

## A study on the predictors of in hospital mortality of patients with acute stroke in Basrah

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### ABSTRACT

**Aim:** to identify predictors of in hospital mortality after acute stroke and to investigate the impact of statins on stroke mortality within a package of other predictors.

**Patient & method:** all patients were admitted to Al-Sadr teaching hospital in Basrah from January 2013 to September 2013 with acute stroke. Diagnosis of acute stroke was based on clinical & imaging criteria as documented in patients medical files.

**Results:** A total of 147 patients (104 males and 43 females) were studied. Common co-morbidity included hypertension which was documented in (68.3%) and diabetes mellitus in (45.8%). Twenty three (16.0%) of stroke patients died while in hospital. Logistic regression analysis indicated significant prediction of mortality by history of old stroke, female gender, use of statins and high diastolic blood pressure at the time of admission.

**Conclusions:** female gender, recurrent stroke, elevated DBP and use of statins were all predicting in hospital mortality.

**Key Words:** Stroke, Basrah, In-hospital mortality, predictor.

دراسة عن التنبؤ في وفيات المستشفى لمرضى السكتة الدماغية الحادة في البصرة

**الهدف:** التنبؤ في وفيات مرضى السكتة الدماغية الحادة داخل المستشفى وللتحقق في مدى تأثير العقاقير المخفضة للكوليسترول على هذه الوفيات ضمن مجموعة من مؤشرات اخرى.

**طريقة العمل:** شملت الدراسة المرضى الذين ادخلوا الى مستشفى الصدر التعليمي في البصرة خلال الفترة من كانون الثاني ٢٠١٣ إلى ايلول ٢٠١٣ من ذوي السكتة الدماغية الحادة. واستند في تشخيص السكتة الدماغية الحادة الى المعايير السريرية والتصويرية كما هو موضح في أضيابير المرضى.

**النتائج:** تمت دراسة ١٤٧ مريضاً (١٠٤ ذكور و ٤٣ إناث). تم توثيق ارتفاع ضغط الدم في (٣، ٦٨٪) منهم، وداء السكري في (٨، ٤٥٪). ثلاثة وعشرون (١٦، ٠٪) من مرضى السكتة الدماغية توفوا أثناء وجودهم في المستشفى. وأشار تحليل الانحدار اللوجستي بان تنبؤاً كبيراً في الوفيات يلاحظ في المرضى ذوي تاريخ سابق في السكتة الدماغية القديمة، وفي جنس الإناث، واستخدام العقاقير المخفضة للكوليسترول و ارتفاع ضغط الدم الانبساطي في وقت دخول المستشفى.

**الاستنتاجات:** جنس الإناث، والسكتة الدماغية المتكررة، و ارتفاع ضغط الدم الانبساطي في وقت دخول المستشفى واستخدام العقاقير المخفضة للكوليسترول كانوا جميعاً مؤشرات تنبئ بوفيات داخل المستشفى.

### INTRODUCTION

The stroke is a condition with an abrupt onset of a neurological deficit that attributable to a focal vascular cause.<sup>[1]</sup> It is the third leading cause of death worldwide.<sup>[2]</sup> Lower-income countries have shown a higher relative stroke burden compared to industrialized ones.<sup>[3]</sup> Despite the significant achievement in management of acute stroke, it remains also a third cause of death in industrialized countries.<sup>[4]</sup> Over a third of stroke

deaths occur in developing countries<sup>[5]</sup> In the United States, 700000 stroke cases responsible for 165000 deaths each year<sup>[6]</sup> Common risk factors for stroke are hypertension (systolic or diastolic) cigarette smoking dyslipidemia, heavy alcohol consumption & contraceptive pills, there is higher incidence of stroke also among male gender & old age<sup>[7]</sup>. Determining predictor of mortality at period of hospitalization could aid a clinical care by

providing valuable prognostic information to patients and their family members and identify those at high risk for poor outcomes who may require more intensive resources'. Various clinical variables have been implicated in the etiology of in hospital mortality of stroke and this study is an attempt to evaluate the effect of a number of these variables and whether they could predict in hospital mortality or not. These predictors included important co-morbidities like diabetes mellitus (DM), ischemic heart diseases (IHD) hypertension (HTN), and role of diastolic blood pressure (DBP) in first few hours after attack, history of old stroke and medications that expected to change the outcome of stroke like statins.

