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REVIEW

Obstetrical complications of thin endometrium in assisted reproductive technologies: a systematic review

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Abstract

Purpose The aim of the systematic review is to describe the obstetrical complications associated with pregnancies in the context of a thin endometrial lining.

Methods Systematic review of the literature.

Results Patients who conceive in the setting of a thin endometrium have a significantly increased risk of early pregnancy loss, namely miscarriage and ectopic pregnancy. These patients also have a twofold increase in low birth weight and preterm delivery, as well as a significantly higher risk of intrauterine growth restriction and composite adverse perinatal outcomes.

Conclusions In addition to the lower probability of conception, a thin endometrium in assisted reproductive technologies appears to be associated with both early and late pregnancy complications. These pregnancies thus warrant special attention and close follow-up from obstetricians.

Keywords Thin endometrium · Obstetrical complications · Miscarriage · Ectopic pregnancy · Low birth weight · Preterm delivery

Background

An endometrial lining of less than 7 mm is associated with a significantly lower probability of achieving and maintaining a pregnancy in the context of assisted reproductive technologies (ART) [1, 2]. And while there is no consensus on a cut-off value below which an endometrium is defined as "thin," the most commonly reported cut-off is 7 mm, which is noted in 2.4% of ART cases [1]. A thin lining however does not prevent the occurrence of pregnancy, and these pregnancies should receive special attention as they are at an increased risk of poor obstetrical outcomes [3–5].

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Although not confirmed by all studies, in vitro fertilization (IVF) pregnancies are generally associated with adverse perinatal outcomes such as preterm birth, low birth weight, and increased incidence of pregnancy-induced hypertension, even when they result in a singleton gestation [6]. The exact underlying pathophysiology that results in adverse obstetrical outcomes is not known; however, defective placentation, which is particularly important in patients with a thin endometrium, seems to be the root cause for many of these obstetrical complications.

Appropriate placentation involves embryonic attachment, proper development of the cytotrophoblastic shell, trophoblastic invasion, and remodeling of maternal spiral arterioles, leading to deep placentation [7]. It is hypothesized that the quality of the functionalis layer in thin endometrium does not sustain the seeding embryo, in part due to the proximity to the oxygen-rich basalis layer which is toxic to the developing embryo [8]. Patients with a thin lining are known to have less vascular endothelial growth factor (VEGF) expression, which leads to poor vascular development and ultimately defective placentation [9].

Recently, significant work has focused on the treatment of thin endometrium in ART in an effort to increase implantation and live birth rates. However, little is known about the obstetrical outcomes of patients that conceive with a thin endometrial lining. These patients may potentially develop early and late pregnancy complications that are related to abnormal

implantation such as miscarriage, abnormal placentation, fetal growth restriction, and preeclampsia. We sought to systematically review the literature and to shed the light on this important, yet overlooked, problem.

Materials and methods

An electronic literature review for articles published in English and pertaining to obstetrical complications in patients with a thin endometrium was conducted in May 2018. The PubMed and Medline online databases were searched with the following MeSH search terms "thin endometrium" or "atrophic endometrium" combined with "miscarriage", "ectopic pregnancy", "low birth weight", "preterm delivery", "growth restriction", "adverse pregnancy outcome", "preeclampsia", and "placenta accreta-percreta". Titles were screened, and relevant articles and their cited references were analyzed for inclusion. We considered abstracts, case reports, and original articles that reported on the association between a thin endometrial lining in ART and obstetrical complications for inclusion in this review. Due to the low incidence of thin endometrium, studies with different types of infertility treatment were considered. Specifically, patients undergoing fresh IVF and intracytoplasmic sperm injection (ICSI), or frozen embryo transfer (FET), as well as those infertile patients who had Asherman's syndrome were included. Institutional Review Board approval was not required since we only included published data.

Results

Several papers reported obstetrical complications related to a thin endometrium both early and late in pregnancy. Mainly, there is an increased risk of miscarriage, ectopic pregnancy, preterm birth, and low birth weight (Table 1).

