Stroke in pregnancy: incidence, investigations and management

Stroke can happen to anyone at any time, even new mothers.

Introduction

The term "stroke" is used to indicate damage to the brain caused by a vascular etiology.
Stroke is defined as a neurological deficit attributed to acute focal injury of the central nervous system by a vascular cause, including cerebral infarction, cerebral vein thrombosis (CVT), intracranial haemorrhage (ICH) and subarachnoid haemorrhage.

2 Types:
1-Haemprrhagic stroke occurs when a blood vessel ruptures and tissue is damaged by the resulting spread of blood into the brain parenchyma.

2-Ischaemic stroke occurs when blood flow to the brain is impaired and tissue dies. Causes of ischemic stroke include atherosclerotic disease, embolisms, thrombi and hypotension.

It is the second leading cause of death and third leading cause of adult disability,
one in six people at risk of experiencing a stroke in their lifetime.
In people under the age of 20 years and young and middle-aged adults (20–64 years) the proportion affected by stroke is increasing.
No longer be regarded as a disease of old age.
Incidence of 30 per 100 000 pregnancies(3x the incidence in nonpregnant female individuals aged 15–44 years).
Most strokes (90%) occur peripartum or in the 6 weeks following delivery.
Antenatal period incidence of 1.5 per 100 000 deliveries(UKOSS)

Overall risk of recurrence is 0.5% outside pregnancy
0-1.8 % in next pregnancy

The independent risk factors for stroke

Maternal age >35 years
Migraine
Gestational diabetes
Pre-eclampsia or eclampsia
Pre- existing hypertension
Case fatality rate ranging from 8.8% to 20.0%.
In haemorrhagic stroke of pregnancy is 13.9%,
Ischaemic stroke in pregnancy 3.4%
Residual disability is50% in haemorrhagic stroke &33%ischaemic stroke
ICH being the single greatest cause of maternal death from stroke
Incidence of pregnancy- associated stroke to be 10.2 per 100 000 deliveries.

Most strokes in the general population are **ischaemic (80–85%),** but in pregnancy, ischaemia, haemorrhage and venous thrombosis have a similar contribution to aetiology.

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19.9% per 100 000 pregnancies from non-haemorrhagic stroke (both arterial and venous thrombosis)
12.2 per 100 000 from haemorrhagic stroke.
In cerebral venous thrombosis :12.2/100 000 pregnancies
in ischaemic stroke 9.1 in cerebral venous thrombosis
12.2 in haemorrhagic stroke per 100 000 pregnancies.
The risk of CVT is increased by the physiological upregulation of clotting factors in pregnancy.

Pregnancy-specific conditions that further increase the hypercoagulability state include:
ovarian hyperstimulation syndrome
hyperemesis gravidarum
Pre-eclampsia.
Pro-thrombotic medical conditions in pregnancy, such as :
antiphospholipid syndrome
sickle cell disease
thrombotic thrombocytopenic purpura
haemolytic uraemic syndrome
mechanical heart valves
Cardiomyopathies, also increase the risk of ischaemic stroke.
Hypertensive disorders of pregnancy, including pre-eclampsia and eclampsia, increase the risk of haemorrhagic or ischaemic stroke and can be associated with posterior reversible encephalopathy syndrome and reversible cerebral vasoconstriction syndrome.
Amniotic fluid embolism is a rare, pregnancy-specific condition that has been associated with stroke.
A curable condition with timely intervention.

Investigation and management of acute stroke

In ischaemic stroke, time-sensitive thrombolysis and thrombectomy improves outcomes.

Clinical presentation, symptoms and signs of stroke
Stroke is a clinical syndrome characterised by rapidly developing symptoms, with signs of focal cerebral loss of function and no cause other than that of a vascular origin.
The symptoms and signs relate to the affected area of the brain
Obtain a good history from the patient or witness to identify the timing and sudden nature of symptom onset.

The onset of stroke is typically sudden, with focal symptoms and clinical deficits conforming to a vascular territory.

Symptoms include:
unilateral numbness or weakness of the face, arm or leg
dysphasia
hemianopia
cerebellar features, such as dysarthria and ataxia.

Non-focal symptoms –
Generalised weakness and/or sensory disturbance
light-headedness
brief loss of consciousness
urinary or faecal incontinence
confusion
tinnitus – are less likely to be caused by a stroke.

