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Original Article

Independent Predictors of Mortality in Intracerebral Hemorrhage Patients: A Retrospective cross-sectional study

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Abstract

Introduction: *Primary (non traumatic) intracerebral hemorrhage (ICH) accounts for approximately 10–15 % of strokes. Morbidity and mortality caused by ICH are high. There has not been reduction of the mortality rate of ICH in the recent decades. Overall mortality also seems to be similar in all regions of the world. The mortality rate of patients with ICH at 30 days varies from 13 to 61%.*

Objective: *This study was undertaken to analyse and evaluate the frequency and risk factors and independent predictors of mortality in intracerebral hemorrhage patients using CT scan..*

Materials and Methods: *The present study was a 1-year cross-sectional study, conducted on 450 patients with primary ICH, admitted in the wards and intensive care units of a tertiary care hospital during the period from January 2017 to December 2017.*

Results: *In this retrospective cross sectional study we analysed 450 patients presented with spontaneous intracerebral hemorrhage. The mortality rate was higher in older age group than younger ones (62.3% vs 37.7%). In this study the location of ICH were was basal ganglia (43.2%), thalamic (26.9%), lobar (17.3%), brain stem (5.1%), cerebellum (3.1%) and multiple hemorrhage (4.4%). The mortality rate of each location was evaluated.*

Conclusion: *Hematoma volume measurement is an easy and bedside tool to assess mortality within first 30 days. ICH score is a sensitive bedside tool to assess prognosis within 24 h. Early expansion of cerebral haematoma of any topography is an important determinant of in-hospital mortality.*

Keywords: *Intracerebral hemorrhage, Intraventricular extension, ICH score, GSC score.*

Introduction

Primary (nontraumatic) intracerebral hemorrhage (ICH) accounts for approximately 10–15 % of strokes [1] .Morbidity and mortality caused by ICH are high. There has not been reduction of the mortality rate of ICH in the recent decades. Overall mortality also seems to be similar in all regions of the world.[3] The mortality rate of patients with ICH at 30 days varies from 13 to 61%.[3] There are many models for prediction the

outcome after intracerebral hemorrhage. Among the predictive models, ICH score is the most popular, due to its simplicity and accuracy.[3] The score consists of 5 characteristics: Age > 80 years, Glasgow Coma Scale (GCS), infratentorial location, hematoma volume and presence of intraventricular hemorrhage.[4] Each characteristic is an independent predictor of mortality at 30 days after onset of stroke. Its clinical importance derives from its frequency and accompanying high mortality. Although the latter strongly depends on hematoma size and, to a lesser extent, on location, the overall mortality rate for this stroke subtype varies between 25 and 60 %. In computed tomography (CT) scans, fresh blood is visualized as a white mass as soon as it is shed. The mass effect and the surrounding extruded serum and edema are hypodense. After 2–3 weeks, the surrounding edema begins to recede and the density of the hematoma decreases, first at the periphery. Gradually, the clot becomes isodense with the brain. There may be a ring of enhancement from the hemosiderin-filled macrophages and the reacting cells that form a capsule for the hemorrhage.[5] Massive hemorrhage refers to hemorrhages several centimeters in diameter; small applies to those 1–2 cm in diameter and <30 mL in volume. The volume and location relate to the outcome and the nature of the initial neurologic deficit.

Material and Methods

The present study was a 1-year cross-sectional study, conducted in the medical and neuromedical department of a tertiary care hospital on patients with intracranial hemorrhage during the period of January 2017 to December 2017 after obtaining an informed written consent. 450 patients with primary (nontraumatic) ICH admitted in the wards and intensive care units of a tertiary care hospital and who have undergone CT imaging were evaluated with following inclusion and exclusion criteria.

Inclusion Criteria

1. Patients with age ≥12 years
2. Patients with spontaneous ICH of nontraumatic origin detected on CT imaging study

(a) Who have presented with history of acute severe headache, altered sensorium, slurring of speech, acute hemiparesis, and accelerated hypertension—suggestive of acute cerebrovascular stroke

Exclusion Criteria

1. Patients <12 years of age
2. Patients with history of trauma
3. Patient with ischemic stroke and venous thrombosis

All raw data were collected, and ICH score and volume were calculated.

