VALUE OF THROMBOPOIETIN LEVEL AND PLATELETS SIZE IN PATIENTS WITH ACUTE ISCHEMIC STROKE

Thesis

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in Clinical and Chemical Pathology

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Dedication

To my Parents, to whom I will never find adequate wordsto express my gratitude.

To my Father In Law, for his continuous support during this work.

To my Wife, for her kind and loving help.

And finally to my Daughter, my small angel and the gift of ALLAH

I Love You All & Thank You


وأنزل الله عليك
الكتاب والحكمة
وعلَّمَكَ مَا لَمْ تَكُن
تَعْلَمُ وكَانَ فَضْلُ
اللَّهِ عَلَيْكَ عَظِيماً
صدق الله العظيم
سورة النساء الآية
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List of Abbreviations

ADP	Adenosine di-phosphate
APS	Antiphospholipid syndrome
ATP.....	Adenosine tri-phosphate
c-AMP	Cyclic adenosine monophosphate
c-GMP	Cyclic guanosine monophosphate
CT	Computed tomography
CTA	C.T arteriogram
DVT	Deep venous thrombosis
ECG	Electrocardiogram
G.CSF	Granulocyte colony-stimulating factor
GM.CSF	Granulocyte-macrophage colony-stimulating factor
GP	Membrane glycoprotein
IL-3.....	Interleukin 3
IL-6.....	Interleukin 6
IP3	Inositol 1,4,5 – trisphosphate
IQR	Interquartile range
IV	Intravenous
LA	Lupus antibody
LMNL	Lower motor neuron lesion
MCV	Mean corpuscular volume
MGDF	Megakaryocyte growth and development factor
MPV	Mean platelet volume
MRA	MR arteriogram

List of Abbreviations (Cont…)

MRI ..... Magnetic resonance imaging

PDGF ..... Growth factors platelet - derived growth factor

PF ..... Platelet factor

PGI ..... Prostaglandin inhibitors

R ..... Pearson's correlation

rs ..... Spearman's rank correlation

rtPA ..... Recombinant tissue plasminogen activator

SD ..... Standard deviation

STAT ..... Signal Transducer and Activator of Transcription

TFPI ..... Tissue factor pathway inhibitor

TPO ..... Thrombopoietin

TxA 2 ..... Thromboxane A2

UMNL ..... Upper motor neuron lesion

VEGF ..... Vascular endothelial growth factor

VWF ..... Von Willebrand Factor

5 – HT ..... 5 - hydroxtryptamine

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INTRODUCTION

Ischemic stroke is a common cerebrovascular disorder associated with increased long term mortality, residual physical, cognitive and behavioral impairments, recurrence, and increased risk of other types of vascular events ***(Cordnnier and Leys, 2008).***

Several factors are known to increase the liability to stroke. The most important of these are hypertension, heart disease such as atrial fibrillation, diabetes mellitus, cigarette smoking, and hyperlipidemia ***(Victor et al., 2009).***

Platelets have essential role in the consistence of ischemic Stroke by developing intravascular thrombosis after the rupture of an atherosclerotic plaque ***(Sahin Balcik et al., 2012)***. Platelet size, detected by mean platelet volume (MPV) is a marker and possible determinant of platelet function; large platelets being potentially more reactive Although platelets are incapable of de novo problem synthesis, they are very active metabolically and respond rapidly to vascular injury or trauma by undergoing a series of reactions (adhesion, release of granular contents, shape change and aggregation) which ultimately result in the formation of a platelet-fibrin plug ***(Renoy, 2009).***Platelet size is also found to be elevated in individuals with hypertension and diabetes mellitus***(Pathansali et al., 2001),*** both conditions that predispose to the development of vascular disease ***(Renoy, 2009).***

The process of platelets proliferation and maturation, megakaryopoiesis, depends on early and late acting hematopoietic Growth factors. Thrombopoietin, also known as megakaryocyte growth and development factor (MGDF), is the most critical cytokine regulator of megakaryopoiesis***(Balcik et al., 2012).*** In humans, it is encoded by the *TPO* gene. Thrombopoietin is a glycoprotein hormone produced mainly by the liver and the kidney. It stimulates the production and differentiation of megakaryocytes, the bone marrow cells that fragment into large numbers of platelets ***(Kaushansky, 2006).***

