Predictors of Outcome for Spontaneous Intracerebral Hemorrhage in Iraqi Stroke Patients

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ABSTRACT:

BACK GROUND:

Primary intracerebral hemorrhage (ICH) is one of the common vascular insults with a relatively high rate of morbidity and mortality and there are many factors which influence the outcome.

OBJECTIVE:

The aim of this study is to determine potential early predictors of outcome within first six days of primary spontaneous supratentorial hemorrhage and to evaluate the influence of those various factors on the mortality and morbidity of patients with intracerebral hemorrhage (ICH).

METHOD:

70 patients (48 men and 22 women) were admitted to Baghdad teaching hospital, for the period from January 2010 to January 2011. They were diagnosed with supratentorial hemorrhage by brain CT. Total Serum cholesterol, the vital signs and the size of hematoma were arranged for each patient at the time of admission, then a modified Rankin scale (mRS) was calculated at 6^{th} day after the onset of this catastrophe.

RESULT:

Of the 70 patients (48 men and 22 women) consecutively admitted with ICH, 24 (38%) were died in the hospital: 31.5% on the first and second days and 82.5% by the fourth, fifth and sixth day of the event. The mRS outcome results were as follow: 8 (12.9%) good outcome mRS = (2), 38 (62.9%) were dependent mRS= (3-5) and 24 (34.3%) were died mRS = (6).

CONCLUSION:

High mortality and morbidity (high mRS scores value) were observed in patient with large hematoma size, low serum cholesterol, and high vital signs readings.

KEYWORDS: intracerebral hemorrhage, cholesterol, size of hematoma, MAP, mRS, vital signs.

INTRODUCTION:

Intracranial hemorrhage accounts for 8-13% of all strokes and results from a wide spectrum of disorders, ICH is more fatal and disabling and least treatable form of stroke. ICH has long been recognized as one of the most severe forms of stroke and among the most devastating neurologic injuries. Between 32% and 50% of patients die within the first month, and only 20% are independent six months after intracerebral bleeding. Tools for prediction of mortality are fundamentally limited in that they do not account for effects of withdrawal of care and are not designed to predict functional recovery.

Substantial displacement of brain parenchyma may cause elevation of intracranial pressure (ICP) and potentially fatal herniation syndromes [1,2,3,4].

The aim of this study is to determine the early predictors of outcome in primary spontaneous supratentorial hemorrhage, usually in the first week and to evaluate the influence of various factors on the mortality and morbidity. This study is the first one done in Iraq and its results may help health giver to improve the outcome of this devastating disease.

PATIENTS AND METHODS:

A prospective study of 70 patients with spontaneous intracerebral hemorrhage (48 men and 22 women) were enrolled in this study, their mean age was 63.34± 8.970 years. The patients were admitted in the medical unit in Baghdad teaching hospital between Jan 2010 to Jan 2011.Specialised medical and nursing personnel were taking care of the patients during their stay in hospital and the same protocols of treatment were followed so that it would be unlikely for the outcome to be varied depending on the facilities. Consent from each

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patient or his companion was taken to be included in the study.

The inclusion criteria for the current study include presence of intracerebral parenchymatous hemorrhage proved by brain CT scanning and the admission of the patients must be on the first day of their illness.

Patients were excluded from the study when there is associated cardiac disease, evidence of chest or urinary infections, evidences of organ failure like renal or hepatic failure and when brain CT scanning was suggestive of other diagnoses like brain tumor or ischemic infarction.

Modified Rankin scale (mRS) was used to assess the disability state of the patients and it was done at the 6th day after the onset of the event. Mean arterial pressure (MAP), temperature, pulse rate, respiratory rate, size of the hematoma [by brain CT] and total serum cholesterols were all done at the first day of admission which must be the first day of the ICH. Average of three readings for each variable was taken as a final result. The correct conditions, perfect instruments and the entire known standard were followed for all patients at times of taking the measurements. Finally all conditions and circumstances that may change the results of the variables at time of measurement were eliminated to the lesser possible limits.

Patients according to Size of the hematoma were divided into 3 groups: ≤ 35 mm, 36-70 mm and ≥ 71mm. Patients according to MAP were divided into 2 groups : ≤ 110 and ≥ 111 mm Hg.

Patients according to Pulse rate were divided into 2 groups : ≤ 100 and ≥ 101 beat /minute.

