Review

The Management of Intracranial Aneurysms During Pregnancy: A Systematic Review

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ABSTRACT

Hemodynamic changes during pregnancy may favor the formation and rupture of intracranial aneurysms. Despite this risk, guidelines for managing intracranial aneurysms during pregnancy have not been clearly defined. The objective of this review is to describe the treatment options for pregnant women with intracranial aneurysms, and to report the maternal and fetal outcomes associated with different treatment strategies. A search of the literature was conducted using the PubMed database for the period January 1991 through June 2015. Aneurysm characteristics and management, pregnancy management, and maternal and fetal outcomes were evaluated. The most recent search was performed in June 2015. In total, 50 aneurysms (44 patients) were evaluated. Rupture was confirmed upon imaging in 36 aneurysms (72%), and most aneurysms ruptured during the third trimester (77.8%). Coil embolization was associated with a lower complication rate than clipping in patients with ruptured aneurysms (9.5% vs 23.1%). For patients with unruptured aneurysms, surgical management was associated with 31.9% fewer complications compared to no treatment. Most patients underwent Cesarean delivery (84%), and a combined neurosurgical-obstetrical procedure was used for 8 patients with ruptured aneurysms near term. Adverse outcomes were reported in 11.9% of children. Treatment of intracranial aneurysms during pregnancy is safe and effective. Furthermore, we suggest that coil embolization be considered a first line treatment over clipping for surgical management of the pregnant population. Going forward, we encourage the establishment of formal guidelines for managing intracranial aneurysms during pregnancy.

KEYWORDS: Intracranial aneurysm, Subarachnoid hemorrhage, Pregnancy

■ INTRODUCTION

Although intracranial aneurysms are uncommon during pregnancy, normal hemodynamic changes in pregnant women may increase vascular stress and the risk of aneurysm formation, progression and rupture (35, 44, 47). Systemically, maternal adaptations to pregnancy include increases in cardiac output (CO) and plasma volume (PV), and a redistribution of the CO between various organs (43). Cerebrovascular changes are thought to result from hormones that increase during pregnancy, such as estrogen, progesterone, and vascular endothelial growth factor (36). Other reported factors that may potentiate aneurysm progression during pregnancy include high levels of relaxin and increased wall tension from intraparenchymal artery hypoplasia (6, 51). It has been estimated that 1.8% of women of childbearing age (16 to 44 years) develop intracranial aneurysms, however the incidence of unruptured intracranial aneurysms during pregnancy is not well established in the literature (25). Rupture of intracranial aneurysms occurs in the range of 1 to 10 per 100,000 pregnancies (1, 33). Case fatality from subarachnoid hemorrhage during pregnancy is reported as high as 83%, but outcomes have improved with better medical care (10, 12).

Cerebrovascular management of aneurysms during pregnancy is complicated by the nature of maternal hemodynamics and their intimate relationship to the developing child. Given the dependence of the fetus on its mother, and the importance of a stable environment during fetal development, risk reduction from an intracranial aneurysm must clearly focus on both the mother and the child (39, 40, 42). Whether these aneurysms



must be treated, as well as the optimum treatment and child delivery modalities, is still unclear. Despite this complexity, guidelines for the management of intracranial aneurysms during pregnancy are not yet established in the literature.

The objective of this review is to better understand how neurosurgical management of intracranial aneurysms translates to the pregnant population. We have conducted a systematic review of the current literature to define the types and the frequency of complications associated with different management options for intracranial aneurysms in pregnant women, as well as with the care and delivery of the unborn child. Our goal is to give insights to the effectiveness and complications of the different treatments available for the management of intracranial aneurysms during pregnancy.

MATERIAL and METHODS

Study Selection

Using the MeSH database system of PubMed, a literature



Figure 1: PRISMA flow chart describing the study selection at different phases of our systematic review process.

search was performed by searching the years between 1991 and 2015 for all articles containing the phrases "pregnancy" and "intracranial aneurysm" [("Pregnancy"(Mesh)) AND "Intracranial Aneurysm" (Mesh)]. Articles were limited to English, and humans were defined as the subjects for this study. Additionally, article types were limited to case reports, clinical trials and randomized controlled trials; reviews, editorials and commentaries were excluded. A general PubMed search was also performed, using combinations of the search terms "aneurysm," "cerebral aneurysm," "intracranial aneurysm" and "pregnancy." Inclusion criteria focused on the management of women who were diagnosed, monitored, or treated for intracranial aneurysms during the course of pregnancy. Articles discussing only diagnostic imaging for intracranial aneurysms were excluded, as were those focused on cerebrovascular pathology in the child. A flow chart of the screening process is illustrated in Figure 1.

One author reviewed the articles and determined which studies to include or exclude, while discrepancies or indecisions were resolved among the other authors. No studies were found to be duplicates. The last search was performed on June 9, 2015.

Data Extraction

The included studies were carefully analyzed based on patient population, diagnosis, aneurysm location, aneurysm size, aneurysm rupture, neurosurgical management, and maternal complications. To better understand the relationship between intracranial aneurysms and the course of pregnancy, we accounted for gestational age at treatment when possible. Delivery modality and child health outcomes were also included in this study. The studies were separated based on aneurysm rupture and gestational age at treatment, at which point they were analyzed for long-term maternal complications, and child outcomes. Data for all patients was reported when available in the literature. No statistical tests were performed.

