

Stroke Around Pregnancy; Protection and Prevention!

Jayasree Manikinda, Subhash Kaul

Department of Neurology, Krishna Institute of Medical Sciences, Secunderabad, Telangana, India

Abstract

As per recent studies, incidence of stroke is increasing in pregnant women. It is essential to be vigilant and well-versed in managing stroke in pregnancy, as both the mother and the baby are prone to stroke-related injury. In this viewpoint article, we have reviewed the current data from research publications on the incidence, prevalence, risk factors, and clinical presentation of stroke in pregnancy. Finally, we have discussed the plan of investigations and the current treatment guidelines for stroke in pregnancy.

Keywords: Management, pregnancy, stroke

INTRODUCTION

Stroke is a neurological emergency and a major cause of death and disability around the world.^[1] Although the risk of stroke among young women is low, pregnancy increases this risk particularly in the peripartum period.^[2] In recent years, the incidence of stroke in pregnancy and puerperium appears to be increasing due to rising rates of obesity, diabetes, and hypertension as well as the trend of delaying pregnancy. The incidence of pregnancy-related strokes including ischemic and hemorrhagic subtypes has recently been estimated to be approximately 34 in 100,000 pregnancies.^[3] The incidence of stroke is high in the third trimester and puerperium, in older women, and in those with hypertensive disorders in pregnancy.^[2,4,5] Peripartum stroke is the most common cause of serious long-term disability after pregnancy.^[6,7] Risk factors for stroke include hypertensive disorders of pregnancy, like preeclampsia and eclampsia, and also the pro-thrombotic state in pregnancy, which increases the risk of arterial and venous thrombosis.^[6]

EPIDEMIOLOGY

Although most of pregnancies have an uneventful course, one should be vigilant toward any new neurological symptoms like headache, blurred vision, giddiness, or weakness in any limb, particularly from the last trimester onward. The incidence of stroke in pregnancy and the postpartum period is approximately 11 to 34 per 100,000 deliveries, which is more frequent than in non-pregnant women (annual incidence, 10.7 per 100,000 women of reproductive age).^[4,8,9] Approximately, 10% of strokes are reported in the antenatal period, 40% are reported proximate to delivery, and 50% are reported in postpartum period and after discharge.^[4] Pregnancy and postpartum period together are associated with a major increase in the relative risk and a minor increase in the absolute risk of all types of stroke, with the highest risk in the puerperium.^[4,10-14] A review of female hospital discharges from central Maryland and Washington DC in 1988 and 1991 determined the magnitude of the effect of pregnancy (including spontaneous and induced

abortions) on stroke risk.^[10] The relative risk for cerebral infarction was 0.7 during pregnancy which increased to 8.7 in the postpartum period (within 6 weeks of live birth or stillbirth). The adjusted relative risk for intracerebral hemorrhage was 2.5 during pregnancy but increased to 28.3 in the postpartum period.^[10] Similar findings were reported in a recent study from France^[11] and also from the nationwide inpatient data analysis of all pregnancy-related discharges in the United States from 2000 to 2001.^[4]

Subarachnoid hemorrhage during pregnancy and postpartum period is usually related to an underlying aneurysm or vascular abnormality. Data from Germany showed an overall incidence of non-traumatic subarachnoid hemorrhage of 11.3 per 100,000 years.^[15] Intracranial hemorrhage can occur in preeclampsia and eclampsia^[16] and is the most common cause of death in women with preeclampsia.^[17]

According to Western data, the incidence of cerebral venous thrombosis (CVT) is approximately 12 per 100,000 deliveries, similar to ischemic stroke.^[18] The incidence and prevalence of CVT in India, however, are much higher.^[19] The third trimester and postpartum period is the highest risk period for CVT, similar to the time frame for the risk of venous thromboembolic events.^[18] The data from the Baltimore–Washington DC population-based study suggested that the

Address for correspondence: Dr. Subhash Kaul,
Block 3, 3rd Floor, C Wing, Neurology Department, KIMS Hospital, Ministers
Road, Secunderabad, Telangana, India.
E-mail: subashkaul@hotmail.com

Submitted: 02-Jun-2023 **Revised:** 17-Jul-2023
Accepted: 18-Jul-2023 **Published:** 09-Oct-2023

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

DOI: 10.4103/aian.aian_492_23

highest risk period for stroke is postpartum.^[1] However, a detailed analysis of the timing of ischemic stroke, hemorrhagic stroke, and subarachnoid hemorrhage in pregnancy showed that the majority of events occur at the delivery period, and the frequency decreases in the postpartum period.^[20]

PATHOPHYSIOLOGY

Pregnancy-related hormonal fluctuations cause wide-ranging physiologic changes. Blood volume expansion, variable vasculature distensibility, and pregnancy-associated hypercoagulable state increase a woman's risk of stroke during pregnancy and postpartum period.

