

**EVALUATE THE CLINICAL PRESENTATIONS WITH S CALCIUM AS A
BIOCHEMICAL PARAMETER IN PATIENTS ADMITTED WITH INTRACEREBRAL
HAEMORRHAGE IN TERTIARY HOSPITALS IN BANGLADESH****Dr. Rajesh Saha^{1*}, Dr. Mohiuddin Ahmmed², Dr. Shekh Md. Abul Fazal³ and Dr. Rahat Amin Chowdhury⁴**¹Assistant Professor, Department of Neurology, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh.²Assistant Professor, Department of Neurology, Dhaka Medical College, Dhaka, Bangladesh.³Assistant Professor, Department of Neurology, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh.⁴Associate Professor, Department of Neurology, Sylhet Women's Medical College, Dhaka, Bangladesh.***Corresponding Author: Dr. Rajesh Saha**

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ABSTRACT

Background: In Bangladesh stroke has been ranked as the third leading cause of death after coronary heart disease and infectious diseases. The World Health Organization (WHO) ranks mortality due to stroke in Bangladesh as number 84 in the world. Spontaneous intracerebral haemorrhage (ICH) accounts for approximately 15% of all strokes and is a leading cause of disability, with a one-month mortality rate of 40%. Whereas factors predicting short-term mortality are well known, data regarding long-term outcome are scarce and imprecise. Aim of this study is to evaluate the clinical presentations with S calcium as A biochemical parameter in patients admitted with intracerebral haemorrhage in tertiary hospitals in Bangladesh. **Methods:** This study was a hospital based observational study and conducted at the Department of Neurology, Neurosurgery and Medicine in Dhaka Medical College Hospital. People who were suffering from intracerebral haemorrhage and were admitted in the department of Neurology, Neurosurgery and Medicine were approached for inclusion in the study according to inclusion and exclusion criteria. Ethical issues were ensured properly. After written informed consent history and physical examination were done. Diagnosis was confirmed by researcher with the aid of CT scan. Total 365 consecutive samples were collected and incompleteness of data was considered exclusion of the study. Following radiological confirmation blood were drawn to measure serum calcium level with maintaining all aseptic precautions. For analysis patients' corrected serum calcium level were divided into three tertiles: T1 = <2.20 mmol/l, T2 = 2.20 to 2.40 mmol/l and T3 = >2.40 mmol/l. The principal investigator interviewed each patient individually and in case of unconscious patient; history was collected from attendant of the patient. All these were registered, documented and analyzed in the statistical program Statistical Package for Social Science (SPSS) version 20.0. **Results:** Out of a total of 365 patients, Mean age of the population was 58.43(±12.33)SD (range 32-75) years and frequent age group was 61-70 (n=145, 39.7%) years. 58% (n=210) were male and 42% (n=155) were female. Univariate analysis comparing the highest and lowest tertiles indicated that an elevated calcium level was associated with 5.1- and 3.1-fold increases in the odds for day 14- and 30-days excellent outcome, respectively. After adjustment for age, sex, and other potential risk factors, patients in the highest quartile still had significantly increased odds of day 14- and 30-day excellent outcome; the corresponding odds ratios (ORs) were 4.6 (95% confidence interval [CI], (2.41 – 8.93) and 3.31 (95% CI, 1.88 – 5.83). **Conclusion:** In conclusion we can say that Intracerebral Hemorrhage Patients also revealed positive association of outcome with serum calcium level and negative correlation with phosphate level.

KEYWORDS: Serum calcium, Spontaneous intracerebral haemorrhage, ischaemic stroke.**INTRODUCTION**

According to an estimates of world health organization (WHO) suggests majority of deaths (86%) related to stroke worldwide occurred in developing countries and South Asia is thought to be the highest contributor, probably accounting for more than 40% of global stroke deaths.^[1,2] In this region, stroke mortality rates might be as high as those for coronary artery disease, and both

stroke and coronary heart disease occur about 10 years earlier, on average, than in the rest of the world.^[3] Estimates of the prevalence of stroke in India and Pakistan range from 44 to 843 and 250 per 100,000 population respectively.^[2] Whereas limited data are available in relation to stroke prevalence in Bangladesh: one study reported an overall prevalence of 3 per 1,000 population, rising as high as 10 per 1,000 in people over

