

ORIGINAL RESEARCH ARTICLE

Hysteroscopy Findings in Women with Thin Endometrium Scheduled for *In Vitro* fertilization in Niger Delta Region, Nigeria

DOI: 10.29063/ajrh2020/v24i2.12

Jude E. Okohue

Assisted Reproduction Unit, Gynescopie Specialist Hospital: 22/24 Gynescopie Drive Port Harcourt, Rivers State

***For Correspondence:** Email: judosca@yahoo.com; Phone: 08177777082

Abstract

The effect of endometrial thickness on *in vitro* fertilization (IVF) outcome is still a subject of debate. It is unclear why a thin endometrium reduces IVF success rates. Our objective was to analyze the hysteroscopic findings in women scheduled for IVF who had an endometrial thickness less than 7 mm. Relevant data of patients scheduled for IVF cycles and found to have an endometrial thickness (ET) of <7 mm on transvaginal ultrasound scan (TVS) between April 1, 2010 and March 31, 2017, at a private fertility and minimal access surgery unit in the Niger-Delta region of Nigeria, were retrieved and documented. A total of 41 patients had ET <7 mm during the study period. These patients accounted for 2.8% of the 1487 IVF cycles performed during the same period. All 41 patients had office hysteroscopies performed, constituting 4.1% of the 1,002 hysteroscopies performed during the study period. The age range of the patients was 23 – 50 years with a mean of 39.9 ± 6.9 years, and the duration of infertility ranged from 3 to 13 years with a mean of 7.2 ± 2.5 years. Most of the patients (32, 78.1%) had secondary infertility. Sixteen patients (39.0%) had intrauterine adhesions. A thin endometrium, though infrequent during IVF treatment cycles, might be associated with undiagnosed intrauterine adhesions. (*Afr J Reprod Health* 2020; 24[2]: 123-128).

Keywords: Thin, endometrium, hysteroscopy, IVF, infertility, adhesions

Résumé

L'effet de l'épaisseur de l'endomètre sur le résultat de la fécondation in vitro (IVF) est toujours un sujet de débat. On ne sait pas pourquoi un endomètre mince réduit les taux de réussite de la IVF. Notre objectif était d'analyser les résultats hystéroscopiques chez les femmes devant subir une FIV qui avaient une épaisseur endométriale inférieure à 7 mm. Données pertinentes des patientes programmées pour des cycles de IFV et ayant une épaisseur endométriale (ET) <7 mm à l'échographie transvaginale (TVS) entre le 1er avril 2010 et le 31 mars 2017, dans une unité de chirurgie privée de fertilité et d'accès minimal à la région du Niger-Delta au Nigeria, ont été récupérées et documentées. Un total de 41 patients avaient ET <7 mm au cours de la période d'étude. Ces patients représentaient 2,8% des 1487 cycles de IVF effectués au cours de la même période. Les 41 patients ont subi une hystérocopie en cabinet, ce qui représente 4,1% des 1 002 hystérocopies réalisées au cours de la période d'étude. La tranche d'âge des patients était de 23 à 50 ans avec une moyenne de $39,9 \pm 6,9$ ans, et la durée de l'infertilité variait de 3 à 13 ans avec une moyenne de $7,2 \pm 2,5$ ans. La plupart des patients (32, 78,1%) avaient une infertilité secondaire. Seize patients (39,0%) avaient des adhérences intra-utérines. Un endomètre mince, bien que peu fréquent pendant les cycles de traitement de IVF, pourrait être associé à des adhérences intra-utérines non diagnostiquées. (*Afr J Reprod Health* 2020; 24[2]: 123-128).

