VOLUME - 14, ISSUE - 06, JUNE - 2025 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper | Obstetrics & Gynaecology

THE CLINICAL EFFECTIVENESS AND SAFETY OF UTERINE ARTERY EMBOLIZATION IN CASES OF REFRACTORY INTRACTABLE HAEMORRHAGE IN TERTIARY CENTRE OF SOUTH INDIA- CASE SERIES AND REVIEW OF LITERATURE.

Dr Kalaivani Thirupathi* MS OG, Assistant Professor, Department Of Obstetrics And Gynaecology , Sri Venkateshwara Medical College And Hospital And Research Centre, Ariyur, Puducherry, India. *Corresponding Author

Dr Jayalakshmi Mega Nathan MS OG, Assistant Professor, Department Of Obstetrics And Gynaecology, Sri Venkateshwara Medical College And Hospital And Research Centre, Ariyur, Puducherry, India.

ABSTRACT Uterine artery embolization has become a standard treatment for life-threatening, intractable hemorrhage in hemodynamically stable patients, often considered in cases of postpartum hemorrhage and gynaecological conditions where conservative management is preferred over surgical interventions. Due to its low invasiveness, high success rate, low morbidity, and the possibility of preserving reproductive functions in women of low parity, it should be considered as a non-surgical alternative approach for intractable hemorrhage instead of a definitive surgical procedure like hysterectomy. Intractable hemorrhage can be successfully managed through a multidisciplinary approach that provides comprehensive care, such as selective angiographic embolization performed by interventional radiologists, serving as a life-saving and fertility-saving procedure. We hereby present a case series of three patients who presented with secondary postpartum hemorrhage, uterine arteriovenous malformation, and abnormal uterine bleeding, and were managed with uterine artery embolization at Villupuram Medical College, Tamil Nadu, India.

KEYWORDS : Intractable Haemorrhage, Uterine artery Embolization (UAE), Secondary Postpartum haemorrhage (PPH), Uterine Arterio venous Malformation (AVM), Heavy menstrual bleeding (HMB), Abnormal Uterine Bleeding.

INTRODUCTION

Uterine artery embolization (UAE) is a minimally invasive, selective endovascular embolization introduced 30 years ago and is an effective and safe intervention for intractable hemorrhage. Unilateral UAE has been observed to be more clinically effective and safer than bilateral UAE in terms of shorter fluoroscopy time, lower requirement for analgesia, and reduced periprocedural pain. According to the NIH, the reported clinical success rate of UAE in intractable hemorrhage ranges from 87% to 98%.[1] Postpartum hemorrhage (PPH) is the leading cause of maternal morbidity and mortality worldwide, occurring in approximately 1% to 3% of all deliveries. In developing countries, PPH accounts for 8% of maternal deaths, whereas it accounts for 20% in developed countries.[2] In India, the incidence of PPH ranges from 2% to 4% in vaginal deliveries and 6% in caesarean sections, contributing to 19.9% of maternal deaths. As a major global concern in low-income and middle-income countries, PPH accounts for one death every six minutes.[1] According to the American College of Obstetricians and Gynecologists (ACOG) recommendations (2017), PPH can be defined as cumulative blood loss of more than 1000 ml with signs and symptoms of hypovolemia within 24 hours of delivery, regardless of the mode of delivery.[3] Based on symptom onset, PPH can be subdivided into primary PPH (occurring between placental delivery and 24 hours after baby delivery) and secondary PPH (occurring after 24 hours of delivery, up to 12 weeks postpartum). Atonic uterus is the primary cause of PPH, accounting for 70%-80% of all haemorrhages. Primary PPH is due to the "4Ts" – tone, trauma, tissue, and thrombus, whereas secondary PPH is associated with retained placenta, sub involution of placental sites, inherited coagulopathies, and infections.[3]