Previous studies have shown higher MPV levels among patients with stroke, myocardial infarction and accompanying diseases which cause vascular risk factors such as diabetes mellitus, hypertension, and hyperlipidemia ***(Kurabayashi et al., 2000)*** however, some studies did not observe such effect ***(Tekbas et al., 2011).*** There is few available data assessing the TPO level in patients with acute ischemic stroke ***(Balcik et al., 2012).***

AIM OF THE WORK

The purpose of this prospective study is to investigate the value of platelet activity determined by the mean platelet volume (MPV) and Thrombopoietin (TPO) level in patients with acute cerebral ischemic stroke.

Chapter (1)

OVERVIEW ON STROKE

I-Physiological consideration

The adult brain, which weighs about 1500 grams or 2% of the total body weight, requires an uninterrupted supply of 150 grams of glucose and 72 litre of oxygen every 24 hours, accounting for 20% of the total body oxygen consumption and blood supply ***(Charles et al,. 2011).***

As the brain does not store these substances, dysfunction results after only a few minutes of deprivation when either the oxygen or the glucose content is reduced below critical levels ***(Philip et al,. 2007 and Luigi et al,. 2011).***

In the resting state, each cardiac contraction delivers about 70 ml of blood into the ascending aorta, 10 to 15 ml are delivered to the brain. Every minute, about 350 ml flows through each internal carotid artery and 100 to 200ml through the vertebrobasilar system to provide a normal total cerebral blood flow of 50-60 ml/minute per 100 gm of the brain ***(Alexander et al., 2010 and Leonardo 2008).***

II-Stroke definition

Stroke is a disease that affects the blood vessels supplying the brain with interruption of blood flow and thus oxygen delivery

to a certain point of the brain with rapid loss of brain function. The area of the damaged brain tissue is called infarct ***(Tatjana and Ralph 2012 and Leonardo 2008).***

III-Types of stroke

Strokes can be classified into two major categories: ischemic and haemorrhagic ***(Andrew et al., 2008 and Tarazona et al., 2010).***

Ischemic strokes are those that are caused by interruption of the blood supply while haemorrhagic strokes are the ones which result from rupture of a blood vessel or abnormal vascular structure ***(Anna and Christine 2010, Conossen et al., 2010).*** About 87% of stokes are caused by ischemia and the remainder by haemorrhages. Some of haemorrhages develop inside areas of ischemia and are called haemorrhagic transformation ***(Antonio et al., 2012 and Mariylin et al., 2009).***

Ischemic stroke is divided into 3 main categories:

1. Thrombotic strokes: occur when a clot (thrombus) forms within a brain blood vessel and blocks blood flow to that area of the brain ***(Bamford et al., 1991& Kate 2009).***Thrombotic strokes cause about 70-80 % of ischemic strokes and about 60% of all strokes ***(Ran et al., 2011).***

   There are two types of thrombotic stroke.

- Large vessel thrombosis: which occurs in large arteries and represents the most common cause of thrombotic strokes ***(Maria and Maria, 2011).***
- Small vessel thrombosis: which occurs when blood flow is blocked to a small arterial vessel.

2. Embolic strokes: occur when a blood thrombus breaks loose in some part of the body such as the heart, travels to and lodges in a brain artery ***(Robert and Heinrich, 2011).*** Most embolic strokes originate from the heart, aorta, carotid or vertebral arteries ***(Harold et al., 2010).*** Embolic strokes account for about 15-20% of all strokes ***(Cnossen et al., 2010).***

3. Systemic hypo perfusion: occurs during severe heart attack, heart arrhythmias or extreme blood loss ***(Rima and Jose, 2008).*** Hypo perfusion is less common than thrombosis or embolism as a cause of stroke ***(Danillo et al., 2013, kazumi et al., 2007).***

IV-Stroke epidemiology

- Stroke is the third most common cause of death worldwide ranking behind diseases of the heart and all forms of cancers ***(Westover et al., 2007).***
- It accounts for 1 of every 16 deaths and causes of deaths every 3 to 4 minutes in the United States. Each year 700,000 people suffer stroke, five hundred thousand of