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# Demographics, Clinical profile, Causes and Outcome of Intracerebral Hemorrhage in Neurosurgical Unit in Manipal Teaching Hospital of Western Nepal

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**Background:** This research article aims to evaluate the demographic variables, clinical profile, causes and outcome determinants of spontaneous intracerebral hematoma (SICH) in a population of Western Nepal. The study represents the cases of SICH reported from Manipal Teaching Hospital, a tertiary center at Gandaki province of Western Nepal.

**Materials and methods:** Retrospective data collection and analysis were done with consecutive cases of SICH admitted to our center between January 2018 and March 2019. The variables analyzed include age, gender, chronic conditions like hypertension, diabetes mellitus, history of tobacco abuse, alcohol abuse, Glasgow coma score (GCS) on admission, radiological(CT scan) findings, treatment modality, an outcome at 6 months period, etc. Modified Rankin score (mRS) was used to assess the outcome at discharge and after six months.

**Results:** Our study group of 237 patients included 171 males and 66 females and the mean age of presentation was 64.02 years. The study group included 121 patients (51.1%) who were previously diagnosed with systemic arterial hypertension and 15 patients diagnosed with diabetes mellitus. The most frequent locations of hematoma were basal ganglia (n=127), lobar (n=94), intraventricular hemorrhage (n=69), cerebellar (n=15) and brainstem (n=11). The mean volume of the blood clot on admission was 25.97 ml. surgical evacuation of hematoma and decompression through craniotomy was done in 52 (21.9%) patients. Independent predictors of unfavorable outcomes includes the variables like headache (p=0.007), aphasia (p=0.017), mean GCS score (p=0.00) and motor GCS score (p=0.00); CT finding of intraventricular extension of hemorrhage (p=0.00), midline shift (p=0.00), intracerebral blood volume (p=0.00); and surgery (p=0.007).

**Conclusion:** ICH predominantly affects a younger population in Nepal in comparison to the Western world. The variables include clinical features like headache, aphasia, pupillary size and reaction, mean GCS score and motor GCS score; CT finding of intraventricular extension of hemorrhage, midline shift, intracerebral blood volume; and surgery were the predictors of an unfavorable outcome. On binary logistic regression, the ICH score was the most consistent predictor of unfavorable outcomes in terms of MRS (OR 2.236, p=0.002).

**Key words:** Demographic variables, Intra cerebral hematoma, Nepal, Outcomes, Risk Factors



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Spontaneous Intra cerebral hemorrhage (SICH) is the second most common type of stroke after ischemic stroke and is a common neuro-critical disease leading to serious morbidity and mortality. ICH refers to any bleeding into the intracranial vault, including the brain parenchyma and surrounding meningeal spaces. Most of the cases are due to the rupture of small penetrating arteries of the brain secondary to hypertensive arteriosclerosis, atherosclerosis, or other vascular abnormalities. ICH accounts for approximately 10-20% of all strokes throughout the world. The overall incidence of spontaneous ICH worldwide is 24.6 per 100,000 person-years.[1] With an increase in the overall life expectancy of the world population, the stroke burden has also increased worldwide. However, the largest number of cases and deaths has occurred in low- and middle-income countries.[2] In Nepal, Intracerebral hemorrhage is responsible for 23.39 deaths by all ages and sexes, per 100,000 population.[3]The definitive management of spontaneous ICH is controversial, and the role of surgery in primary management is debatable. So in developing countries like Nepal, with severe constraints in resources, skilled manpower, and sophisticated facilities, treatment goals need to be stratified given the high disability and death associated with spontaneous ICH. The goal of our single institution based study was to analyze the demographic variables, clinical profile, risk factors and to assess the functional outcome and to identify the prognostic factors after spontaneous intracerebral hemorrhage in a tertiary care hospital located in a metropolitan city of Western Nepal.

**Methods and Materials:**

A retrospective analytical study was conducted in the Department of Neurosurgery, Manipal Teaching Hospital, Nepal from January 2018 to March 2019 including 238 consecutive patients admitted with intracranial hemorrhage (ICH) intending to study various clinico-socio-demographic features of ICH and various features associated with outcome.

