

Stroke in pregnancy and puerperium

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Disclosures and specific domain

1. Nothing to disclose
2. Specific domain: to address diagnosis and treatment of stroke during pregnancy and puerperium



Introduction

- pregnancy and puerperium- female-specific stroke risk factor
- pregnancy-associated stroke : 18% of strokes in women <35 years
- stroke incidence - 25–34 cases / 100,000 deliveries

➤ 9x increased stroke rate at time of delivery

➤ 3x increased stroke rate in early postpartum period

Gear KE, Bushnell CD. Stroke and pregnancy: clinical presentation, evaluation, treatment and epidemiology. Clin. Obstetr. Gynecol. 2013; 56, 350–359.
Feske SK, Singhal AB. Cerebrovascular disorders complicating pregnancy. In: Continuum, Ed. American Academy of Neurology 2014. Continuum (Minneapolis Minn). 2014;20:80–99. Cordonnier C et al. Stroke in women — from evidence to inequalities. Nat Rev Neurol. 2017;13:521–32.
Miller EC et al. Risk of pregnancy-associated stroke across age groups in New York State. JAMA Neurol. 2016; 73:1461–467.

Significant increase in hormonal activity, significant cardiovascular, hemodynamic and coagulation changes

A. PHYSIOLOGICAL CHANGES IN CARDIOVASCULAR SYSTEM AND COAGULATION

Decrease in

- peripheral vascular resistance (35-40%)
- blood pressure (5-10mmHg)
- anticoagulants (protein S)
- fibrinolytic system (increase in PAI-1/PAI-2, decrease in tPA activity)

Increase in

- renal plasma flow and glomerular filtration rate (~50%)
- left ventricular wall thickness
- cardiac output (~45%)
- heart rate (20-25%)
- blood volume (~40%)
- red blood cell mass (~25%)
- vasomotor sympathetic activity
- baroreceptor sensitivity
- major coagulation factors (fibrinogen, factors VII, VIII, X and XII, vWF)



B. PREGNANCY COMPLICATIONS

- Hypertensive disorders of pregnancy: chronic hypertension, gestational hypertension, preeclampsia, eclampsia
- Gestational diabetes
- HELLP syndrome
- Hyperemesis gravidarum
- Cesarean section
- Postpartum infection
- Postpartum hemorrhage
- Blood transfusion
- DVT, pulmonary embolism

C. CHARACTERISTICS OF THE PREGNANT WOMAN

- Age, race
- Substance abuse: smoking, alcohol, illicit drugs
- Vascular and cardiac malformations: arteriovenous malformations, aneurysms, moyamoya, patent foramen ovale
- Genetic disorders: sickle cell trait, CADASIL
- Hematological disorders: anemia, thrombocytopenia, thrombophilia
- Heart disease: valvular heart disease, cardiomyopathy, heart failure, atrial fibrillation
- Rheumatoid diseases: SLE, antiphospholipid syndrome
- Other comorbidities: dyslipidemia, diabetes, migraine

