ORIGINAL ARTICLE

Primary Intracerebral Haemorrhage in Malaysia: In-hospital Mortality and Outcome in Patients from a Hospital Based Registry

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SUMMARY

Primary intracerebral haemorrhage (ICH) results in significant morbidity and mortality among patients. There is a paucity of epidemiological data on this condition in Malaysia. The purpose of this hospital based study was to define the clinical profile in patients with primary spontaneous intracerebral haemorrhage at University of Malaya Medical Centre (UMMC) and to determine the mortality rate of intracerebral haemorrhage at the time of discharge, the prognostic factors and one year outcome of this cohort of patients. Sixty-six patients were admitted at the Neurosurgical unit of University of Malaya Medical Centre for a period of 13 months from March 2002 to March 2003. Fifty percent of the subjects were female. The mean age was 61.6±16.7 years. Among our patients with intracerebral haemorrhage, the common risk factors were: hypertension (80.3%), diabetes mellitus (25.7%) and smoking (27.2%). Common presenting features for our series were: weakness (61.8%), LOC (58.5%), headache (56.3%) and speech disturbances (45.3%). On neuroimaging, the lesions were seen in basal ganglia/thalamus (45.1%), lobar (32.9%), brainstem (13.4%) and cerebelli (8.5%). The overall 30 days mortality rate for intracerebral haemorrhage (ICH) was 43.9%. The important predictors of for mortality were the GCS score on admission (p<0.0001), haematoma volume>30mls (p<0.0001), evidence of intraventricular extension (p=0.011) and ICH score (p<0.0001). At one year follow up, 48.5% (n=32) were dead, 33.3% (n=11) obtained good recovery, 36.4% (n=12) moderate disability, 18.2% (n=6) severe disability and 3% remain vegetative state. The overall mortality rate for our series of patients with primary intracerebral haemorrhage is quite similar to previously published epidemiological studies. ICH scoring is useful in the prognostication.

KEY WORDS:
Primary intracerebral haemorrhage, Clinical profile, ICH score, Outcome, Malaysia

INTRODUCTION

Spontaneous intracerebral haemorrhage accounts for 10-15% of the total cases of stroke worldwide and is associated with a high mortality rate with only 38% of patients surviving in the first year[1]. A higher proportion of ICH has been observed in Asian populations while the percentage of ICH in stroke patients in South-East Asian (SEA) countries varies from 17.2% to 38.6%[2-3]. The available epidemiological data for stroke in Malaysia had been derived mainly from hospital-based studies. A prospective hospital based stroke study in Northeast region of Malaysia in 2002 revealed the overall mortality from primary intracerebral haemorrhage was 37%, and most patients died in the first month after the event (34%)[4]. In another large hospital-based study, 2% of all hospital admissions admitted in 1996 were stroke patients while 33% of them were intracerebral hemorrhages[5,6]. In a comparative study, Ng WK *et al* observed that ICH was more common in Malaysian population 17.2% vs Australian population 11.7%. On the other hand, cardioembolic strokes were more common among Australians 20.8% versus 10.9% in Malaysians[7]. However, no previous study in Malaysia has documented the clinical profile, outcome and prognostic variables of primary intracerebral haemorrhage.

The purpose of this hospital-based prospective study was to define the clinical profile in patients with primary spontaneous intracerebral haemorrhage at the UMMC, an urban 900-bed teaching hospital serving Kuala Lumpur-Petaling Jaya with the population of 1.5 million and to determine the mortality rate of intracerebral haemorrhage at the time of discharge, common presenting symptoms and prognosis of intracerebral haemorrhage at one year by using the ICH score[8].