History and clinical examination were performed in all patients and the diagnosis of ICH was made with the CT imaging of the brain. Data was collected from the Medical Records Department, ICU census, patient files, operation theater register, and discharge sheets and were charted in a pre-structured proforma. Patients of all ages and both genders admitted in the neurosurgery ward and ICU were included in the study. Data was collected on social demographical characteristics like age, gender and clinical characteristics like duration before the presentation, ICH site, clinical features, past medical history, family history, personal history, Glasgow Coma Scale (GCS) at the Emergency Room, serum electrolytes (sodium and potassium), serum urea, serum creatinine, CT findings, the volume of the bleed, presence or absence of midline shift, Intracerebral Hemorrhage Score (ICH score), surgery. The outcome was categorized into a good outcome group and a poor outcome group. Good outcome was defined as a modified Rankin Scale (*mRS*) score of <= 3 and poor outcome was defined as the mRS score of ≥4 at the end of six months after hospital discharge. Patients were followed up till 6 months with telephone conversation using a pre-structured questionnaire or scheduled OPD visit after the telephone conversation. All the continuous variables were compared with the outcome using the student's t-test and the categorical data were compared using Chi-Square and Fischer Exact test. Data analysis was done using SPSS 20.0 software.

**Results:**

The cases of patients who met all the inclusion and exclusion criteria were retrospectively studied. 262 patients were initially included in the study but 25 cases were lost either in follow up or expired during treatment or left to other medical centers against medical advice. The final analysis was done for 237 patients. There were 171 male patients (72.15%) and 66 female patients (27.84 %). The mean age of presentation of ICH in our study was 64.02 years.

**Table 1.Clinico-Demographic parameters of Patients with ICH Vs Outcome**

| S. N | Clinico-Demographic Parameters | Favorable outcome | Unfavorable outcome | P-value |
|---|---|---|---|---|
| 1. | Mean age (in years) | 62.45±13.984 | 65.89±14.721 | 0.067 |
| 2 | Male | 89 (52%) | 82 (48%) | 0.236 |


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| | | | | |
|---|---|---|---|---|
| | **Female** | 40 (60.6%) | 26 (39.4%) | |
| **3** | **Smoking** | 42(56.0%) | 33(44.0%) | 0.741 |
| **4** | **Drinking** | 71(57.7%) | 52(42.3%) | 0.290 |
| **5** | **Family history** | 14(51.9%) | 13(48.1%) | 0.775 |
| **6** | **Previous stroke** | 10(37.0%) | 17(63.0%) | 0.054 |
| **7** | **Hypertension** | 60(49.6%) | 61(50.4%) | 0.126 |
| **8** | **Diabetes Mellitus** | 7(46.7%) | 8(53.3%) | 0.533 |
| **9** | **Antiplatelet/ Anticoagulant** | 13(44.8%) | 16(55.2%) | 0.268 |
| **10** | **Surgery** | 13 (25.0%) | 39 (75.0%) | 0.000* |

Systemic hypertension was present in 51.1%(n=121)of cases, a history of diabetes in 6.3%(n=15), a history of tobacco abuse in 31.6%(n=75), and alcohol abuse in 51.9%(n=123),anticoagulant use in 5.5%(n=13) and anti-platelet use was present in 7.6%(n=18) of total ICH cases(n=237).

**Table 2.**

| S.N. | Presenting Features | Favorable outcome | Unfavorable outcome | P-value |
|---|---|---|---|---|
| **1** | **Headache** | 51 (63.8%) | 21(36.2%) | 0.007* |
| **2** | **Vomiting** | 51(50.5%) | 50(49.5%) | 0.294 |
| **3** | **Seizure** | 12(38.7%) | 19(61.3%) | 0.059 |
| **4** | **Weakness** | 81(49.1%) | 84(50.9%) | 0.120 |
| **5** | **Visual symptoms** | 8(66.7%) | 4(33.3%) | 0.382 |
| **6** | **Aphasia** | 38(44.2%) | 48(55.8%) | 0.017* |
| **7** | **Cerebellar signs** | 7(77.8%) | 2(22.2%) | 0.152 |
| **8** | **Pupils** | 13(22.0%) | 46(78.0%) | 0.000* |
| **9** | **Mean GCS** | 13.97±1811 | 10.78±3.751 | 0.00* |
| **10** | **Motor GCS Score** | 5.82 ±0.423 | 4.85±1.471 | 0.00* |
| **11** | **ICH score** | 0.68±0.729 | 1.91±1.227 | 0.00* |

The median GCS on admission was 14 (mean=12.51); median motor GCS was 6(mean=5.38), and 31 patients presented with a GCS of ≤ 8.

