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REVIEW ARTICLE

Intracerebral Hemorrhage in Women: A Review with Special Attention to Pregnancy and the Post-Partum Period

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Abstract

Non-traumatic intracranial hemorrhage includes subarachnoid hemorrhage, subdural hemorrhage, and intracerebral hemorrhage (ICH), which can be classified as primary or secondary. Primary ICH is due to arterial hypertension or cerebral amyloid angiopathy, and secondary ICH is due to cerebral vascular malformations, coagulopathies, infectious complications, brain tumors, and illicit stimulant drug use. This review explores the epidemiology and management of non-traumatic ICH in women, with a focus on pregnancy and the post-partum period, defined as 6 weeks post-delivery.

Keywords: Cerebral hemorrhage, Pregnancy, Pregnancy complications, Subarachnoid hemorrhage, Arteriovenous malformations, Vascular malformations

Methods

We searched PubMed using the MeSH terms "pregnancy and intracerebral hemorrhage" and "women and intracerebral hemorrhage." Additionally, we conducted focused PubMed searches with the terms "arteriovenous malformation and pregnancy," "cerebral venous thrombosis and pregnancy," "cerebral cavernous malformation," "subarachnoid hemorrhage and pregnancy," "moyamoya," and "pituitary apoplexy and pregnancy." To identify additional relevant citations, we reviewed reference lists of recent original articles and reviews. We only included studies published in English and prioritized original and contemporary studies. Our local institutional review board approved publication of the case report and images shown in Fig. 1.

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Basic Physiologic Changes in Pregnancy

Before reviewing vascular pathology in non-pregnant and pregnant women, it is important to highlight key normal hematologic, cardiac, and vascular physiologic changes that occur throughout pregnancy. Blood volume increases by 50% in pregnancy, with most of the increase occurring early in gestation. This increase in blood volume leads to a 30–50% increase in cardiac output that plateaus by the end of the second trimester. Blood pressure decreases due to a decrease in systemic vascular tone [1]. There is also a decrease in cerebral vascular resistance, as well as an increase in blood–brain barrier (BBB) permeability [2]. Importantly, pregnancy also leads to a hypercoagulable state, with changes in both coagulation and fibrinolysis [1].

All-Cause Intracerebral Hemorrhage in Pregnant and Non-pregnant Women

While some studies report an increased prevalence of intracerebral hemorrhage (ICH) in women compared to men [3, 4], this observation is not reported in all studies [5]. Among women with ICH from any cause, there may be an increased risk during pregnancy, mostly in the

