

Stroke and pregnancy

**Essay submitted for partial fulfillment of master degree in
neuropsychiatry**

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LIST OF ABBREVIATIONS

a PTT	Activated partial thromboplastin time
ACAs	Anticardiolipin antibodies
ACE	Angiotensin converting-enzyme
ADAMTS13	A disintegrin and metalloprotease with thrombospondin type 1 motif, number 13
AFE	Amniotic fluid embolism
APA	Antiphospholipid Antibodies
APC	Activated protein C
AT1-AA	Angiotensin II type 1 receptor autoantibodies
AVM	Arteriovenous malformation
cAMP	Cyclic adenosine monophosphate
CBF	Cerebral blood flow
CPP	Cerebral perfusion pressure
CT	Computed tomography scan
CVT	Cerebral venous thrombosis
DIC	Disseminated intravascular coagulopathy
DSA	Digital subtraction angiography
DVT	Deep venous thrombosis
ECMO	Extracorporeal membrane oxygenation
ET	Essential thrombocythemia

ET-1	Endothelin-1
HELLP	Hemolysis, elevated liver enzymes, and low platelet count
HUS	Hemolytic uremic syndrome
ICA	Internal carotid artery
ICH	Intracerebral hemorrhage
IgG	Immunoglobulin G
INR	International normalized ratio
LMWH	Low-molecular-weight heparins
MAP	Mean arterial pressure
MI	Myocardial infarction
MMD	Moyamoya disease
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
MTHFR	Methylene tetrahydrofolate reductase
NIS	Nationwide Inpatient Sample
NO	Nitric oxide
PAI	Plasminogen activator inhibitor
PE	Pulmonary embolism
PRES	Posterior reversible leucoencephalopathy
PV	Polycythemia vera

RCVS	Reversible cerebral vasoconstriction syndromes
ROS	Reactive oxygen species
RPL	Recurrent pregnancy loss
rt-PA	Recombinant tissue plasminogen activator
RUPP	Reduced uterine perfusion pressure
SAH	Subarachnoid haemorrhage
sFlt-1	Soluble fms-like tyrosine kinase-1
TPR	Total peripheral resistance
TTP	Thrombotic thrombocytopenic purpura
TTP-HUS	Thrombotic thrombocytopenic purpura–hemolytic uremic syndrome
TX	Thromboxane
Va	Activated factor V
VIIIa	Activated factor VIII
VTE	Venous thromboembolism

Introduction

A stroke is the rapidly developing loss of brain function due to disturbance in blood vessels supplying blood to the brain. This can be due to ischemia caused by thrombosis or due to hemorrhage. As a result the affected area of the brain is unable to function, leading to inability to move one or more limbs on one side of the body, inability to understand or formulate speech or inability to see one side of the visual field. Stroke can be classified into two major categories; ischemic and hemorrhagic. Ischemia is due to interruption of the blood supply, while hemorrhage is due to rupture of blood vessels or abnormal vascular structure. 80% of strokes are due to ischemia and 20% are due to hemorrhage. Some hemorrhages develop inside areas of ischemia leading to hemorrhagic transformation **(Donnan et al., 2008)**.

Stroke symptoms typically start suddenly, over seconds to minutes, and in most cases don't progress further. The symptoms depend on the area of the brain affected. Some forms of stroke can cause additional symptoms; in intracranial hemorrhages, the affected area may compress other structures. Sudden onset face weakness, arm drift, and abnormal speech are the finding

most likely to identify a case of stroke. Loss of consciousness, headache and vomiting usually occur more often in hemorrhagic stroke. Risk factors for stroke include: advanced age, hypertension, previous stroke or transient ischemic attacks, diabetes, high cholesterol, cigarette smoking, hyperurecemia, homocysteinemia and atrial fibrillation. High blood pressure is the most important modifiable risk factor of stroke **(Goldstein and Simel., 2005).**