On the basis of location of hematoma, out of total ICH cases(n=237), basal ganglia bleed accounts for 53.6%(n=127), lobar hematoma in 39.7%(n=94), intraventricular extension in 29.1%(n=69), cerebellar bleed in 6.3%(n=15) and brainstem bleed in 4.6%(n=11).The mean volume of hematoma was 25.97 ml.

**Table 3**

| S.N. | CT Parameters | Favorable outcome | Unfavorable outcome | P-value |
|---|---|---|---|---|
| **1.** | **Lobar Hematoma** | 45 (47.9%) | 49 (52.1%) | 0.100 |
| **2.** | **Cerebellar** | 10(66.7%) | 5(33.3%) | 0.326 |
| **3.** | **Ganglionic** | 74(58.3%) | 53(41.7%) | 0.202 |
| **4.** | **Brainstem** | 6(54.5%) | 5(45.5%) | 0.994 |
| **5.** | **Intraventricular** | 21(30.4%) | 48(69.6%) | 0.000* |
| **6.** | **Midline shift** | 9(19.6%) | 37(80.4%) | 0.000* |
| **7.** | **Volume** | 16.43±27.963 | 37.36±30.675 | 0.00* |

The parameters associated with statistically significant(p-value <=0.05) unfavorable outcomes include clinical features like headache, aphasia, pupillary size and reaction, mean GCS score and motor GCS score; CT finding of intraventricular extension of hemorrhage, midline shift, intracerebral blood volume; and Surgery.

A binary logistic regression was done amongst all the parameters having significant association outcomes in univariate analysis and tabulated in **Table 4**.

**Table 4**

| S.N. | Variables | B | P-value | Odds (Exp B) | 95% CI for Odds |
|---|---|---|---|---|---|
| **1** | **IVH** | -0.557 | 0.170 | 0.573 | 0.258-1.270 |
| **2** | **Headache** | 0.640 | 0.750 | 1.896 | 0.937-3.838 |
| **3** | **Aphasia** | -0.651 | 0.056 | 0.522 | 0.268-1.017 |
| **4** | **Glasgow Coma Scale** | -0.073 | 0.518 | 0.930 | 0.746-1.159 |
| **6** | **GCS motor score** | -0.416 | 0.248 | 0.660 | 0.325-1.337 |
| **7** | **Volume** | 0.006 | 0.336 | 1.006 | 0.994-1.018 |
| **8** | **Midline Shift** | - | 0.137 | 0.456 | 0.162-1.285 |

| | | | | | |
|---|---|---|---|---|---|
| | | 0.786 | | | |
| **9** | **ICH Score** | 0.805 | 0.002* | 2.236 | 1.329-3.762 |
| **10** | **Surgery** | 0.145 | 0.781 | 1.156 | 0.416-3.210 |

Following adjustment of all other variables associated with a significant association with outcome, only the ICH score was independently associated with unfavorable outcome in terms of MRS (OR 2.236,p=0.002).

**Discussion**:

Spontaneous Intracerebral Hemorrhage (SICH) is a common medical emergency, often with severe and devastating consequences as per the patient and their families. Intracerebral Hemorrhage is classified further depending on the underlying cause of bleeding, either primary or secondary. Primary intracerebral hemorrhage accounts for approximately 78-88% of cases originated from the spontaneous rupture of small vessels secondary to chronic hypertension or amyloid angiopathy.[4] Secondary ICH occurs in a small group of patients with vascular abnormalities (aneurysms and AV malformations), tumors, or impaired coagulation. The first-month mortality rate ranges from 35% to 52% and only 20% of survivors are expected to have full functional recovery at 6 months.[5]Approximately 50% of deaths occur within the first 24 hours, emphasizing the crucial role of early and effective treatment in the primary setting.[6]

The definitive risk factors for SICH include systemic arterial hypertension and cerebral amyloid angiopathy (CAA). Hypertension-related SICH is more likely to occur in deep brain structures (basal ganglia), and the risk increases with uncontrolled blood pressure and irregular medications. In developed countries, the incidence of hypertensive ICH has decreased with the improvement of blood pressure control. However, in developing countries, the burden of ICH has not decreased. ICH is twice as frequent in low to middle-income countries compared to high-income countries.[2,7] CAA is associated with old age and the bleed tends to occur in lobar regions.

