



# Outcome in women undergoing uterine artery embolization for arterio-venous malformation diagnosed post-pregnancy-A retrospective study

## Gebelik sonrası tanı konulan arteriyovenöz malformasyon nedeniyle uterin arter embolizasyonu uygulanan kadınlarda sonlanım-Retrospektif bir çalışma

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<sup>1</sup>Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, New Delhi, India

<sup>2</sup>Department of Radiodiagnosis, All India Institute of Medical Sciences, New Delhi, India

### Abstract

**Objective:** To analyse the outcome of patients with symptomatic arterio-venous malformation (AVM), formed following pregnancy and managed by uterine artery embolization (UAE).

**Materials and Methods:** This retrospective study was conducted after ethical approval and included 15 patients presenting with abnormal uterine bleeding following pregnancy, who were suspected to have an AVM which later was confirmed by angiography and managed with UAE. Presenting symptoms, post-UAE complications and subsequent fertility outcomes were noted. Follow-up period ranged from 6 months to 2.5 years.

**Results:** The mean age was 28.4±3.82 years and mean parity was 1.3. Out of 15 cases, 9 (60%) presented after abortion, 4 (26.6%) after normal vaginal delivery and 2 (13.3%) after cesarean delivery; of these 10/15 (66.7%) patients had a history of curettage. The most common presenting symptom was continuous bleeding per-vaginum since the antecedent pregnancy in 9/15 (60%) patients and 6/15 (40%) patients had irregular bleeding. The mean duration of symptoms was 91±85.7 (30-360) days. For UAE, embolic agents used were polyvinyl alcohol (PVA) particles (300-500 µm) in 2 (13.3%), 30% glue injection in 3 (20%), the combination of PVA with glue injection in 4 (26.6%) and PVA with gelfoam in 6 (40%) patients. After UAE, bleeding responded within 3.6±0.97 (3-6) days in all but one patient who required repeat UAE one month later. All women resumed their normal menstrual cycle in 31.3±5.2 (24-42) days. Ten patients desired conception, of whom 5 (50%) conceived within 13.2±5.1 (6-19) months after UAE. Two women carried pregnancy to term, one underwent preterm cesarean for growth restriction with oligohydramnios. One patient had postpartum hemorrhage, which was managed medically. One had spontaneous abortion at 6 weeks gestation and the other is 13 weeks pregnant at present.

**Conclusion:** UAE is an effective treatment modality for the management of symptomatic post-pregnancy AVMs.

**Keywords:** Uterine artery embolization, arteriovenous malformation, post-pregnancy, outcomes

### Öz

**Amaç:** Gebelikten sonra oluşan ve uterin arter embolizasyonu (UAE) ile tedavi edilen semptomatik arterio-venöz malformasyonlu (AVM) hastaların sonuçlarını analiz etmek.

**Gereç ve Yöntemler:** Bu retrospektif çalışma, etik onay alındıktan sonra yapıldı ve gebelik sonrası anormal uterin kanama ile başvuran, AVM'si olduğundan şüphelenilen ve daha sonra anjiyografi ile doğrulanan ve UAE ile tedavi edilen 15 hastayı içeriyordu. Başvuru semptomları, UAE sonrası komplikasyonlar ve sonraki doğurganlık sonuçları not edildi. Takip süresi 6 ay ile 2,5 yıl arasında değişmekteydi.

**PRECIS:** UAE for management of symptomatic AVMs following pregnancy is an effective treatment modality.

**Address for Correspondence/Yazışma Adresi:** Vatsla Dadhwal MD,

Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, New Delhi, India

**Phone:** +09811015979 **E-mail:** vatslad@hotmail.com **ORCID ID:** orcid.org/0000-0003-0280-5833

**Received/Geliş Tarihi:** 22.01.2022 **Accepted/Kabul Tarihi:** 05.06.2022

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Turkish Journal of Obstetrics and Gynecology published by Galenos Publishing House.

