

ORIGINAL RESEARCH ARTICLE

The Effect of Endometrial Thickness on *In vitro* Fertilization (IVF)-Embryo Transfer/Intracytoplasmic Sperm Injection (ICSI) Outcome

Okohue JE^{1,2}, Onuh SO^{1,2}, Ebeigbe P³, Shaibu I^{1,2}, Wada I^{1,2}, Ikimalo JJ⁴ and Okpere EE⁵

ABSTRACT

The value of measuring the endometrial thickness and studying the endometrial receptivity in the context of assisted conception remains a contentious issue. A prospective analysis was carried out to determine the effect of endometrial thickness on IVF - embryo transfer / ICSI outcome in dedicated Assisted Reproductive Technology (ART) units in Abuja and Rivers State, Nigeria. Two hundred and fifty one patients who met the inclusion criteria were analysed. They were grouped on the basis of endometrial thickness into 3 groups; <7 mm, 7 – 14 mm and >14 mm. The main outcome measure was clinical pregnancy. There were significantly more pregnancies in the 7 – 14 mm endometrial thickness group compared to the <7 mm and >14mm groups, $p=0.004$ and $p<0.0001$ respectively. The findings suggest that following IVF/ICSI, significantly more pregnancies occurred when the endometrial thickness was between 7 and 14 mm (*Afr J Reprod Health 2009; 13[1]:113-121*).

RÉSUMÉ

L'effet de l'épaisseur endomètre sur la fécondation in vitro (FIV) le transfert de l'embryon/le résultat de l'injection intracytoplasmique du sperme. La valeur obtenue quand on mesure l'épaisseur d'endomètre et quand on étudie la réceptivité d'endomètre dans le contexte d'une conception assistée reste un problème controversé. Une analyse prospective a été menée pour déterminer l'effet de l'épaisseur d'endomètre sur la FIV-le transfert de l'embryon/IIS dans les centres de la Technologie de la Reproduction Assistée à Abuja et dans l'état de Rivers, au Nigéria. Deux cent cinquante patientes qui ont satisfait les critères d'inclusion ont été analysées. Elles ont été regroupées selon l'épaisseur d'endomètre en trois groupes : < 7mm, 7-14mm et > 14mm. Le résultat de la mesure le plus important était la grossesses parmi le groupe de < 7mm et > 14mm, $p=0,004$ et $p<0,0001$ respectivement. Les résultats indiquent qu'à travers la FIV/IIS, ils se produisaient de manière significative, plus de grossesses quand l'épaisseur d'endomètre était entre 7 et 14mm (*Afr J Reprod Health 2009; 13[1]: 113-121*).

KEYWORDS: Endometrial thickness, IVF/ICSI, Pregnancy

¹Nordica Fertility Centre @ Nisa Premier Hospital, Jabi Abuja; ²PortHarcourt Fertility Centre, PortHarcourt Rivers State; ³Department of Obstetrics and Gynaecology, College of Health Sciences, Delta State University, Abraka; ⁴Department of Obstetrics and Gynaecology, University of PortHarcourt Teaching Hospital, Rivers State; ⁵University of Benin Teaching Hospital, Benin city, Edo State.

For Correspondence: Dr Jude Okohue. PortHarcourt Fertility centre @ Prime Medical Consultants, 4 Prime Close Rumuogba, PortHarcourt, Rivers State. *E-mail:* judosca@yahoo.com

Introduction

The endometrium is the inner lining of the uterus and has receptors for gonadotrophins and ovarian hormones. In response to estradiol from the ovaries (or exogenously) the endometrial lining grows in a typical pattern which is recognizable by transvaginal ultrasound scan.

During the menstrual cycle, the endometrium undergoes cyclic proliferative and secretory changes in preparation for implantation¹. The endometrial growth has been found to be at the rate of 0.5 mm/day in the proliferative phase and 0.1mm/day in the luteal phase². The endometrial thickness on transvaginal scan is usually taken as the maximum distance between the echogenic interfaces of the myometrium and the endometrium measured in a plane through the central longitudinal axis of the uterus.²

Implantation is the most crucial stage in the establishment of pregnancy.³ It is defined as a process by which the embryo attaches to the uterine wall and first penetrates the epithelium and then circulatory system of the mother to form the placenta.^{4,5} Throughout the menstrual cycle, changes take place that prepare the endometrium for implantation.