Patients according to oral temperature were assessed by centigrade unit and divided into those ≤ 37.2 and ≥ 37.3.Patients according to Respiratory Rate (breath /min) was divided into those ≤ 20 and those ≥21. Patients according to Serum cholesterol were assessed using (mg/dl) units and divided into those with level ≤ 200 and ≥ 201. All these patients' clinical characters and Para- clinical parameters were studied for correlation with mortality.

Statistical analysis: Statistical Package of Social Sciences (SPSS) v. 18 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-values less than 0.05 are regarded as statistically significant. [5]

RESULTS:

Of the 70 patients (48 men and 22 women) consecutively admitted with ICH, 24 (38%) died in the hospital: 31.5% on the first and second days and 68.5% by the fourth, fifth to seventh day of the event. The mean age of ICH patients was 63.34± 8.970 years. At first day of admission the MAP was 109.3671±18.37511, the mean Pulse Rate (pulse/minute) was 85.91±13.621, the mean temperature (C) 37.4129±1.37734, the mean Respiratory Rate 17.10±3.452, the mean Cholesterol (mg/dl) 206.84±46.350, the mean Size of Hematoma (ml) 69.37±26.305, and the mean MRS Score 4.39±1.448. See table 1.

We tried to find the interrelationship between mRS and different study variables which showed significant correlation regarding MAP, respiratory rate, pulse rate, size of hematoma and other variables as shown in table 2. Of the 70 studied patients, the outcome results were as follow: 8 (12.9%) good outcome (MRS = 2).38 (62.9%) were dependent (mRS= 3-5). 24 (34.3%) were died MRS= 6. The distribution of patients according to their mRS score is shown in figure 1.

On comparing the results of variables between patients who died and those who survive, we found the following results: The MAP for those who died was 113.9667 ± 20.36 compared to 106.96± 16.98 for surviving patients (p=0.044). The mean pulse rate for those who died was 87.63±16.455 compared to 85.02± 11.98 for surviving patients (p=0.452). The mean temperature for those who died was 38.11±2.06227 compared to 36.9± 0.82 for surviving patients (p = 0.04). The mean respiratory Rate for those who died was 20.38±4.726 compared to 15.91± 1.63 for surviving patients (p=0.001). Size of Hematoma for those who died was 80.29±20.127 compared to 63.67± 27.51 for surviving patients (p = 0.011). S. Cholesterol for those who died was 184.50±40.849 compared to 201.22± 27.296 for surviving patients (p = 0.046). Table 3

The relationship between serum cholesterol and mRS shown in figure 2 which showed significant inverse relation with mRS (p =0.047).

Table 1: Distribution of cases according to their (mRS) cores and different characteristics

Characteristic	N %	mRS (mean ± SD)	mRS 6th day			P value
			2	3-5	6	
			%	%	%	
Sex M F	 60 40	 4.64 ± 1.37 4.00 ± 1.49	 7.1 21.4	 52.4 53.6	 40.5 25.0	0.068[A]
Age y <50 50-64 ≥65	 4.3 60.0 35.7	 2.67 ± 1.15 3.95 ± 1.43 5.32 ± 0.90	 66.7 16.7 0.0	 33.3 59.5 44.0	 0.0 23.8 56.0	0.000[B]
Size of hematoma (cm^3) ≤ 35 35-70 >70	 5.7 38.6 45.7	 2.91 ± 1.38 4.19 ± 1.39 5.06 ± 1.07	 54.5 11.1 0.0	 36.4 63.0 40.0	 9.1 25.9 60.0	0.002[B]
MAP (mmHg) <110 >110	 51.4 48.6	 4.11 ± 1.56 4.68 ± 1.27	 22.2 2.9	 47.2 58.8	 30.6 38.2	0.103[A]
Pulse Rate (pulse /min) <100 ≥100	 75.7 24.7	 4.23 ± 1.50 4.88 ± 1.16	 15.1 5.9	 52.8 52.9	 32.1 41.2	0.104[A]
Temperature (C^0) ≤37.2 >37.2	 54.3 45.7	 4.16 ± 1.62 4.66 ± 1.18	 21.1 3.1	 42.1 60.1	 31.3 36.8	0.04[A]
Respiratory Rate (breath /min) ≤15 >15	 78.6 21.4	 4.00 ± 1.37 5.80 ± 0.56	 60.7 2.00	 23.3 21.6	 16.0 76.4	0.001[A]
Serum cholesterol (mg/dl) ≤200 >200	 58.6 41.4	 4.80 ± 1.38 3.79 ± 1.35	 7.3 20.7	 65.5 43.9	 48.8 13.8	0.003[A]

A: using t test for two independent samples.
B: using ANOVA test.