#### **PATIENTS AND METHODS**

This is an eight - month hospital-based study conducted from January until September 2013. All patients admitted to Al-Sadr teaching hospital in Basrah with the diagnosis of stroke on the basis of clinical & imaging criteria enrolled in medical records. Cases with transient ischemic attacks (TIA) and subarachnoid hemorrhage were excluded from this study. Each patient included in this study was followed up until being discharged and outcome on the day of discharge was one of two alternatives: either died or left the hospital alive. The data used were based on patients records. These data included age, gender, systolic pressure in first few hours of admission & considered elevated when pressure  $\geq 140$  mmHg.& diastolic blood pressure (DBP) in first few hours of admission also considered elevated when  $\geq 90$  mmHg, The data include also history of hypertension (HTN), diabetes mellitus (DM), ischemic heart disease (IHD), history of old stroke. statins used early in study including simvastatin or atorvastatin at dose around 20-40 mg/day, there is no document about use of statins prior to

stroke onset Hypertension was diagnosed by either blood pressure 180/110 mmHg or above in single measurement<sup>[8]</sup> or blood pressure more than 140/90 mmHg in at least two measurements or the patient on regular anti hypertensive medications. Diagnosis of IHD based on medical records also. A total of 147 patients were included in the analysis for the purpose of this study. The in hospital mortality sorted as patients died while in hospital & the cause of death was not recorded

The statistical analysis was done using Statistical Package for Social Sciences (SPSS-for windows version 15). Chi square test or t test (ANOVA)used when appropriate. Logistic regression analysis was also done to identify the independent predictors of in hospital mortality. A P. of less  $< 0.05$  was considered as significant

#### **RESULTS**

Of the 147 patients with acute stroke,104(70.7%) were males and 43(29.3%) patients were females thus the male: female ratio was 2.4:1. The mean age of patients was  $64.1 \pm 11.7$  years and the range was 29-95 years. There was no significant difference ( $P > 0.05$ ) in the mean age between males ( $63.5 \pm 11.6$ ) and females ( $65.6 \pm 12.2$ ). In this study, 66 patients (45.8%) were with diabetes mellitus, while history of hypertension was observed in patients (68.3%). The systolic blood pressure in first few hours was elevated in100 patients (69.4%) and the diastolic blood pressure in first few hours found to be elevated in 52( 36.4%) patients. History of old stroke was reported in 38 (26.6%) patients. Statins (simvastatin, atorvastatin) were used in 108(75.5%) patients. History of IHD was observed in 37 (26.6%). A total of 23 patients (16.0%) died during hospital stay, 13 males and 10 females. Details are shown in (Table-1).

**Table 1. Distribution of patients by gender and selected variables.**

Variable	Male		Female		Total		P-value
	No.	%	No.	%	No.	%	
<i>Age</i>							
<50	7	7.1	5	21.2	12	8.6	<b>0.337**</b>
50-59	28	28.6	7	17.1	35	25.2	
60-69	30	30.6	8	19.5	38	27.3	
70 and above	33	33.7	21	51.2	54	38.8	
<b>Total</b>	98	100.0	41	100.0	139	99.9	
<b>Mean ±SD</b>	63.5 ± .01.6		65.6 ± 12.2		64.1 ± 11.7		
<i>Diastolic BP at admission</i>							
Elevated	34	34.0	18	41.9	52	36.4	<b>0.049*</b>
normal	66	66.0	25	58.1	91	63.6	
<b>Total</b>	100	100.0	43	100.0	143	100.0	
<i>Systolic BP at Admission</i>							
<140	32	31.7	12	27.9	44	30.6	<b>0.697*</b>
140+	69	38.3	31	72.1	100	69.4	
<b>Total</b>	101	100.0	43	100.0	144	100.0	
<i>Use of statin</i>							
User	77	76.2	31	73.8	108	75.5	<b>0.159*</b>
Non-users	24	23.8	11	26.2	35	24.5	
<b>Total</b>	101	100.0	42	100.0	143	100.0	
<i>History of hypertension</i>							
Hypertensive	65	63.7	34	79.1	99	68.3	<b>0.030*</b>
Normotensive	37	36.3	9	20.9	46	31.7	
<b>Total</b>	102	100.0	43	100.0	145	100.0	
<i>Old stroke</i>							
Present	26	26.0	12	27.9	38	26.6	<b>0.157*</b>
Absent	74	74.0	31	72.1	105	73.4	
<b>Total</b>	100	100.0	43	100.0	143	100.0	
<i>Diabetes mellitus</i>							
Present	45	44.5	21	48.8	66	45.8	<b>0.129*</b>
Absent	56	55.4	22	51.1	78	54.2	
<b>Total</b>	101	100.0	43	100.0	144	100.0	
<i>Ischemic diseases</i>							
Present	28	28.2	9	21.9	37	26.4	<b>0.128*</b>
Absent	71	71.7	32	78.1	103	73.5	
<b>Total</b>	99	100.0	41	100.0	140	99.9	
<i>Fate</i>							
Dead	13	12.6%	10	24.4%	23	16.0%	<b>0.045*</b>
Alive	90	87.4%	31	75.6%	121	84.0%	
<b>Total</b>	103	100.0	41	100.0	144	100.0	