**Bulgular:** Ortalama yaş 28,4±3,82 yıl ve ortalama parite 1,3 idi. On beş olgunun 9'u (%60) kürtaj, 4'ü (%26,6) normal vajinal doğum ve 2'si (%13,3) sezaryen sonrası başvurdu. On (%66,7) hastanın küretaj öyküsü vardı. En sık başvuru semptomu, 9/15 (%60) hastada önceki gebelikten beri sürekli vajinal kanama idi ve 6/15 (%40) hastada düzensiz kanama mevcuttu. Ortalama semptom süresi 91±85,7 (30-360) gündü. UAE için kullanılan embolik ajanlar, 2 hastada (%13,3) polivinil alkol (PVA) partikülleri (300-500 µm), 3 hastada (%20) %30 tutkal enjeksiyonu, 4 hastada (%26,6) PVA ile tutkal enjeksiyonu kombinasyonu ve 6 hastada (%40) PVA ile jel köpüğü kombinasyonu kullanıldı. BAE'den sonra, bir ay sonra UAE'nin tekrarlanması gereken bir hasta dışında tüm hastalarda kanama 3,6±0,97 (3-6) gün içinde durduruldu. Tüm kadınlar 31,3±5,2 (24-42) günde normal adet döngüsüne döndüler. UAE'den sonra 10 hasta gebe kalmak istedi ve 5 hasta (%50) 13,2±5,1 (6-19) ay içinde gebe kaldı. İki kadında terme kadar gebelik devam ederken, bir kadına oligohidramnios ve gelişme geriliği nedeniyle erken sezaryen uygulandı. Bir hastada medikal olarak tedavi edilen doğum sonu kanama vardı. Biri 6 haftalık gebeyken spontan düşük yaptı ve diğeri şu anda 13 haftalık hamiledir.

**Sonuç:** UAE gebelik sonrası semptomatik AVM'lerin yönetiminde etkili bir tedavi yöntemidir.

**Anahtar Kelimeler:** Uterin arter embolizasyonu, arteriyovenöz malformasyon, gebelik sonrası, sonlanım

## Introduction

Uterine arterio-venous malformations (AVM) are rare, representing 1-2% of all genital hemorrhages<sup>(1)</sup>. AVMs are characterized by abnormal communications between arteries and veins in the same vicinity, which can be of varying sizes. Uterine AVMs may be congenital or acquired. Congenital AVMs are the result of defect in embryonic vascular differentiation<sup>(2)</sup> and usually present as pubertal heavy menstrual bleeding. Acquired uterine AVMs are usually traumatic, resulting from prior curettage, uterine surgery, or direct uterine trauma. Less commonly, these may also be associated with neoplasm, infection, endometriosis, diethylstilbestrol and intrauterine devices<sup>(3)</sup>.

AVMs usually occur in women of reproductive age but have been reported up 72 years and are rare in nulliparous women. Patients mostly present with abnormal uterine bleeding (AUB) due to the disruption of thin walled abnormal vessels. Bleeding may be insidious or acute<sup>(3)</sup>; heavy, irregular, or scanty but prolonged. Patients with AVM formed post-pregnancy may present as postpartum hemorrhage or bleeding may ensue post-instrumentation of the gravid uterus following abortions<sup>(4,5)</sup>. Patients may also present with pain in the lower abdomen, anemia, and rarely congestive heart failure due to a large AV shunt. Approximately 30% AVM cases require blood transfusion<sup>(6)</sup>.

Treatment options for uterine AVMs include expectant management in women with mild symptoms, medical management for symptomatic relief and surgical management in severe cases. Though hysterectomy is the definitive cure, uterine sparing unilateral or bilateral uterine artery ligation is also an option. In today's era, uterine artery embolization (UAE) is emerging as a promising conservative treatment due to its potency and safety<sup>(7,8)</sup>. However, the literature-regarding post-pregnancy AVM is limited. This retrospective study was conducted to evaluate the efficacy and safety of UAE for symptomatic uterine AVMs developing the following pregnancy.

## Materials and Methods

The study was conducted in the Department of Obstetrics and Gynecology, All India Institute of Medical Sciences New Delhi India, a tertiary care hospital, from July 2017 to December 2019.

