Profile and predictors of outcome in Patients of Intracranial Hemorrhage

Amit Gupta*, S. N. Mahajan**, S. K. Diwan***, Sourya Acharya****

Abstract

Aims:
To study the profile of patients admitted with intracranial hemorrhage and to study the outcome of patients admitted with intracranial hemorrhage at 30 days.

Methods:
75 intracranial hemorrhage patients were studied. For the purpose of comparison of risk factors between intracranial hemorrhage and cerebral infarct group, 276 patients of cerebral infarct group were also taken in study.

Results:
The ratio of cerebral infarct to intracranial hemorrhage group was found to be 3.68: 1. Intracranial hemorrhage was more common in 5th and 6th decade of life (53.33 %) and was more common in males (58.66%). Hypertension (54.67 %) was the most common risk factor for stroke. High mean systolic and diastolic blood pressures on admission are more strongly correlated with intracranial hemorrhage than cerebral infarct. Mean waist/hip ratio and total cholesterol were more strongly associated with cerebral infarct group than hemorrhage. The most common presentation were hemiplegia (66.67) followed by loss of consciousness (58.66 %), headache (53.33 %) and vertigo (44 %). The most frequent site of bleed was basal ganglia (50.66 %) and cortex (33.33 %). The major predictors of mortality at 30 days were volume of bleed, GCS score, MRS score and Barthel's score on admission. Patients requiring ventilator had a poorer outcome. The overall mortality rate in our study was 41.33 % at 30 days.

Conclusions:
In patients presenting as stroke high blood pressure on admission with altered consciousness are more likely to have bleed. Low GCS and Barthel's , and high MRS score with high volume of bleed predicts poor short term outcome.

Key words: stroke, risk factors, mortality.

Introduction:
Intracerebral hemorrhage (ICH) is a spontaneous extravasation of blood into brain parenchyma. The overall incidence is 12 to 15 cases per 100,000 population per year[1], and it is the cause of 10% to 15% of first-ever strokes[2]. It is more common in the elderly [3] and in those of African [4] or Asian ethnicity [5], and the incidence is substantially increased in those receiving anticoagulant therapy[6].

More than 85% of ICH occurs as a primary (spontaneous) event related to rupture of small penetrating arteries and arterioles that have been damaged by chronic arterial hypertension or amyloid angiopathy. Sixty percent to 70% of primary ICH is hypertension related [7] and, in the elderly, amyloid angiopathy accounts for up to one-third of the cases. Secondary ICH can be related to multiple causes[8].
Non-modifiable risk factors for ICH include male

Address for correspondence
* Resident, ** Professor & HOD, *** Professor, **** Professor,
Department of Medicine, JNMC, Sawangi (M), Wardha

gender, older age, and African or Asian ethnicity [3]. Cerebral amyloid angiopathy is an important risk factor in the elderly and can occur in isolation or in association with Alzheimer disease or familial apolipoprotein syndromes[8, 9].

Modifiable risk factors include hypertension, which is one of the most important, especially in the elderly or in those with untreated or uncontrolled hypertension, when the risk of ICH is doubled [3, 7]. The risk of recurrent hypertensive ICH is <1.5% if arterial blood pressure (BP) is well controlled [10]. Warfarin anti-coagulation is associated with an 8- to 19-fold increase in the risk of ICH [11, 12]. High-dose aspirin is also associated with increased risk in the elderly particularly in those with untreated hypertension [13]. The recreational use of cocaine[3] and alcohol intake, either moderate or heavy acute use or chronic abuse (>60 mg/d), are also a risk factor for ICH[14].

Though the information on ICH is available in the medical literature, there has been no systematic study on the clinical profile of subjects with ICH and its outcome in Indians especially the central part of India, Therefore, this prospective study has been undertaken in patients of non traumatic intracranial haemorrhage admitted to AVBRH over a period of 30 months (May 2009 – October 2011) to study profile of patients of ICH and its outcome at 30 days.

Aims & Objectives

1. To study the profile of patients admitted with intracranial hemorrhage.
2. To study the outcome of patients admitted with intracranial hemorrhage at 30 days

Materials and Methods

STUDY DESIGN:

This was a prospective study. The study was carried out in 75 subjects admitted in Acharya Vinoba Bhave Rural Hospital (AVBRH), Sawangi (M), Wardha with intracranial haemorrhage. Duration of study – 24 months (Sept 2009 to August 2011).

