IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 3 Ver.16 March. (2018), PP 60-67
www.iosrjournals.org

Study on Clinical Outcome in Cases of Hypertensive Hemorrhagic Stroke In Relation To Size and Site of The Hemorrhage.

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Abstract: *The term stroke is applied to a sudden focal neurologic syndrome, specifically the type caused by cerebrovascular disease. The term cerebrovascular disease designates any abnormality of the brain resulting from a pathologic process of the blood vessels, including occlusion of the lumen by embolus or thrombus, rupture of a vessel, an altered permeability of the vessel wall, or increased viscosity or other change in the quality of the blood flowing through the cerebral vessel.[1] The intracerebral hemorrhage remains an area where different confluenting views on CT scan findings of hematoma and its effects are prevalent. Public awareness regarding various risk factors is still quite poor in our society. Many times it becomes an important task for the physician to predict the functional outcome from a single CT scan of the brain done at the time of the hospital admission. The present study was conducted out in the patients admitted in the Department of Medicine of Rajendra Institute of Medical Sciences, Ranchi with intraparenchymal brain hemorrhage proven by CT scan of brain from November 2016 to October 2017. The present study was an observational study in which a total of 110 patients were followed from the time of admission till 30th day. Out of various parameters studied age, hypertension, smoking & prior CVA history as risk factors; hemorrhagic volume; blood pressure at the time of admission; intraventricular extension of blood; midline shift; GCS and ICH score at the time of admission were the parameters which were strongly related to poor outcome in the patients of intracerebral hemorrhagic stroke.*

Keywords*: hemorrhagic stroke, site and size, prognostic significance, jharkhand.*

Date of Submission: 16-03-2018 Date of acceptance: 30-03-2018

I. Introduction

Stroke is the second leading cause of death worldwide, and one of the leading causes of disability[2]. With increasing life expectancy the burden of stroke is likely to increase worldwide with middle and low income countries particularly affected. The Global Burden of Disease 2010 Study[3] showed a 47% increase in the absolute number of hemorrhagic stroke (including ICH and subarachnoid hemorrhage) worldwide between 1990 and 2010. Intracerebral hemorrhage occurs when a blood vessel within the brain parenchyma ruptures. Hypertension or any other cause which weakens the endothelial lining of the vessel leads to the rupture of the blood vessel of a focal region of brain and collection of blood in brain parenchyma leading to acute hemorrhagic stroke. In hemorrhagic stroke, the injury of neuronal tissue is caused by the compression of the tissue from expanding hematomas. In addition, pressure may lead to loss of blood supply causing infarction.

In contrast to industrialized western countries where there has been a steady decline in stroke over the past 30 years, India is currently facing the challenge of a high stroke incidence. The major reason is that the common risk factors of stroke, namely, hypertension, diabetes, smoking, and dyslipidemia are not being adequately controlled. Public awareness in this regard is still quite poor in our society. Cardiovascular disease including stroke, which comprised 19% of death in India in 2001-2003, is estimated to rise to 36% by 2030.

Intracerebral hemorrhage is the second most common subtype of stroke after ischemic stroke and accounts for approximately 20 % of all strokes. Multivariate analysis using the technique logistic regression identified three variables, the Glasgow coma scale score, hemorrhage size and intraventricular extension of blood to be most predictive of prognosis[2]. The intracerebral hemorrhage remains an area where different confluenting views on CT scan findings of hematoma and its effects are prevalent. Public awareness regarding various risk factors is still quite poor in our society. Also in rural area where resources are limited, CT scan cannot be done repeatedly. Therefore, many times it becomes an important task for the physician to predict the functional outcome from a single CT scan of the brain done at the time of the hospital admission. This study was undertaken to resolve some of the confusions and try to reach a better insight into the complex problem.

II. Material And Method

The present study was conducted out in the patients admitted in the Department of Medicine of Rajendra Institute of Medical Sciences, Ranchi with intraparenchymal brain hemorrhage proven by CT scan of brain from November 2016 to October 2017. The present study was an observational study in which a total of 110 patients were followed from the time of admission till 30th day.

