Use of Magnetic Resonance Imaging (MRI) in the Management of Diagnostic Uncertainty in Low-Resource Settings: A Case Report of Cesarean Ectopic Pregnancy in a Tertiary Hospital in Ghana

ABDEF 1 Anna Sarah Erem
ADE 2 Thomas Okpoti Konney
ADE 3 Adu Appiah-Kubi
AD 4 Kwasi Ankomah
B 4 Adu Tutu Amankwa
B 2 John Jude Kweku Annan
B 2 Augustine Tawiah
B 2 Benjamin Kwame Amoako-Adjei
B 5 Kwabena Fosu Lariedy
ABDE 6 Emma R. Lawrence

1 Department of Obstetrics and Gynecology, Saba University School of Medicine, Saba, Netherlands Antilles
2 Department of Obstetrics and Gynecology, Komfo Anokye Teaching Hospital, Kumasi, Ghana
3 Department of Obstetrics and Gynecology, University of Health and Allied Sciences, Ho, Ghana
4 Department of Radiology, Komfo Anokye Teaching Hospital, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana
5 Department of Anesthesiology, Komfo Anokye Teaching Hospital, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana
6 Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI, U.S.A.

Corresponding Author: Anna Sarah Erem, e-mail: a.erem@saba.edu
Conflict of interest: None declared

Patient: Female, 35-year-old
Final Diagnosis: Cesarean section ectopic pregnancy
Symptoms: Amenorrhea
Medication: —
Clinical Procedure: Exploratory laparotomy • MRI • ultrasonography
Specialty: Obstetrics and Gynecology

Objective: Management of emergency care
Background: Low- and middle-income countries (LMICs) account for the overwhelming majority of maternal deaths worldwide. Cesarean section rates have increased globally over the last 10 years, including in LMICs, and are an important intervention to decrease neonatal and maternal mortality. However, cesarean sections also contribute to increased complications in subsequent pregnancies, including invasive placentaion and cesarean scar ectopic pregnancies (CSEP). Potential CSEP complications include rupture of the uterus, bladder invasion, and maternal mortality.

Case Report: We present the case of a 35-year-old Ghanaian woman (gravidity 5, parity 3) with a positive urine pregnancy test and 2 months of amenorrhea. Ultrasound scanning demonstrated a gestational sac with a fetal pole and absent cardiac activity located in the lower uterine segment. Myometrium infiltration was present, with only 2 mm of anterior myometrium between the gestational sac and the urinary bladder. Owing to concern for CSEP with uncertain bladder invasion, a pelvic MRI was obtained for preoperative planning. Following the MRI, which demonstrated an intact bladder, the patient underwent an uncomplicated exploratory laparotomy and excision of the CSEP.

Conclusions: In LMICs, pelvic ultrasound continues to be the diagnostic tool of choice for CSEP. However, in cases with diagnostic uncertainty or possible bladder invasion, MRI is an additional imaging tool that can optimize preoperative planning and minimize the risk of maternal mortality and potential post-surgical complications.

MeSH Keywords: Cesarean Section • Ghana • Magnetic Resonance Imaging • Pregnancy, Ectopic • Ultrasonography

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/927496
Background

Low- and middle-income countries (LMICs) account for approximately 99% of the estimated 300 000 maternal deaths per year worldwide [1,2]. Disparities in maternal outcomes are a consequence of poor access to healthcare, which is commonly very centralized, patient inability to afford basic procedures, utilization of unverified traditional treatments [3–5], and low patient education [6,7]. Cesarean section rates have increased globally in the last decade [8] but range widely, from less than 10% in LMICs to 42% in the southeastern region of the United States [8]. Medically-induced cesarean delivery has been shown to decrease neonatal and maternal mortality in low-income but not in medium- and high-income countries [9]. Although cesarean sections can mitigate complications that can result in maternal death [10], they contribute to future reproductive complications, including invasive placentation and cesarean scar ectopic pregnancies (CSEP) [11].

The West African country of Ghana has had rapid development in obstetrics and gynecology (OBGYN) training, leading to an increased capacity for cesarean delivery, but also increased cesarean-related challenges. Cesarean section rates in Ghana increased from an average of 5.01% in 2003–2011 to 15.6% in 2018 [12], and the maternal mortality ratio decreased from 371 per 100 000 in 2005 to 308 per 100 000 in 2017 [13]. The rates of cesarean section in Ghana rise with increasing socioeconomic status [14].

