Original Article

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Surgery Section

Predictors of Mortality in Spontaneous Intracerebral Haemorrhage: A Prospective Interventional Study from a Tertiary Care Centre, Kerala, India

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ABSTRACT

Introduction: Spontaneous Intracerebral Haemorrhage (SICH) is a potentially life-threatening condition associated with a high mortality and morbidity. Early assessment of outcome is important to optimise the therapeutic efforts. This study helps in the prediction of outcomes in SICH based on clinical and radiological predictors, so as to effectively utilise the treatment resources.

Aim: To assess clinical and radiological predictors of mortality and morbidity in patients with SICH at a Tertiary Care Centre, Kerala, India.

Materials and Methods: This prospective interventional study included 100 patients admitted with SICH at Government Medical college, Kozhikode, Kerala, India, from 1st May 2019 to 30th January 2020. The assessed variables include age, sex, mean Glasgow Coma Scale (GCS) score on admission, Intracerebral Haemorrhage (ICH) volume, ICH site, ICH score and treatment provided (conservative/surgery). The dependent variable was 30 day mortality. Univariate analysis was performed to determine the association between the mortality and independent variables. A binary logistic regression was also performed. Statistical analysis performed using Statistical Package for the Social Sciences (SPSS) software version 22.0. The p-value <0.05 was considered significant.

Results: Among the total of 100 SICH patients, males were 52% and females were 48%; the mean age was 67±11 years. The medical history of SICH patients predominantly showed hypertension (90%), diabetes (45%) and alcohol abuse (33%). Out of total, 70% cases were managed conservatively, and 30% cases were managed surgically. The short-term outcome of 30 day mortality was 40% and the survival rate was 60%. Univariate analysis inferred that the location of bleed (p-value=0.0002), volume of ICH (p-value <0.001), ICH score (p-value 0.003) and type of management (p-value <0.001) were statistically significant predictors for 30 day mortality in SICH patients.

Conclusion: The location of bleed, volume of ICH, ICH score and type of management were statistically significant predictors for 30 day mortality in SICH patients.

Keywords: Clinical, Determinants, Intracerebral haemorrhage score, Prognosis, Radiological

INTRODUCTION

The Spontaneous Intracerebral Haemorrhage (SICH) occurs within brain parenchyma without any history of recent trauma or surgery. Common causes are hypertension, coagulopathy, amyloid angiopathy, tumors and vascular anomalies. Of these major risk factors identified are advancing age and hypertension [1].

Approximately, 4-14% of all strokes comprises SICH, with a higher incidence in Asian countries compared to the West [2,3]. Intracerebral Haemorrhage (ICH) is more common as well as more likely to result in death (30 day mortality of 44%) or major disability compared to cerebral infarction or Subarachnoid Haemorrhage (SAH) [4].

The American Heart Association/American Stroke Association (AHA/ASA) guidelines for management of spontaneous intracerebral bleed recommended to use widely accepted severity assessing scores like Glasgow Coma Scale (GCS) and ICH scores for clear communication among medical professionals and objective assessment [5]. National Institute of Health Stroke Scale (NIHSS) is the most extensively used deficit rating scale for stroke [6]. Modified Rankin Scale (mRS) is used for measurement of neurologic disability affecting daily activities of patients suffering from stroke or any other neurological disease [7].

Various studies have been conducted determine the relationship between clinical and radiological factors and poor outcome in ICH [8-10]. Some biochemical and haematological parameters like increased white blood cell count elevated renal function and liver function tests at the time of admission in ICH patients have been associated with poor outcome in patients [11].

Most of the literature on morbidity and mortality predictors is available from the West and some East Asian countries. Computerised Tomography (CT) scanning is the initial diagnostic modality of choice in SICH, as it clearly differentiates haemorrhagic from ischemic stroke. Magnetic Resonance Imaging (MRI) and angiography may be considered wherever appropriate [12,13]. The radiological predictors of poor outcome in ICH patients include- haematoma location, haematoma volume, haematoma expansion, perihaematomal edema, intraventricular haemorrhage, hydrocephalus, spot sign and swirl sign [14].

