vaghani, Mehul R Marwadi, Gaurang K Gheewala3 Viral A. Barfiwala. A Study On Clinical Profile, Risk Factors And Mortality In Hypertensive Intracerebral Hemorrhage In A Tertiary Care Hospital In Surat City. *National Journal of Medical Research*. Volume 3 | Issue 4 | Oct – Dec 2013: 381-4.
17. Sia SF, K S Tan, V Waran, Primary Intracerebral Haemorrhage in Malaysia: In-hospital Mortality and Outcome in Patients from a Hospital Based Registry. *Med J Malaysia* Vol 62 No 4 October 2007: 308-12
18. Broderick J, Brott T, Tomsick T: Management of intracerebral hemorrhage in a large metropolitan population. *Neurosurgery* 1994, 34:882-887
19. Mansoorh Togha* and Khadigeh Bakhtavar, Factors associated with in-hospital mortality following intracerebral hemorrhage: a three-year study in Tehran, Iran, *BMC Neurology* 2004, 4
20. Daniel Woo, Mary E. Comeau, Simone Uniken Venema, Christopher D. et al , Risk Factors Associated With Mortality and Neurologic Disability After Intracerebral Hemorrhage in a Racially and Ethnically Diverse Cohort *JAMA Network Open*. 2022;5(3):e221103. doi:10.1001/jamanetworkopen.2022.1103

21. 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; 15:263-6
22. Zia E, Hedblad B, Pessah-Rasmussen H, Berglund G, Janzon L, Engström G. Blood pressure in relation to the incidence of cerebral infarction and intracerebral hemorrhage. Hypertensive hemorrhage: debated nomenclature is still relevant. *Stroke* 2007; 38:2681-2685.
23. Martini SR, Flaherty ML, Brown WM, Haverbusch M, Comeau ME, Sauerbeck LR, et al. Risk factors for intracerebral hemorrhage differs according to hemorrhage location. *Neurology* 2012;79:2275-2282
24. Chun-Yu Chen, Po-Tso Lin, Yun-Huei Wang, Ruei-Wun Syu, Shao-Lun Hsu, Li-Hsin Chang, et al, Etiology and risk factors of intracranial hemorrhage and ischemic stroke in young adults, *Journal of Chinese Medical Association*. (2021) 84: 930-936
25. Vigneshwar Kasirajana, Nicholas G. Smediraa*, James F. McCarthy, Filip Casselmana, Navdeep Boparaib, Patrick M. McCarthy, Risk factors for intracranial hemorrhage in adults on extracorporeal membrane oxygenation, *European Journal of Cardio-thoracic Surgery* 15 (1999) 508–514
26. Flaherty ML, Woo D, Haverbusch M, Sekar P, Khoury J, Sauerbeck L, et al. Racial variations in location and risk of intracerebral haemorrhage. *Stroke* 2005;36934-7
27. Nilsson OG, Lindgren A, Brandt L, Säveland H. Prediction of death in patients with primary intracerebral hemorrhage: A prospective study of a defined population. *J Neurosurg*. 2002; 97:531–6. [PubMed]
28. Lindsey R. Kuohn, Audrey C. Leasure, Julian N. Acosta,, Kevin Vanent, Santosh B. Murthy, et al Cause of death in spontaneous intracerebral hemorrhage survivors, *Neurology* | Volume 95, Number 20 | November 17, 2020
29. Arboix A, Comes E, Garcia-Eroles I: Site of bleeding and early outcome in primary intracerebral hemorrhage. *Acta Neurol Scand* 2002, 105:282-288.
30. Zhang B, Pu S, Zhang W, Yang N, Shen G, Yin J, et al. Sex differences in risk factors, etiology, and short-term outcome of cerebral infarction in young patients. *Atherosclerosis* 2011; 216:420–5.
31. Morgan TC, Dawson J, Spengler D, et al; CLEAR and VISTA Investigators. The Modified Graeb score: an enhanced tool for intraventricular hemorrhage measurement and prediction of functional outcome. *Stroke*. 2013; 44(3):635-641. doi:10.1161/STROKEAHA.112. 670653