Study Design: Prospective observational study

Study Location: This was a tertiary care teaching hospital based study done in Department of General Medicine, at Rajendra Institute of Medical Sciences, Ranchi

Study Duration: November 2016 to October 2017.

Sample size: 110 patients.

Inclusion criteria:

In the present study those patients who presented to the hospital with sign and symptoms of stroke like sudden onset headache, loss of consciousness, aphasia, slurring of speech, weakness (hemiplegia/hemiparesis), ataxia etc. within 24 hours of onset were immediately and thoroughly examined in the emergency room and then CT scan of brain was performed on the same day. Those patients who had intraparenchymal hemorrhage proved by CT scan of brain within 24 hours of onset of their illness were included in the study. Consent from each patient or his/her companion was taken for including patient in the study and the study was approved by ethical committee.

Exclusion criteria:

Present study did not take into account those cases of hemorrhagic stroke which were due to:-

- Trauma
- Aneurysm
- Coagulopathy
- Brain CT scanning suggestive of other diagnosis like brain tumor or ischemic infarction.
- Age <40 years
- Patients presenting in hospital after 24 hours of onset of their illness.
- Patients who did not show up after 30 days for follow-up

Various parameters for observation-

- Age
- Sex
- Hemorrhagic location
- Hemorrhagic volume[14]
- Blood pressure at the time of admission
- Midline shift in CT scan
- Presence of intraventricular extension
- Glasgow coma scale
- ICH score at the time of admission

Method of calculating volume of blood of the CT scan

The hematoma volume of a spontaneous ICH, using patient in the acute phase, can be measured by two different methods (ABC/2 and the planimetric method) of computed tomography (CT) scans. Both methods are widely accepted and commonly used. Both methods are fairly accurate and there is no significant difference of results in these two methods. In the present study, ABC/2 method was used.

The ABC/2 volume estimation is based on a simplification of the ellipsoid volume equation as described by Kothari et al[14], 2007 to estimate ICH volume. A simple method of measuring the volume of hematoma (in cc) on the CT scan is by using the formula: - **A*B*C/2** where A= maximum length of the bleed in cm along the falx, B= maximum width of the bleed (not necessarily measured on the same head CT slice as A) andC=the number of slices multiplied by the slice thickness.

Statistical analysis

Pair wise comparison between various variable was done for different parameters. The Range, Mean value, Standard Deviation (S.D.), Standard error of Mean, 't' value and 'p' values were calculated as per the applicability by using appropriate formulas. Statistical Package of Social Sciences (SPSS) v. 22 was used for the purpose of data entry and data analysis. Data are summarized as appropriate tables and charts showing different variables are demonstrated. Chi-square test was used to find out associations (relations) between 2 categorical variables, ANOVA test was used to find out associations between multiple categorical variables. Pearson's correlation coefficient was used for numerical variables. P-value less than 0.05 was regarded as statistically significant.

III. Result

Following are the observations in this study involving 110 cases of hemorrhagic stroke after 30-day follow-up.

Observation 1- Age distribution of cases

Age	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
<60 yrs	12	25.5	21	33.3	12.343	0.0020
60-70 yrs	20	42.5	38	60.3		
>70 years	15	31.0	4	6.4		

Observation 2- Sex distribution of cases

Sex	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
Male	28	59.6	40	63.5	0.175	0.6756
Female	19	40.4	23	36.5		

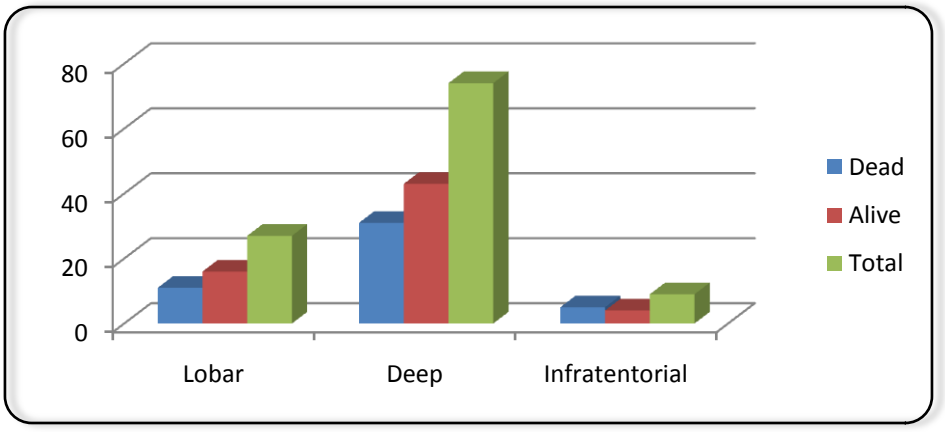
Observation 3- Categorization of cases in tribal and non-tribal groups with mortality

