Etiology and outcome determinants of intracerebral hemorrhage in a south Indian population, A hospital-based study

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Abstract

Background: There is paucity of methodologically sound published studies on intracerebral hemorrhage (ICH) from India, on pub med/embase search. **Aims:** To explore etiology of ICH and correlate the causes, location, and size of hemorrhage to clinical outcome. **Materials and Methods:** A hospital-based descriptive study from South Indian eastern coastal town of Puducherry; 60 consecutive subjects aged > 12 years, predominantly of inbred Tamil population, with head CT evidence of intracerebral hemorrhage not associated with trauma and brain tumors, were recruited. Outcome at three months was measured using Glasgow Outcome scale, NIHSS and mortality. SPSS v 19 was used for statistical analysis. **Results:** Commonest etiological factor was hypertension, followed by bleeding diathesis, thrombolysis for myocardial infarction, and cortical vein thrombosis. Most frequent locations of hematoma were basal ganglia, thalamus, internal capsule, and cerebral and cerebellar parenchyma. Hematoma volume correlated significantly with systolic and mean arterial pressure but not with diastolic blood pressure. Poor outcome was correlated to size ($P < 0.05$) and intraventricular extension of hematoma ($P < 0.05$), and to systolic, diastolic and mean arterial pressure, but not to age, gender, smoking, alcoholism, ischemic heart disease, and blood sugar level. Among diabetic patients with ICH, the size of hematoma ($P = 0.04$) and severity of coma ($P = 0.01$) at admission were significantly worse compared to the non-diabetic, but not the outcome at three months [Glasgow outcome scale or mortality ($P = 0.94$ and 0.14)]. **Conclusions:** The location of hemorrhage and correlation with outcome agreed with the patterns described for the non-white races in prior reports. Independence of outcome to diabetic status despite a more severe initial presentation may indicate importance of good care, even in high risk groups.

Key Words

Etiology, intracerebral hemorrhage, outcome

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Introduction

Spontaneous intracerebral hemorrhage (ICH) accounts for 10% to 15% of all strokes.[1] In the eastern nations, ICH appears to be more common, accounting for up to 30% of strokes.[2] In spite of advances in medical and neurosurgical treatment, ICH remains a condition with poor outcome, with an overall mortality of 40% to 50%.[3] Identification of factors determining and modifying the clinical presentation and outcome of ICH is, therefore, very important for every population. Among the etiologies implicated in spontaneous intracerebral hemorrhage, chronic arterial hypertension is considered the most important[4]; other established causes include alcohol consumption,[5,6] anti-coagulant treatment,[4,7] and to a lesser extent, anti-platelet use,[8] thrombolytic therapy,[9] and use of amphetamines or cocaine[4] and possibly statins. Current smoking does not seem to increase the risk of ICH.[5,10]

There have been very few prospective studies on ICH in India. Further, in view of vastness and heterogeneity of Indian population, systematic studies from different regions of the country may be justified. Through a prospective hospital-based study of 60 consecutive patients with ICH, we sought to investigate the risk factors for ICH and correlate the causes, location, and size of hemorrhage to clinical outcome.

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Subjects and Methods

This is a prospective descriptive-analytical study, which comprised of 60 consecutive patients with CT scan proven

ICH, aged > 12 years , admitted to the Jawaharlal institute of Postgraduate Medical Education and Research, Puducherry, over a period of 18 months. Subjects consisted predominantly of Dravidian ethnic Tamil patients of low and middle income from Puducherry and neighboring districts of Tamilnadu. Traumatic and brain tumor-related ICH were excluded. Written informed consent was obtained from every patient or guardian as applicable. All patients were subjected to detailed history and physical examination followed by relevant laboratory investigations. Initial examination included recording of vital signs, assessment of Glasgow Coma Scale Score, neurological examination as per a performa and assessment of National Institute of Health Stroke Scale (NIHSS) score. Non-contrast Head CT Scan was done in all patients. A battery of investigations including electrocardiogram, and echocardiogram, renal function tests, blood sugar level estimation, lipid profile, liver function tests, complete blood picture, were used to work up for hypertension, diabetes mellitus, hyper/hypolipidemia and bleeding/clotting disorders. Computerized tomographic angiogram (CTA) and magnetic resonance imaging (MRI) were done, wherever indicated.

