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REVIEW ARTICLE

# Spontaneous Intracranial Hemorrhage in Pregnancy: A Systematic Review of the Literature

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## Abstract

Stroke in pregnant women has a mortality rate of 1.4 deaths per 100,000 deliveries. Vascular malformations are the most common cause of hemorrhagic stroke in this population; preeclampsia and other risk factors have been identified. However, nearly a quarter of strokes have an undeterminable cause. Spontaneous intracranial hemorrhage (ICH) is less frequent but results in significant morbidity. The main objective of this study is to review the literature on pregnant patients who had a spontaneous ICH. A systematic review of the literature was conducted on PubMed and the Cochrane library from January 1992 to September 2016 following the PRISMA guidelines. Studies reporting pregnant patients with spontaneous intraparenchymal hemorrhage (IPH), subarachnoid hemorrhage (SAH), and subdural hemorrhage (SDH) were selected and included if patients had non-structural ICH during pregnancy or up to 6 weeks postpartum confirmed by imaging. Twenty studies were included, and 43 patients identified. Twenty-two patients (51.3%) presented with IPH, 15 patients (34.8%) with SAH, and five patients (11.6%) with SDH. The most common neurosurgical management was clinical in 76.7% of patients, and cesarean section was the most common obstetrical management in 28% of patients. The most common maternal outcome was death (48.8%), and fetal outcomes were evenly distributed among term delivery, preterm delivery, and fetal or neonatal death. Spontaneous ICH carries a high maternal mortality with IPH being the most common type, most frequently presenting in the third trimester. Diagnosis and management do not differ for the parturient compared to the non-pregnant woman.

**Keywords** Pregnancy · Intracranial hemorrhage · Intraparenchymal hemorrhage · Spontaneous subarachnoid hemorrhage · Subdural hemorrhage · Systematic review

## Introduction

When stroke—ischemic or hemorrhagic—occurs during pregnancy, both woman and child may have devastating outcomes [1]. The incidence of strokes in pregnant patients is estimated at 34.2 per 100,000 deliveries, and the mortality rate is 1.4 per 100,000 [2] deliveries, accounting for both types.

Vascular anomalies, preeclampsia/eclampsia, and coagulopathy have been described as leading causes of intracranial hemorrhage (ICH) [3, 4]. Aneurysmal subarachnoid hemorrhage (SAH) is a type of ICH, which has been found to have a lower risk of incidence during pregnancy, labor, or puerperium (RR 0.40, 95% CI 0.20–0.90) [5]. Intraparenchymal hemorrhage (IPH) or intracerebral hemorrhage and subdural hemorrhage (SDH) are other types of ICH, and they have identifiable etiologic factors. However, 24% of ICHs arise from undeterminable

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causes [4]. These undetermined cases are categorized as "spontaneous ICH."

Identified ICH risk factors are migraine headache, thrombophilia, systemic lupus erythematosus, heart disease, sickle-cell disease, thrombocytopenia, postpartum hemorrhage, preeclampsia, transfusion, gestational hypertension, and postpartum infection [1, 2]. Arteriovenous malformations (AVMs) are the most common cause of IPH [1]. Moyamoya disease and cerebral venous sinus thrombosis are less common, known etiological factors. However, the pathophysiology and etiology of spontaneous ICH differ from the other types of ICH since they do not relate to a specific structural abnormality.

Besides neurosurgical aspects, the overall management of pregnant women is challenging for additional reasons. First, gravidity represents important limitations for diagnostic imaging studies (because of possible radiation side effects to the unborn child) and for treatment. Second, the low incidence of ICH in this population makes it difficult to create standard management guidelines. Third, the maternal–fetal dyad needs to be addressed and optimal management of both the mother and fetal statuses must be individually assessed. The risks of prematurity for the fetus must be balanced with the risks of ongoing expectant management of the pregnancy for the parturient. Because of the absence of both guidelines and systematic reviews for these cases, we decided to systematically review the available literature to explore the etiology, management, and outcomes of spontaneous ICH in pregnant women.

## Methods

A systematic review of the literature was performed regarding spontaneous ICH in pregnancy, according to the PRISMA guidelines for systematic reviews and meta-analyses [6]. For this study, spontaneous ICH was defined as any hemorrhage of the cerebral vascular circulation without a specific source after appropriate imaging and evaluation. Such ICH includes SAH, IPH, SDH as well as extradural hemorrhages. Our main objective was to review the etiology, management options, and perinatal outcomes of pregnant patients with spontaneous ICH with the potential of formulating management recommendations following a review of the literature, with the addition of a case vignette reflecting the management and outcomes in our institution.

### Studies Selection Criteria

Studies utilized included case reports, case series, or observational studies that enrolled pregnant women over 18 years old, that were pregnant or up to 6 weeks postpartum, and presented with spontaneous ICH. The period covered was from January 1992 to September 2016 to capture reports that were generated in the modern imaging (CT/MRI) era. ICH diagnosis must have been confirmed by either imaging modality. ICHs resulting from structural abnormalities such as trauma, tumors, or vascular malformations were excluded. For the purpose of this systematic review, spontaneous ICH was classified as follows: SDH, IPH, SAH, and extradural hemorrhages. The search was conducted in the PubMed and Cochrane library databases using MESH-indexed keywords as search commands, date filters and limited to English and Spanish languages. Search terms used were: "spontaneous," "cranial" or "intracranial," "hemorrhage," "pregnancy," "epidural," "subdural" and "subarachnoid." These commands were combined using the algorithmic terms "AND" and "OR."

