

# Impact of the Extent of Intraventricular Hemorrhage on Functional Outcome in Spontaneous Intracerebral Hemorrhage

TAPU SD<sup>1</sup>, HASSANUZZAMAN M<sup>2</sup>, RAHMAN T<sup>3</sup>, AHAMMED Z<sup>4</sup>, MARZUK RM<sup>5</sup>, SEN S<sup>6</sup>, CHOWDHURY MMH<sup>7</sup>, DAS A<sup>8</sup>, ADNAN SM<sup>9</sup>, HASSAN K<sup>10</sup>

## Abstract

**Background:** The impact of the extent of Intraventricular hemorrhage (IVH) on functional outcomes in patients with Spontaneous intracerebral hemorrhage (sICH) needs to be better established. This study estimated the extent of IVH by the Graeb score (a valid and reliable semiquantitative score to measure IVH volume) in patients with sICH. **Objective:** It explored the impact of the magnitude of IVH on functional outcomes after one month of stroke onset. **Methods:** This study prospectively analyzed 104 patients of sICH from the Department of Neurology and Neurosurgery of Chattogram Medical College Hospital from July 2021 to June 2022. The primary outcome was defined as a functional outcome one month after ICH, assessed using the modified Rankin Scale (MRS) dichotomized into favorable (MRS = 0–3) and unfavorable outcome (MRS = 4–6). Secondary outcomes included mortality at one month and a Graeb score-based threshold analysis for the association of the extent of IVH with unfavorable clinical outcomes. **Results:** The mean age was 60.9±13.6 years, 51% were male, and in 91.3% of the cases, the hematoma was supratentorial. The mortality rate was 39.4%, and 19.2% had a good functional outcome. The Graeb score had a significant positive correlation with the 30-day mRS score ( $p < 0.001$ , Pearson correlation coefficient = 0.344). Graeb score was good for discriminating 30-day poor functional outcomes with having an area under the ROC curve of 0.699 (95% CI: 0.0.572-.0826;  $P=0.006$ ). The risk of having a poor one-month functional outcome was 1.32 times higher in patients with Graeb scores 5-12 than those with Graeb scores 0-4 (RR: 1.32, 95% CI: (1.17-1.50). Admission Graeb score was an independent predictor of 30-day mortality (OR: 1.28; 95% CI: 1.06-1.54,  $p=0.011$ ). **Conclusion:** As large amounts of IVH (Graeb score  $\geq 5$ ) is associated with unfavorable outcome or death after sICH, medical caregivers could use this score in making decisions regarding the use of care resources and other medical care.

**Keywords:** Intraventricular hemorrhage, Graeb score, stroke outcome, spontaneous ICH.

## Introduction

Primary or spontaneous ICH (sICH) comprises 10-15% of all strokes and is associated with high morbidity and mortality.<sup>1</sup> The one-month case-

fatality rate is around 40%, less than half of patients survive one year, and less than a third survive five years. Most survivors are left with severe disabilities.<sup>2,3</sup> Accurate prediction of ICH clinical

1. Dr. Shagor Deb Tapu, Medical Officer, Khagrachhari Modernized Sadar Hospital, Khagrachhari, Bangladesh.
2. Prof. Dr. Md. Hassanuzzaman, Head, Department of Neurology, Chittagong Medical College, Chattogram, Bangladesh.
3. Dr. Touhidur Rahman, Assistant Professor, Department of Neurology, Chittagong Medical College, Chattogram, Bangladesh.
4. Dr. Zaman Ahammed, Assistant Professor, Department of Neurology, Chittagong Medical College, Chattogram, Bangladesh.
5. Dr. Riyadh Muhammad Marzuk, Medical Officer, Banskhalia Upazila Health Complex, Chattogram, Bangladesh.
6. Dr. Suman Sen, Medical Officer, Shahid Syed Nazrul Islam Medical College Hospital, Kishoreganj Sadar, Kishoreganj, Bangladesh.
7. Dr. Md. Mubinul Huq Chowdhury, Emergency Medical Officer, Khagrachhari Modernized Sadar Hospital, Khagrachhari, Bangladesh.
8. Dr. Aditi Das, MD (Neurology), Phase-B Resident, Chittagong Medical College, Chattogram, Bangladesh.
9. Dr. Samee M Adnan, Student of MD (Neurology), Phase-B, Chittagong Medical College, Chattogram, Bangladesh.
10. Dr. Kamrul Hassan, MD (Neurology), Phase-B Resident, Chittagong Medical College, Chattogram, Bangladesh.