Miscarriage

Chen and colleagues analyzed the effect of endometrial thickness and pattern, measured on the day of hCG administration in fresh IVF and ICSI cycles on miscarriage rates. In this retrospective study, the authors reviewed a total of 2896 cycles from patients with average age of 31.1 ± 3.9, and compared three groups based on endometrial thickness as follows: EMT ≤ 7 mm or EMT > 7 mm but ≤ 14 mm or EMT > 14 mm. Embryo transfer was performed 2–5 days after oocyte retrieval and the average number of embryo transfer was 2.3 ± 0.5. The overall clinical pregnancy rate for the cohort was 48.4%. There was no statistically significant difference in miscarriage rates between the three groups based solely on endometrial thickness (8.3% vs. 8.9% vs. 6.6% for EMT ≤ 7 mm vs. EMT > 7 mm but ≤ 14 mm vs. EMT > 14 mm respectively) [10]. In the subanalysis where endometrial pattern was included, the miscarriage rate was significantly higher in the group where the EMT > 7 mm but ≤ 14 mm with a triple line endometrium vs. when a triple line was absent (8.3% vs. 16.9%, $P < 0.05$), but this effect was negated when the endometrial thickness was greater than or equal to 14 mm. When the EMT was less than 7 mm and a triple line was absent, only one cycle achieved clinical pregnancy but ended up in miscarriage [10].

In a study by Yang et al., the effect of endometrial thickness on miscarriage rates in both natural FET and medicated FET cycles was assessed. In the medicated cycles, endometrial preparation was achieved with 2 mg of daily oral estradiol on days 1 to 4, then 4 mg daily on days 5 to 8, and then 6 mg daily on days 9 to 12 of the cycle. When the endometrial thickness ≥ 8 mm, 40 mg intramuscular progesterone was given daily for 3 days. A total of 1512 single-embryo transfer cycles at the blastocyst stage from patients aged 30.3 ± 4.2 were retrospectively analyzed. Miscarriage rates were calculated for EMT ≤ 8 mm vs. > 8 mm with or without a triple line pattern measured by transvaginal ultrasound on the day of progesterone supplementation. The overall pregnancy rate was 66.7%, and the reported miscarriage rates were 16.7% vs. 16.2%, $P = 0.90$ for EMT ≤ 8 mm vs. EMT > 8 mm with a triple line, respectively, and 16.2% vs. 16.7%, $P = 0.91$ for EMT ≤ 8 mm vs. EMT > 8 mm without a triple line respectively [11].

Yuan et al. also studied the relationship between endometrial thickness measured on the day of hCG administration and miscarriage in fresh IVF/ICSI cycles. A total of 10,787 cycles of patients with an average age of 32.7 ± 4.8 were retrospectively analyzed and subjects were divided into four groups in the following manner: EMT <8 mm vs. EMT ≥ 8 mm but ≤ 11 mm vs. EMT > 11 mm but ≤ 15 mm, vs. EMT > 15 mm. Embryo transfer was carried at either the cleavage or blastocyst stage and patients received between one and three embryos. The overall clinical pregnancy rate of the cohort was 40.5%. The authors found that an endometrial lining of less than 8 mm on the day of hCG administration was associated with a significantly higher miscarriage rate (26.7%). The rate of miscarriage decreased with increasing endometrial thickness (26.7% vs. 23.8% vs. 19.9% vs. 17.5% for EMT <8 mm vs. EMT ≥ 8 mm but ≤ 11 mm vs. EMT > 11 mm but ≤ 15 mm vs. EMT > 15 mm, respectively) [2]. There was a significant negative correlation between EMT measured on the day of hCG and miscarriage (OR = 0.948, $P = 0.001$) [2].

Recently, Baradwan et al. retrospectively analyzed the pregnancy outcomes in infertile patients with a persistently thin lining (≤ 5 mm) after having undergone hysteroscopic treatment of Asherman's syndrome. A total of 41 patients with an average age of 32.2 ± 4.6 were included, 26 of them had an EMT ≤ 5 mm (group A), while 15 had an EMT > 5 mm (group B). Patients were then followed up to 2 years after the procedure and natural conception was recorded. Patients with tubal factor and those who did not conceive naturally within 1 year

Table 1 Studies that reported obstetrical complications related to thin endometrium

