A Dynamical Study of Risk Factors in Intracerebral Hemorrhage using Multivariate Approach

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Abstract: The purpose of this study is to investigate the effects of clinical covariates to the outcome of Intracerebral Hemorrhage (ICH) patients in terms of best fitted and excellent discriminate model of binary response variable.

Clinical data of 985 patients with ICH have collected using the International classification of diseases, Ninth revision codes. The diagnosis of ICH was confirmed by neuro-imaging in all patients.

Univariate analysis revealed that out of 88 covariates 46 were found to be significant ($p<0.05$). The multivariable analysis using multiple logistic regressions, exhibited a significant negative relationship between ICH and hypertension. The improvement among ICH patients having hypertension was 0.5 ($p=0.001$, ARR=0.5, 95% C.I. 0.3 – 0.8). The improvement among ICH patients using antihypertensive medicine was 1.3 ($p = 0.016$, ARR=1.3, 95% C.I. 1.1 – 1.5). Thus present study showed that ICH has strong relationship with use of antihypertensive medicine. The improvement of patients who were using antihypertensive medicine at the time of discharge was 3.0 times ($p < 0.0001$, ARR=3.0, 95% C.I. 2.7 – 3.2) as compared to those who did not use antihypertensive medicine. The change in ARR from 1.3 to 3.0 times shows that the use of antihypertensive medicine and ICH outcome variable are positively associated. The change in ARR of hypertensive range of SBP also indicates that the blood pressure range and ICH outcome variable are negatively associated. The neurological symptomatology, slurred speech and double vision are important factors of proposed statistical models. Moreover, a clear decrease was found in mental status from normal to coma in applicable model.

Surgery is an important part of recovery, and estimated that the improvement among the ICH patients, who were treated with surgery, was 1.4 times with significant p-value in best fitted models. The complication of pneumonia during treatment of ICH subjects has highly significant negative association with outcome variable.

Present Model has 0.892 area under the curve with sensitivity (0.852), specificity (0.793) and p-value (0.204). This indicates that the model gives the impression to fit quite well for predictive performance of the ICH outcome variable and the model is excellent model.

Keywords: Intracerebral Hemorrhage, clinical covariates, multivariable analysis, logistic regression, discriminate model, sensitivity and specificity.

INTRODUCTION

The brain is an "end organ" and gets its blood supply through network of blood vessels in the body. These vessels are the least prepared to handle the chronic increase in blood pressure. At the same time, they are responsible for carrying a larger amount of blood to a very vital area, at relatively high pressures. Thus, over the years, they can develop microscopic outpouchings called Charcot Aneurysms (place where a blood vessel has become swollen). Rupture of blood vessel causes Intracerebral Hemorrhagic stroke. Intracerebral Hemorrhage (ICH) thus refers to bleeding into parenchyma of the brain that may extend into the ventricles or rarely into subarachnoid spaces.

The global rate of occurrence of Intracerebral Hemorrhage (ICH) is 10-20 / 100,000 populations. It is noted that male suffer more than female. Moreover people aged more than 55 years have been noted to be at the maximum risk [1, 2]. Intracerebral Hemorrhage is not only a major issue in third world countries but it is reported to be a major issue also in the USA and UK. Regrettably it is estimated that mortality of ICH is expected to become two fold by the year 2050. The unidentified reason is increase in aging population as well as changing in racial demographics [3-5].

Stroke is the third leading cause of death and the first leading cause of disability [2, 5]. Morbidity is more

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severe and mortality rates are higher for hemorrhagic stroke than for ischemic stroke. Spontaneous Intracerebral Hemorrhage accounts for 10 to 15% of all strokes [6]. The 30-day mortality rate for hemorrhagic stroke is 40-80%. Approximately 50% of all deaths occur within the first 48 hours. The survival rate in Intracerebral Hemorrhage is only 38% in one year [4, 5, 7].