All studies retrieved by automated search or hand searching underwent title and abstract screening and included for full-text review if relevant. A full-text review was conducted, and studies were included when inclusion criteria were met. Studies with discrepancies were reviewed and resolved by consensus among the authors (Fig. 1). Quality assessment of case reports was performed using the Joanna Briggs Institute Reviewer's Manual [7] for case reports.

### Data Collection

Variables collected were the following: maternal age, gestational age, time of presentation (in weeks), trimester of presentation, obstetric-gynecologic history, clinical presentation, gestational age when symptoms presented, type of hemorrhage, non-gestational maternal comorbidities, history of chronic hypertension (defined as increased blood pressure before the 20th gestational week), or pregnancy-related hypertension, which included: gestational hypertension (defined as newly increased blood pressure after the 20th gestational week without preeclampsia or eclampsia), preeclampsia/eclampsia, or hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome. Neurosurgical management was stratified as clinical or surgical. Obstetrical management was stratified as cesarean section, normal delivery, or expectant (no obstetrical intervention performed at the time of the onset of the hemorrhage). Maternal outcomes were stratified as uneventful, neurological disability of any kind and, death. Fetal outcomes were stratified as a term delivery (any liveborn neonate delivered vaginally or by cesarean section between the gestational age of 37 (0/7 days) weeks and 41 weeks), preterm birth (defined as any liveborn neonate delivered by either vaginal delivery or cesarean section between the gestational age of 20 weeks and 36 (6/7 days) weeks), and abortion/stillbirth.

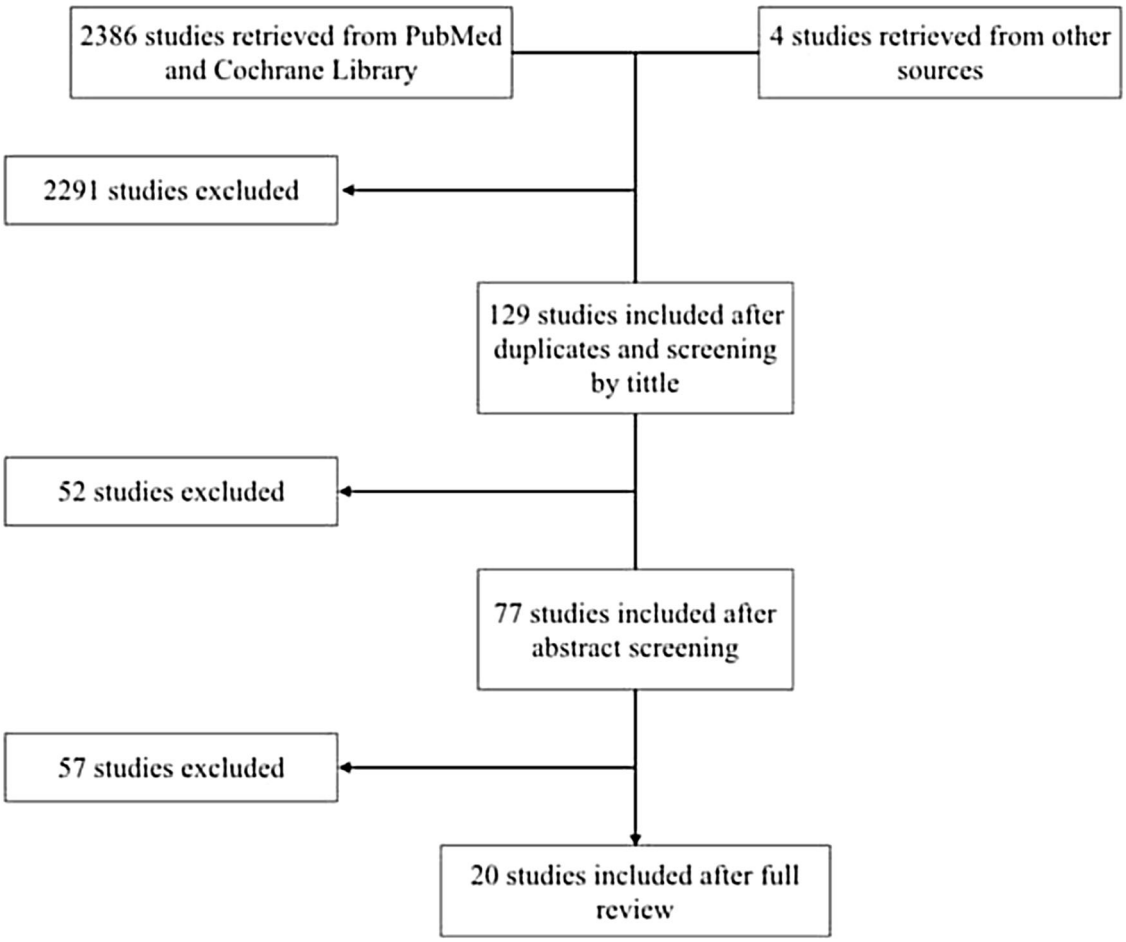


**Fig. 1** Study selection flowchart

Minimal variables needed for patients' inclusion for analysis were: time of symptom onset in gestational weeks, trimesters or within 6 weeks postpartum and hemorrhage etiology confirmed by imaging.