RESULTS

Study Characteristics

The initial PubMed search, before restrictions, returned 392 articles. Restricting the search for article type, language, subject and year yielded 109 full-text articles that required assessment for eligibility. After excluding articles that did not fit the specified content parameters described above, 17 case reports, 5 case series, and 1 retrospective study for a total of 44 patients and 50 intracranial aneurysms during pregnancy were included in our analysis. Data from these 23 articles are summarized in Table I.

Patient Characteristics

Patient age ranged from 15 to 43 years, with a mean of 28.0 years. Parity was only reported for 17 patients, the majority (88.2%) of whom were primigravida (n = 6) or secundogravida (n = 9). Patient identifying data from the included studies are summarized in Table I.

Aneurysm Characteristics

Of the 50 aneurysms, 36 presented with subarachnoid

Table I: Study Chi	aracteris	stics (of Intra	cranial Ar	neurysms Duri	ing Pregn	ancy						
Author & Year	Study design	Pts - no.	Age (yrs)	Parity	Aneurysm _F Location(s)	Rupture?	Largest dimension (mm)	Management of aneurysm(s) [*]	Gestational Age at Management	Type of Delivery	Child Outcome	Maternal Outcome	Notes
Couldwell et al., 2010 (7)	СВ	-	26		MCA	~	1.6	SC	18 wks	CS	Favorable	Favorable	Initial attempt to manage w/ IVCE unsuccessful
D'Haese et al., 1997 (10)	CR	-	34	G2P1	ICA (2)	Y (1)	12 (1), 4 (1)	CS + SC (1), None (1)	PP (1)	cs	Favorable	Favorable	SC of untreated aneurysm 4 mo postpartum
Dogan et al., 2011 (13)	CR	-	38		ICA	≻	Ŋ	IVCE	ЪР	CS	Favorable	Reduced visual acuity	IVCE of ICA and cavernous sinus for suspected CCF
Duggan et al., 2007 (14)	CR	-	22	G1P0	AICA	z	ı	None	ı	CS	Low Apgar, improved	Favorable	IVCE 2 mo postpartum
Georgantopoulou et al., 2003 (16)	CB		32	ı	ICA-PCoM	≻	·	SC	12 wks	CS	Favorable	Favorable	
Goto et al., 2015 (17)	CR	-	34	1	MCA	~	4.3	SC	ЪР	CS	Favorable	Favorable	Initial false-negative CTA at 34 wks gestation
Hussain et al., 2001 (22)	CB	-	29	ı	ICA-PCoM	≻	ı	None	ı	S	ı	ı	Aneurysm ruptured during labor
Jaeger et al., 2000 (23)	СВ	. 	38	ı	ICA	~		CS + SC	£	S		Favorable	Emergency CS performed due to fetal bradycardia while under anesthesia for SC
Kim et al., 2014 (24)	СВ	-	35	ı	PICA	≻	6.08	IVCE	16 wks	S	Favorable	Favorable	First reported case of PICA aneurysm coiling during pregnancy
Kizilkilic et al., 2003 (26)	Case series	- ო	mean: (30 (31P0 (2), G2P1 (1)	ACA-ACoM (1), ICA (1), ICA-PCoM (1)	~	20 (1), 10 (1), 3 (1)	IVCE	10 wks (1), 18 / wks (1), 28 wks ¹ (1)	Abortion (1), Unspecified (2)	Favorable (2)	Favorable (2)	Abortion performed 3 d post-IVCE due to risk of fetal deficits
Kriplani et al., 1995 (27)	Case series	ε	mean: (25	G2P1 (1), G2P1 (2)	ACA-ACoM (1), ICA (1), PICA (1)	~		CS + SC (1), SC (1), SC + CS (1),	37 wks (1), PP (2)	CS (2), Vaginal (1)	Favorable	Favorable	Ruptured during labor (1)
Mavromatidis et al., 2011 (30)	CR		30	G1P0	ACA-ACoM	z	ı	None (previously treated)	ı	cs	Favorable	Favorable	IVCE for aneurysm 2 yrs before pregnancy