\*Using X<sup>2</sup> test , \*\* Using ANOVA

Note: Variable with missing values were excluded

**Logistic regression analysis to predict in hospital mortality**

In order to identify independence prediction of in hospital mortality, a logistic regression analysis was done. Factors which were significantly associated with in hospital mortality among the studied variables are shown in( Table-2). These were diastolic hypertension at admission, use of statins, history of old stroke and female gender. Variables which could not

be shown to predict in hospital mortality were history of hypertension, diabetes mellitus, history of ischemic heart disease, age and systolic blood pressure in first few hours of admission. Non-predictors were history of hypertension, history of diabetes mellitus, history of ischaemic heart disease and age.

**Table 2. Logistic regression analysis to predict in hospital mortality of stroke patients.**

Variable	B	SE	WALD	DF	SIG.	EXP (B)
<b>Predictors</b>						
<b>Diastolic BP at admission</b>	0.033	0.016	4.004	1	0.045	1.033
<b>Use of statin</b>	2.225	0.680	10.717	1	0.001	9.258
<b>Old stroke</b>	-2.080	0.743	7.832	1	0.005	0.125
<b>Gender</b>	1.192	0.599	3.357	1	0.046	3.293

**DISCUSSION**

At the present study, the allover in hospital mortality was 15.6%. This result was comparable to the mortality in neighboring Arab countries, Benamer HT et al, showed that case fatality in 30 days was around 10% -17% in these countries [9] interestingly, a study in southern part of Iran the figure of in hospital mortality was 20% [10] which showed a higher level as compared to our study & developed countries. In a study in USA in California, the in hospital mortality was 8.4% [11] & in a Spanish study the results appeared somewhat higher 12.9% than the figure for the USA but still lower than our results. [12] In a Japanese study, a figure of 7.2% was reported. [13] The marked variation in these results is attributable to several possible explanations; of them is a increase the time between the stroke onset and admission to hospital and consequently less benefit of thrombolytic therapy which revolutionized the management of stroke. In centers which adapted thrombolytic therapy in stroke unit or neurology department, there were three fold reduction of in-hospital mortality [12] but absolutely thrombolytic therapy was no longer used in this study and we could not be able to judge how useful it is. It had been stated that no more than three hours was necessary to use thrombolytic agent to have a proper effect. [14] In the present study, female gender appeared as an independent predictor of in-hospital mortality, a result which contradicts some evidence [15] but consistent with Italian study which concluded the same result in this regard [16] and also consistent with a study in university of California. [11] Furthermore,