MATERIALS AND METHODS

Our hospital-based study involved all the patients diagnosed to have primary ICH admitted to the University of Malaya Medical Centre (UMMC) from March 2002 to March 2003. The cases were detected prospectively in the Accident and Emergency department, medical neurology and the neuro-surgical operation registry of the UMMC. Primary intracerebral haemorrhage was defined as the presence of a neurological deficit on clinical examination and further documented by a brain computed tomography (CT) confirming the presence of intracerebral haemorrhage in the absence of trauma or surgery. Exclusion criteria were patients with haemorrhage secondary to brain tumours, trauma, haemorrhagic transformation of cerebral infarction, subarachnoid haemorrhage or rupture of arteriovenous malformations. All patient admission data, clinical assessments and neuroimaging findings were obtained

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prospectively by the same investigators and entered into a standardised questionnaire. We collected data on the following risk factors including hypertension, diabetes mellitus and cigarette smoking. In our patients, hypertension was defined as a history of treatment with antihypertensive medication and/or systolic and diastolic blood pressure levels of greater than 160 mmHg and 90 mmHg documented during previous outpatient reviews.

We used several widely accepted assessment scales including the Glasgow Coma Scale (GCS) and the ICH score. The ICH Score is a clinical grading score for primary ICH proposed by Hemphill *et al*[8] based on important prognostic variables based on the hospital records of 161 patients in an American teaching hospital. This scale has also been subsequently validated in geographically and socioculturally diverse populations[9-13]. Briefly, the ICH score is made up of several parameters including a basic neurological status examination, assigned as GCS score (2 points were given for GCS score of 3 to 4, 1 point for GCS score of 5 to 12, and 0 points for GCS score 13 to 15.) age (1 point for ≥ 80 years old and 0 point for < 80 years), infratentorial origin (1 point); ICH volume (1 point for ≥30cm^3, 0 point for <30cm^3) and presence of intraventricular haemorrhage (1 point).

Accordingly, neuroimaging data was reviewed and the location, size and the presence of intraventricular extension of intracerebral haemorrhage was noted. Haematoma volume was estimated by measuring the greatest diameter "A" and perpendicular diameter "B" of haematoma and the thickness of each CT slices by adding the number of CT slices visualizing the haematoma. These values are multipled and the product (AxBxC) is divided by two to yield the approximated volume. The neurological outcome of the patients' used the Glasgow Outcome Scale[14] with grade 1 dead, grade 2 vegetative, grade 3 severe disability, grade 4 moderate disability and grade 5 good recovery

The collected data was analysed using the Statistical Package for Social Science (SPSS) (Version 10.0). X^2 and t tests were used to assess association between demographic and other categorical variables, including age, sex, risk factors, GCS score, pulse pressure, ICH score, volume haemorrhage and evidence of intraventricular extension at the univariate level. Logistic regression was employed using mortality as the dependent variable. These independent variables were entered into the analysis and any non -significant variables were then eliminated using a backwards stepwise procedure.

Data on functional outcome was obtained upon discharge from hospital at two different time intervals namely at one month and one year after the first ICH either by assessment of patients in the outpatient clinic or by telephone interviews. The Glasgow outcome score was used with the following categories: Grade 5=good recovery, Grade 4=moderate disability, Grade 3=severe disability, Grade 2=vegetative, Grade 1=dead.

RESULTS

Intracerebral haemorrhage (ICB)

Demographic/ clinical profile

During the 13 month period from 1 March 2002 to 31 March 2003, there were 66 patients with primary ICH. There were 33 men (50%) and 33 women (50%) with a male to female ratio of 1:1. The age range was from 26-92 years with mean age for patients presenting with ICH was 61.6 years. There were 29 Malays (43.9%), 26 Chinese patients (39.4%), 8 Indian patients (12.1%) and 3 others (4.5%). The age and the patients' gender did not show any statistical significant affecting the admission mortality. (Table I). Initial Glasgow Coma Scale (GCS) showed that 45.5% (30) of patients had a score > 12. Mean GCS on admission were 9.9. The admitting GCS had a strong statistical association with mortality with p value <0.0001. Approximately 50% of patients were detected to have motor deficit. The most common clinical features for primary ICH were weakness (61.8%), lost of consciousness (58.5%) and headache (56.3%). Language disorders were present in 45% of patients. Other related presenting complaints were sensory disturbances (11.6%), fits (11.0%), visual disturbances and behavioral changes (5.8%) respectively.