PATIENTS AND METHODS

Patients

Retrospective clinical data of 985 patients with Intracerebral Hemorrhage (ICH) over an 18 years period (1988-2005), were collected from one of the largest tertiary care hospital situated in Karachi. Patients were identified through medical records at the hospital using the International classification of diseases, Ninth revision coding system. Diagnostic codes (434 for stroke and 431 for ICH) were used to identify patients. The diagnosis of ICH was confirmed by neuro-imaging in all patients.

Statistical Approaches

The clinical data was processed by coding, editing, tabulating, recoding, re-tabulating and finally analyzed using different statistical tools. In analysis, we first assessed the univariate association between the response variable and a covariate using Chi- square test and logistic regression analysis. All variables with p-value less than 0.25 on univariate analysis were then included in multivariable analysis. A stepwise procedure was used to select the variable with a value of $p<0.25$ as the inclusion criteria for best fitted multivariable model. A number of models containing all possible combinations of variables were significant according to defined criteria, comparing the models through the likelihood ratio test.

The association between the various causal variables associated with each other biologically was also assessed. These variables, having statistically significant p-values, were possible confounders and their odd ratios changed significantly in multivariable analysis but were not strongly associated with each other because of p-value > 0.05. After developing main effect model, a relationship was tried to seek out with the interactions which were biologically meaningful but none of them were found to be significant.

In the present study, Hosmer-Lemeshow test statistics was used to assess the goodness of fit for logistic regression model. It is frequently used in risk prediction models; particularly during the assessment of human disease models [8-14].

Finally, the discrimination of the predictive models is determined by measuring the area under the receiver operating characteristic (ROC) curve and obtains the cutoff which can best predict the outcome. In current study sensitivity and specificity analysis is based on binary classification of actual outcome and predictive probabilities of outcome of models. The SPSS software (ver. 12) is used to perform all the statistical analysis.

ANALYSIS AND RESULT

In univariate analysis Pearson Chi-square and likelihood ratio test were performed for p-value and test of association , and logistic regression was used for RR (relative risk) with 95% confidence interval. It was revealed that out of 88 covariates 46 were significant according to p-value <0.05 (Table **1**).

After preliminary analysis, any variable whose p-value was found to be less than 0.25 on univariate analysis or otherwise thought to be biologically meaningful [10, 15-17] were entered into multivariable analysis using forward stepwise logistic regression, likelihood ratio test were used for variable selection. We only had two continuous variables which were age and length of stay. After analyzing the associations of the two continuous variables with outcome variable, it was found that both are statistically insignificant.

We tried to investigate the interactions which are biologically meaningful but none were found to be significant according to the p-value criteria (Table **2**).

After the process of including, deleting, refitting with different combinations of all important (statistically and /or clinically) variables and their interactions (biologically), different models were obtained using multiple logistic regression. One best fitted multiple logistic regressions model is as follows:

g(x): 0.9- 1.17(htn) -1.3(coag)+ 0.58(mahtn) -0.57(slusp) -1.88(dbvis) + 0.13(mssl1)-0.67(msco2) -0.13(mspr3) -0.92(msur4) -1.16(msco5) – 1.1(lsbp1) + 0.04(lsbp2)-0.9(lsbp3)-1.19(lsbp4)+ 0.12(mtnor) + 2.06(mtrmp) -0.06(lorbg) +0.68(loput)-0.3(lopon) +1.2(locer) + 0.46(lofrl) + 0.3(lopal)-0.3(memidsh) + 0.43(meintb)- 0.4(mehydr) -0.9(menorm)-1.5(wbclp1) + 0.15(wbclc2)- 0.2(reivab)- 0.5(reoxyg)+1.1(surger)-1.3(pnem1)- 0.6(pnem2) +2.6(dmant) + 0.7(dmasa).