The modifiable risk factors of spontaneous intracerebral hemorrhage (SICH)includes systemic arterial hypertension, current cigarette/tobacco smoking, excessive ethanol consumption, use of antiplatelet drugs like aspirin, anticoagulants, and sympathomimetics.[8]

According to Hemphill et al, the poor prognostic factors for SICH includes advanced age (≥ 80 years), low GCS scale score, ICH volume of ≥30 ml, an intraventricular extension of hemorrhage, infra-tentorial origin, advanced white matter lesions, hyperglycemia at admission, and chronic kidney disease (estimated glomerular filtration rate <60 mL/minute/m2).[8]Our retrospective study showed a statistically significant and direct relationship of ICH blood volume (p=0.000), midline shift (p=0.000), an intraventricular extension of hematoma (p=0.000) to be associated with poor outcome. As reported each ml increase in baseline clot volume increases the mortality risk by 1% and for each 10% increase in hematoma volume growth, the risk of death increases by 5%.[9]It has been repeatedly considered a negative prognostic predictor and powerful predictor of mortality.[10,11] Many studies have also shown there is a poor prognosis with the increased midline shift. In 40-60% spontaneous ICH patients, an intraventricular extension was seen and is a significant predictor of 30-day mortality and long term outcome. [12,8] One prospective study done in Nepal showed GCS at admission, size of the hematoma, midline shift in cerebral tomography scan (CT), and presence of IVE as a predictor of outcome in supratentorial spontaneous intracranial hemorrhage.[13]

Headache is more common in patients with large hematomas and is attributed to traction on meningeal pain fibers, increased intracranial pressure, or blood in the cerebrospinal fluid.[6] Our study showed the presence of headaches during the presentation to be associated with poor outcomes of the patient (p=0.007). In spontaneous ICH patients in one study, it was also an independent predictor of the residual cavity volume(Odds Ratio 6.49).[14]

Global aphasia is usually associated with a large left hemisphere bleed. The location of the lesion is more important than the size of the lesion in determining the prognosis of aphasia in stroke patients.[15] Since we had a significant number of lobar hemorrhage 39.7% (n=94), this may be the

reason for the statistical association between aphasia at presentation and the poor outcome of intracerebral hemorrhage in our study.

All over the world pupil size and reflex are commonly used for the evaluation and management of ICH patients. Our study also showed a statistically significant relation between pupillary reaction and the ICH outcome. Fixed dilated pupils are usually associated with increased intracranial pressure secondary to large hematoma or due to brain herniation. Both of these conditions carry a poor outcome of intracranial hemorrhage.

GCS score is one of the most consistent predictors in most of the studies. The association between low GCS score and poor outcome of ICH has been further verified by our study (p=0.00). We observed a mean GCS of 10.78±3.751 for an unfavorable outcome. According to Bhatia et al. and Wang et al. 72.9% and 68.4% fatality were reported respectively with poor GCS on presentation.[12,16]

Surgical treatment of spontaneous ICH is controversial. Many techniques such as open craniotomy, decompressive craniectomy, neuroendoscopy, etc. are favored according to the surgeons. It has many benefits as it can prevent mass effect and cerebral herniation, reduction of Intracranial pressure, and decrease of excitotoxicity and neurotoxicity of blood products.[17] Our study also showed a statistically significant relation between surgical intervention and the outcome of ICH emphasizing the importance of timely intervention (p=0.000). Patients who underwent surgical therapy had a higher survival rate compared to patients who received the conservative best medical treatment. However, this survival advantage was not statistically significant.