Blood volume expansion starts during the first weeks of pregnancy, and the volume of whole blood continues to increase until it reaches levels 45% higher than pre-pregnancy levels.^[21] Blood volume expansion, combined with underlying vessel wall damage due to hypertension, preeclampsia, or eclampsia can increase the risk of stroke.^[22,23]

Cardiac output increases to 45% above the pre-pregnant state by 24th week of gestation.^[21] During labor, cardiac output can increase up to 60% to 80% above pre-pregnant levels.^[21] This increased cardiac output can exacerbate the structural changes around cardiac or major vessels abnormalities, increasing the risk of ischemic strokes.

Pregnancy is a hypercoagulable state. From around 11 weeks of gestation, there is an increase in factors I, VII, VIII, IX, X, XII, XIII, and von Willebrand factor; all of which promote coagulation.^[24] There is a decrease in levels of factors that inhibit coagulation, including protein S and protein C.^[22] These changes in clotting factors along with a decrease in fibrinolytic activity in pregnancy increase the risk of thrombosis and subsequently increase risk of ischemic strokes.^[25]

RISK FACTORS

Traditional risk factors

The risk factors for ischemic stroke in pregnancy also include those for non-pregnant patients, such as hypertension, smoking, atherosclerosis, heart diseases, hyperlipidemia, thrombophilia, infection, paradoxical embolism, and substance abuse. Additional risk factors include age over 35, migraine with aura, and black race.^[4] In particular, undetected heart diseases like rheumatic mitral stenosis, atrial septal defect (ASD), and patent foramen ovale (PFO) can decompensate during delivery and can lead to cardioembolic stroke. Pregnant women with sickle cell disease are also at increased risk for thromboembolic events.

Pregnancy-related risk factors

Risk factors related to ischemic stroke in pregnancy include pregnancy-induced hypertension,^[1,3] cesarean delivery, peripartum infection,^[4,26,27] and multiple gestations.^[28] Several conditions unique to pregnancy also can present as a stroke or a stroke-like event, which include preeclampsia/eclampsia,

postpartum cerebral angiopathy, and gestational trophoblastic disease. Amniotic fluid embolism is an important but rare cause of focal cerebral ischemia in pregnancy.^[29]

Risk factors for intracerebral hemorrhage in a US study of pregnant women were advanced maternal age, pre-existing and gestational hypertension, preeclampsia/eclampsia, pre-existing hypertension superimposed on preeclampsia/eclampsia, coagulopathy, tobacco abuse, and black race.^[12] Several other studies identified preeclampsia, eclampsia, and HELLP (hemolysis, elevated liver enzymes, low platelet counts) syndromes as the most common causes of ischemic and hemorrhagic strokes in pregnancy.^[10,11,16,30-32] Although intracranial hemorrhage is less common than ischemic stroke, mortality is higher. Retrospective data from a large UK study showed that mortality from intracranial hemorrhage was the single greatest cause of maternal death from stroke.^[33] In a review of approximately 60,000 deliveries, out of 11 hemorrhagic strokes, four were due to rupture of an AVM.^[33] In retrospective data of 154 women with spontaneous intracerebral hemorrhage during pregnancy, 23% were attributable to AVM rupture and 77% to aneurysmal rupture.^[34] It was noted that aneurysms and AVMs bled more frequently with increasing gestational age. Hemodynamic, angiogenic, and endocrine changes associated with pregnancy are considered to affect the growth and rupture of aneurysms in the gravid patient.^[35] Subarachnoid hemorrhage occurs as a consequence of aneurysmal rupture in pregnancy and is most frequent in the third (55%) and second trimesters (31%).^[34]

Risk factors for CVT may be the pregnancy induced thrombophilic tendency in some individuals, but in past anemia, increased coagulability of blood, slowing of the blood stream and dehydration aggravated by the local custom of withholding fluid intake in puerperium were thought to contribute to high prevalence of postpartum CVT in India.^[36] Pregnancy and the puerperium predispose to an increased risk of venous thrombotic events both in cerebral and non-cerebral territories. The average incidence of CVT during pregnancy and the puerperium range from one in 2500 to one in 10,000 deliveries in Western countries.^[37,38] The highest risk periods for CVT include the third trimester and the early postpartum period up to 2 weeks. Headache is the most common presenting feature and can precede other symptoms by many days. This can be followed by encephalopathy, focal signs, and/or seizures.

Causes of stroke/stroke-like events in pregnancy and postpartum period [Table 1]:^[39,40]

Posterior reversible encephalopathy syndrome

The cerebrovascular disturbance associated with preeclampsia and eclampsia is posterior reversible encephalopathy syndrome (PRES), which occurs as a result of impaired cerebrovascular autoregulation. Neurologic manifestations of this syndrome include headache, visual blurring, scotomas, cortical blindness, and seizures. Patients may progress to coma if untreated. Imaging of the brain shows vasogenic edema in the subcortical white matter of the parietal and occipital lobes.