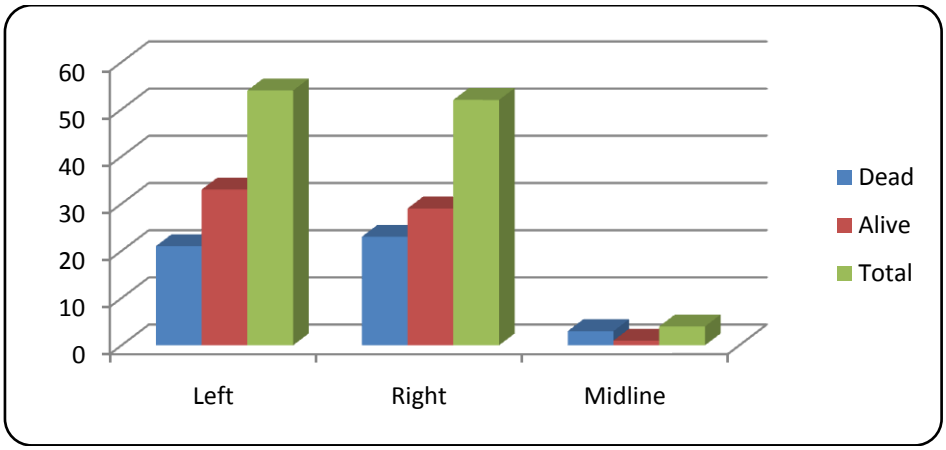
Tribal and Non-tribal	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
Tribal	19	40.4	25	39.7	0.006	0.9372
Non-tribal	28	59.6	38	60.3		

Observation 4- Categorization of cases on the basis of site of hemorrhage

Site (side)	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
Left	21	44.7	33	52.4	2.076	0.3542
Right	23	48.9	29	46.0		
Midline	3	6.4	1	1.6		

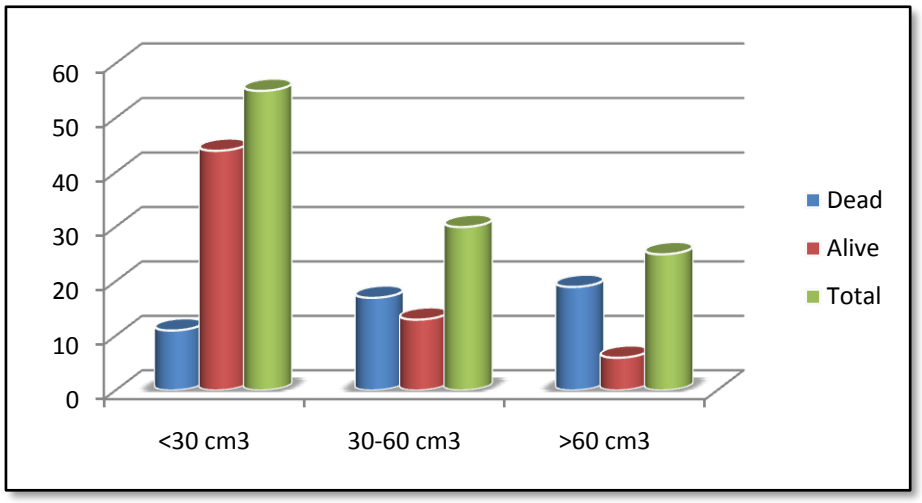
Site (location)	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
Lobar	11	23.4	16	25.4	0.715	0.6699
Deep	31	65.9	43	68.3		
Infratentorial	5	10.7	4	6.3		