The inclusion criteria were patients with angiography confirmed AVM who presented with AUB following a pregnancy and who were managed with UAE. Exclusion criteria were patients with no history of antecedent pregnancy before AVM diagnosis; patients in whom angiography report was not available and patients who were not managed with UAE.

After obtaining ethical approval from the Institute Ethics Committee (IEC-660/03.07.2020), data for these cases were retrieved from the hospital records. The patients were followed up telephonically after obtaining verbal consent. Patient's socio-demographic profile was noted. Detailed history, including presenting symptoms with duration, details of antecedent pregnancy and its outcome, obstetric history, previous menstrual history, investigations, ultrasonography and Doppler findings were extracted from case records.

All patients underwent UAE after discussion regarding their need and feasibility based on the severity of symptoms, failed medical management and ultrasound findings. Pelvic digital subtraction angiography (DSA) was performed in all patients at the time of UAE, which confirmed AVM. UAE was performed under local anesthesia with asepsis. The bilateral common femoral artery was punctured using an 18 gauge needle and a 6F sheath was placed inside the internal iliac artery under fluoroscopic guidance. Embolization was performed using polyvinyl alcohol (PVA) particles, 30% glue injection (Endocryl, Samarth Life Sciences Pvt. Ltd., India) or gelfoam (Spongostan, Ferrosan Medical Devices A/S, Søborg, Denmark), as per availability.

Procedural details such as the type of embolic agent used and intra-procedural difficulty or complications were noted. Post procedure imaging for vascularity and resolution of the lesion was performed after 24 hr. Time taken for the relief of symptoms was noted. The menstrual pattern and any subsequent pregnancy in women keen on conception were determined on telephonic interview. Follow-up period ranged from 6 months to 2.5 years.

## Statistical Analysis

Data was analyzed using the statistical package STATA version 12.0 (Texas, USA). Descriptive statistics such as mean, standard deviation and range values were computed for all continuous variables.

## Results

Total 15 women underwent UAE for AVM, which developed post-pregnancy, over a span of two years. The mean age and parity were  $28.4 \pm 3.82$  years and 1.3 respectively. Nine (60%) patients presented after abortion, including two 2<sup>nd</sup> trimester abortions, 4 (26.6%) patients presented after normal vaginal delivery and 2 (13.4%) after cesarean section. Symptoms started immediately the following pregnancy in 5/15 (33%) patients and there was no history of curettage. Rest 10 (67%) patients had symptoms following curettage performed for managing antecedent pregnancy complications. Details of patients included in the study are shown in Table 1 and Figure 1.

The mean hemoglobin at hospital admission was  $8.9 \pm 1.97$  gm/dL. The most common presenting symptom was continuous bleeding per vaginum (BPV) since the antecedent pregnancy in 9/15 (60%) patients, 6/15 (40%) patients had irregular but heavy BPV and four of these required blood transfusions. The mean time interval since symptom onset and UAE was  $91 \pm 85.7$  (30-360) days (Table 1).

The embolic agents used for UAE were PVA particles (300-500  $\mu$ m diameter) in 2 (13.3%) patients, 30% glue injection in 3 (20%) patients, the combination of PVA with glue injection in 4 (26.6%) and PVA with gelfoam in 6 (40%) patients, as per availability (Table 1). Bilateral UAE was successful in 14/15 (93.3%) patients; with complete symptomatic relief achieved

in  $3.6 \pm 0.97$  (3-6) days (mean  $\pm$  standard deviation, range). One patient required a repeat embolization due to persistent vascularity on Doppler and had symptomatic relief five days after the 2<sup>nd</sup> UAE. Hence, failure rate in the present study was 6.7%. Figure 2 and Figure 3 show DSA spot images and pre- and post-embolization ultrasound Doppler images, respectively.

Procedure related complications were seen in 3 (20%) patients. One patient developed a 2 cm hematoma at the femoral puncture site, which was managed conservatively by pressure bandage and resolved in three days. Two patients developed mild fever with lower abdominal pain and were managed with antipyretics and analgesics. None of the patients had any severe adverse event.