This prospective interventional study was designed to primarily assess the clinical and radiological predictors of mortality and morbidity in patients with SICH at a tertiary care institution in Kerala.

MATERIALS AND METHODS

This hosital-based, prospective, interventional study was conducted in Department of Neurosurgery, Government Medical College, Kozhikode, Kerala, India, between 1st May 2019 to 30th January 2020. The ethical approval was obtained (IEC no. GMCKKD/RP2019/IEC/176).

Inclusion and Exclusion criteria: Patients attending the casualty with SICH during the study period were included in the study. Patients with subdural and epidural haematoma, patients with

anticoagulant or coagulopathy related haemorrhage, patients who denied informed consent and patients aged <15 years and >70 years were excluded from the study.

Sample size calculation: According to a prospective study done by Rahmani F et al., 10 patients with ICH were included and it was found that the 30 day mortality rate was 57% [6]. Taking this study as a reference, we have considered the values for calculating sample size.

Required minimum sample size (n_r) based on proportion is given by the formula:

$$n_r=\frac{4pq}{d^2}$$

Here, p=% mortality (57%)

q=100-p (43%)

d=precision (10%)

Therefore, $n_r=4\times57\times43/10^2$

nr=98.04≈98

Data collection: Presenting complaints of patients at the time of admission like headache, vomiting, seizure altered consciousness, fever and focal neurological deficits were recorded. Clinical examination findings like vitals, systemic examination findings, GCS sore and ICH score at the time of admission were also noted [15,16].

Study Procedure

All patients took plain CT at the time of admission, after 24 hours and later at the time of discharge or if there was deterioration of score. Details on CT scan like site of bleed, volume of haematoma (using ABC/2 formula), presence or absence of intraventricular extension or hydrocephalus and extent of midline shift in millimeters were recorded.

- Haematoma volume was estimated by ABC/2 method [17],

where

  - A is the greatest diameter on slice with the largest haemorrhage,
  - B is the diameter which is perpendicular to A, and
  - C is the number of axial slices with bleeding multiplied by slice thickness .

- The location/site of haematoma was broadly divided into
  - supratentorial (lobar and basal ganglia)
  - infratentorial (cerebellum and brainstem).
- The depth of bleeding from the cortical surface (<10 mm or >10 mm) was recorded.
- Details of neurosurgical intervention whether surgical or conservative, time of surgical intervention was also recorded.

The treatment provided was either medical conservative therapy or early surgical evacuation, which is done within 72 hours of diagnosis of ICH. Primary outcome was either death or survival within the hospital. Follow-up was done up to 30 days of occurrence. The observations were made to assess the short-term outcome and short-term mortality.

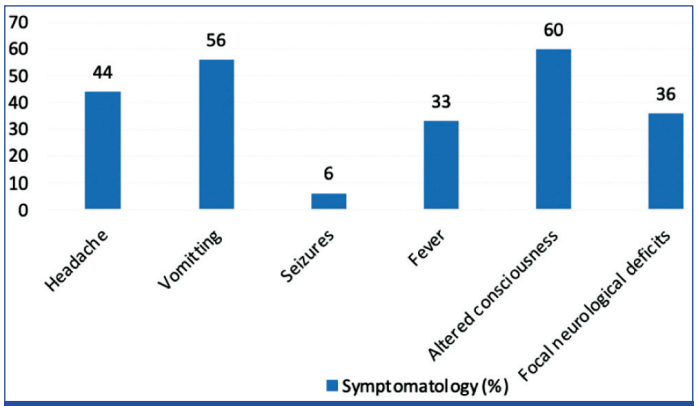
STATISTICAL ANALYSIS

The assessed variables include age, sex, ICH volume, ICH site and treatment provided (conservative/surgery). The dependent variable was 30 day mortality. Univariate analysis was done using chi-square test for qualitative variables and t-test for quantitative variables. A binary logistic regression was also performed. Statistical analysis performed using Statistical Package for the Social Sciences (SPSS) software version 22.0. The p-value <0.05 was considered significant.