The ICH score is a simple clinical grading scale that allows risk stratification on presentation with ICH. The use of a scale such as the ICH score could improve standardization of clinical treatment protocols and clinical research studies in ICH [7].

Components of score are as follows:

1. GCS 3–4=2, 5–12=1, and 13–15=0
2. ICH volume (in milliliter) [6]: >30 mL=1, <30 mL=0
3. Intraventricular hemorrhage: yes=1, no=0
4. Age: >80=1, <80=0
5. Infratentorial: yes=1, no=0

Thirty-day mortality can be calculated, and thus, it helps to decide the prognosis. ICH volume is measured by ABC/2 formula (ellipsoid method) [4], where A=longest diameter, B=diameter perpendicular to A, and C=number of slices multiplied by their thickness. The data obtained were tabulated and analyzed by proportion and percentages.

All patients in our study were treated with conservative treatment. Localization of ICH, based on CT scan findings, was divided into the following groups: lobar, subcortical, infratentorial, intraventricular hemorrhage, and multiple hematomas. The volume of intracerebral hematoma was calculated according to the formula $V = 0.5 \times a \times b \times c$ (a is the largest diameter of hematoma, b the diameter versus a, and c the number of scans that shows hematoma)

[8]. The thickness of the scan through the back of the skull was 4mm and 6mm through the other parts.When the first or the last scan recorded only a small amount of blood, the computer value *c* was calculated as 0.5 (half the thickness of the scan) and not as 1 (6, resp., 4 mm). Intracerebral hematomas are divided by the volume into three groups (0–29 mL, 30–60 mL, and >60 mL). Short term outcome was defined as survival or death and functional dependence six months after ICH [12].

Results

In this retrospective cross sectional study we analysed 500 patients presented with spontaneous intracerebral hemorrhage. Out of them 50 cases were excluded based on exclusion criteria. The average age of presentation in males and females was 59.4 and 65.3 yr respectively (16–86). The mortality rate was higher in older age group than younger ones (62.3% vs 37.7%). Mortality was also higher in males than females (68.8% vs 31.2%). Males were observed to be affected more in comparison to females, 66.2% and 33.8 % respectively. In this study the location of ICH was basal ganglia (43.2%) (Figure 1), thalamic (26.9%) (Figure 3), lobar (17.3%), brain stem (5.1%) (Figure 4,5), cerebellum (3.1%) (Figure 6) and multiple hemorrhage (4.4%) (Table-2). The mortality rate of each location was basal ganglia (22.1%), thalamic (47.5%), lobar (7.4%), brain stem (15.6%), cerebellum (3.3%) and multiple hemorrhage (4.1%). We observed presence of intraventricular hemorrhage in 47.1% of cases and it was a important predictor of mortality being seen in 90.2% of mortality patients (Figure 2). We observed Systolic blood pressure at presentation more than 200 mmHg in 248 (55.1%), 140-200 mmHg in 172 (38.2%) and less than 140 mmHg in 30 (6.7%) cases. 62.4% of the patients who died within 30 days presented with systolic blood pressure of more than 200 mmHg. We observed Glasgow coma scale score of 3-4,5-11,12-15 in 17.6%,29.5% and 52.9% of cases respectively. Highest number of patients (79) who died have GCS score of 3-4 (64.8%). We observed volume of ICH to be <30 ml in 344 (76.4%), 30-60 ml in 84(18.7%) and >60ml in 22(4.9%) of cases respectively. But among the patients who died, ICH volume was <30 ml in 43 (35.2%),30-60 ml in 60 (49.2%) and >60ml in 19 (15.6%) of cases respectively (Table -1). The highest mortality rate was recorded in patients with the hematoma volume more than 60mL (86.3%), followed by the group of 30 to 60mL (71.4%), and the lowest mortality rate was among the patients with a hematoma volume less then 29mL (12.5%) (Table- 4).. In this study all patients with ICH score 0 (n = 74, 16.4%) survived at 30 days. Patients with ICH score 1 (n = 176, 39.1 %), ICH score 2 (n = 114, 25.3%), ICH score 3 (n = 63, 14%) , ICH score 4 (n = 11, 2.5%) and ICH score 5 (n = 12, 2.7%) had mortality rate of 11.4%, 37.7%, 60.3% , 81.8% and 100% respectively (Table -3).. No patient had ICH score of 6. As shown, increasing ICH score correlated with increasing mortality at 30 days. We observed midline shift in 190 (42.2%) cases and no midline shift in 260 (57.8%) cases. we found mortality in 104 (54.7%) of cases with midline shift and 18 (6.9%) of cases without midline shift (Table -5) (Figure 1).