All patients resumed the menstrual cycle in  $31.3 \pm 5.2$  (24-42) days post-procedure. Five (33.3%) patients complained of hypomenorrhoea with mean  $1.9 \pm 0.7$  bleeding days. Three (20%) patients had an increased frequency of cycles (mean  $20.6 \pm 2.5$  days) compared to their previous cycles.

Ten out of 15 patients (66.7%) desired conception, of whom 5 (50%) conceived within  $13.2 \pm 5.1$  (6-19) months after UAE.

Two patients carried pregnancy to term with no complications, one delivered vaginally and the other underwent cesarean for failed induction. The third patient had preterm cesarean at 34 weeks' gestation done for severe oligohydramnios with fetal growth restriction and had PPH, which was managed

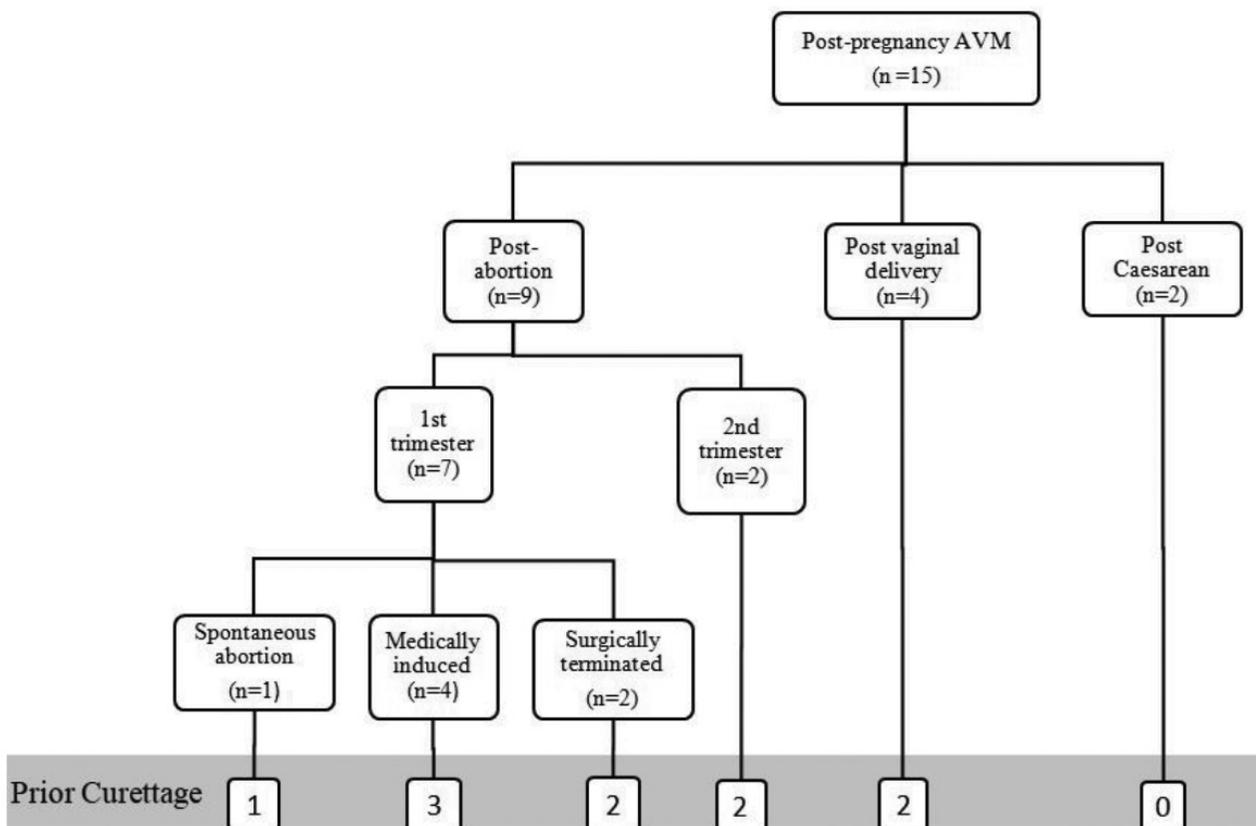


Figure 1. Showing antecedent pregnancies and history of curettage in women included in study

medically. One patient had spontaneous abortion at 6 weeks gestation and pregnancy is ongoing in another patient who is 13 weeks pregnant (Table 2). However, 3 patients who developed hypomenorrhoea tried for conception but none of them conceived with in follow-up duration.