70 years of age. The lack of authentic incidence and prevalence data from Pakistan, Bangladesh is a major limitation, and a pressing need exists for population-based studies.^[1]

Intracerebral hemorrhage occurs when a blood vessel within the brain parenchyma ruptures as a complication of a pre-existing lesion (vascular malformation or tumor) or in the absence of a single clear underlying lesion (Ikram, M.A., Wieberdink, R.G. & Koudstaal, P.J., 2012).^[4] It is the second most common subtype of stroke after ischemic stroke and accounts for approximately 10 % to 20 % of all strokes.^[1] Different meta-analysis suggest almost double incidence of ICH in Asian populations than others (i.e. Black, Indian, Hispanic, Maori, White. In south east Asia ICH percentage are ranged from 19–46% and it is hypothesized due to high prevalence and poor control of Hypertension. Moreover, prevalence of ICH is especially high in younger patients (15–45 years of age) with stroke (32–43%) and the pattern has similarity in this country (31–33 in according to hospital based study).^[2]

Hospital admissions for intracerebral hemorrhage have increased by 18% in the past 10 years, probably because of increase in the number of elderly people, many of whom lack adequate blood-pressure control, and the increasing use of anticoagulants, thrombolytics, and antiplatelet agents. Thus it becomes one of the major causes of mortality and morbidity in worldwide. Not only loss of lives but also imposing an enormous economic burden on individuals and society overall.^[6]

METHODOLOGY

| | |
|--------------------|---------------------------------------------------------------------------------------------|
| Type of study | It was an observational study |
| Place of study | Department of Neurology, Neurosurgery and Medicine, Dhaka Medical College Hospital. |
| Study period | This study was conducted for a period of 2 years started from July 2015 to June 2017 |
| Study population | Patients suffering from non-traumatic intracerebral hemorrhage. |
| Sample Size | Total 365 patient were included in the study. |
| Sampling technique | Non-probability purposive consecutive sampling method was used to select sample population. |

Selection criteria

Inclusion criteria

- Age ≥ 18 years
- All cases and both sexes of acute intracerebral hemorrhage confirmed by CT scan of head
- Patient who willing to give informed written consent
- Patient who are willing to give blood sample for serum calcium estimation

Exclusion criteria

- Secondary cause acute intracerebral hemorrhage
- Diagnosed case of hypercalcemia due to any cause
- Multi-organ failure at the time of diagnosis

Data collection technique

All of the study population were counseled regarding the study aim, objectives, and usefulness of the study. Written informed consent were collected from each

Despite aggressive and newer management strategies, the prognosis of Spontaneous intracerebral hemorrhage (ICH) remains very poor: case-fatality at 1 month is over 37-52 % and this proportion has not changed over the past 20 years.^[6] At the same time, of those who survive only a small proportion reaches independent life after 1 year, with estimates varying between 12% and 39%. These numbers show that intracerebral hemorrhage is not only a very lethal disease, but that remaining survivors pose a significant burden on health care resources.^[4] Several studies were conducted to find out the risk factors and the predictors of short term and long-term survival of ICH patients. Among them two important predictor were identified and they are baseline hematoma volume and hematoma expansion. It has been suggested that a lower serum calcium level is associated with higher hematoma volume in patients with ICH, as well as hemorrhagic transformation after intravenous thrombolysis for acute ischemic stroke.

OBJECTIVES

General Objective

- 1) To assess the clinical presentations with S calcium as a biochemical parameter in patients admitted with intracerebral haemorrhage in tertiary hospitals in Bangladesh.

Specific Objective

- 1) To observe the corrected calcium level on admission
- 2) To find out the short time outcome of the patients according to modified rankin scale (MRS)

patient and interview was taken by the researcher himself with a semi-structured questionnaire. Patient with intracerebral haemorrhage following admission in the department of Neurology, Neurosurgery and Medicine were sorted out according to inclusion and exclusion criteria and was confirmed by a consultant neurologist.