Mots-clés: Mince, endomètre, hystérocopie, IVF, infertilité, adhérences

Introduction

The endometrium, which is the inner lining of the uterine cavity, has receptors for gonadotrophins and ovarian hormones. Cyclic proliferative and secretory changes occur within the endometrium during the menstrual cycle in preparation for possible implantation¹. During the proliferative

phase of the menstrual cycle, the endometrium is reported to grow at a rate of 0.5 mm per day, decreasing to 0.1 mm per day in the luteal phase². A recent study analyzed the endometrial thickness of 849 premenopausal women attending a gynecological clinic using transvaginal ultrasound scan (TVS) and found that the thickness increased from 5.4 mm immediately after menstruation to

9.2 mm on days 13 to 14, further increasing to 11.1 mm on day 18³.

During IVF treatment cycles, the endometrial thickness measured in the midsagittal plane of the uterus in its widest diameter is routinely used to assess patient progress and response to treatment^{4,5}. While the effect of endometrial thickness on *in vitro* fertilization (IVF) outcome is still a subject of debate, numerous studies suggest that a thin endometrium of less than 7 mm on the day of human chorionic gonadotrophin (hCG) administration significantly reduces IVF success rates⁵⁻⁷. It is unclear why a thin endometrial lining would negatively impact IVF success rate, but it has been reported that endometrial thickness less than 7 mm occurs infrequently⁸.

Hysteroscopy remains the gold standard in the evaluation of the uterine cavity⁹. It involves visualization of the uterine cavity with the help of a telescopic-like device called a hysteroscope. Hysteroscopy can detect conditions that otherwise would be missed by transvaginal ultrasound scan¹⁰. The etiology of thin endometrium during IVF cycles has not been fully studied. We therefore set out to document the hysteroscopic findings in women undergoing IVF treatment with a thin endometrial lining below 7 mm, measured by TVS.

Methods

This is a retrospective, descriptive study, carried out at a private fertility and minimal access surgery unit in the Niger-Delta region of Nigeria. The medical records of 1,002 patients who had hysteroscopy between April 1, 2010 and March 31, 2017 were retrieved. Of this, 41 patients scheduled for IVF/ICSI cycles but found to have an ET of <7 mm on TVS were analyzed. Data including age, duration of infertility, gravidity and parity, and findings at hysteroscopy were documented. The data collated were analyzed using the Statistical Package for Social Sciences (SPSS version 24). All the scans were performed by the same trained sonologist with over 13 years of experience. The Institutional Ethics Committee gave approval for the conduct of this study and

informed consent was obtained from the patients to use their data.

Outcome Measure: Findings at hysteroscopy.

Results

A total of 41 patients scheduled for IVF/ICSI had ET <7 mm during the study period. This represented 2.8% of the 1487 IVF/ICSI cycles performed during the same period. All 41 patients had office hysteroscopies performed, constituting 4.1% of the 1,002 hysteroscopies performed during the study period. As shown in Table 1, the age range of the patients was 23 – 50 years with a mean of 39.9 ± 6.9 years, and the duration of infertility ranged from 3 to 13 years with a mean of 7.2 ± 2.5 years. Most of the patients (32, 78.1%) had secondary infertility. As shown in Table 2, 20 patients (48.8%) had normal findings, while 16 patients (39.0%) had intrauterine adhesions. Table 3 shows the relationship between the number of terminations of pregnancy (TOP) and hysteroscopic findings in patients with thin endometrium. While 60.0% of the patients who had no abnormal findings at hysteroscopy had no previous TOP or had only one previous TOP, 57.2% of the patients with intrauterine adhesions had more than 3 previous TOP. All 4 patients who had tunnel-shaped uterine cavities had previous open myomectomy.

Discussion

With over 8 million babies delivered via IVF worldwide, the technology has indeed grown substantially¹¹. Unfortunately, the success rate of each IVF cycle remains low¹². While embryo aneuploidy remains one of the most important contributors to poor IVF outcome, the condition of the uterus also has a significant role to play^{5,13,14}. Some researchers have advocated for the cancellation of treatment cycles whenever the endometrial thickness is less than a critical value, such as 7 mm, while others suggest various ways of increasing the thickness with the use of adjuncts, such as granulocyte colony stimulating factor, human chorionic gonadotrophins (hCG) or prostaglandins^{5,15-17}.

