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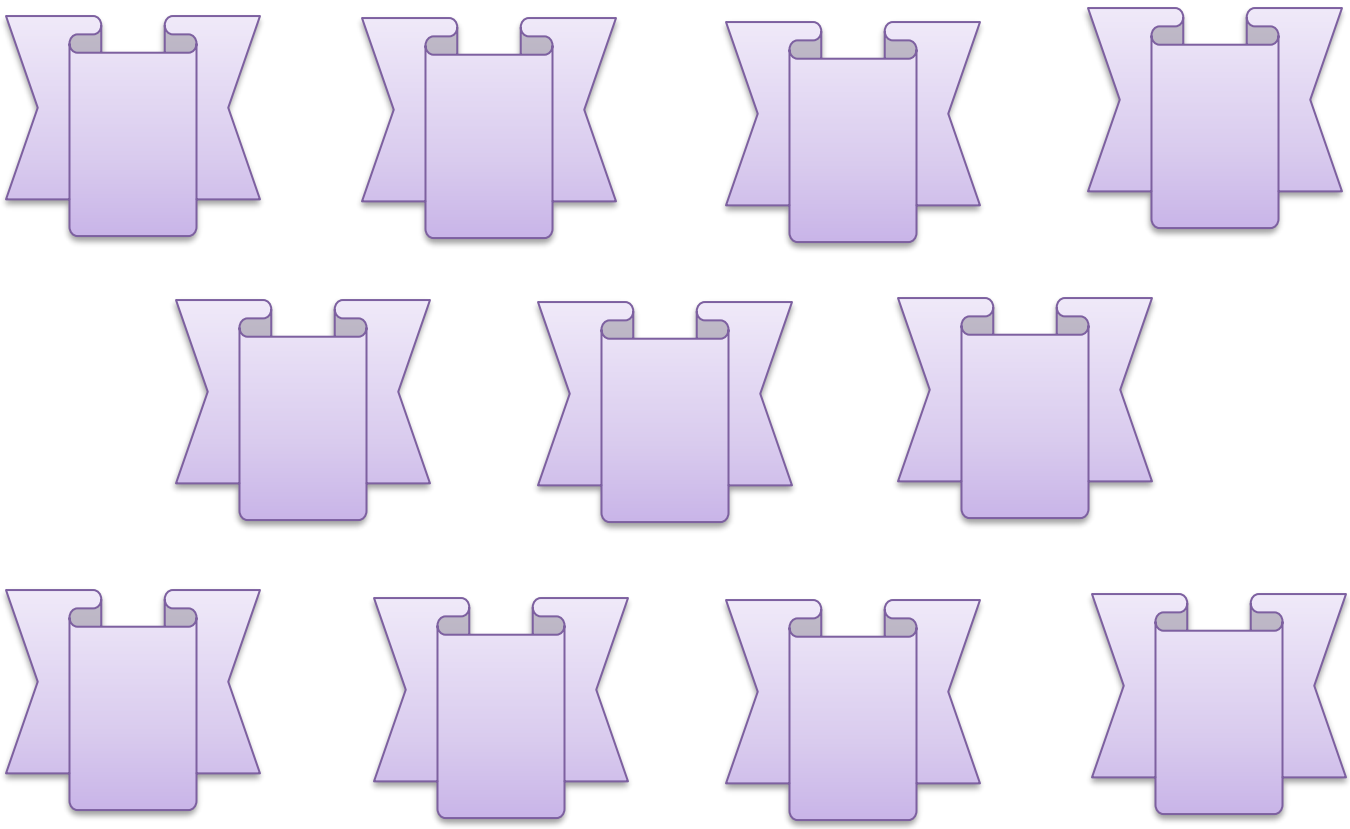

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Original Article

Rates and Risk Factors of Acute Ischemic Stroke Mortality [A Multi-Center Prospective Cohort Study]

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ABSTRACT

Background: Treatment of stroke had recent advances. However, and irrespective of these advances, it remains the second commonest cause of death and the chief cause of disability all over the world.

The Aim of the work: To estimate the incidence and risk factors associated with in- hospital ischemic stroke mortality.

Patients and Methods: In the prospective cohort study, 128 patients who had ischemic stroke. The diagnosis was built on the clinical and radiological basis. They were selected from the emergency department or stroke unit, Al-Azhar University Hospitals, between the start of December 2022 to the end of May 2023. Patients who survived were compared with the subgroup with lethal outcome regarding different factors.