Inclusion criteria: All subjects of non- traumatic intracranial haemorrhage.

Exclusion criteria: All subjects of intracranial hemorrhage who were on anti-coagulant therapy.

STUDY PROCEDURES

The study was conducted on 75 subjects admitted with intracranial haemorrhage, in AVBRH hospital over a period of 2 years. Informed consent was obtained from the subjects prior to enrolment. The study procedure was explained to them.On admission basic information like name, age, sex, registration no and address were noted. Presenting symptoms on admission were noted along with any history of risk factors like hypertension, diabetes mellitus, smoking, alcohol consumption and previous history of cerebrovascular episode. Vital signs on admission were recorded. Waist / Hip ratio was also noted on admission of all subjects. GCS score, MRS score and Barthel's score on admission were noted. After CT scan of brain was done, information about location of hemorrhage, extent and volume of hemorrhage were noted. Among blood investigations lipid profile was done. Information whether ventilator was needed or not was also noted. The subjects were followed up after 30 days for outcome either at OPD or telephonically. For comparison of risk factors between intracranial hemorrhage and cerebral infarct, data on 276 cases of cerebral infarct was also taken. Risk factors studied were age, sex, history of hypertension, diabetes mellitus, smoking, alcohol consumption, previous history of cerebrovascular episode, waist/hip ratio, admission systolic and diastolic blood pressures and lipid profile.

Methods:

Volume of ICH was measured using the ABC/2 method.[15]

Where A = greatest diameter of hemorrhage by CT.

B = diameter 90 degrees to A

C = number of CT slices showing haemorrhage multiplied by slice thickness.

The Computed tomography (CT) machine used in our hospital for this study was Brilliant Model of Phillips 16 slice CT scan with slice thickness of 3mm.

The Glasgow Coma Scale (GCS) was used as a measure of the level of consciousness[16]

The Modified Rankin scale (MRS) was used to assess the functional disability (measure of handicap) particularly in the long term [17].

Barthel's scoring index was used to assess functional status[17].

The statistical tests used in our study were Chi – square test, Z test for proportions, Odd's ratio, Relative risk, Probability value (p)

Statistical significance is indicated by conventional symbols:

$p < 0.05$: Statistically significant

$p < 0.001$: Statistically highly significant

Observation tables

Table 1: ***Comparison of Risk factors in Hemorrhage and Infarct group***

Parameters	Hemorrhage	Infarct	p value
Total cases	75	276	
Age in years (Mean)	58.18 ± 13.45	60.82 ± 12.22	0.10, NS, p>0.05
Sex (M:F)	44 MALE (58.66%) 31 FEMALE(41.33%) χ= 2.47 (NS)	194 MALE (70.28 %) 82 FEMALE (29.71 %) χ = 45.44 **(S)**	0.10, NS, p>0.05
Hypertension	41(54.67 %)	144 (52.17 %)	0.67, NS, p>0.05
Smoking	16 (21.33 %)	72 (26.08 %)	0.40, NS, p>0.05
Alcohol	17 (22.67 %)	63 (22.82 %)	1.00, NS, p>0.05
Diabetes	10 (13.33 %)	23 (8.33 %)	0.62, NS, p>0.05
Previous stroke	07 (9.09 %)	12 (4.34 %)	0.15, NS, p>0.05
W/H ratio (mean)	0.89 ± 0.07	0.91 ± 0.55	0.01, **S**, p<0.05
Systolic BP (mean)	171.89 ±31.08	142.71 ± 19.05	p < 0.0001,**S**
Diastolic BP (mean)	98.74 ±17.00	78.43 ± 8.40	P < 0.0001,**S**

Table 2: co-relation of region of bleed with outcome at 30 days

S.no	Region of brain	No	Deaths	Remained same	Partially improved	Totally improved	Z VALUE
1	Basal ganglia	38	11 (28.94%)	7	16	4	5.52,S
2	Cortex	25	16 (64 %)	4	4	1	11.54,S

S.no	Region of brain	No	Deaths	Remained same	Partially improved	Totally improved	Z VALUE
3	Thalamus	4	-	1	3	-	-
4	Mid-brain	1	1 (100 %)	-	-	-	-
5	Pons	2	-	-	2	-	-
6	Cerebellum	1	-	-	1	-	-
7	Corona radiata and peri-ventricular bleed	1	1 (100 %)	-	-	-	-
8	Primary ventricular bleed	3	2 (66.67 %)	-	-	1	12.54,S
	TOTAL	75	31	12	26	6	

Table 3: Table showing mean values of GCS, MRS, Barthel's score and volume of bleed among patients who died and survived and their significance.