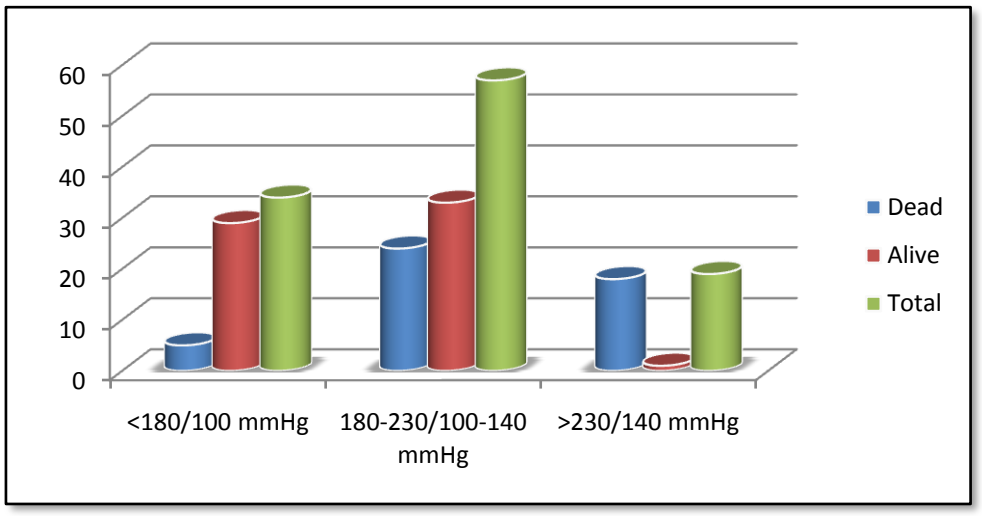
Observation 5- Categorization of cases on the basis of volume of hemorrhage with mortality

Volume	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
<30 cc	11	23.4	44	69.8	25.301	<0.0001
30-60 cc	17	36.2	13	20.6		
>60 cc	19	40.4	6	9.6		



Observation 6- Categorization of cases on the basis of blood pressure at time of admission with mortality

BP (mmHg)	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
<180/100	5	10.6	29	46.0	31.921	<0.0001
180-230/100-140	24	51.0	33	52.4		
>230/140	18	38.4	1	1.6		

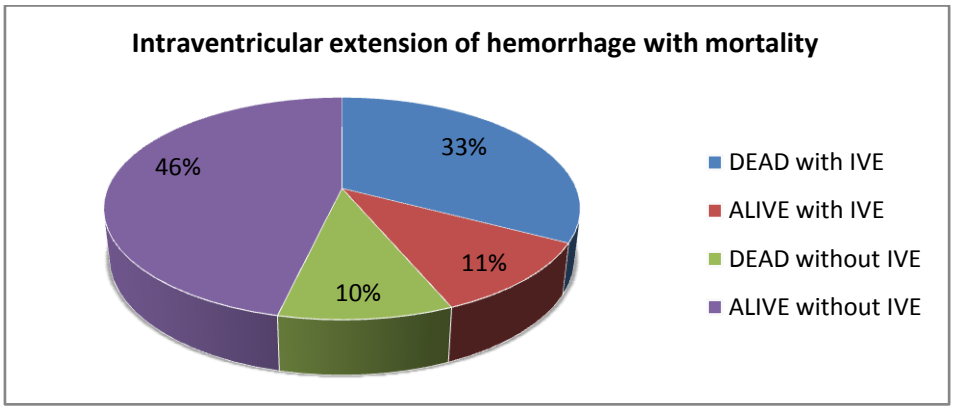


Observation 7- Categorization of cases on the basis of midline shift with mortality

Midline shift	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
<3 mm	3	6.4	43	68.3	56.209	<0.0001
3-5 mm	10	21.3	15	23.8		
>5 mm	34	72.3	5	7.9		

Observation 8- Categorization of cases on the basis of intraventricular extension of hemorrhage with mortality

IVE	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
Present	36	76.6	12	19.0	36.246	<0.0001
Absent	11	23.4	51	81.0		