Table 1 Incidence of patients with ICH according to its volume

Volume of hematoma	n (450)	%
< 30 ml	344	76.4 %
30-60 ml	84	18.7 %
> 60 ml	22	4.9 %

Table 2 Sites of ICH and percentage

Site of ICH	n (450)	%
Basal ganglia	178	39.6 %
Thalamus	121	26.9 %
Lobar	78	17.3%
Brain stem	23	5.1%
Cerebellum	14	3.1 %
Multiple	20	4.4 %
Intraventricular hemorrhage	16	3.6 %

Table 3 Mortality according to ICH Score

ICH Score	n (%)	Survived, n (%)	Expired ,n (%)
0	74 (16.4)	74 (100 %)	0 (0 %)
1	176 (39.1)	165 (88.6 %)	20 (11.4%)
2	114 (25.3)	54 (62.3%)	43 (37.7%)
3	63 (14)	15 (39.7%)	38 (60.3%)
4	11 (2.5)	2 (18.2%)	9 (81.8%)
5	12 (2.7%)	0 (0%)	12 (100%)

Table 4 Mortality in ICH patients according to its volume

Volume of hematoma	n	30 – days mortality
< 30 ml	344	43 (12.5 %)
30-60 ml	84	60 (71.4 %)
> 60 ml	22	19 (86.3 %)

Table 5 Mortality in ICH patients according to the Midline shift

Midline shift	Death	
	Yes	No
Yes	104 (54.7%)	86 (45.3 %)
No	18 (6.9 %)	242 (93.1 %)

Table 6 Analysis of parameters predictive of mortality in ICH patients by 30 days

Patient characteristic		n = 450 , (%)	30 – days mortality, n = 122 (%)
Sex	Male	298 (66.2%)	84 (68.8%)
	Female	152 (33.8%)	38 (31.2%)
Age > 80 yr	Yes	199 (44.2 %)	76 (62.3 %)
	No	251 (55.8%)	46 (37.7%)
Location	Basal ganglia	194 (43.2 %)	27 (22.1%)
	Thalamus	121 (26.9 %)	58 (47.5%)
	Lobar	78 (17.3%)	9 (7.4%)
	Brain stem	23 (5.1%)	19 (15.6%)
	Cerebellum	14 (3.1 %)	4 (3.3%)
	Multiple	20 (4.4 %)	5 (4.1%)
Presence of IVH	Yes	212 (47.1%)	110 (90.2%)
	No	238 (52.9%)	12 (9.8%)
Systolic blood pressure (mmHg)	<140	30 (6.7 %)	8 (6.5 %)
	140 – 200	172 (38.2 %)	38 (31.1%)
	>200	248 (55.1 %)	76 (62.4%)
GCS score	3 - 4	79 (17.6 %)	79 (64.8 %)
	5 - 11	133 (29.5 %)	20 (16.4 %)
	12 - 15	238 (52.9 %)	23 (18.8 %)
ICH volume (ml)	< 30 ml	344 (76.4 %)	43 (35.2 %)
	30-60 ml	84 (18.7 %)	60 (49.2 %)
	> 60 ml	22 (4.9 %)	19 (15.6 %)
Midline shift	Yes	190 (42.2%)	104 (85.2%)
	No	260 (57.8%)	18 (14.8)

