Original Article

Predictors of outcome after acute ischemic stroke among Egyptians

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Abstract

Background: Stroke has a high health burden, which make it among the disabilities leading disorders, especially among middle- income and high-income countries. Various factors can affect ischemic stroke prognosis, such as age group, initial stroke severity, stroke subtype, infarction site, comorbid diseases, and associated complications.

Objectives: To study the potential predictors of outcome after acute ischemic stroke among Egyptians.

Patients and Methods: One hundred first-ever AIS patients without any pre-morbid handicap who were recruited. They were subjected to MRI brain with diffusion weighted image volume infarct size assessment, stroke scales and scores and laboratory investigations.

Results: Forty-one patients had high level of high sensitive CRP and IL-6, 59 with low levels of insulin, 51 with dyslipidemia as they had high levels of LDL-C and only 2 patients with high level of homocysteine. Elevated total cholesterol level, lowered HDL level and high level of LDL had statistical significant correlation with the stroke outcome. Reduction of HDL, high level of total cholesterol, higher NIHSS at admission and larger DWI volume more than 55.8 cm3 were the significant independent predictors of outcome.

Conclusion: Initial ischemic stroke severity at time of presentation defined by higher NIHSS scores, higher levels of cholesterols with low HDL levels and larger diffusion weighted image volume of infarction are associated with poor outcome after acute ischemic stroke in Egyptians.

Keywords: DWI volume, ischemic stroke, IL-6, stroke outcome, dyslipidemia.

INTRODUCTION

Stroke has a high health burden, which make it among the disabilities leading disorders. In middle- income and high-income countries around the world, stroke is the leading neurologic cause of lost disability-adjusted life years(1). The mean survival time after stroke is 6 to 7 years with approximately 85% of patients living past the first year of stroke(2). Clinicians are often asked to predict outcome after stroke by the patient, family, other healthcare workers, and insurance providers(3).

A wide variety of factors influence stroke prognosis, including age, stroke severity, stroke mechanism, infarct location, comorbid conditions, clinical findings, and related complications(4). These are not only the confounding factors affecting ischemic stroke prognosis, but also interventions like intravenous thrombolysis, mechanical thrombectomy, high standard stroke unit, and well equipped rehabilitation center (5).

Racial factor actually affect ischemic stroke prognosis. This is evident as Hispanic patients have high stroke burden in comparison with white patients. In addition, black patients have ischemic stroke at younger age. Hispanic individuals appear to be at greater risk for stroke as compared with non-Hispanic whites sharing the same environmental factors (6). These findings consolidate the concept that the racial factor should be highly considered in the prognosis.

Knowledge of the important factors that affect prognosis is necessary for the clinician to make a reasonable prediction for individual patients, to provide a rational approach to patient management, and to help the patient and family understand the course of the disease.

Aim of the work

To study the predictors of outcome after acute ischemic stroke among Egyptians.

PATIENTS AND METHODS

One hundred patients with first ever-acute ischemic stroke were recruited at Neurology department, Mansoura University for a prospective cohort study between April 2019 until June 2022. The study protocol was clarified with all participants or their relatives, and then written informed consents were obtained from the patient or surrogate.

One hundred Egyptian patients with first ever-acute ischemic stroke with no any previous morbidity who were admitted to the Neurology Department, Mansoura university hospital between April 2019 and June 2022 were recruited.

The exclusion criteria included those with previous history of stroke either ischemic or hemorrhagic, previous non-stroke related disability, those having chronic liver disease, chronic renal disease, comorbid psychiatric disorders or any chronic disease that may affect the quality of life.

Initial assessment included; gender, age and body mass index (BMI). The investigators collected information about the medical history as hypertension, diabetes mellitus, dyslipidemia, smoking history, previous cardiovascular disease, and a history of transient ischemic attack (TIA). Specific reperfusion therapy at admission were clearly included in the study as (IV thrombolysis and/or mechanical thrombectomy). Initial evaluation was done using National Institute of Health Stroke Scale (NIHSS) score at their admission(7). Classification od ischemic stroke was done according to TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification(8).