Table 1: Causes of stroke/stroke like events in pregnancy and postpartum period

Hematologic causes	Vascular abnormalities	Pregnancy-related disorders
Essential thrombocythemia	Aneurysms	Preeclampsia, eclampsia
Sickle cell disease	AV malformations	HELLP syndrome
Thrombophilias (inherited or acquired)	Vasculopathy (moya moya disease, takayasu)	Peripartum cardiomyopathy
Thrombotic thrombocytopenia purpura	Cervical artery dissection	Amniotic fluid embolism
Cardiac causes	Cerebral venous thrombosis	Air embolism
Valvular abnormalities	Reversible cerebral vasoconstriction syndrome	Gestational lymphoblastic disease
Arrhythmias esp. atrial fibrillation	Posterior reversible encephalopathy syndrome	
Cardiomyopathy	Atherosclerotic cerebrovascular disease	
Infective endocarditis		
Atrial septal defect		
Patent foramen ovale		

A study from Mexico of 240 women with cerebrovascular complications in pregnancy like preeclampsia/eclampsia was associated with both ischemic stroke (23 of 64 cases [36%]) and intracerebral hemorrhage (22 of 40 cases [55%]).^[31] In another study from France comprising 31 pregnancy-related strokes, eclampsia accounted for 47% of cerebral infarctions and 44% of intracerebral hemorrhages.^[11]

Thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS)

TTP and HUS are acute syndromes with microangiopathic hemolytic anemia, thrombocytopenia, and abnormalities in multiple organ systems. Neurologic features include coma, confusion, seizures, transient ischemic attack, stroke, reversible posterior leukoencephalopathy syndrome, and headache.^[41] TTP and HUS must be distinguished from severe preeclampsia and the HELLP (hemolysis, elevated liver enzymes, low platelet counts) syndrome, which can also have a similar clinical presentation but are expected to resolve spontaneously within several days after delivery. The distinction between TTP, HUS, and severe preeclampsia or HELLP is important for therapeutic and prognostic considerations.^[41]

Hypercoagulability and antiphospholipid syndrome

Pregnancy is a hypercoagulable state due to the increase in resistance to activated protein C in the second and third trimesters, decreased protein S activity, increased factors II, VII, VIII, X, XII, and von Willebrand factor, increased fibrinogen, and increased activity of fibrinolytic inhibitors. The risk of stroke is increased in women with antiphospholipid syndrome (APS) or an inherited thrombophilia, such as factor V Leiden, the prothrombin gene mutation, or a deficiency of antithrombin, protein C, or protein S.

Antiphospholipid syndrome (APS) is pro-thrombotic condition especially in pregnancy, and even after treating women with aspirin and low molecular weight heparin for prior ischemic stroke, the rate of recurrence in pregnancy was 10.7% in one study.^[42]

Postpartum angiopathy

Postpartum angiopathy belongs to the group of reversible cerebral vasoconstriction syndromes (RCVS) with similar

clinical and radiographic features characterized by thunderclap headache and diffuse, segmental, reversible cerebral vasospasm.^[43] Clinical features include severe headaches and a combination of neurologic findings such as visual disturbances, hemiplegia, dysarthria, aphasia, numbness, ataxia, seizure, and encephalopathy.^[44] Vasogenic cerebral edema, ischemic stroke, intraparenchymal hemorrhage, subarachnoid hemorrhage, and even death have been reported.^[44,45] Narrowing of multiple segments of intracranial arteries can be seen on cerebral angiography. The angiographic changes are usually reversible, but may persist for days to months. Recent reports suggest that sympathomimetic drugs may increase the risk of postpartum angiopathy.^[46] In a retrospective study of 18 patients with postpartum angiopathy from three tertiary care centers, pregnancy was complicated by preeclampsia or eclampsia in 7 (39%).^[44]

Peripartum and other dilated cardiomyopathies

Peripartum cardiomyopathy is a rare disorder characterized by severe cardiac dysfunction at the end of pregnancy or within several months of delivery without any other cause for cardiac failure. Pre-existing dilated cardiomyopathy may also become obvious in pregnancy due to increased cardiac demands. This can lead to the formation of cardiac thrombi and subsequent embolism.^[47] This entity should be considered in women who present with new stroke and marked global impairment of cardiac function.

Carotid and vertebral artery dissection

Dissection of the carotid or vertebral artery is rare in women of childbearing age, but as per recent data, they occur more commonly in the postpartum period.^[48] Early diagnosis is important to prevent complete vessel occlusion and other thromboembolic sequelae. In a small case series of 27 pregnant women, advanced maternal age (mean age 34 years) appeared to be the only common risk factor. A recent European observational study of women with prior history of dissection did not suggest a high rate of recurrence in pregnancy.^[49]

Amniotic fluid embolism (AFE)

AFE occurs when there is a breach in the maternal-fetal physiological barrier during labor and leading to a

proinflammatory response. Definitive diagnosis is difficult as there are no universally accepted diagnostic criteria. Maternal stroke has been attributed to AFE. In an Australian study of approximately 600,000 deliveries, 20 cases of AFE were reported^[50]; out of which there were four cases of cerebral infarction.^[50] Hypercoagulable state resulting from AFE was considered to be the cause of stroke.