**Corresponding Author:** Dr. Shagor Deb Tapu, Medical Officer, Khagrachhari Modernized Sadar Hospital, Khagrachhari, Bangladesh.

outcomes following admission is crucial for families confronted with a patient's need for intensive care. Parameters such as age, ICH volume, Glasgow Coma Scale (GCS), or infratentorial origin of hemorrhage, the presence of intraventricular hemorrhage (IVH) represents an established parameter independently impacting functional outcome after ICH.<sup>4,5</sup>

IVH occurs in up to 45% of ICH patients.<sup>6</sup> Previous studies have suggested an influence of the extent of IVH on functional outcomes.<sup>7,8</sup> The ICH score, which incorporates IVH as a binary variable being present or absent, is an established prediction model for sICH outcomes.<sup>5</sup> However, the ICH score cannot comment on the critical threshold in the extent of IVH, only beyond which clinical outcome is affected. The Graeb score is a semiquantitative scoring tool based on gross hemorrhage size and dilation within each ventricle, ranging from 0 to 12 points, with higher scores denoting increased IVH volumes.<sup>9</sup> Graeb score was introduced decades ago but has recently gained attention for its accuracy, simplicity, applicability, and reliability for predicting the outcome following sICH.<sup>10-12</sup> However, knowledge was scarce regarding the impact of IVH volume assessed by Graeb Score in predicting functional outcomes of sICH patients in Bangladesh.

Contemplating this background, this study was designed to evaluate the impact of the extent of the IVH as assessed by the Graeb score on Functional outcomes in patients with sICH. Based on the study findings, a recommendation could be made for its broader use in Bangladesh for preferential allocation of resources to those sICH patients who would benefit most.

## Methods

This prospective analytic study was conducted in the Department of Neurology and Neurosurgery, Chattogram Medical College Hospital (CMCH), Chattogram, Bangladesh, from July 2021 to June 2022. The study protocol was approved by the ethical review committee of Chittagong Medical College, and written informed consent was taken from the caregivers of the patients. Consecutive 110 radiologically confirmed cases of sICH with IVH,

aged more than 18 years, were included in the study. Patients with traumatic intracranial hemorrhages, subarachnoid hemorrhage, hemorrhagic transformation of a recent ischemic stroke, hemorrhage inside a space-occupying lesion, and suspected arteriovenous malformation were excluded.

Every patient suspected of acute stroke was subjected to an urgent non-contrast CT scan of the brain. Patients were enrolled after confirmation of ICH with IVH, and Graeb scores were then calculated [for each lateral ventricle: 1= trace of blood or mild bleeding, 2= Less than 50% filled with blood, 3= More than 50% filled with blood, 4= ventricle filled with blood and expanded; for 3rd and 4th ventricle: 0= No blood, 1= Blood present, ventricle size normal, 2= Ventricle filled with blood and expanded]<sup>9</sup>. The demographic and clinical data of the study subjects were collected by interviewing the patients' legal relatives. Physical examination and neurological assessment were done soon after the hemodynamic stabilization of the patients.

Patients received medical treatment as per standard institutional protocol for ICH with IVH. Functional outcome was assessed using a modified Rankin scale (mRS) at one month. Any case fatality following inclusion in the study was recorded. All relevant data was noted in the pretested datasheet. Functional outcome at one month was determined by mRS score which was dichotomized as good functional outcome (mRS score 0–3 points) and poor functional outcome (mRS score 4–6 points).

Data were analyzed by using SPSS version 23.0. Continuous data were expressed as mean  $\pm$  standard deviation (SD) for normally distributed data or median and 25%–75% interquartile range for non-normally distributed data. Categorical variables were presented as frequency and percentages. Unpaired t-test was used to analyze normally distributed continuous variables, while Mann–Whitney U-test was used for nonnormally distributed continuous variables. Categorical variables were compared using the Chi-square test and Fisher's exact test. The discriminatory values

of the Graeb score for predicting poor Functional outcome and mortality at one month were studied using receiver operating characteristic (ROC) curve analyses with the calculation of the area under the curve (AUC). An optimal cutoff value of the Graeb score for predicting Functional poor outcomes at one month was defined by calculating Youden's index. Correlation analysis was performed using Pearson's correlation test. The Strength of association between the Graeb score and the 30-day functional outcome was expressed as a risk ratio with a 95% confidence interval (CI). Binary logistic regression analysis was performed to determine the independent predictors of 30-day mortality. The results were expressed as odds ratio (OR) and 95% CI for OR.  $P < 0.05$  was considered statistically significant.