Complication	Author [ref] year	Study design	No. of cases	Endometrial thickness (mm)	Rate of complication	*P* value/CI
Miscarriage	Chen [10] 2010	Retrospective	2896 fresh IVF/ICSI	≤ 7 mm vs. > 7 mm	8.3% vs. 8.9%	N/S
	Yuan [2] 2016	Retrospective	10,787 fresh IVF/ICSI	< 8 vs. 8 ≤ EMT ≤ 11 vs. 11 < EMT ≤ 15 vs. EMT > 15	OR = 0.948 for EMT < 8 mm	0.001
	Yang [11] 2018	Retrospective	1512 FET	1A ≤ 8+ triple line vs. 1B ≤ 8 without triple line vs. 2A > 8 mm + triple line vs. 2B > 8 without triple line	16.7% vs. 16.2% for 1A vs. 2A	N/S
	Baradwan [12] 2018	Retrospective	41	≤ 5 mm vs. > 5 mm	50% vs. 8.3%	< 0.001
	Liu [13] 2018	Retrospective	21,914 fresh IVF	EMT ≥ 8 mm vs. 7.0–7.9 mm vs. 6.0–6.9 mm vs. 5.0–5.9 mm	22% vs. 26.4% vs. 27.1% vs. 30%	*P* = 0.01
			18,942 FET cycles	EMT ≥ 8 mm vs. 7.0–7.9 mm vs. 6.0–6.9 mm vs. 5.0–5.9 mm vs. 4.0–4.9 mm	26% vs. 28.4% vs. 25.2% vs. 47.8% vs. 22.2%	*P* = 0.09
Ectopic pregnancy	Yuan [2] 2016	Retrospective	2896 fresh IVF/ICSI	≤ 7 mm	OR = 0.851	< 0.001
Preterm birth	Chung [14] 2006	Case-control	435 fresh IVF/ICSI	≤ 10 mm	OR = 2.04	95% CI, 1.09–3.83
Low birth weight	Chung [14] 2006	Case-control	435 fresh IVF/ICSI	≤ 10 mm	OR = 2.04	95% CI, 1.09–3.83
	Moffat [15] 2017	Retrospective	764 fresh IVF/ICSI	< 7 mm	Estimate 0.036, std. error 0.015	0.017

IVF in vitro fertilization, *ICSI* intracytoplasmic sperm injection, *FET* frozen embryo transfer

were treated with superovulation and intrauterine insemination or IVF/ICSI. In the IVF/ICSI group, embryo transfer was carried out at either the cleavage or blastocyst stage, and patients had 1–2 embryos transferred unless they were older than 40 with multiple IVF failures. The overall pregnancy rate of the cohort was 78% with 38.4% vs. 80% for group A vs. group B, respectively. The authors found that in patients with thin lining of ≤ 5 mm, there was a significantly higher miscarriage rate (50% vs. 8.3%, $P < 0.001$) [12].

Most recently, Liu et al. conducted a large retrospective analysis of the impact of thin endometrial lining on pregnancy outcomes in fresh IVF and frozen-thawed embryo transfers. A total of 40,856 autologous and donor cycles were included in this analysis. In autologous and donor fresh IVF cycles, patients had either day 3 or 5/6 embryo transfers, and the miscarriage rate significantly increased with every millimeter decrease in endometrial thickness below 8 mm (22% vs. 26.4% vs. 27.1% vs. 30%; $P = 0.01$ for EMT ≥ 8 mm vs. 7.0–7.9 mm vs. 6.0–6.9 mm vs. 5.0–5.9 mm respectively). Endometrial preparation was not described in the FET cycles and patients had day 5/6 embryo transfers. A similar trend in miscarriage rate was seen in autologous and donor frozen-thawed embryo transfers however that did not reach statistical significance (26% vs. 28.4% vs. 25.2% vs. 47.8% vs. 22.2%; $P = 0.09$ for EMT ≥ 8 mm vs. 7.0–7.9 mm vs. 6.0–6.9 mm vs. 5.0–5.9 mm vs. 4.0–4.9 mm respectively [13].

Ectopic pregnancy

A thin endometrial stripe (≤ 8 mm) discovered in patients with suspicion for ectopic pregnancy appears to be a good predictor of the diagnosis of ectopic pregnancy [16]. Furthermore, it also appears that in patients undergoing IVF-ICSI and who have an EMT < 8 mm, there is an increased risk of developing an ectopic pregnancy. In the previously described retrospective analysis by Yuan et al. [2], the authors showed that the rate of ectopic pregnancy increased with decreasing EMT measured on the day of hCG administration (10.0% vs. 4.3% vs. 2.1% vs. 2.2% for EMT <8 mm vs. EMT ≥ 8 mm but ≤ 11 mm vs. EMT > 11 mm but ≤ 15 mm vs. EMT > 15 mm, respectively). There was a significant negative correlation between EMT measured on the hCG trigger day and ectopic pregnancy (OR = 0.851, $P < 0.001$) [2].