Table I: Cont.													
Meyers et al., 2000 (32)	Case series	с С	iean: G5 35.3 G7	5P3 (1), 7P6 (1) (Basilar (1), ICA-PCoM (1), PCA (1), SCA (1)	Y (3)	20 (1), 7 (2), 1.4 (1)	CS + IVCE (1), IVCE (1), None (1), SC (1)	11 wks (1), Mid-third trimester (1), PP (1)	CS (1), Unspecified (1), Vaginal (1)	Favorable	Favorable	IVCE required 14 wks post-SC due to aneurysm enlargement
Nelson, 2005 (35)	CR	-	19 G	31P0 /	ACA-ACoM	≻	15	SC	16 wks	Vaginal	Favorable	Favorable	
Ortiz et al., 1997 (37)	CR	-	15		ICA	z	18	None	ı	CS	Favorable	No new neurological defects	Enlargement of an aneurysm present since age 12
Piotin et al., 2001 (38)	Case series	,, T	1ean: 29.5		ICA	≻	4	IVCE (1), CS + IVCE (1)	22 wks (1), PP (1)	CS (1), Vaginal (1)	Favorable	Favorable (1), Third nerve palsy (1)	ı
Pumar et al., 2010 (39)	Case series	د د	lean: G	1912	ACA-ACoM (3), Basilar (2), ICA- PCoM (2), PCA (1)	≻	8 (1), Unspecified (7)	IVCE	Third trimester	S	Favorable	Favorable	ı
Riviello et al., 2004 (40)	СВ	-	37 G	31P1	ACA	≻	10	INCE	Ч	cs	Favorable	Favorable	ı
Roman et al., 2004 (42)	Retro.	Ω Ω	iean: G2 1.5 ± G2 4.8	2P1(2), I(2P2 (2)	CA (7), MCA (2)	Y (6)		CS + IVCE (1), None (4), SC (4)	First trimester (1), Third trimester (1), PP (3)	CS (5), No delivery (1), Vaginal (2)	Death (3), Favorable (4), Neurological retardation (1), (entriculomegal) (1)	Death (3), Favorable (4), Reduced visual acuity (1), Chronic ventriculomegaly (1)	IVCE 6 mo postpartum for untreated aneurysm in one pt; No delivery of one child due to fetal death <i>in utero</i>
Shutter et al., 1993 (45)	СВ		43	1	ICA (4)	z	6 (2), 2 (2)	SC (1), W (1), None (2)	12 wks	Terminated	r	Reduced visual acuity	Termination after amniocentesis confirmed trisomy 21
Surico et al., 2015 (48)	CR	-	ı	ı	ICA	≻	ı	IVCE	27 wks	CS	Favorable	Favorable	Patient also presented with a posterior fossa hemangioblastoma
Tarnaris et al., 2011 (50)	CR	-	21	ı	ICA-PCoM	z	ı	INCE	29 wks	CS	Favorable	Third nerve palsy	I
Weir et al., 1991 (51)	CR	. 	34	ı	SCA	z	n	SC	20 wks	CS	Favorable	Favorable	Dramatic post- operative course, deficits gradually resolved
ACA: Anterior cere Computed tomogre PCoM: Posterior <i>&</i> W: Wrapping, +: Pe	bral arter tphy ang mmunic rformed	y, AC iograp ating ¿ immec	M: Ante hy, G : G. artery, PI liately be	erior com travidity, ICA: Pos efore, *: L	Imunicating art ICA: Internal c terior inferior co Defined as the p	ery, AIC . arotid a. erebellaı <i>seriod</i> bı	A: Anterior infi rtery, IVCE: In r artery, PP: P< etween conce	erior cerebellar ar travascular coil eı ostpartum period, ption and 6 wks p	tery, CCF: Carot mbolization, MC retro: Retrospe oostpartum.	id-cavernous A: Middle cer sctive study, S	fistula, CR: Cas ebral artery, P: I :C: Surgical clip	e report, CS : Cesa ^p arity; PCA: Poste ping, SCA: Superio	rean section, CTA: ior cerebral artery, or cerebellar artery,

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hemorrhage (72%). The distribution of ruptured and unruptured aneurysms in our review is compared to that of the general population in Table II.

Seventy-eight percent (n = 28) of ruptured aneurysms occurred during the third trimester, including two during labor; the remaining aneurysms ruptured during the first (8%) and second (11%) trimesters (22, 27). None of the aneurysms included in this review ruptured during the postpartum period. Aneurysms with a greatest dimension of 6 millimeters or larger were nearly twice as likely to have ruptured when compared to those measuring less than 6 millimeters (91% vs 50%). Aneurysm size data with respect to location and rate of rupture are represented in Figure 2.

Aneurysm Treatment

Choice of treatment for ruptured and unruptured aneurysms is presented in Table III.

Through this review, we found that ninety-two percent of ruptured aneurysms were treated, with most treatments (76%) occurring during the third trimester or postpartum period. Coil embolization was used more often than surgical clipping (56% vs 36%). Two untreated aneurysms ruptured during labor; one aneurysm was treated (surgical clipping) immediately after delivery while the other was monitored without surgery (22, 27).

The majority of unruptured aneurysms were monitored without surgery (64.3%). In the remaining cases, surgical clipping was used more often than coil embolization (21.4% vs 7.1%). Aneurysm wrapping was used for one unruptured aneurysm

(45). The average size of unruptured aneurysms that received surgical treatment was 4.4 millimeters.

Pregnancy Management

A total of thirty-eight childbirths were included in our analysis. Cesarean delivery was performed more often than vaginal



Figure 2: The distribution of aneurysm size with respect to location (bar chart) and percentage ruptured (line chart).