Results: The in-hospital mortality was reported in 11 patients [8.6%]. Mortality was significantly associated with arterial fibrillation, older age, progression of stroke, hemorrhagic transformation, edema, respiratory and gastrointestinal [GIT] complications. In addition, mortality was associated with higher assessment scores. Respiratory and GIT complications and atrial fibrillation remains the significantly associated with mortality after adjusting for all factors.

Conclusion: The mortality rate is comparable with reported data from some developed and developing countries. Development of hemorrhagic transformation, cerebral edema, pneumonia, GIT bleeding at admission appears to be associated with in-hospital mortality.

Keywords: Mortality; Morbidity; Stroke; Ischemia.

INTRODUCTION

Stroke is the second commonest cause of mortality and a significant cause of morbidity [disability] worldwide regardless the recent improvement and advances in the management options [1]. Stroke [ischemic or hemorrhagic] is the commonest known cerebrovascular disease. It could be induced by modifiable and non-modifiable risk factors. The commonest non-modifiable risk factors are age and race. On the other side, the modifiable risk factors include elevated blood pressure [hypertension] or blood sugars [diabetes mellitus], dyslipidemia, obesity, physical inactivity and cardiovascular disorders [2-5]. Other nontraditional risk factors are linked to ischemic stroke [e.g., inflammatory bowel disease [6], blood pressure and nocturnal heart rate variability, endothelial function and recurrent cerebrovascular accidents [7]. However, there are heterogeneity in results and paucity of data.

The stroke-related comorbidities are frequently reported in the first week after the stroke. The mortality risk is higher during hospital admission and remains high during the whole duration of hospital stay. Intensive care unit [ICU] admission is increasing and this is especially for aged populations [8]. ICU admission is extremely critical for the management of critically-ill stroke patients. The ICU admission criteria include dysfunction/ failure of single or multiple organs, low score of Glasgow Coma Scale, need for advanced and continuous monitoring and postoperative observation [9].

The neurocritical care aimed principally directed to prevention, early identification and treatment of secondary brain insults [e.g., cerebral edema, intracranial hypertension, cerebral circulation impairment, hypo-or hyper-tension, hypoxia, hypercapnia and hyperthermia]. Thus, it is critically important to recognize the potential modifiable risk factors in critically ill patients with stroke. Thus, this could improve the overall patient outcome [9]. This study aimed to determine the incidence and risk factors associated with in- hospital ischemic stroke mortality to improve the patient survival [in acute phase of ischemic stroke].

PATIENTS AND METHODS

In this prospective cohort study, 128 with acute ischemic stroke were included. The diagnosis was based on the clinical and radiological findings. They were selected from the emergency department [ED] and stroke-treatment unit, department of neurology, Al-Azhar University hospitals. They were selected from those admitted between the first of December 2022 to the end of May 2023.

The inclusion and exclusion criteria: Patients above 18 years old and clinically evident first time acute ischemic stroke within first week, radiologically confirmed were included. Otherwise, patients with transient ischemic attacks or recurrent ischemic stroke, patients with intracranial hemorrhage, traumatic brain injury, cranial interventions/surgery except mechanical thrombectomy or endovascular stenting were excluded.

Ethical consideration: The study protocol was reviewed and approved by the ethical committee of the Faculty of Medicine, Al-Azhar University. The patient or his/her guardian signed an informed consent and an administration approval was approved. The study was completed in accordance with research and reporting guidelines.

Every patient was assessed on the clinical and radiological basis. The clinical assessment included socioeconomic data [e.g., age, sex, residence, marital status, occupation], clinical data [e.g., vascular risk factor, body temperature, blood pressure, pulse, and respiration rate] and state of consciousness [Glasgow coma scale, NIHSS score, and APACHEII score]. Investigations included the computed tomography [CT] brain and magnetic resonance imaging [MRI] brain with diffusion. Laboratory investigations included fasting blood sugar [FBS], complete blood count [CBC], Electrolytes, Renal function tests, and lipid profile]. Treatment included antiplatelet drugs, tissue plasminogen activator [tPA], thrombectomy, antihypertensive, and anti-hyperlipidemia drugs.

Statistical analysis of data: The qualitative data were presented as frequencies and percentages. Otherwise, the quantitative data were presented by their means ± standard deviation [SD] when normally distributed. Median and interquartile range [IQR] were used for preservation of non-normally distributed data. Patients were then categorized into alive and dead. Simple and multivariate analysis was performed to estimate the mortality associated risk factors. P value < 0.05 was set as the value of significant differences. The association between groups were calculated by independent samples student "t" test or Chi square test for quantitative and qualitative data respectively. All statistical analyses were achieved by the statistical package for social sciences [SPSS], version 20 [IBM®, Armonk, USA].