## Discussion

Surgical manipulations such as curettage lead to an increased immune response and angiogenesis, disturbing uterine physiology<sup>(9,10)</sup>. Peitsidis et al.<sup>(9)</sup> in a systematic review of 91 studies, reported acquired AVM after curettage in 95 of 103 patients with

AVM. Obstetric association of AVM even without prior curettage is also reported; proposed mechanism being aberrant regression of the placental bed or abnormal vascular communication after chorionic villi necrosis<sup>(5)</sup>. In a retrospective study by Kim et al.<sup>(1)</sup>, of 19 patients who developed AVM following delivery, approximately a quarter of patients had no history of curettage, which was almost similar to this study, with about 30% patients lacking prior curettage; though in Vilos et al.'s<sup>(10)</sup> case-series of five patients 60% did not have prior curettage.

In the past, AVMs have been diagnosed incidentally on histopathology after hysterectomy performed for heavy

**Table 1.** Overview of patients developing AVM following pregnancy and managed with UAE

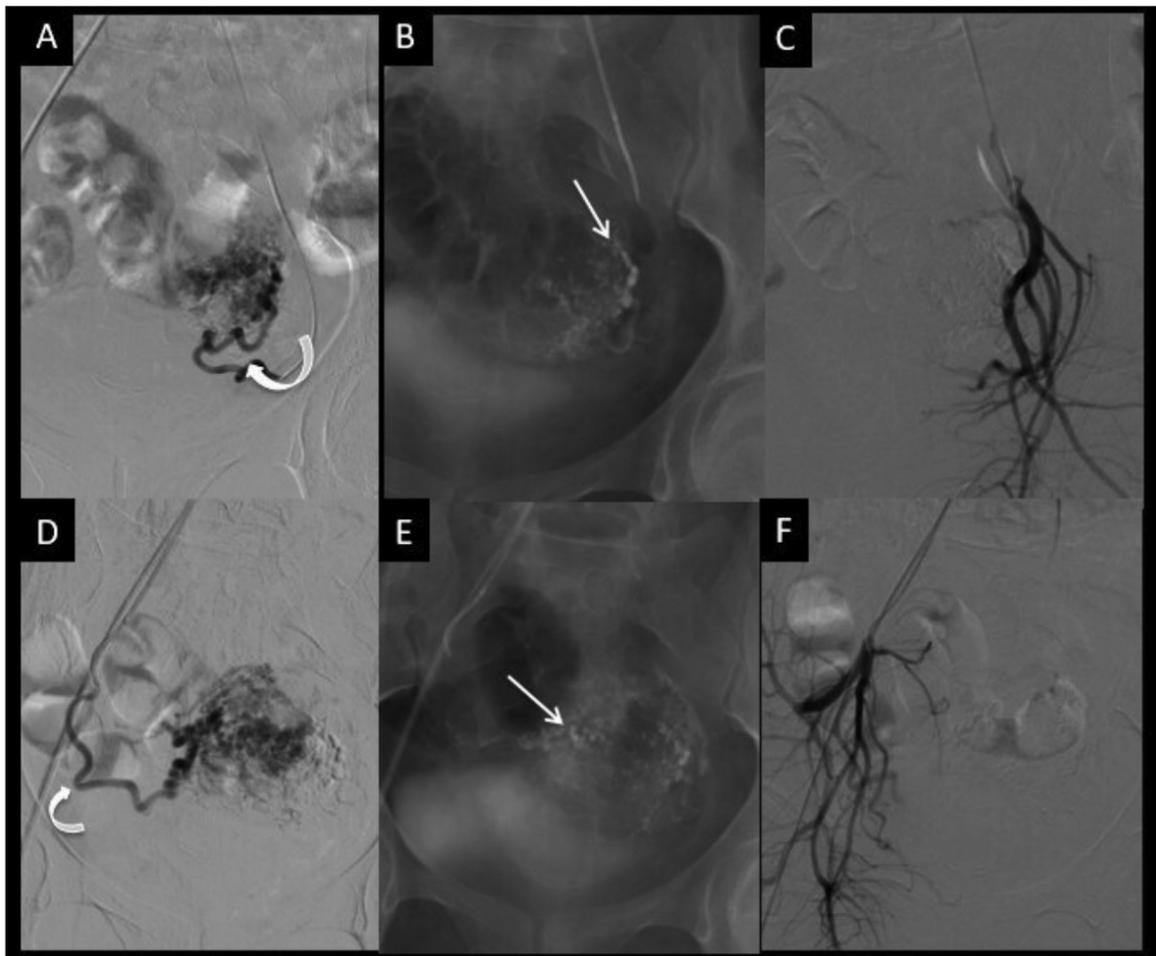
Case	Age (in years)	Parity	Antecedent pregnancy	Symptoms duration at presentation (In days) <sup>1</sup>	Clinical presentation	Medical treatment prior to UAE	Embolic agent	Pregnancy	Interval between UAE and conception (months)