Data processing and analysis

To test for significant associations between MRS distribution at day 14 and day 30 and serum levels of albumin-corrected calcium, logistic regression analyses were used. Excellent outcome were considered MRS 0-1. For logistic regression models and Cox proportional hazard models, adjusted variables with p values < 0.05 were selected by univariate analysis. Differences between the groups were analyzed using the χ^2 test for categorical variables and the Student t-test or the Mann-Whitney U test for continuous variables.

RESULT

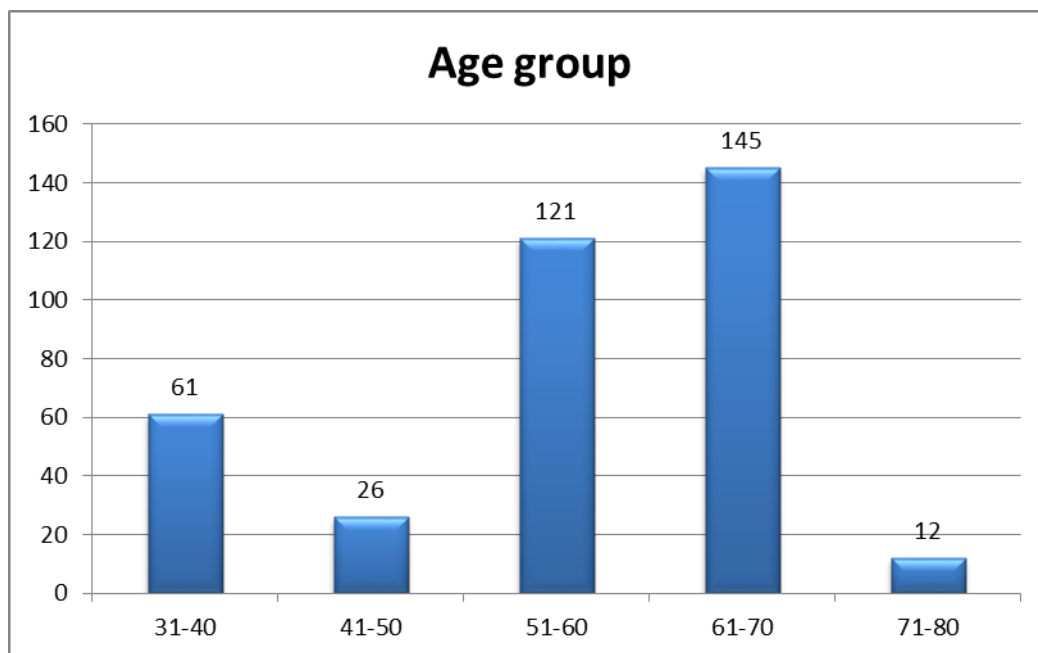


Figure 1: Age group of the patients (n=365).

Total 365 patients were studied. Minimum age was 32 and maximum age was 75 years. Mean age was $58.43(\pm 12.33)$. Most of the patients (145, 39.7%) were aged in between 61 to 70 years followed by 121 patients (33.2%) in between 51 to 60 years of age. Among rest 61

patients (16.7%) was from 31 to 40 years group, 26 patients (7.1%) were from group 41 – 50 years and 12 patients (3.3%) were from group 71 to 80 years. figure 1 shows a column chart of the distribution.