Uterine arteriovenous malformation (AVM) is a rare and life-threatening condition characterized by the proliferation of arterial and venous channels with fistula formation and a mixture of capillary-like vessels, with a reported mortality rate of 1% to 4%. It may be either congenital or acquired. Congenital AVM is due to anomalous differentiation of capillaries and abnormal communication between arteries and veins, mainly resulting from arrested vascular embryologic development, which may invade surrounding structures and is often found as isolated cases. Acquired AVM commonly occurs after uterine trauma, such as caesarean section, curettage procedures, retained products of conception (RPOC), gestational trophoblastic diseases, gynaecological malignancies, pelvic surgeries, and diethylstilbestrol exposure. Ultrasound color Doppler is commonly used to detect this condition, but digital subtraction angiography remains the gold standard for diagnosis.[1,4]

Abnormal uterine bleeding (AUB) can be characterized by menorrhagia, metrorrhagia, polymenorrhea, dysfunctional uterine bleeding, and heavy menstrual bleeding. In India, the reported prevalence of AUB is 17.9%, and heavy menstrual bleeding (HMB) is 24.1%. Uterine artery embolization (UAE) is an effective treatment for symptomatic adenomyosis with a reasonable long-term success rate. However, given the more than 40% rate of treatment failure and recurrence, all patients should be counselled before the procedure about the possibility of treatment failure and the potential need for hysterectomy.[1–4]

We hereby report a case series of three patients with intractable hemorrhage who were treated with UAE, its clinical outcome, and also review the literature on the clinical effectiveness and safety of UAE.

Case Series

Case 1

A 23-year-old woman, P1L1, delivered a live term male baby weighing 3.1 kg by emergency caesarean section due to fetal distress at a private hospital. Her postoperative period was uneventful, and she was discharged on postoperative day 5. She presented to our obstetric casualty on postoperative day 21 with a history of 5 episodes of vaginal bleeding, soaking 10-12 pads, associated with clots. She had similar complaints with 3 episodes of bleeding on postoperative day 16, for which she was conservatively managed with Antifibrinolytics. For a haemoglobin level of 7.2 g/dl, 2 units of packed RBCs were transfused at a private clinic, and she was discharged the next day with a haemoglobin level of 9.1 g/dl and reassurance. Her past medical and surgical history was insignificant.

On examination, her vitals were stable, with a pulse rate of 92/min, blood pressure of 110/70 mmHg, SpO2 of 100% on room air, and a respiratory rate of 16/min. Per abdominal

examination revealed an involuting uterus, and no palpable mass was felt. On bimanual examination, the cervical os was open, and 650 grams of clots were removed from the vaginal canal; all fornices were free, and there was no forniceal tenderness. An abdominal ultrasound with color Doppler revealed a bulky uterus and a blood-filled endometrial cavity. A provisional diagnosis of secondary postpartum hemorrhage was made, and she was conservatively managed with 1 gram of Tranexemic acid, 2 units of packed RBCs, and 4 units of fresh frozen plasma transfused for a haemoglobin level of 8.1 g/dl. Her platelet count was 276,000/mm^3, total count was 16,000, bleeding time was 2 minutes 40 seconds, clotting time was 4 minutes 40 seconds, prothrombin time was 13 seconds, INR was 1.0, and an intrauterine Foley tamponade was inserted.

After 4 hours of observation in the obstetric ICU, she had 3 episodes of bleeding, with 500 grams of clots removed from the vaginal canal, and she was managed conservatively with 3 units of packed RBC transfusion to maintain hemodynamic stabilization. After 24 hours of admission, she had no further episodes of bleeding per vaginum and was observed in the obstetric ICU. MRI of the abdomen revealed a bulky uterus with no evidence of uterine arteriovenous malformation. After 2 days of admission, she had 4 episodes of bleeding per vaginum on her postoperative day 24, with removal of 500 grams of clots. In view of her low parity index (P1L1), young age (23 years), and persistent refractory bleeding episodes, uterine artery embolization was considered by a multidisciplinary team to preserve her reproductive functions. Bilateral uterine artery embolization was performed on postoperative day 25 using gelatin sponge particles as embolic agents, under fluoroscopic guidance, which were inserted into the uterine arteries. Post-procedural angiography was performed in the immediate postoperative period after UAE to confirm blocked uterine arteries for blood flow cessation. Her postoperative period after UAE was uneventful, and she was discharged on postoperative day 33.