### Exclusion Criteria

Studies that reported traumatic ICH, structural causes of ICH (such as aneurysmal SAH, or ICH secondary to tumors, AVMs or any other vascular malformation) were not included. Studies without abstract available, not written in English or Spanish, non-relevant after screening or full-text review, without individual patient data for detailed assessment, were also excluded.

### Statistical Analyses

Frequencies and percentages were used to report categorical data and measures of central tendency and dispersion were used to analyze continuous data. Three subgroups were created to perform subgroup analyses based on the type of ICH: IPH, SAH, and SDH. The statistical software used was IBM® SPSS Statistics® version 20 (Chicago, Illinois).

## Results

### Studies' Characteristics

Our initial automatic search retrieved 2386 articles, whereas four additional articles were retrieved by hand searching of the reference list. Of these, 129 papers were selected after title screening. Next, abstract screening was performed leading to the inclusion of 77 studies for full-text review (75 in English and two in Spanish). Only 20 studies were included for data extraction and analysis after a full-text review (Fig. 1). Pooling all patients from these 20 studies lead to a total of 773 patients. From these, only 43 patients met our inclusion criteria. There was no patient overlapping among the studies included. More information of the included studies is found in supplemental Table 1.

The most common type of study was "case report" with 15 studies identified [8–22] (78.9%), followed by "retrospective study" with four such studies [23–26] (21.1%) and one "cross-sectional" study [27]. Most cases included were taken from these retrospective studies with a total of 26 patients who could be identified in detail (66.6%).

## Pooled Patients' Characteristics

The mean maternal age was 30.5 years with a standard deviation of ± 6.9 years. The median gestational age at admission was 33 weeks with a range of 8–41 weeks. Per ICH etiology, IPH was the most common type of ICH with 22 cases identified (51.3%), followed by SAH with 15 cases (34.8%). Also, five SDH cases (11.6%) and one simultaneous ICH + SDH case (2.3%) were identified. No studies were identified reporting any spontaneous epidural hematoma in pregnancy. Obstetrical history was available only in 15 patients (34.8%), most of them multiparous (18.5%). Thirty-four patients did not have a history of chronic hypertension (79.1%), and 28 (65.1%) denied other comorbidities. No patients had gestational hypertension. Preeclampsia was observed in 12 patients (27.9%), eclampsia in one patient (2.3%) and three patients were diagnosed with HELLP syndrome (7.3%). Twenty-six (60.4%) of patients did not have pregnancy-related hypertension. One patient with IPH had chronic hypertension with superimposed preeclampsia, and one patient with SAH had chronic hypertension with superimposed eclampsia/HELLP syndrome. At the time of symptomatic presentation, 30 (72.1%) of the patients in our cohort were diagnosed with ICH antepartum, in which 23 out of 30 occurred within the third trimester (53.5%).

On investigation of the obstetrical management, we found that only 19 (44.3%) of patients had their obstetrical management reported. Within this group, 11 patients underwent emergent cesarean section, two underwent scheduled cesarean section, three underwent normal vaginal delivery, and three were managed in an expectant fashion. All patients had their neurosurgical management reported, which was expectant without surgical intervention in 33 patients (76.7%). Surgery was carried out in 10 patients (23.3%), being hematoma evacuation the most common surgical procedure performed (16.4%). Only 19 patients (44.1%) had both obstetrical and neurosurgical management reported, in which nine patients (47.4%) were managed surgically and 10 patients (52.6%) were managed clinically. Nine patients presented with ICH before 28 weeks of gestation. Of those, eight patients (88.9%) were managed medically and one patient underwent surgery (11.1%). Twenty-two patients presented with ICH after 28 weeks of gestation and before delivery. Of those, 15 cases (68.2%) were managed medically and seven cases (31.8%) were managed surgically.

On maternal outcome analysis, 21 patients expired (48.8%) succumbing to their disease, whereas only 15 patients (35%) were reported to achieve uneventful maternal outcomes. With respect to pregnancy outcomes, only 15 (34.8%) of cases had their fetal outcomes reported: Five were liveborn term births, five were liveborn preterm births, and five were fetal demises. Appearance, pulse, grimace, activity and respiration (APGAR) scores and birth weight were available in six patients, and therefore, further statistical analysis was not performed (Table 1).

## IPH Subgroup Characteristics

Twenty-two patients were identified with IPH. The mean age was 30.0 years with a standard deviation of 7.0 years. The median gestational age at the time of symptom onset was 33 weeks. Eighteen patients presented with their symptoms at some point in time antepartum, and of those, 12 (59.1%) had their symptoms become apparent in the third trimester. The majority of women with reported obstetrical history were multiparous (four patients, 18.1%). The majority of women (18 patients, 81.8%) had neither chronic hypertension nor other maternal comorbidities. Seven patients (31.7%) were found to pregnancy-related hypertension including preeclampsia.