RESULTS

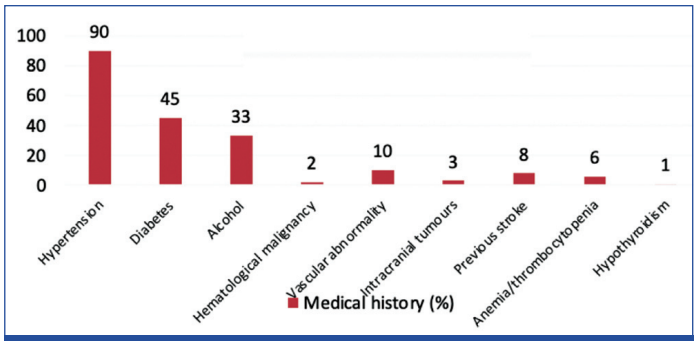
A total of 100 patients with SICH, were studied whose details fulfilled the inclusion criteria. The mean age was 67±11 years with males 52% and females 48%.

[Table/Fig-1] shows the distribution of symptoms in SICH patients. These included headaches in 44 patients (44%), vomiting in 56 (56%), seizures in 6 (6%), fever in 33 (33%), altered consciousness in 60 (60%), and focal neurological deficits in 36 (36%).



[Table/Fig-1]: Distribution of symptoms in SICH patients (%).

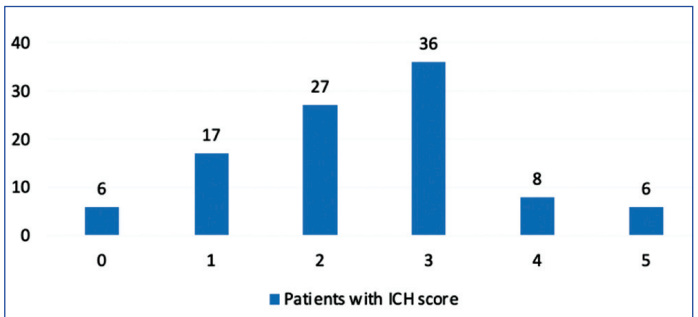
[Table/Fig-2] shows medical history of patients with SICH. These include: hypertension (90%), diabetes (45%), alcohol abuse (33%), haematological malignancy (2%), known vascular abnormality (10%), intracranial tumors (3%), previous stroke (8%), anaemia/ thrombocytopenia (6%), and hypothyroidism (1%). On examination, the average pulse rate was 56/minute, blood pressure was more than 160/90 mmHg (in 90% of cases) and temperature was 102°F (in 30% of cases). Forty patients (40%) of cases had an initial GCS in the range of 9 to 12. The mean GCS score was 9±3.



[Table/Fig-2]: Medical history (%).

[Table/Fig-3] shows the distribution of ICH score among the patients with SICH. Most of the patients (36%) had an ICH score of 3.

[Table/Fig-4] shows the location of ICH as per the CT scan findings. The most common location was basal ganglia (45%), followed by



[Table/Fig-3]: Patients with ICH score.

Location		Number	Percentage	
Supratentorial	Lobar	45	45%	88%
	Basal Ganglia	43	43%	
Infratentorial	Cerebellum	6	6%	12%
	Brainstem	6	6%	

[Table/Fig-4]: Site of bleed.