MRI was performed with the use of echo planar imaging on a 1.5-Tesla ("Magentom Symphony, Siemens Medical solutions, Version VA 12A, Erlangen, Germany"). Multi-slice whole-brain DWI was performed and DW images were acquired in the x, y, and z directions. The x-, y-, and z-direction.

Blood samples were obtained after informed written consent in the second day morning after admission or within two days of stroke onset. After that, plasma and serum were separated. Storage of the samples at − 80 °C was done, until further analysis. Assessment of lipid profile was done to include; total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and high sensitivity C-reactive protein (Hs-CRP). In addition to this, IL-6, Homocysteine, Fasting serum glucose and Fasting insulin (FINS) were measured.

The Modified Rankin Scale (mRS)(Banks & Marotta, 2007) can be considered as a tool to evaluate the degree of disability among stroke survivors. Follow up was designed to be done at 6 months via well trained investigators. Theses follow ups were either telephone or face to face according to the patient condition. Secondary endpoints was stroke related mortality within 6 months.

Statistical Analysis

All statistical analyses were performed using "Statistical Package for the Social Sciences (SPSS) Statistics version 21.0" (IBM Corp., Armonk, New York, USA). The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Qualitative data were described using number and percent. Association between categorical variables was tested using Chi-square test.

Continuous variables were presented as mean ± SD (standard deviation) for parametric data and Median for non-parametric data. The two groups were compared with Student t test (parametric data) and Mann–Whitney test (non- parametric data). Multivariate logistic regression model to explore the factors associated with outcomes.

RESULTS

One hundred first-ever AIS patients without any pre-morbid handicap who were admitted to the Neurology Department, Mansoura university hospital between April 2019 and June 2022 at Mansoura University Hospital were recruited. They were subjected to NIHSS, mRS, MocA, MRI brain, and laboratory assesment. Collected data was statistically analyzed. It revealed the following:

In our study, the age range was 18-45 years (Mean ± SD = 61.97 ± 7.07). Forty-nine were males and mean BMI was 29.49 ± 3.81 (range was 24-38). Smoking history revealed that twenty-eight were mildly smokers, sixteen were heavy smokers and nine were ex-smokers.

About fifty patients were Hypertensive, forty one diabetic (type 2), thirteen had atrial fibrillation, fourteen with previous history of myocardial infarction and about thirteen with previous history of transient ischemic attack. Pre-event treatment fifty patient were on antihypertensive medications, forty-one on treatment for diabetes and seventy-four on antiplatelet while no one was on anticoagulants. Only twelve of the studied group received reperfusion therapy in the form of recombinant tissue plasminogen activator (r-tPA). NIHSS mean among studied cases was 13.61 ± 5.61(range 5-27).

The studied group were classified into three different groups according to the DWI lesion volume. Eighteen patients had volume between 7.9 and 31.35 cm3, forty patients had lesion volume between 31.36 and 55.8 cm3 and forty-two patients had lesion volume more than 55.8 cm3 .

Analysis of routine laboratory results and others for metabolic syndrome revealed that 41 patients had high level of high sensitive CRP and IL-6, 59 with low levels of insulin, 51 with dyslipidemia as they had high levels of LDL-C and only 2

patients with high level of homocysteine. (Figure 1)