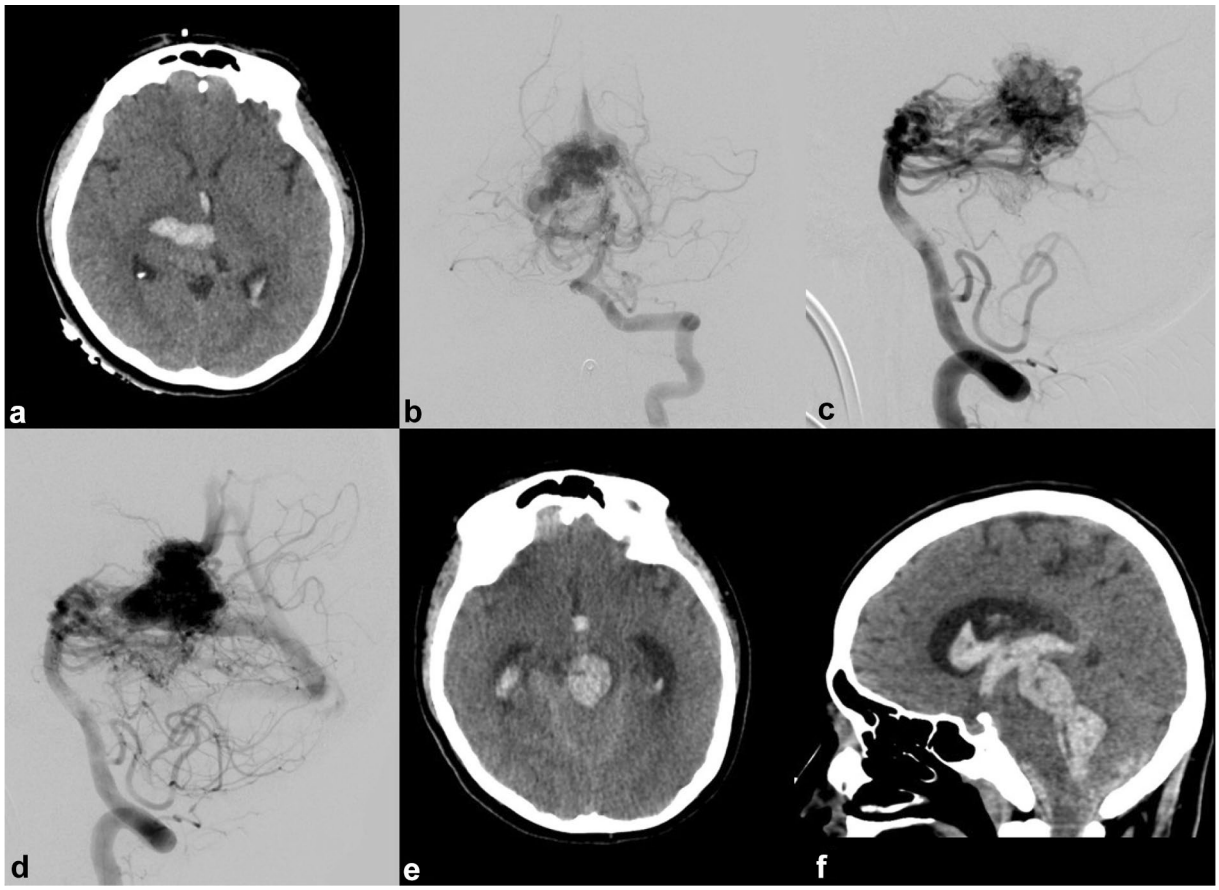

Fig. 1 Case of a 33-year-old woman, gravida 4 para 3, with a history of known unruptured intracranial AVM presenting with acute left hemiplegia and depressed level of consciousness. Initial non-contrast head CT **a** showed a right thalamic intracerebral hemorrhage with intraventricular extension. Digital subtraction angiogram **b**, **c**, **d**) showed an AVM with arterial supply from the bilateral posterior cerebral arteries, bilateral superior cerebellar arteries, and thalamoperforator arteries from the basilar trunk, with deep venous drainage. No intranidal aneurysms were identified, and the AVM was deemed to be inoperable given that the arterial feeders to the AVM also provided blood supply to normal brain. Hydrocephalus was treated with a ventriculostomy drain. Given that the fetus was previable, the AVM was unable to be secured, and the high risk of harm to the patient should the AVM re-rupture, the pregnancy was terminated at 18 weeks fetal gestational age. Thirteen days following dilation and evacuation, patient became acutely altered with a new left dilated, unreactive pupil and displayed spontaneous posturing on motor exam. Non-contrast head CT (e,f) demonstrated acute ICH in the midbrain with extensive intraventricular hemorrhage causing hydrocephalus. Another ventriculostomy drain was placed. Patient's examination remained poor throughout her hospitalization following AVM re-hemorrhage, and failure to wean the ventriculostomy resulted in ventriculoperitoneal shunt placement. Family ultimately elected for tracheostomy and percutaneous endoscopic gastrostomy tube placement, and she was transferred to a long-term acute care hospital

third trimester or post-partum period [6–9]. In a retrospective analysis of all female patients aged 15 through 44 who were discharged from 46 hospitals, Kittner et al. [7] found that the relative risk of ICH (irrespective of etiology) was 2.5 (95% CI 1.0–6.4) during pregnancy and 28.3 (95% CI 13.0–61.4) in the post-partum period. In a recently published meta-analysis, the pooled estimate of pregnancy-related ICH was 12.2 per 100,000 deliveries [10], though there are higher estimates reported in the Japanese and Taiwanese populations [11, 12]. Despite being relatively rare overall, ICH has profound consequences and is responsible for up to 7.1% of all maternal mortality [6]. Over a 23-year period in one study, ICH related to arteriovenous malformations (AVMs) and aneurysms accounted for 4.4% of all maternal deaths [13] (Table 1).