We also observed the common sites of primary intracerebral bleed in our population. Most lesions were located in the basal ganglia such as in the putamen and thalamus. These sites account for more than half (56.1%) of the bleeding locations. Other sites were lobar 40.9% (n=27), brainstem 16.6% (n=11) and cerebellum 10.6% (n=7). (Table II) Almost half of the patients showed evidence of intraventricular extension. Out of 66 patients with intracerebral bleed, 33.4% (22) bled with the clots volume of more than 30 mls. Fifty three percents (n=35) of the ICB patients obtained ICH score 2 and above. Mean ICH score for intracerebral haemorrhage was 1.85 + 1.5. It was found to have strong statistical association with ICH mortality if patients score 2 and above.

Risk Factors

There were multiple risk factors of intracerebral haemorrhage in this series. Hypertension was the most common cause of ICH which accounts for 84.8% of the patients. Mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) on admission were 180.6 mmHg and 99.8 mmHg respectively. Half of the patients had DBP more than 100mmHg at the time of admission. The level of blood pressure was not related to mortality (Table I) Normal pulse pressure on admission (< 40mmHg) was found in 4.5% (n=3) of cases, 22.7% (n=15) had mild elevation (41-65 mmHg) and 72.7% (n=48) had moderate to severe elevation (>65mmHg) with mean pulse pressure 80.8 mmHg. However, pulse pressure was not a statistically significant variable with ICH mortality. In addition, smoking and the presence of diabetes mellitus showed no statistical association with admission mortality.

Outcome

Twenty-nine patients with primary ICH died in hospital prior to discharge. Consequently, admission mortality rate was 43.9%. Survival analysis showed a large clustering of deaths within the first three weeks of admission. Approximately one third of patients had good recovery or moderate disability, 22.7% (n=15) had severe disability. (Table III) The patients who survived were followed up from time of admission till April 2004. Follow up duration ranging from 12 months to 24 months. Mean survival of the follow up patients was 20.7 weeks.

Follow up data at one month and one year was available in 93.9% of cases. No death was reported at one month follow

Table I: Association of demographic and clinical profile with ICH admission mortality

Variables	Alive % (n)	Dead % (n)	Test	P Value
Demographic and clinical profile				
Age (in years) *	62.1 (14.4)	62.0 (17.4)	t Test	0.556
Gender				
Male	57.6 (19)	42.4 (14)	x^2	0.447
Female	66.6 (22)	33.4 (11)		
Risk factors				
HPT				
Yes	66.0 (35)	34.0 (18)	x^2	0.432
No	46.2 (6)	53.8 (7)		
DM				
Yes	62.5 (10)	37.5 (6)	x^2	0.908
No	62.0 (31)	38.0 (19)		
Smoking				
Yes	72.3 (13)	27.7 (5)	x^2	0.772
No	58.3 (28)	41.7 (20)		
SBP *	181.1 (36.6)	179.8 (41.3)	t Test	0.890
DBP *	96.9 (20.2)	102.5 (23.1)	t Test	0.258
Pulse Pressure *	84.1 (26.6)	77.3 (28.0)	t Test	0.275
Outcome				
GCS Score				
>12	80.0 (24)	20.0 (6)	x^2	0.000
<11	44.4 (16)	55.6 (20)		
ICH Score *	1.0 (0.9)	3.0 (1.3)	t Test	<0.0001
Size of Haematoma >30cc volume				
Yes	38.1 (8)	61.9 (13)	x^2	<0.0001
No	73.3 (33)	26.7 (12)		
Intraventricular Extension				
Yes	39.3 (11)	60.7 (17)	x^2	0.011
No	78.9 (30)	21.1 (8)		

* Contain mean values with standard deviation values in parenthesis.