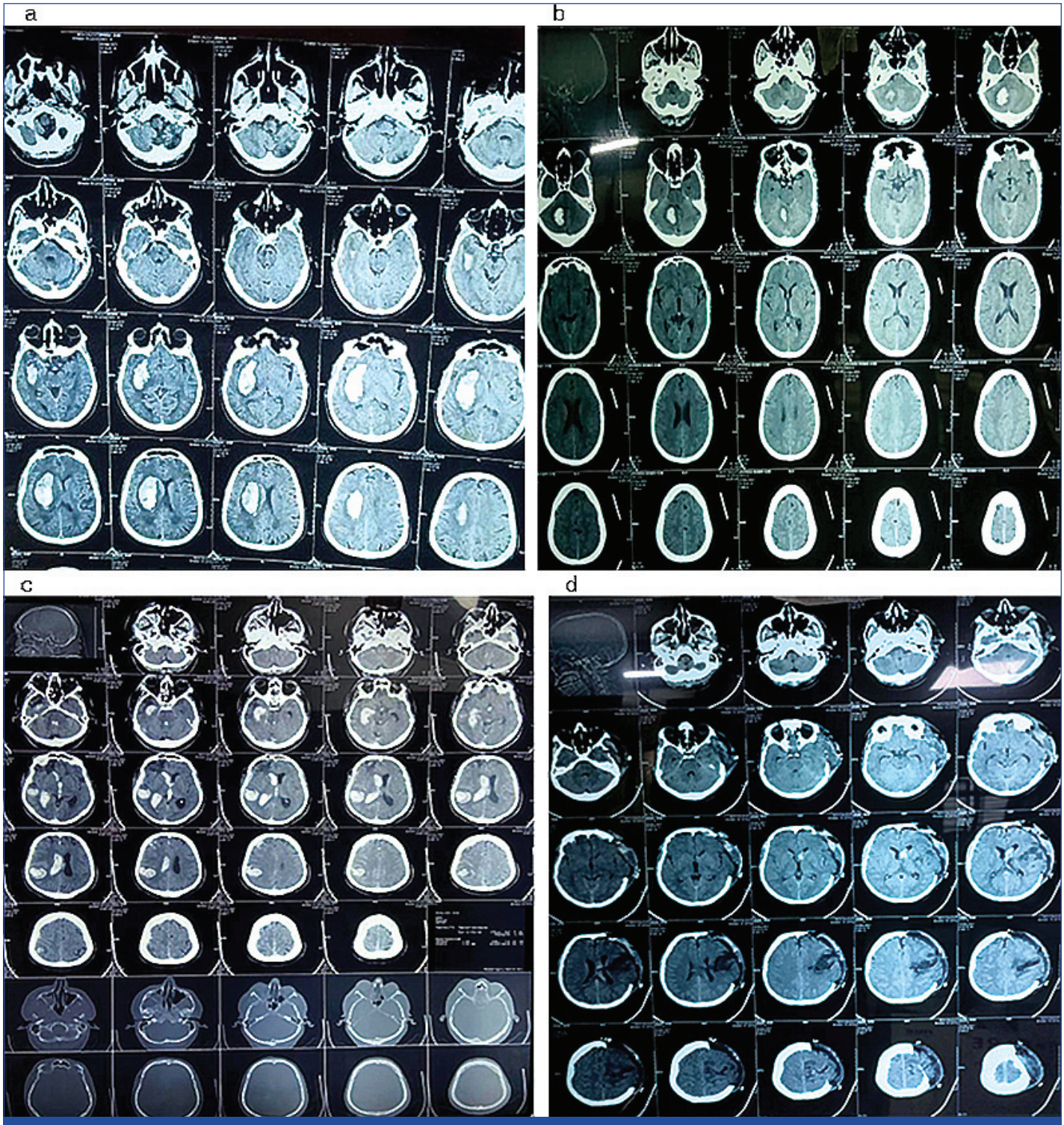
lobular (43%), cerebellum (6%), and brainstem (6%). It can be inferred that ICH haemorrhage more commonly involves supratentorial region than infratentorial region. There were 12 patients (12%) with infratentorial bleed and 88 (88%) patients with supratentorial bleed.

The CT scan showed intraventricular extension in 43% of cases; subarachnoid haemorrhage in 11% of cases; and hydrocephalus in 6% of cases. The mean ICH volume was 44±16 mL. The mean midline shift was 6.6±4.4 mm. The depth of haematoma was <10 mm in 30%, and >10 mm in 70%.

Conservative treatment was given to 70% patients, while surgery was performed in 30% patients. Radiographic Images of various sites of ICH, pre and postoperative images are given below in [Table/Fig-5].