Mean	Deaths (31)	Survivors (44)	Z value	p value
GCS score	6.13 ± 3.00	8 ± 3.19	7.33	0.0001 S
MRS score	4.5 ± 1.02	3.37 ± 1.11	4.56	0.0001 S
Barthel's score	23.38± 19.84	52.60 ± 19.94	6.29	0.0001
Volume of bleed	47.38± 18.65	25.45 ± 25.30	4.19	0.0001

Discussion:

In present study out of total 351 cases of stroke studied over a period of 2 years, 276 (78.63 %) were in cerebral infarct group and 75 (21.37 %) were in intracranial hemorrhage group. This ratio between two groups was 3.68:1. Similarly, in a study conducted by ***Mohr JP et al*** [18], 84 % of patients were in cerebral infarct group and 16 % of patients were in intracranial hemorrhage group. In another study conducted by ***Zia E et al*** [19], 87.44 % were in cerebral infarct group and 12.56 % were in intracranial hemorrhage group.

Risk factors in intracranial hemorrhage and cerebral infarct group

1. Age:

In our study, the peak incidence of both cerebral infarct and intracranial hemorrhage was in the 5th and 6th decade of life with almost half of the cases (53.33 % for intracranial hemorrhage and 59.06 % for cerebral infarct) falling in that group. The mean age for intracranial hemorrhage group was 58.18 ± 13.45 years and for cerebral infarct was 60.82 ± 12.22 years. This difference between two groups was not statistically significant. (p = 0.1053). ***Fogelholm R et al*** [20] in a study of 411 patients reported that the incidence of hemorrhage was higher in older age group with mean age of 64.9 years. Similarly, ***P.Daverat et al*** [21] in a study of 166 patients of intracranial hemorrhage found that 66 % of patients were in 5th and 6th decade of life with mean age of 61 years.

2. Sex:

In our study, the incidence of intracranial hemorrhage was more in males (58.66 %) than females (41.33 %)

but this result was not statistically significant (χ = 2,47). In a study conducted by ***Zia E et al [19]***, a total of 474 cases of intracranial hemorrhage were studied out of which 54 % were males and 46 % were females. Similarly, in a study conducted by ***P.Daverat et al*** [21] in 166 patients of intracranial hemorrhage, 113 (68 %) were males and 53 (32 %) were females, sex ratio being 2:1.

3. Blood pressure:

In our study, history of hypertension was the most important risk factor in both intracranial hemorrhage (54.67 %) and cerebral infarct group (52.17 %), Z value for each being 9.51 and 17.35 respectively which was statistically significant. However the difference beween history of hypertension between the two groups was not statistically significant (p = 0.67). Similar to our findings, in a study conducted by ***Fauziah Jaya et al*** [22] in 1997 – 1998 in Malaysia, hypertension was a risk factor in both cerebral infarct and intracerebral haemorrhage patients at almost the same rate (65.2 and 69.2%, respectively) and the difference between the two groups was not statistically significant. ***Sia et al [23], Anderson CS et al [24]***, ***Thrift AG et al [25], Manno EM et al [26]*** also had similar findings.

4. The mean systolic BP on admission in intracranial hemorrhage group was 171.89 ± 31.08 mm of Hg and in cerebral infarct group was 142.71 ± 19.05 mm of Hg. The mean diastolic BP on admission in intra cranial hemorrhage group was 98.74 ± 17 mm of Hg and in cerebral infarct group was 78.43 ± 8.40 mm of Hg. This difference between mean systolic and diastolic BP between the two groups was highly statistically significant (p <0.0001). Thus in our study high mean systolic and diastolic BP on admission were more strongly correlated with intracranial hemorrhage than in cerebral infarct group. A study conducted by ***Jared D. Sturgeon et al*** [27], concluded that patients with mean systolic BP more than 160 mm of Hg and mean diastolic BP more than 110 mm of Hg had 5.5 times the risk of developing intracranial hemorrhage as compared to cerebral infarct.