1	33	P3L4A1	Abortion	30	Continuous BPV	TA	PVA	Not desired	
2	27	A3	Abortion	60	Irregular&HMB	TA	Glue	Conceived <sup>2</sup> (Caesarean)	19
3	22	P1I1A1	FTNVD	180	Irregular & HMB	TA	Glue	Not conceived	
4	27	P1L1A2	Abortion	96	Continuous BPV	TA& OCP	PVA and glue	Conceived (Caesarean)	17
5	32	P2L2A1	Abortion	120	Continuous BPV	TA	PVA and glue	Not desired	
6	30	P3L3	FTLSCS	90	Irregular &HMB	OCP	PVA	Not desired	
7	28	P1L1A1	Abortion	45	Continuous BPV	TA	Glue	Conceived (VD)	13
8	30	PLL1A3	Abortion	360	Irregular &HMB	TA	PVA and glue	Not conceived	
9	24	P1L0A1	Abortion	60	Continuous BPV	TA	PVA and glue	Conceived <sup>3</sup> (abortion at 8 week)	11
10	31	P1L1A1	Abortion	50	Continuous BPV	TA	PVA and Gelfoam	Not conceived	
11	27	P1L1	FTNVD	54	Continuous BPV	TA& OCP's	PVA and Gelfoam	Conceived (ongoing pregnancy-13 weeks)	6
12	25	P1L1	FTNVD	30	Continuous BPV	TA	PVA and Gelfoam	Not conceived	
13	26	P1L1A2	PTVD	30	irregular & HMB	OCP's	PVA and Gelfoam	Not conceived	
14	28	P1L2	PTLSCS	40	Continuous BPV	TA	PVA and Gelfoam	Not desired	
15	37	P2L2A1	Abortion	120	irregular & HMB	TA	PVA and Gelfoam	Not desired	

<sup>1</sup>: Onset of symptoms was immediately following pregnancy in 5/15 (33%) patients without history of curettage. Rest 10 (67%) patients had onset of symptoms following curettage done for the management of antecedent pregnancy complications.