Physiological changes in pregnancy

- hypercoagulable state- characteristic of pregnancy

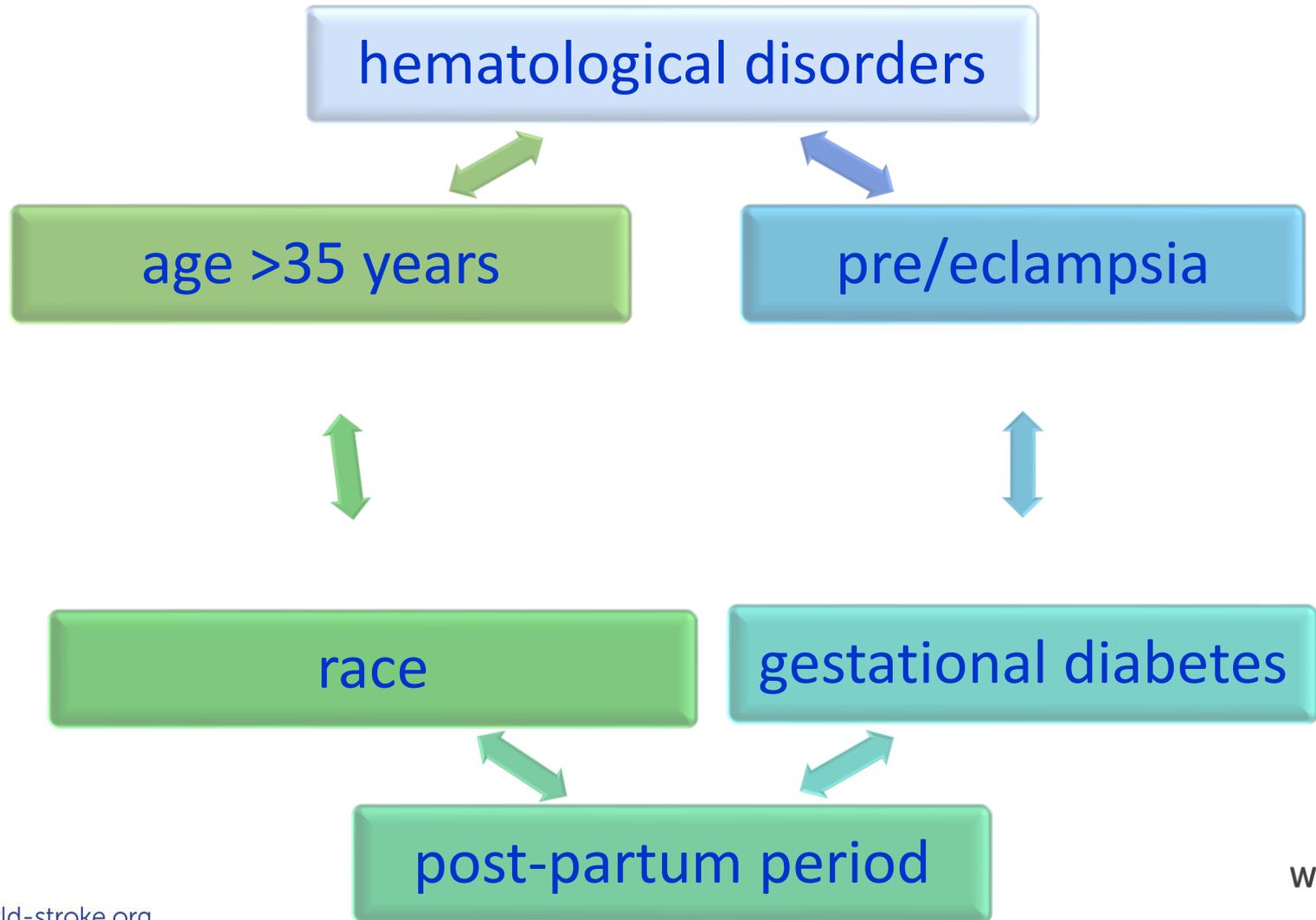
- marked increase in fibrinogen and factor VIII

- fibrinolytic activity is depressed during pregnancy and labour

- DVT- common complication (1-2% for vaginal delivery; 2-10% for C-section delivery)

-pulmonary embolism- potential complication

Risk factors for pregnancy related stroke





Age >35 years

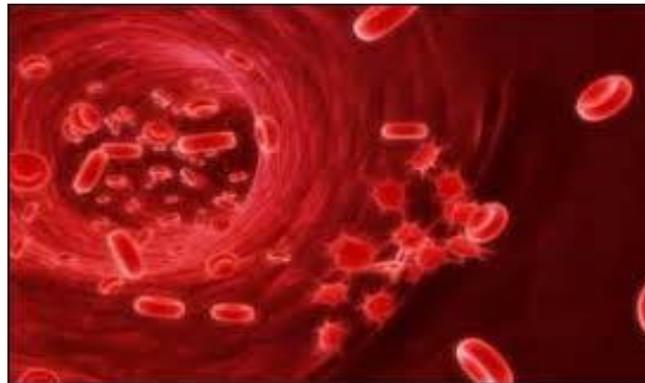
- risk of stroke generally increases with age