Although two-thirds of patients had no obstetrical management described in the study, cesarean section was the most common obstetrical management chosen in 14.5% of the cases, and non-surgical management was the most common neurosurgical management, observed in 16 patients (72.7%). Eight patients had both their obstetrical and neurosurgical management reported, in which five patients were managed surgically and three patients were managed clinically. Death was the most common maternal outcome in 15 (68.1%) patients. In contrast, fetal outcomes were only available in nine patients. From these, a full-term live birth was the most common fetal outcome (22.7%) of patients (Table 2).

## SAH Subgroup Characteristics

Fifteen patients were identified with SAH. The mean age was 31.9 years with a standard deviation of 7.1 years. Eight patients (53.3%) presented with symptoms antepartum, and most commonly in the third trimester (33.3%). Conversely to the ICH group, most women with reported obstetrical history were nulliparous (13.2%). The majority (86.7%) of patients did not have preexisting chronic hypertension, and 66.6% did not have pregnancy-related hypertension. A third (33.4%) of patients had pregnancy-related hypertension, primarily eclampsia (26.7%). Of note, 9 patients (60%) had no comorbidities. The

**Table 1** Pooled patients' characteristics

| | | |
|---|---|---|
| Number of patients (*n*, %) | 43 | 100 |
| Age in years[a] (mean ± SD) | 30.5 | ± 6.9 |
| Gestational age in weeks[b] (median, range) | 33 | 8–41 |
| Type of ICH | *n* | % |
| IPH | 22 | 51.3 |
| SAH | 15 | 34.8 |
| SDH | 5 | 11.6 |
| IPH + SDH | 1 | 2.3 |
| Total | 43 | 100 |
| Time of presentation | | |
| Antepartum | 30 | 72.1 |
| First trimester | 3 | 7.0 |
| Second trimester | 5 | 11.6 |
| Third trimester | 23 | 53.5 |
| Postpartum | 12 | 27.9 |
| Total | 43 | 100 |
| Obstetrical history | | |
| Nulliparous | 7 | 16.3 |
| Multiparous | 8 | 18.5 |
| Not reported | 28 | 65.2 |
| Total | 43 | 100 |
| Maternal comorbidities | | |
| Anemia | 1 | 2.3 |
| Asthma | 1 | 2.3 |
| Coagulopathy | 1 | 2.3 |
| Convulsion | 1 | 2.3 |
| ITP | 1 | 2.3 |
| Purpura | 1 | 2.3 |
| SLE | 1 | 2.3 |
| Valvulopathy | 1 | 2.3 |
| No comorbidities | 28 | 65.1 |
| Not reported | 7 | 16.5 |
| Total | 43 | 100 |
| Chronic hypertension | | |
| Yes | 2 | 4.7 |
| No | 36 | 83.7 |
| Not reported | 5 | 11.6 |
| Total | 43 | 100 |
| Pregnancy-related hypertension | | |
| Yes | 16 | 37.2 |
| Gestational hypertension | 0 | 0 |
| Preeclampsia | 12 | 27.9 |
| Eclampsia | 1 | 2.3 |
| HELLP syndrome | 3 | 7.3 |
| No | 26 | 60.5 |
| Not reported | 1 | 2.3 |
| Total | 43 | 100 |
| Obstetrical management | | |
| Cesarean section | 12 | 28 |
| Scheduled | 2 | 4.7 |
| Emergent | 11 | 26.6 |
| Vaginal delivery | 3 | 7.0 |
| Expectant | 3 | 7.0 |
| Not reported | 24 | 55.7 |
| Total | 43 | 100 |
| Neurosurgical management | | |
| Clinical | 33 | 76.7 |
| Surgery | 10 | 23.3 |
| EVD insertion | 1 | 2.3 |
| EVD insertion and VP shunt | 1 | 2.3 |
| Evacuation | 7 | 16.4 |
| Unspecified | 1 | 2.3 |
| Total | 43 | 100 |
| Maternal outcome | | |
| Uneventful | 15 | 35 |
| Neurological Disability | 6 | 13.9 |
| Death | 21 | 48.8 |
| Not reported | 1 | 2.3 |
| Total | 43 | 100 |
| Fetal outcome | | |
| Term delivery | 5 | 11.6 |
| Preterm delivery | 5 | 11.6 |
| Fetal or neonatal death | 5 | 11.6 |
| Not reported | 28 | 65.2 |
| Total | 43 | 100 |

*EVD* External ventricular drain; *HELLP* hemolysis, elevated liver enzymes and low platelet count; *ICH* intracranial hemorrhage; *IPH* intraparenchymal hemorrhage; *ITP* idiopathic thrombocytopenic purpura; *SAH* subarachnoid hemorrhage; *SD* standard deviation; *SDH* subdural hemorrhage; *SLE* systemic lupus erythematosus; *VP* ventriculo-peritoneal

[a]Missing value in 1

[b]Missing values in 10

obstetrical management was available for five patients; three patients underwent a cesarean section. In contrast to ICH, neurosurgical management was clinical in all patients. Maternal outcomes were significantly better than outcome observed in the IPH subgroup, being uneventful in 10 (66.7%) SAH patients. Nevertheless, maternal death occurred in 26.7% of patients. Unfortunately, most studies did not report fetal outcomes (Table 3).