Table 1: Characteristics of women with thin endometrium scheduled for IVF/ICSI in Niger Delta, Nigeria

Patient characteristics	Mean $\pm$ SD (Range)
Age (years)	39.9 $\pm$ 6.9 (23 – 50)
Gravidity	2.17 $\pm$ 1.9 (0 – 8)
Parity	1.17 $\pm$ 0.52 (0 – 3)
Duration of infertility (years)	7.2 $\pm$ 2.5 (3 – 13)
Infertility type (primary/secondary)	9/32

Table 2: Hysteroscopy findings among women with thin Endometrium scheduled for IVF/ICSI in Niger Delta, Nigeria

Findings	Frequency	Percentage
Normal	20	48.8
Intrauterine adhesions	16	39.0
Tunnel-shaped (narrow) cavity	4	9.8
Subseptate uterus	1	2.4
Total	41	100

Our study found a 2.8% incidence of thin endometrium among the study population. This was lower than the 5.0% reported in a recent study and similar to the 2.7% reported in another systematic review^{8,18}. The low incidence supports the notion that a thin endometrium is infrequent during IVF cycles. There is still no consensus on whether routine hysteroscopy improves IVF success rate. While some studies found an increase in live birth rates following routine hysteroscopy before IVF, others concluded otherwise¹⁹⁻²². The discovery of previously undiagnosed pathologies in over half (51.2%) of the patients with thin endometrium in our study, supports the importance of hysteroscopy as a diagnostic tool. Faterni *et al*²³ reported previously unsuspected pathologies in 11.0% of women being planned for IVF. A higher figure of 14.2% missed pathologies was recorded in a more recent study¹⁰, while Cenksoy *et al*²⁴ documented 44.9% abnormal hysteroscopy findings in patients with two or more previous failed IVF cycles, despite normal ultrasound scan features.

Intrauterine adhesions were the most common pathology found in our patients with thin endometria (39.0%). Of the 13 patients with a persistently thin endometrial lining during IVF treatment, Shufaro *et al*²⁵ found intrauterine adhesions in four (30.8%), like our findings.

Intrauterine adhesions have been associated with IVF treatment failure and recurrent pregnancy losses^{26,27}.

In countries with highly restrictive abortion laws, intrauterine adhesions are a common problem because of unsafe abortions⁹. The frequency of intrauterine adhesions is due to the significant proportion of the terminations of pregnancy that are still performed via dilatation and curettage in such environments²⁸. Dilatation and curettage of a pregnant or recently pregnant uterus seems to be the most common predisposing factor for intrauterine adhesions because it causes damage to the basal layer of the endometrium²⁹. It is therefore not surprising that 32 (78.0%) of the patients had one or more previous terminations of pregnancy, while 9 (22.0%) had no history of a previous termination of pregnancy, as shown in Table 3.

Myomectomy has been associated with intrauterine adhesions, with intrauterine adhesions still possible even in cases where the endometrium was not breached³⁰. We however found tunnel-shaped uterine cavities in all four patients who had previously undergone abdominal myomectomy. It is our belief that all were probably caused by the myomectomies. It was interesting to note that in all four cases of a tunnel-shaped cavity, no intrauterine adhesions were observed.

To the best of our knowledge, the majority of the previous studies that compared the effect of a thin endometrial lining on IVF success rates did not take into consideration the effect of missed pathologies such as intrauterine adhesions, found in our study, which have the potential of reducing the IVF pregnancy rate. This might explain some of the discrepancies in the eventual conclusions reached by some of the studies. Numerous studies correctly suggest that the number of oocytes and age of the woman are potential cofounders of endometrial thickness, as the higher the woman's age and the lower the oocyte yield are, the thinner the endometrium³¹⁻³³. This, however, does not rule out an associated missed pathology, such as intrauterine adhesions, as shown from our findings. This has important implications in developing countries where patients pay for IVF treatment out-of-pocket. In Nigeria, for example,