NEUROIMAGING

The main aim of evaluation is to determine the type of stroke that the patient is suffering from. Neuroimaging with non-contrast head computed tomography (CT) or magnetic resonance imaging (MRI) is necessary to differentiate between infarction and hemorrhage, regardless of cause.^[51] MRI in combination with MR venography is the most sensitive imaging modality for CVT.^[52]

The advantages of CT are widespread access and speed of acquisition. MRI with diffusion-weighted sequences is superior to CT for the diagnosis of early infarction. Imaging abnormalities of reversible posterior leukoencephalopathy syndrome are also best seen on MRI fluid-attenuated inversion recovery (FLAIR) sequences. Radiation exposure to the fetus with head CT, cerebral angiography, and chest radiography is approximately 50, 10, and 1 milliradians, respectively, which are considered safe.^[51]

WORKUP

Echocardiography and carotid Doppler studies should be done in all patients. Other evaluation includes electrocardiogram, complete blood count, metabolic profile, peripheral blood smear, HIV testing, urine drug screen, and antinuclear antibody.^[15] Laboratory evaluation for an inherited or acquired thrombophilia is indicated for women presenting with a cryptogenic ischemic stroke or transient ischemic attack during pregnancy.^[16] Thrombophilia screening should be done six weeks postpartum to exclude underlying thrombophilia

MANAGEMENT OF STROKE IN PREGNANCY AND POSTPARTUM PERIOD

Initial management of stroke in pregnant or postpartum women does not differ from that of non-pregnant patients, with care focused on adequate oxygenation, maintaining circulatory integrity and euglycemia.

Acute ischemic stroke

Early aspirin therapy is recommended for pregnant or postpartum women with acute ischemic stroke not receiving thrombolysis, intravenous heparin, or oral anticoagulants. This recommendation is in accordance with the current guidelines.^[53,54] All ischemic stroke patients should be considered for acute intravenous thrombolysis as per the current guidelines. According to a recent study of 338 pregnant or postpartum women and over 24,000 non-pregnant women ages 18 to 44 years with ischemic stroke, rates of reperfusion therapy were

similar in pregnant or postpartum women (40/338 [11.8%]) compared with non-pregnant women (2545/24,303 [10.5%]).^[55] Rate of symptomatic intracranial hemorrhage was higher in pregnant or postpartum women (3/40 [7.5%]) compared with non-pregnant women (66/2545 [2.6%]) but was not statistically significant.^[55] There was no significant difference between pregnant or postpartum women and non-pregnant women for rates of in-hospital death (2.1 versus 2.7%), discharge to home (75 versus 73%), or independent ambulation at home (74 versus 71%) after reperfusion therapy.^[55] The American Heart Association/American Stroke Association 2019 guidelines state that intravenous alteplase administration may be considered in pregnancy when the anticipated benefits of treating moderate or severe stroke outweigh the increased risks of uterine bleeding.^[54] Endovascular treatment with mechanical thrombectomy may be preferred over intravenous thrombolytic therapy for women with a high risk of hemorrhage, such as those with placenta previa or a history of obstetric hemorrhage.^[55]

Cerebral venous thrombosis (CVT)

For treatment of CVT in the pregnant and postpartum period, American Heart Association/American Stroke Association guidelines recommend low molecular weight heparin in full anticoagulant doses to be continued throughout pregnancy and low molecular weight heparin or a vitamin K antagonist (target INR of 2 to 3) to be continued for at least six weeks postpartum for a total duration of therapy of six months.^[18] Symptomatic management includes the control of seizures and intracranial hypertension.

Intracranial hemorrhage

Initial management of hemorrhagic stroke involves both medical and, if necessary, surgical intervention. Medical therapy should be targeted toward the control of hypertension and discontinuation of all antithrombotic medication, if any.^[56] Raised intracranial pressure should be controlled with osmotic diuretics and, if warranted, surgical evacuation of hematoma. Seizures can elevate intracranial pressure and so anti-epileptic medication may be needed. Ruptured intracranial aneurysms or AVMs in pregnant women are managed as they would be in non-pregnant patients. Endovascular coiling is preferred to surgical clipping for appropriately shaped aneurysms.^[57-60] Stable, unruptured asymptomatic aneurysms can be observed without intervention during pregnancy, whereas symptomatic or enlarging unruptured aneurysms can be treated.^[61] There are a few case reports of successful embolization of hemorrhagic AVMs during pregnancy via the endovascular approach, followed by surgical resection of the AVM.^[62,63]

SECONDARY PREVENTION STRATEGY IN PREGNANCY-RELATED STROKE

Secondary prevention of stroke depends on the type and underlying mechanism of stroke, whereas antithrombotic agents are the mainstay in ischemic stroke, removal of an underlying vascular anomaly if any has to be done in

hemorrhagic stroke. Strict control of vascular risk factors like hypertension, diabetes, hyperlipidemia, and smoking has to be ensured.

Aspirin, clopidogrel, and the combination of aspirin-extended-release dipyridamole are reasonable options for preventing recurrent non-cardioembolic ischemic stroke. An aspirin dose of 60 to 81 mg/day has been considered safe in pregnancy.^[64,65] Clopidogrel (pregnancy category B) and the combination of aspirin and dipyridamole (pregnancy category D) have not been evaluated in large numbers of patients or over prolonged periods of time, but can be administered in the postpartum period.