Table 1: Result of Univariate Analysis, Showing Iimproved Percentage, Relative Risk with 95% Confidence Interval and P-Value of Statistically Significant Variables

Variables of Interest	Count	Improved %	RR(95% C.I.)	p-value
Risk Factors				
Recent Stroke(not present)	930	56.5	1	
Present	55	72.7	1.3(1.04,1.47)	0.01
Coagulopathy (not present)	948	58.4	1	
Present	37	29.7	0.5(0.3,0.8)	0.001
Medication				
Warfarin (No)	974	57.7	1	
Yes	11	27.3	0.5(0.15,1.02)	0.04
Antihypertansive (No)	339	49	1	
Yes	646	61.8	1.3(1.1,1.4)	0.0001
First Symptom				
Headache (No)	783	55.3	1	
Yes	202	65.3	1.2(1.04,1.3)	0.009
Weakness (No)	514	52.5	1	
Yes	471	62.6	1.2(1.09,1.3)	0.001
Faintness (No)	774	61.6	1	
Yes	211	41.7	0.6(0.5,0.8)	0.0001
Numbness (No)	965	56.9	1	
Yes	20	80	1.4(1,1.6)	0.03
Dizziness (No)	873	55.7	1	
Yes	112	70.5	1.3(1.1,1.4)	0.002
Slurred Speech (No)	774	55.4	1	
Yes	211	64.5	1.2(1,1.3)	0.018
Unable to Walk (No)	945	56.6	1	
Yes	40	75	1.3(1.04,1.5)	0.018
Initial SBP				
90-140, Normal	206	60.7		0.006
<90, Mild hypo.	15	26.7	0.4(0.2,0.9)	
141-160,Mild htn	215	59.5	1.0(0.8,1.1)	
161-200,Mod.htn.	379	59.9	1(0.8,1.1)	
>200,Sev.htn.	170	47.6	0.8(0.6,0.9)	
Mental Status				
Normal	286	77.3		0.0001
Sleepy	230	67.4	0.9(0.7,1.0)	
Confused	78	67.9	0.9(0.7,1.0)	
Poorly Responsive	57	45.6	0.7(0.3,0.8)	
Unresponsive	204	37.3	0.5(0.3,0.7)	
Coma	102	14.7	0.3(0.1,0.3)	

(Table 1). Continued.

Variables of Interest	Count	Improved %	RR(95% C.I.)	p-value
CN Palsy				
Troch Lear (No)	976	57.7	1	
Yes	9	22.2	0.4(0.1,1)	0.031
Trigeminal (No)	974	57.7	1	
Yes	11	27.3	0.5(0.2,1.02)	0.042
Abducent (No)	958	57.9	1	
Yes	27	37	0.6(0.2,0.97)	0.031
Facial (No)	515	53.4	1	
Yes	470	61.7	1.2(1.04,1.3)	0.008
Speech				
Normal	608	55.1	1	0.0001
Dysarthria	194	74.2	1.3(1.2,1.5)	
Global Aphasia	111	37.8	0.7(0.5,0.9)	
wernick'e Aphasia	12	91.7	1.7(1.04,1.79)	
Brocas	60	55	1(0.8,1.23)	
Motor				
Normal (Yes)	227	49.8	1	0.009
No	758	59.6	1.2(1.05,1.34)	
Rt.monopaeesis (No)	975	57	1	
Yes	10	90	1.6(0.9,1.7)	0.022
Lt.hemiparesis (No)	697	54.5	1	
Yes	288	64.2	1.2(1.04,1.3)	0.005
Rt.hemiplegia (No)	890	58.4	1	
Yes	95	47.4	0.8(0.6,0.99)	0.039
Lt.hemiplegia (No)	845	59.3	1	
Yes	140	45.7	0.8(0.6,0.9)	0.003
Sensory				
Normal	873	54.9		0.0001
Hemihypoasthesia	94	77.7	1.4(1.2,1.6)	
Neglect	18	72.2	1.3(0.9,1.6)	
Location				
Cerebellum (No)	936	56.3	1	
Yes	49	77.6	1.4(1.1,1.6)	0.002
Temporal Lobe (No)	923	58.2	1	
Yes	62	45.2	0.8(0.5,1)	0.046
Mass Effect				
Midline Shift (No)	766	64.8	1	
Yes	219	31.5	0.6(0.4,0.6)	0.0001
Intraventricular Blood (No)	718	63.5	1	
Yes	267	40.8	0.7(0.5,0.8)	0.0001
Hydrocephalus (No)	889	60.1	1	
Yes	96	32.3	0.5(0.4,0.7)	0.0001
Normal (Yes)	566	70.7	1	0.0001
No	419	39.4	0.6(0.5,0.7)	

(Table 1). Continued.