5. History of smoking, alcohol consumption, diabetes mellitus and previous stroke:

The other risk factors studied were history of smoking (21.33 % in hemorrhage and 26.08 % in infarct group), history of alcohol consumption (22.67 % in hemorrhage and 22.82 % in infarct group), history of diabetes mellitus (13.33 % in hemorrhage and 8.33 % in infarct group) and history of previous stroke (9.09 % in hemorrhage and 4.34 % in infarct group). All these risk factors individually were significant risk factors in both intracranial hemorrhage and cerebral infarct group. Similarly, in a study conducted by ***Sia et al*** [23] in Malaysia, the common risk factors were smoking (27.2%) and diabetes mellitus (25 %). ***Ariesen MJ et al,*** [3] also concluded that diabetes, smoking and alcohol were significant risk factors for intracranial hemorrhage.

6. Waist to hip ratio:

In our study, the mean waist/hip ratio in intracranial hemorrhage group was 0.89 ± 0.08 while in cerebral infarct group it was 0.92 ± 0.006, this difference between two groups was statistically significant. (p = 0.01) showing that waist/hip ratio is more strongly associated with cerebral infarct group rather than in intracranial hemorrhage group. In a prospective study conducted by ***Xianglan Zhang et al*** [28], in women less than 60 years, it was found that women with WHR > 0.85 had a twofold higher risk of stroke than women with WHR <0.80 and this association was more marked for ischemic than for hemorrhagic stroke. Another similar study conducted by ***Gang Hu et al*** [29], concluded that men with high mean waist/hip ratio (> 0.9) had a higher risk of total stroke and ischaemic stroke rather than intra cerebral hemorrhage.

7. Lipid profile:

In our present study, though the mean total cholesterol values were in the normal range in intracranial hemorrhage (161.01 ± 30.89) and in cerebral infarct group (169.37 ± 26.47), there was a trend towards higher total cholesterol values in the infarct group which was statistically significant (p = 0.020). This suggests that higher total cholesterol values were more closely associated with infarct rather than hemorrhage. The rest of the lipid parameters like triglycerides, LDL, HDL, and VLDL were not statistically different in both the groups. (p = 0.40, 0.54, 0.97, 0.49 respectively). A study conducted by ***Carlos Iribarren et al*** concluded that low serum cholesterol levels (< 178 mg/dl) were associated with a significantly higher risk of intracerebral hemorrhage in men aged 65 years and older [30]. Another study conducted by Suzuki K *et al*

[31], concluded that serum total cholesterol (TC) <160 mg/dl was a risk factor for hemorrhagic stroke, whereas TC >280 mg/dl increased the risk of ischaemic stroke.

Presenting symptoms

In our study the most common presenting symptoms were hemiplegia (66.67 %), loss of consciousness (58.66 %), headache (53.33 %), vertigo (44 %), speech defect (42.67 %), vomiting (38.66 %), seizures (18.67 %) and respiratory difficulty (17.33 %). These were all also individually statistically significant ($p < 0.0001$), Z value for each being 12.25, 10.75, 9.26, 7.68, 7.47, 6.88, 4.15 and 3.97 respectively. Similarly, in a study conducted by ***Sia et al*** [23], common presenting features were: hemiplegia (61.8%), loss of consciousness (58.5%), headache (56.3%) and speech disturbances (45.3). Also ***Hung TP et al*** in Taiwan [32] reported that, the most common presenting symptoms were motor dysfunction (80 %), loss of consciousness (50 %), speech difficulty (31.1 %), vomiting (30.8 %) and headache (27 %).