Table 3: Relationship between previous Termination of Pregnancy (TOP) and findings at Hysteroscopy

Previous TOP	Normal findings (%)	IUA (%)	Tunnel-shaped uterus (%)	Subseptate uterus	Total
0	6 (30.0)	1 (7.2)	2 (50.0)	0 (0)	9
1	6 (30.0)	4 (28.6)	0 (0)	0 (0)	10
2	2 (10.0)	3 (21.4)	1 (25.0)	0 (0)	6
3	3 (15.0)	4 (28.6)	0 (0)	0 (0)	7
≥4	3 (15.0)	4 (28.6)	1 (25.0)	1 (100)	9
Total	20 (100)	16 (100)	4 (100)	1 (100)	41

most of the population lives below the poverty line of less than 2 USD a day. Patients are often sponsored for IVF by religious organizations, family members, friends, and communities. The result is that such patients might only be able to afford one IVF cycle in their lifetime. Missing a pathology that can negatively impact the success of the IVF program might quite literally be a death sentence. There are numerous reports in Nigeria, for example, of women not allowed any inheritance following the death of their spouses either because they were childless or only conceived female children, while some were even murdered because of childlessness³⁴. A case might therefore be made for routine hysteroscopy before IVF treatment in patients with thin endometrium, especially in such an environment. Unfortunately, our patient pool is too small, and the study lacks enough power for a proper deduction to be made.

While observing that endometrial thickness below 7 mm was associated with a lower pregnancy rate, Kasius *et al*⁸, in a systematic review and meta-analysis, suggested that further research was needed to determine the real independent significance of endometrial thickness in IVF treatment cycles. When such a study is eventually carried out, we recommend that hysteroscopy be performed in all the patients with thin endometrial thickness to ensure that only those with no endometrial pathology are included.

Conflict of Interest

The author declares that they have no conflict of interest.

Funding

The author did not receive any funding for this study.

References

1. Kovacs P, Matyas S, Boda K and Kaali SG. The effect of endometrial thickness on IVF/ICSI outcome. *Hum Reprod* 2003; 18(11): 2337-41
2. Malhotra N and Malhotra J. Transvaginal sonography in infertility. In: Rao K. (ed) *The infertility manual* 2nd ed. 2004; 19-41
3. Tsuda H, Ito YM, Todo Y, Iba T, Tasaka K, Sutou Y, Hirai K, Dozono K, Dobashi Y, Manabe M, Sakamoto T, Yamamoto R, Ueda K, Akatsuka M, Kiyozuka Y, Nagai N, Imai M, Kobiki K, Fujita H, Itamochi H, Oshita T, Kawarada T, Hatae M and Yokoyama Y. Measurement of endometrial thickness in premenopausal women in office gynecology. *Reprod Med and Biol* 2017; 17(1): 29 – 35.
4. Zhang T, Li Z, Ren X, Huang B, Zhu G, Yang W and Jin L. Endometrial thickness as a predictor of the reproductive outcomes in fresh and frozen embryo transfer cycles. A retrospective cohort study of 1512 IVF cycles with morphologically good-quality blastocyst. *Medicine (Baltimore)*. 2018; 97(4): e9689
5. Okohue JE, Onuh SO, Ebeigbe P, Shaibu I, Wada I, Ikimalo JI and Okpere EE. The effect of endometrial thickness on invitro fertilization (IVF)-embryo transfer/intracytoplasmic sperm injection (ICSI) outcome. *Afri J Reprod Health* 2009; 13(1): 113-21
6. Oliveira JB, Baruffi RL, Mauri AL, Petersen CG, Borges MC and Franco JG Jr. Endometrial ultrasonography as a predictor of pregnancy in an IVF programme after ovarian stimulation and gonadotrophin releasing hormone and gonadotrophins. *Human Reprod* 1997; 12(11): 2515-8.
7. Zhao JI, Zhang Q and Li Y. The effect of endometrial thickness and pattern measured by ultrasonography on pregnancy outcomes during IVF-ET cycles. *Reprod Biol Endocrinol* 2012; 10: 100
8. Kasius A, Smith JG, Torrance HL, Ejikemans MJC, Mol BW, Opmeer BC and Broekmans FJM. Endometrial thickness and pregnancy rates after IVF. A systematic review and meta-analysis. *Hum Reprod Update* 2014; 20(4): 530-41.
9. Okohue JE. Adhesions and abortion. In: Tinelli A,