RESULTS

The present study included 128 patients with acute ischemic stroke. They were followed up during hospitalization. Females represented 53.1%. Venous thrombosis was reported among 14 patients [12 of them were females]. However, arterial thrombosis was reported in 114 patients with nearly equal distribution of males and females. The majority of them were married [68.8%] [Table 1]. Death was reported among 11 patients [8.6%].

When searching factors associated with mortality, we found significant association between mortality and each of atrial fibrillation, older age, progression of stroke, hemorrhagic transformation, edema, respiratory and GIT complications [Table 2].

Table [3] showed significant association between mortality and each of NIHSS, mRS, APACHE-II and GCS at admission. There was a significant increase of all scores in died than alive patients.

The logistic regression model showed that patients who had respiratory complications were 6.4 times more likely to die compared to patients without respiratory complications [post stroke pneumonia] and adjusted to demographic and comorbid factors [adjusted OR = 6.4, p = 0.04]. Additionally, GIT complications [GIT bleeding] were 7.9 time more associated with death among stroke patients during the in-hospital period adjusted to demographic and comorbid factors [adjusted OR = 7.9, p = 0.03]. Moreover, AF patients were 11.8 times more likely to have death during the in- hospital period compared to non-AF patients adjusted to other variables in the model [Table 4, Figure 1].

The area under the ROC curve is significantly higher than the area of chance, which is 0.5, concluding that the model has a significant prediction ability [Table 5].

Table [1]: Demographic data of the studied patients

Demographics		Frequency	Percent
Sex	Female	68	53.1
	Male	60	46.9
Sex regarding venous thrombosis	Female	12	85.7
	Male	2	14.3
Sex regarding arterial thrombosis	Female	56	49.1
	Male	58	50.9
Marital status	Divorced	1	0.8
	Married	88	68.8
	Single	10	7.8
	Widow	28	21.9
Age, mean ± SD		58.91	17.094

Table [2]: Demographics, comorbid conditions and hospital events in relationship with mortality

Variables		Alive [n = 117]		Died [n = 11]		p-value
		Frequency	Percent	Frequency	Percent	
Sex	Female	63	53.8	5	45.5	0.59
	Male	54	46.2	6	54.5	
DM		41	35.0	6	54.5	0.21
HTN		63	53.8	7	63.6	0.75
AF		18	15.4	6	54.5	**0.006***
Smoking		34	29.1	2	18.2	0.73
High BP on admission		71	60.7	10	90.9	**<0.05***
Age [mean]		57.78		71.00		**0.001***
Stroke progression		3	2.6	1	9.1	0.305
Hemorrhagic transformation		4	3.4	5	45.5	**< 0.001***
Edema		9	8.0	6	54.5	**<0.001***
Seizures		3	2.6	0	0.0	> 0.5
DVT		2	1.7	1	9.1	0.238
Respiratory complications		23	19.7	7	63.6	**0.003***
Cardiac complications		3	2.6	1	9.1	0.305
GIT complications		13	11.1	5	45.5	**0.009***
Depressive symptoms		25	21.4	2	18.2	> 0.5
Duration [median; IQR]		7 [5-10]		9 [5-16]		0.502
Radiological localization	Posterior	14	13.6	3	27.3	0.199
	Anterior	89	86.4	8	72.7	

Table [3]: Scores of strokes at admission in relation to mortality

		Alive [n=117]	Died [n=11]	P value
NIHSS	Mean	10	17	**<0.001***
	Min.-Max	3-18	15-23	
mRS	Mean	3	4.8	**<0.001***
	Min.-Max	2-5	4-5	
APACHE-II	Mean	6	16	**<0.001***
	Min.-Max	0-23	12-22	
GCS	Mean	14.9	12.5	**<0.001***
	Min.-Max	10-15	9-14	

Table [4]: Logistic regression for mortality prediction using complications, comorbidities, and demographic data

Independent variables	Beta	S.E.	p-value	Adj. OR
Age	0.05	0.044	0.251	1.051
Male	1.378	1.014	0.174	3.966
DM	1.266	0.918	0.168	3.548
HTN	-1.061	0.964	0.271	0.346
AF	2.472	0.992	0.013	11.84
Smoking	-1.009	1.331	0.449	0.365
Cardiac complication	1.773	1.699	0.297	5.889
Respiratory complication	1.862	0.9	0.039	6.435
GIT complication	2.065	0.976	0.034	7.887
Constant	-8.442	3.233	0.009	0.00