This paper utilizes a case study of CSEP in Ghana to address several key points in the management of diagnostic uncertainty in LMICs. The importance of training and utilization of lower-cost diagnostic imaging, such as ultrasound, is emphasized. We also recognize that access to advanced medical technology, including magnetic resonance imaging (MRI), is increasing in LMICs like Ghana. This case demonstrates that the utilization of MRI in the management of CSEP involves a careful balance of cost and diagnostic benefit.

Case Report

A 35-year-old woman, with gravidity 5 and parity 3, presented with a positive urine pregnancy test result and 2 months of amenorrhea to the emergency department at the Komfo Anokye Teaching Hospital, a tertiary hospital and the second largest hospital in Ghana. Her past obstetric history was significant for 1 stillbirth delivered via spontaneous vaginal delivery, 2 prior scheduled low transverse cesarean sections, 1 spontaneous abortion managed expectantly, and 1 spontaneous abortion managed with manual vacuum aspiration. The indication for the patient’s most recent cesarean section was fetal macrosomia. During prenatal screening, the patient tested negative for diabetes, syphilis, hepatitis B and C, HIV, and rheusus incompatibility. Her other past medical history was unremarkable, although a hypercoagulability and antiphospholipid syndrome workup had not been performed.

On admission, the patient was hemodynamically stable. A pelvic examination demonstrated a nontender, retroverted uterus with nonpalpable adnexa. The laboratory evaluation was notable for serum beta-HCG level of 450 IU/L, hemoglobin level of 12.2 g/dL, and a normal white blood cell count. The patient’s electrolytes and liver and kidney function test results were also normal.

The urinalysis result was negative for hematuria. A pelvic ultrasound performed on admission demonstrated a gestational sac with a fetal pole and absent cardiac activity, located in the lower uterine segment. Myometrium infiltration was present, with only 2 mm of anterior myometrium between the gestational sac and the urinary bladder. There was no free fluid in the cul-de-sac. The findings were suggestive of CSEP and raised concern for possible bladder invasion. Owing to our uncertainty regarding bladder invasion, we decided to proceed with a pelvic MRI, which was performed 3 days after the patient’s presentation. The MRI demonstrated a gestational sac within the myometrium of the lower uterine segment in the region of the cesarean scar (Figures 1, 2). Also noted was extension of the posterior aspect of the gestational sac into the endometrial cavity of the lower uterine segment (Figure 2). The anterior myometrium was thin (Figure 2); however, the urinary bladder appeared normal with no radiologic evidence of invasion (Figures 1, 2). The risks and benefits of expectant management and the necessity of a series of follow-up visits were discussed with the patient. After carefully assessing the logistics and the likelihood of compliance, which included educating the patient on family planning and the importance of serial visits, the patient opted for surgical intervention. She underwent an uncomplicated exploratory laparotomy and excision of the gestational sac. Operative findings demonstrated a soft, vascular 3×5 cm mass in the region of the previous cesarean scar. An incision over the mass in the lower uterine segment revealed products of conception, which were removed (Figures 3, 4). The uterine cavity was digitally explored to remove the products of conception. The edges of the dehisced lower uterine segment scar were excised, and the incision was closed in a continuous fashion with Vicryl 2 sutures. On postoperative day 3, after an uncomplicated postoperative course, the patient was discharged. The pathological report of the samples confirmed the products of conception were normal.

Discussion

In high-income countries, up to two-thirds of ectopic pregnancies are treated before uterine rupture [15]. In Ghana,
only 1.9% to 8.5% of ectopic pregnancies are diagnosed before uterine rupture [7,16], with case fatalities as high as 27.9 per 1000 [16]. CSEP is the least common manifestation of ectopic pregnancy [17,18]. However, the frequency of CSEP has dramatically increased in recent years [19], comprising 4.2% of all ectopic pregnancies [20]. This is likely a consequence of increasing cesarean section rates, as well as other diagnostic improvements over the past 2 decades [21–23]. Technically, CSEP is harder to diagnose than tubal ectopic pregnancy and requires a careful differentiation from an ectopic pregnancy in the cervix. Although rare, CSEP has significant clinical consequences, including uterine rupture in 9.9% of cases [24] and death in 191.2 per 100 000 cases [25].