Anticoagulants are recommended to prevent stroke due to cardioembolic sources as well as due to antiphospholipid syndrome. The 2014 American Heart Association/American Stroke Association (AHA/ASA) guidelines recommend short- or long-term anticoagulation for patients with an inherited thrombophilia who have recurrent ischemic stroke of undefined origin, depending on the clinical and hematologic circumstances.^[66]

Stroke remote from term

When a stroke occurs in a pregnant woman who is <24 weeks of gestation, the stroke should be managed as dictated by the patient's clinical condition. Every effort should be made to protect the salvageable brain tissue, prevent medical complications (e.g., aspiration), control maternal physiologic factors that may worsen the stroke, such as blood pressure, and facilitate long-term physical rehabilitation. Pregnancy termination is an option if thrombolytic therapy is being considered.

As mentioned earlier, some women with ischemic stroke or cerebral venous thrombosis will require anticoagulation throughout the pregnancy.

Stroke near term

For women who have a stroke between 24 and 32 weeks gestation, antenatal glucocorticoids can be administered to accelerate fetal lung maturation. A multidisciplinary approach in consultation with neurology, neurosurgery, anesthesia, neonatology, and perinatology should take place to stabilize the mother and assess fetal status. As long as maternal and fetal well-being are not deteriorating, plans can be made to continue the pregnancy with a scheduled controlled delivery between 34 and 39 weeks gestation to optimize fetal outcome.

For pregnant women diagnosed with ischemic stroke or cerebral venous sinus thrombosis, anticoagulation with unfractionated heparin, LMWH, or antiplatelet therapy with aspirin should be considered in consultation with neurologists throughout the remainder of the pregnancy.

After 36 weeks of pregnancy, LMWH can be changed over to unfractionated heparin until a scheduled labor induction at 39 weeks can take place, and LMWH can resume in the postpartum period. Aspirin should be stopped within one

week of a planned delivery (i.e., induction of labor or cesarean delivery).

Blood pressure management

For pregnant women with a previous history of hemorrhagic or ischemic stroke, blood pressure control is vital. The antihypertensives considered safe in pregnancy are methyldopa, labetalol, and nifedipine. In women with intracranial hemorrhage, blood pressure should be controlled in relation to intracranial pressure. Intravenous labetalol and hydralazine can be safely used for acute blood pressure management.^[67] NICE recommends labetalol as first-line agent to treat hypertension in pregnancy and postpartum period.^[68]

Statins

Currently, statins are contraindicated in pregnancy due to higher rates of birth defects.^[69] For those already on statins, a short interruption for the duration of pregnancy is unlikely to cause any harm. Lipid levels should not be measured during pregnancy as interpretation of results is unreliable.^[69]

Anticoagulation

The 2012 ACCP guidelines recommend low molecular weight heparin (LMWH) instead of unfractionated heparin for prevention and treatment of venous thromboembolism during pregnancy or puerperium and recommend LMWH instead of vitamin K antagonist antenatally.^[64] The ACCP guidelines also recommend to continue anticoagulant therapy for at least six weeks postpartum and for a minimum total duration of three months.

As per ACCP guidelines, discontinuation of LMWH is recommended 24 h before induction of labor, cesarean section, or expected time of neuraxial anesthesia.^[70] Unfractionated heparin or LMWH can be restarted 4 to 6 h after vaginal delivery or 6 to 12 h after cesarean delivery, unless there was significant intraoperative or postpartum bleeding.^[70]

BREASTFEEDING

Breastfeeding is not contraindicated for postpartum women on unfractionated heparin or low molecular weight heparin. Similarly, nursing mothers can safely take warfarin as there is no evidence that it can exert an anticoagulant effect on the breastfed infant. A small fraction of iodinated or gadolinium contrast agents is secreted in maternal milk. Hence, women who require neurovascular imaging are advised to discontinue breastfeeding for 24 h after receiving intravenous contrast agents and discard milk expressed during that interval before starting normal breastfeeding.

PROGNOSIS

For women with previous pregnancy-related stroke, the recurrence rate during a subsequent pregnancy and postpartum period is low ($\leq 1\%$).^[71,72] This was demonstrated in a review of 441 women with a history of ischemic stroke (373 with arterial ischemic stroke and 68 with cerebral venous thrombosis);

after a follow-up of 5 years, there were 13 recurrent arterial ischemic strokes and no recurrent cerebral venous thrombosis.^[71] The risk of recurrence during pregnancy or the puerperium was 1.8%. Untreated ruptured brain arteriovenous malformations (AVMs) are prone to rebleed with or without pregnancy. In one study, the annual rate of hemorrhage recurrence in women with a brain AVM was approximately 31% in the first year following an initial hemorrhage and 6% in subsequent years.^[73] Hence, brain AVMs should be treated by surgical excision or endovascular embolization in women before deciding future pregnancy, if possible.