Variables of Interest	Count	Improved %	RR(95% C.I.)	p-value
White Blood Cells				
$4x10^3$-10^4/cc, normal	355	65.4		0.0001
<$4x10^3$/cc, leukopenia)	15	40	0.6(0.3,1.0)	
>10^4/cc, leukocytosis)	540	52.4	0.8(0.7,0.9)	
Lowest SBP				
90-140, Normal	566	65.5		0.0001
<90, Mild hypo.	106	18.9	0.2(0.2,0.4)	
141-160,Mild htn	140	66.4	1(0.9,1.1)	
161-200,Mod.htn.	65	43.1	0.7(0.4,0.9)	
>200,Sev.htn.	11	36.4	0.6(0.2,1.0)	
Lowest DBP				
60-90, Normal	544	65.1		0.0001
<60, Hypo.	203	40.9	0.7(0.6,0.7)	
91-110,Mild htn	117	60.7	0.9(0.8,1.1)	
111-120,Mod.htn.	17	41.2	0.6(0.2,1.0)	
>120,Sev.htn.	7	14.3	0.2(0.03,0.9)	
Received				
IVABX (No)	789	61.3	1	
Yes	196	41.3	0.7(0.5,0.8)	0.0001
NG (No)	720	61.7	1	
Yes	265	45.7	0.7(0.6,0.9)	0.0001
Foley Catheter (No)	708	60.6	1	
Yes	277	49.1	0.8(0.7,0.9)	0.001
Oxygen (No)	820	62.3	1	
Yes	165	32.7	0.5(0.4,0.6)	0.0001
Complication				
Pneumonia (not present)	229	72.5	1	
Present	154	31.2	0.5(0.3,0.6)	0.0001
Don't know	602	58.3	0.8(0.7,0.9)	
MI (not present)	315	62.2	1	
Present	12	33.3	0.5(0.2,1.0)	0.033
Don't know	658	55.5	1.9(0.8,1.0)	
Gastro I. bleed (not present)	319	61.8	1	
Present	10	30	0.5(0.2,1.0)	0.041
Don't know	656	55.6	0.9(0.8,1.0)	
Discharge Medicine				
Antihypertensive (No)	437	28.1	1	
Yes	548	80.7	2.9(2.7,3.0)	0.0001
ASA (No)	937	56	1	
Yes	48	83.3	1.5(1.2,1.6)	0.0001
Antilipidemics (No)	916	55.7	1	
Yes	69	79.7	1.4(1.2,1.6)	0.0001

(Table 1). Continued.

Variables of Interest	Count	Improved %	RR(95% C.I.)	p-value
Disposition				
Home	674	82.3		0.0001
Hospital	26	7.7		
Died	259	0		
Length of Stay (days)	Mean (S.E.)			
Not Improved	5.38(0.36)			
Improved	8.22(0.29)		1.03(1.01,1.1)	<0.0001

Table 2: Biologically Meaningful Interaction Terms

Variable's Combination	-2 log likelihood	G – Statistics	Degree of freedom	p-value
age x htn	632.325	0.066	1	>0.05
age x mahtn	629.526	2.925	1	>0.05
age x lsbp	625.036	7.415	4	>0.05
age x dmant	632.445	0.006	1	>0.05
htn x mahtn	629.117	3.334	1	>0.05
htn x lsbp	626.382	6.069	3	>0.05
htn x dmant	630.836	1.615	1	>0.05
memidsh x surger	631.483	0.968	1	>0.05
mehydr x surger	632.439	0.012	1	>0.05
reoxyg x pnem	632.394	0.057	2	>0.05

-2 log likelihood of main effect model = λ= 632.451.

The discrimination of the prediction model was determined by measuring the accuracy, sensitivity, specificity and area under the receiver operating characteristic (ROC) curve (Table **4**).