CSEP is believed to be a precursor of an abnormally adherent placenta, leading to placenta accreta, increta, and percreta [26]. One of its proposed mechanisms involves the implantation of a blastocyst into a microscopic tract within the cesarean scar [27,28]. Many factors could be responsible for the formation of a defect in the wound, including fibrosis, poor vasculature and oxygenation, poor approximation of the uterine incision, and poor wound healing (due to infection or fluid collection) [17].
As was the case with our patient, about one-third of CSEP cases present with asymptomatic secondary amenorrhea [23]. Common presenting signs include abdominal pain with or without vaginal bleeding [23]. Vague symptoms may be easily overlooked by the patient who later presents with late-stage complications including hemoperitoneum, uterine rupture, and hemodynamic instability. The mean gestational age of presentation is typically 7.5±2.5 weeks [23].

Risk factors for the development of CSEP include multiparity, advanced maternal age, history of multiple cesarean sections, history of multiple induced abortions, and iatrogenic uterine defect [29]. In vitro fertilization and fertility-conserving myomectomies for fibroids are also important risk factors [30]. During the first 5 years after the last cesarean section, there is an increased risk for CSEP, with the highest risk in the first 2 years [29]. CSEP risk factors may have compound effects [29]. As in our case, women with a history of cesarean section before the onset of labor are most at risk for CSEP because of the poor development of the lower uterine segment [23]. Elective cesarean section is also a risk factor for post-cesarean dehiscence, which is an independent risk factor for CSEP [31]. Interestingly, our patient had a retroflexed uterus, which is also a risk factor for CSEP. Mechanical tension is a plausible proposed mechanism for the increased risk of CSEP, which reduces the blood perfusion and oxygenation at the cesarean incision site [32,33]. Risk-increasing procedures, including myomectomy, dilatation and curettage, metroplasty and hysteroscopy [30], are currently available in private and public practices in Ghana. As minimally invasive gynecologic procedures become more accessible to the general population, education on their complications will become increasingly relevant when updating the OBGYN curriculum.

Transabdominal ultrasound can be used as a first step for quick visualization of the pelvis and may be helpful for evaluating suprapubic pathology or an abdominal ectopic pregnancy [34]. However, its reliability for the diagnosis of ectopic pregnancy is 70%, and the imaging can be limited by a large body habitus [35]. The diagnostic modality of choice for CSEP is transvaginal ultrasound, which has a sensitivity of 84.6% [36]. Ultrasound is a relatively inexpensive imaging technique with bedside optionality that is available in all tertiary and regional hospitals in Ghana and is becoming more available in Ghana’s district hospitals. In Ghana, ultrasound technique is a focused course during the OBGYN residency, with further refresher courses and self-directed ultrasound learning available throughout residency. Despite its advantages, ultrasonography evaluation of CSEP is limited by the differentiation of CSEP from cervical ectopic pregnancy and evaluation of possible bladder involvement. The presence of a thin myometrial layer between the bladder and the gestational sac is important to evaluate, and MRI should be considered if the anterior myometrium is <2.15 mm [37]. MRI is a relatively new imaging modality in Ghana. In CSEP, MRI is a highly accurate technique that can be used to assess the extent of implantation into the cesarean scar and possible bladder involvement. Due to its superiority in evaluating soft tissue, an MRI can identify a cesarean scar defect, the trophoblastic layer, and the myometrium separately, thus guiding the surgeon in preparation for intervention and surgical decision-making [11,38–40]. In contrast, ultrasound is less accurate in distinguishing between adjacent soft tissues and is therefore less accurate than MRI at evaluating CSEP [39]. This is significant because up to 13.6% of cesarean scar pregnancies are initially misdiagnosed as cervical ectopic pregnancies [41]. An MRI can better distinguish between them by more clearly distinguishing the location of the gestational sac [42] and detecting the presence of any deep stromal infiltration of the cervix [43]. Furthermore, MRI is superior to ultrasound in distinguishing the myometrial thinning between the sac and the bladder, which is characteristic of CSEP [44], and in detecting CSEP invasion into the bladder wall [45]. In some LMIC settings, MRI, through its ability to better characterize soft tissue and provide more detailed anatomical information, may allow physicians to consider minimally invasive procedures such as uterine artery embolization as a first-line treatment [46].