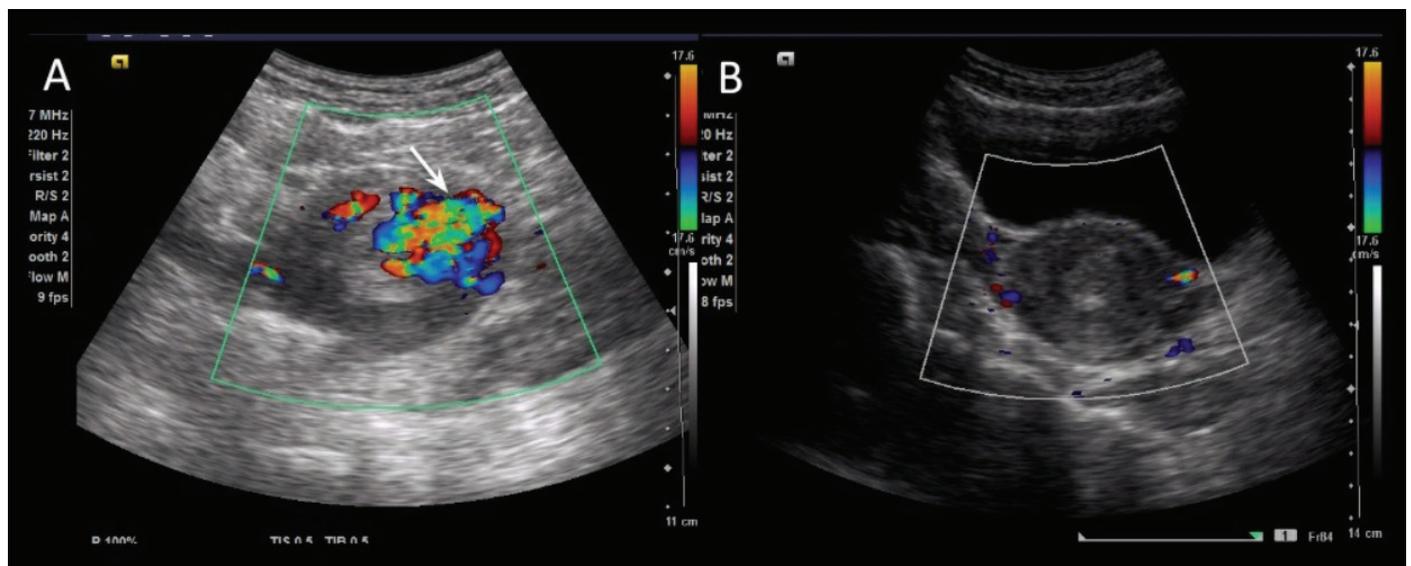
<sup>2</sup>: This patient underwent repeat UAE 48 hours after first UAE due to persistent bleeding and persistent vascularity on Doppler.

<sup>3</sup>: This patient developed a 2 cm hematoma.

TA: Tranexamic acid, VD: Vaginal delivery, HMB: Heavy menstrual bleeding, PVA: Polyvinyl alcohol, UAE: Uterine artery embolization, AVM: Arterio-venous malformation



**Figure 2.** Diagnostic subtraction angiography (DSA) spot images of UAE: A & D showing bilateral hypertrophied uterine arteries supplying the nidus of uterine AVM (curved arrow); B & E showing vessels being embolized sequentially using glue mixed with lipiodol (arrows); C & F showing post embolization angiograms showing non filling of the uterine AVM suggestive of successful embolization



**Figure 3.** (A) Pre-embolization ultrasound Doppler image (A) showing bunch of vascular channels within the uterine wall (arrow) suggestive of uterine AVM. (B) Post embolization Doppler image (B) showing complete obliteration of nidus of AVM

**Table 2.** Pregnancy outcomes in patients of AVM who conceived after UAE

Pregnancy	Total n=5	Complication	Particle used for UAE	Interval between UAE & conception(months)
Full term delivery				
<b>Total</b>	2			
Caesarean	1		PVA and glue	17
Vaginal	1		Glue injection	13
Prterm	1	Severe oligohydramnios, FGR, PPH	Glue injection	19
Caesarean	1			
Abortion	1	Spontaneous abortion at 6 weeks	PVA and glue	11
Ongoing	1 (at 13weeks gestation)		PVA and gel foam	6

UAE: Uterine artery embolization, FGR: Fetal growth restriction, PPH: Postpartum haemorrhage, AVM: Arterio-venous malformation

bleeding<sup>(9)</sup>. The advent of imaging modalities such as colour-Doppler ultrasonography, magnetic resonance imaging, computed tomography and pelvic angiography has made diagnosis easy and early. Pelvic angiography remains the gold standard for diagnosing AVM<sup>(11)</sup>, though not used routinely as ultrasonography with color Doppler has good detection<sup>(6)</sup>. In the present study, all cases could be diagnosed with Doppler ultrasound, and confirmed with angiography at the time of UAE.