CONCLUSION

Stroke during pregnancy and postpartum period, though uncommon, has a significant maternal mortality morbidity often leading to long-term consequences. Hence, one should screen all pregnant women for major stroke risk factors and keep a close watch on them during the peripartum period. Pregnancy should not be a barrier to timely diagnosis, and appropriate treatment of stroke and multidisciplinary working can ensure favorable outcomes.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Bushnell C, McCullough LD, Awad IA, Chireau MV, Fedder WN, Furie KL, *et al.* Guidelines for the prevention of stroke in women: A statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014;45:1545-88.
- Ban L, Sprigg N, Abdul Sultan A, Nelson-Piercy C, Bath PM, Ludvigsson JF, *et al.* Incidence of first stroke in pregnant and nonpregnant women of childbearing age: A population-based cohort study from England. *J Am Heart Assoc* 2017;6:e004601. doi: 10.1161/JAHA.116.004601.
- Kremer C, Gdovinova Z, Bejot Y, Heldner MR. European Stroke Organisation guidelines on stroke in women: Management of menopause, pregnancy and postpartum. *Eur Stroke J* 2022;7:1-XIX. 10.1177/23969873221078696.
- James AH, Bushnell CD, Jamison MG, Myers ER. Incidence and risk factors for stroke in pregnancy and the puerperium. *Obstet Gynecol* 2005;106:509-16.
- Scott CA, Bewley S, Rudd A, Spark P, Kurinczuk JJ, Brocklehurst P, *et al.* Incidence, risk factors, management, and outcomes of stroke in pregnancy. *Obstet Gynecol* 2012;120:318-24.
- Treadwell SD, Thanvi B, Robinson TG. Stroke in pregnancy and the puerperium. *Postgrad Med J* 2008;84:238-45.
- Sells, CM, Feske, SK. Stroke in pregnancy. *Semin Neurol* 2007;37:669-78.
- Petiitti DB, Sidney S, Quesenberry CP Jr, Bernstein A. Incidence of stroke and myocardial infarction in women of reproductive age. *Stroke* 1997;28:280-3.
- Davie CA, O'Brien P. Stroke and pregnancy. *J Neurol Neurosurg Psychiatry* 2008;79:240-5.
- Kittner SJ, Stern BJ, Feeser BR, Hebel R, Nagey DA, Buchholz DW, *et al.* Pregnancy and the risk of stroke. *N Engl J Med* 1996;335:768-74.
- Sharshar T, Lamy C, Mas JL. Incidence and causes of strokes associated with pregnancy and puerperium. A study in public hospitals of Ile de France. *Stroke in Pregnancy Study Group. Stroke* 1995;26:930-6.
- Bateman BT, Schumacher HC, Bushnell CD, Pile-Spellman J, Simpson LL, Sacco RL, *et al.* Intracerebral hemorrhage in pregnancy: Frequency, risk factors, and outcome. *Neurology* 2006;67:424-30.
- Lanska DJ, Kryscio RJ. Risk factors for peripartum and postpartum stroke and intracranial venous thrombosis. *Stroke* 2000;31:1274-82.
- Kamel H, Navi BB, Sriram N, Hovsepian DA, Devereux RB, Elkind MS. Risk of a thrombotic event after the 6-week postpartum period. *N Engl J Med* 2014;370:1307-15.
- van Lieshout JH, Fischer I, Kamp MA, Donders ART, Cornelius JF, Steiger HJ, *et al.* Subarachnoid haemorrhage in Germany between 2010–2013: Estimated incidence rates based on a nationwide hospital discharge registry. *World Neurosurg* 2017;104:516-21.
- Martin JN Jr, Thigpen BD, Moore RC, Rose CH, Cushman J, May W. Stroke and severe preeclampsia and eclampsia: A paradigm shift focusing on systolic blood pressure. *Obstet Gynecol* 2005;105:246-54.
- Saving Lives Improving Mothers Care – Surveillance of maternal deaths in the UK 2012–14 and lessons learned to inform maternity care from the UK and Ireland confidential enquiries into maternal deaths and morbidity 2009–14.
- Saposnik G, Barinagarrementeria F, Brown R, Bushnell CD, Cucchiara B, Cushman M, *et al.* Diagnosis and management of cerebral venous thrombosis: A statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2011;42:1158-92.
- Dash D, Prasad K, Joseph L. Cerebral venous thrombosis: An Indian perspective. *Neurol India* 2015;63:318-28.
- Ros HS, Lichtenstein P, Bellocco R, Petersson G, Cnattingius S. Increased risks of circulatory diseases in late pregnancy and puerperium. *Epidemiology* 2001;12:456-60.
- Sanghavi M, Rutherford JD. Cardiovascular physiology of pregnancy. *Circulation* 2014;130:1003-8.
- Beal CC, Faucher MA. Stroke and pregnancy: An integrative review with implications for neuroscience nurses. *J Neurosci Nurs* 2015;47:76-84; quiz E71.
- Razmara A, Bakhadirov K, Batra A, Feske SK. Cerebrovascular complications of pregnancy and the postpartum period. *Curr Cardiol Rep* 2014;16:532.
- Blackburn ST. *Maternal, Fetal, and Neonatal Physiology: A Clinical Perspective*. 4th ed. Maryland Heights, MO: Elsevier; 2013.
- Brenner B. Haemostatic changes in pregnancy. *Thromb Res* 2004;114:409-14.
- Miller EC, Gallo M, Kulick ER, Friedman AM, Elkind MSV, Boehme AK. Infections and risk of peripartum stroke during delivery admissions. *Stroke* 2018;49:1129-34.
- Miller EC, Wen T, Elkind MSV, Friedman AM, Boehme AK. Infection during delivery hospitalization and risk of readmission for postpartum stroke. *Stroke* 2019;50:2685-91.
- Ros HS, Lichtenstein P, Bellocco R, Petersson G, Cnattingius S. Pulmonary embolism and stroke in relation to pregnancy: How can high-risk women be identified? *Am J Obstet Gynecol* 2002;186:198-203.
- Mas JL, Lamy C. Stroke in pregnancy and the puerperium. *J Neurol* 1998;245:305-13.
- Wabnitz A, Bushnell C. Migraine, cardiovascular disease, and stroke during pregnancy: Systematic review of the literature. *Cephalalgia* 2015;35:132-9.
- Cantu-Brito C, Arauz A, Aburto Y, Barinagarrementeria F, Ruiz-Sandoval JL, Baizabal-Carvallo JF. Cerebrovascular complications during pregnancy and postpartum: Clinical and prognostic observations in 240 Hispanic women. *Eur J Neurol* 2011;18:819-25.
- McDermott M, Miller EC, Rundek T, Hardy T. Preeclampsia: Association with posterior reversible encephalopathy syndrome and stroke. *Stroke* 2018;49:524-30.
- Skidmore FM, Williams LS, Fradkin KD, Alonso RJ, Biller J. Presentation, etiology, and outcome of stroke in pregnancy and puerperium. *J Stroke Cerebrovasc Dis* 2001;10:1-10. doi: 10.1053/jscd.2001.20977.
- Dias MS, Sekhar LN. Intracranial hemorrhage from aneurysms and arteriovenous malformations during pregnancy and the puerperium. *Neurosurgery* 1990;27:855-66.