In our case, MRI imaging was utilized to guide surgical planning, including the timing of the patient’s surgery. It was also used for deciding whether urology or urogynecology teams needed to be involved and whether specialized surgical instruments needed to be available. In LMIC settings, there is limited availability of trained personnel and surgical equipment for a safe surgery addressing bladder involvement. Further, complications of unanticipated bladder involvement can have clinically significant and costly consequences. The use of MRI in LMICs must be carefully considered despite its benefits (Figure 5). While ultrasound can be performed quickly at bedside, MRI may take significant time to schedule and hours to perform, and thus should only be considered in hemodynamically stable patients. Cost is the largest barrier to the use of MRI in LMICs. In Ghana, MRI is not covered under Ghana’s national health insurance scheme. The approximate out-of-pocket cost of a pelvic MRI is 200 USD, which is a major expense considering that the minimum wage is just 2.05 USD per day in Ghana [47]. In addition to cost, access to MRI is limited in LMICs, and MRIs are usually available only in tertiary hospitals in major urban centers.

In populations with highly reliable patients and the ability to conduct close follow-up, medical management of CSEP with systemic methotrexate and intra-gestational sac injection of methotrexate or potassium chloride could be considered [48]. In Ghana, systemic methotrexate is available; however, the capacity and training for intra-sac injection are not currently available in public hospitals. Notably, medical management...
necessitates serial follow-up of beta-HCG values and ultrasound imaging [15]. In Ghana, the ability of patients to access and adhere to repeated follow-up visits is limited. Consequently, patients’ missing follow-up is a risk that may outweigh the benefits of medical management of CSEP in many LMIC settings.

In our case, operative management was carried out via laparotomy. In high-income settings, minimally invasive operative techniques, including laparoscopy and hysteroscopy, are the standard of care. Although hysteroscopic procedures have been reported to result in better outcomes and fewer reported obstetric complications for women with recurrent miscarriages, like our patient [49], hysteroscopy is not readily available throughout Ghana. Laparoscopic excision of CSEP has demonstrated a high degree of efficacy and low complication rates [48]. However, barriers to laparoscopic management of CESP in low-resource settings like Ghana include lack of access to laparoscopic equipment, limited laparoscopic gynecologic training, increased cost and operative times, and lack of national health insurance coverage for laparoscopy. Therefore, laparotomy is the standard of care for operative management of CESP at the Komfo Anokye Teaching Hospital and most LMIC public hospitals.

Conclusions

In LMICs, such as Ghana, the diagnosis and management of CSEP requires an understanding of the costs and benefits of ultrasound and MRI techniques. To improve care for women with CSEP, the primary focus should be on building the capacity for early identification of CSEP and the evaluation of potential bladder invasion on ultrasound. This is especially important in remote regions, where MRI is not available. If bladder invasion is suspected and the patient is hemodynamically stable, prompt transfer to a tertiary care facility with MRI capability should be considered. Overall, ultrasound continues to be the diagnostic tool of choice in CSEP. However, in cases with diagnostic uncertainty or in complicated CSEP with the potential of bladder invasion, MRI is a complementary imaging tool that can optimize preoperative planning and minimize the risk of maternal mortality and potential post-surgical complications.
References:

1. World Health Organization: Trends in maternal mortality: 1990 to 2013. Estimates by WHO, UNICEF, UNFPA, The World Bank and the United Nations Population Division, 2014.
2. World Health Organization, Unicef. Trends in maternal mortality: 1990 to 2010. WHO, UNICEF, UNFPA and The World Bank estimates, 2012.
3. Aizato L, Antwi HO: Facilitators and barriers of herbal medicine use in Accra, Ghana: An inductive exploratory study. BMC Complement Altern Med, 2016; 16(1): 142.
4. Aizato L, Odai PN, Omoyen CN: Religious beliefs and practices in pregnancy and labour: An inductive qualitative study among post-partum women in Ghana. BMC Pregnancy Childb, 2016; 16(1): 138.
5. Fischer M: Childbearing in Ghana: How beliefs affect care. African Diaspora JSpA, 2002; 76.
6. Weitzman A: The effects of women’s education on maternal health: Evidence from Peru. Soc Sci Med, 2017; 180: 1–9.
7. Obed S, Wilson J, Elkins T: Diagnosing unruptured ectopic pregnancy. Int J Gynecol, 1994; 4(1): 25.
8. Betrán AP, Torloni MR, Zhang J et al: WHO statement on caesarean section rates. BJOG, 2016; 123(5): 667–70.
9. Althabe F, Sosa C, Belzán JM et al: Cesarean section rates and maternal and neonatal mortality in low-, medium-, and high-income countries: An ecological study. Birth, 2006; 33(4): 270–77.
10. Harrison MS, Goldberg RL: Cesarean section in sub-Saharan Africa. Matern Health Neonatal Perinatal, 2016; 2: 6.
11. Rosen T: Placenta accreta and cesarean scar pregnancy: Overlooked costs of the rising cesarean section rate. Clin Perinatol, 2008; 35(3): 519–29.
12. Yaya S, Utman OA, Amouzou A, Bishwajit G: Disparities in caesarean section prevalence and distributions across sub-Saharan Africa countries. Glob Health Res Policy, 2018; 3: 19.
13. World Health Organization: Trends in maternal mortality 2000 to 2017. Estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division, 2019.
14. Cavalarro F, Cresswell J, Hurt L et al: Wealth disparities in obstetric surgery for absolute maternal indications in Ghana. Int J Epidemiol, 2015; 44(Suppl. 1): i46.
15. Murano T, Shaker L, Marco CA: Evaluation and management of ectopic pregnancy in the Emergency Department. Emerg Med Rep, 2019; 40(14).
16. Baffoe S, Nkyekyer K: Ectopic pregnancy in Korle Bu Teaching Hospital, Ghana: A three-year review. Trop Doct, 1999; 29(1): 18–22.
17. Jurkovic D, Hillaby K, Woelfer B et al: Cesarean scar pregnancy. Ultrasound Obstet Gynecol, 2003; 21(3): 310–10.
18. Seow KM, Huang LW, Lin YH et al: Cesarean scar pregnancy: Issues in management. Ultrasound Obstet Gynecol, 2003; 21(3): 310–10.
19. Ngu SF, Cheung VY: Non-tubal ectopic pregnancy. Int J Gynecol, 2011; 115(3): 295–97.
20. Fylstra DL: Ectopic pregnancy within a cesarean scar: A review. Obstet Gynecol Surv, 2002; 57(8): 537–43.
21. Fystrail DL: Ectopic pregnancy within a cesarean scar: A review. Obstet Gynecol Surv, 2002; 57(8): 537–43.
22. Osbom DA, Williams TR, Craig BM: Cesarean scar pregnancy: Sonographic and magnetic resonance imaging findings, complications, and treatment. J Ultrasound Med, 2012; 31(9): 1449–56.
23. Rotas MA, Haberman S, Leugur M: Cesarean scar ectopic pregnancies: Etiology, diagnosis, and management. Obstet Gynecol, 2006; 107(6): 1373–81.
24. Cali G, Timer-Tritsch IE, Palacios-Jaraquemada J et al: Outcome of Cesarean scar pregnancy managed expectantly: Systematic review and meta-analysis. Ultrasound Obstet Gynecol, 2018; 51(2): 169–75.
25. Ben-Nagi I, Jurkovic D: Deaths in early pregnancy. The eighth report of the confidential enquiries into maternal deaths in the United Kingdom. BJOG, 2011; 118(11): 1403–2.
26. Hab RHM, Knight M, Bottomley C et al: Cesarean scar pregnancy in the UK: A national cohort study. BJOG, 2018; 125(13): 1663–70.