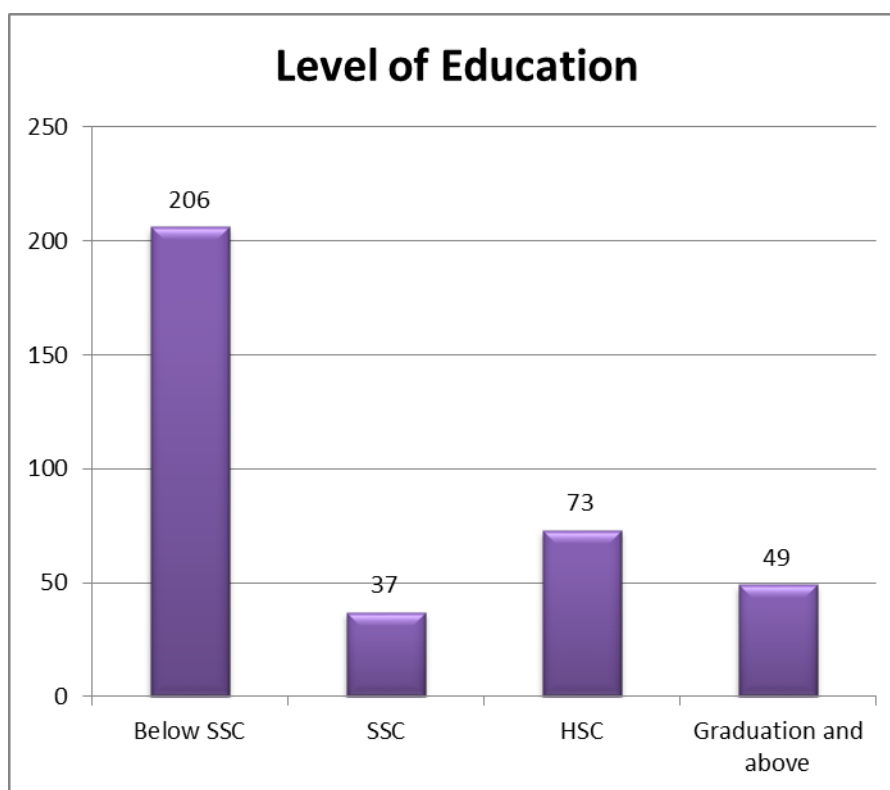


Figure 2: Distribution of patients according to level of education (n =365)

206 out of 365 patients (56.4%) had education below SSC. 37 patients (10.1%) completed SSC, 73 patients

(20%) completed HSC and 49 patients (13.4%) were able to achieve graduation and above.

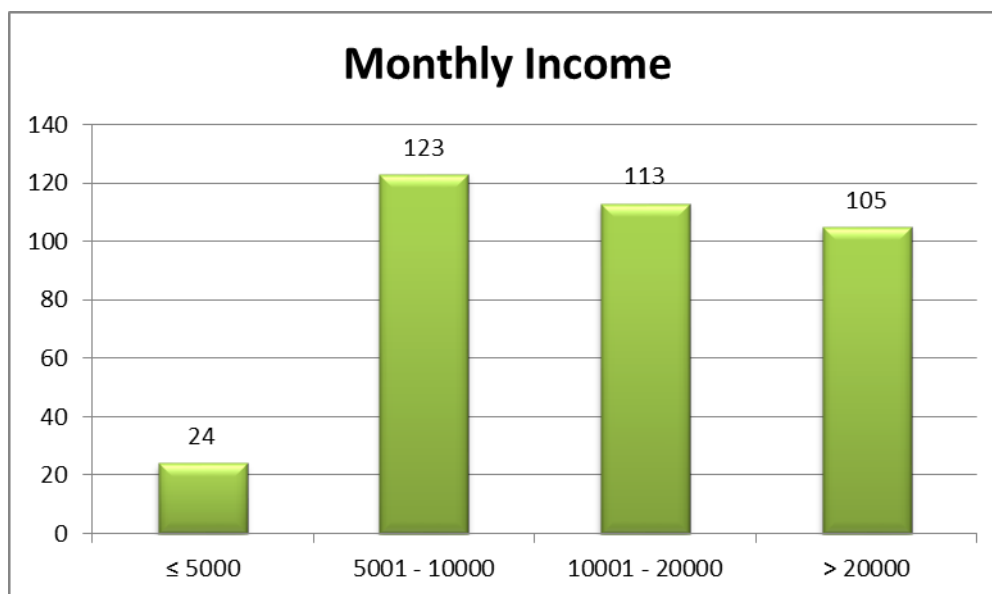


Figure 3: Monthly income status of study patients in taka (n = 365).