Risk factors for pregnancy-related ICH include advanced maternal age, African-American race, hypertensive diseases, coagulopathy, tobacco abuse, and baseline vascular lesions such as AVMs and cerebral aneurysms [6, 14]. Regarding the etiology of pregnancy-related ICH, one retrospective multicenter study observed that 44% of cases were due to eclampsia, 37% due to vascular malformations, and the remaining causes

Table 1 Summary of epidemiology and key highlights

Disease process	Epidemiology in the general adult population	Epidemiology in pregnancy and post-partum	Highlights	References
Preeclampsia ICH	N/A	14–50% of pregnancy-associated ICH	ICH due to preeclampsia is clustered around delivery and post-partum	Jaigobin et al. [8].; Sharshar et al. [9].; Takahashi et al. [14].; Salonen Ros et al. [16]
Arteriovenous malformation	Incidence 1/100,000. Prevalence 15–18/100,000. Annual rupture risk 1–4%	5.59% annual hemorrhage rate pregnancy and post-partum	OR of 2.19 hemorrhage in pregnancy, either in 2nd or 3rd trimester. If left untreated, risk of re-bleed 27%	Kittner et al. [7].; Yoshida et al. [12].; Al-Shahi et al. [22].; Al-Shahi et al. [23].; Ondra et al. [24].; Stapf et al. [25].; Gross et al. [26].; Zhu et al. [29].; Sadasivan et al. [31]
Aneurysmal subarachnoid hemorrhage	Incidence 9–15/100,000 in US, 19–23/100,000 in Japan and Finland	2.4–17.1/100,000	Higher incidence by 25-45% in women over 55 years old. In pregnancy, most frequent time of ICH is the third trimester, HTN being the biggest risk factor	Salonen Ros et al. [16].; Ingall et al. [32].; de Rooij et al. [33].; Labovitz et al. [34].; Shea et al. [35].; Giroud et al. [36].; Huang et al. [37].; Bateman et al. [39].; Robba et al. [42]
Cavernous malformations	CCM prevalence 0.4-0.8% of population. Annual ICH rate of ICH 0.6% without prior CCM-related hemorrhage, 4.5% if prior CCM-related hemorrhage	Hemorrhage rate not increased in pregnancy or post-partum	Higher risk of ICH with CCMs located in brainstem. Hemorrhage rate is higher in woman than in men	Dalyai et al. [43].; Kondziolka et al. [46].; Al-Shahi Salman et al. [47].; Moriarity et al. [49].; Witiw et al. [50]
Cerebral Venous Sinus thrombosis	Incidence of 0.3-1.57/100,000	9.1-11.6/100,000 deliveries	Male-to-female ratio 1:3. Particularly greater risk in obese women. Increased risk in pregnancy, and even greater risk post-partum. Higher risk with cesarean delivery	Jaigobin et al. [8].; Swartz et al. [10].; Stam et al. [51].; Devasagayam et al. [52].; Cantu et al. [56].; Zuurbier et al. [57].; Lanska et al. [58]
Pituitary apoplexy	Occurs in up to 10% of pituitary adenomas	Unknown	Male-to-female ratio 1.6:1. Presents with severe headache, visual deficits, critical hormonal deficiency	Wakai et al. [60].; Nawar et al. [61]
Moyamoya	Incidence 0.35–0.94/100,000	Unknown	Male-to-female ratio 1:1.8 to 1:2.2. No increased risk during pregnancy, though MMD-related ICH clusters late in pregnancy or early post-partum	Baba et al. [66].; Wakai et al. [67].; Kuriyama et al. [68].; Liu et al. [70]