Hypertension was defined as blood pressure in excess of 140 (systolic) and/or 90 (diastolic) mm Hg blood pressure. [11] A fasting blood glucose of ≥126 mg/dl or two random blood glucose values of more than 200 mg/dl were taken as diagnostic of diabetes mellitus.[12] Hypercholesterolemia and hypocholesterolemia were defined by serum cholesterol value greater than 200 mg/dl and less than 160 mg/dl, respectively.[13] Platelet count of less than 150,000/μl defined thrombocytopenia.[14]

CT scans were studied to document the anatomical location, number and size of hemorrhage and the presence of intraventricular hemorrhage. Approximate volume of the hematoma was calculated using the formula, ABC/2, where A is the longest diameter of the hematoma measured in centimeter (cm), B the diameter perpendicular to A, and C the product of slice thickness in cm and the number of slices of the CT scan in which the hematoma is visible.[15]

All patients received the optimal treatment for ICH as per protocols of the hospital for various etiologies of ICH. Recombinant factor VII was not administered to any, due either to late presentation or cost factor. Osmotic agents, anti-hypertensive, anti-epileptic agents and hypoglycemic agents including insulin were given as per indications. Surgical interventions and mechanical ventilator support were provided as and when necessary.

Patients were followed up for a period of three months to assess short term clinical outcome by Glasgow Outcome Scale (GOS) and NIHSS at 3 months. For statistical analysis, GOS 1, 2 and 3 were grouped together as poor outcome groups and GOS 4 and 5 as good outcome.[16] Baseline parameters were correlated to NIHSS and GOS at 3 months through appropriate statistical tests. Statistical analysis was done using SPSS software v 19.

Results

The baseline characteristics of the study population with respect to age and gender are summarized in Figure 1. The most common clinical presentation was hemiplegia. Baseline NIHSS was 0 to 15 in 20 (33.3%) patients, 16 to 30 in 32 (53.3%), and > 31 in 8 (13.3%) patients. GCS at baseline was 3 to 8 in 23 patients (38%), 9 to 12 in 24 (40%), and 13 to 15 in 13 (22%) patients. Hypertension was the most common etiological risk factor, 50% of patients having been diagnosed hypertensive in the past, another 36.7% newly diagnosed. Other etiologies included bleeding/clotting disorders (6.67%), anti-platelets/thrombolytic use (5%), and ICH in association with cerebral venous sinus thrombosis (1.67%).

Baseline data pertaining to the location of the bleed as seen on CT scan are given in Figure 2. The mean ICH volume was 49.97 ± 28.3 cubic cm. ICH volume was significantly associated with systolic and mean arterial pressures but not with diastolic pressure. (P=0.001, 0.023 and 0.11 respectively). Intraventricular hemorrhage was found maximally in the group of ICH with > 60 cubic cm volume [14 (66.67%)]. While 20% (12) of the ICH subjects had a good outcome, the remaining 80% did have a poor functional outcome as defined above. Diabetic status was seen to significantly correlate with hematoma Volume and low GCS but not with NIHSS score, GCS score or mortality at 90 days [Table 1].

Of the 30 patients who died, 20 (66.7%) were men. While 20 (66.7%) died within a period of 24 hours, remaining 10 patients survived up to 30 days. The majority of patients who died were hypertensives [25 (83.3%)], of which 18 (72%) were male and 7 (28%) female.

Poor outcome was correlated to size (P<0.05) and intraventricular extension(P<0.05) of hematoma, and blood pressures (systolic, diastolic and mean arterial; P=0.004, 0.027 and 0.005 respectively). ICH volume was significantly associated with poor outcome (P < 0.05); same was true of the intraventricular hemorrhage (IVH) [Table 2]. The 3-month GOS was also significantly correlated to NIHSS at baseline (P < 0.05), with the poor outcome group having a significantly higher mean baseline NIHSS of 23.8 (± 8.1) compared to a mean baseline NIHSS of 8.8 (± 4.0) in the good outcome group.

Analysis of the outcome did not reveal any significant association with age, gender, diabetes mellitus, ischemic heart disease, smoking or alcoholism.

Discussion

This is one of the few systematic studies on intracerebral hemorrhage from India, albeit a modest sample size. The study was conducted in a Ministry of Health-funded University hospital which provides quality medical care free of cost to poor patients and thus caters to the needs of and enjoys the patronage and confidence of low and middle income Tamil population in and around the union territory of Puducherry and the neighboring districts of the Arcot region of Tamilnadu such as Cuddalore and Villupuram. Uncontrolled hypertension was the most common etiology for ICH in our study, as has been the case in earlier studies across the globe.[17-19] The most common site of hematoma was the basal ganglia (45%) followed by thalamus, cerebral lobes, and cerebellum (43, 38, and 5%, respectively), which is in agreement with the pattern described for the non-white races in the United States as well.[20]

Table 1: Comparison of clinical and radiological features of ICH between diabetic and nondiabetic patients

Parameter	DM (*N* = 16) Mean (SD)	Non DM (*N* = 44) Mean (SD)	*P* value
Initial ICH volume (milliliters)	72.1 (28.4)	42 (13.6)	0.04 (student's *t*)
GCS at day 0	8 (3)	10 (3)	0.01 (student's *t*)
NIHSS Score at day 0	23 (7)	20 (6)	0.21 (student's *t*)
NIHSS at day 90	7 (2)	10 (3)	0.36 (student's *t*)
Poor outcome*	13 (81.3)**	35 (79.5)**	0.94 (χ^2)
Mortality	11 (68.8)**	19 (43.2)**	0.14 (χ^2)