Case 2

A 28-year-old woman, Gravida 2, Para 1, Live 1 (G2P1L1), at a gestational age of 9 weeks and 3 days, presented with complaints of vaginal bleeding associated with clots. She had one previous caesarean section a year ago at a private clinic due to meconium-stained liquor/fetal distress. Her past medical and surgical history was insignificant. Upon examination, her vitals were stable, her abdomen was soft and non-tender, and bimanual examination revealed a bulky uterus with products of conception felt through the os with bleeding per vaginum. Basic investigations were sent and found to be within normal range. A trans abdominal ultrasound was performed, which showed retained products of conception. A provisional diagnosis of incomplete abortion was made, and an emergency dilatation and curettage procedure was done. Her post-abortal period was uneventful, and she was discharged on day 2 of the post-abortal period.

After 3 days of discharge, she presented to our obstetric casualty with complaints of 3 episodes of vaginal bleeding, and her vitals were stable. Bimanual examination revealed a bulky uterus, and 250 grams of blood clots were removed from the vaginal canal. Initially, she was conservatively managed with Antifibrinolytics and blood products (1 unit of packed RBC) transfusion. A trans abdominal ultrasound with color Doppler was done, which revealed retained products of conception of size 1.2 cm with absent vascularity. Therefore, she was managed with misoprostol (dose 400 mcg kept pervaginally), followed by passage of clots, and discharged the next day with no evidence of RPOC on check ultrasound abdomen.

On post-abortal day 9, she again presented with complaints of 5 episodes of vaginal bleeding, and 300 grams of blood clots were removed from the vaginal canal. She was hemodynamically stabilized with adequate fluid and blood products. A trans abdominal ultrasound with color Doppler and MRI abdomen was performed, which showed features of uterine arteriovenous malformation with RPOC of size 0.5 cm and prominent vascularity in the myometrium. Although CT angiography is considered a diagnostic modality for uterine arteriovenous malformation, in this case, ultrasound and MRI were used for diagnosis. Bilateral uterine artery embolization was performed using gelatin sponge particles as embolic agents under fluoroscopic guidance. After the procedure, angiography was done to confirm the blocked uterine arteries for blood flow cessation. Her postoperative period was uneventful, and a stat dose of injection methotrexate was given for RPOC, and she was discharged on postoperative day 5.

Case 3

A 32-year-old woman, P2L2, presented to our emergency department with complaints of heavy menstrual bleeding per vaginum for 5 days, with a history of 3 episodes of bleeding per vaginum. She had 2 normal deliveries previously, had regular menses of 3/28-day cycles until her 2nd childbirth, and irregular cycles were observed for the last three months with a history of heavy menstrual bleeding (HMB). She had no significant past medical or surgical history. On examination, her vitals were stable, abdominal examination was soft and non-tender, and bimanual examination revealed a bulky uterus, free fornices, and 200 grams of clots were removed from the vaginal canal. Initially, she was conservatively managed with Antifibrinolytics and blood products transfusion for a haemoglobin level of 6.5 g/dl (3 units of packed RBC), and her coagulation profile was found to be normal. A trans abdominal ultrasound was done, suggesting features of adenomyosis with a bulky uterus. A diagnosis of abnormal uterine bleeding-adenomyosis (AUB-A) was made as per the PALM-COEIN classification, endometrial biopsy revealed proliferative endometrium, and hormonal drugs containing progesterone were given. The patient was discharged after 5 days of observation.

After 2 months, the patient again presented with a history of 5 episodes of bleeding per vaginum, 350 grams of blood clots were removed from the vaginal canal, and she was hemodynamically stable. She was conservatively managed with Antifibrinolytics and blood products transfusion for a haemoglobin level of 8.1 g/dl (2 units of packed RBC). During her admission, she had 3 episodes of bleeding per vaginum, and an MRI abdomen was performed to rule out uterine arteriovenous malformation. She was discharged with reassurance and advice for regular follow-up. After 1 month, she again had 2 episodes of bleeding per vaginum, with 150 grams of blood clots removed from the vaginal canal. Hysteroscopic-guided endometrial ablation was performed this time, and a Levonorgesterol-releasing intrauterine system (LNG-IUS) was inserted, and she was discharged.

