

## Early Neurological Deterioration in Acute Ischemic Stroke: potential Predictors, causes and relation to infarct growth

#### Thesis

Submitted for Partial Fulfillment of MD Degree of Neurology **By** 

#### **Ehab AbdElbaset Abdulsamad**

M.B.B.Ch., M.Sc. Neuropsychiatry Supervised by

### Prof. Dr. Samia Ashour Mohamed Helal

Professor of Neurology Faculty of Medicine - Ain Shams University

### Prof. Dr. Hany Amin Aref

Professor of neurology Faculty of medicine- Ain Shams University

### **Prof. Dr. Ayman Mohammed Nassef**

Professor of neurology Faculty of medicine- Ain Shams University

### Prof. Dr. Ramez Reda Moustafa

Assistant Professor of Neurology

Faculty of Medicine-Ain Shams University

#### **Prof. Dr. Mohammed Amir Tork**

Assistant professor of Neurology Faculty of Medicine - Ain Shams University

2019



## CKNOWLEDGMENT

First and foremost, thanks to "**Allah**, whose magnificent help is the first factor in every thing we can do in our life.

I would like to express my deep gratitude and sincere thanks to *Prof. Dr. Samia Ashour Mohamed Helal*, Professor of neurology, Ain Shams University, for great help offered to me and endless scientific support all through this work.

My warmest thanks to *Prof. Dr. Hany Amin Aref*, Professor of neurology, Ain Shams University, for submitting his effort and skill to the conduction of this work along with the generous provision of his vast experience.

Also, my profound gratitude to *Prof. Dr. Ayman Mohamed Nassef*, Professor of neurology, Ain Shams University, for continuous guidance and support.

I am really thanks to *Prof. Dr. Ramez Reda Moustafa*, Professor of neurology, Ain Shams University, for his advice, scientific support and continuous effort sincere.

I would like to thank *Prof. Dr. Mohammed Amir Tork*, Professor of neurology, Ain Shams University, for scientific support and continuous effort.

My great thanks and gratitude to all patients who were sharing in this work.

Lastly but not least, my deepest gratitude to my family especially *Father and Mother* for their unflagging love and support throughout my life. I owe my loving thanks to my *wife*, without their encouragement it has been impossible to me to finish this work, my lovely kissing to my kids (*Mohammed*, *Hager and Mariam*).

Finally, I can't forget all the favors of *Prof. Gamal Youssof*, (*Professor of Neurology, KFS general hospital*) for his help and support greatly guided me all through my work

## Contents

Subject	Page
• List of Abbreviation	Ι
• List of Tables	V
• List of Figures	VII
• Introduction	1
• Aim of the work	5
• Review Of Literature	
- Predictors of early neurological deterioration	6
- Mechanisms of early neurological deterioration	18
- Management of early neurological deterioration	32
- Outcome	37
• Patients And Methods	38
• Results	48
• Discussion	93
• Conclusion	110
• Recommendations	111
• Summary	112
• References	115
• Appendix	140
• Arabic summary	١