Gomara E. et al, in a published article in 2014 stated that the influence of gender is unclear on stroke mortality [17] while Rathore JA, et al) in large Indian study reported also no association between gender & Stoke mortality. [2] The existence of variation of gender effects on stroke patients need assessment of cultural and social background as well as additional selected study taking in account the profile of sex hormone especially on vascular and endothelial system as pivotal aspect. [18] A significant association of in-hospital mortality had been observed in our study with presence of history of old stroke and the old stroke appeared to be independent predictor of in-hospital mortality, a similar result observed by Nedelter K et al [4] and Henon H et al [19] as well. Conversely in 2004 The Copenhagen stroke study described that old stroke had negative impact on early outcome of acute stroke. [20] However this point needs further researches. Using statins was associated with higher in hospital mortality but such conflicting effect needs special attention interestingly cholesterol level itself appeared to have variable effect on stroke itself and determined by the type of stroke. The fact that there is opposite effect on ischemic stroke than hemorrhagic stroke [21,22] but Becker K et al, reported that early statin use was associated with increased post stroke infection, this risk may in part be related to increase plasma IL-Ir. [23] Furthermore, it had been shown that statins provide high level of protection for all causes of mortality in non hemorrhagic strokes but caution remained for patient at risk of bleeds. [24] A recent Iraqi study supports this

view and showed that low serum cholesterol was associated with high mortality and morbidity after hemorrhagic stroke.<sup>[25]</sup> In general the evidence with and against the role of statins and cholesterol in affecting post-stroke mortality is controversial and conflicting results were reported by a number of studies.<sup>[26-30]</sup> Furthermore, the Stroke Prevention by Aggressive Reduction in Cholesterol Level (SPARCL) study showed that statins exert limited benefit on stroke prevention but this beneficial effect is lost by increase risk of intracerebral hemorrhage.<sup>[31]</sup> Finally a meta-analysis published in 2007 illustrates that statins have a significant reduction of both ischemic or hemorrhagic stroke with somewhat insignificant increase in risk of hemorrhagic stroke.<sup>[32]</sup> With respect to the effect of diabetes mellitus, our results did not document any prediction on the mortality after stroke and this result is in agreement with study by Akhter et al,<sup>[2]</sup> Nadri et al<sup>[11]</sup> and Sweileh, et al<sup>[33]</sup> who all concluded that diabetes did not predict the mortality after stroke but this was against the view of Bolanle, et al that elevated serum glucose was independent predictor of in-hospital mortality.<sup>[8]</sup> Other controversial studies reported a significant prediction of in-hospital mortality.<sup>[34,35]</sup> Diabetes however, can commonly causes small infarcts which less likely to lead to a fatal stroke.<sup>[36]</sup> Age in this study was not significant predictor of in-hospital mortality. Such result is compatible with observations made by other researchers.<sup>[11, 33]</sup> But the Risk score designed by Smith, et al for in hospital death after stroke showed a strong impact of age<sup>[37]</sup> Similarly others shown significant impact on one year mortality & recurrence of stroke<sup>[38]</sup> In addition to previously mentioned predictors we found that history of hypertension was not a predictor of in hospital mortality; a result which is similar to that of Nadir et al<sup>[11]</sup> but contradicts the result of Smith et al.<sup>[37]</sup> Early admission diastolic blood pressure was elevated in 44.7%, a finding which is in agreement with Bentsen L, et al who reported

that admission BP strongly affects short and long term outcome after stroke and he reported that low or high admission BP indicates increase morbidity because of preexisting cardiac diseases so that close monitoring for stroke patient low or high BP is warranted.<sup>[39]</sup> However, Kvistad et al showed an inverse association between elevated BP and stroke severity on admission where elevated BP was associated with mild stroke and lack of elevated BP was associated with severe stroke. This may be attributable to protective effect of elevated BP on acute phase of stroke.<sup>[40]</sup> in this study IHD was not independent predictor of in hospital mortality & in 2010 an inverse result observed by Smith E et al who concluded that IHD is characteristically associated with significant in hospital mortality after stroke<sup>[37]</sup> Other studies reported a significant impact on in hospital mortality as well<sup>[11]</sup> But the extent of the association between IHD and stroke is not fully elucidated. The relationship of ischaemic heart disease to the outcome of stroke is not clear yet. Some investigators claimed that biomarkers is likely play Key role.<sup>[41]</sup>

**Conclusion,** this study evaluated the predictors of in hospital mortality of stroke, these predictors are, female gender, recurrent stroke, elevated DBP and use of statins. Physicians should have extreme attention to limit their impact on stroke mortality & Orientation to these factors is first step for success. Finally, this study conclude that use of statin carry some hazard when used in acute stroke, further research is needed to clarify this point.

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