CVT is a diagnosis not to be missed, as it can result in both venous ischemic and hemorrhagic infarctions. The hemorrhage arises from the venous congestion as a result of backflow of blood from the occlusion of a major sinus. CVT often presents as a severe headache with symptoms of increased intracranial pressure, such as nausea and vomiting. Frequently, papilledema is present on physical exam.
CVT can be variable in its clinical presentation, with only 40% of patients presenting with typical stroke symptoms and signs a headache; drowsiness or confusion can also occur with deep vein occlusion of the thalamus.
The FAST campaign was created to promote public awareness of the symptoms and signs of stroke and to encourage rapid response.

Subarachnoid haemorrhage is a consequence of the bleed, rather than being caused by hypertension itself.
Severe intracranial bleeds can also be associated with a relative bradycardia. If a hypertensive patient is relatively bradycardic, this may lead to suspicion of an intracranial bleed, rather than a stroke.

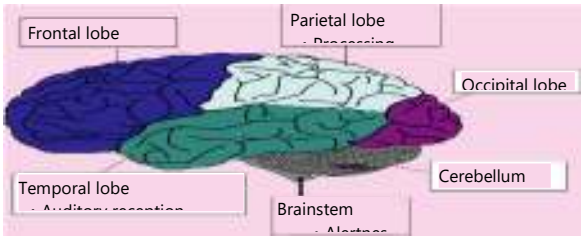

Figure 1. Brain anatomy and functions. Symptoms and signs of stroke relate to the affected area of the brain.

Clinically difficult to distinguish an intracerebral haemorrhage from an ischaemic stroke at the bedside.
Headache, nausea, vomiting and a depressed level of consciousness are more common in haemorrhagic strokes.
Systemic blood pressure tends to be higher in ICH than in acute ischaemic stroke (AIS); a relative bradycardia may also be seen in severe intracranial haemorrhages with associated raised intracranial pressure.

Seizures can occur following a stroke .

Rule of thumb in pregnancy is that **most new-onset seizures after 20 weeks of gestation and up to 2 weeks postnatally are caused by eclampsia** unless proven otherwise.
Importantly, focal neurological deficits are not typical of eclampsia(visual symptoms seen) .These include blurring of vision, diplopia, amaurosis fugax, photopsia, scotomata and homonymous hemianopia; could be caused by cortical blindness, serous retinal detachment, Purtscher-like retinopathy, central retinal vein occlusions and retinal or vitreous haemorrhages, which may occur as a complication of pre-eclampsia.

Imaging is necessary if there are focal neurological symptoms and signs or visual symptoms persist despite optimisation of blood pressure control.

History

Specific questions to ask when taking a history

- Where were you when you experienced the symptoms of stroke?
- What were you doing at the time?
- What did you first notice was wrong?
- When were you last free of symptoms?
- Then what happened?

- **The FAST campaign, outlining how to recognise symptoms of stroke**
- F – Face drooping
- A – Arm weakness
- S – Speech difficulty
- T – Time to call

Investigations and management of stroke
A brief history of time of onset, symptoms and premorbid status, along with potential contraindications to thrombolysis, is taken. Scores on the National Institutes of Health Stroke Scale (NIHSS; Table 1) and modified Rankin Scale should be recorded.

Imaging
Should be done promptly in pregnancy.
All patients with suspected AIS should have brain imaging on arrival to hospital.

Non-contrast CT-In most cases, non-contrast computed tomography will provide the necessary information to make decisions about acute management, such as intravenous thrombolysis.
ICH is a contraindication to thrombolysis.Management is focused at maintaining haemostasis and correction of coagulopathy.Sometimes surgery has to be done if required.

CT angiogram-In anticipation of throbectomy when a large vessel occlusion is suspected.
Considered better in detecting higher degrees of cereberal arterial stenosis
Safe in pregnancy as less radiation exposure as compared to CT perfusion

Theoretical risk of fetal thyroid suppression so neonatal thyroid function tests indicated within 2 weeks of birth.
CT perfusion-more specific in detecting infarction and ischaemia of brain tissue.

CT -The most appropriate tool for initial rapid diagnosis as readily accessible.Fetal radiation exposure is <0.1 Gy not associated with higher risk of adverse event .

Combination of CT angiogram and CT perfusion -Offers most accurate assessment of site of occlusion ,infant core and salvageable brain tissue and collateral circulation.