After 3 months, she presented to our emergency department with complaints of 5 episodes of bleeding per vaginum, with 200 grams of blood clots removed from the vaginal canal. She was hemodynamically stable, and abdominal ultrasound with color Doppler suggested features of adenomyosis with a bulky uterus and normal vascularity noted. Uterine artery embolization was planned, considering her low parity and age of 32 years, and bilateral UAE was done with the help of a multidisciplinary team. She was discharged after 5 days with instructions for regular follow-up. After 6 months, she had 4 episodes of bleeding per vaginum. Due to conventional treatment failure, a life-saving definitive procedure of hysterectomy was performed.

Table 1. Clinical Summary of Refractory Intractable Haemorrhage case series and Effectiveness of Uterine

artery Embolization.

Case	Clinical scenario	Management strategy	Clinical outcome	Clinical insight
Case 1	A 23 year old P1L1/ Post LSCS had intractable bleeding per vaginum since POD 16 and diagnosed as Secondary PPH	Conservatively managed with Blood products , due to its Refractory condition, UAE was performed as a fertility saving procedure.	Excellent maternal outcome	Emphasizes early diagnosis and collaborative management approach
Case 2	A 28 year old G2P1L1/ Previous LSCS had Incomplete Abortion at 9 weeks of gestation, had intractable bleeding per vaginum on Post abortal day 4, USG abdomen with Doppler and MRI Abdomen suggested Uterine AV malformation	UAE was performed as a life saving procedure.	Maternal survival	Significance of identifying D&C related Uterine AV malformation
Case 3	A 32 years old P2L2 presented with heavy bleeding per vaginum, had Adenomyosis features in USG, diagnosed as AUB- A	Conservatively managed with LNG-IUD, Refractory bleeding results in UAE, but Intractable Haemorrhage leads to Hysterectomy as a life saving procedure.	Full recovery	Emphasizes the need for tailored surgical planning

DISCUSSION

The success rate of uterine artery embolization (UAE) has been reported as 88.4% after the first procedure, 79.2% after a single UAE, and 66.7% after repeated embolization. As a first-line modality of management in cases of intractable hemorrhage, its success rate depends on its clinical effectiveness, safety, and fertility-preserving technique due to its less time-consuming nature and few long-term complications. The key factors responsible for its success depend on the availability of well-equipped infrastructure and a well-trained multidisciplinary team of obstetricians, anaesthetists, and interventional radiologists in a tertiary center.[1–2]

The most common cause of intractable hemorrhage in obstetric cases is postpartum hemorrhage (PPH), which leads to severe morbidity and mortality due to placental abnormalities like placenta accreta and placenta praevia. After spontaneous delivery of the placenta, uterine contractions draw blood from nearby collaterals, and excessive bleeding occurs if placental tissue remains. The reported success rate of UAE for PPH management is 87.2%, and the most common cause of UAE failure is constricted uterine arteries.[3]

During delivery, hemodynamic stability can be maintained by considering prophylactic occlusion of the aorta through a balloon catheter, but reported vascular complications are higher, and its effectiveness is reduced due to the extensive collateral circulation of the uterus. Due to its risk of radiation exposure and vascular complications, its prophylactic role remains debatable. The prompt use of UAE in cases of intractable obstetric hemorrhage effectively controls bleeding by decreasing the occurrence of re-bleeding from collaterals, as more distal occlusion of vessels improves the chances of fertility and uterine preservation. The timing of UAE plays a pivotal role, as delayed diagnosis and treatment in PPH can challenge its effectiveness; therefore, a proactive approach to UAE in PPH management is essential.