This study demonstrates that the ICH Score is a valid clinical grading scale for stratifying the likelihood of a favorable functional outcome in the first 6 months after acute ICH. This is in addition to prior studies that have demonstrated the ICH Score is a validated predictor of the risk of 30-day mortality.[18,19] Importantly, in this study, the ICH Score was valid and significant regardless of the specific cut-point chosen to define a favorable functional outcome. The component of the Intracerebral hemorrhage score (ICH score) includes GCS at presentation, ICH volume, Intraventricular Extension, the origin of ICH, and Age of the patient. **Table 5** shows how to calculate the ICH score.

**Table 5**

| Variable | Scores |
|---|---|
| **GCS at presentation** | |
| **13-15** | 0 |
| **5-12** | 1 |
| **3-4** | 2 |
| **ICH volume(cm3)** | |
| **≥30** | 1 |
| **≤30** | 0 |
| **IVH** | |
| **Yes** | 1 |
| **No** | 0 |
| **Infratentorial origin of ICH** | |
| **Yes** | 1 |
| **No** | 0 |
| **Age(In years)** | |
| **≥80** | 1 |
| **≤80** | 0 |
| **Total ICH Score** | 0-6 |

Our study is unambiguous with the findings of J. C Hemphill et al about the prognostic value of ICH score with the p-value of 0.00.8 S. Turhim et al found that the volume of intraventricular hemorrhage is an important determinant of outcome in supratentorial intracerebral hemorrhage.[20] Our study also found a statistically significant relation between intraventricular hemorrhage and the outcome of intracerebral hemorrhage (p=0.000).

The incidence of ICH increases with advanced age. The mean age of presentation in our study was 64.02 years. In the Indian subcontinent, comparatively younger age patients were reported to have a characteristic feature of SICH.[12,21]Consistent with other peer-reviewed researches, neither sex nor age was a significant outcome predictor.

Our study even showed no significant association between the 6 months outcome and the presence of comorbidities such as systemic hypertension, diabetes mellitus, smoking, or alcohol abuse. The failure of a statistically significant relationship

between systemic hypertension and the outcome of intracerebral hemorrhage may be because patients with medication-controlled hypertension were labeled as hypertensive patients in our study. Additionally, current smokers also failed to show a higher incidence of ICH in the study which may be because patients who smoke infrequently were also labeled as smokers in our study and were not quantified according to the pack years during the beginning of the study. Similarly, all drinkers regardless of quantity and duration were also labeled as drinkers, and the alcohol dependence was not staged based on the CAGE questionnaire, which may be the reason why our study did not find the statistical significance between alcohol consumption and the outcome of ICH. Similarly, patients under antiplatelet and/or anticoagulants also did not show a statistically significant association with ICH. It may be because of the small sample size of patients under antiplatelet /anticoagulants in our study.

There are several limitations to be considered while analyzing our data. The retrospective nature of the study aids to incomplete documentation of the various analyzed variables. As the decision on the treatment modality (surgical or conservative) was made individually by the treating surgeon and as there are no definitive nationwide guidelines, it probably contributed to the diverse distribution of the variables in operated and non-operated groups. One of the important limitations in our study is a relatively short period of follow up of 6 months and a relatively small number of ICH cases (n=237).

## Conclusion:

In developed countries, the incidence of spontaneous intracerebral hematoma has decreased with the improvement of blood pressure control. However, in developing countries, the burden of ICH has notreduced.2The need to identify potential risk factors, causes and demographic variables to initiate corrective measures and customize treatment cannot be overemphasized, especially in a resource limited country like Nepal. In this retrospective research study, we summarized the demographics, risk factors, clinical profile, and favorable and unfavorable prognostic factors of ICH. The parameters associated with statistically significant unfavorable outcomes were clinical features like headache, aphasia, pupillary size and reaction, mean GCS score and motor GCS score; CT findings of intraventricular extension of hemorrhage, midline shift, intracerebral blood volume; and Surgery. On binary logistic regression, the ICH score was the most consistent predictor of unfavorable outcome in terms of mRS. Intracranial hemorrhage (ICH), as it carries a high mortality risk and prolonged disability requiring extended rehabilitation, more researches needs to be done to get the true estimate of the burden of ICH in the context of Nepal.

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