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Original Article

Predictors of in-Hospital Mortality after Acute Stroke: Impact of Gender

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Abstract: The purpose of this study was to identify predictors of in-hospital mortality after acute stroke and investigate the impact of gender on stroke mortality. All patients admitted to Al-watani governmental hospital in Palestine from September 2006 to August 2007 and diagnosed with acute stroke were included in the study. Diagnosis of stroke was confirmed by computerized tomography scan. Demographics and clinical data pertaining to the patients were obtained from their medical files. The main outcome measure in this study was vital status at hospital discharge. Multiple logistic regression analysis was used to identify the independent predictors of in-hospital mortality. Statistical analysis was carried out using SPSS 15.A total of 186 acute stroke cases (95 females and 91 males) were included in the study. Hypertension (69.9%) and diabetes mellitus (45.2%) were the most common risk factors among the patients. Thirty nine (21%) of the stroke patients died in hospital. Multiple logistic regression analysis indicated that chronic kidney disease (P = 0.004), number of post-stroke complications (P= 0.037), and stroke subtype (P = 0.015) were independent predictors of in-hospital mortality among the total stroke patients. Knowledge of in-hospital mortality predictors is required to improve survival rate after acute stroke. The study showed that gender was not an independent predictor of mortality after acute stroke. More research is required to understand gender differences in stroke mortality.

Key Words: Predictors, hospital mortality, acute stroke, gender

Introduction

Stroke is one of the leading causes of morbidity and mortality world-wide [1]. In developing countries, the health burden of stroke is high. For example, in 2001, death from stroke in developing countries accounted for 85.5% of stroke deaths worldwide [2]. The high death rates in stroke patients could be reduced by implementing preventive and specific therapeutic strategies. Application of such strategies could be enhanced once the mortality predictors are identified. So far, different predictive models of mortality after stroke have been proposed from different countries [3-8] indicating ethnic and racial variations in stroke outcome [9-14]. Although data from many developing countries including some Arab countries regarding stroke have emerged in the past twenty years [15 – 17], there is a lack of such data from Palestine. The purpose of this study was to identify predictors of in-hospital mortality after acute stroke and investigate the impact of gender on stroke mortality.

Methodology

This is a one-year, hospital-based study conducted from September 01, 2006 until August 31, 2007. All patients admitted to Al-Watani hospital in Palestine with acute stroke were included in the study. Diagnosis of stroke was confirmed by Computerized Tomography (CT) scan. Patients with no confirmed CT scan or those suspected of having transient ischemic attack (TIA) were excluded from the study. Each patient included in the study was followed up until either death in hospital, or discharge alive, whichever come first. The data

Table 1. Univariate analysis of in-hospital stroke mortality by gender and after categorical risk factors

	Total (n=186)		Males (n = 91)		Females (n=95)	
Risk factor	Number of stroke (%)	Death (% mortality)	Number of stroke (%)	Death (% mortality)	Number of stroke (%)	Death (% mortality)
Stroke Subtype	153 (82.3)	26 (17)	70(76.9)	14 (20)	83(87.4)	12 (14.5)
Ischemic	33 (17.7)	13 (39.4)**	21(32.1)	11 (52.4)**	12(12.6)	2 (16.7)
Hemorrhagic						
Tobacco smoking	39 (21)	12 (30.8)	38(41.8)	12 (31.6)	1(1.1)	0 (0%)
Present	147 (79)	27 (18.4)	53(58.2)	13 (24.5)	94(98.9)	14 (14.9)
Absent						
HTN						
Present	130 (69.9)	30 (23.1)	66(72.5)	20(30.3)	64(67.4)	10 (15.6)
Absent	56 (31.1)	9 (16.1)	25(27.5)	5(20)	31(32.6)	4(12.9)
DM						
Present	84 (45.2)	23 (27.4)	39(42.9)	15 (38.5)*	45(47.4)	8 (17.8)
Absent	102 (54.8)	16 (15.7)	52(57.1)	10 (19.2)	50(52.6)	6 (12)
CHF						
Present	23 (12.4)	3 (13)	6(6.6)	1 (16.7)	17(17.9)	2 (11.8)
Absent	163 (87.6)	36 (22.1)	85(93.4)	24 (28.2)	78(82.1)	12 (15.4)
AF						
Present	26 (14)	4 (15.4)	11(12.1)	1 (9.1)	15(15.8)	3 (20)
Absent	160 (86)	35 (21.9)	80(87.9)	24 (30)	80(84.2)	11(13.8)
IHD						
Present	14 (7.5)	3 (21.4)	8(8.8)	2 (25)	6(6.3)	1 (16.7)
Absent	172 (92.5)	36 (20.9)	83(91.2)	23 (27.7)	89(93.7)	13 (14.6)
Previous Stroke	74 (39.8)	24 (32.4)**	43(47.3)	15 (34.9)	31(32.6)	9 (29)**
Present	112 (60.2)	15 (13.4)	48(52.7)	10 (20.8)	64(67.4)	5 (7.8)
Absent						
Obesity						
Present	31 (16.7)	7 (17.9)	12(13.2)	4 (33.3)	19(20)	3 (15.8)
Absent	155 (83.3)	22 (82.1)	79(86.8)	21(26.6)	76(80)	11(14.5)
CKD						
Present	63(33.9)	21(53.8)**	32(35.2)	14(56)*	31(32.6)	7(50)
Absent	123(66.1)	18(46.2)	59(64.8)	11(44)	64(67.4)	7(50)
Gender						
Male	91 (48.9)	25 (27.5) *				
Female	95 (51.1)	14 (14.7)				