Table II: Distribution of Ruptured and Unruptured Aneurysms Compared to the General Population

Location	Unruptured	aneurysms – %	Ruptured a	neurysms – %
	Current series (N = 14)	General population ^a (N = 4,060)	Current series (N = 36)	General population ^b (N = 2,143)
Internal carotid artery ^c	64	38	33	7.9
Internal carotid-posterior communicating artery	7	8.5	17	25
Basilar artery	0	20	8	<1
Middle cerebral artery	0	29	11	14
Posterior cerebral artery	0	-	6	<1
Anterior cerebral artery ^d	0	12	3	5.2
Anterior cerebral-anterior communicating artery	7	12	17	45
Superior cerebellar artery	14	-	0	<1
Anterior inferior cerebellar artery	7	-	0	-
Posterior inferior cerebellar artery	0	_	6	<1

^aBased on data from the International Study of Unruptured Intracranial Aneurysms Investigators (ISUIA) by Wiebers et al. (53). ^bBased on data from the International Subarachnoid Aneurysm Trial (ISAT) by Molyneux et al. (34). ^cThis category includes the internal carotid artery paraclinoid location, carotid-ophthalmic bifurcation, and internal carotid artery cavernous portion, but excludes the internal carotid-posterior communicating artery. ^dThis category includes the pericallosal artery and the anterior cerebral artery proximal to the anterior communicating artery, but excludes the anterior cerebral-anterior communicating artery. Table III: Choice and Timing of Aneurysm Treatment in the Presented Studies

	Unruptured Aneurysms – no. (%)	Ruptured Aneurysms – no. (%)
Surgical clipping	3 (21.4)	13 (36.1)
First trimester	2 (14.3)	3 (8.3)
Second trimester	1 (7.1)	1 (2.8)
Third trimester	-	2 (5.6)
Postpartum period	-	7 (19.4)
Intravascular coil embolization	1 (7.1)	20 (55.6)
First trimester	-	1 (2.8)
Second trimester	-	3 (8.3)
Third trimester	1 (7.1)	11 (30.6)
Postpartum period	-	5 (13.9)
No treatment	9 (64.3)	3 (8.3)

delivery in patients with ruptured (87% vs 13%) and unruptured (71% vs 29%) aneurysms. All twelve patients who gave birth before receiving treatment for aneurysm rupture underwent Cesarean deliveries (10, 13, 22, 23, 27, 32, 38, 40, 42). Six of these were part of a combined neurosurgical-obstetrical approach in which treatment (clipping, n = 3; coiling, n = 3) immediately followed delivery (10, 23, 27, 32, 38, 42). Two additional patients with ruptured aneurysms underwent combined procedures in which treatment (surgical clipping) preceded Cesarean delivery (27, 42).

Five patients went into labor with previously untreated and unruptured aneurysms (14, 22, 27, 42). Among these, one patient experienced aneurysm rupture during vaginal delivery and the child was immediately delivered via Cesarean section (27). A second patient also experienced aneurysm rupture during vaginal delivery (22).

Maternal Outcome

The complication rate of all patients included in our study was 18.2%. When taking into consideration only patients that received aneurysm treatment, the complication rates for ruptured and unruptured aneurysms were to 8.8% and 14.3%, respectively. Maternal complications were more than twice as frequent in patients who underwent clipping versus coiling for aneurysm rupture (23.1% *vs.* 9.5%). Maternal outcomes are listed in Table I.

Aneurysm rupture was fatal in three cases (42). Of these patients, two presented during the third trimester with highgrade subarachnoid hemorrhage after MCA aneurysm rupture, and both died from cerebral herniation before treatment was initiated; the third patient died during the postpartum period from cerebral edema and herniation due to ICA aneurysm rebleeding 12 days after surgical clipping (42). Other complications from aneurysm rupture were third nerve palsy (n = 1) and chronic ventriculomegaly (n = 1) (38, 42). Complications secondary to unruptured aneurysms were third nerve palsy (n = 1) and reduced visual acuity (n = 2). Two studies reported patients with reduced visual acuity, including one case that persisted after coil embolization for a suspected cavernous-carotid fistula (13, 45).

Fetal Outcome

Adverse outcomes related to maternal aneurysms were reported in five children (11.9%) (26, 42). Two children died at birth, and a third child died *in utero* after maternal death from cerebral herniation following aneurysm rupture (42). One child was aborted at ten weeks gestation due to the risk of fetal radiation damage from coil embolization of a ruptured aneurysm (26). Neurological retardation and ventriculomegaly developed in one child (42).

DISCUSSION

Selecting a strategy for the treatment of intracranial aneurysms is challenging, and balancing the risks to the fetus and mother adds further complexity (10, 12, 30). However, guidelines for the management of intracranial aneurysms during pregnancy are not currently available. We address here some of the principle aspects unique to managing the pregnant patient.

Risk of Rupture During Pregnancy

We found that 78% of the ruptured aneurysms in our review occurred during the third trimester, compared to only 8% and 11% in the first and second trimesters, respectively. This may be explained by the nature of the vascular changes during pregnancy, which fluctuate according to gestational age (18, 28, 54). Blood pressure is reported to fall during the second trimester, which corresponds to the lower rate of aneurysm rupture seen during that time (18, 54). The decrease in blood pressure that occurs during the second trimester is followed by a rise back to or above the patient's normal blood pressure range throughout the third trimester and postpartum period (28, 54). We suggest that this hemodynamic pattern be considered in the management of aneurysms. The neurosurgeon should be cautious not to overlook patients who harbor small or asymptomatic aneurysms early in the course of pregnancy, as later changes may progressively increase the risk of aneurysm enlargement and rupture. One patient in our review presented during the third trimester with worsening headaches and blurred vision after enlargement to 18 millimeters of an untreated aneurysm that was present before the pregnancy (37). A second patient required coil embolization during the third trimester due to 40% enlargement and rupture of an aneurysm that was clipped during the first trimester (32).