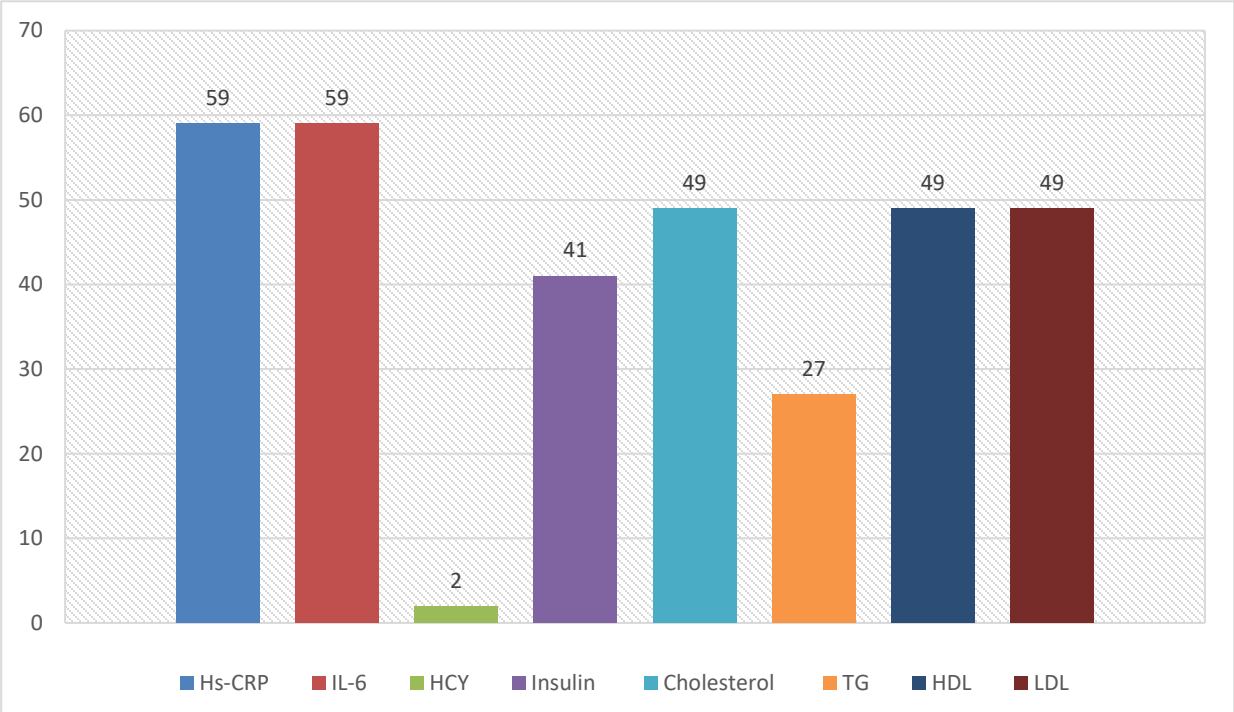

Figure (1): Analysis of laboratory data among the studied cases

Elevated total cholesterol level, lowered HDL level and high level of LDL had statistical significant correlation with the stroke outcome defined by higher mRS scores (ρ-value <0.001). However, elevated CRP, IL-6, hyperglycaemia, high levels of homocysteine, lowered insulin levels and higher levels of triglycerides failed to prove statistical significant correlation with the ischemic stroke outcome at six months follow-up (ρ-value > 0.005). (Table 1)

Table (1): Relation between outcome (defined by mRS at 6 months) with laboratory findings

	Not disabled (n=53)		Disabled (n=47)		Test of significance
	N	%	N	%	
Elevated CRP	28	52.8	31	66	χ^2= 1.775 P= 0.183
Elevated IL-6	28	52.8	31	66	χ^2= 1.775 P= 0.183
Elevated HGY	2	3.8	0	0	FET= 1.810 P= 0.179
Elevated glucose level	21	39.6	20	42.6	χ^2= 0.088 P= 0.776
Decreased insulin level	21	39.6	20	42.6	χ^2= 0.088 P= 0.776
Elevated total cholesterol level	18	34	31	66	**χ^2= 10.204** **P= 0.001***
Elevated TGs level	12	22.6	8	17	χ^2 = 0.709 P= 0.702
Decreased HDL	18	34	31	66	**χ^2= 10.204** **P= 0.001***
Elevated LDL	18	34	31	66	**χ^2= 10.204** **P= 0.001***

MC: Monte-carlo test

χ^2: Chi-square test

After logistic regression analysis of independent predictors for poor out come and mortality, reduction of HDL, high level of total cholesterol, higher NIHSS at admission and larger DWI volume more than 55.8 cm3 were the significant independent predictors (table 2).