DISCUSSION

The inference of data through univariate analysis revealed that out of 88 covariates 46 were found to be significant (Table **1**) according to p-value < 0.05.

Statistical analysis showed that 84.8 % subjects were found to have hypertension as major risk factor. The inference of data through univariate analysis, revealed that hypertensive subjects showed apparent improvement (1.12 times) as compared to non hypertensive patients (95% C.I.: 0.95 – 1.27) for outcome variable. Contrary to this the multivariable analysis using multiple logistic regressions, interestingly exhibited a significant negative relationship between ICH and hypertension; when these data were adjusted for other variables in the statistical model. The improvement among ICH patients having hypertension was 0.5 (p=0.001, ARR=0.5, 95% C.I. 0.3 – 0.8) as compared to non hypertensive's when adjusted for other variables in the model.

Results of present study as reported in multivariable analysis were in accordance to the results of a previous study [18]. Other studies [2, 14, 19-25] showed a clear relationship between hypertension and ICH. The results of present study intensely support the scientific concept of direct relation of hypertension with ICH.

Recent data showed that 65.6 % subjects were using antihypertensive medicine. Multivariable analysis exhibited a significant relationship between ICH and antihypertensive medicine when these data were adjusted for other variables in given best fitted model (Table **3**). The improvement among ICH patients using antihypertensive medicine was 1.3 (p = 0.031, ARR=1.3, 95% C.I. 1.1 – 1.5) as compared to those who were not using antihypertensive medicine when adjusted for other variables in the model. Thrift *et al*. (1998) [22], reported that the use of antihypertensive

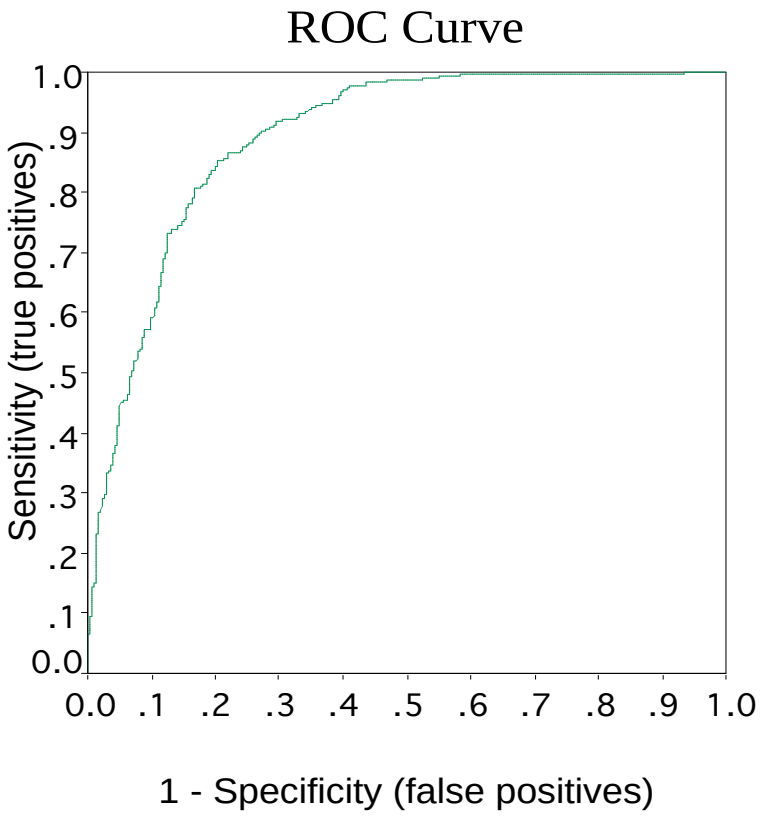
Table 3: Multiple Logistic Regression Estimates of Covariates of given Model, Showing Relative Risk and Adjusted Relative Risk with 95% Confidence Interval and p-Value for the Outcome Variable of ICH