$p < 0.05$, ** $p < 0.01$, HTN: hypertension; DM: diabetes mellitus; CHF: congestive heart failure; AF: atrial fibrillation; IHD: ischemic heart disease; CKD: chronic kidney disease.

collection was approved by the hospital administration and was performed by the clinical pharmacists at the hospital. The data collected included: age, gender, risk factors present, and post stroke medical complications. Data on pre-stroke risk factors for each patient were recorded both from the records of hospital or general practitioner and as self reported by the patient and included: hypertension (HTN), diabetes mellitus (DM), congestive heart failure (CHF), atrial fibrillation (AF), ischemic heart disease (IHD), smoking, recurrent stroke attack, chronic kidney disease (CKD) and obesity. Hypertension was diagnosed by either BP readings > 160/95 mmHg obtained from patients medical files and/or the use of anti-hypertensive medication for treatment of an elevated BP. Diabetes mellitus was diagnosed based on history of fasting blood glucose levels > 126 mg/dL obtained from medical records and/ or the use of anti-diabetic agents. Congestive heart failure was defined based on both written medical history. Atrial fibriallation (AF) was defined as any positive history of AF based on ECG recordings. Ischemic heart

Table 2. Univariate analysis of continuous variable risk factors for fatal and non-fatal stroke by gender

Risk factors	Total (n=186)		Males (n = 91)		Females (n=95)	
	Deaths Mean ±S.D	Survivors Mean± SD	Deaths Mean ±SD	Survivors Mean± SD	Deaths Mean± S.D	Survivors Mean± SD
Age	71.1±11.3	68.6±10.8	70.7±2.3	69±1.3	71.7±3.1	68±1.2
No. of risk factors	4.64±1.3**	3.9 ±1.3	5 ±0.3	4.9±0.1	3.9 ±0.2*	3.6 ±0.1
No. of post-stroke complications.	1.6±0.2***	1±0.1	1.2 ±0.2	1±0.1	2.3±0.3***	1 ±0.1

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

disease was defined as a history of any type of angina or myocardial infarction. Obesity was defined as having a body mass index (BMI) value >30 for both genders. Creatinine Clearance (CrCl) was calculated for all patients using Cockroft-Gault equations and values for females were obtained by multiplying the result by 0.85. Patients with CrCl less than 60 ml/min were considered to have CKD (stages 3 – 5). Post-stroke complications were defined as sudden onset of symptoms or identified complications that arouse during the period spent in hospital after admission. These complications included seizures, anxiety/ depression, infection, limb pain, and constipation [18, 19]. These complications were assessed and documented by the neurologist and/or the internist in the patients' medical files. The number of risk factors and number of post-stroke complications for each patient were counted and included in the analysis.

Statistical analysis

Analysis of data was carried out using the "Statistical Program for Social Sciences" (SPSS) for windows version 15.0. Categorical variables were expressed as frequency and percentage while continuous variables were expressed as mean ± standard deviation. Pearson Chi-square and independent student's (t) test were used in univariate analysis. P value < 0.05 was used as a significance level. Variables with P < 0.05 in the univariate analysis were included in multiple logistic regression analysis to identify the independent predictors of in-hospital mortality.

Results

During the study period, 186 patients with acute stroke were admitted to Al-Watani hospital. All patients were admitted alive and within the first 48 hours of the attack. Forty-nine per cent of the patients were males; giving a male: female ratio of ~ 1: 1. The average age of the stroke patients was 69.1± 10.9 years (range: 41 – 90 years) and there was no significant difference in the mean age between males and females (69.46 ±10.76 years for males versus 68.74 ± 11.09 years for females). One hundred and fifty three (82.3%) of the stroke cases were of the ischemic subtype and 33 (17.7%) cases were of the hemorrhagic subtype. Seventy four patients (39.8%) had recurrent stroke attacks while 112 (60.2%) had a first-ever stroke. Patients included in the study had an average of 3.4 ± 1.2 risk factors prior to the attack. The most common risk factors were HTN (n = 130, 69.9%) followed by DM (n = 84, 45.2%). None of the risk factors, except smoking, was significantly associated with either gender.