- risk increased dramatically among women aged 35-39 years
(58.1 per 100, 000 deliveries)

- highest risk among women > 40 years
(90.5 per 100,000 deliveries)

Hematological disorders

- anemia may result from blood loss that results in cerebral hypoperfusion
- thrombocytopenia
- Sickle cell disease





Preeclampsia/eclampsia

✓ new onset of hypertension and proteinuria/ new onset of hypertension and significant end-organ dysfunction with or without proteinuria after 20 weeks of gestation or postpartum in a previously normotensive patient

- increased risk associated with 1st pregnancy, adv. maternal age, black heritage and past diabetes and hypertension

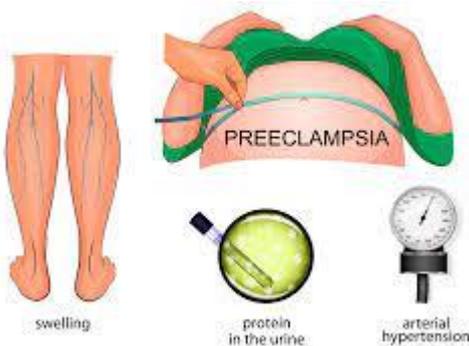
- occurs in 5 - 7 % of all pregnancies

- 1 out of 200 women who have preeclampsia, blood pressure becomes high enough to have seizures (eclampsia)



Preeclampsia and eclampsia

- strongest risk factors for stroke (24% - 48%)
- risk potentiated by genitourinary tract infection, hypertension, prothrombotic states and coagulopathies



ECLAMPSIA

New, otherwise unexplained, seizures in a pregnant lady
Typically 3rd trimester up to 48 hrs after delivery
Consider other causes (e.g. check BM)
Confirmed if hypertensive AND heavy proteinuria (catheterise and check)

ECLAMPSIA BOX in Resus Cupboard

ED MANAGEMENT

CALL OBSTETRICS, PAEDIATRICS & ANAESTHETICS
(baby will need delivered)
Turn on to left side to avoid aortocaval compression
Support airway and deliver high flow oxygen
IV access + bloods (FBC, U&E, LFT's, COAG)
Catheterise

MAGNESIUM

LOADING
4g IV bolus over 5 mins
8mils of 50% Mg²⁺ (4g) mixed with 12mils of saline (total 20mils)

then

INFUSION
1g per hour IV
20mils of 50% Mg²⁺ (10g) mixed with 30mils of saline (total 50mils)
Infuse at 5ml/hr

RECURRENT SEIZURES ON INFUSION
2g IV bolus over 5 mins
4mils of 50% Mg²⁺ (2g) mixed with 6mils of saline (total 10mils)

BP CONTROL

Sys >150, Dia >110, MAP >125

LOADING
Labetalol 50mg IV over 5mins
(Can be repeated x1)

then

INFUSION
Labetalol 50mg/hr
Draw 40mils of Labetalol (200mg) undiluted and infuse in syringe driver (10mls/hr)

Can increase every 15mins (max 200mg/hr) until BP controlled

SECOND LINE
Hydralazine 5mg IV bolus
Hydralazine infusion (10mg/hr)

FLUIDS

High risk for pulmonary oedema

FLUID RESTRICT
1ml/kg/hr (max 85mls/hr)
inclusive of infusions

URINE OUTPUT
Aim for around 25ml/hr

3rd STAGE

AVOID Ergometrine/Syntometrine
Can give Syntoclonon 10IU IM/IV

PARALYSE & VENTILATE IF FITS ARE PROLONGED OR RECURRENT

GRI ED 2017

Bushnell, C, Chireau M. Preeclampsia and stroke: risks during and after pregnancy. Stroke Res. Treat. 2011; 858134.
Kittner SJ et al. Pregnancy and the risk of stroke. N Engl J Med. 1996. 335:768-774
Salonen HR et al. Increased risks of circulatory diseases in late pregnancy and puerperium. Epidemiology.2001; Vol 12, 456-460.