CCM cerebral cavernous malformation, *HTN* hypertension, *ICH* intracerebral hemorrhage, *MMD* moyamoya disease, *N/A* not applicable, *OR* odds ratio

of undetermined etiology [9]. In pregnancy-related ICH secondary due vascular lesions, there are differing reports on the most frequent vascular culprits. In a retrospective review, Takahashi et al. [14] identified 97 hemorrhagic strokes associated with pregnancy, of which AVMs were the most frequent cause of hemorrhage at a rate of 25.8%, followed by aneurysms (16.5%) and moyamoya disease (10.3%). This study showed that AVMs were 1.8 times more frequent than cerebral aneurysms as a bleeding source in pregnancy-associated ICH [14]. In another retrospective study, Yoshida et al. identified aneurysm rupture as the most frequent cause of pregnancy and post-partum-related ICH (19.8%), followed by AVMs (17.1%) [12]. The higher rate of aneurysmal hemorrhage in Yoshida et al.'s study may be related to the higher prevalence of aneurysmal rupture in the Japanese population, given results of a pooled analysis of 6 prospective cohort studies of aSAH showing a 2.8 times increased risk of aneurysm rupture in the Japanese population compared to populations from North America and Europe [15].

Specific Etiologies of Intracerebral Hemorrhage

Preeclampsia, Eclampsia, and HELLP Syndrome

Preeclampsia and eclampsia are risk factors for pregnancy-associated ICH, reported to be present in 14–50% of cases [8, 9, 16, 17]. Preeclampsia is defined as blood pressure greater than 140/90 mm Hg with significant proteinuria, and eclampsia is defined as new onset seizures in a woman with preeclampsia [18]. A syndrome of hemolysis, elevated liver enzymes, and low platelet count (HELLP) may represent a severe form of preeclampsia (though this relationship is controversial [19]) in which there is a risk for developing spontaneous ICH due to an acquired coagulopathy [12, 20].

The pathophysiology of these disorders is similar to hypertensive encephalopathy. The increase in blood pressure with these disorders leads to disturbed cerebral autoregulation, cerebral hyperperfusion, BBB disruption and formation of cerebral edema. The observation that many women who develop eclampsia do so at pressures that are lower than those causing hypertensive encephalopathy suggests that pregnancy affects cerebral autoregulatory capacity and/or the autoregulatory curve is shifted to lower pressures [2]. It is possible that the change in range of cerebral autoregulation and increased BBB permeability observed in pregnancy, in conjunction with the relative hypertension of preeclampsia and eclampsia, lead to ICH at lower pressures than observed in non-pregnant women [1]. In addition to acute hypertensive vascular changes and loss of cerebral autoregulation, preeclampsia and eclampsia may lead to ICH due to hypertension-induced vessel wall damage and a possible association with coagulation disorders that are frequently demonstrated in eclampsia [21]. ICH due to these disorders tends to cluster around the time of delivery [12].

Cerebral Arteriovenous Malformations

Cerebral AVMs are vascular malformations formed by abnormal vessels, both arterial and venous, with no intermediate capillary vessels or normally functioning brain parenchyma. They are likely congenital lesions and account for approximately one-third of primary ICH in young adults [22]. The incidence of cerebral AVMs is approximately 1 per 100,000 per year with prevalence estimates of 15–18 per 100,000 adults [22, 23]. In a large retrospective series, the annual rupture risk was estimated at 4% [24]; however this estimate includes patients who suffered recurrent hemorrhages. A prospective study of initial hemorrhage rate of AVMs was as low as 1% [25].