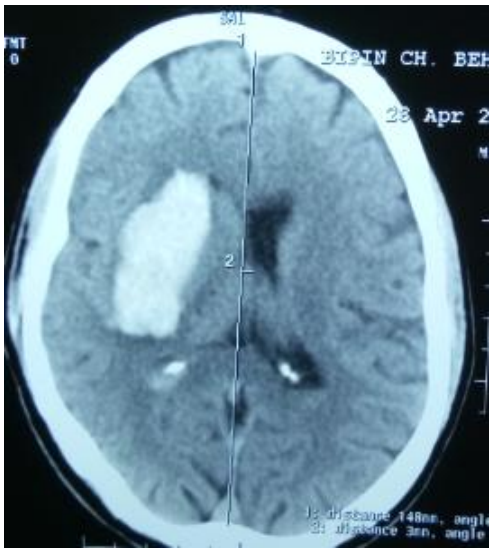

Figure 1 – Basal ganglia hemorrhage with midline shift

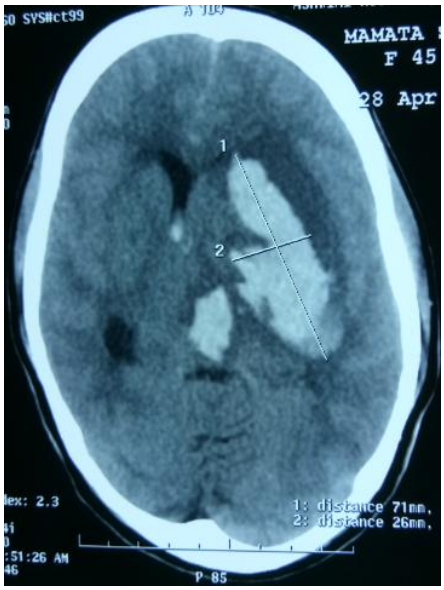

Figure 2 – Basal ganglia hemorrhage with intraventricular extension

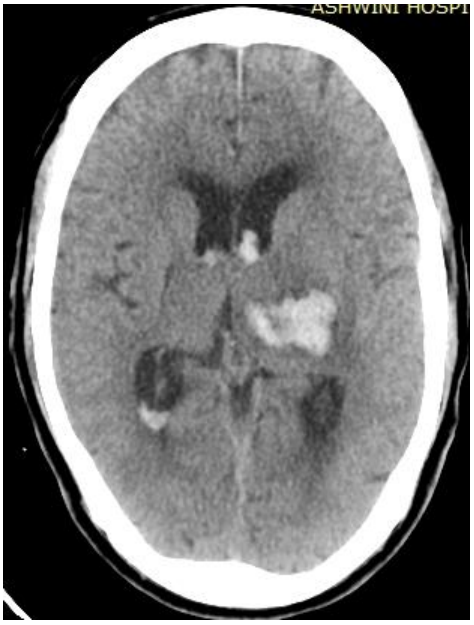

Figure 3 – Thalamic hemorrhage

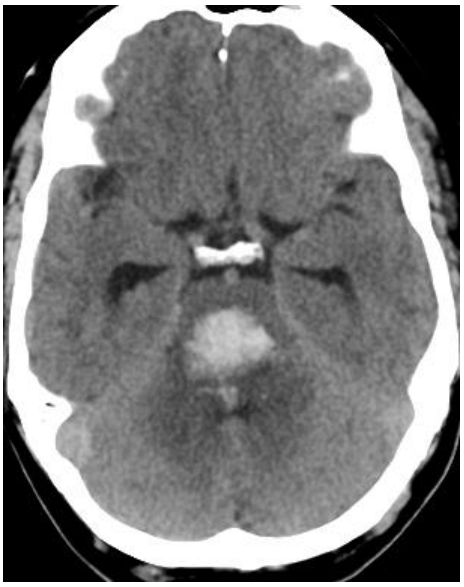

Figure 4 – Brain stem hemorrhage

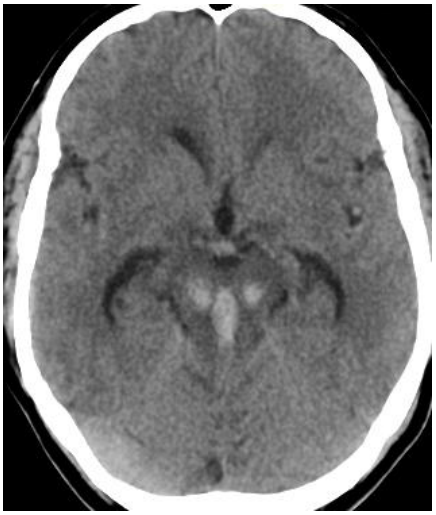

Figure 5 – Multiple brain stem bleed

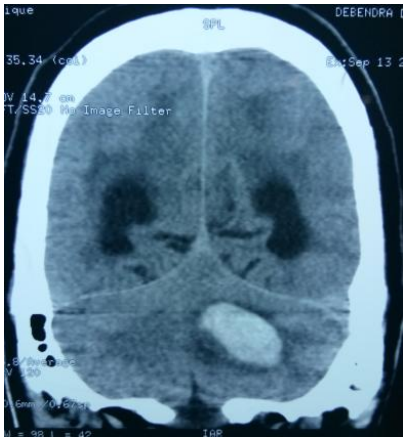

Figure 6 – Cerebellar hemorrhage

Discussion

CT is presently the imaging modality of choice to identify ICH. This method has the potential to provide quantitative data, with implications for use as a predictor of treatment benefit[9].

In this present study we have analysed 450 patients presented with spontaneous intracerebral hemorrhage. We observed that the average age of presentation in males and females was 59.4 and 65.3yr respectively (16–86). The mortality rate was higher in older age group than younger ones (62.3% vs 37.7%). Mortality was also higher in males than females (68.8% vs 31.2%). Males were observed to be affected more in comparison to females (66.2% and 33.8 %). Similar to our study Hiten N et al [9] observed females to be affected more than males, 52 and 48 %, respectively and the average age of presentation in males and females was 58.6 and 62.4 years, respectively. In contrast to us Sombat Muengtaweepongsa *MD* et al[10] found overall incidence of ICH more in males (63.6%). Adrià Arboix et al[18] observed increased in death rate with increase in age. Daverat el al.[20] studied age as the most important predictor of death and functional outcome after spontaneous intracerebral haemorrhage.