Preeclampsia and Pregnancy: Recommendations

- women with chronic hypertension/ history of pregnancy-related hypertension should take **low-dose aspirin** from **12th week** of gestation until **delivery** (Class I Level A)
- control hypertension: methyldopa, labetalol, nifedipine (Class I Level A)

– Atenolol, ACEI, ARBS are contraindicated!



- consider screening women with preeclampsia 6 months to 1 year post-partum
- evaluate and treat other stroke risk factors (hypertension, obesity, smoking, dyslipidemia) (Class IIa, Level C)
- document preeclampsia as a stroke risk factor

Gestational Diabetes



- inability to process carbohydrates during pregnancy
- all pregnant women should be screened for gestational diabetes
- in many cases blood glucose levels return back to the pre-pregnancy state after delivery
- **diabetes is a risk factor for stroke**

Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes—2021

American Diabetes Association (ADA)

- lifestyle behavior change

- **Insulin** is the **preferred medication** for treating hyperglycemia in gestational diabetes mellitus



- **Metformin and glyburide should not be used as first-line agents, as both cross the placenta to the fetus!**

- other oral and noninsulin injectable glucose-lowering medications lack long-term safety data



Post-partum period

- risk of developing thromboembolic disease increased 6-8 weeks after delivery
 - complications result from injuries during delivery
 - greater risk after a cesarean section than after vaginal delivery
-
- extremely high relative risk due to decrease in blood volume/ rapid changes in hormonal status/ hemodynamic, coagulative or vessel-wall changes



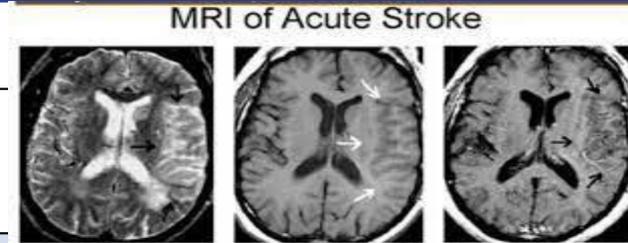
Stroke risk in puerperium

- women with preterm birth and small for gestational age infants have higher rates of cerebrovascular events
- increased risk for women with prior stroke
- absolute risk depends on presence of vascular risk factors

Bushnell C, McCullough LD, Awad IA et al. American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Council for High Blood Pressure Research. Guidelines for the prevention of stroke in women: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014 May;45(5):1545-88.

Diagnosis of stroke in pregnancy and puerperium

imaging done promptly



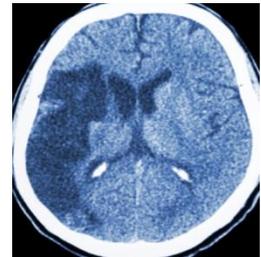
MRI - preferred first-line imaging modality in pregnancy

potential hazards: theoretical biological damage, tissue heating; and potential damage to the fetal ear

no harmful short- or long-term effects on fetus at <T1.5

CT- most appropriate tool for rapid diagnosis

- fetal radiation dose in non-contrast CT is 5% of naturally occurring background radiation dose during a full-term pregnancy (0.5–1.0 mGy)
- fetal radiation dose < 0.1 Gy not associated with increased risk of adverse effects
- fetal exposure - below regulatory limits with use of standard shielding of 0.5 mm lead equivalent