Independent Factors Include in the Model	Field Name	RR(95.0% C.I.)	ARR(95.0% C.I.)	p-value
Hypertension	htn	1.12(0.95,1.27)	0.5(0.3 , 0.8)	< 0.001
Coagulopathy	coag	0.5(0.3,0.8)	0.5(0.2 , 0.9)	0.018
Antihypertansive	mahtn	1.3(1.1,1.4)	1.3(1.1 , 1.5)	0.031
Slurred Speech	slusp	1.2(1,1.3)	0.8(0.6 , 1.0)	0.032
Double Vision	dbvis	0.95(0.6,1.3)	0.4(0.2 , 1.0)	0.038
Mental Status(Normal)				0.002
Sleepy	mssl1	0.9(0.7,1.0)	1.0(0.9 , 1.1)	
Confused	msco2	0.9(0.7,1.0)	0.8(0.5 , 1.0)	
Poorly Responsive	mspr3	0.7(0.3,0.8)	1.0(0.7 , 1.1)	
Unresponsive	msur4	0.5(0.3,0.7)	0.7(0.5 , 0.9)	
Coma	msco5	0.3(0.1,0.3)	0.7(0.3 , 0.9)	
Normal(90-140)				0.006
Mild.hypo.(< 90)	lsbp1	0.2(0.2,0.4)	0.6(0.2 , 0.9)	
Mild.htn.(141-160)	lsbp2	1(0.9,1.1)	1.0(0.8 , 1.2)	
Mod.htn.(161-200)	lsbp3	0.7(0.4,0.9)	0.7(0.4 , 1.0)	
Sev.htn.(> 200)	lsbp4	0.6(0.2,1.0)	0.6(0.2 , 1.3)	
Normal(Motor)	mtnor	1.2(1.05,1.34)	1.0(0.8 , 1.3)	0.477
Rt.monoparesis	mtrmp	1.6(0.9,1.7)	1.6(0.8 , 1.7)	0.063
Rt.Basal Ganglia	lorbg	0.96(0.85,1.1)	1.0(0.8 , 1.2)	0.793
Putamen	loput	1.08(0.9,1.2)	1.3(1.0 , 1.5)	0.041
Pons	lopon	0.85(0.6,1.1)	0.8(0.4 , 1.3)	0.594
Cerebellum	locer	1.4(1.1,1.6)	1.4(1.0 , 1.7)	0.025
Frontal Lobe	lofrl	0.9(0.7,1.1)	1.2(0.8 , 1.5)	0.333
Parietal Lobe	lopal	1.04(0.9,1.2)	1.1(0.9 , 1.3)	0.301
Midline Shift	memidsh	0.6(0.4,0.6)	0.9(0.7 , 1.2)	0.445
Intraventricular Blood	meintb	0.7(0.5,0.8)	1.1(0.9 , 1.3)	0.266
Hydrocephalus	mehydr	0.5(0.4,0.7)	0.9(0.5 , 1.1)	0.303
Normal	menorm	0.6(0.5,0.7)	0.7(0.5 , 1.0)	0.04
WBC($4x10^3$ to 10^4/cc, nor.)				0.083
<$4x10^3$/cc, leukopenia)	wbclp1	0.6(0.3,1.0)	0.4(0.2 , 1.0)	
>10^4/cc, leukocytosis)	wbclc2	0.8(0.7,0.9)	1.1(0.9 , 1.2)	
IVABX	reivab	0.7(0.5,0.8)	0.9(0.6 , 1.2)	0.566
Oxygen	reoxyg	0.5(0.4,0.6)	0.8(0.5 , 1.1)	0.148
Surgery	surger	1.2(0.9,1.3)	1.4(1.1 , 1.6)	0.014
Pneumonia				0.001
Present	pnem1	0.5(0.3,0.6)	0.6(0.3 , 0.8)	
Don't know	pnem2	0.8(0.7,0.9)	0.8(0.6 , 1.0)	
Antihypertansive	dmant	2.9(2.7,3.0)	3.0(2.7 , 3.2)	< 0.001
ASA	dmasa	1.5(1.2,1.6)	1.3(0.8 , 1.6)	0.18

-2 log likelihood = 647.239.