Total 123 subjects (33.7%) had monthly income between 5001 to 10000 tk. Followed by 113 patients (31.0%) who had monthly income between 10001 to 20000 tk and 105 patients (28.8%) who had monthly income more than

20000 taka. 24 patients (6.6%) had monthly income less than and equal to 5000 tk. Monthly income status is shown in figure 4.

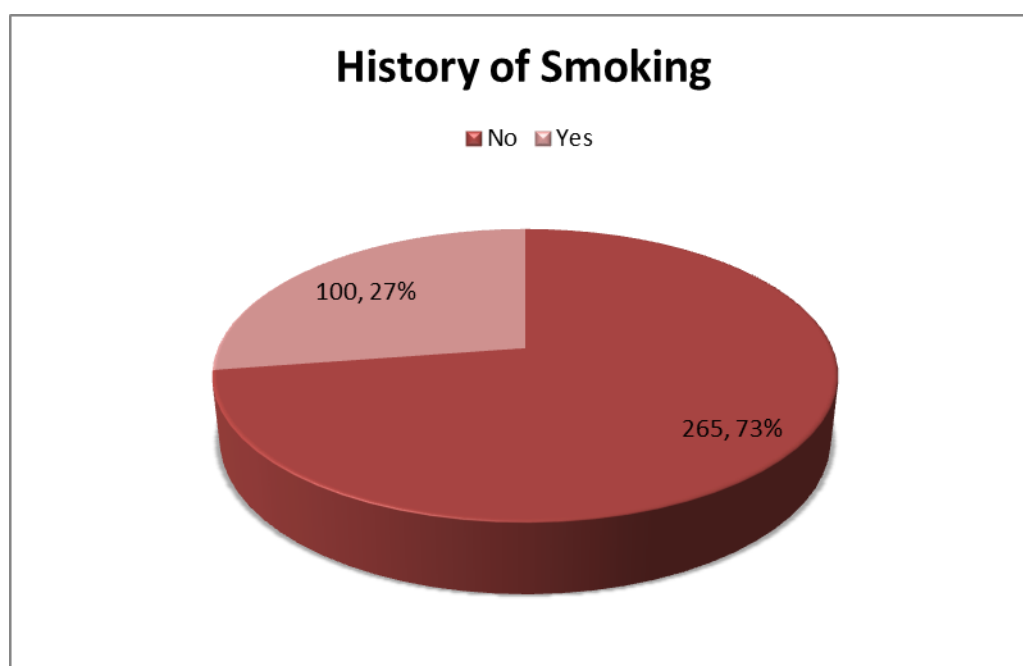


Figure 4: Distribution of patients according to history of smoking (n= 365)

265 patients (73%) out of 365 were not smokers. 100 patients (27%) had history of smoking.

Table 1: Outcome and mortality of patients at day 14 and day 30.

| Out come at day 14 and day 30 | Number of patients | Percentage |
|-------------------------------|--------------------|------------|
| Excellent outcome at day 14 | 135 | 37.0 % |
| Excellent outcome at day 30 | 185 | 50.7 % |
| Mortality at day 14 | 106 | 29% |
| Mortality at day 30 | 136 | 37.3% |

Excellent outcome is defined by having MRS score 0 and 1 at follow up. 37.0% patients had excellent outcome at day 14 and 50.7% patients had excellent outcome at day

30. 29% patients died at day 14 and 37.3% patients died at day 30.

Table 2: Odds ratios and 95% confidence intervals for 14 day and 30 day excellent outcome according to serum calcium quartiles among acute intra-cerebral hemorrhage stroke patients (n= 365)