### Results

A total of 110 subjects were enrolled out of 139 subjects screened for eligibility. Six patients were lost to follow-up at the end and were excluded from the analysis. The mean ( $\pm$ SD) age was  $60.9 \pm 13.6$  years, and 51% were male. The most frequent comorbidity was hypertension (98.2%), followed by diabetes mellitus (19.1%) and dyslipidemia (15.5%). The median (IQR) GCS was 9 (IQR:7-12). The median hematoma volume was 5 (8-20) ml. In most cases (91.8%), the hematoma was located in the deep cerebrum. The median Graeb score was 3 (IQR:2-5) and 13.5% had hydrocephalous (Table I). Out of 104 patients, 41 expired within 30 days with a 30-day mortality rate of 39.4% (Table II). Only twenty (19.2%) patients had good functional outcome, and the rest, 84 (80.8%), had poor functional outcome on 30-day follow-up (Table II).

The Graeb score of the patients assessed at enrollment had a significant positive correlation with the mRS assessed after 30 days from stroke onset ( $p$ -value =  $<0.001$ , Pearson correlation coefficient = 0.344) (Figure 1). The AUC value of the admission Graeb score for predicting 30-days poor functional outcomes was 0.699 (Figure 2). A cut-off value of the admission Graeb score was tested

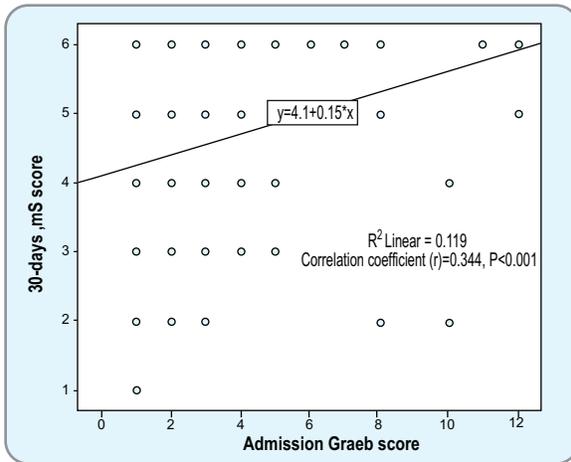
**Table-I**  
*Baseline clinical and radiological characteristics of the patients (n=104)*

Variables	Mean $\pm$ SD/ Frequency (%)/median (IQR)
Age, years	60.9 $\pm$ 13.6
Sex	
Male	53 (51.0)
Female	51 (49.0)
Current or ex-smoker	29 (37.5)
Hypertension	102 (98.1)
Diabetes mellitus	21 (20.1)
Dyslipidemia	16 (15.4)
Ischemic heart disease	5 (4.8)
Chronic Kidney DiseaseSystolic blood pressure, mm of Hg	4(3.8)169.3 $\pm$ 25.8
Diastolic blood pressure, mm of Hg	99.5 $\pm$ 12.2
Glasgow coma scale score	9 (7-12)
Hematoma volume, mlLocation of hematoma	5 (8-20)
Lobar	6 (5.8)
Deep	95 (91.3)
Infratentorial	3 (2.9)
Admission Graeb Score	3 (2-5)
Hydrocephalus	14 (13.5)

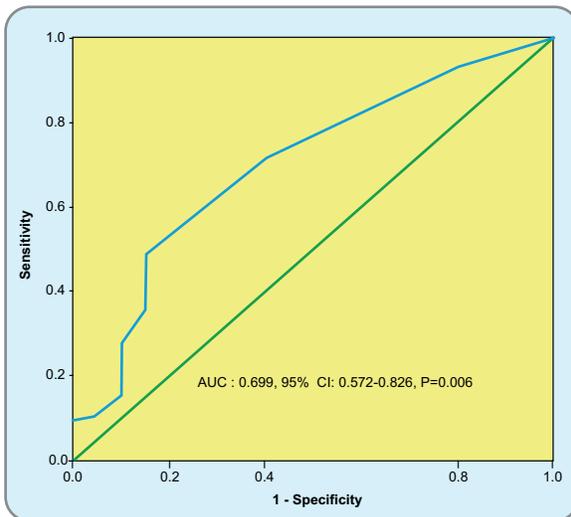
IQR: Interquartile range.