Low birth weight and preterm delivery

Chung and colleagues conducted a case-control study in 2006, to delineate the effect of various IVF treatment components on perinatal outcomes. A total of 455 viable pregnancies were identified over the study period of which 20 were excluded as those patients contributed two pregnancies over the study time period and the first pregnancy was included. Of the remainder cases, 159 served as the study group while 276 served as the control group. The study group was comprised of pregnancies complicated with preterm delivery, low birth weight, and intrauterine fetal demise. The authors found that with increasing endometrial thickness, there was a significant reduction in the risk for developing poor outcomes. Specifically, there was a twofold increased risk for adverse perinatal outcomes, namely low birth weight and preterm delivery, when the endometrial thickness was ≤ 10 mm (OR, 2.04; 95% CI, 1.09–3.83). The

authors also noted a 12% increase in the risk of adverse perinatal outcomes with each millimeter decrease in EMT [14].

Recently, Moffat et al. retrospectively analyzed 764 singleton deliveries from fresh embryo transfer IVF/ICSI cycles between 1997 and 2014. Of those 764 singleton deliveries, 570 were uneventful whereas 194 developed obstetrical complications including premature labor, gestational diabetes, growth restriction, hypertensive disorders, antepartum hemorrhage in the second and third trimesters, placenta previa, and cholestasis of pregnancy. The authors found that the endometrial thickness measured on the day of hCG trigger was a strong positive predictor of neonatal birth weight [15]. Specifically, the univariate regression analysis showed that EMT < 7 mm on the trigger day strongly predicted neonatal birth weight (estimate 0.036, std. error 0.015, $P = 0.017$).

In their oral communication at the American Society for Reproductive Medicine meeting in 2016, Juneau et al. showed that patients who conceived after FET with an EMT < 7 mm had a significantly lower live birth rate, lower estimated gestational age at birth, and lower birth weight in grams. Low birth weight (< 2500 g) was significantly more common in patients with EMT < 7 mm vs. those with EMT > 7 mm (24.8% vs. 15.9%, $P = 0.0003$) [17].

Oron et al. also showed that there is a strong correlation between an EMT < 8 mm during fresh IVF cycles and intrauterine growth restriction and composite adverse perinatal outcomes, in an oral presentation at the ESHRE 2016 meeting. Specifically, the rate of intrauterine growth restriction was 17.6% vs. 10.3%, $p = 0.006$, whereas the rate of composite adverse outcomes was 19.9% vs. 12.8%, $p = 0.014$ (EMT < 8 mm vs. ≥ 8 mm respectively).

Discussion

A thin endometrium in ART is not only a frustrating obstacle for reproductive endocrinologists, but it seems to be associated with obstetrical complications that pose a challenge to the obstetrician after a pregnancy is achieved. However, pregnancies do occur and many patients cannot afford gestational carriers, and thus embryo transfer is certainly not contraindicated. However, the paucity of the published articles related to this issue clearly reflects the lack of attention given to it. Given that it occurs in about 2.4% of infertility cases, it is not an uncommon occurrence and it requires special attention from all providers involved [1]. Previously, research has mainly focused on improving pregnancy rates in patients with a thin lining; however, little attention has been given to the obstetrical outcomes of those successful pregnancies [18, 19]. Pregnancies achieved with IVF are clearly associated with increased risk of obstetrical complications, adverse pregnancy outcomes, and lower birth weight [6, 20]. Controlled ovarian hyperstimulation, fresh vs. frozen embryo transfers, culture media, duration of culture, the number of embryos transferred, advanced maternal age, and male neonate have been investigated as possible causes of low birth weight in ART pregnancies [21].

EMT however seems to be an important independent predictor of early and late pregnancy complications. Although in Chen and Yang's [10, 11] studies the rate of miscarriage was not different between patients with respect to endometrial thickness alone, the opposite was later confirmed in larger trials. In Yuan's trial, the miscarriage rate was as high as 26.7% in patients who conceived with IVF and had an endometrial thickness ≤ 8 mm, whereas in Liu's trial, there was an increase in miscarriage rates with every 1-mm decrease in endometrial thickness below 8 mm [2, 13]. The effect of endometrial thickness on miscarriage rate seems to be even more profound in patients with Asherman's syndrome who have a persistent thin lining after lysis of intrauterine adhesions [12].