Table 2: The interrelationship between mRS and different study variables.

Characteristics	r [a]	P
Mean Arterial Pressure (mg Hg)	0.254*	0.034
Respiratory Rate breath/minute	0.514**	0.000
Temperature (C^0)	0.027	0.04
Pulse Rate pulse/minute	0.312**	0.075
Serum Cholesterol (mg/dl)	0.173	0.047
Size of haematoma	0.531	0.001
Age (year)	0.615**	0.000

[a] (Pearson's correlation coefficient).
** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

Table 3: THE results of different study variables, according to ultimate health outcomes.

Variables	Died		Not Died		t - Test	
	Mean	Std. Deviation	Mean	Std. Deviation	t	Significance
Mean Arterial Pressure (mm Hg)	113.9667	20.36	106.96	16.98	1.527	0.044
Pulse Rate (pulse/minute)	87.63	16.455	85.02	11.98	0.757	0.452
Temperature (C^0)	38.11	2.06227	36.90	0.82	-1.194	0.04
Respiratory Rate (breath/minute)	20.38	4.726	15.91	1.63	4.505	0.001*
S. Cholesterol (mg/dl)	184.50	40.849	201.22	27.296	0.767	0.046
Size of Hematoma (ml)	80.29	20.127	63.67	27.51	2.613	0.011*
Age (year)	69.50	8.288	60.13	7.582	4.753	0.000*

- Significant difference

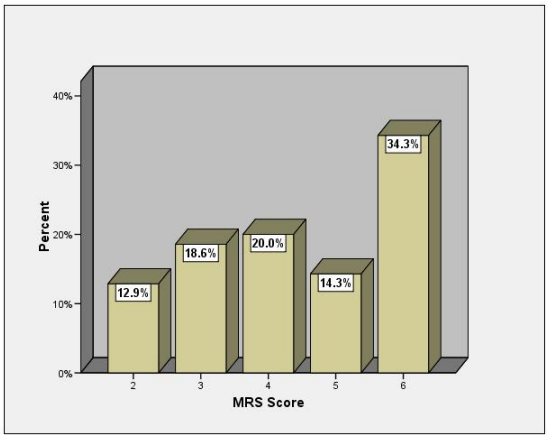

Figure1: Distiribution of patients according to their (mRS) scores.

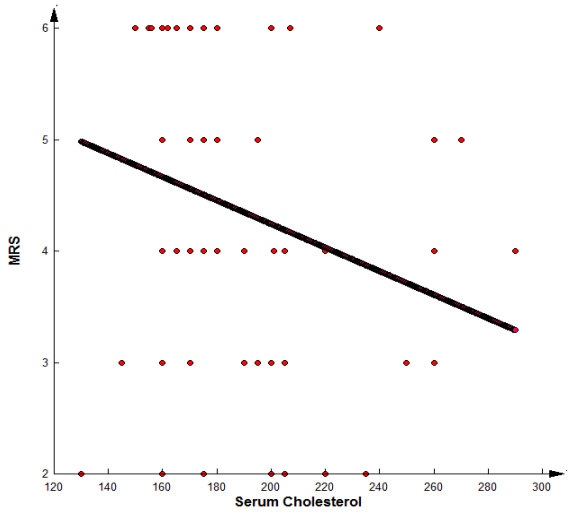

Figure 2: Distiribution of the study sample according to both cholesterol and mRS.

DISCUSSION:

In the present study we will discuss the predictors of (6th day in hospital) mortality and morbidity using mRS, which is a scale that reflects neurological deficit of the patient, predicts morbidity as well as mortality. The present study showed that there is significant inverse relationship between serum cholesterol and mRS ($p<0.047$) and this reflect the effect of total cholesterol on mortality. 48.8% of patient with serum cholesterol (≤200 mg/dl) were died in comparison to 13.8% with serum cholesterol (>200 mg/dl). This results reflect the significant relationship between serum cholesterol and in hospital mortality, this figure is in agreement with the Multiple Risk Factor Intervention Trials which showed higher mortality with ICH and total cholesterol <160 mg/dl, (P=0.042) [6]. Moreover, Roquer J et al showed that low total cholesterol in the first hours after ICH are strong independent predictors of in-hospital mortality[7]. In other side surprisingly higher cholesterol levels have been associated with better short-term outcomes after acute hemorrhagic strokes(8, 9,10). Many studies showed that very low serum cholesterol concentration increased mortality from hemorrhagic stroke[11,12]. Only one reported study which showed no significant correlation between cholesterol and markers of ICH severity [13].