Co-relation of region of bleed with outcome at 30 days

In our study, the most common region of bleed was Basal Ganglia (50.66 %) followed by cortex (33.33 %), thalamus (5.33 %), brainstem (4 %), primary ventricular bleed (4 %), cerebellum (1.33 %) and corona radiata with periventricular bleed (1.33%). The mortality rate was more in cortical bleed (64 %) than in basal ganglia bleed (28.9%). However since the number of patients in other regions were very few, the mortality rate in these areas could not be compared. Similarly, ***Sia et al*** in Malaysia also found that the commonest site for intracranial hemorrhage was basal ganglia (45.1 %), followed by cortex (32.9 %), followed by brainstem (13.4 %) and cerebellum (8.5 %) [23]. A study conducted by ***Hung TP et al*** in **Taiwan** [32], the most common region of bleed was basal ganglia (41 %), followed by thalamus (23%), putaminothalamus (9.7%), subcortical white mater (9.3%), brainstem (6.5%), and cerebellum (5.9%)

Co-relation of volume of bleed with outcome at 30 days

In present study, there was significant co-relation between volume of bleed and outcome of patients at 30 days. In our study, patients whose volume of bleed was less than 40 ml, the mortality rate was 17.02 %, while patients whose volume of bleed was more than 40 ml, the mortality rate shot up to 82.14 %. This finding was also statistically significant $p = 0.0001$) and proves that more the volume of bleed higher the mortality. Also the Relative Risk (RR) of mortality above 40 ml of bleed was 2.89 times more than that below 40 ml of bleed. The odd's ratio for the same was 13.78 which is also statistically significant.

In a study conducted by ***S Helweg-Larsen et al*** [33], the volume of hematoma was a significant determinant for the immediate prognosis. The crucial limit was 50 ml with a mortality rate of 90 % above and 10 % below. Similarly, ***Broderick JP et al*** [34] also reported that volume of bleed is a powerful predictor of 30 day mortality. Patients with a parenchymal hemorrhage volume of 60 cm3 or more on their initial computed tomogram had a predicted 30 day mortality of 91 % while those with a volume of less than 30 cm3 had a mortality rate of 19 %.

Co-relation of GCS score with outcome at 30 days

GCS score was found to be a strong predictor of 30 day outcome. Subjects with a low GCS score on admission (< 5) had a higher rate of mortality, 94.44 % as compared to those with a higher GCS score on admission (> 10), mortality rate being 11.53 %. This difference was found to be statistically highly significant ($p < 0.0001$). Patients who died (31) had a significantly low mean GCS score on admission (6.13 ± 3.00) as compared to survivors (8 ± 3.19. ***Broderick JP et al*** [34] reported that GCS score at presentation is a powerful predictor of 30 day mortality. Glasgow Coma Scale score of 8 or less had a predicted 30-day mortality of 91% while a GCS score of 9 or more had a predicted 30-day mortality of 19%. A study conducted by ***Sia et al*** [23], concluded that the GCS score on admission was an important predictor of mortality ($p < 0.0001$).

Correlation of mortality with MRS and Barthel's score

In our present study, patients who died (31 patients) had a higher mean MRS score on admission (4.5 ± 1.02) and lower mean Barthel's score on admission (23.38 ± 19.84) which was found to be statistically significant indicating that high MRS score and lower Barthel's scores on admission are good predictors of mortality at 30 days.

Correlation between need for ventilator and mean GCS score

In our study out of total 75 patients of intracranial

hemorrhage, 17 (22.67 %) required ventilatory support and 58 (77.33 %) did not require ventilatory support. Patients who needed ventilatory support also had low mean GCS score (5.64) on admission and higher mortality (82.35 %). This was statistically significant ($p < 0.0001$). Hence low GCS score on admission is a good marker for requirement of ventilatory support and also of subsequent mortality.

Outcome at 30 days

In our study, all 75 patients were followed up at 30 days either at OPD or telephonically. The mortality rate at 30 days was **41. 33 %,** 34.67 % of subjects partially improved & 16 % of subjects remained same while 8 % totally improved.

Conclusions

The ratio of cerebral infarct to intracranial hemorrhage group was found to be 3.68: 1. Intracranial hemorrhage was more common in 5th and 6th decade of life (53.33 %) and was more common in males (58.66%). Hypertension (54.67 %) was the most common risk factor for stroke. High mean systolic and diastolic blood pressures on admission are more strongly correlated with intracranial hemorrhage than cerebral infarct. Mean waist/hip ratio and total cholesterol were more strongly associated with cerebral infarct group than hemorrhage. The most common presentation were hemiplegia (66.67) followed by loss of consciousness (58.66 %), headache (53.33 %) and vertigo (44 %). The most frequent site of bleed was basal ganglia (50.66 %) and cortex (33.33 %). The major predictors of mortality at 30 days were volume of bleed, GCS score, MRS score and Barthel's score on admission. Patients requiring ventilator had a poorer outcome. The overall mortality rate in our study was 41.33 % at 30 days.