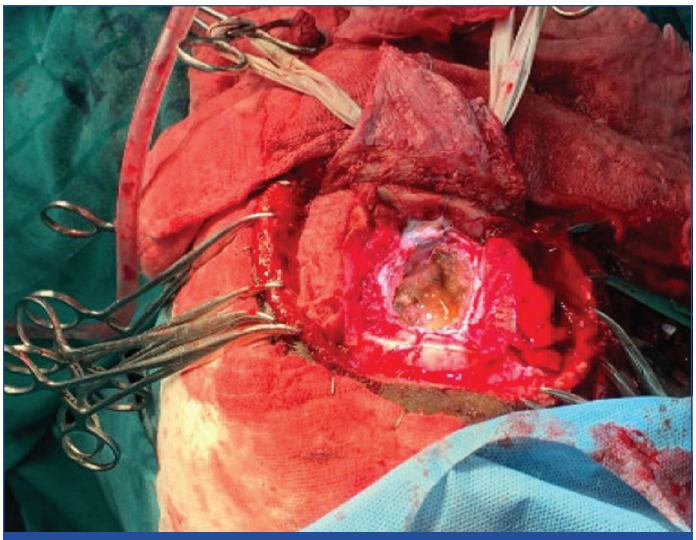
Intraoperative image of lobar ICH is presented in [Table/Fig-6]. It was seen that 40% patients died during the follow-up period of 30 days, i.e., 30 day mortality was 40%. The survival rate for the 30 day follow-up period was found to be 60%. Details of study are given in [Table/Fig-7].

Short-term outcome (30 days): 40 patients died within the 30 day follow-up period; among which 22 died during the first 48 hours of diagnosis. Hence, the 30 day mortality for our study was 40%; and the survival rate was 60%. Univariate analysis was performed to compare the variables in the two groups, i.e., survived group and died group. The characteristics of both the study groups referring to the 30 day mortality are as shown below in [Table/Fig-8]. The factors that were found to be significant in univariate analysis were also tested using binary logistic regression. The R^2 value which shows the percentage of variation that could be explained with the model was 0.606. The factors which were found to be significantly associated with 30 days mortality in patients in ICH were ICH volume, location of bleed, ICH score and type of management. A critical bleeding volume of 33 mL (supratentorial)



[Table/Fig-5]: Intracerebral Haemorrhage (ICH), radiographic images of different sites of bleed and postoperative image; A) Capsuloganglionic bleed; B) Cerebellar haemorrhage; C) Lobar bleed with intraventricular haemorrhage; D) Postoperative image of lobar haemorrhage.

and 22 mL (infratentorial) were found to be associated with poor short-term outcome.



[Table/Fig-6]: Intraoperative image of lobar Intracerebral Haemorrhage (ICH).

Patients (n)	N=100
Male/female; (%)	52/48
Age (years); mean±SD	67±11
Co-morbidities (%)	
• Hypertension	90
• Diabetes	45
• Alcoholism	33
Imaging (CT scan) characteristics of ICH	
Location/site of ICH:	
• Basal ganglia	45
• Lobular	43
• Cerebellum	6
• Brainstem	6
Intraventricular Haemorrhage (IVH); (%)	43
Subarachnoid haemorrhage; (%)	11
ICH volume (mL); mean±SD	44±16
Midline shift (mL); mean±SD	6.6±4.4
Depth of haematoma; <10 mm/>10 mm; (%)	30/70
Treatment	
Conservative/Surgery (%)	30/70

[Table/Fig-7]: Characteristics of 100 patients with Spontaneous ICH (SICH).

Characteristics	Survived group (n=60)	Died (within 30 days) group (n=40)	Statistical test
Gender			
Male	30 (57.7%)	22 (42.3%)	χ^2 value=0.240 p-value=0.388#
Female	30 (62.5%)	18 (37.5%)	
Age (year)			
Mean age, Mean±SD	67.02	67.42	p-value=0.711*
Glasgow coma scale			
Mean±SD (on admission)	10±3	6±3	p-value=0.59*
Imaging (CT scan) characteristics of ICH			
Location of Intra cranial bleed			
Basal ganglia	36 (80%)	9 (20%)	χ^2=16.1 p-value=**0.0002**#
Lobar	21 (48.83%)	22 (51.17%)	
Cerebellum	0	6 (100%)	
Brainstem	3 (50%)	3 (50%)	
ICH volume (mL); mean±SD	4.75±2.2	7.82±2.39	p-value **<0.001***
ICH score±SD	2.12±1.1	2.85±1.25	p-value=**0.003***
Management			
Conservative	52 (74.3%)	18 (25.7%)	χ^2 value=19.8 p-value **<0.0001**#
Surgical	8 (26.7%)	22 (73.3%)	