In this study we observed the location of ICH in basal ganglia (43.2%), thalamus (26.9%), lobar (17.3%), brain stem (5.1%), cerebellum (3.1%) and multiple hemorrhage (4.4%) of cases. The mortality rate of each location was basal ganglia (22.1%), thalamic (47.5%), lobar (7.4%), brain stem (15.6%), cerebellum (3.3%) and multiple

hemorrhage (4.1%). Similar to our study Hiten N et al [9] observed the incidence of ICH in basal ganglia (40%), thalamus (25%), lobar (23%), brain stem (8%) and cerebellum (4%) of cases. In contrast to us Sombat Muengtaweepongsa *MD* et al[10] studied the locations of ICH in basal ganglia (48.5%), lobar (25.8%), infratentorial (15.2%), combined supra and infratentorial (7.6%), and thalamic hemorrhage (3.0%) of cases. Celikbilek A et al[2] observed bleeding localization as supratentorial in 89.6% and infratentorial in 10.4% of cases. In the supratentorial hemorrhage group, 48.1% patients bled in the cortex, 0.9% bled in the subcortical white matter, 39.6% bled in the basal ganglions and 0.9% in the capsula interna while in the infratentorial group, 9.4% patients bled in the cerebellum and 0.9% in the brainstem. Sunil K. Narayan et al[6] observed the location of ICH in basal ganglia (45%), thalamus (43%), lobar (38%), internal capsule (41.5%), and cerebellum (5%) of cases.