Limitations:

The limitation of our study was that since the number of cases were very few in regions other than basal ganglia, the mortality rates in these areas could not be compared. Hence it is recommended that similar studies should be conducted over longer periods of time and with larger number of cases so that this limitation can be overcome.

References:

1. *Gebel JM, Broderick JP. Intracerebral hemorrhage. Neurol Clin 2000;18:419-38.*
2. *Broderick J, Connolly S, Feldmann E, Hanley D, Kase C, Krieger D, Mayberg M, Morgenstern L, Ogilvy CS, Vespa P, Zuccarello M. Guidelines for the management of spontaneous intracerebral hemorrhage in adults: 2007 update: a guideline from the American Heart Association/American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Outcomes in Research Interdisciplinary Working group. Stroke 2007;38:2001-23.*
3. *Ariesen MJ, Claus SP, Rinkel GJ, Algra A. Risk factors for intracerebral hemorrhage in the general population: a systematic review. Stroke 2003;34:2060-5.*
4. *Flaherty ML, Woo D, Haverbusch M, Sekar P, Khoury J, Sauerbeck L, Moomaw CJ, Schneider A, Kissela B, Kleindorfer D, Broderick JP. Racial variations in location and risk of intracerebral hemorrhage. Stroke 2005;36:934-7.*
5. *Mayer SA, Rincon F. Treatment of intracerebral haemorrhage. Lancet Neurol 2005;4:662-72.*
6. *Hart RG, Tonarelli SB, Pearce LA. Avoiding central nervous system bleeding during antithrombotic therapy: recent data and ideas. Stroke 2005;36:1588-93.*
7. *Thrift AG, McNeil JJ, Forbes A, Donnan GA. Three important subgroups of hypertensive persons at greater risk of intracerebral hemorrhage. Melbourne Risk factor Study group. Hypertension 1998;31:1223-9.*
8. *Qureshi AI, Tuhrim S, Broderick JP, Batjer HH, Hondo H, Hanley DF. Spontaneous intracerebral hemorrhage. N Engl J Med 2001;344:1450-60.*
9. *Skidmore CT, Andrefsky J. Spontaneous intracerebral hemorrhage: epidemiology, pathophysiology, and medical management. Neurosurg Clin N Am 2002;13:281-8.*
10. *Arakawa S, Saku Y, Ibayashi S, Nagao T, Fujishima M. Blood pressure control and recurrence of hypertensive brain hemorrhage. Stroke 1998;29:1806-9.*
11. *Fang MC, Go AS, Chang Y, Hylek EM, Henault LE, Jensvold NG, Singer DE. Death and disability from warfarin-associated intracranial and extracranial*

hemorrhages. Am J Med 2007;120:700-5.