[Table/Fig-8]: Characteristics of both study groups (survived and died) referring to 30 day mortality.
*T-test p-value; #Chi-square; p-value <0.05 was considered as statistically significant

The ICH volume had a p-value of 0.001 and an odds ratio of 1.64, ICH score had a p-value of 0.044 and odds ratio of 1.728, Mode of management had p-value of 0.034 and odds ratio of 0.23 on logistic regression. A higher ICH volume and a higher ICH score were found to be risk factors for morality whereas conservative management was found to be protective with less mortality. The location of bleed even though was found to be significantly associated with mortality in univariate analysis was not found to be significant in binary logistic regression. Details are given in [Table/Fig-9].

Factor	p-value	Exp (B)	95.0% CI for EXP (B) Lower	95.0% CI for EXP (B) Upper
ICH volume	**0.001**	1.64	1.210	2.224
ICH score	**0.044**	1.728	1.01	2.944
ICH location	0.940	0.908	0.074	11.143
Management	**0.034**	0.23	0.62	0.898

[Table/Fig-9]: Association between 30 day mortality ICH volume and ICH score.
p-value <0.05 was considered as statistically significant

DISCUSSION

The SICH is a medical emergency with potentially life-threatening consequences for the patients. Hence, its optimum management is of utmost importance, so that appropriate treatment option is provided by virtue of the prediction of 30 day mortality [18].

This study was designed to evaluate the short-term outcome and the predictors of 30 day mortality. Our study showed a 30 day mortality rate of 40%. In a study by Bhatia Ret al., 30 day mortality was 32.7% (70 out of 214 patients) [19]. Consistent with the previous study [20], the age, gender, co-morbidities like hypertension, diabetes, and alcohol abuse were not the significant outcome predictors in the present study. The present study confirmed that the ICH volume was one of the strongest predictors of outcome in patients with SICH. In study by Hegde A et al., volume more than 30 mL with intraventricular extension and hydrocephalus was indicator of poor outcome [21].

It was shown that initial GCS and ICH volume can be considered to determine the suitable treatment for the patient. In general, conservative treatment is advised if GCS is atleast 13, or if ICH volume is <30 mL irrespective of GCS score. Surgical treatment is advised if GCS is less than 12 and ICH volume is atleast 30 mL. GCS score less than 8 was associated with poor outcome [21]. Endoscopic surgery is less invasive and effective in removal of ICH at GCS of >9 [22].

The current study showed that an and a critical bleeding volume of 33 mL (supratentorial) and 22 mL (infratentorial) are associated with poor short-term outcome. This is consistent with the study done by Safatli DA et al., where supratentorial bleeding volume more than 32 mL and infratentorial bleeding volume more than 21 mL correlate with poor outcome [23]. However, the cut-off values for ICH volume significantly differ with various studies [23]. The present study observation that infratentorial location of ICH has a higher 30 day mortality, is also consistent with the aforementioned study [23].

There is a vague insignificant observation showing that early surgical intervention is associated with a higher survival rate. Similar results were obtained in a study conducted by Luostarinen T et al., early surgery is associated with lower mortality [24]. This could possibly emphasise the importance of "timely" surgical intervention in reviving the patient. The present study also showed the importance of validated outcome grading scores like ICH score and ICH-GS in the accurate prediction of 30-day mortality in SICH patients.

The current study showed that 30 day mortality increased in accordance with increasing ICH score values. Most of the surviving patients was disabled at discharge. Surgery had no significant improvement in mortality. Similar were the results of study by Prasad K et al., which considered further randomised controlled studies were needed to determine who might benefit from surgery [25].

Limitation(s)

This was a short-term outcome study and there is a definite need for more studies evaluating the long-term outcomes in patients with SICH. The decision for surgical or conservative management varies between various physicians/neurosurgeons, based on their subjective knowledge and risk prediction.

CONCLUSION(S)

The 30 day mortality in patients with SICH was 40%. The outcome grading scores like ICH score predict the 30 day mortality accurately. The imaging findings of baseline ICH volume and its location were found to be the most important radiological predictors of 30 day mortality in patients with spontaneous primary ICH.

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