## SDH Subgroup Characteristics

Five patients were identified with SDH; this being the smallest subgroup and with the youngest mean maternal age of all subgroups (27.5 years). The median gestational age was 33 weeks. Four patients presented during the third trimester, and one patient presented immediately postpartum. The majority (60%) of women with reported

**Table 2** Intraparenchymal hemorrhage subgroup

| | |
|---|---|
| Number of patients (*n*, %) | 22 (100) |
| Age (mean ± SD) | 30.0 ± 7.0 |
| Gestational age in weeks[a] (median, range) | 33 (8–41) |
| Time of presentation | *n* (%) |
| Antepartum | 18 (81.8) |
| First trimester | 2 (9.1) |
| Second trimester | 3 (13.6) |
| Third trimester | 12 (59.1) |
| Postpartum | 4 (18.2) |
| Total | 22 (100) |
| Obstetrical history | |
| Nulliparous | 3 (13.6) |
| Multiparous | 4 (18.1) |
| Not reported | 15 (68.3) |
| Total | 22 (100) |
| Chronic hypertension | |
| Yes | 2 (9.1) |
| No | 18 (81.8) |
| Not reported | 2 (9.1) |
| Total | 22 (100) |
| Pregnancy-related hypertension | |
| Yes | 7 (31.8) |
| Gestational hypertension | 0 (0) |
| Preeclampsia | 5 (22.7) |
| HELLP Syndrome | 2 (9.1) |
| No | 15 (68.2) |
| Total | 22 (100) |
| Maternal comorbidities | |
| Anemia | 1 (4.5) |
| Convulsion | 1 (4.5) |
| SLE | 1 (4.5) |
| No comorbidities | 16 (72.7) |
| Not reported | 3 (13.6) |
| Total | 22 (100) |
| Obstetrical management | |
| Cesarean section | 4 (14.5) |
| Scheduled | 1 (10) |
| Emergent | 3 (4.5) |
| Vaginal delivery | 2 (9.1) |
| Emergent delivery | 1 (4.5) |
| Expectant | 1 (4.5) |
| Not reported | 14 (63.6) |
| Total | 22 (100) |
| Neurosurgical management | |
| Surgical | 6 (27.3) |
| EVD | 1 (4.5) |
| EVD and VP shunt | 1 (4.5) |
| Evacuation | 3 (13.6) |
| Unspecified | 1 (4.5) |
| Clinical | 16 (72.7) |
| Total | 22 (100) |
| Maternal outcome | |
| Uneventful | 2 (9.1) |
| Disability | 4 (18) |
| Death | 15 (68.1) |
| Not reported | 1 (4.8) |
| Total | 22 (100) |
| Fetal outcome | |
| Term delivery | 5 (22.7) |
| Preterm delivery | 1 (4.5) |
| Fetal or neonatal death | 3 (13.5) |
| Not reported | 13 (59.1) |
| Total | 22 (100) |

*EVD* External ventricular drain; *HELLP* hemolysis, elevated liver enzymes and low platelet count; *SD* standard deviation; *SLE* systemic lupus erythematosus; *VP* ventriculo-peritoneal

[a]Missing values in three patients

obstetrical history were multiparous. No patients were found to have chronic hypertension, but 60% of pregnant patients with spontaneous SDH had other underlying comorbidities. Three of the patients in this subgroup had preeclampsia. Comorbidities were found in three out of five individuals of this group including asthma, idiopathic thrombocytopenic purpura, and a cardiac valvulopathy.

All five patients underwent emergent cesarean delivery, while surgical evacuation was the most common neurosurgical management (three patients, 60%). Maternal outcome was described as uneventful in three patients, and death was reported for two patients. Death was the most common fetal outcome (Supplemental Table 3).

## Case Vignette

Considering few studies reporting patients with spontaneous ICH in pregnancy, we present a case vignette from our institution to highlight how cases with these characteristics should be reported, to share how these patients are managed in our institution and to add another case to the literature.

A 29-year-old woman, 36 weeks and 6 days of gestation, G2P0010, presented to an outside hospital after waking up at 4 am with a significant headache, associated with dizziness, nausea, and vomiting. She was treated with IV fluids, acetaminophen, and metoclopramide. She was transferred to our institution for further management. Upon arrival, her status was alert and conversant. Over the next few hours, she became sleepy and minimally verbal. Her past medical history was unremarkable, while her