The proven action of cholesterol as a buffer neutralizing free radicals is a finding to be taken into consideration when we want to explain this finding. When cholesterol is exposed to oxidative stress, it provides an antioxidant protection through its own oxidation, which results in oxsterols, substances that are less toxic for cells than the initial free radicals. This action might limit the extent of cerebral lesions [14]. So many previous studies and our recent one proved that adequate cholesterol levels may be important for maintaining the integrity of vessels and their resistance to rupture.

The present study showed highly statistical association of hematoma size and mortality; the Mean of the hematoma size in died patients was 80.29 ml and 63.67 ml in surviving patients (P=0.046). Large volume ICH is commonly associated with high ICP and brain tissue shifts related to ICP gradients and compartmentalized mass effect. This problem can be exacerbated by intraventricular hemorrhage, which leads to acute obstructive hydrocephalus[15].This result is in agreement to Alexander et al who showed that 7-day mortality was (39.8%) and associated with larger ICH volume at presentation [16]. one previous report by S. M. Davis shown that Hematoma growth is an independent determinant of both mortality and functional outcome after intracerebral hemorrhage [17], and this was against our study.

In our study we found that 30.6% patient with MAP ≤110 mmHg were died, while 38.2% of patient with MAP > 110 were died [P=0.044]. This reflects the positive significant relation of MAP and first week mortality. This result is similar to high first-day MAP (especially if >145 mm Hg) that worsened the survival rate reported by Castellanos et al [18], Ohwaki et al study confirmed significant positive relationship between maximum

systolic BP and hematoma growth as hematoma enlargement was reported more often in patients with a systolic BP greater than 160 mmHg[19].

Suri MF et al study stated that reduction of blood pressure in patients with acute ICH is safe and suggests that aggressive reduction might reduce the risk of neurological deterioration in first 24 hours of admission [20], Terayama et al and Fogelholm etal 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[21,22]. Also Tetri et al showed that the patients who died with ICH had significantly higher MAP at admission ($p < 0.001$) [23].

Comitia et al reported that MAP was at 153.78 ± 34.5 for those who died compared to 154.23 ± 33.1 for surviving patients $p = 0.641$[24], which is inconsistent with our study.

Our study found that 31.3% of patients with body temperature ≤37.2 celiuses had died in comparison to 36.8 patients with body temperature > 37.2 ($p<0.04$)

A meta-analysis of patients with stroke and other neurological injuries found that fever was consistently associated with worse outcomes across multiple outcome measures, and it supports the suspicion that therapeutic hypothermia may be beneficial in part by preventing fever[25]. Shuttered et al study observed a statistically significant association between high temperature and mortality within 7 days of the hemorrhagic stroke ($p<0.03$)[26] All above studies are in consistent with our study

Elevated temperatures have a direct neurotoxic effect, and therefore, unsurprisingly affect outcome detrimentally. However, the extent of this and the pathogenic mechanisms involved have not been fully elucidated [27].

In the present study we found that death rate was 32.1 % in patient with pulse rate ≤100 and 41.2% with pulse rate >101 ($p = 0.075$). This non significant correlation was in agreement with previous two studies [28,29].

Our results showed that 16% of patients with RR ≤20 were died and 76.4% of patients with RR >20 were died ($p< 0.001$)

Other studies like WhaSook et al showed that a higher respiratory rate on admission was associated with a higher level of functional and cognitive disability after brain injury and hemorrhagic stroke ($p = 0.00$), [28.29].

CONCLUSION :

High mortality and morbidity (patients with high mRS) were observed in patients with large haematoma size, low serum cholesterol, and high vital signs.

According to the above results we recommend admission of patients with ICH into a stroke unit, early evaluation of haematoma size and vital signs to determine the patient at risk for better management and elimination of these adverse effects, and lastly we recommend early referral of high risk patients for neurosurgical intervention (e.g. large size haematome).

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