| Variables | Serum Calcium Tertiles | | | P value* |
|---------------------------------------------------------------------------------------------------------------------|------------------------|--------------------|--------------------|------------------------|
| | T1 | T2 | T3 | |
| Adjusted Calcium (mmol/L) | <2.20 | 2.20 – 2.40 | >2.40 | |
| No. of cases of excellent outcome | 20 | 52 | 63 | |
| At 14 days | | | | |
| Crude | 1 | 3.53 (1.94 – 6.44) | 5.14 (2.83 – 9.34) | T2 <0.001 T3 <0.001 |
| Adjusted* | 1 | 2.44 (1.24 – 4.81) | 4.67 (2.41 – 8.93) | T2 0.009 T3 <0.001 |
| At 30 days | | | | |
| No. of cases of excellent outcome | 41 | 67 | 77 | |
| Crude | 1 | 2.20 (1.13 – 3.70) | 3.14 (1.85 – 5.32) | T2 0.003 T3 <0.001 |
| Adjusted* | 1 | 2.23 (1.22 – 4.06) | 3.31(1.88 – 5.83) | T2 0.001 T3 <0.001 |
| * Adjusted for age, history of DM, history of HTN, smoking, SBP, DBP, FBS, Serum lipid profile and Serum creatinine | | | | |

Modified Rankin Score 0 or 1 was considered as excellent outcome at follow up. Patients who had adjusted serum calcium level at admission in between 2.20 to 2.40mmol/l have significantly higher odds of having excellent outcome at day 14 and day 30 after discharge than patients who had adjusted serum calcium level below 2.20 mmol/l. Patients in the T3 group (ie

serum calcium >2.40 mmol) had still higher odds of having excellent outcome than T1 group and this finding was significant. When adjusted for age, h/o smoking, HTN, DM, SBP, DBP, FBS, Serum creatinine and serum lipid profile overall odds ratio decreased at 14 days but slightly increased at 30 days.

Table 3: Odds ratios and 95% confidence intervals for 14 day and 30 day mortality according to serum calcium quartiles among acute intra-cerebral hemorrhage stroke patients(n= 365)

| Variables | Serum Calcium Tertiles | | | P value* |
|---------------------------------------------------------------------------------------------------------------------|------------------------|--------------------|-------|-----------------------|
| | T1 | T2 | T3 | |
| Adjusted Calcium (mmol/L) | <2.20 | 2.20 – 2.40 | >2.40 | |
| No. of cases died | 46 | 32 | 28 | |
| At 14 days | | | | |
| Crude | 2.16 (1.23 – 3.79) | 1.18 (0.65 – 2.11) | 1 | T1 0.007 T2 0.577 |
| Adjusted* | 2.07 (1.13 – 3.80) | 1.36 (0.73 – 2.55) | 1 | T1 0.018 T2 0.323 |
| At 30 days | | | | |
| No. of cases died | 62 | 42 | 32 | |
| Crude | 3.15 (1.83 – 5.40) | 1.45 (0.84 – 2.52) | 1 | T1 <0.001 T2 0.179 |
| Adjusted* | 3.09 (1.74 – 5.50) | 1.64 (0.92 – 2.93) | 1 | T1 <0.001 T2 0.089 |
| * Adjusted for age, history of DM, history of HTN, smoking, SBP, DBP, FBS, Serum lipid profile and Serum creatinine | | | | |

Patients who had adjusted serum calcium level at admission less than 2.20mmol/l have significantly higher odds of mortality at day 14 and day 30 after discharge than patients who had adjusted serum calcium level more

than 2.40 mmol/l. Patients in the T2 group (ie serum calcium in between 2.20 and 2.40 mmol/l) had higher odds of mortality than T3 group, although this finding was not significant. When adjusted for age, h/o smoking,

HTN, DM, SBP, DBP, FBS, Serum creatinine and serum lipid profile overall odds ratio decreased slightly for T1 and increased slightly for T2.

DISCUSSION

Total 365 patients of intracerebral haemorrhage were taken for this study. Minimum age was 32 and maximum age was 75 years. Mean age was 58.43(\pm 12.33). Majority of the patients (39.7%) were aged in between 61 to 70 years followed by 33.2% in between 51 to 60 years of age. This implies total 72.9% of stroke patients were from 51 to 70 years of age. In a socio-demographic study of stroke patients conducted in a tertiary care hospital of Bangladesh. Another study showed that majority of the stroke patients were from 51-60 age group (29%) followed by 61-70 age group (22%).^[7] When both groups are combined 51% patients are found in between 51 to 70 years. This finding is lower than the present study. But it is similar with this study in that majority of the patients were from 51 to 70 years in both of the studies. In this study majority 58% were male and 42% were female. This is consistent with the findings of Abegunde.^[8] They found 64.3% male and 35.7% female among haemorrhagic stroke patients.