In 2002 Al-Shahi et al. [23] studied the prevalence of adults with cerebral AVMs based on a community study in Scotland and found that AVMs were less frequent in women (43%) than in men, and women were significantly older at time of diagnosis. However, AVMs remain an important etiology of cerebral hemorrhage in women especially during pregnancy. Regarding timing of AVM-related hemorrhage, some studies have reported a predilection for the second trimester [7, 12], possibly related to the impressive increase in cardiac output that starts early in pregnancy and peaks by the end of the second trimester. This finding has not been consistent, however, with another study reporting an increased rate in the third trimester [26].

Whether pregnancy itself increases AVM rupture rate is controversial, with some studies indicating no increased risk of AVM-related hemorrhage during pregnancy and post-partum in women without a previous hemorrhage [27, 28], and others reporting an increased risk [26, 29, 30]. In a recent retrospective study by Zhu et al. [29], hemorrhage rates in 264 female patients with AVM at a single institution were pooled with data from 8 other published studies to identify an annual hemorrhage rate of 5.59% in pregnancy and post-partum versus 2.52% in non-exposure periods (odds ratio 2.19, $p=0.002$). If left untreated, the risk of AVM re-bleed in the same pregnancy has been reported to be as high as 27% [31].

Aneurysmal Subarachnoid Hemorrhage

About 10% of all strokes are due to subarachnoid hemorrhage (SAH). The most common non-traumatic cause of SAH is aneurysm rupture. The incidence of SAH varies by geographic location, likely due to the differing prevalence of cerebral aneurysms. In the USA, the incidence is roughly 9–15 cases annually per 100,000 people. The highest reported incidences are in Japan and Finland (19–23 cases annually per 100,000 people) [32–35].

SAH is the only intracranial hemorrhage subtype that has an increased prevalence in women. A recent French retrospective study identified 4614 stroke cases and showed a lower overall incidence of ischemic stroke and ICH in women across all age groups; however there was an increased incidence of SAH in women over time [36]. This increased incidence of SAH in women was again demonstrated in a retrospective analysis of 1689 patients with spontaneous SAH in Taiwan, with an overall male-to-female ratio of 1:1.45, though this gender difference did not hold true for those younger than 50 years old [37]. In a review of 51 studies across 58 study populations in 21 countries, De Rooij et al. [33] also demonstrated increased incidence of SAH in women, finding a 1.24 times higher incidence in women, with the gender difference starting at 55 years old and increasing with greater age.

While aneurysmal SAH (aSAH) is relatively rare, it accounts for 5–12% of total mortality during pregnancy, making it the leading cause of death from non-obstetric causes [38]. SAH is estimated to occur in 2.4–5.8 per 100,000 deliveries during pregnancy and post-partum [16, 39]; however some institutions have reported rates up to 17.1 per 100,000 deliveries [39]. There is conflicting data about whether there is an increased risk of aneurysm rupture during pregnancy, delivery, and post-partum, with one study finding a higher risk [16], and some studies finding no association [40, 41]. Risk factors for pregnancy-related SAH include hypertensive disorders (present in up to 40% of cases), age, African-American race, Hispanic ethnicity, coagulopathy, hypercoagulability, sickle cell disease, intracranial venous thrombosis, and tobacco or drug abuse [39]. The most frequent period of aSAH in pregnancy is during the third trimester [12, 42]. In a retrospective review, Robba et al. identified 52 cases of aSAH in pregnant patients, with 73.1% occurring in the third trimester, 19.2% in the second trimester, and 7.7% in the first trimester [42]. Hypertension was the most common risk factor, affecting 30% of cases [42].