During the study period, 21% (39 patients; 25 males and 14 females) died in hospital. Results of univariate analysis in 186 stroke patients according to vital status at discharge are shown in **table 1 and 2** based on the type of variable. **Table 1** included all categorical variables while **table 2** included all continuous variables. Factors significantly associated with in-hospital mortality among the study sample included: gender (P= 0.033), stroke subtype (P= 0.004), recurrent stroke (P= 0.002), CKD (P = 0.003), number of risk factors (P=0.001) and number of post-stroke complications (P< 0.0001). However, DM (P= 0.04), stroke

Table 3. Independent factors associated with in-hospital mortality in stroke patients using multiple logistic regression analysis (enter method)

Variable	Wald value	Significance (P)	B	S.E	Odds Ratio (95% CI)
Chronic kidney disease	8.44	0.004	- 1.22	0.42	0.29 (0.13-0.67)
Number of risk factors	2.77	0.09	0.32	0.19	1.38 (0.94-2)
Number of post-stroke complications	4.36	0.037	0.90	0.43	2.47 (1.06-576)
Stroke subtype	5.9	0.015	1.14	0.47	3.13 (1.25-7.85)
Recurrent stroke	1.86	0.17	0.61	0.45	1.85 (0.76-4.46)
Gender	2.41	0.12	- 0.65	0.42	0.52 (0.23-1.19)

subtype (P=0.004) and CKD (P= 0.01) were found to be significantly associated with in-hospital mortality in male stroke patients. On the other hand, recurrent stroke (P= 0.006), number of risk factors (P= 0.038) and number of post-stroke complications (P= 0.001) were significantly associated with in-hospital mortality in female stroke patients (**table 1 and 2**). Regression analysis of the total study sample indicated that CKD (P = 0.037), number of post-stroke complications (P= 0.001), and stroke subtype (P= 0.015) were independent predictors of in-hospital mortality. The model was significant with a Chi-square of 33.03, DF = 6; P < 0.0001 (**table 3**).

Discussion

In this study, the overall in-hospital mortality was 20.96%. In male patients, mortality was 27.5% while in female patients, mortality was 14.7%. The in-hospital mortality reported in this study was within the range of in-hospital mortalities (10 – 37%) reported in studies from other neighboring countries [20-22]18 - 20]. Independent predictors of in-hospital mortality among the total stroke patients were stroke subtype, CKD, and number of post-stroke complications. Patients having hemorrhagic subtype had a higher risk of mortality than those diagnosed with ischemic stroke subtype. Other studies had found that hemorrhagic stroke was a risk factor of mortality and poor functional outcome [23]. A study carried out in Western Australia has also found that survival after 28 days was the lowest in patients with hemorrhagic stroke [24]. In our study, in-hospital mortality was significantly more common in patients with CKD. This is in agreement with the few publications in this regard. A study has found that decreased GFR was associated with higher in-hospital mortality [25]. Several publications have indicated that the severity of post-stroke complications was a strong independent predictor of in-hospital mortality and long-term outcome in stroke patients. For example, a study indicated that post-stroke infection is a bad prognostic factor in stroke patients [10]. Another study indicated that post-stroke neurological complications like seizures are bad prognostic factors [26]. In this study, we believe that the number of post-stroke complications was a reflection of the severity of stroke attack and therefore was a significant risk factor and an independent predictor of in-hospital mortality in stroke patients.

In this study, gender, DM and age were not independent predictors of in-hospital mortality. Our findings regarding gender were in agreement with a Copenhagen study which concluded that stroke is equally severe in men and women and short-term survival is also similar. The Copenhagen also indicated that once they survived the stroke, women live longer than men [27]; other studies have found that male gender is an independent prognostic factor of in-hospital mortality [28, 29].

In the present study, the impact of DM on in-hospital mortality was at the border of significance in the overall stroke patients. Diabetes mellitus was a significant risk factor of mortality for males but not for females. Different findings have been reported in the literature regarding the impact of DM on mortality among stroke patients. The German Stroke Study found that DM has a significant impact on early outcome [10]. However; a

Polish study suggested that DM has no effect on the course and outcome of ischemic stroke [30].

In this study, age was not a predictor of in-hospital mortality in patients with stroke. The influence of age on stroke outcome is still a matter of debate. While several studies showed a negative influence, other studies showed no influence [31-37]. It is difficult to establish whether age influences stroke outcome per se, or through other factors associated with it. The German Stroke Study on the predictors of in-hospital mortality after ischemic stroke found that in women, higher age, severity of stroke, and atrial fibrillation were independent predictors of in-hospital mortality, while in men, DM, and previous stroke had a significant negative impact on early outcome [10].

Limitation

Although this study shed some lights on the potential predictors of in-hospital mortality after acute stroke, yet it has few limitations. First, hyperlipidima, which is a known risk factor for stroke, was not considered in this study since the information regarding lipid profile was missing in most patients. Therefore no accurate data regarding hyperlipidemia could be used in the analysis. Second, no differentiation between pre vs. post menopausal women in stroke risk stratification, as well as women who have had a hysterectomy or an oophorectomy was made. Such analysis was not feasible given the difficulty of obtaining accurate information from patient's close relatives. There are multiple risk factors that need to be addressed for both men and women for there to be a consideration if gender plays a role in stroke.

Conclusion

This study indicated that several factors, particularly CKD, were associated with high risk of in-hospital mortality. Screening and better control of these factors is required to decrease the risk of in-hospital mortality in patients after acute stroke. Finally, the study showed that gender was not an independent predictor of mortality after acute stroke. More research is required to understand gender differences in stroke mortality.

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