Methods of Aneurysm Treatment

Coil embolization was performed more often than clipping for patients in our review (47.7% vs 36.4%) (20). The less invasive nature of coiling results in shorter operating times and shorter hospital stays than surgical clipping (4, 20). In cases that require aneurysm treatment before childbirth, reducing the operation time by performing an endovascular procedure translates into decreased fetal exposure to anesthesia and possibly improved outcomes. Fetal complications during anesthesia may cause permanent deficits to the newborn (10, 27).

Although coil embolization offers the advantage of reducing fetal exposure time to anesthesia, the use of systemic heparinization that comes with it is potentially dangerous (35). Heparinization poses a greater risk of bleeding complications if emergency Cesarean section is needed, such as when anesthesia causes fetal bradycardia (23, 35). Another concern associated with coil embolization is that radiation used during angiography may damage the embryo or early fetus (29). Such concerns are most pressing during the first trimester, when the risk for radiation-induced defects, namely congenital abnormalities and death, is highest (31). One study in our review documented a case in which embolization during the 8th week of pregnancy lead to elective abortion because of "probable injury to the fetus from radiation exposure" (26). Digital subtraction angiography (DSA) is currently used more often than computed tomography (CT) in the diagnosis of intracranial aneurysms, as well as during the embolization procedure; however, DSA is known to deliver higher doses of radiation (29). Nonetheless, it has been reported that the amount of radiation delivered during these situations is negligible (5, 39). Fetal shielding, excluding fluoroscopy near the uterus, and safer technologies have been used successfully to combat radiation damage (26). These results, along with those of our study, point to the value of treatment in reducing complications, especially since complications may be fatal.

Treatment of Ruptured Aneurysms

Neurosurgical treatment of ruptured aneurysms during pregnancy should be approached the same as in the nonpregnant population (46). Furthermore, our results suggest that the treatment of ruptured aneurysms during pregnancy is safe and effective. Maternal mortality among treated patients was 2.7%; the overall complication rate was 8.8%. Similar results were reported in a large study by Kim et al., in which treatment of ruptured aneurysms reduced maternal mortality to 6.7% (25). Among the cases presented in our review, coil embolization was associated with a lower complication rate for ruptured aneurysms (9.5% *vs* 23.1%). Notably, one patient required coil embolization 14 weeks after clipping for aneurysm enlargement (32).

In our review, two patients and their children died from highgrade subarachnoid hemorrhage before receiving treatment (42). Although these particular patients were in critical condition upon presentation, we note that early signs of hemorrhage may be difficult to detect. Since plasma volume is 30% higher in pregnant women, onset of clinical signs after aneurysm rupture may be delayed (49). Importantly, compensatory mechanisms after major hemorrhage may decrease blood flow to the placenta in an attempt to maintain adequate perfusion pressure in the mother, and fetal distress may be an early sign of blood loss in the mother (9).

Treatment of Unruptured Aneurysms

In our review, we found that patients who were treated for unruptured aneurysms had 32% fewer complications than those who did not receive treatment. It is currently accepted that unruptured aneurysms during pregnancy should be treated only when symptomatic or enlarging (46). However, our review showed a clear trend of aneurysm rupture at sizes traditionally considered to be at low risk of rupture. Sixty-two percent of aneurysms measuring between three and six millimeters in our review were ruptured, as well as 91% of aneurysms measuring at least six millimeters. Thus, it seems prudent to be more aggressive with the treatment of smaller aneurysms in pregnancy to prevent rupture and the risks associated with it. Based on our review of the literature, we suggest that neurosurgical treatment is indicated for unruptured aneurysms that are either symptomatic, show signs of instability, or measure at least six millimeters, as these aneurysms seem to represent a higher risk of unfavorable maternal and fetal outcomes. Furthermore, smaller aneurysms such as those between three and six millimeters must be monitored carefully and considered for treatment if they become larger, unstable or asymptomatic. As previously discussed, coil embolization results in shorter operating times, less anesthesia exposure and shorter hospital stays than surgical clipping, and thus serves as a better management option for unruptured aneurysms when possible, especially when the patient is not near term.