Cerebral Cavernous Malformations

Cerebral cavernous malformations (CCMs), also known as cavernous angiomas or cavernomas, are collections of vascular spaces lined by thin walls that lack smooth muscle, with no brain tissue intervening between these vascular channels. The estimated prevalence is 0.4–0.8% of the general population [43]. Cavernous malformations present with seizure (most commonly), focal neurologic deficit and headache, with the diagnosis typically made with magnetic resonance (MR) imaging of the brain parenchyma as these lesions are not detectable on vascular imaging studies [44]. There is a higher risk of hemorrhage with CCMs located in the brainstem compared with non-brainstem locations, and a higher rate of recurrent hemorrhage compared to initial hemorrhage [45–47]. The annual rate of hemorrhage is reported to be as low as 0.6% in those without a prior CCM-related hemorrhage, with the annual hemorrhage rate as high as 4.5% in those with a prior hemorrhage [46]. In a meta-analysis of data from 7 cohorts including 1620 patients with CCM, the 5-year estimated risk of ICH was 3.8% for those with non-brainstem CCM presenting without ICH or focal neurologic deficit, and as high as 30.8% in those with brainstem CCM presenting with ICH or focal neurologic deficit [45]. In another prospective study of 134 adults with CCM, Al-Shahi Salman et al. found that the 5-year risk of first hemorrhage in those without intracranial hemorrhage at the time of initial CCM diagnosis was 2.4%; however the 5-year risk of second hemorrhage in those who had presented with a first hemorrhage was 29.5% ($p < 0.001$) with the risk of recurrent hemorrhage deceasing each year following the initial hemorrhagic presentation [47].

While the overall incidence of CCM is thought to be similar for men and women, there is a higher prevalence of CCM hemorrhage in women [44, 47, 48]. In the study by Al-Shahi Salman et al. [47], the annual risk of recurrence of ICH or focal neurologic deficit was higher for women than men ($p = 0.01$). In another prospective study, irrespective of symptoms and findings at initial CCM presentation, the hemorrhage rate was 4.2% per year in women compared to 0.9% in men [49].

The precise reason for the gender disparity in CCM hemorrhage risk is unclear, though hormonal differences between men and women are hypothesized to be the main determinant of CCM enlargement and bleeding [44, 48]. If hormonal differences are the culprit, however, it is interesting that there is no proven relationship between CCM hemorrhage and pregnancy. In a study of 186 women of childbearing age with cerebral cavernous malformations, Witiw et al. [50] found no increased risk of intracranial hemorrhage during pregnancy, delivery or post-partum across 349 pregnancies compared with hemorrhagic events during non-pregnancy periods.

Cerebral Venous Sinus Thrombosis

Cerebral venous sinus thrombosis (CVST) can lead to both ischemic and hemorrhagic stroke. The venous thrombosis results in increased cerebral venous pressure, development of cerebral edema, and potential venous hemorrhage. It most commonly affects younger adults and children, reported to have an incidence of 3–4 per 1 million in adults and 7 per 1 million among children [51]. Recent studies have observed CVST to be much more common than previously reported, with the incidence as high 15.7 per 1 million [52].

CVST is more common in women than men with a ratio of about three to one, largely attributable to gender-specific risk factors including oral contraceptive (OCP) use [53, 54], pregnancy (a prothrombotic state), and hormone replacement therapy [51, 55]. In cases of CVST due to a gender-specific risk factor, women have a better prognosis than both men and women without gender-specific risk factors [55, 56]. Gender-nonspecific risk factors include genetic prothrombotic states, acquired prothrombotic states such as antiphospholipid syndrome, malignancy, infections, inflammatory diseases, hematologic conditions such as polycythemia, trauma, and dehydration [51].

A recent study explored obesity as a risk factor for CVST, and its relationship to gender and OCP use. The case–control study by Zuurier et al. [57] included 186 cases of CVST and 6134 controls and found that women with a body mass index of 30 or greater who use OCPs have an almost 30-fold increased risk of CVST compared with men and with women of normal weight who do not use OCPs. The reasons for this effect may be multifactorial and synergistic, including higher plasma prothrombotic factors in obesity, increased activated protein C resistance and higher factor VIII concentrations in obesity, and increased activated protein C resistance seen with use of OCPs [57].