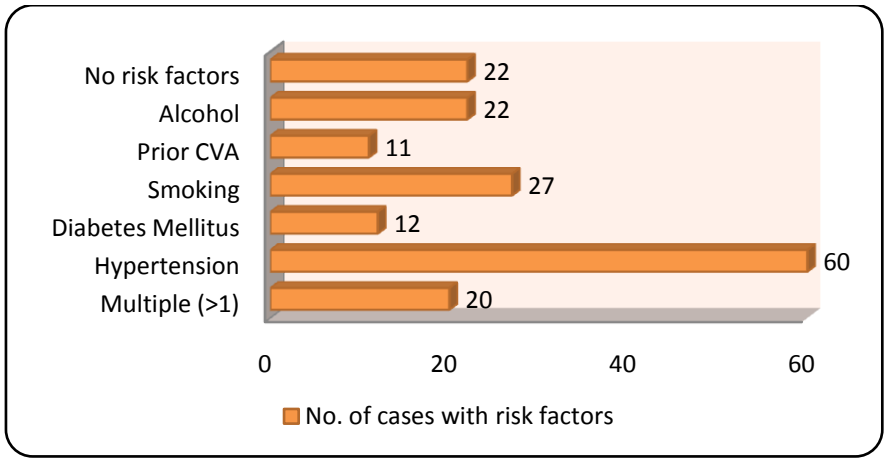


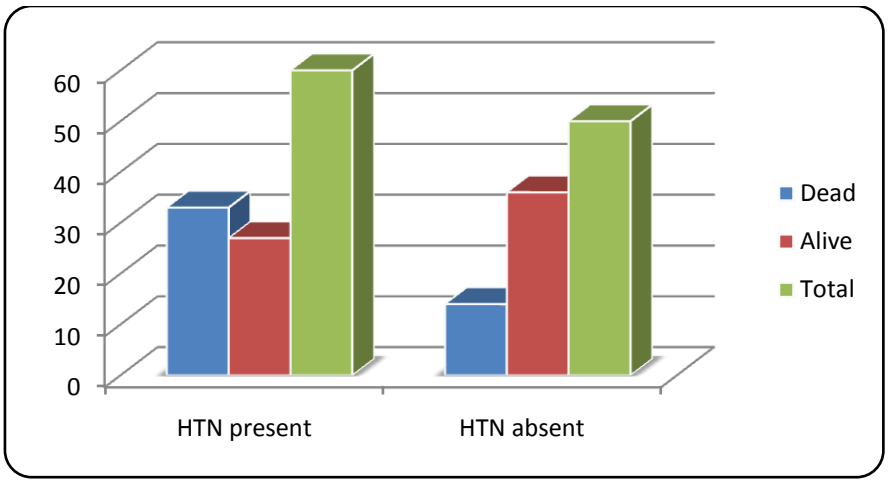
Observation 9- Categorization of cases on the basis of GCS score at the time of admission with mortality

GCS	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
<8	39	83.0	13	20.6	41.975	<0.0001
≥8	8	17.0	50	79.4		

Observation 10- Mortality in the patients with hypertension as a risk factor

HTN	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
Present	33	70.2	27	42.9	8.124	0.0339
Absent	14	29.8	36	57.1		





Observation 11- Categorization of cases on the basis of ICH score at the time of admission with mortality

ICH score	Dead (n=47) 42.7%	%	Alive (n=63) 52.3%	%	X^2	P
1-2	3	6.4	36	57.1	54.348	<0.0001
3-4	14	29.8	25	39.7		
5-6	30	63.8	2	3.2		

IV. Discussion

Mortality- Among the 110 patients studied 47 patients died in 30-day follow-up. Mortality in this study was 42.7%. Recent reports of 3 large prospective studies from India have suggested a higher proportion of mortality attributable to ICH (30%–42%) in comparison with the Global Burden of Disease study, 2010.

Age and sex- Mean age in this study was 63 years with minimum age of 40 years and maximum age of 85 years. Age in this study was divided into three groups: <60 years, 60-70 years and >70 years. Majority of the patients were of age between 60 and 70 (52.7%). There was a strong correlation between age and mortality ($p<0.05$). So, higher the age, poorer was the outcome. In this study, male were 68 (61.82%) in total out of which 28 (41.2%) died and female were 42 (38.18%) in total out of which 19 (45.2%) died after 30 days follow-up. In most of the Indian studies, males were in larger number than females. This is probably due to the fact that males are keener towards seeking medical attention than females especially in low socio-economic classes due to social & cultural beliefs. There was no statistical difference in mortality between males and females ($p>0.05$).