## Tist of Abbreviations

**ACA** Anterior Cerebral Artery

**ACWSI** Anterior Cortical Watershed infarction

**AF** Atrial Fibrillation

**AIS** Acute Ischemic Stroke

**ALT** Alanine Transaminase

**AST** Aspartate Transaminase

**BA** Basilar Artery

**BBB** Blood Brain Barrier

**BP** Blood Pressure

BUN Blood Urea Nitrogen

**CA** Calcium

**CCA** Common Carotid Artery

**CPP** Cerebral Perfusion Pressure

**CT** Computed Tomography

**DBP** Diastolic Blood Pressure

**DM** Diabetes Mellitus

**DNA** Deoxyribo Nucleic Acid

**DVT** Deep Venous Thrombosis

**DWI** Diffusion-Weighted Imaging

**DWI** Diffusion-Weighted Image

**DWSI** Deep Watershed Infarction

**ECAS** Extracranial Arterial Stenosis

**EEG** Electroencephalogram

**EF** Ejection Fraction

**END** Early Neurological Deterioration

**EPSS** European Progressing Stroke Study

SSS Scandinavian Stroke Scale

**NIHSS** National Institute of Health Stroke Scale

**EVT** Endovascular Treatment

**EXPRESS** Existing Preventive Stroke Study

**FLAIR** Fluid Attenuated Inversion Recovery

**FSE** Fast Spin Echo

GCS Glasgow Coma Scale

**HB** Hemoglobin

**HbA**<sub>1C</sub> Glycosylated Hemoglobin

**HDL** High Density Lipoprotein

**HS** Highly Significant

**HTN** Hypertension

IAT Intra Arterial Thrombolysis

ICA Internal Carotid Artery

ICAS Intracranial arterial Stenosis

ICU Intensive Care Unit

**IHD** Ischaemic Heart Disease

**INR** International Normalized Ratio

**IQR** Inter-Quartile Range

**K** Potassium

**LAD** Left Arial Diameter

**LDL** Low Density Lipoprotein

**LT** Left

MCA Middle Cerebral Artery

MI Myocardial Infarction

MRA Magnetic Resonance Angiography

MRI Magnetic Resonance Imaging

MRS Modified Rankin Scale

MT Mechanical Thrombectomy

MTT Mean Transit Time

NA Sodium

**NADPH** Nicotinamide Adenine Dinucleotide

Phosphate

NCSE Non Convulsive Status Epileptics

**ND** No Deterioration

NS Non Significant

**PCA** Posterior Cerebral Artery

**PCWSI** Posterior Cortical Watershed

**PLT** Platelets

**PSV** Peak Systolic Velocity

**PVEEG** Prolonged Video EEG

**PWI** Perfusion Weighted Image

**RBS** Random Blood Sugar

**RNA** Ribo Nucleic Acid

**ROS** Reactive Oxygen Species

**RT** Right

**rT-PA** Recombinant Tissue Plasminogen Activator

S Significant

**SAP** Stroke Associated Pneumonia

**SBP** Systolic Blood Pressure

**SD** Standard Deviation

SE Status Epilepticus

**sICH** Symptomatic Intracerebral Hemorrhage

TCD Transcranial Doppler

**TG** Triglycerides

TIA Transient Ischemic Attack

TLC Total Leucocytic Count.

**TOF** Time-Of-Flight

**TTP** Time To Peak

**UTI** Urinary Tract Infection

VA Vertebral Artery

WSI Watershed Infarction

# List of Tables

Table No.	Title	Page
1	Basic demographic data among 300 AIS patients.	48
2	Co-morbidities among 300 AIS patients	50
3	Baseline clinical and neurological data among 300 AIS patients.	51
4	Laboratory data among 300 AIS patients.	52
5	Echocardiography and Carotid Duplex data among 300 AIS patients.	53
6	Follow up clinical data among 300 AIS patients.	56
7	Follow up neurological outcomes among 300 AIS patients.	57
8	Comparison between the 2 groups as regards basic demographic data.	58
9	Comparison between the 2 groups as regards co-morbidities.	59
10	Comparison between the 2 groups as regards clinical and neurological data.	62
11	Comparison between the 2 groups as regards laboratory data.	64
12	Comparison between the 2 groups as regards	66
	Echocardiography and Carotid Duplex data.	
13	Comparison between the 2 groups as regards	67
	MRI data (Type of stroke).	

Table No.	Title	Page
14	Comparison between the 2 groups as regards	69
	MRA data.	
15	Comparison between the 2 groups as regards	71
	Follow up clinical outcomes (Causes of	
	END).	
16	Follow up imaging for patients with END.	72
17	Causes of END.	72
18	Comparison between the 2 groups as regards	75
	Follow up neurological outcomes.	
19	Relation between seasons and (3-month	78
	mRS) and END using Mann-Whitney's U	
	and Chi square tests	
20	Spearman's correlation analysis for some	80
	baseline Factors associated with NIHSS	
	change.	
21	Spearman's correlation analysis for some	85
	baseline Factors associated with MRS (3-	
	month).	
22	Logistic regression model for the Factors	92
	affecting END occurrence.	

## List of Figures

Figure No.	Title	Page
1	Summary of pathophysiological cascade in	12
	diabetic stroke	
2	proposed mechanisms by which	13
	hyperglycemia worsens stroke related brain	
	ingury	
3	Impact of collateral flow on clot lysis and	19
	reperfusion	
4	Imaging data in 3 patient showing clot	20
	progression	
5	Non contrast CT brain of showing malignant	23
	brain edema	
6	Subtype of hemorrhagic transformation	25
7	Mechanisms oh hypoxia in Ischemic Stroke	28
	Damage	
8	Reperfusion therapy in acute ischemic stroke	34
9	Digital subtraction angiography (DSA)	43
	showing Parts of major intracerebral arteries.	
10	Gender among 300 AIS patients.	49
11	MRI data (type of stroke) among 300 AIS	54
	patients	
12	Site of arterial disease among 300 AIS	55
	patients.	
13	Comparison between the 2 groups as regards	60
	duration of DM.	
14	Comparison between the 2 groups as regards	61
	AF.	