27. Herman A, Weinaub Z, Arevch O et al: Follow up and outcome of isthmic pregnancy located in a previous caesarean section scar. Br J Obstet Gynaecol, 1995; 102(10): 839–41.
28. Qian ZD, Guo QY, Huang LL: Identifying risk factors for recurrent cesarean scar pregnancy: A case-control study. Fertil Steril, 2014; 102(1): 129–34.e1.
29. Zhou X, Li H, Fu X: Identifying possible risk factors for cesarean scar pregnancy based on a retrospective study of 291 cases. J Obstet Gynaecol Res, 2020; 46(2): 272–78.
30. Patel MA: Scar ectopic pregnancy. J Obstet Gynaecol India, 2015; 65(6): 372–75.
31. Chen Y, Han P, Wang Y-L, Li Y-K: Risk factors for incomplete healing of the uterine incision after cesarean section. Arch Gynecol Obstet, 2017; 296(2): 355–61.
32. Schugart RC, Friedman A, Zhao R, Sen CK: Wound angiogenesis as a function of tissue oxygen tension: A mathematical model. Proc Natl Acad Sci, 2008; 105(7): 2628–33.
33. Lofrumento DS, Di Nardo MA, De Falco M, Di Lieto A: Uterine wound healing: A complex process mediated by proteins and peptides. Curr Protein Pept Sci, 2017; 18(2): 125–28.
34. Condous GS: Ultrasound diagnosis of ectopic pregnancy. Semin Reprod Med, 2007; 25(2): 85–91.
35. Gurel S, Sarikaya B, Gurel K, Akata D: Role of sonography in the diagnosis of ectopic pregnancy. J Clin Ultrasound, 2007; 35(9): 509–17.
36. Gonzalez N, Tulandi T: Cesarean scar pregnancy: A systematic review. J Minim Invasive Gynecol, 2017; 24(5): 731–38.
37. Sharma C, Surya M, Soni A et al: Sonographic prediction of scar dehiscence in women with previous cesarean section. J Obstet Gynaecol India, 2015; 65(2): 97–103.
38. Maymon R, Halperin R, Mendlovic S et al: Ectopic pregnancies in a Caesarean scar: Review of the medical approach to an iatrogenic complication. Hum Reprod Update, 2004; 10(6): 515–23.
39. Peng KW, Lei Z, Xiao TH et al: First trimester caesarean scar ectopic pregnancy evaluation using MRI. Clin Radiol, 2014; 69(2): 123–29.
40. Riaz RM, Williams TR, Craig BM, Myers DT: Cesarean scar ectopic pregnancy: Imaging features, current treatment options, and clinical outcomes. Abdom Imaging, 2015; 40(7): 2589–99.
41. Timor-Tritsch IE, Montesagudo A: Unforeseen consequences of the increasing rate of cesarean deliveries: Early placenta accreta and cesarean scar pregnancy. A review. Am J Obstet Gynecol, 2012; 207(1): 14–29.
42. Koroglu M, Kayhan A, Soylu FN et al: MR imaging of ectopic pregnancy with an emphasis on unusual implantation sites. Jpn J Radiol, 2013; 31(2): 75–80.
43. Maxsell G, Derme M, Piccioni MG et al: To evaluate the feasibility of magnetic resonance imaging in predicting unusual site ectopic pregnancy: A retrospective cohort study. Eur Radiol, 2018; 28(6): 2444–54.
44. Mahajan D, Kang M, Sandhu MS et al: Rare complications of cesarean scar. Indian J Radiol Imaging, 2013; 23(3): 258–61.
45. Caserta NMM, Bacha AM, Grassiotto OR: Cesarean scar ectopic pregnancy: Invasion of the bladder wall detected by magnetic resonance imaging. Radiol Bras, 2017; 50(3): 197–98.
46. Awad FM, Kamal E: MRI in Cesarean scar ectopic pregnancy. Med Clin Rev, 2015; 1(1): 2.
47. Ghana Daily minimum wage increased by 11%, effective 2020. August 30, 2019; 2020. https://ghanatalksbusiness.com/2019/08/ghanadaily-minimum-wage-increased-by-11-effective-2020/.
48. Society for Maternal-Fetal Medicine (SMFM), Miller R, Timor-Tritsch IE, Gyamfi-Bannerman C: Society for Maternal-Fetal Medicine (SMFM) Consult Series #49: Cesarean scar pregnancy. Am J Obstet Gynecol, 2020; 222(5): B2–14.
49. De Franciscis P, Riemma G, Schiattarella A et al: Impact of hysteroscopic metropotomy on reproductive outcomes of women with a dysmorphic uterus and recurrent miscarriages: A systematic review and meta-analysis. J Obstet Gynecol Hum Reprod, 2020; 49(7): 101763.