We observed presence of intraventricular hemorrhage in 47.1% of cases and it was an important predictor of mortality being seen in 90.2% of mortality patients. Similar to us Sombat Muengtaweepongsa *MD* et al[10] studied presence of intraventricular hemorrhage in 48.5% of cases and mortality in 91.7% of cases with intraventricular hemorrhage. Sunil K. Narayan et al observed intraventricular hemorrhage in 36.8% of cases and found maximally in the group of ICH with > 60 cubic cm volume. They also studied higher incidence of mortality in cases with IVH than without IVH (56.4% vs 22.4%) of cases (66.67%). Sunil K. Narayan et al[6] found Intraventricular hemorrhage maximally in the group of ICH with > 60 cubic cm volume.

We observed systolic blood pressure at presentation, more than 200 mmHg in 248 (55.1%), 140-200 mmHg in 172 (38.2%) and less than 140 mmHg in 30 (6.7%) cases.. 62.4% of the patients who died within 30 days were presented with systolic blood pressure of more than 200 mmHg. Similarly to us Sombat Muengtawe-epongsa *MD* et al[10] observed systolic blood pressure at presentation more than 200 mmHg, 140-200 mmHg and less than 140 mmHg in 53%,39.4% and 7.6% of cases respectively. They also seen 50% of mortality cases have presented with systolic blood pressure of more than 200 mmHg. Hiten N et al[9] in their study also seen hypertension as the most common risk factor for ICH seen in 50% of their study population. Sunil K. Narayan et al[6] also studied hypertension was the most common etiological risk factor, 50% of patients having been diagnosed hypertensive in the past, another 36.7% newly diagnosed.

We observed Glasgow coma scale score of 3-4,5-11,12-15 in 17.6%,29.5% and 52.9% of cases respectively. Highest number of patients (79) who died have GCS score of 3-4 (64.8%). In accordance with us Sombat Muengtaweepongsa *MD* et al[10] observed GCS score of 3-4,5-11,12-15 in 9.1%,28.8% and 62.1% of cases respectively. They also studied 50% of mortality cases have presented with GCS score 3-4. Sunil K. Narayan et al[6] observed GCS at baseline was 3 to 8 in 38%, 9 to 12 in 40% and 13 to 15 in 22% of patients.

We observed volume of ICH to be <30 ml in 344 (76.4%),30-60 ml in 84(18.7%) and >60ml in 22(4.9%) of cases respectively. But among the patients who died , ICH volume was <30 ml in 43 (35.2%),30-60 ml in 60 (49.2%) and >60ml in 19 (15.6%) of cases respectively. The highest mortality rate was recorded in patients with the hematoma volume more than 60mL (86.3%), followed by the group of 30 to 60mL (71.4%), and the lowest mortality rate was among the patients with a hematoma volume less then 29mL (12.5%). In contrast to us Hiten N et al[9] observed 78% of patients had hematoma volume < 30ml and 22% had volume > 30ml. They found 64.7% of mortality cases had volume > 30 ml. Hiten N et al [9] also observed hematoma volume measurement is an effective method to predict the mortality in patients of ICH within 30 days of presentation. They observed greater the volume, the higher was the mortality. Increment in mortality rate when ICH volume was >30 mL. Sombat Muengtaweepongsa *MD* et al[10] observed ICH

volume of < 10 ml, 10-30 ml, >30 ml in 36.4%,25.8% and 37.9% respectively. They also studied 66.7% of mortality cases had volume >30 ml. Denisa Salihovic et al[11] observed that the best six-month survival was in patients with a volume up to 29 mL; 30 of them (64%) survived. They recorded the highest mortality rate in patients with the hematoma volume more than 60mL (85%), followed by the group of 30 to 60mL (62.5%), and the lowest mortality rate among the patients with a hematoma volume up to 29mL (36%). M. Togha et al[13] observed volume of hematoma as an independent factor influencing mortality in patients with ICH. D. A. Godoy et al[14] and M. Togha et al[13] showed that unfavorable outcome (mortality) was higher in the groups with greater hematoma volume, which is similar to the results of our study. Castellanos et al[15] noted that the higher hematoma volume, deep localization, intraventricular spreading of hematoma, mass effect was significantly associated with a worse outcome. Broderick JP et al[16] studied volume of ICH in combination with initial GSC as the powerful and easy-to-use predictor of 30-day mortality and morbidity in patients with spontaneous ICH. Divani et al[17]

