



بسم الله الرحمن الرحيم

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Value of C-reactive Protein Level to Distinguish between Ischemic and Hemorrhagic Stroke

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

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List of Abbreviations

Abb.	Full term
<i>ACA</i>	<i>Anterior cerebral artery</i>
<i>ACoA</i>	<i>Anterior communicating artery</i>
<i>ANA</i>	<i>Antinuclear antibodies</i>
<i>aPTT</i>	<i>Activated partial thromboplastin time</i>
<i>ASA</i>	<i>American stroke association</i>
<i>ATACH</i>	<i>Acute Cerebral Hemorrhage</i>
<i>AVM</i>	<i>Arteriovenous malformation</i>
<i>BBB</i>	<i>Blood-brain barrier</i>
<i>BP</i>	<i>Blood pressure</i>
<i>CAA</i>	<i>Cerebral amyloid angiopathy</i>
<i>CMBs</i>	<i>Cerebral microbleeds</i>
<i>CPP</i>	<i>Cerebral perfusion pressure</i>
<i>CRP</i>	<i>C-reactive protein</i>
<i>CRT</i>	<i>Cognitive rehabilitation therapy</i>
<i>CSF</i>	<i>Cerebrospinal fluid</i>
<i>CT</i>	<i>Computerized tomography</i>
<i>CTA</i>	<i>CT angiogram</i>
<i>CVD</i>	<i>Cardiovascular diseases</i>
<i>DSA</i>	<i>Digital subtraction angiography</i>
<i>DVST/CVT</i>	<i>Dural venous sinus (or cerebral vein) thrombosis</i>
<i>ED</i>	<i>Emergency department</i>
<i>ENLS</i>	<i>Emergency neurological life support</i>
<i>ESR</i>	<i>Erythrocyte sedimentation rate</i>
<i>FAST</i>	<i>Acute Hemorrhagic Stroke Treatment</i>
<i>FFP</i>	<i>Fresh frozen plasma</i>
<i>GCS</i>	<i>Glasgow coma scale</i>
<i>GRE</i>	<i>Gradient echo</i>

List of Abbreviations (Cont...)

Abb.	Full term
<i>HRT</i>	<i>Hormone replacement therapy</i>
<i>HU</i>	<i>Hounsfield units</i>
<i>IA</i>	<i>Intra-arterial</i>
<i>IBD</i>	<i>Inflammatory bowel diseases</i>
<i>ICH</i>	<i>Intracranial hemorrhage</i>
<i>ICP</i>	<i>Intracranial Pressure</i>
<i>IgG</i>	<i>Immunoglobulin G</i>
<i>IL-1β</i>	<i>Interleukin-1β</i>
<i>IL-6</i>	<i>Interleukin-6</i>
<i>IL-8</i>	<i>Interleukin-8</i>
<i>INTERACT</i>	<i>Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial</i>
<i>IVH</i>	<i>IntraVentricular Hemorrhage</i>
<i>MAC</i>	<i>Membrane attack complex</i>
<i>MCA</i>	<i>Middle cerebral artery</i>
<i>MDCTA</i>	<i>Multidetector CT angiography</i>
<i>MISTIE</i>	<i>Intracerebral Hemorrhage Evacuation</i>
<i>MRI</i>	<i>Magnetic resonance imaging</i>
<i>nCRP</i>	<i>Native CRP</i>
<i>NO</i>	<i>Nitric Oxide</i>
<i>NPM-SAH</i>	<i>Non-perimesencephalic SAH</i>
<i>oxLDLs</i>	<i>oxidized low-density lipoproteins</i>
<i>PCA</i>	<i>Posterior cerebral artery</i>
<i>PCAs</i>	<i>Posterior cerebral arteries</i>
<i>PCh</i>	<i>Phosphocholine</i>
<i>PCoA</i>	<i>Posterior communicating artery</i>
<i>PEG</i>	<i>Percutaneous endoscopic gastrostomy</i>
<i>PICA</i>	<i>Posterior inferior cerebellar artery</i>
<i>PT</i>	<i>Prothrombin time</i>

List of Abbreviations (cont...)

Abb.	Full term
<i>RCVS</i>	<i>Reversible cerebral vasoconstrictive syndrome</i>
<i>rFVIIa</i>	<i>Recombinant activated factor VII</i>
<i>rt-PA</i>	<i>Recombinant tissue plasminogen activator</i>
<i>SAH</i>	<i>Subarachnoid hemorrhage</i>
<i>SBP</i>	<i>Systolic blood pressure</i>
<i>SLE</i>	<i>Systemic lupus erythematosus</i>
<i>STICH</i>	<i>Surgical Trial in Intracerebral Haemorrhage</i>
<i>TNF-α</i>	<i>Tumor necrosis alpha</i>
<i>WBC</i>	<i>White blood cell</i>

INTRODUCTION

Stroke is considered as a life threatening condition in neurological patients. It is one of the leading causes of morbidity and mortality worldwide, as cerebrovascular accidents rank first in the frequency and importance among all neurological disease (*Roudbary et al., 2011*).

Spontaneous ICH accounts for approximately 20% of all strokes, and it is characterized by high rates of mortality and residual disability among survivors (*Lattanzi et al., 2017*).

Low- grade inflammation is increasingly recognized as a key player in the pathophysiology underpinning many different medical conditions. Serum biomarkers related to increases in systemic inflammatory activity are significant predictors of cardiovascular diseases (CVD) and mortality (*Guarner et al., 2015*).

C-reactive protein (CRP) is a glycoprotein produced by the liver, which is normally absent from the blood in the presence of acute inflammation causing tissue destruction within the body stimulates CRP production, it typically rises within 6 hours of the start of inflammation, allowing the inflammation to be confirmed (*Ridker et al., 2008*).