MRI is the preferred first line investigation in pregnancy
It further distinguishes stroke subtypes and vascular imaging.
Potential hazards of MRI :theoretical biological damage ,tissue heating and potential damage to fetal ear
No harmful short or long term fetal effects at T 1.5 or less
On MRI white matter lesions are :
Hyper intense on T2
Hypo intense on T1
Gadolinium chelate may be used to enhance MRI studies .Only 0.01%
Remain in fetus after 4 hours;just traces persist after 24 hours.Well documented informed consent should be taken and extreme caution should be taken.

Investigations for underlying causes of stroke
Investigations for underlying causes of stroke in a young woman

Investigations	Risk factors
12-lead electrocardiogram	Atrial fibrillation, cardiac ischaemia
24-hour cardiac/Holter monitor	Atrial fibrillation
Prolonged cardiac monitor/ implantable loop recorder	Paroxysmal atrial fibrillation
Transoesophageal echocardiogram	Patent foramen ovale Patent foramen ovale
Transthoracic echocardiogram with 'bubble test'	
Full blood count, urea and electrolytes, liver function tests, uric acid, coagulation profile	Pre-eclampsia
Lipid profile Thrombophilia screening	Hypercholesterolaemia
Carotid and lower limb Dopplers	Antiphospholipid syndrome Inherited thrombophilias*
	Venous thromboembolism

Limited benefit of inherited thrombophilia screening in pregnancy.
**In presence of patent foramen ovale, to rule out paroxysmal thromboembolic event.

Management of stroke

"Time is brain" approach is adopted

Time-sensitive and reperfusion therapies are associated with improved functional outcomes.

Intravenous thrombolysis

Recombinant tissue plasminogen activator (rt-PA) significantly improves overall outcome when administered within 4.5 hours of onset

Risk of haemorrhagic stroke development is 2-6%

Though does not cross placenta but thortical risk of placental bleding and IUFD

Earlier intervention is proportionally beneficial

Contraindications to thrombolysis

Absolute contraindications

- Intracerebral haemorrhage
- Suspected subarachnoid haemorrhage, even if normal computed tomography
- Neurosurgery, head trauma within the last 3 months
- Systolic blood pressure >185 mmHg, diastolic blood pressure >150 mmHg
- History of ICH
- Known intracerebral arteriovenous malformation, neoplasm or aneurysms
- Active internal bleeding
- Suspected/confirmed endocarditis
- Known bleeding diathesis
- Platelets <100 000
- Heparin within 48 hours
- Current use of warfarin with

Table 2. Modified Rankin Scale

Score	Score description
0	No symptoms at all
1	No significant disability despite symptoms; able to perform all usual duties and activities
2	Slight disability; unable to perform all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

Relative contraindications

- Age >80 years

- National Institutes of Health Stroke Scale >25 and coma
- Multilobar infarction on CT
- Previous stroke within the last 3 months
- Diabetes mellitus and previous stroke
- Minor or rapidly improving stroke
- Major surgery or serious non-head trauma within 14 days
- Gastrointestinal or urinary tract haemorrhage within 21 days
- Seizure at stroke onset
- Recent arterial puncture at non-compressible site
- Recent lumbar puncture
- Post myocardial infarction pericarditis
- Pregnancy

Post-stroke thrombolysis care

- 24 hours of bedrest (may not be essential if very stable)
- Maintain O_2 saturations above 95%
- Maintain normal temperature; use paracetamol if >37.5°C
- Maintain blood glucose <10 mmol/l
- Deep vein thrombosis prophylaxis with intermittent pneumatic compression devices (as per the CLOTS-3 study)
- No arterial lines, nasogastric tubes or central lines for 24 hours
- No urinary catheter until at least 1 hour after infusion ends
- Avoid suctioning and careful mouth care
- No aspirin,clopidogrel ,dipyridamole or anticoagulants for 24 hours.
- Repeat CT in 24-36 hours
- Maintain hydration and nutrition
- Risk assessment and prevention of falls
- Stop rt-PA if neurological deterioration of 2 points on Glasgow eye/motor scale
- Observe for signs of systemic bleeding and stop rt-PA
- Monitor BP,stop rt-PA if for more than 5 minutes the systolic BP<100 or >180 mmHg and diastolic BP >105

  Observe for signs of anaphylaxis -stop rt-PA

Mechanical thrombectomy

Mechanical thrombectomy with stent retriever devices is superior to IV RFT-PA alone.Benefits if administered within 6 hours.
All eligible patients should be considered for clot retrieval and urgently referred to higher specialized centre;can be done upto 24 hours after onset of stroke.Appropriate in 10 % cases of AIS.
Thrombectomy plus standard care have better outcomes for disability at 90 days as compared to standard care alone.