In addition to miscarriage, ectopic pregnancy appears to be another early pregnancy complication of concern in patients with a thin endometrium. While the reported rate of ectopic pregnancy in the general population is around 2%, it could be as high as 10% in patients with a thin endometrium [2, 22]. It is unclear how a thin endometrium is a risk factor for ectopic pregnancies, but the association has been previously reported [2, 22]. More studies are clearly needed to confirm or refute this association.

All the reviewed studies have their inherent limitations, specifically with respect to their retrospective designs, which subject them to selection bias. Only one (Yuan et al.) out of the five reviewed papers addressing the rate of miscarriage in patients with thin lining had assessed whether the embryos where euploid or not as preimplantation genetic testing for aneuploidy was not performed in the other four studies. Although the retrospective nature of these studies likely precluded them from addressing this issue, the role of aneuploidy remains extremely important when discussing potential causes of miscarriage. The reviewed studies used different cut-offs to define "thin endometrium" (7 mm or 8 mm or 10 mm), making it difficult to generalize their results due to this inconsistency. It is also important to note that while Chung et al. controlled for maternal age, race, parity, and body mass index (BMI), their study included twins and triplets in their analysis. When those were excluded from the secondary analysis, a thin EMT was still associated with an almost threefold increase in poor perinatal outcomes however that did not reach statistical significance most likely due to low number. When triplets were excluded, the adjusted OR for endometrial thickness was statistically significant and similar to the primary analysis (OR, 0.89; 95% CI, 0.80–0.99) [14]. Another important limitation to note is that Chung and colleagues [14] analyzed obstetrical outcomes at an endometrial lining less than 10 mm which is not considered thin; therefore, their data cannot be easily pooled with that of thin endometrium, and it is safe to assume that their findings could be extrapolated to a thinner cut-off. While the two mentioned oral communications (Juneau and Oron) showed an association between thin

endometrium and low birth weight, intrauterine growth restriction, and composite adverse perinatal outcomes, those results have not been published in a peer-reviewed journal to date.

While Moffat's [15] study design was also retrospective and had controlled for maternal age, race, parity, and body mass index (BMI), the authors excluded multiple gestations and frozen embryo transfers which are both known to have a strong association with neonatal birth weight. And while the two published studies that assessed the association between endometrial thickness and late pregnancy complications have their limitations, it is important to note that monitoring infant and maternal outcomes following ART is not always easy. The lack of published data addressing the possible occurrence of other obstetrical complications such as preeclampsia, pregnancy-induced hypertension, and abnormal placentation does not preclude their existence. There is increasing evidence exposing that such complications originate from an early-stage pathological interaction between the placenta and the endometrium, but more studies are needed to further elucidate this relationship [7]. With the limited available literature, it is safe to assume that the influence of a thin endometrium on perinatal outcome might be greater than what it is thought to be.

In conclusion, proper communication between the trophoblasts and the endometrium seems to be a key factor in preventing adverse perinatal outcomes [7]. A thin endometrium (< 7 mm) appears to be associated with early and late pregnancy complications; thus, these pregnancies warrant special attention, such as an early ultrasound to confirm an intrauterine pregnancy, and subsequently serial growth ultrasounds and antenatal testing. More research is needed to further elucidate the relationship between a thin lining and pregnancy complications.

Compliance with ethical standards

Institutional Review Board approval was not required since we only included published data.

