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# Predictors of Outcome for Spontaneous Intracerebral Hemorrhage in Iraqi Stroke Patients

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## Abstract

**Background:** Intracerebral hemorrhages (ICHs) comprise approximately 10% of all strokes with a thirty-day case fatality rate of 30% to 50%.

**Objectives:** To determine potential early predictors of outcome within first week of primary intracerebral hemorrhage and to evaluate the influence of those various factors on the mortality and morbidity of patients with intracerebral hemorrhage (ICH).

**Methods:** 70 patients (48 men and 22 women) were admitted to Baghdad teaching hospital, between May 2009 and 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 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), 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; Size of haematoma; Mortality rate

## Introduction

Intracranial hemorrhage (ICH) accounts for 8-13% of all strokes and results from a wide spectrum of disorders, ICH is most severe, more fatal and disabling and least treatable form of stroke. Between 32% and 50% of patients die within the first month, and 80% of survival are disabled six months after intracerebral bleeding. Tools for prediction of mortality are fundamentally limited 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 [1-4].

The aim of this study is to determine hematoma size, serum cholesterol, mean arterial pressure and vital signs readings within first week of intracerebral hemorrhage as potential early predictors of the mortality and morbidity outcomes of primary spontaneous Intracranial hemorrhage.

# **Patients and Methods**

A prospective study of 70 consecutive patients with spontaneous intracerebral hemorrhage (48 men and 22 women) were enrolled in this study, their mean age was  $63.34 \pm 8.970$  years. The patients were admitted in the medical unit in Baghdad teaching hospital in the center of Baghdad 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 patient or his companion was taken to be included in the study and the study was approved by ethical committee of Iraqi board council for medical specilization.

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 diagnosis 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 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. Patients according to the hematoma Size were divided into 3 groups: less than 35 mm, 36-70 mm and more than 71 mm.

Patients according to Mean Arterial Pressure (MAP) were divided into 2 groups: Less than 110 and more than 111.

Patients according to Pulse rate divided into 2 groups: less than 100 and more than 101 beat /minute.

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Patients according to oral temperature were assessed by centigrade unit (°C) and divided into 2 groups those less than 37.2°C and those with more than 37.3°C.

Patients according to Respiratory Rate (breath /minute) was divided into 2 groups those less than 20 and those with more than 21/ minute.

Patients according to Serum cholesterol were assessed using (mg/ dl) units and divided into 2 groups those with level less than 200 and those with level above 201 mg/dl.

All these patients were followed for one month from ICH onset.

### 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-value 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  $63.34 \pm 8.970$  years. At first day of admission the MAP was  $109.3671 \pm 18.37511$ , the mean Pulse Rate (pulse/minute)  $85.91 \pm 13.621$ , the mean temperature (°C)  $37.4129 \pm 1.37734$ , the mean Respiratory Rate  $17.10 \pm 3.452$ , the mean Cholesterol (mg/dl) 206.84  $\pm$  46.350, the mean Size of Hematoma (ml)  $69.37 \pm 26.305$ , and the mean mRS Score  $4.39 \pm 1.448$  (Table 1).

We tried to find the interrelationship between mRS and different study variables which is shown in Table 2.

Of 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 (Figure 1).

On comparing the results of variables between patient who died and those who survive, we found the following results (Table 3).

The MAP for those who died was 113.9667  $\pm$  20.36 compared to 106.96  $\pm$  16.98 for surviving patients (p=0.044).

The mean pulse rate for those who died was  $87.63 \pm 16.455$  compared to  $85.02 \pm 11.98$  for surviving patients (p=0.452).

The mean temperature for those who died was  $38.11 \pm 2.06227$  compared to  $36.9 \pm 0.82$  for surviving patients (p=0.04).

The mean respiratory Rate for those who died was  $20.38 \pm 4.726$  compared to  $15.91 \pm 1.63$  for surviving patients (p =0.001).