Management of ICH

Haemostasis,correction of coagulopathy, thrombocytopenia and hyper/hypoglycaemia
BP control and VTE prophylaxis
Use anti-epileptic medication to treat seizures

Consider surgical decompression in cerebellar haemorrhage with deteriorating neurological function.

Management of Cereberal Venous Thrombosis(CVT)
Anticoagulation with LMWH or UH
If anticoagulation contraindicated or patient does not respond then thrombolysis should be considered
Patients with raised intracranial pressure can be treated with I/V mannitol and considered for decompressive Craniectomy.

Management of pre-eclampsia /eclampsia and PRES(Posterior reversible encephalopathy syndrome)
If pre-eclampsia is suspected, full blood count, liver function tests, urea and electrolytes and uric acid levels should be checked to rule out HELLP (haemolysis, elevated liver enzymes, low platelets) syndrome or thrombocytopaenia.

MgSO4 is well documented in treatment and prevention of eclampsia,as it raises threshold for seizures and decreases neuroinflammation
PRES is associated with PET/Eclampsia ,hypertension ,infection /sepsis,shock
Autoimmune disorders ,chemotherapy and massive blood transfusion.
Optimise BP by removing /treating suspected causative factors.
Deliver the baby in case of PET/Eclampsia
Most cases resolve on their own within days to weeks

Stroke Unit Care
Multidisciplinary unit with focused nursing care ,specialist medical treatment with specific protocols ,coordination of rehabilitation services and patient education.
Patients treated here are more likely to be alive ,independently living at their homes at 1 year after stroke.
Affects mother-baby bonding and feeding due to separation of mother and baby.

Secondary prevention strategies

Recurrent stroke -in 25-30% of all strokes
Aggressive BP management is central to secondary prevention
Gradual & sustained lowering of BP is recommended for ALL stroke patients
Increased maternal mortality with a systolic BP >160 & diastolic BP>100 mmHg mainly due to ICH
Aspirin therapy is recommended in AIS within 24-48 hours of onset.If patient receiving thrombolysis, for 24 hours delay aspirin (when ICH has been excluded)
In minor stroke or TIA ,dual anti-platelet therapy like aspirin and clopidogerel,started within 24 hours and continued over next 21 days may be beneficial for early secondary stroke prevention.Should be used cautiously as associated with higher risk of major haemorrhage at 90 days as compared to patients on aspirin alone

Clopidogerel is category B drug
Treatment should not be withheld due to pregnancy
Should be stopped 7-10 days before a scheduled delivery
If patient goes into spontaneous labour avoid neuroaxial anaesthesia

Patients with AIS/Atrial fibrillation ,then initiate oral anticoagulation within 4-14 days of onset of neurological symptoms
High intensity statin therapy should be initiated or continued as first line therapy in all patients with atherosclerotic cardiovascular disease if no contraindication exists

Smoking caesation is important for secondary prevention
The incidence of patent foramen ovale in general population is about 20%

Mode of delivery

MDT input- obstetrics, neurology, radiology, neurosurgery, cardiology, anaesthesiology and haematology
Individualized plan

Postpartum management
Highest risk period for VTE & Stroke
Continue anticoagulation for 6 weeks postpartum
MDT care
Factor V Leiden hetrozygosity and persistent Lupus anticoagulant are associated with increased risks of transient ischaemic attacks ,amaurosis fugax and ischaemic stroke.
Full thrombophilia screen at 6 weeks postnatal appointment
Brestfeeding is safe if patient is on aspirin,warfarin or LMWH

Contraception
Combined harmonal contraception is contraindicated
Progesteron only contraception can be considered
Use non-harmonal contraception

Pre-conception care
Individualized care for women with prior stroke
No specific secondary prevention strategy available
Closely monitor future pregnancies as high risk of recurrence.

obstetrics, neurology, radiology, neurosurgery, cardiology, anaesthesiology and haematology