**Table 3** Subarachnoid hemorrhage subgroup

| | |
|---|---|
| Number of patients (*n*, %) | 15 (100) |
| Age (mean ± SD) | 31.9 ± 7.1 |
| Gestational age in weeks[a] (median, range) | 34 (8–38) |
| Time of presentation | *n* (%) |
| Antepartum | 8 (53.3) |
| First trimester | 1 (6.7) |
| Second trimester | 2 (13.3) |
| Third trimester | 5 (33.3) |
| Postpartum | 7 (46.7) |
| Total | 15 (100) |
| Obstetrical history | |
| Nulliparous | 2 (13.2) |
| Multiparous | 1 (6.6) |
| Not reported | 12 (80.2) |
| Total | 15 (100) |
| Pregnancy-related hypertension | |
| Yes | 5 (33.4) |
| Gestational hypertension | 0 (0) |
| Preeclampsia | 4 (26.7) |
| Eclampsia | 1 (6.7) |
| No | 10 (66.6) |
| Total | 15 (100) |
| Chronic hypertension | |
| Yes | 0 (0) |
| No | 13 (86.7) |
| Not reported | 2 (13.3) |
| Total | 15 (100) |
| Maternal comorbidities | |
| Coagulopathy | 1 (6.7) |
| Purpura | 1 (6.7) |
| No comorbidities | 9 (60) |
| Not reported | 4 (26.6) |
| Total | 15 (100) |
| Obstetrical management | |
| Cesarean section | 3 (20.1) |
| Scheduled | 1 (6.7) |
| Emergent | 2 (13.4) |
| Expectant | 2 (13.4) |
| Not reported | 10 (66.5) |
| Total | 15 (100) |
| Neurosurgical management | |
| Clinical | 15 (100) |
| Total | 15 (100) |
| Maternal outcome | |
| Uneventful | 10 (66.7) |
| Disability | 1 (6.6) |
| Death | 4 (26.7) |
| Total | 12 (100) |
| Fetal outcome | |
| Term delivery | 2 (13.4) |
| Not reported | 13 (86.6) |
| Total | 15 (100) |

[a]Missing values in six patients

*SD* Standard deviation

obstetrical history included one prior spontaneous abortion. She had no pertinent family or social history. On admission, she was afebrile with a blood pressure of 87/70 mmHg and a heart rate of 97 beats per minute. On neurological examination, the patient was sleepy, minimally cooperative but oriented. She was nonverbal, and cranial nerves examination was normal. Motor examination revealed left-sided drift and hyperreflexia, while her sensory examination was normal. Fetal assessment on a non-stress test was reassuring.

## Imaging

Admission MRI showed a large IPH measuring 6.7 × 4.1 cm on axial FLAIR, and 8.3 cm in longitudinal dimension on sagittal imaging (Fig. 2a, b). IPH involved the right parietal and posterior/superior temporal lobe with intraventricular extension. There was compression of the third ventricle and a 3.8-mm leftward midline shift. Magnetic resonance angiography and magnetic resonance venography did not show vascular abnormalities.

## Management

A multidisciplinary team including neurology, neurosurgery, anesthesia, and maternal–fetal medicine was formulated. The patient was taken for emergent cesarean section followed by immediate right-sided decompressive hemicraniectomy for decompression (Fig. 2c).

Under general anesthesia, the patient underwent a cesarean section resulting in the birth of a viable male infant. The newborn weighed 3090 g, and APGAR scores were 8 and 9 at minutes 1 and 5, respectively. The patient was kept intubated and repositioned in the lateral position for a right-sided hemicraniectomy and duraplasty, after which adequate closure was performed. There were no complications.

## Hospital Course

The patient remained neurologically stable, and postpartum evolution was uneventful. A postoperative cerebral angiography was normal. The patient was discharged from the floor on day 17 in neurologically stable condition without motor or sensory deficits other than a limited hemianopia.