12. *Rosand J, Eckman MH, Knudsen KA, Singer DE, Greenberg SM. The effect of warfarin and intensity of anticoagulation on outcome of intracerebral hemorrhage. Arch Intern Med 2004;164:880-4.*
13. *Saloheimo P, Juvela S, Hillbom M. Use of aspirin, epistaxis, and untreated hypertension as risk factors for primary intracerebral hemorrhage in middle-aged and elderly people. Stroke 2001;32:399-404.*
14. *Thrift AG, Donnan GA, McNeil JJ. Heavy drinking, but not moderate or intermediate drinking, increases the risk of intracerebral hemorrhage. Epidemiology 1999;10:307-12.*
15. *Rashmi U. Kothari; Thomas Brott; Joseph P. Broderick; William G. Barsan. The ABCsof measuring intracerebral hemorrhage volumes Stroke 1996;27:1304 - 130.*
16. *John P. Kress, Jesse B.Hall, Glasgow coma scale, Principles of critical care medicine Harrison's textbook of internal medicine chapter 261 page 1674.*
17. *Geert Sulter, MD; Christel Steen, MS; Jacques De Keyser, MD, PhD; Use of Barthel Index And Modified Ranking Scale in Acute Stroke Trials; Stroke 1999;30:1538 - 1541.*
18. *Mohr JP, Caplan LR, Melski JW, Goldstein RJ, Duncan GW, Kistler JP, Pessin MS, Bleich HL; The Harvard Cooperative Stroke Registry: a prospective registry. Neurology. 1978;28(8):754.*
19. *Zia E, Hedblad B, Pessah-Rasmussen H, Berglund G, Janzon L, Engström G; Blood pressure in relation to the incidence of cerebral infarction and intracerebral hemorrhage; Stroke. 2007;38(10):2681.*
20. *Fogelholm R, Murros K, Rissanen A, Avikainen S. Long term survival after primary intracerebral haemorrhage: a retrospective population based study. J Neurol Neurosurg Psychiatry 2005;76:1534-8.*
21. *P Daverat, JP Castel, JF Dartigues and JM Orgogozo, Death and functional outcome after spontaneous intracerebral hemorrhage, Stroke1991;22;1-6.*
22. *Fauziah Jaya, M. Nyunt Win, Mohd Riduan Abdullah, Mohamed Rusli Abdullahb, Jafri Malin Abdullahc; Stroke Patterns in Northeast Malaysia: A Hospital-Based Prospective Study; Neuroepidemiology 2002;21:28-35.*
23. *Sia SF, Tan KS, Waran V. Primary intracerebral haemorrhage in Malaysia:in-hospital mortality and outcome in patients from a hospital based registry. Med J Malaysia. 2007 Oct;62(4):308-12.*
24. *Anderson CS, Chakera TM, Stewart-Wynne EG, Jamrozik KD; Spectrum of primary intracerebral haemorrhage in Perth, Western Australia, 1989-90: incidence and outcome; J Neurol Neurosurg Psychiatry. 1994;57(8):936.*
25. *Thrift AG, McNeil JJ, Forbes A, Donnan GA; Risk factors for cerebral hemorrhage in the era of well-controlled hypertension. Melbourne Risk Factor Study (MERFS) Group; Stroke. 1996;27(11):2020.*
26. *Manno EM, Atkinson JL, Fulgham JR, Wijdicks EF. Emerging medical and surgical management strategies in the evaluation and treatment of intracerebral hemorrhage. Mayo Clin Proc. 2005;80:420-433.*
27. *Jared D. Sturgeon, Aaron R. Folsom, W.T. Longstreth, Jr, Eyal Shahar, Wayne D. Rosamond and Mary Cushman; Risk Factors for Intracerebral Hemorrhage in a Pooled Prospective Study; Stroke 2007, 38:2718-2725.*
28. *M.L U, H.O.Adami & E.Weiderpass; Prospective study of body size and risk for stroke amongst women below age 60; Journal of Internal Medicine 2006; 260: 442–450*
29. *Gang Hu, Jaakko Tuomilehto, Karri Silventoinen, Cinzia Sarti; Satu Ma¨nnisto¨, ; Pekka Jousilahti; Body Mass Index, Waist Circumference,and Waist-Hip Ratio on the Risk of Total and Type-Specific Stroke; Arch Intern Med. 2007;167(13):1420-1427.*
30. *Carlos Iribarren, MD, MPH, PhD; David R. Jacobs, Jr, PhD; Marianne Sadler, MPH; Ami J. Claxton, MS; Stephen Sidney, MD; Low Total Serum Cholesterol and Intracerebral Hemorrhagic Stroke: Is the Association Confined to Elderly Men? Stroke. 1996;27:1993-1998.*
31. *Suzuki K, Izumi M, Sakamoto T, Hayashi M; Blood*

pressure and total cholesterol level are critical risks especially for hemorrhagic stroke in Akita, Japan; Cerebrovascular Dis. 2011;31(1):100-106.

32. *Hung TP, Chen ST; Cerebral hemorrhage in Taiwan; J Formos Med Assoc. 1993 Dec;92 Suppl 4:S161-8.*
33. *S Helweg-Larsen, W Sommer, P Strange, J Lester and G Boyse; Prognosis for patients treated conservatively for spontaneous intracerebral hematomas, Stroke 1984;15;1045-1048*
34. *Broderick JP, Brott TG, Duldner JE, Tomsick T, Huster G. Volume of intracerebral hemorrhage. A powerful and easy-touse predictor of 30-day mortality. Stroke 1993;24:987-93.*