Clinical presentation- The most common clinical presentation of patients with ICH was weakness of limbs or focal neurological deficit which was seen in 77.2% cases. Other clinical presentations in decreasing order of frequencies were- loss of consciousness (72.7%), aphasia (36.4%), headache (33.0%), vomiting (31.8%), seizure (11.8%) and ataxia (1.8%). There was a considerable overlap of clinical features. A headache was more commonly seen with lobar hemorrhage. There was no strong association between clinical symptoms and hematoma size or mortality outcome.

Risk factors- The major risk factors identified in a recent North Indian study were hypertension (a diastolic blood pressure >95 mmHg), hyperglycemia, tobacco use, and low hemoglobin levels <10 gm% (Srinivasrao Bandaru VC, Kaul S et al, 2009).[4] Hypertension was the most common risk factor present in 54.5%

of the cases. Mortality in the patients with hypertension as a risk factor was 55.0% and on comparison, it was statistically significant ($p<0.05$). Diabetes was present in 10.9% of the patients with mortality of 50.0%. But in chi-square test it was not significant ($P>0.05$). The non-relation of diabetes with mortality in present study was perhaps due to smaller number of patients with history of diabetes present in this study. Similarly mortality in patients with alcohol intake was 45.5% and it was also statistically insignificant ($P>0.05$). In Jharkhand most of the people consume alcohol on regular basis and various local forms of drinks are very common. So, collecting accurate data were difficult in the current situation which might have affected the results regarding alcohol intake and ICH. Mortality of patients with history of prior CVA, chronic smoking and with more than one risk factor were 72.7%, 59.3% and 75.0% respectively. All had strong correlation with outcome ($P<0.05$).

Volume of hemorrhage- In the present study, hemorrhage size ranged from 10 cm^3 to 90 cm^3. The mean volume of hemorrhage was 37.5 cm^3. 55 (50.0%) patients in this study were having bleed volume less than 30 cm^3 out of which 11 (20.0%) died. 30 (27.3%) patients had bleed volume between 30 to 60 cm^3 out of which 17 (56.7%) died. There were 25 (22.7%) patients with bleed volume more than 60 cm^3 out of which 19 (76.0%) died after 30 days. Statistical analysis performed to correlate the patient's outcome with volume of ICH using chi-square test showed significant correlation ($P<0.05$) in this study. Many different studies have also found similar results. Zaki Noah Hasan, Kareem M. Al Tameemi et al[5] (2012) performed study which showed highly statistical association of hematoma size and mortality. Flemming et al[6] identified 40 ml as a critical volume predicting a poor outcome in his study with a population of patients with lobar hemorrhage who were primarily medically treated.

Midline shift and intraventricular extension- IVH is an independent risk factor for mortality rather merely a proxy for large hemorrhage size. (Tuhrim et al, 2010). In the present study, intraventricular extension of the hemorrhage was seen in 48 (43.6%) patients out of which 36 (75.0%) died. There were 62 (56.4%) patients without intraventricular extension of hemorrhage out of which only 11 (17.07%) died after 30-day follow-up. Chi square test for correlation showed significant relationship between mortality and IVE of the bleed ($P<0.05$). Similarly midline shift on the initial CT scan has been consistently shown to predict high mortality rate. Midline shift was found to be statistically significant in mortality of ICH patients ($P<0.05$).