Pregnancy increases the risk of CVST likely because it induces prothrombotic changes in the coagulation system that persist into the early post-partum period. It is estimated that CVST complicates 9.1–11.6 per 100,000 deliveries [10, 58]. The majority of cases become symptomatic in the post-partum period [8], with one study [56] finding a 13 times greater risk during the post-partum period compared to during pregnancy. This may be secondary to worsened hypercoagulability post-delivery due to trauma and rapid fluid shifts that cause volume depletion [59]. Additionally, cesarean delivery is associated with a higher risk of CVST (OR 3.10, 95% CI 2.26-4.24) [58].

Pituitary Apoplexy

Sudden hemorrhage into the pituitary gland is known as pituitary apoplexy. It occurs most often into a pituitary tumor, reportedly occurring in 0.6–10% of pituitary adenomas and affecting men more commonly than women with a 1.6:1 male-to-female ratio [60, 61]. It is a very rare cause of ICH in the pregnant woman, and the true incidence of pituitary apoplexy in pregnancy is unknown. As of late 2015, only 33 cases of pregnancy-related pituitary apoplexy have been described in the literature [62]. While pituitary apoplexy may occur in pregnant women with an underlying adenoma, it may also occur without an underlying mass given the physiological increase in pituitary size during pregnancy and the post-partum [63]. The enlarged pituitary may lead to increased intracapsular pressure, infarction, and hemorrhage, leading to severe headache, visual deficits, and life-threatening hormonal deficiency [62]. Pituitary apoplexy is a neurologic emergency, and rapid replacement of pituitary hormones, circulatory support, and early evaluation for surgical management are imperative.

Moyamoya Disease and Syndrome

Moyamoya disease (MMD) is a cerebrovascular disorder characterized by progressive bilateral arterial stenosis of the terminal internal carotid arteries accompanied by the formation of extensive collateral vessels, in the absence of associated risk factors. Patients with the characteristic vasculopathy who also have an associated risk factor (sickle cell disease, neurofibromatosis type 1, cranial therapeutic irradiation, Down's syndrome, congenital cardiac anomaly, renal-artery stenosis, giant cervicofacial hemangiomas, or hyperthyroidism) are said to have moyamoya syndrome [64]. Moyamoya is most common in Japan and Korea, with the incidence in Europe being one-tenth of the incidence in Japan [65]. The estimated incidence in Japan ranges from 0.35 to 0.94 per 100,000 persons, with the male-to-female ratio ranging from 1:1.8 to 1:2.2 [66–68]. Clinical presentations include ischemic stroke, hemorrhagic stroke, seizures, headaches, and cognitive impairment. Compared to primary ICH, MMD-related ICH is mostly intraventricular and associated with higher rates of recurrent hemorrhage [69].

There is no increased risk of ICH from MMD during pregnancy compared to non-pregnancy periods, though MMD-related ICH tends to occur late in gestation or early in the post-partum period [70]. As such, careful attention should be paid to hemodynamic management of patients with MMD during this period. Regarding method of delivery, although a survey of delivery methods in patients with known MMD in Japan showed that over two-thirds were scheduled cesarean section deliveries, successful vaginal deliveries that address optimal blood pressure and ventilation strategies have been reported [71–74].

Intracerebral Hemorrhage Management in Pregnancy

A detailed discussion of ICH management in the general population is beyond the scope of this review and is well described in the American Heart Association guidelines [75]. Here we will review key unique considerations and management principles as they apply to the pregnant patient.

In a pregnant woman with an acute neurologic change, immediate assessment and stabilization of the patient's airway, breathing, and hemodynamic status should be followed by rapid imaging with a non-contrast head computed tomography (CT) scan to confirm the diagnosis

of ICH. Given that pregnancy-related ICH is commonly secondary to a ruptured vascular lesion [9, 12, 14], intracranial vessel imaging should be strongly considered. Additionally, contrast-enhanced CT may help to identify women at risk for hematoma expansion [76]. Note that iodinated contrast may cross the placenta and thus there is a risk of neonatal hypothyroidism [1]. If a vascular lesion is identified, or still highly suspected after an unrevealing CT angiogram, digital subtraction angiography should be pursued.