In the present study majority had education below SSC (56.4%). This gives a nearly similar picture to the study done in Dhaka Medical College Hospital where author had found total 63% of patient having education below SSC. In a Brazilian three-year population based study involving stroke patients Cabral and colleagues found a negative co-linearity of incidence of stroke with years of education.^[9] This means incidence of stroke were higher among patients who had lesser number of completed years of education. Findings of the present study suggest a similar picture which needs further evaluation in context of Bangladesh.

64.7% patients had monthly income less than 20000 tk and 28.8% patients had monthly income more than 20000 taka. In contrast to present study, Riaz and colleagues found 55.7% patients having monthly income more than 30000 tk and 44.3% patients having monthly income less than 30000 tk. But their study involved only 70 patients of haemorrhagic stroke.

Total 27% patients had history of smoking. This includes patients who smoked regularly and who had previous history of smoking. In a prospective study involving 22067 apparently healthy male physicians Tobias Kurth and colleagues found an increased risk of intracranial haemorrhage in current smokers.^[10] In a review article published in journal Nature entitled "Stroke in South Asian Countries" a prevalence of smoking of 15 – 20% in South Asian region was noted.^[2] 27% smokers (past and current combined) among intracranial haemorrhage patients in this study suggests important link of intracerebral hemorrhage with smoking which needs to be studied systematically.

Excellent outcome was defined by having mRS score 0 and 1 at follow up. 37.0% patients had excellent outcome at day 14 and 50.7% patients had excellent outcome at day 30. 29% patients died at day 14 and 37.3% patients died at day 30. Shoujiang You and colleagues followed up ICH patients at discharge and at 90 days.^[11] In their study they found 45.2% patients having excellent outcome at day 90.^[11] Flaherty and colleagues found one month mortality of 48% and 44% in two cohorts of haemorrhagic stroke patients.^[12]

They reported 42% mortality at one month from other population based studies. Findings of the present study correspond with above mentioned studies.

When the highest and lowest tertiles were compared in univariate models, an elevated serum calcium level was associated with a 5.14- fold increase in odds for excellent outcome at day 14 (OR, 5.14; 95% CI, 2.83-9.34, P = <0.001) and a 3.14-fold increase in odds for 30 days excellent outcome (OR, 3.14; 95% CI, 1.85-5.32; P = .003). After multivariate adjustment, the patients in the highest quartile still had significantly increased odds of 14 day and 30 day excellent outcome; 4.67(95% CI, 2.41-8.93) and 3.31 (95% CI, 1.88-5.83), respectively. This is similar to the findings of China study (You, S. *et al.* 2016).^[11] When highest and lowest quartiles were compared they found 2.28 fold increase in odds for 90 days outcome (OR, 2.28; 95% CI, 1.25-4.15; P for trend = .009) which did not change much after adjustment. This means high serum calcium level at admission is associated with excellent short term outcome in patients of acute cerebral haemorrhage.

Again when the lowest and highest tertiles were compared in univariate models, an decreased serum calcium level was associated with a 2.16- fold increase in odds for mortality at day 14 (OR, 2.16; 95% CI, 1.23-3.79, P = 0.007) and a 3.15-fold increase in odds for 30 day mortality (OR, 3.15; 95% CI, 1.83-5.40; P = <0.001). After multivariate adjustment, the patients in the lowest quartile still had significantly increased odds of 14 day and 30 day mortality; 2.07(95% CI, 1.13-3.80) and 3.09 (95% CI, 1.74-5.50), respectively. This implies that adjusted serum calcium level less than 2.20 mmol/l in haemorrhagic stroke patients at admission is associated with increased short term mortality.

CONCLUSIONS

In conclusion we can say that Intracerebral Hemorrhage Patients also revealed positive association of outcome with serum calcium level and negative correlation with phosphate level. There is no such study is seen in this country and therefore the study is designed to explore the short-term hospital outcome of intracerebral hemorrhage on the basis of admission serum calcium level.

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