Treatment of Aneurysms in Patients Near Term

Special consideration is required for the treatment of aneurysms near term. Many authors suggest that clipping or coiling should be performed immediately before or after delivery when possible (23, 27, 32, 38, 42). Six studies in our review presented cases in which a combined management strategy was employed (10, 23, 27, 32, 38, 42). Delivering the child first, before neurosurgical treatment, is expected to result in better outcomes for the fetus (27, 42). By doing so, the fetus is protected from potential anesthesia-related problems or changes in maternal blood pressure dynamics that may result from aneurysm re-bleeding intraoperatively, as well as postoperative maternal complications such as cerebral vasospasm (27). Moreover, the fetus is spared from the risk of hypoxia, dehydration and acidosis, which may result from poor uterine perfusion and increased vascular resistance as a consequence of hyperventilation and osmotic diuretics often used during surgery (2, 10, 27, 52). Aneurysm treatment after childbirth in a combined procedure also benefits the anesthesiologist, who is better able to create optimal operating conditions for the neurosurgeon without harming the child (10). Additionally, performing both neurosurgical and obstetrical operations under the same general anesthesia spares the mother from undergoing multiple anesthetic procedures. In consideration of these data, we suggest that child delivery prior to treatment in patients near term may improve child outcomes and facilitate the neurosurgical and anesthesiological management of patients during surgery.

Methods of Child Delivery

Childbirth in a patient with an intracranial aneurysm covers the scope of both neurosurgery and obstetrics, and there must be a coordinated approach between physicians in each field. Our analysis of the current literature shows a clear preference for Cesarean section delivery (84.2%) in pregnant women with intracranial aneurysms, when compared to the reported rate of Cesarean delivery in the general population (32.8%) (19). Vaginal delivery was deemed inappropriate by some studies because of the associated methods of anesthesia delivery, high-pressure Valsalva maneuvers needed by the patient, or existing aneurysm-related complications such as cranial defects from prior clipping (16, 30). Lumbar puncture involved with spinal and epidural anesthesia (both commonly used for vaginal delivery) has been reported to increase the risk of aneurysm rupture due to loss of CSF and increased vessel transmural pressure (3, 8). Whether straining during vaginal delivery causes aneurysm rupture is argued in the literature, however our data suggests that this depends on whether the aneurysm has been treated prior to delivery (4, 11, 15, 21, 41). We reported three patients who went into labor with previously untreated and unruptured aneurysms; two of these patients experienced aneurysm rupture during vaginal delivery (27). Conversely, no complications were reported in patients who underwent vaginal delivery with previously treated aneurysms (32, 35, 38, 42).

Limitations

Limitations of the present review stem from the nature of reported data and its sample size. We have presented our findings from a set of case reports, case series and one retrospective study, the original reports of which are subject to reporting bias and selection bias. Incomplete data reporting and the tendency to report favorable outcomes more often than unfavorable ones may have affected aneurysm management in ways that are unrecognizable to the authors of this study. We presented fifty aneurysms in forty-four patients, however this is only a small subset of the pregnant population that is managed for intracranial aneurysms. Taking these limitations into account, our intention to provide a concise summary of the literature to outline the management of intracranial aneurysms during pregnancy. To best establish a set of guidelines for neurosurgical practice, we strongly suggest the need for large prospective studies dedicated to correlating management options to maternal and fetal outcomes and complications.

■ CONCLUSION

Based on our review of the published literature, neurosurgical treatment of intracranial aneurysms in pregnancy is safe and effective. We found that coil embolization following aneurysm rupture resulted in fewer maternal complications than clipping, and it is important to realize the advantages and disadvantages unique to each procedure in pregnancy. The use of endovascular methods has steadily increased, and associated reductions in operating time and hospital stay are beneficial to both the mother and child. The most serious complications of aneurysms in pregnant women appear after rupture, at which point the probability of poor outcomes increases and may be fatal. Unfortunately, most ruptured aneurysms are diagnosed after the fact. Aneurysms that are found intact should be critically assessed for treatment, realizing that the adverse effects of pathological progression outweigh those of neurosurgical treatment.

Our review of the literature suggests that maternal and neonatal outcomes of combined neurosurgical-obstetrical procedures are favorable, as no adverse outcomes were reported. However, because of the limited follow-up data on aneurysm enlargement and re-bleeding in the pregnant population, it is uncertain whether surgical clipping or coil embolization provides greater long-term stability. Stronger documentation and additional trials are needed in this regard.

The major finding of our review is a much higher rate of Cesarean section delivery in pregnant women affected by intracranial aneurysms; however absolute guidelines for delivery in this specific patient population are not yet available in the literature. Management of pregnant patients with an intracranial aneurysm ultimately lies in the hands of the neurosurgeon, but we encourage a coordinated approach with obstetrical personnel to ensure comprehensive treatment. Going forward, we suggest the establishment of formal guidelines for neurosurgical and obstetrical management of intracranial aneurysms during pregnancy after large prospective studies are completed.

REFERENCES

- Barrett JM, Van Hooydonk JE, Boehm FH: Pregnancy-related rupture of arterial aneurysms. Obstet Gynecol Surv 37(9): 557-566, 1982
- Battaglia F, Prystowsky H, Smisson C, Hellegers A, Bruns P: Fetal blood studies. XIII. The effect of the administration of fluids intravenously to mothers upon the concentrations of water and electrolytes in plasma of human fetuses. Pediatrics 25: 2-10, 1960
- Bottiger BW, Diezel G: Acute intracranial subarachnoid hemorrhage following repeated spinal anesthesia. Anaesthesist 41(3):152-157, 1992