The post-procedural complications of uterine artery embolization (UAE) include fever, catheter site hematoma, pelvic abscess, contrast allergy, ischemia, and rarely, perforation of the iliac artery.[4] During UAE, ascending spread of infection may occur through the endometrial cavity, adnexa, bowel, and blood. Post-embolization syndrome can be misdiagnosed as pyomyoma due to its similar triad of features, including pelvic pain, sepsis, unknown source of infection, and elevated total cell count.[5] According to a study report by Brat et al. (2007), unilateral UAE was performed in 48 patients based on angiographic findings, which included a smaller and less tortuous uterine artery supplying normal myometrium, whereas a larger and more tortuous artery supplied fibroid tissue. Resolution of symptoms was achieved in 76-85% of cases.[5] Stall et al.'s study (2011) reviewed 1500 patients who underwent UAE, including 28 cases of unilateral UAE compared with bilateral UAE cases. Significant clinical differences were not observed between the two groups, except for a lower dose of radiation exposure in unilateral UAE.

According to Vishalakshi et al.'s study reports, 5 cases were successfully treated with complete control of bleeding, and a high success rate was reported in cases presented later than 6 hours. Additionally, 1 patient conceived after 11 months of UAE.[6] Jung HN et al.'s study suggested that UAE successfully managed 14 cases of postpartum hemorrhage (PPH), with only 3 cases undergoing hysterectomy due to its failure.[7] Park JK et al.'s study evaluated the clinical effectiveness of UAE in 23 cases of PPH due to uterine atony, placenta accreta spectrum, puerperal hematoma, and placental polyp. Of these cases, only 2 underwent hysterectomy due to severe vasoconstriction.[8]

In a study conducted by Cheng H et al., post-procedural complications of UAE included hypomennorhea (55.6%), abdominal pain (4 cases), frequent micturition (2 cases), and pelvic inflammatory disease (1 case). Menstruation and pregnancies were not affected by UAE, but it increased the risk of placenta praevia in subsequent pregnancies.[9] UAE can affect subsequent pregnancies, such as miscarriages, abnormal placentation, and PPH. However, a well-planned fertility preservation technique protects the ovaries, which is considered a safe and effective procedure for women who plan to conceive in the future. During UAE, minimizing the risk of exposure to the ovarian artery preserves fertility functions.

A systematic review study conducted in 2021 compared UAE and medical treatment of uterine arteriovenous malformation, and the success rate was reported to be similar. Due to hormonal changes in pregnancy, there may be proliferation of latent uterine AVM after a D&C procedure, possibly through an unknown etiology, such as enhanced myometrial vascularity and retained products of conception. Soro et al.'s study suggested that UAE has no direct effect on placental blood supply and does not affect fetal growth due to the formation of collateral circulation after UAE. However, heterogeneous rates of infertility, uterine synechiae, and premature ovarian failure may occur following UAE.[10]

According to a study report by Brat and Walker (2008), 27 cases of adenomyosis were managed with UAE using PVA

particles, and 14 cases had co-existing uterine fibroids. These cases were followed clinically at 6 and 12-month intervals after UAE.[5] Of these, 88% of cases showed improvement in menorrhagia at 6 months, which dropped to 79% at one-year follow-up. Cases with adenomyosis without fibroids showed 80% improvement in menorrhagia at one-year follow-up. Unilateral UAE was performed in one woman due to unfavourable anatomical conditions, and she underwent hysterectomy after 2 months due to persistent symptoms. At a 3-year follow-up study on 14 cases, 63% of cases showed complete resolution of dysmenorrhea, and 54% showed complete resolution of fibroid-related symptoms.[11] In our case, due to the failure of UAE at 6 months in adenomyosis-related intractable hemorrhage, hysterectomy was performed.

CONCLUSION

The role of UAE as a minimally invasive procedure in the management of refractory intractable hemorrhage should be considered early when conventional treatment fails. Its clinical efficacy can be achieved by obtaining rapid haemostasis, hemodynamic stability, and fertility preservation. Maternal morbidity and mortality can be reduced by adopting measures such as early diagnosis, prompt and proactive decision-making, and a multidisciplinary team approach in a tertiary center. In the future, studies related to unilateral UAE in the treatment of uterine fibroids should be considered to potentially avoid hysterectomy.

Funding- Not Required
Conflicts Of Interest- No

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