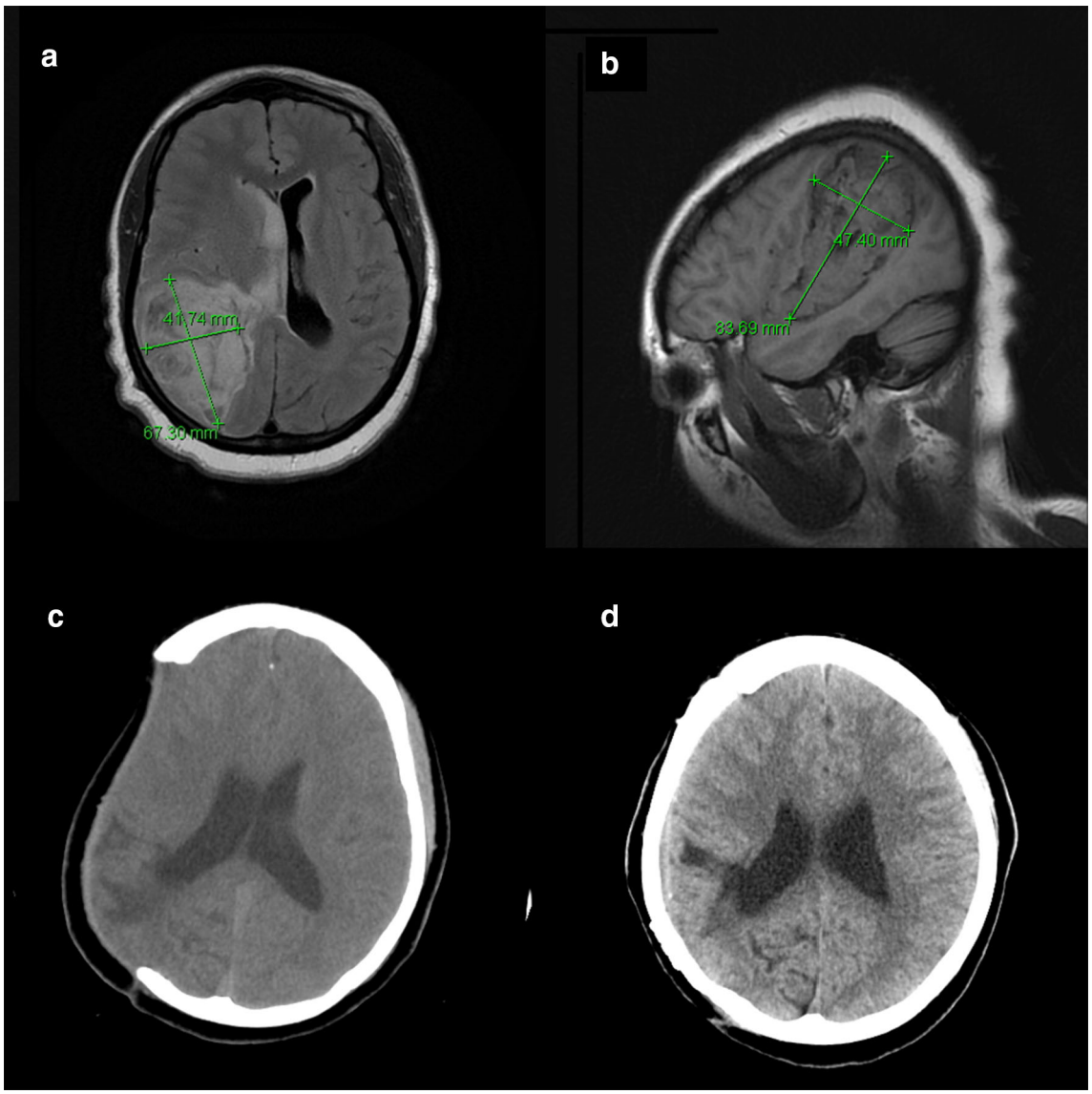


**Fig. 2** Axial (Panel **a**) and sagittal (Panel **b**) MRI sequences at admission show a right parietal and temporal IPH with intraventricular extension. Panel **c** shows an MRI post-right hemicraniectomy for hemorrhage evacuation. Three months later, the patient underwent a right cranioplasty. Panel **d** shows the patient's MRI at 6-month follow-up

### Follow-Up

The patient underwent elective autograft cranioplasty 3 months later without complications. At the last follow-up, her neurologic examination was normal except for persistent hemianopia. Head CT scan showed an expected post-ICH and postoperative changes (Fig. 2d).

## Discussion

### Etiology

ICH is a devastating condition regardless of pregnancy status and can lead to long-term disabilities or death. SAH and IPH represent $\leq 50\%$ of hemorrhagic strokes encountered in pregnant women [28]. Although the incidence of spontaneous SAH is approximately 10–20 cases per 100.000 pregnancies [29], it is not known how many of the other types of ICHs are due to structural anomalies (e.g., vascular) and how many are of unidentified etiology.

Most causes of ICH in pregnant women are from vascular malformations such as AVMs, aneurysms, or moyamoya disease. Less often but equally devastating are spontaneous ICHs. Preeclampsia and other pregnancy-related hypertensive disorders are common comorbidities [4]. Kittner et al. reported 14% of patients suffering from ICH with either preeclampsia or eclampsia, while Sharshar et al. attributed 44% of the ICHs to eclampsia in their cohort

[30, 31]. Another risk factor for ICH in pregnancy is reversible cerebral vasoconstriction syndrome [9].

Studies have categorized ICH as of undetermined cause if no structural reason was found. The number of such spontaneous ICH may vary, though Liang et al. estimated this number to be about 24% [4]. Kittner et al. reported a relative risk of intracerebral hemorrhage of 2.5 (95% CI 1.0–6.4) during pregnancy and 18.2 (95% CI 8.7–38.1) relative risk in the first 6 weeks postpartum [30].

Block et al. reported that non-structural ICH was linked to preeclampsia in both IPH and SAH and linked HELLP syndrome and disseminated intravascular coagulation to IPH [32]. This is consistent with results from our study, showing that 28% of pregnant ICH patients carried the diagnosis of preeclampsia.

## Comorbidities

The physiology of pregnant women is different from non-pregnant women due to increases in total body fluid volume, cardiac output increase, vascular remodeling, and existence of a hypercoagulable state [28]. Specific risk factors that have been identified for ICH in pregnancy are preeclampsia/eclampsia, chronic kidney disease, chronic hypertension, smoking, pregnancy-related hematological disorders, gestational diabetes, and black race [33].

In our study, only four patients were found to have a hematological disorder, whereas 64% of maternal patients did not have identifiable comorbidities. Contrary to what was found in other pregnancy-related ICH cases reported in the literature, chronic hypertension was less often encountered in our cohort.

Pregnancy-related hypertension is an independent risk factor associated with ICH [3, 34]. ICH in pregnancy is associated with preeclampsia in 25–45% of cases [3]. However, despite being a leading risk factor for ICH, subgroup analysis showed that the majority of patients in this study did not have pregnancy-related hypertension. This observation was made across the subgroup analysis.