- Brunken M, Kehler U, Fiehler J, Leppien A, Eckert B: Coiling vs. clipping: Hospital stay and procedure time in intracranial aneurysm treatment. Rofo 181(10):989-995, 2009
- Chandra V, Dorsey C, Reed AB, Shaw P, Banghart D, Zhou W: Monitoring of fetal radiation exposure during pregnancy. J Vasc Surg 58(3):710-714, 2013
- Cipolla MJ: The adaptation of the cerebral circulation to pregnancy: Mechanisms and consequences. J Cereb Blood Flow Metab 33(4):465-478, 2013
- Couldwell SM, Kraus KL, Couldwell WT: Regression of cerebral arteriovenous malformation in the puerperium. Acta Neurochir (Wien) 153(2): 359-362, 2011
- Coursange F, Aubert M, Gosset S, Carpentier JP, Cornen L: Rupture of an intracranial aneurysm after spinal anesthesia. Ann Fr Anesth Reanim 6(2):113-114, 1987
- 9. Curran CA: Intrapartum emergencies. J Obstet Gynecol Neonatal Nurs 32(6):802-813, 2003
- D'Haese J, Christiaens F, D'Haens J, Camu F: Combined cesarean section and clipping of a ruptured cerebral aneurysm: A case report. J Neurosurg Anesthesiol 9(4):341-345, 1997
- 11. Dias MS: Neurovascular emergencies in pregnancy. Clin Obstet Gynecol 37(2): 337-354, 1994
- Dias MS, Sekhar LN: Intracranial hemorrhage from aneurysms and arteriovenous malformations during pregnancy and the puerperium. Neurosurgery 27(6):855-65; discussion 865-866, 1990
- Dogan S, Salman MC, Deren O, Geyik S: Carotid-cavernous fistula in term pregnancy due to spontaneous rupture of carotid-cavernous aneurysm. J Obstet Gynaecol Res 38(2): 427-430, 2012
- Duggan T, Simpson A: An unusual intracranial aneurysm presenting in pregnancy. Int J Obstet Anesth 17(2):194-195, 2008
- Fliegner JR, Hooper RS, Kloss M: Subarachnoid haemorrhage and pregnancy. J Obstet Gynaecol Br Commonw 76(10): 912-917, 1969
- Georgantopoulou C, Jha R: Intracranial aneurysm in pregnancy presenting as hyperemesis gravidarum. J Obstet Gynaecol 23(1):74-75, 2003
- Goto Y, Ebisu T, Mineura K: Ruptured intracranial aneurysm during pregnancy with false-negative computed tomography angiography findings: A case report. Emerg Radiol 22(3): 343-346, 2015
- Grindheim G, Estensen ME, Langesaeter E, Rosseland LA, Toska K: Changes in blood pressure during healthy pregnancy: A longitudinal cohort study. J Hypertens 30(2):342-350, 2012
- Hamilton BE, Hoyert DL, Martin JA, Strobino DM, Guyer B: Annual summary of vital statistics: 2010-2011. Pediatrics 131(3):548-558, 2013
- Huang MC, Baaj AA, Downes K, Youssef AS, Sauvageau E, van Loveren HR, Agazzi S: Paradoxical trends in the management of unruptured cerebral aneurysms in the United States: Analysis of nationwide database over a 10-year period. Stroke 42(6):1730-1735, 2011
- 21. Hunt HB, Schifrin BS, Suzuki K: Ruptured berry aneurysms and pregnancy. Obstet Gynecol 43(6):827-837, 1974

- Hussain SA, Chitnavis B, Connor S, Strong AJ, Gullan RW: Spontaneous thrombosis of a giant aneurysm following pregnancy. Case illustration. J Neurosurg 94(4):680, 2001
- 23. Jaeger K, Ruschulte H, Muhlhaus K, Tatagiba M: Combined emergency Caesarean section and intracerebral aneurysm clipping. Anaesthesia 55(11):1138-1140, 2000
- 24. Kim KD, Chang CH, Choi BY, Jung YJ: Endovascular treatment of a ruptured posterior inferior cerebellar artery aneurysm during pregnancy. J Korean Neurosurg Soc 55(5): 273-276, 2014
- 25. Kim YW, Neal D, Hoh BL: Cerebral aneurysms in pregnancy and delivery: Pregnancy and delivery do not increase the risk of aneurysm rupture. Neurosurgery 72(2):143-149; discussion 150, 2013
- 26. Kizilkilic O, Albayram S, Adaletli I, Kantarci F, Uzma O, Islak C, Kocer N: Endovascular treatment of ruptured intracranial aneurysms during pregnancy: Report of three cases. Arch Gynecol Obstet 268(4):325-328, 2003
- Kriplani A, Relan S, Misra NK, Mehta VS, Takkar D: Ruptured intracranial aneurysm complicating pregnancy. Int J Gynaecol Obstet 48(2):201-206, 1995
- Macdonald-Wallis C, Lawlor DA, Fraser A, May M, Nelson SM, Tilling K: Blood pressure change in normotensive, gestational hypertensive, preeclamptic, and essential hypertensive pregnancies. Hypertension 59(6):1241-1248, 2012
- Marshman LA, Aspoas AR, Rai MS, Chawda SJ: The implications of ISAT and ISUIA for the management of cerebral aneurysms during pregnancy. Neurosurg Rev 30(3):177-180; discussion 180, 2007
- Mavromatidis G, Dinas K, Mamopoulos A, Delkos D, Vosnakis C, Michailidis K, Rousso D: Uneventful delivery with caesarean section in a woman with a history of endovascular management of an intracranial aneurysm. J Obstet Gynaecol 31(7):664, 2011
- McCollough CH, Schueler BA, Atwell TD, Braun NN, Regner DM, Brown DL, LeRoy AJ: Radiation exposure and pregnancy: When should we be concerned? Radiographics 27(4): 909-917; discussion 917-918, 2007
- 32. Meyers PM, Halbach VV, Malek AM, Phatouros CC, Dowd CF, Lawton MT, Lempert TE, Higashida RT: Endovascular treatment of cerebral artery aneurysms during pregnancy: Report of three cases. AJNR Am J Neuroradiol 21(7):1306-1311, 2000
- 33. Miller HJ, Hinkley CM: Berry aneurysms in pregnancy: A 10 year report. South Med J 63(3):279 passim, 1970
- 34. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, Holman R: International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: A randomized trial. J Stroke Cerebrovasc Dis 11(6):304-314, 2002
- 35. Nelson LA: Ruptured cerebral aneurysm in the pregnant patient. Int Anesthesiol Clin 43(4): 81-97, 2005
- Nevo O, Soustiel JF, Thaler I: Cerebral blood flow is increased during controlled ovarian stimulation. Am J Physiol Heart Circ Physiol 293(6): H3265-9, 2007