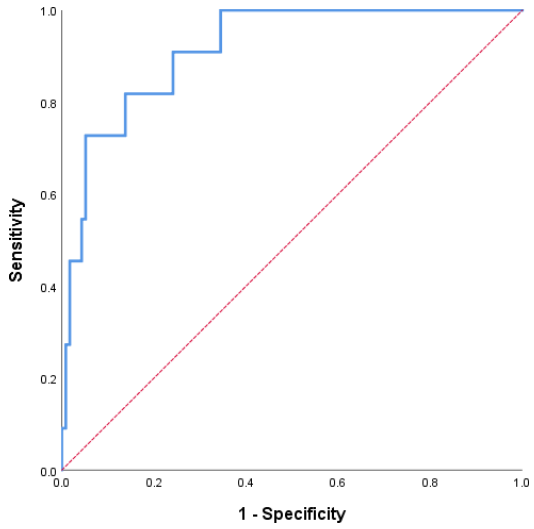

Figure [1]: ROC curve for prediction of mortality among patients with stroke

Table [5]: ROC curve characteristics of the logistic regression model

			Asymptotic 95% Confidence Interval	
Area	**SE**	**p-value**	Lower Bound	Upper Bound
0.916	0.036	<0.05	0.846	0.987

DISCUSSION

This study aimed to determinate the incidence of in-hospital mortality rate of ischemic stroke patients in addition to risk factors and complications associated with mortality. The study included 128 patients, and in-hospital mortality was reported among 11 patients [8.6%]. There was no significant difference between anterior and posterior circulation ischemic stroke as regard mortality rate. This is supported by the study **Jalali *et al.*** [10] who showed that the origin of emboli or thrombus were not an outcome predictor in ischemic strokes. The most important predictor was baseline NIHSS. In addition, **Zürcher *et al.*** [11] showed that there were specific differences in clinical presentation, etiology, and arterial pathology between posterior and

anterior circulation strokes. But did not affect the clinical outcome.

The in-hospital mortality rate was 8.6% with significant older age and higher coma score in died than alive patients. **Kortazar-Zubizarreta *et al.*** [12] revealed in-hospital mortality rate was 7.13%. **Viderman *et al.*** [9] in-hospital mortality rate of ischemic stroke was 36%. The mean age was 63 years, 45% were male and the mean GCS at baseline was 10.3. low mean GCS and involvement of recurrent stroke patients in this study explain the cause of high mortality rate.

In the hospital-based follow-up study by **Alhazzani *et al.*** [13], the in-hospital mortality was comparable to ours [9.7%], with an average length of stay of 10.67 days and a median of 7 days.

In logistic regression, we showed significant association between atrial fibrillation and in hospital mortality, and this explained by that cardiac causes of death are common in acute stage of ischemic stroke. In addition, ischemic stroke in patients with AF was also associated with higher incidence of acute kidney injury, bleeding and infectious complications and severe disability, as reported by **Alkhouli *et al.*** [14].

In a study of **Hannawi *et al.*** [15] the case fatality rate was significantly associated with increased age and mortality was higher in ischemic stroke patients with AF than in those without AF [13.0% vs 7.3%; P <0.001]. AF was a significant predictor of in-hospital mortality [OR 1.30; 95% CI 1.28-1.31; P <.001].

In logistic regression we showed significant association between pneumonia, GIT bleeding and in hospital mortality. In majority of SAP [Stroke-associated pneumonia], the causative factor was hospital-acquired infection. **Keller *et al.*** [16] included parapneumonic effusion, necrotizing pneumonia, empyema, pneumatocele and lung abscess formation, as risk factors for mortality in addition to pneumonia. However, **Kortazar-Zubizarreta *et al.*** [12] reported that, post-stroke pneumonia was not associated with the intensive care unit mortality but was associated with a 1.6-fold increase in ICU length of stay with an increase in 1- year mortality rate. However, this study is different than the current one. They focused on critically-ill acute ischemic stroke patients requiring invasive MV “whatever the reason”.

In our study, there was a significant association between high NIHSS and in hospital mortality. This is supported by **Kortazar-Zubizarreta *et al.*** [12], **Liu *et al.*** [17] and **Heuschmann *et al.*** [18]. In addition, the significant older age associated with in-hospital mortality is supported by **Liu *et al.*** [16] and **Heuschmann *et al.*** [18] who showed the same association in females only.

In conclusion, higher age, high stroke severity, coma, hypertension, atrial fibrillation on admission were found to be independent predictors for in-hospital mortality after ischemic stroke in routine clinical care. Development of hemorrhagic transformation, cerebral edema, pneumonia, GIT bleeding during admission appears to be associated with poor outcome. However, the small number of cases and lower rate of mortality are limiting steps for generalization of results. Future large-scale studies are recommended.

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