Table II: Site of Intracerebral Haemorrhage

Location	n	%
Lobar	27	32.9
Basal/thalamus	37	45.1
Brainstem	11	13.4
Cerebelli	7	8.5
Intraventricular extension	29	35.3

Table III: Glasgow Outcome Score at Different Interval Follow-Up

Glasgow Outcome Score	Discharge % (n)	1 Month % (n)	1 Year % (n)
1. Dead	43.9 (29)	-	9.1 (3)[a]
2. Vegetative	1.5 (1)	3.0 (1)	3.0 (1)[b]
3. Severe Disability	22.7 (15)	24.2 (8)	18.2 (6)[c]
4. Moderate Disability	27.3 (18)	51.5 (17)	36.4 (12)[d]
5. Good Recovery	4.5 (3)	21.2 (7)	33.3 (11)[e]
Total	66	33	33

a) Two patients deteriorated from moderate disability group and 1 from severe disability group
b) One patient remain unchanged in vegetative stage.
c) Three patients remain unchanged, three patients deteriorated from moderate disability group
d) Four improved from severe disability, two patients deteriorated from good recovery and 6 remain unchanged
e) Six improved from moderated disability and five remain unchanged

Table IV: Multivariate analysis for predictor of ICH mortality and 95 % CI relative risks of Intracerebral Haemorrhage

Variables	p Value	Crude OR (95% CI)	Adjusted OR (95% CI)
GCS Score	0.000	3.78 (2.10 - 6.83)	0.90 (0.30 - 2.68)
ICH Score	<0.0001	4.92 (2.30 - 10.54)	8.83 (2.10 - 37.96)
Size Volume $\geq$ 30 cc	<0.0001	9.41 (2.60 - 33.10)	3.20 (0.40 - 25.49)
Intraventricular extension	0.011	3.65 (1.32 - 10.11)	0.46 (0.81 - 2.58)

up. Four patients were lost due to default in treatment, invalid telephone number or house address.

At one year follow up, 9.1% (3) were dead (two patients were from moderate disability group and one patient from severe disability group). Secondary pneumonia was the main cause of death. Good or full recovery was reported by 33.3% (11) of patients (six improved from moderate disability and five remain unchanged). Two patients from the good recovery group deteriorated to moderate disability at one year follow-up. Fifty percent (4) of the severe disability patients improved to moderate disability at one year and 37.5% (3) of the patients in this group remain unchanged. 35.3% (6) of the patients with moderate disability had a good recovery in one year. 17.6% (3) of patients with moderate disability deteriorated one grade lower and 35.5% (6) of them remained unchanged at one year. (Table III)

The significant predictors of acute ICH mortality at univariate level were depressed GCS score, elevated ICH score (2 and above), size of haemorrhage (volume greater than 30 cc) and evidence of intraventricular extension. (Table I) After the final multivariate analysis, only the ICH score remained as an independent prognostic factor of in-hospital mortality. (Table IV)

DISCUSSION

In the present study, we found that two major races, Malays and Chinese were present in nearly equal proportions accounting for 43.9% and 39.4% respectively. This is in contrast to an earlier study by Jaya F *et al*[4] who studied the stroke pattern in Northeast Malaysia. The main reason for this difference is the concentration of the various racial groups in urban and rural Malaysia. Our study is probably representative of cities with a higher concentration of Chinese patients in the West Coast of Peninsular Malaysia, whereas Jaya's study is representative of the rural population of Malaysia in the east coast states. This study reflects better the multiracial nature of our population. Indian patients constituted 12.1% of the total number of patients in our study while no Indian patients were noted in Jaya's study.

Over the same period, a total of 41,439 patients were admitted to our hospital, of which sixty-six (0.16%) were admitted for spontaneous intracerebral haemorrhage. This figure is slightly less if compared to unpublished data of Hanip MR's study [6] where he reported 0.66% of the hospital admission in 1996 were due to cerebral hemorrhage. Most of the patients from this series were from age group of 41-70 years. This finding was similar to Fogelholm R's study in Finland where he reported an early peak incidence of primary intracerebral haemorrhage occurred in the age group of 51-70 years[15].