Stroke is a recognized complication of pregnancy, contributing to more than 12% of all maternal deaths. Pregnancy is associated with an increased risk of both ischemic and hemorrhagic strokes. The majority occurs in the third trimester or puerperium. Etiological factors important in pregnancy include: hypercoagulability due to maternal physiological changes, pre-eclampsia and eclampsia, cerebral venous sinus thrombosis, paradoxical embolism, postpartum cerebral angiopathy and peripartum cardiomyopathy. The management of stroke related to pregnancy should generally proceed as in the non - pregnant state, with special consideration of the pregnancy -specific causes outlined **(Treadwell et al., 2008).**

Pre-eclampsia is a pregnancy-specific multi-system disorder affecting 2-10 % of pregnancies: It is defined as a new onset of raised blood pressure with proteinuria after 20 weeks of pregnancy. Eclampsia is characterized by the new onset of seizures in a woman with pre-eclampsia. The association between eclampsia and cerebral hemorrhage has been recognized since 1881 and this is reported to be the most common cause of death in patients with eclampsia. The definitive treatment for pre-eclampsia and eclampsia is the delivery of the fetus and placenta. Hydralazine is the antihypertensive agent of-choice. Magnesium sulfate is the first line therapy for seizures **(James et al., 2005)**.

Post partum cerebral angiopathy belongs to a group of disorders termed reversible cerebral vasoconstriction syndromes. Post partum cerebral angiopathy usually occurs few days after delivery. Presenting features are sudden thunder clap headache, photo sensitivity, vomiting, altered consciousness, seizures and transient or permanent focal neurological symptoms. Vasoconstriction can cause a variety of focal deficits due to transient ischemia, cerebral infarction and intracranial hemorrhage. The process is self-limiting, however, cerebral hemorrhage, maternal death and

recurrence in subsequent pregnancies have all been reported (**Neudecker et al., 2006**).

Subarachnoid hemorrhage is the third leading cause of non-obstetric-related maternal death. Most cases of cerebral hemorrhage are due to ruptured cerebral aneurysm. The presenting features are thunder clap headache, vomiting, seizures, and reduced level of consciousness. Presentation in pregnancy may be confused with eclampsia and the diagnosis should be confirmed with neuroimaging or cerebrospinal fluid analysis. Surgical treatment after aneurysmal subarachnoid hemorrhage during pregnancy improves both maternal and fetal outcome. Endovascular techniques have been successfully demonstrated during pregnancy (**Shah., 2003**).

Pregnancy and puerperium carry an increased risk of cerebral venous thrombosis (CVT) with a fatality rate ranging from 4-36%. In the majority of patients symptoms develop within 3 weeks after delivery. Approximately 2% of strokes occurring during pregnancy can be attributed to venous thrombosis. Typical presenting features include: headache, disturbance of consciousness, focal neurological signs and seizures. A stroke like presentation has been described as a manifestation of cortical vein thrombosis.

CT imaging of the brain may show venous infarcts with or without hemorrhage. MRI studies may be useful in identifying CVT. The conventional treatment for cerebral venous thrombosis is anti coagulation. In general full heparinization is safe once 24 hours have elapsed since delivery. Warfarin therapy may be started 2-3 days after birth. Both heparin and warfarin are safe during breast feeding **(Canhao et al., 2005)**.

Peripartum cardiomyopathy (PPCM) is an established risk factor for cardioembolic stroke. PPCM is a disorder of unknown cause occurring in the peripartum period, characterized by symptoms of heart failure due to left ventricular systolic dysfunction in women without preexisting heart disease. The treatment follows that of heart failure unrelated to pregnancy with agents such as diuretic, angiotensin converting enzyme (ACE) inhibitors, antithrombotic for high risk thromboembolic conditions **(Crawford et al., 2004)**.

Investigation such as head CT involves exposure to ionizing radiation. The potential effects of ionizing radiation on the fetus include: death, malformation, growth retardation, mental retardation and cancer induction. The risk is assessed on the basis of dose of absorbed radiation,

if it less than 5000 mrad there is no additional risk factor to the fetus. MRI doesn't involve ionizing radiation, and no adverse effects on the developing fetus have been documented. Guidance from the American college of radiology suggests that pregnant patients can undergo MRI scanning (**Kanal et al., 2007**).

Aim of the Work

1. To review the risk factors and mechanisms of stroke related to pregnancy.
2. To review the management of different stroke types and their impact on pregnancy.