In a pregnant woman, there may be a temptation to choose MR as the initial imaging modality given the radiation associated with CT; however CT is more rapid, more readily available, and is more sensitive for detecting acute blood. The shielded fetal radiation exposure from a maternal non-contrast head CT is estimated to be less than 0.005 mGy, with the generally considered threshold for development of fetal malformations from radiation exposure is 100 mGy [1, 77]. Two-dimensional digital subtraction angiography has a radiation burden of 10.5 mSV, and a fetal radiation dose of 4.9 mSv, which are below the fetal teratogenic dose [42].

Once the diagnosis of ICH is made, management should be direct at blood pressure control. The exact target blood pressure range in acute ICH has not been rigorously studied in pregnant patients. While it is important to rapidly decrease blood pressure to prevent hematoma expansion and, in the case of vascular lesions, aneurysm or AVM rebleed, it is equally important to avoid hypotension as this may cause placental hypoperfusion and fetal hypoxia. It is important to utilize fetal monitoring to ensure the fetus is tolerating maternal hemodynamic manipulation.

Patients with ICH due to a known coagulation factor deficiency or platelet disorder should receive factor or platelet replacement in the same manner as non-pregnant patients. Patients who are coagulopathic due to pharmacologic agents (vitamin K antagonists, direct thrombin inhibitors, direct factor Xa inhibitors, unfractionated and low molecular weight heparin) should receive the appropriate reversal agent with prothrombin complex concentrates, fresh frozen plasma, vitamin K, or protamine sulfate depending on the pharmacologic agent used [75]. In the case of hemorrhage secondary to CVST, anticoagulation therapy should be started immediately to prevent venous clot propagation and hemorrhage expansion from increasing venous pressure. Vitamin K antagonists are contraindicated in pregnancy due to teratogenicity, and treatment with full-dose low molecular weight heparin or unfractionated heparin should be instituted as soon as the diagnosis of CVST is made [59].

In cases of large ICH leading to mass effect, efforts to minimize cerebral edema and reduce intracranial hypertension in the non-pregnant patient include keeping the head of the bed at 30°, sedation, induced hyperventilation for a short temporizing period to induce cerebral vasoconstriction and lower intracranial pressure, administration of hyperosmolar therapy, removal of cerebral spinal fluid with an external ventricular drain, and decompressive craniectomy. In the intubated pregnant patient, the dose and type of sedation should be chosen cautiously given placental transfer and risk of fetal toxicity. Benzodiazepines, as well as opiates if used in high doses near term or for extended durations, can lead to neonatal withdrawal and respiratory depression [78]. In the pregnant patient, hyperosmolar therapy should be avoided if possible given the potential for severe fetal dehydration and electrolyte abnormalities. Hyperventilation should be used in moderation given the potential for decreased placental oxygen transfer [1]. If decompressive craniectomy or operative management of a vascular lesion is indicated in a pregnant woman, attention should be paid to intraoperative positioning. After 24 weeks of pregnancy, inferior vena cava compression may be significant, and thus the woman should ideally be placed in a partial left lateral position.

Summary

While rare, ICH during pregnancy and post-partum is a significant contributor to maternal mortality. There may be an increased risk of ICH during the third trimester of pregnancy and post-partum, particularly in cases related to aneurysm rupture and CSVT. Whether pregnancy increases the rate of initial AVM rupture is controversial, however if left untreated, pregnancy increases the rate of recurrent hemorrhage. ICH during pregnancy may pose unique challenges in ICH management, and a multidisciplinary approach including obstetricians, neurointensivists, neonatologists, vascular neurologists, and vascular neurosurgeons knowledgeable in endovascular and surgical techniques is recommended.

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ST involved in manuscript concept and design, literature review, manuscript preparation, and critical revision of the manuscript. AM involved in manuscript concept and critical revision of the manuscript.

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Conflict of interest
The authors declare that they have no conflict of interests.

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