Suggested that the measurement techniques such as ABC/2 may introduce significant errors. So protocols for measurement of hematoma volume and its characteristics should be incorporated into CT scanner consoles, which would allow the operator to obtain such information accurately in a timely manner. Celikbilek A et al[2] observed 47.2% patients had small (0-9.9 cm^3), 34.9% had medium (10-29.9 cm^3), 14.2% had large (30-59.9 cm^3), and 3.8%) patients had very large (≥60 cm^3) hemorrhages. Sunil K. Narayan et al[6] observed mean ICH volume of 49.97 ± 28.3 cubic cm in their study. they found good outcome in 20% and poor outcome in 80% of the ICH subjects and the ICH volume was significantly associated with systolic and mean arterial pressures but not with diastolic pressure. Adrià Arboix et al[18] observed stroke-related deaths in 40.5% of intraventricular haemorrhage cases. Steinke et al.[19] found that in-hospital mortality occurred in 52% of thalamic haematomas with ventricular extension and that intraventricular extension is an powerful independent predictor of mortality.

In this study all patients with ICH score 0 (n = 74, 16.4%) survived at 30 days. Patients with ICH score 1 (n = 176, 39.1 %), ICH score 2 (n = 114, 25.3%), ICH score 3 (n = 63, 14%) , ICH score 4 (n = 11, 2.5%) and ICH score 5 (n = 12, 2.7%) had mortality rate of 11.4%, 37.7%, 60.3% , 81.8% and 100% respectively. No patient had ICH score of 6. As shown, increasing ICH score correlated with increasing mortality at 30 days. Hiten N et al [9] observed patients with ICH score 0 in (18%) , ICH score 1 in 40%, ICH score 2 in 26%, ICH score 3 in 14%, ICH score 4 in 2% of cases. They have not studied any patients with ICH score 5 and 6. They found mortality rate of 0%, 10%, 53.84% , 71.42% and 100% in patients with ICH score 0,1,2,3,4 respectively.

We observed midline shift in 190 (42.2%) cases and no midline shift in 260 (57.8%) cases.we found mortality in 104 (54.7%) of cases with midline shift and 18 (6.9%) of cases without midline shift. Celikbilek A et al[2] in a series with 106 patients observed the presence of shift in 41.5% of cases with mortality in 59.1% of cases with shift and 17.8% of cases with no midline shift. Celikbilek A et al[2] found that mortality increased with older age , advancing bleeding volume and development of ventricular extension of hemorrhage, and the presence of midline shift ($P < 0.001$), but not with gender ($P > 0.05$) or the development of subarachnoidal extension of hemorrhage

Conclusion

Hematoma volume measurement is an easy and bedside tool to assess mortality within first 30 days. ICH score is a sensitive bedside tool to assess prognosis within 24 h. Early expansion of cerebral haematoma of any topography is an important determinant of in-hospital mortality. Recent studies have shown that ultra-early

haemostatic therapy with recombinant activated factor VII (rFVIIa) within four hours after the onset of intracerebral hemorrhage limits the growth of the haematoma, reduces mortality, and improves functional outcomes. Early detection and pharmacological rapid control of hypertension is the key intervention to decrease the incidence of this devastating type of stroke. Future genetic and epidemiologic studies will help identify at-risk populations and hopefully allow for primary prevention. Randomized, controlled studies focusing on novel therapeutics should aid in minimizing secondary injury and hopefully improve morbidity and mortality.

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Abbreviations

1. CT - Multidetector computerized tomography
2. ICH – Intracerebral hemorrhage
3. IVH - Intraventricular hemorrhage
4. GCS – Glasgow coma scale