35. Marshman LA, Aspoas AR, Rai MS, Chawda SJ. The implications of ISAT and ISUIA for the management of cerebral aneurysms during pregnancy. *Neurosurg Rev* 2007;30:177-80.
36. Srinivasan K. Cerebral venous and arterial thrombosis in pregnancy and puerperium: A study of 135 patients. *Angiology* 1984;34:731-46.
37. Lanska DJ, Kryscio RJ. Peripartum stroke and intracranial venous thrombosis in the National Hospital Discharge Survey. *Obstet Gynecol* 1997;89:413-8.
38. Francois P, Fabre M, Lioret E, Jan M. Vascular cerebral thrombosis during pregnancy and post-partum. *Neurochirurgie* 2000;46:105-9.
39. Carmargo EC, Singhal AB. Stroke in pregnancy: A multidisciplinary approach. *Ostet Gynecol Clin North Am* 2021;48:75-96.
40. Hung SK, Lee MS, Lin HY, Chen LC, Chuang CJ, Chew CH, *et al.* Impact of hypertensive disorders of pregnancy on the risk of stroke stratified by subtypes and follow up time. *Stroke* 2022;53:338-44.
41. Scully M. Thrombotic thrombocytopenic purpura and atypical hemolytic uremic syndrome microangiopathy in pregnancy. *Semin Thromb Hemost* 2016;42:774-9.
42. Fischer-Betz R, Specker C, Brinks R, Schneider M. Pregnancy outcome in patients with antiphospholipid syndrome after cerebral ischaemic events: An observational study. *Lupus* 2012;21:1183-9.
43. Singhal AB, Bernstein RA. Postpartum angiopathy and other cerebral vasoconstriction syndromes. *Neurocrit Care* 2005;3:91-7.
44. Fugate JE, Ameriso SF, Ortiz G, Schottlaender LV, Wijidicks EF, Flemming KD, *et al.* Variable presentations of postpartum angiopathy. *Stroke* 2012;43:670-6.
45. Fugate JE, Wijidicks EF, Parisi JE, Kallmes DF, Cloft HJ, Flemming KD, *et al.* Fulminant postpartum cerebral vasoconstriction syndrome. *Arch Neurol* 2012;69:111-7.
46. Bakhru A, Atlas RO. A case of postpartum cerebral angiitis and review of the literature. *Arch Gynecol Obstet* 2011;283:663-8.
47. Lamy C, Sharshar T and Mas JL. Cerebrovascular diseases in pregnancy and puerperium. *Rev Neurol* 1996;152:422-40.
48. Kelly JC, Safain MG, Roguski M, Edlow AG, Malek AM. Postpartum internal carotid and vertebral arterial dissections. *Obstet Gynecol* 2014;123:848-56.
49. Reinhard M, Munz M, von Kannen AL, Griesser-Leute HJ, Dittrich R, Engelter ST. Risk of recurrent cervical artery dissection during pregnancy, childbirth and puerperium. *Eur J Neurol* 2015;22:736-9.
50. Roberts CL, Algert CS, Knight M, Morris JM. Amniotic fluid embolism in an Australian population-based cohort. *BJOG* 2010;117:1417-21.
51. Committee opinion No 723: Guidelines for diagnostic imaging during pregnancy and lactation. *Obstet Gynecol* 2017;130:e210-6.
52. Rizzo L, Crasto SG, Ruda R, Gallo G, Tola E, Garabello D, *et al.* Cerebral venous thrombosis: Role of CT, MRI and MRA in the emergency setting. *Radiol Med* 2010;115:313-25.
53. Lansberg MG, O'Donnell MJ, Khatri P, Lang ES, Nguyen-Huynh MN, Schwartz NE, *et al.* Antithrombotic and thrombolytic therapy for ischemic stroke: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2012;141:e601S-36S.
54. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, *et al.* Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2019;50:e344-418.
55. Leffert LR, Clancy CR, Bateman BT, Cox M, Schulte PJ, Smith EE, *et al.* Treatment patterns and short-term outcomes in ischemic stroke in pregnancy or postpartum period. *Am J Obstet Gynecol* 2016;214:723.e1-11.