**Table II**  
*30-day outcome of the patients*

Outcome measures	Frequency	Percentage
30-day mortality		
Survived	63	60.6
Expired	41	39.4
Functional outcome		
Good (mRS 0-3)	20	19.2
Poor (mRS 4-6)	84	80.8



**Figure 1:** Scatter plot showing the correlation between admission Graeb score and mRS score after 30 days from stroke onset



**Figure 2:** Receiver operating characteristic curve for admission Graeb score in predicting 30-days functional outcome

to identify the highest possible Youden's index. The admission Graeb score of 3.5 has the best Youden index (sensitivity + specificity - 1). With this score, the admission Graeb score predicted 30-days poor functional outcomes with a sensitivity of 48.8% and specificity of 85.0%.

Table III depicted that none of the patients with Graeb score 5-12 had good functional outcome compared to 24.4% of patients with Graeb score 0-4 (p=0.01). The risk of having poor one-month functional outcome was 1.32 times higher in patients with Graeb score 5-12 than the patients with Graeb score 0-4 (RR: 1.32, 95% CI:(1.17-1.50)). In univariate analysis, age, GCS score, hematoma volume, and Graeb score were associated with poor outcome (p < 0.05) (Table 4.5). The mean age, median hematoma volume, and median Graeb score of the patients with poor functional outcomes were higher than those with good functional outcomes (p=0.011, p=0.015, and p=0.005, respectively). On the other hand, median GCS was significantly lower in the patients with poor functional outcome than in the patients with good functional outcome (p<0.001) (Table IV). Upon multivariate analysis using logistic regression analysis, the independent predictors of mortality included a higher age (p=0.022, OR:1.05; 95% CI:1.01-1.09), lower GCS (P = 0.035, OR:0.82, 95% CI 0.68-0.99), higher baseline hematoma volume (P = 0.021, OR:1.05; 95% CI 1.01-1.10), and admission Graeb score (P = 0.011 OR: 1.28; 95% CI:1.06-1.54).

**Table-III**

*Association between Graeb score and Modified Rankin Scale Score after one month of ICH onset*

Graeb score	One-month functional outcome			RR with 95% CI	Pvalue*
	Good (mRS 0-3)	Poor (mRS 4-6)			
Score 5-12	0 (0)	22 (100.0)		1.32	0.010
Score 0-4	20 (24.4)	62 (75.6)		(1.17-1.50)	

RR: Relative risk; CI: Confidence interval; \*Chi-square test.

**Table-IV**  
Association between different clinical factors with the 30-day functional outcome (n=104)

Variables	One-month functional outcome by mRS score		Pvalue*
	Good (mRS 0-3) (n=20)	Poor (mRS 4-6) (n=84)	
Age, years	54.0±12.1	62.5±13.4	0.011†
Sex			
Male	10 (50.0)	43 (51.2)	0.924*
Female	10 (50.0)	41 (48.8)	
Smoking	6 (30.0)	33 (39.3)	0.441*
Alcohol	0 (0)	1 (1.2)	1.0**
Hypertension	19 (95.0)	83 (98.8)	0.349**
Diabetes mellitus	6 (30.0)	15 (17.9)	0.224*
IHD	0 (0)	5 (6.0)	0.580**
CKD	1 (5.0)	3 (3.6)	0.580**
SBP, mm of Hg	160.5±25.6	169.8±25.3	0.145†
DBP, mm of Hg	101.5±14.9	98.5±11.5	0.317†
GCS	13 (9-15)	9 (6-11)	<0.001‡
Hematoma volume, ml	6.0 (3.4-8.0)	10.0 (5.2-21.7)	0.015‡
Hematoma location			
Lobar	0 (0)	6 (7.1)	
Deep	18 (90.0)	77 (91.7)	0.056*
Infratentorial	2 (10.0)	1 (1.2)	
Hydrocephalous	2 (10.0)	12 (14.3)	0.614*
Graeb score	2 (2-3)	3 (2-6)	0.005‡

‡Mann-Whitney U test; †Independent sample t-test; \*Chi-square test; \*\*Fisher's exact test.

### Discussion

The present study results showed that sICH patients with a large score of IVH (Graeb score  $\geq 5$ ) were significantly associated with 30-day poor functional outcomes, which indicates that the degree of IVH severity had a negative impact on the functional outcome.