## Survival Predictors

Moulin and Cordonnier [35] reported recently a review of predictors of survival and functional outcome among all ICH patients. They found that hematoma volume is the strongest predictor of 30-day mortality and functional outcome. Also, hematoma location is an identified risk factor for short-term and long-term prognosis. Samarasekera et al. [36] found that patients with lobar ICH had better outcomes than patients with non-lobar ICH. Although sex was not significantly different, neither between lobar ICH and non-lobar ICH nor in patient's mortality, these studies did not include pregnant women with ICH. These findings cannot be extrapolated to our study population, and there are no studies looking at predictors of ICH in pregnancy. Additionally, in our study, most studies report neither the size nor the volume of the ICH; therefore, analysis cannot be made.

## Management

In our systematic review we found that the neurosurgical and obstetrical management of spontaneous ICH does not differ significantly from the neurosurgical and obstetrical management of ICH in non-pregnant patients. In neurosurgical cases involving a pregnant woman, a multidisciplinary team is needed to assess and care for the patient; management decisions are based on maternal clinical presentation, gestational age, and fetal status. Of critical importance is the concept that maternal hemodynamic stability is directly correlated with the fetal status. Neurosurgical evaluation with urgent head CT imaging is needed to start the diagnosis and management of a pregnant patient with a potential intracranial bleed. Head CT imaging should be performed expeditiously for maternal evaluation purposes without delay; there is minimal risk developing fetus given the limited radiation exposure [37]. MRI imaging can be utilized if deemed helpful for surgical decision making.

Management of spontaneous ICH in pregnancy needs to be individualized based on the maternal status and the gestational age of the pregnancy. Overall, care for the parturient with a spontaneous ICH should be managed similarly to a non-pregnant patient. As many pregnant women will present with a spontaneous ICH in the third trimester, attention needs to be directed to immediate maternal and fetal evaluation and stabilization which may include emergent delivery. Consideration of delivery prior to neurosurgical management is reasonable and may often be preferable, particularly in the late third trimester. However, there may be beneficial in delaying delivery in selected cases, particularly those preterm, to decrease the risk of prematurity and those undergoing medical management of the ICH.

There are no studies comparing management strategies of acute ICH in pregnancy; therefore, care of the individual patient is made based on expert opinion and multidisciplinary care. Prior studies have provided guidance outlining various management plans based on the gestational age of the pregnancy. Caution should be taken in strictly interpreting these algorithms based on the limitations of available data. Management of the fetal status, particularly in the periviable period, needs to be tailored after detailed counseling by a multidisciplinary team with the patient or her health care proxy. In 2008, Ng and Kitchen described three relevant periods that define neurosurgical

management for aneurysmal SAH in pregnant women. They indicated that management of ICH before week 26 should focus on protecting maternal health over the survival of the developing fetus. After 34 weeks, management should address both the needs of mother and fetus by performing cesarean section. Between 26 and 34 weeks of gestation, management will be individualized [29]. Yoshitani et al. described in detail how the neurosurgical approach should be decided. They considered the 28th week of gestation the turning point for neurosurgical intervention [38]. Women with an acute intracerebral bleed and hemodynamic instability will likely require urgent delivery via cesarean if neurosurgical management (rather than medical management) is indicated; however, in select patients delivery may not need to be cesarean. An operative assisted vaginal delivery with regional anesthesia is reasonable. This mode of delivery has the potential to minimize Valsalva while limiting blood loss compared to a cesarean delivery and can be considered particularly if medical management of the ICH is undertaken.

In our study, 22 patients presented with ICH after 28 weeks of gestation. Of those, 15 cases (68.2%) were managed medically and seven cases (31.1%) were managed surgically. Despite other expert opinion suggesting neurosurgical intervention after week 28th and the case vignette presented, medical management remains as the first line of treatment for most women with ICH in the third trimester in our systematic review and in our institution.

## Conclusions

Spontaneous ICH carries a high maternal mortality with IPH being the most common type most frequently presenting in the third trimester. Diagnosis and management do not differ during pregnancy. Care of the parturient with a spontaneous ICH needs to be individualized; however, paramount to the care of the maternal–fetal dyad is maternal optimization and delivery for obstetric indications as needed. However, managing the pregnancy until the late third trimester should be considered to reduce the risk of extreme prematurity to the neonate as long the parturient's neurological and obstetrical conditions remain stable.

### Limitations

Our search for this systematic review revealed that most studies on the topic included for analysis were case reports and small case series. Therefore, the results of this pooled analysis are rather descriptive and stand-alone observations, rather than systematic trials with control groups.

Neither randomized clinical trials nor prospective studies were found in our search. Fetal outcomes were not reported as often or in as much detail as maternal outcomes.

Given the low incidence of ICH in pregnancy, the pooled data have limitations and larger case series are not available. Given the limitations of these data, this should be an incentive to expeditiously create multicenter registries (e.g., online/web-based) to gather all the data we can obtain from individual cases to further optimize the best treatment strategies and to derive more definitive conclusions for the care of this complex patient population.

## Compliance with Ethical Standards

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

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