56. Pollack CV Jr, Reilly PA, Eikelboom J, Glund S, Verhamme P, Bernstein RA, *et al.* Idarucizumab for dabigatran reversal. *N Engl J Med* 2015;373:511-20.
57. Tarnaris A, Haliasos N, Watkins LD. Endovascular treatment of ruptured intracranial aneurysms during pregnancy: Is this the best way forward? Case report and review of the literature. *Clin Neurol Neurosurg* 2012;114:703-6.
58. Pumar JM, Pardo MI, Carreira JM, Castillo J, Blanco M, Garcia-Allut A. Endovascular treatment of an acutely ruptured intracranial aneurysm in pregnancy: Report of eight cases. *Emerg Radiol* 2010;17:205-7.
59. Meyers PM, Halbach VV, Malek AM, Phatouros CC, Dowd CF, Lawton MT, *et al.* Endovascular treatment of cerebral artery aneurysms during pregnancy: Report of three cases. *AJNR Am J Neuroradiol* 2000;21:1306-11.
60. Piotin M, de Souza Filho CB, Kothimbakam R, Moret J. Endovascular treatment of acutely ruptured intracranial aneurysms in pregnancy. *Am J Obstet Gynecol* 2001;185:1261-2.
61. Stoodley MA, Macdonald RL, Weir BK. Pregnancy and intracranial aneurysms. *Neurosurg Clin N Am* 1998;9:549-56.
62. Dashti SR, Spalding AC, Yao TL. Multimodality treatment of a ruptured grade IV posterior fossa arteriovenous malformation in a patient pregnant with twins: Case report. *J Neurointerv Surg* 2012;4:e21. doi: 10.1136/neurintsurg-2011-010059.
63. Jermakowicz WJ, Tomycz LD, Ghiassi M, Singer RJ. Use of endovascular embolization to treat a ruptured arteriovenous malformation in a pregnant woman: A case report. *J Med Case Rep* 2012;6:113.
64. Sibai BM, Caritis SN, Thom E, Klebanoff M, McNellis D, Rocco L, *et al.* Prevention of preeclampsia with low-dose aspirin in healthy, nulliparous pregnant women. The National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. *N Engl J Med* 1993;329:1213-8.
65. Duley L, Henderson-Smart D, Knight M, King J. Antiplatelet drugs for prevention of pre-eclampsia and its consequences: Systematic review. *BMJ* 2001;322:329-33.
66. Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, *et al.* Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014;45:2160-236.
67. Magee LA, von Dadelszen P, Rey E, Ross S, Asztalos E, Murphy KE, *et al.* Less-tight versus tight control of hypertension in pregnancy. *N Engl J Med* 2015;372:407-17.
68. NICE. Hypertension in pregnancy: Diagnosis and management, 2010.
69. Bateman BT, Hernandez-Diaz S, Fischer MA, Seely EW, Ecker JL, Franklin JM, *et al.* Statins and congenital malformations: Cohort study. *BMJ (Clin Res Ed)* 2015;350:h1035.
70. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, *et al.* Antithrombotic therapy for VTE disease: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2012;141:e419S-96S.
71. Lamy C, Hamon JB, Coste J, Mas JL. Ischemic stroke in young women: Risk of recurrence during subsequent pregnancies. French Study Group on stroke in pregnancy. *Neurology* 2000;55:269-74.
72. Coppage KH, Hinton AC, Moldenhauer J, Kovilam O, Barton JR, Sibai BM. Maternal and perinatal outcome in women with a history of stroke. *Am J Obstet Gynecol* 2004;190:1331-4.
73. Mast H, Young WL, Koennecke HC, Sciacca RR, Osipov A, Pile-Spellman J, *et al.* Risk of spontaneous haemorrhage after diagnosis of cerebral arteriovenous malformation. *Lancet* 1997;350:1065-8.