Treatment options for post-pregnancy AVM remain the same as AVM of other etiologies and include medical treatment, uterine sparing UAE or hysterectomy, which is the definitive treatment. Forssman et al.<sup>(12)</sup> in 1982 reported the first conservative treatment of uterine arteriovenous aneurysm which was occluded at laparotomy by introducing gelfoam into the uterine artery. In a review including a hundred women with iatrogenic AVM after diagnostic curettage and presenting with acute abnormal uterine bleeding, 59% patients underwent UAE, 29% had hysterectomy, 6% responded to methylergometrine, and 6% had a spontaneous resolution<sup>(9)</sup>. All patients in our study were managed conservatively with UAE and only one patient required the second session of embolization, which is comparable to 5.3% (1/19) reported by Kim et al.<sup>(1)</sup>, though 60% (3/5) patients required repeated embolization in the study by Vilos et al.<sup>(10)</sup>.

The embolic agent most commonly used in patients desiring fertility is gelfoam because of its temporary nature<sup>(10,13)</sup>, but no difference is reported in clinical outcome with other embolic agents<sup>(14,9)</sup>.

Reported complications of the procedure are puncture site superficial hematoma in 0.6-14.8%, uterine artery rupture during manipulation, contrast allergy, adult respiratory distress syndrome and femoral artery hematoma, pseudoaneurysm and arterio-venous fistula<sup>(1,13,15)</sup>. In present study, one patient had puncture site hematoma which was managed with compression. There is concern of diminished ovarian function and consequent amenorrhea and subfertility post-UAE. However, in Peitsidis' review, most patients resumed normal menstruation within two months and none developed amenorrhea<sup>(9)</sup>. As in our series, evidence also suggests that the ovarian function might not be

affected or, if affected, recovers in young patients undergoing UAE<sup>(16)</sup>. Fifty percent (5/10) of our patients desiring pregnancy conceived spontaneously within two years of UAE and only one of them had placental insufficiency requiring pre-term delivery. Pregnancy in other patients were uneventful. Two patients were delivered by cesarean due to obstetric indications and other delivered vaginally. Peitsidis et al.<sup>(9)</sup> reported a pregnancy rate of up to 29% following UAE for AVM with 15 months as mean time to conceive, whereas up to 50% pregnancy rate was reported by Delplanque et al.<sup>(8)</sup> within mean 38 months from UAE who also studied peak systolic velocity with the success of UAE in AVMs. Post-UAE pregnancy outcomes in a meta-analysis of 227 pregnancies conceived after UAE performed for leiomyoma showed 35.2% risk of abortion, which was three fold higher than controls; 66% caesarean rate; with no increase in preterm delivery rate<sup>(17)</sup>.

In this study, UAE was successful in the symptomatic management of all fifteen patients presenting with post-pregnancy AVM with no significant complications, and half of the woman desiring pregnancy conceived. Hence, UAE can be offered to young patients with post-pregnancy AVM, though the retrospective nature and small sample size are the limitations of this study.

## Conclusion

UAE is an effective and safe option for managing symptomatic AVMs developing post-pregnancy in women of reproductive age.

## Ethics

**Ethics Committee Approval:** After obtaining ethical approval from the Institute Ethics Committee (IEC-660/03.07.2020), data for these cases were retrieved from the hospital records.

**Informed Consent:** Retrospective study.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Concept: V.K., Sw.S., J.M., S.G., S.S., N.S., S.K., V.D., Design: V.K., Sw.S., J.M., S.G., S.S., N.S., S.K., V.D., Data Collection or Processing: V.K., Sw.S., J.M., S.G., S.S., N.S., S.K., V.D.,

Analysis or Interpretation: V.K., Sw.S., J.M., S.G., S.S., N.S., S.K., V.D., Literature Search: V.K., Sw.S., J.M., S.G., S.S., N.S., S.K., V.D., Writing: V.K., Sw.S., J.M., S.G., S.S., N.S., S.K., V.D.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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