Figure	Title	Page
No.		
15	Comparison between the 2 groups as regards IHD.	61
16	Comparison between the 2 groups as regards SBB-1 and DBP-1.	63
17	Comparison between the 2 groups as regards uric acid.	65
18	Comparison between the 2 groups as regards Territorial strokes.	68
19	Comparison between the 2 groups as regards MCA stenosis or occlusion.	70
20	Comparison between the 2 groups as regards day-2 SBP and DBP.	72
21	Comparison between the 2 groups as regards day-3 SBP and DBP.	73
22	Comparison between the 2 groups as regards chest complications.	73
23	Comparison between the 2 groups as regardsday-2 and 3 NIHSS scores.	76
24	Comparison between the 2 groups as regards MRS (3-months).	77
25	Correlation between NIHSS change and Duration of DM.	81
26	Correlation between NIHSS change and AIS duration.	82
27	Correlation between NIHSS change and DBP-1.	82
28	Correlation between NIHSS change and NIHSS-1.	83

Figure No.	Title	Page
29	Correlation between NIHSS change and uric	83
	acid.	
30	Correlation between NIHSS change and RBS.	84
31	Correlation between NIHSS change and HbA1C.	84
32	Correlation between MRS (3-month) and age.	87
33	Correlation between MRS (3-month) and Duration of HTN.	87
34	Correlation between MRS (3-month) and Duration of DM.	88
35	Correlation between MRS (3-month) and DBP-1.	88
36	Correlation between MRS (3-month) and NIHSS-1.	89
37	Correlation between MRS (3-month) and TLC.	89
38	Correlation between MRS (3-month) and albumin.	90
39	Correlation between MRS (3-month) and RBS.	90
40	Correlation between MRS (3-month) and LAD.	91

## Early Neurological Deterioration in Acute Ischemic Stroke: potential Predictors, causes and relation to infarct growth

#### **Abstract**

**Background:** Worsening of acute stroke early in its course (within 48–72 h of its onset) is a common occurrence and has potentially serious short term and long term consequences. The incidence of early neurological deterioration (END) among hospitalized patients varies widely in different studies between 13% and 38%.

**Aim of the Work:** To define incidence and timing of END in relation to acute ischemic stroke (AIS) onset. To identify possible causes and predictors associated with END. To assess the relation between END and the patient functional level at three months post stroke.

**Patients and Methods:** Three hundred patients were recruited into this hospital prospective comparative study. Clinical history, laboratory indices, structural brain imaging, Magnetic Resonance Angiography (MRA) and Carotid Duplex ultrasonography were done. Patients were examined on NIHSS and Glasgow Coma Scale (GCS) in day 1, 2, 3 and patients with END did a follow up (MRI diffusion film or CT brain) at day4 or 5 and all patients were followed up by Modified Rankin scale (MRs) at three-month post stroke.

**Results:** Of the Three hundred patients included in the study, the incidence of END was 16.7%. The median NIHSS on admission was 9.25. END was associated with long duration of DM (P 0.012), IHD (p 0.015), AF (p 0.048), severe stroke (p 0.0044), low blood pressure on admission (p 0.0079), high uric acid (p 0.033) and MCA occlusion (p 0.0007). END was associated with significant increase in MRS at 3 month (p<0.0001) and mortality rate (44% vs 4.4). Patients with END are more prone for aspiration pneumonia (p 0.0001) and hemorrhagic transformation.

**Conclusion:** Early neurological deterioration is a frequent complication after acute stroke, with a poor short-term prognosis. This study provides that hyperglycemia, hyperuricemia and cardiac disease (IHD and AF) may increase the risk of END.

**Keywords:** Early Neurological Deterioration, Acute Ischemic Stroke.

Worsening of acute stroke early in its course (within 48– 72 h of its onset) is common and has potentially serious short term and long term consequences for the patient (Thanvi et al., 2008). Various terms, such as "progressive stroke", "stroke in evolution", and "stroke in progression" have been used to describe this worsening (Sumer et al., 2003). Now most commonly termed early neurological deterioration (END) (Helleberg et al., 2014).

In one of the earlier studies, neurologic worsening was determined to be present if worsening of the neurologic condition, including consciousness level, was observed by trained neurologists and nurses at and after admission to the stroke unit (Yamamoto et al., 1998).

END was defined in the European progressing stroke study (EPSS) as any significant neurological deterioration from baseline to 72 hours (Brichel et al., 2004).

A significant neurological deterioration was primarily defined as a decrease in the Scandinavian stroke scale (SSS) items score for consciousness, speech, gaze, arm, or leg by at least 2 points. Consciousness was given precedence over the other signs (Brichel et al., 2004).