Table 4: Sensitivity and Specificity Analysis with 95% C.I. of Good Fitted Multiple Logistic Regression Model

Cutoff Value	0.521
Area under ROC curves (95% C.I.)	0.892 (0.869 , 0.915)
Sensitivity (95% C.I.)	0.852 (0.816 , 0.883)
Specificity (95% C.I)	0.793 (0.746 , 0.834)
Positive Predictive Value (95% C.I.)	0.849 (0.812 , 0.879)
Negative Predictive Value (95% C.I.)	0.798 (0.750 , 0.838)



medicine decrease the risk of ICH due to hypertension. Thus results of present study showed that ICH has strong relationship with use of antihypertensive medicine and it can be hypothesized that the use of antihypertensive medicine decreases the risk of occurrence of ICH due to hypertension. The result of this study clearly presented that 84.8 % ICH patients have a risk factor of hypertension, 65.6 % ICH patients take antihypertensive medicine while 31.9 % do not take any medicine. So we can conclude that improvement in ICH patients, who develop hypertension was 0.5 times (ARR=0.5) as compared to those who did not develop hypertension. In the same way at the time of discharge, 56 % subjects were using antihypertensive medicine. Multivariable analysis showed that there is a relationship between ICH and antihypertensive medicine. The improvement among ICH patients who were using antihypertensive medicine at the time of discharge as resulted from multiple logistic regression model was 3.0 times ($p < 0.001$, ARR=3.0, 95% C.I. 2.7 – 3.2) as compared to those who did not use antihypertensive medicine. Thus the change in adjusted relative risk (ARR) from 1.3 to 3.0 times in antihypertensive medicine shows that the use of antihypertensive medicine and ICH outcome variable are positively associated.

Since hypertension is a significant risk factor, the different group of level or range of blood pressure plays an important role in improvement of subjects. Before discussion of different groups of range of blood pressure, it is important to inform that there are four groups of range of blood pressure in the present study. Two, at the time of admission after ICH, i.e., initial SBP

and DBP and two, during the period of admission in hospital, i.e., lowest SBP and DBP.

In the analysis of present data for different range of blood pressure, it was revealed that, in initial systolic blood pressure a large number of patients (78 %) belongs to the hypertensive blood pressure group of range (141-200 mm Hg) and 21 % patients have normal blood pressure group of range (90-140 mm Hg). Similarly in initial diastolic blood pressure group, 56 % belong to the hypertensive blood pressure group of range (>90 mm Hg) and 40.9 % patients have normal diastolic blood pressure group of range (60-90 mm Hg). In the same way during the hospitalization of patients with SBP it was found that 25 % belong to the hypertensive blood pressure group of range(141-200 mm Hg) and 64 % patients have normal blood pressure group of range (90-140 mm Hg). Similarly with reference to diastolic blood pressure during the hospitalization, 10 % of patients belong to the hypertensive blood pressure group of range(>90 mm Hg) and 62 % patients have normal diastolic blood pressure group of range (60-90 mm Hg).

The improvement among ICH patients who belong to hypertensive lowest systolic blood pressure group (141–160 mm Hg) was 1.02 times (p = 0.006, ARR=1.02, 95% C.I. 0.8 – 1.2), for the range of (161–200 mm Hg) was 0.7 times (p = 0.006, ARR=0.7 , 95% C.I. 0.4 – 0.9) and for the range of (>200 mm Hg) was 0.6 times (p = 0.006, ARR=0.6 , 95% C.I. 0.2 – 1.3) as compared to the normal range (90 – 140 mm Hg) of blood pressure when adjusted for other variables in the best fitted model. Thus the change in adjusted relative risk (ARR) of hypertensive range of systolic blood pressure also indicates that the blood pressure range and ICH outcome variable are negatively associated.

Results of current data analysis as reported in multivariable case are in accordance to the results of previous studies. Leppala *et al*. (1999) [26] showed that the risk of ICH is increased with increasing systolic and diastolic blood pressure. Song *et al*. (2004) [27] supported the closer relationship between hemorrhagic stroke and blood pressure level. Kin *et al*. (2005) [24] indicated the risk ratio of blood pressure level and hemorrhage was associated. Hence it can be concluded that the risk of ICH is increased with increasing systolic blood pressure, as already hypothesized above in discussion of hypertension that ICH has strong relationship with hypertension.