The reported 30-day mortality of patients with spontaneous ICH ranges from 25 to 53.4% 12-15, and in the present study, it was

39.4%. Concerning the short-term outcome (after 30- days), only one-fifth of the patients had good functional outcomes (mRS score  $\leq 3$ ). In a meta-analysis, good functional outcome rates range between 12 and 39%, corresponding to the present study's findings.<sup>16</sup>

The admission Graeb score has good discriminatory power for predicting 30-days poor

functional outcomes (AUC 0.699) in the present study and a cut-off value of 3.5 had a sensitivity and specificity of 48.8% and 85%, respectively. In the study of Wayan et al.<sup>12</sup> predictive power of Graeb score in hospital patients unfavorable outcome with cutoff point  $\geq 1$  was similar to the present study (AUC: 0.6365) but with a higher sensitivity (77.6%) and lower specificity (53.3%). Two independent groups showed that IVH extension severity, measured as a continuous variable by the Graeb scale, is associated with poor outcome in sICH.<sup>17,18</sup>

Predictors of outcome in early studies of ICH included age, ICH location, electrocardiographic abnormalities, and history of hypertension. More recent studies have also identified lesion size, level of consciousness, midline shift, blood pressure or pulse pressure, kidney dysfunction, IVH, and pupillary abnormality, as factors influencing

outcome<sup>13,19,20</sup>. A review of these studies reveals considerable variability in the factors identified. This is likely as many factors are likely to interact strongly with each other. In the current study, independent predictors for 30-days mortality were higher age, low GCS score, larger volume of hematoma, and high Graeb score. Radiological findings seem to be closely associated with predicting mortality and clinical behavior<sup>9,13,19,21</sup>.

The present study has some important clinical implications. Tuhim et al. were the first to demonstrate that IVH volume is associated with higher 30-day mortality rates.<sup>22</sup> Another report identified that a threshold IVH volume of 20 mL was predictive of poor outcome.<sup>23</sup> However, IVH extension volumes as low as 6 mL have increased the likelihood of poor functional outcomes after sICH.<sup>24</sup> Performing volumetric analysis requires imaging reprocessing software not typically available in clinical practice. This drawback has been circumvented using semiquantitative IVH extension severity scales that estimate IVH extension volume using visual grading systems. In this regard, the Graeb score, a simple semiquantitative score is a valid and reliable measure of IVH volume. Present study findings have shown that the Graeb score has good predictive accuracy for 30-days functional outcome following sICH. These results may evaluate the chance of recovery and guide an appropriate care plan for such patients.

### Conclusion

In conclusion, the study showed that increased IVH extension severity, defined by a Graeb score  $\geq 5$ , was associated with poor functional outcome 30 days after sICH. A Higher Graeb score was an independent predictor of 30-day poor functional outcome after sICH.

### References

1. Ziai WC, Carhuapoma JR. Intracerebral hemorrhage. *Continuum: Lifelong Learning in Neurology*. 2018 Dec 1;24(6):1603-22.
2. Poon MT, Fonville AF, Salman RA. Long-term prognosis after intracerebral haemorrhage: systematic review and meta-

- analysis. *Journal of Neurology, Neurosurgery & Psychiatry*. 2014 Jun 1;85(6):660-7.
3. Krishnamurthi RV, Ikeda T, Feigin VL. Global, regional and country-specific burden of ischaemic stroke, intracerebral haemorrhage and subarachnoid haemorrhage: a systematic analysis of the global burden of disease study 2017. *Neuroepidemiology*. 2020;54(2):171-9.
4. Qureshi AI, Mendelow AD, Hanley DF. Intracerebral haemorrhage. *The Lancet*. 2009 May 9;373(9675):1632-44.
5. Hemphill III JC, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. *Stroke*. 2001 Apr;32(4):891-7.
6. Hallevi H, Albright KC, Aronowski J, Barreto AD, Martin-Schild S, Khaja AM, et al. Intraventricular hemorrhage: anatomic relationships and clinical implications. *Neurology*. 2008 Mar;70(11):848-52.
7. Rusalleda J, Peiro A. Prognostic factors in intraparenchymatous hematoma with ventricular hemorrhage. *Neuroradiology*. 1986 Dec;28(1):34-7.
8. Morgan TC, Dawson J, Spengler D, Lees KR, Aldrich C, Mishra NK, Lane K, Quinn TJ, Diener-West M, Weir CJ, Higgins P. The Modified Graeb Score: an enhanced tool for intraventricular hemorrhage measurement and prediction of functional outcome. *Stroke*. 2013 Mar;44(3):635-41.
9. Graeb DA, Robertson WD, Lapointe JS, Nugent RA, Harrison P. Computed tomographic diagnosis of intraventricular hemorrhage. Etiology and prognosis. *Radiology*. 1982 Apr;143(1):91-6.
10. Roeder SS, Sprügel MI, Sembill JA, Giede-Jeppe A, Macha K, Madar D, Lücking H, Hoelter P, Gerner ST, Kuramatsu JB, Huttner HB. Influence of the extent of intraventricular hemorrhage on functional outcome and mortality in intracerebral hemorrhage. *Cerebrovascular Diseases*. 2019;47(5-6):245-52.