- Ortiz O, Voelker J, Eneorji F: Transient enlargement of an intracranial aneurysm during pregnancy: Case report. Surg Neurol 47(6):527-531, 1997
- Piotin M, de Souza Filho CB, Kothimbakam R, Moret J: Endovascular treatment of acutely ruptured intracranial aneurysms in pregnancy. Am J Obstet Gynecol 185(5):1261-1262, 2001
- 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 17(3): 205-207, 2010
- Riviello C, Ammannati F, Bordi L, Lamassa M, Mennonna P, Parretti E, Tondi F, Mello G: Pregnancy and subarachnoid hemorrhage: A case report. J Matern Fetal Neonatal Med 16(4): 245-246, 2004
- Robinson JL, Hall CJ, Sedzimir CB: Subarachnoid hemorrhage in pregnancy. J Neurosurg 36(1): 27-33, 1972
- Roman H, Descargues G, Lopes M, Emery E, Clavier E, Diguet A, Freger P, Marpeau L, Proust F: Subarachnoid hemorrhage due to cerebral aneurysmal rupture during pregnancy. Acta Obstet Gynecol Scand 83(4): 330-334, 2004
- 43. San-Frutos L, Engels V, Zapardiel I, Perez-Medina T, Almagro-Martinez J, Fernandez R, Bajo-Arenas JM: Hemodynamic changes during pregnancy and postpartum: A prospective study using thoracic electrical bioimpedance. J Matern Fetal Neonatal Med 24(11):1333-1340, 2011
- 44. Selo-Ojeme DO, Marshman LA, Ikomi A, Ojutiku D, Aspoas RA, Chawda SJ, Bawa GP, Rai MS: Aneurysmal subarachnoid haemorrhage in pregnancy. Eur J Obstet Gynecol Reprod Biol 116(2):131-143, 2004
- Shutter LA, Kline LB, Fisher WS: Visual loss and a suprasellar mass complicated by pregnancy. Surv Ophthalmol 38(1):63-69, 1993

- 46. Sloan MA, Stern BJ: Cerebrovascular disease in pregnancy. Curr Treat Options Neurol 5(5): 391-407, 2003
- 47. Stoodley MA, Macdonald RL, Weir BK: Pregnancy and intracranial aneurysms. Neurosurg Clin N Am 9(3):549-556, 1998
- Surico D, Amadori R, Garofalo G, Nuzzi NP, Carriero A, Surico N: "One-shot" endovascular management of cerebral aneurysm and fourth ventricle hemangioblastoma in a pregnant woman. Int J Gynaecol Obstet 129(1):79-80, 2015
- Tan EK, Tan EL: Alterations in physiology and anatomy during pregnancy. Best Pract Res Clin Obstet Gynaecol 27(6):791-802, 2013
- 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 114(6):703-706, 2012
- Weir BK, Drake CG: Rapid growth of residual aneurysmal neck during pregnancy. Case report. J Neurosurg 75(5):780-782, 1991
- Whitburn RH, Laishley RS, Jewkes DA: Anaesthesia for simultaneous caesarean section and clipping of intracerebral aneurysm. Br J Anaesth 64(5): 642-645, 1990
- 53. Wiebers DO: Unruptured intracranial aneurysms: Natural history and clinical management. Update on the international study of unruptured intracranial aneurysms. Neuroimaging Clin N Am 16(3):383-390, vii, 2006
- 54. Wilson M, Morganti AA, Zervoudakis I, Letcher RL, Romney BM, Von Oeyon P, Papera S, Sealey JE, Laragh JH: Blood pressure, the renin-aldosterone system and sex steroids throughout normal pregnancy. Am J Med 68(1):97-104, 1980