Table (2): Multivariate regression analysis for prediction of disability

Predictors	P value (by univariate regression)	Multivariate regression			
				95% C.I. for odds ratio	
		P value	Odds ratio	Lower	Upper
Elevated total cholesterol level	**0.002***	0.373	1.145	0.735	1.800
Elevated TGs level	0.995				
Decreased HDL	**0.002***	0.336	1.127	0.864	1.966
Elevated LDL	**0.002***	0.342	1.138	0.822	1.887
DWI volume >55.8 cm3	**<0.001***	**<0.001***	2.465	1.47	4.25
NIHSS	**<0.001***	**<0.001***	2.364	1.11	3.78

Multivariate Logistic regression analysis of independent predictors of cases

Discussion

Outcome after stroke remains a big challenge for neurologists, patients and investigators. Clinical assessment in the acute setting usually give us an overview about the disease process and the possible pathway in the disease process but unfortunately, this is not right forever. Clinical assessment may be of great value if it is combined with the use of blood biomarkers that can evaluate any step in the pathological mechanisms in acute ischemic stroke as oxidative stress, homeostasis, neuronal injury, glial injury and inflammation. Ischemic stroke and inflammation are considered to have a potential large interaction. These findings indicate that inflammation markers and homeostasis can open the door for the potential prediction of outcome after acute ischemic stroke.(9)

Numerous studies tried to assess the potential prognostic factors in acute ischemic stroke, and they found promising results. These studies mostly were outside Mediterranean region, which may reveal different ethnicity, genetic, different body composition and environmental factors. Therefore, we try to assess these findings among Egyptians with AIS.

Metabolic syndrome "is a group of metabolic-related risk factors. Behavioral, environmental, and genetic factors can explain the main pandemic of metabolic syndrome".(10) Metabolic syndrome itself is considered as an alarm for the possible occurrence of coronary, peripheral vascular and cerebrovascular disorders.(11) numerous researches highlights the positive correlation of low HDL-C and high CRP levels and IL-6 with stroke morbidity and or mortality.(12)

Higher levels of total cholesterol and low HDL levels were independent prognostic factors for acute ischemic stroke out come among Egyptians. These findings were consistent with findings observed by Sohail et al, who studied one hundred and sixteen patients with acute ischemic stroke. Their findings revealed that higher levels of total cholesterol were associated with poor stroke presentation and poor outcome and defined by high mRS score at admission and even at discharge.(13)

Inflammation following acute ischemic stroke not usually considered as a poor process, It has both pros and cons as it may result in further damage, leading to neuronal damage and network failure, on the other hand it may have a valuable role, via endorsing the recovery.(14) The pro-inflammatory molecules, cytokines and interleukins secreted from the nearby damaged tissue and immune residue cells within the brain and upregulation of adhesive molecules, encourage wide range of inflammatory cells to pass the blood brain barrier and causing more brain damage.(15)

Reperfusion therapy including mechanical thrombectomy and thrombolysis efficacy need s surrogate marker of their efficacy. This can be done via ischemic stroke volume measurement as in DWI volume. It is not only the case in reperfusion therapy but also as a prognostic tool. However, it should be correlated accurately with an outcome characteristic like disability score assessment. This was the case in our study which revealed that larger volume of infarction at DWI were associated with poor outcome especially volume more than 55.8 cm3. These findings were in concordance with the findings observed by Thijs et al, who concluded that DWI lesion volume measured within 48 hours of symptom onset is an independent risk factor for functional independence.(16) Baird et al, reported that, DWI volume of infarction within 48 hours of ischemic stroke onset after excluding the effect of age, NIHSS score is an independent predictor of acute ischemic stroke outcome.(17)

Summary and Conclusion

Initial ischemic stroke severity at time of presentation defined by higher NIHSS scores, higher levels of cholesterols with low

HDL levels and larger diffusion weighted image volume of infarction are associated with poor outcome after acute ischemic stroke in Egyptians.

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