Notably, over recent decades CRP has been the focus of an intense investigation to explore its role in the setting of intracerebral

hemorrhage (ICH) and currently is proposed as a risk assessment tool and prognostic marker (*Di Napoli et al., 2018*).

The serum CRP concentration has close associations with the risk of coronary heart disease, ischemic stroke, and vascular mortality (*Kaptoge et al., 2010*).

Several studies have assessed the value of CRP in the very early phases of stroke as a prognostic factor of functional outcome. Many of these studies evaluated only the relation between CRP and mortality instead of functional outcome. The findings were inconclusive, some found a positive association but others were found negative correlation (*Topakian et al., 2008*).

There is no evidence providing a clear relationship with the risk of ICH. In the last decade, a number of epidemiological studies across multiple ethnicities have been conducted, but none demonstrated a meaningful link between circulating CRP levels and ICH risk (*Di Napoli et al., 2018*).

Verification of the role of CRP as an early prognostic factor of functional outcome after ischemic stroke may be of clinical importance, because it is an easily measured and readily available inflammatory marker.

AIM OF THE WORK

To detect the value of serum CRP level in differentiation between ischemic and hemorrhagic stroke.

Chapter 1**ISCHEMIC STROKE**

Stroke is the third leading cause of mortality in the United States. Of the approximately 700,000 strokes occurring each year, about 550,000 are first strokes. About 400,000 strokes are ischemic. Stroke is the leading cause of adult disability with more than 4 million stroke survivors in the United States alone. Approximately 90% of stroke survivors are left with some residual deficit (*Alkhouli et al., 2019*).

Pathophysiology

Stroke is defined as an “acute neurologic dysfunction of vascular origin with sudden (within seconds) or at least rapid (within hours) occurrence of symptoms and signs corresponding to the involvement of focal areas in the brain” (*Feigin et al., 2018*).

The two main types of stroke are ischemic and hemorrhagic, accounting for approximately 85% and 15%, respectively. When an ischemic stroke occurs, the blood supply to the brain is interrupted, and brain cells are deprived of the glucose and oxygen they need to function (*Hickey, 2003*).

Ischemic stroke is a complex entity with multiple etiologies and variable clinical manifestations. Approximately 45% of ischemic strokes are caused by small or large artery

thrombus, 20% are embolic in origin, and others have an unknown cause (*Kurisu et al., 2018*).

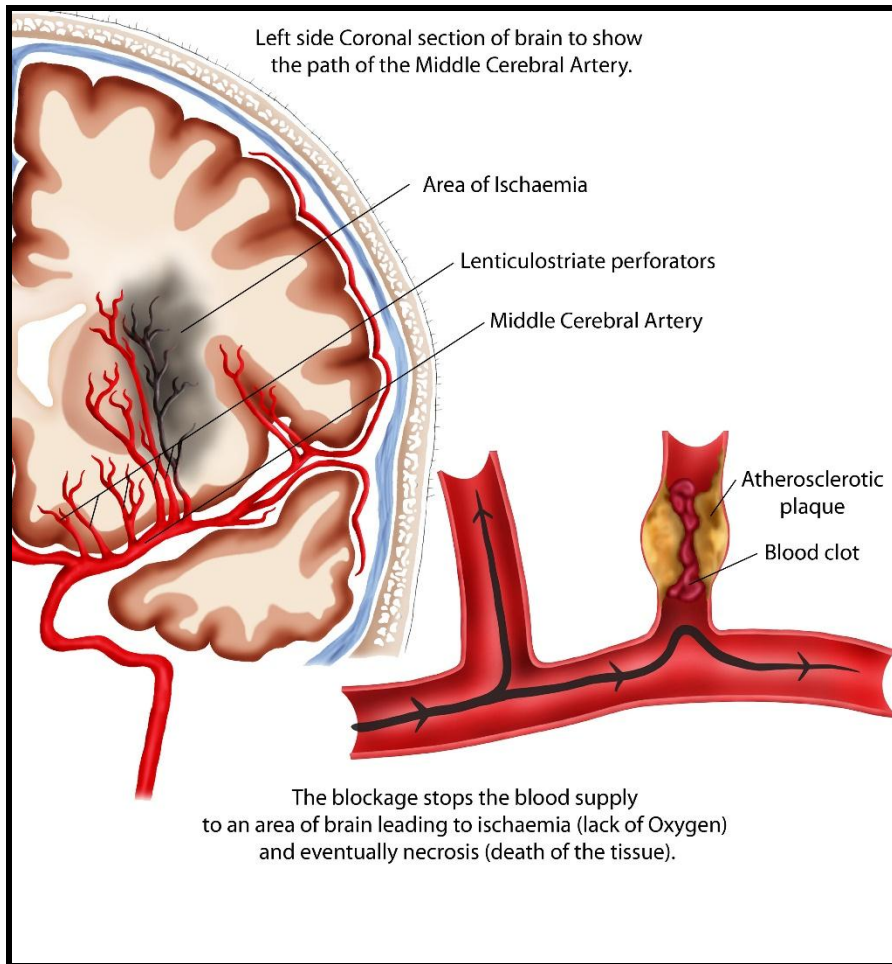


Figure (1): Pathology in Ischemic cerebral stroke
(*Bailey et al., 2012*)

Thrombosis can form in the extracranial and intracranial arteries when the intima is roughened and plaque forms along the injured vessel. The endothelial injury (roughing) permits platelets to adhere and aggregate, then coagulation is activated and thrombus develops at site of plaque. Blood flow through the