CT angiogram/CT perfusion



- ❖ no mutagenic or teratogenic effects in human pregnancies after administration of iodinated contrast
- ❖ theoretical risk of fetal thyroid suppression
- ❖ American College of Radiology recommends that iodinated contrast be used in pregnant women only when no alternative test is available

Contrast MRI with gadolinium chelate

- it traverses the placenta and may accumulate in the amniotic cavity, with contrast medium cycling through the fetal GIT and GUT

- 0.01% of the gadolinium dose remains present in the fetus after 4 hours

- American College of Radiology- gadolinium based agents be used with extreme caution and informed consent

European Stroke Organisation guidelines on stroke in women: Management of menopause, pregnancy and postpartum

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Abstract

Pregnancy, postpartum and menopause are regarded as periods women are more vulnerable to ischaemic events. There are conflicting results regarding stroke risk and hormone replacement therapy (HRT) during menopause. Stroke in pregnancy is generally increasing with serious consequences for mother and child; therefore, recommendations for acute treatment with intravenous thrombolysis (IVT) and/or mechanical thrombectomy (MT) are needed. The aim of this guideline is to support and guide clinicians in treatment decisions in stroke in women. Following the “Grading of Recommendations and Assessment, Development and Evaluation (GRADE)” approach, the guidelines were developed according to the European Stroke Organisation (ESO) Standard Operating Procedure. Systematic reviews and meta-analyses were performed. Based on available evidence, recommendations were provided. Where there was a lack of evidence, an expert consensus statement was given. Low quality of evidence was found to suggest against the use of HRT to reduce the risk of stroke (ischaemic and haemorrhagic) in postmenopausal women. No data was available on the outcome of women with stroke when treated with HRT. No sufficient evidence was found to provide recommendations for treatment with IVT or MT during pregnancy, postpartum and menstruation. The majority of members suggested that pregnant women can be treated with IVT after assessing the benefit/risk profile on an individual basis, all members suggested treatment with IVT during postpartum and menstruation. All members suggested treatment with MT during pregnancy. The guidelines highlight the need to identify evidence for stroke prevention and acute treatment in women in more vulnerable periods of their lifetime to generate reliable data for future guidelines.

In pregnant women with AIS, does IVT improve outcome as compared to no IVT?

- **Evidence-based recommendation**
no specific recommendation



- **Expert consensus statement**
 - pregnant women with disabling AIS, who otherwise meet eligibility criteria, can be treated with IVT after assessing individual benefit/risk profile



In women with AIS during pregnancy, does MT or IAT improve outcome compared to MT and/or IVT or IAT?

- **Evidence-based recommendation**
 - no specific recommendation



- **Expert consensus statement**



- pregnant women with disabling AIS, who otherwise meet eligibility criteria, can be treated with MT after assessing individual benefit/risk profile
- MT alone should be preferred over IVT or bridging therapy (IVT+MT)

In women with AIS during the postpartum period, does IVT improve outcome compared to no IVT?

- **Evidence-based Recommendation**

- no specific recommendation



- **Expert Consensus Statement**

- postpartum women with disabling IS, occurring at least 10 days after delivery, who otherwise meet eligibility criteria, can be treated with IVT with alteplase after individual assessment of benefit/ risk profile



In women with AIS during the postpartum period, does MT or IAT improve outcome compared to no MT and/or IVT or IAT?

Evidence-based Recommendation

- no specific recommendation



Expert Consensus Statement

-postpartum women with AIS, who otherwise meet eligibility criteria, might benefit from MT after individual benefit/risk profile assessment
- prefer MT alone over IVT or bridging therapy (IVT + MT) on individual basis



Conclusion

- team approach is essential
- planning is important
- management of these cases should be individualized
- future studies focusing on identification of mechanisms, prevention and management strategies for stroke during pregnancy and puerperium are needed

THANK YOU FOR YOUR KIND ATTENTION