- Alonso Pacheco L, Haimovich S. (eds) Hysteroscopy. Springer, Cham, Switzerland 2018; 697-708
10. Bahadar A, Malhotra N, Singh N, Gurunath S and Mittal S. Comparative study on the role of diagnostic hysteroscopy in evaluation of the uterine cavity prior to invitro fertilization in a developing country. Arch Gynecol Obstet 2013; 288(5): 1137-43.
11. De-Geyter C. More than 8 million babies born from IVF since the world's first in 1978. European Society of Human Reproduction press release, 3 July 2018. Available at <https://www.eshre.eu/ESHRE2018/Media/ESHRE-2018-Press-releases/De-Geyter.aspx>. Accessed on 5 August 2018
12. Ferraretti AP, Goossens V, Kupka M, Bhattacharya S, de Mouzon J, Castilla JA, Erb K, Korsak V and Nyboe Andersen A. Assisted reproductive technology in Europe, 2009: results generated from European registers by ESHRE. Hum Reprod. 2013; 28(9): 2318-31.
13. Sills ES, Li X, Federick JL, Khoury CD and Potter DA. Determining parental origin of embryo aneuploidy: analysis of genetic error observed in 305 embryos derived from anonymous donor oocyte IVF cycles. Mol. Cytogenet 2014; 7: 68
14. Kader MA, Abdelmeged A, Mahran A, Samra MA and Bahaa H. The usefulness of endometrial thickness, morphology and vasculature by 2D Doppler ultrasound in prediction of pregnancy in IVF/ICSI cycles. The Egyptian J of Radiology and Nuclear Medicine 2016; 47(1): 341-46
15. Xu B, Zhang Q, Hao J, Xu D and Li Y. Two protocols to treat the endometrium with granulocyte colony-stimulating factors during frozen embryo transfer cycles. Reprod Biomed Online 2015; 30: 349-58
16. Check JH, Choe JK and Summers-Chase D. Failure to increase the thickness of thin endometria with intrauterine infusion of granulocyte colony stimulating factor (G-CSF). Clin Exp Obstet Gynecol 2016; 43: 332-3
17. Nakagawa K, Ojio Y, Iywen H, Nishi Y, Sugiyama R, Kuribayashi Y and Sugiyama R. Prostaglandin Therapy during the proliferative phase improves pregnancy rates following frozen embryo transfer in a hormone replacement cycle. J. Obstet Gynecol Res 2014; 40:1331-7.
18. Griesinger G, Trevisan S and Cometti B. Endometrial thickness on the day of embryo transfer is a poor predictor of IVF treatment outcome. Human Reprod Open 2018; 2018(1): hox031
19. Pundiv J, Pundiv V, Omanwa K, Khalaf Y and EL-Toukhy T. Hysteroscopy prior to the first IVF cycle, a systematic review and meta-analysis. Reprod Biomed Online 2014; 28:151-61
20. Elsetohy KA, Askalany AH, Hassan M and Dawood Z. Routine office Hysteroscopy prior to ICSI vs ICSI alone in patients with normal transvaginal ultrasound: A randomized controlled trial. Arch Gynecol Obstet 2015; 291: 193-99
21. EL-Toukhy T, Campo R, Khalaf Y, Tabanelli C, Gianaroli L, Gordts SS, Gordts S, Mestdagh G, Mardesic T, Voboril J, Marchino GL, Benedetto C, Al-Shawaf T, Sabatini L, Seed PT, Gergolet M, Grimbizis G, Harb H and Coomarasamy A. Hysteroscopy in recurrent invitro fertilization failure (TROPHY): a multiculture randomized controlled trial. Lancet 2016; 387(10038): 2614-21