*Poor Outcome: Glasgow outcome scales 1-3; **N (%)

Table 2: Correlation of baseline and radiological parameters to outcome

Parameter	Poor outcome *N*= 48 [Mean (SD)]	Good outcome *N*=12 [Mean (SD)]	Significance(*P*) Student's *t*
Age (yrs)	59 (15)	57 (15)	0.686
Systolic BP (mm Hg)	195 (37)	169 (22)	0.004
Diastolic BP (mm Hg)	110 (24)	99 (12)	0.027
Mean Arterial Pressure (mm Hg)	140 (27)	126 (10)	0.005
Random Blood Glucose (mg/dl)	178 (98)	154 (57)	0.271
Mean ICH volume (cubic cm)	59.8 (46.4)	10.7 (14.7)	<0.05
Number of patients with Intraventricular haemorrhage	*25 (52.1)	*1 (0.08)	**<0.05
NIHSS at baseline	23.81 (8.09)	8.83 (4.00)	<0.05

**N* (%); * *χ^2 (Fisher's exact) test Glasgow outcome scales: 1-3 (Poor outcome); 4-5 (Good outcome)

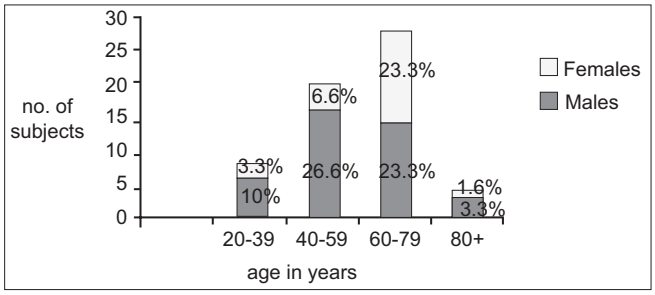

Figure 1: Age and sex distribution in the study population

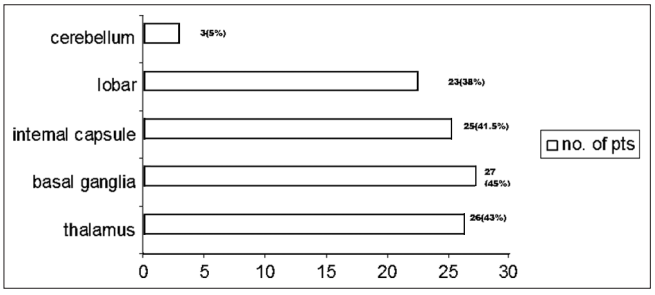

Figure 2: Location of Intracerebral hemorrhage

Based on the Glasgow outcome scale, 80% of the patients had poor outcome in our study. Predictors of death or severe disability included lower baseline Glasgow Coma Score, larger baseline ICH volume, and the presence of IVH at baseline, conforming to a pattern described previously.[1,21-24] While one study from Cincinnati, USA described a high sensitivity (96%) and specificity (98%) for the combined ICH volume and baseline GCS score to predict the 30 day mortality,[23]another from Heidelberg, Germany ascribed clinical outcome and increased mortality from ICH, more to the very presence of IVH and its early growth in size.[24]

In our study, patients with a poor outcome had significantly higher initial blood pressure. A multicentric study including centers from Asia (China and Singapore), Europe, Australia, and America had shown a similar association.[21,25] However, an Asian multicentric study (including centers from India) opined against such an association.[22] While previous studies from Japan, Sweden, and Finland found age to be a significant predictor of outcome,[26-28] our limited data did not find this association.

Diabetes has been reported as an independent predictor of death after ICH.[29] In our study, outcome did not differ significantly between diabetics and non-diabetics though there was a trend towards poor outcome in diabetic group. Diabetic status; however, showed a significant correlation to larger hematoma volume at admission, in our population too, agreeing with earlier studies.[23,29]

Limitations

This hospital-based study from a single center does not aim to provide true prevalence or burden of ICH in the community.

Sample size is modest here and the follow-up period of three months allowed only short term outcome assessment. Non-availability of sequential CT scans precluded studies on evolution of changes in hematoma volume.

Conclusions

In a quarternary university hospital-based ICH patient sample of predominantly Tamil population from the South Indian eastern coastal town of Pondicherry, poor outcome was significantly associated with size and location of hematoma, arterial blood pressures, NIHSS at baseline, and presence of IVH but not with age, smoking, alcoholism, ischemic heart disease, and diabetic status. Larger, well-designed studies

with a longer period of follow-up will be necessary to draw more robust conclusions on various etiologies of ICH and their correlation to the clinico-radiological parameters in our population.

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