The second and third highest frequencies of risk factor noted in this study were diabetes mellitus (24.3%) and hyperlipidemia (13.4%). As far as these two major risk factors are concerned; results are quit interesting. Work done by researchers [18, 28-31] showed that diabetes mellitus is not an independent risk factor for the development of ICH. However it increases mortality rate in subjects with ICH since hyperglycemia is reported to increase edema and infarct size and with reduction in cerebral blood flow and cerebrovascular reserves. These indicate an indirect correlation of DM and hyperlipidemia with ICH. Sturgeon *et al*. 2007 [25] also showed that diabetes mellitus is not associated (p > 0.05) with ICH either in univariate and multivariate models. Arboix *et al*. (2000) [29] showed that diabetes mellitus increases the mortality rate in subjects with ICH. The univariate and multivarible analysis of present data showed insignificant relationship between ICH and these risk factors. Diabetes mellitus subjects with ICH outcome variable indicated less improvement (0.9 times) with non significant relationship (p<0.17) as compared to non-diabetic subjects. Diabetes mellitus and hyperlipidemia were not selected in the model as a candidate of best fitted model, when adjusted for other variables in the model.

The assessment of coagulopathy expected that 3.7 % subjects had this risk factor. The univariate analysis showed less clinical improvement (0.5 times) in coagulopathy subjects with ICH, as compared to non coagulopathic subjects (95% C.I.: 0.3 – 0.8) for outcome variable. Multivarible analysis showed a negative significant relationship between ICH and coagulopathy when adjusted for other variables in the best fitted model. The improvement among ICH patients with coagulopathy was 0.5 times (p = 0.018, ARR=0.5, 95% C.I. 0.2 – 0.9) as compared to without coagulopathy when adjusted for other variables in the model.

Present Model has 0.892 area under the curve with sensitivity (0.852), specificity (0.793) and p-value (0.204). This indicates that the model give the impression to fit quite well for predictive performance of the ICH outcome variable. The value of the area under the curve, sensitivity and specificity showed that the model is applicable.

CONCLUSION

The present statistical model of multiple logistic regression suggested that ICH has strong relationship with hypertension and the use of antihypertensive medicine was found to play a pivotal role in reduction of

the risk of ICH due to hypertension. They showed a clear improvement (1.3 times) in ICH patients as compared to those not using antihypertensive medicine. Likewise, statistical analysis showed a clear improvement (3.0 times) among ICH patients who were using antihypertensive medicine at the time of discharge. Thus the change in adjusted relative risk from 1.3 to 3.0 times illustrate that the use of antihypertensive medicine and ICH outcome variable are positively associated. Similarly, the change in adjusted relative risk of different range of level of blood pressure showed that the blood pressure level and ICH outcome are significantly associated. Therefore, it can be tested that the risk of ICH is increased with increase in blood pressure. From other risk factors, coagulopathy was found as a negatively significant risk factor for ICH outcome in the fitted model.

Multiple logistic regressions revealed that neurological symptomatology, slurred speech and double vision are important factors of proposed statistical models. Moreover, multivariable analysis discovered a clear decrease in mental status from normal to coma in applicable model. Putamen and cerebellum were positively significant with ICH outcome.

Multivariable analysis pointed out insignificant relationship between white blood cells and ICH; however WBC was selected as a candidate in the multiple logistic regression model. Hence white blood cells are essential for the best fitted model. Current statistical evaluation found that the surgery is an important part of recovery of ICH patients and estimated that the improvement among the ICH patients, who were treated with surgery, was 1.4 times with significant p-value in best multiple logistic regression models. Multivariable analysis showed that the complication of pneumonia during treatment of ICH subjects has highly significant negative association with outcome variable.

The above findings also intended that the multivariable analysis using multiple logistic regressions and statistical diagnostic tools are better techniques of binary response variable because multiple logistic regressions provides an easy interpretation and identify the most important factors from the multiple factor diseased data.

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