22. Smit JG, Kasius JC, Ejikemans MJC, Koks CAM, Van Golde R, Nap AW, Scheffer GJ, Manger PAP, Hoek A, Schoot BC, van Heusden AM, Kuchenbecker WKH, Perquin DAM, Fleischer K, Kaaijk EM, Sluijmer A, Friederich J, Dykgraaf RHM, van Hooff M, Louwe LA, Kwee J, de Koning CH, Janssen ICAH, Mol F, Mol BWJ, Broekmans FJM and Torrance H. Hysteroscopy before in vitro fertilization (in SIGHT): a multicenter randomized controlled trial. Lancet 2016; 387: 2622-29.
23. Fatemi HM, Kasius JC, Timmermans A, van Disseldorp J, Fauser BC, Devroey P and Broekmans FJ. Prevalence of unsuspected uterine cavity abnormalities diagnosed by office hysteroscopy prior to invitro fertilization. Hum Reprod 2010; 25(8): 1959-65.
24. Cenksay P, Ficicoglu C, Yildirim G and Yesiladali M. Hysteroscopic findings in women with recurrent IVF failures and the effect of correction of hysteroscopic findings on subsequent pregnancy rates. Arch Gynecol Obstet 2013; 287(2): 257-60
25. Shufaro Y, Simon A, Laufer N and Fatum M. Thin unresponsive endometrium-a possible complication of surgical curettage compromising ART outcome. J Asst Reprod Genet.2008; 25(8): 421-25
26. Coughlan C, Ledger W, Wang Q, Liu F, Demirel A, Gurgan T, Cutting R, Ong K, Sallam H and Li TC . Recurrent implantation failure: definition and management: Reprod Biomed Online 2014; 28(1): 14-38.
27. Young BK. A multidisciplinary approach to pregnancy loss: the pregnancy loss prevention centre. J Perinatal Med 2018 pii:/j/jpmc. ahead of print /jpm-2018-0135
28. Enabudoso EJ, Gharoro EP, Ande ABA, Ekpe UP and Okohue EJ. Five-year review of complicated induced abortions in university of Benin teaching hospital, Benin City. Ben J Postgrad Med 2007; 9(1): 13-21
29. Harick H, Akin O, Sala E, Ascher SM and Levine D. Diagnostic imaging in gynecology 1st ed. Amyris Inc: Salt Lake City. UT. 2007; 68-77
30. Bhandari S, Ganguly I, Agarwal P, Singh A and Gupta N. Effect of myomectomy on endometrial cavity: a prospective study of 51 cases J Hum Reprod Sci 2016; 9(2): 107-11

31. Bozalag G, Esinler I and Yarali H. The impact of endometrial thickness and texture on intracytoplasmic sperm injection outcome. *J. Reprod Med* 2009; 5: 303-11
32. Chen SL, Wu FR, Luo C, Chen X, Shi XY and Zheng HY. Combined analysis of endometrial thickness and pattern in predicting outcome of invitro fertilization and embryo transfer: a retrospective cohort study *Reprod Biol Endocrinol* 2010; 8:30
33. Kuc P, Kuzcynska A, Topczewska P and Kuczynski W. The dynamics of endometrial growth and the triple layer appearance in three different controlled ovarian hyperstimulation protocols and their influence on IVF outcomes. *Gynecol Endocrinol* 2011;11: 867-73
34. Violence affecting women and girls in select Nigerian States. Quarterly reports 8 (Feb – Apr 2016). Available at <http://www.nsrp-nigeria.org/wp.content/uploads/2016/06/VAWG-Quarterly-Report-Feb-Apr-2016.pdf>. Accessed on July 25, 2018.