References

1. Kasius A, Smit JG, Torrance HL, Eijkemans MJC, Mol BW, Opmeer BC, et al. Endometrial thickness and pregnancy rates after IVF: a systematic review and meta-analysis. Hum Reprod Update. 2014;20(4):530–41.
2. Yuan X, Saravelos SH, Wang Q, Xu Y, Li TC, Zhou C. Endometrial thickness as a predictor of pregnancy outcomes in 10787 fresh IVF-ICSI cycles. Reprod BioMed Online. 2016;33:197–205.
3. Sundström P. Establishment of a successful pregnancy following in-vitro fertilization with an endometrial thickness of no more than 4 mm. Hum Reprod. 1998;13(6):1550–2.
4. Check JH, Dietterich C, Check ML, Katz Y. Successful delivery despite conception with a maximal endometrial thickness of 4 mm. Clin Exp Obstet Gynecol. 2003;30(2–3):93–4.
5. Dix E, Check JH. Successful pregnancies following embryo transfer despite very thin late proliferative endometrium. Clin Exp Obstet Gynecol. 2010;37:15–6.
6. Qin JB, Sheng XQ, Wu D, Gao SY, You YP, Yang TB, et al. Worldwide prevalence of adverse pregnancy outcomes among singleton pregnancies after in vitro fertilization/intracytoplasmic sperm injection: a systematic review and meta-analysis. Arch Gynecol Obstet. 2017;295:285–301.
7. Burton GJ, Jauniaux E. The cytotrophoblastic shell and complications of pregnancy. Placenta. 2017;60:134–9.
8. Catt JW, Henman M. Toxic effects of oxygen on human embryo development. Hum Reprod. 2000;15:199–206.
9. Miwa I, Tamura H, Takasaki A, Yamagata Y, Shimamura K, Sugino N. Pathophysiologic features of "thin" endometrium. Fertil Steril. 2009;91(4):998–1004.
10. Chen S, Wu F, Lou C, Chen X, Shi X, et al. Combined analysis of endometrial thickness and pattern in predicting outcome of in vitro fertilization and embryo transfer: a retrospective cohort study. Reprod Biol Endocrinol. 2010;8:30.
11. Yang W, Zhang T, Li Z, Ren X, Huang B, Zhu G, et al. Combined analysis of endometrial thickness and pattern in predicting clinical outcomes of frozen embryo transfer cycles with morphological good-quality blastocyst: a retrospective cohort study. Medicine. 2018;97(2):e9577.
12. Baradwan S, Shafi D, Baradwan A, Bashir MS, Al-Jaroudi D. The effect of endometrial thickness on pregnancy outcome in patients with Asherman's syndrome post-hysteroscopic adhesiolysis. Int J Women's Health. 2018;10:77–82.
13. Liu KE, Hartman M, Hartman A, Luo ZC, Mahutte N. The impact of a thin endometrial lining on fresh and frozen-thaw IVF outcomes: an analysis of over 40 000 embryo transfers. Hum Reprod. 2018;33(10):1883–8.
14. Chung K, Coutifaris C, Chalian R, Lin K, Ratcliffe S, Castelbaum A, et al. Factors influencing adverse perinatal outcomes in pregnancies achieved through use of in vitro fertilization. Fertil Steril. 2006;86:1634–41.
15. Moffat R, Beutler S, Schötzau A, De Geyter M, De Geyter C. Endoemtrial thickness influences neonatal birth weight in pregnancies with obstetric complications achieved after fresh IVF/ICSI cycles. Arch Gynecol Obstet. 2017;296:115–22.
16. Spandorfer S, Barnhart K. Endometrial stripe thickness as a predictor of ectopic pregnancy. Fertil Steril. 1996;66:474–7.
17. Juneau CR, Franasiak JM, Morin SJ, Molinaro TA, Scott RT. Obstetric outcomes following frozen embryo transfer (FET) in patients with an endometrial thickness measuring < 7mm. [Abstract]. ASRM. 2016;106(3):e214.
18. Mouhayar Y, Sharara FI. Modern management of thin lining. Middle East Fertil Soc J. 2017;20:1–12.
19. Mouhayar Y, Sharara FI. G-CSF and stem cell therapy for the treatment of refractory thin lining in assisted reproductive technology. J Assist Reprod Genet. 2017;34:831–7.
20. De Geyter C, De Geyter M, Steimann S, Zhang H, Holzgreve W. Comparative birth weights of singletons born after assisted reproduction and natural conception in previously infertile women. Hum Reprod. 2006;21:705–12.
21. Nakashima A, Araki R, Tani H, Ishihara O, Kuwahara A, Irahara M, et al. Implications of assisted reproductive technologies on term singleton birth weight: an analysis of 25,777 children in the national reproduction registry of Japan. Fertil Steril. 2013;99:450–5.
22. Ectopic pregnancy—United States, 1990–1992. Centers for Disease Control and Prevention (CDC). MMWR Morb Mortal Wkly Rep. 1995;44:46–8.