11. Trifan G, Arshi B, Testai FD. Intraventricular hemorrhage severity as a predictor of outcome in intracerebral hemorrhage. *Frontiers in neurology*. 2019 Mar 12;10:217.
12. Wayan N, Anne S, Tjokorda M. Combination Intracerebral Hemorrhage-graeb Score Improves Prediction of Outcome in Spontaneous Intracerebral Hemorrhage. *Biomedical and Pharmacology Journal*. 2019 Mar 25;12(1):463- 7.
13. Bhatia R, Singh H, Singh S, Padma MV, Prasad K, Tripathi M, Kumar G, Singh MB. A prospective study of in-hospital mortality and discharge outcome in spontaneous intracerebral hemorrhage. *Neurology India*. 2013 May 1;61(3):244-48.
14. Godoy DA, Pinero G, Di Napoli M. Predicting mortality in spontaneous intracerebral hemorrhage: can modification to original score improve the prediction?. *Stroke*. 2006 Apr 1;37(4):1038-44.
15. Sacco S, Marini C, Toni D, Olivieri L, Carolei A. Incidence and 10-year survival of intracerebral hemorrhage in a population-based registry. *Stroke*. 2009 Feb 1;40(2):394-9.
16. 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. *The Lancet Neurology*. 2010 Feb 1;9(2):167-76.
17. Morgan TC, Dawson J, Spengler D, Lees KR, Aldrich C, Mishra NK, Lane K, Quinn TJ, Diener-West M, Weir CJ, Higgins P. The Modified Graeb Score: an enhanced tool for intraventricular hemorrhage measurement and prediction of functional outcome. *Stroke*. 2013 Mar;44(3):635-41.
18. Hansen BM, Morgan TC, Betz JF, Sundgren PC, Norrving B, Hanley DF, Lindgren A. Intraventricular extension of supratentorial intracerebral hemorrhage: the modified graeb scale improves outcome prediction in lund stroke register. *Neuroepidemiology*. 2016;46(1):43-50.
19. Kim KH. Predictors of 30-day mortality and 90-day functional recovery after primary intracerebral hemorrhage: hospital based multivariate analysis in 585 patients. *Journal of Korean Neurosurgical Society*. 2009 Jun;45(6):341-45.
20. Tetri S, Juvela S, Saloheimo P, Pyhtinen J, Hillbom M. Hypertension and diabetes as predictors of early death after spontaneous intracerebral hemorrhage. *Journal of neurosurgery*. 2009 Mar 1;110(3):411-7.
21. Tshikwela ML, Longo-Mbenza B. Spontaneous intracerebral hemorrhage: Clinical and computed tomography findings in predicting in-hospital mortality in Central Africans. *Journal of neurosciences in rural practice*. 2012 May;3(02):115-20.
22. Tuhim S, Horowitz DR, Sacher M, Godbold JH. Volume of ventricular blood is an important determinant of outcome in supratentorial intracerebral hemorrhage. *Critical care medicine*. 1999 Mar 1;27(3):617-21.
23. Young WB, Lee KP, Pessin MS, Kwan ES, Rand WM, Caplan LR. Prognostic significance of ventricular blood in supratentorial hemorrhage: a volumetric study. *Neurology*. 1990 Apr 1;40(4):616-20.
24. Hwang BY, Bruce SS, Appelboom G, Piazza MA, Carpenter AM, Gigante PR, Kellner CP, Ducruet AF, Kellner MA, Deb-Sen R, Vaughan KA. Evaluation of intraventricular hemorrhage assessment methods for predicting outcome following intracerebral hemorrhage. *Journal of neurosurgery*. 2012 Jan 1;116(1):185-92.