A history of hypertension is major risk factor for ICH as reported by a number of authors[15,16,17]. Hypertension was also reported as a major risk factor for mortality amongst patients with ICH in a study by Mase G *et al* in Italy[18]. Diabetic patients have a poorer outcome after ICH than the non diabetic group[19,20,21]. Arboix *et al* and Togha *et al* showed that diabetes mellitus was an independent factor for mortality among ICH patients[24,25]. Pulse pressure has been studied and shows a linear relationship with acute intracerebral hemorrhage mortality, thus providing strong evidence for the role of pulse pressure in predicting the outcome[22]. However, in present study, we observed that our data did not show any statistically significant in mortality rates among the elderly, hypertensive, diabetic or smoking and pulse pressure on admission.

The Intracerebral Haemorrhage score (ICH score) has been shown to be a useful, simple reliable clinical grading scale that allows risk stratification and prognostication on patients with ICH[8,13]. The ICH Score [8] was the sum of individual points assigned as GCS score 3 to 4 (= 2 points), 5 to 12 (=1 point) 13 to 15 (=0 points); Age >= 80 years old yes(=1), no(=0); infratentorial origin yes(=1), no(=0); ICH volume >= 30cm^3 (=1), <30cm^3 (=0) and evidence of intraventricular haemorrhage yes(=1), no(=0). The size of the haemorrhage and the intraventricular spread seems to be important predictors of acute ICH mortality at the univariate level in our study. Our data suggested that elevation of ICH score is associated with significantly increase mortality rates in patients with intracerebral haemorrhage. (OR 8.8; 95% CI 2.1-37.9). This was similar to that found by Hemphill JC in 2001[8].

Twenty-nine with primary ICH patients died in hospital before discharge yielding a admission mortality rate of 43.9%. The 43.9% acute intracerebral haemorrhage mortality found in this study is comparable to figures reported in previous study on South Asia and Caucasian population[17,22]. Mortality rates of 40-50% have been reported world wide for spontaneous ICH. Almost 40% of all deaths within the first month were observed in the first three days (<72 hours) following admission in our survival analysis, a finding similar to that reported in previous studies[22,23]. The most important predictors of early mortality in this series are depressed GCS score on admission, elevated ICH score, size of haemorrhagic clots and evidence of intra-ventricular extension of haemorrhage.

To our knowledge, this is the first paper to describe the outcome of primary intracerebral haemorrhage in a prospective cohort of urban Malaysian patients. There was an increase of patients in the good recovery categories when compared with outcome at discharge. (Table III) The improved outcome of the respective categories may be attributed to aggressive rehabilitation and functional physiotherapy programmes in hospital[26]. Moreover, spontaneous neurological recovery and natural improvement with family support may play an important role in the convalescence of the patients[27].

Our study had several limitations. Firstly, the number of patients were small and may account for some of the discordant results when compared to the published literature. Secondly, our study may be affected by selection bias as hospital based studies emphasised on moderate to severe strokes requiring admission while rapidly fatal or very mild strokes may not have been directly admitted into hospital. The strength of our study was our follow up rate at one year which was 93.9%. Furthermore, all the patients were seen consistently by at least one designated investigator.

CONCLUSION

Data from our hospital-based registry is important as we have been able to demonstrate the clinical and neuroimaging profile of our cohort of patients with primary intracerebral haemorrhage. This is the first study to document the clinical profile and prognosis of a prospective cohort of patients with intracerebral haemorrhage in our population. Secondly, the overall mortality rate (43.9%) in our patients is quite similar to previously published epidemiological studies. The most common risk factor for intracerebral haemorrhage was hypertension which accounted for 84.8% of all cases. Significant predictors of mortality at 30 days were depressed GCS score (less than 8), elevated ICH score, size of haematoma >30 cc and evidence of intraventricular extension. However, other predictors of mortality in primary intracerebral haemorrhage such as age, elevated blood pressure during admission, hypertension, diabetes, smoking and elevated pulse pressure were not found to be significant in our study. ICH scoring is useful in Malaysian population as a prognostic tool.

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