Size of Hematoma for those who died was  $80.29 \pm 20.127$  compared to  $63.67 \pm 27.51$  for surviving patients (p=0.011).

Serum Cholesterol for those who died was  $184.50 \pm 40.849$  compared to  $201.22 \pm 27.296$  for surviving patients (p=0.046).

The distribution of patients according to their mRS score is shown in Figure 1.

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

# Discussion

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 ( $\leq 200 \text{ mg/dl}$ ) 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 result 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 is strong independent predictor of in-hospital mortality [7]. On other side surprisingly higher cholesterol levels have been associated with better short-term outcomes after acute hemorrhagic strokes [8-10]. Many studies showed that very low serum cholesterol concentration increased mortality

Characteristic	N %	mRS (mean ± SD)	mRS 6 <sup>th</sup> day			Byoluo
			2	3-5	6	r value
			%	%	%	
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 <sup>A</sup>
Age y <50 50-64 ≥65	4.3 60.0 35.7	$2.67 \pm 1.15$ $3.95 \pm 1.43$ $5.32 \pm 0.90$	66.7 16.7 0.0	33.3 59.5 44.0	0.0 23.8 56.0	0.000 <sup>B</sup>
Size of hematoma (cm³) ≤ 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 <sup>в</sup>
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 <sup>A</sup>
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 <sup>A</sup>
Temperature (°C) ≤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 <sup>A</sup>
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 <sup>A</sup>
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 <sup>A</sup>

A: Using t test for two independent samples

B: Using ANOVA test.

 $\label{eq:table_table_table} \ensuremath{\text{Table 1: Distribution of cases according to their (mRS) scores and different characteristics.}$ 

Characteristics	r <sup>a</sup>	Р
Mean Arterial Pressure (mg Hg)	0.254*	0.034
Respiratory Rate breath/minute	0.514**	0.000
Temperature (°C)	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 0.05 level (2-tailed).

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

<sup>\*\*</sup> Correlation is significant at the 0.01 level (2-tailed).



Variables	Died		Not Died		t - Test	t
	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)	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

 $\label{eq:table_table_table} \textbf{Table 3:} The results of different study variables, according to ultimate health outcomes.$ 

from hemorrhagic stroke [11,12]. Only one reported study showed no significant correlation between cholesterol and markers of ICH severity [13].

The proven action of cholesterol as a buffer neutralizing free radicals; when cholesterol is exposed to oxidative stress, it provides an antioxidant protection through its own oxidation, which results in oxysterols- substances that are less toxic for cells than the initial free radicals. This action might limit the extent of cerebral lesions and proved that adequate cholesterol levels may be important for maintaining the integrity of vessels and their resistance to rupture. [14].

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 intracranial pressure (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 Davis showed that hematoma growth is an independent determinant of both mortality and functional outcome after intracerebral hemorrhage [17].

In our study we found that 30.6% patients with MAP  $\leq$  110 mmHg were died, while 38.2% of patients 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), 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 and hematoma enlargement was reported more often in patients with a systolic BP greater than 160 mmHg [19]. Suri 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 et al. 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  $153.78 \pm 34.5$  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  $\leq$  37.2°C had died in comparison to 36.8% deaths in patients with body temperature >37.2°C (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  $\leq 100$  and 41.2% with pulse rate >101 (p=0.075). This non significant correlation was in agreement with previous two studies [28,26].

Our results showed that 16% of patients with respiratory rate (RR)  $\leq$  20 were died and 76.4% of patients with RR >20 were died (p<0.001).

See et al. showed that a higher respiratory rate on admission was associated with a higher level of functional disability and a lower cognitive ability after brain injury and hemorrhagic stroke (p=0.00), only for those with an admission respiratory rate of greater than 15 per minute [28,26].

The smallness of the study sample was the main problem faced by our study which was a result of the rarity of the intracerebral hemorrhage disease in Iraq.

In 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 haematoma).

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Page 4 of 4

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