Site of the hemorrhage- A total of 54 (49.1%) patients in this study were having bleed in left side. 52 (47.3%) patients had bleed towards the right side and 4 (3.6%) patients had midline bleed. On applying chi-square test, there was no statistically significant correlation between the side of bleed with mortality ($p>0.05$). But maximum mortality was seen with patients of midline bleed, which were actually bleeds in midbrain and pons. Sites of bleed in this study were also categorized as deep, lobar and infratentorial bleeds which included midbrain, pons and cerebellar bleeds. A total of 27 (24.55%) patients in this study were having lobar bleed out of which 11 (40.7%) died. 74 (67.27%) patients had deep bleed out of which 31 (41.9%) patients died. There were 9 (8.2%) patients with infratentorial bleed out of which 5 (55.5%) died after 30-day follow-up. Hence majority of the patients in this study had deep hemorrhage. But there was no statistically significant difference in mortality based upon the site of bleed ($p>0.05$). Bhatia R, Singh H et al[7], 2013, found poor correlation of mortality with site of ICH. Majority of the patients with history of hypertension in this study had deep bleed (53.4%). Hence from this study, site of bleed was not an important factor in outcome of ICH, but it does help in determining the risk factors.

Blood pressure- Blood pressure of the patients at the time of admission was recorded in 3 categories: (1) <180/100 mmHg, (2) 180-230/100-140 mmHg, (3) >230/140 mmHg. Whenever systolic or diastolic BP was falling in two different categories, higher category was chosen. More than half of the patients were in second category of blood pressure but maximum mortality was seen with third category having very high blood pressure. On applying chi-square test, relation of blood pressure with mortality was statistically significant ($P<0.05$). Similar reports were found by AR Massero et al, 2007. Terayama et al[8] and Fogelholm et al[9] in their studies claimed that high MAP at the time of hospital admission (>140 mmHg) is an independent risk factor of mortality in ICH patients.

GCS at the time of admission- Level of consciousness is an important determinant of outcome in patients with ICH (Tuhrim S, Dambrosia et al, 1998, Huang et al, 2007). In the present study, patients were categorized in two categories based upon GCS at the time of admission: (1) GCS<8, (2) GCS ≥8. Lowest GCS score was 3 and highest GCS score was 14 with mean value 7.62. The statistical analysis performed to correlate the patient outcome with GCS at the time of admission using chi-square test showed a significant correlation ($P<0.05$).

Tribal and Non-tribal patients- In this study a total of 44 (40.0%) tribal patients were present out of which 19 (43.2%) patients died. Remaining 66 (60.0%) patients were non-tribal out of which 28 (42.4%) died at the end of 30-day follow-up. There was no statistically significant difference of mortality between tribal and non-tribal patients ($P>0.05$). In a previous study done in RIMS[12], hypertension and alcohol abuse was found to be associated with intracerebral hemorrhage in tribal subjects. In present study, hypertension was statistically significant as a risk factor in tribal as well as in non-tribal. However, more than half (54.4%) of the tribal

patients did not have history of hypertension, diabetes and other risk factors. This was perhaps due to lack of awareness and medical facilities in tribal areas.

ICH score and outcome- ICH score calculated at the time of admission was predictor of poor outcome ($p<0.05$). 30 (93.8%) out of 32 patients with ICH score more than 4 died within 30 days of follow-up. Basu AK et al[10] found the same statistical significance of ICS score in his study. In this study modified Rankin Scale[15] was used to see the outcome of hemorrhagic stroke after one month. A total of 63 patients were alive at the end of 30-day follow-up while 47 patients died. 33 (52.4%) of the alive patients were having mild to moderate disability (mRS<4). Those patients were moderately disabled, needed someone's help to carry out their daily activities but were able to walk without assistance. 30 (47.6%) of the alive patients were having severe disability (mRS ≥4). Such patients were unable to walk and were unable to do their own body needs without assistance. On statistical analysis volume of blood or size of hemorrhage had significant relationship with functional outcome in patients of hemorrhagic stroke. Similar conclusion was seen in the study of Kamel H, Navi BB et al[11]

V. Conclusion

Cerebrovascular disease is very serious disorder, mainly of middle and old ages and is one of the leading causes of mortality in India and world. India is currently facing the challenge of a high stroke incidence. The major reason is that the common risk factors of stroke, namely, hypertension, diabetes, smoking, and dyslipidemia are not being adequately controlled. Out of various parameters studied age, hypertension, smoking & prior CVA history as risk factors; hemorrhagic volume; blood pressure at the time of admission; intraventricular extension of blood; midline shift; GCS and ICH score at the time of admission are the parameters which are strongly related to poor outcome in the cases of intracerebral hemorrhagic stroke in this study.

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