The value of measuring the endometrial thickness and studying the endometrial receptivity in the context of assisted conception remains a contentious issue.⁶⁻⁹ In one study, the authors reported that endometrial thickness on the day before oocyte recovery was significantly

greater in pregnant than in non pregnant women and suggested that it may predict the likelihood of implantation.¹⁰ Another retrospective analysis studied the impact of endometrial thickness on the day of embryo transfer on *in vitro* fertilization (IVF) outcome. It found that increased endometrial thickness was significantly associated with higher pregnancy rates.¹ This finding supported those of Yakin et al.¹¹

In a more recent study, clinical pregnancy was found to be positively associated with increased endometrial thickness and peak estradiol concentrations in serum and negatively associated with advanced age.¹² Using leuprolide acetate with Human Menopausal gonadotrophin (hMG) for ovarian stimulation, Sher et al¹³ also described a positive outcome between a thicker immature endometrium with a matured grade as opposed to a thinner immature endometrium. A more recent Turkish study concluded that endometrial thickness of at least 6.5 mm correlated with a higher rate of conception¹⁴ while no pregnancy occurred in a similar study when the endometrial thickness was less than 6mm.¹⁵ Bergh et al¹⁶ concluded that an endometrium of at least 9 mm before oocyte retrieval was required for pregnancy, while Oliveira et al¹⁷ put the cut off at 7 mm.

On the other hand, several researchers found that measurement of endometrial thickness had no predictive value for pregnancy.¹⁸⁻²⁰ Eichler et al²¹ failed to relate endometrial thickness or grade with outcome using either clomiphene citrate with hMG or

gonadotrophin releasing hormone agonist and hMG. One study prospectively evaluated the predictive value for pregnancy of the endometrial thickness and pattern assessed by vaginal ultrasonography on the day of human chorionic gonadotrophin (hCG) injections and the day of embryo transfer in 74 stimulated cycles for IVF. The presence of a 'poor quality' endometrial pattern on the day of hCG administration, while associated with lower pregnancy rates compared to those with 'good quality' endometrial pattern, was not statistically significant.²²

Another prospective study found that endometrial growth and its pattern transformation during the stimulation did not influence the pregnancy outcome.²³ Weissman et al²⁴ in their retrospective analysis found that patients with endometrial thickness greater than 14mm on the day of hCG administration, had significantly reduced implantation and pregnancy rates with an increase in the rates of miscarriage contrary to a more recent report.²⁵ Yaman et al²⁶ also concluded that sonographic measurement of endometrial thickness on the day of hCG treatment is not useful in predicting IVF outcome.

Although De Geyter et al²⁷ had advised against cancellation of treatment cycles for the simple reason of inadequate endometrial thickness, treatment cycles have been known to be abandoned for the above reason with the attendant losses to the patients. This study therefore aims to evaluate whether or not there exist a relationship between endometrial thickness and pregnancy

rates in an African population. This becomes relevant considering other studies, which have shown some differences in the response to ovarian stimulation and complication rates between an African population (Yorubas) and their Caucasian counterparts.²⁸

Methods

A prospective analysis of pregnancy rates in women undergoing IVF/ICSI between May 2005 and April 2006 at Nordica Fertility Centre, a dedicated IVF centre in Abuja Nigeria and its subsidiary in Rivers State, Nigeria was carried out. An average of 60 and 15 cycles per month are carried out at the Abuja and Rivers State centres respectively. Ovarian stimulation was achieved using the standard long protocol, of pituitary desensitization with GnRH-a followed by administration of hMG. Endometrial thickness was measured with a Transvaginal scan on the day of hCG administration, 36 hours before oocyte retrieval. Measurement was taken as the maximum distance between the echogenic interfaces of the myometrium and the endometrium measured in a plane through the central longitudinal axis of the uterus. All measurements were done by the same physician.

Embryos were transferred after 48 hours. Pregnancy tests were done 15 days after embryo transfer. Transvaginal ultrasound scans were done three weeks after a positive pregnancy test. The uterine ultrasonographic scoring system by Baruffi et al²⁹ was used to grade the endometrial thickness. Cycle parameters

were compared between pregnant and non pregnant patients.

Exclusion criteria included women who were above 35 years of age and those using donor eggs. Those with abnormal FSH, LH and Prolactin levels were also excluded.

Main outcome measures were endometrial thickness and clinical pregnancy.

Results obtained were recorded on a data collection sheet designed for the study. The coded data was then fed into the computer using Epi Info programme and analysed. Observed differences were evaluated for statistical significance using the Chi square test and the Fisher's exact test. Level of significance was set at $p < 0.05$.

Results

Overall, 298 patients met the inclusion criteria during the study period. Fourteen patients had their treatment cycles cancelled due to poor follicular response to stimulation with GnRH α . Two patients were found to be pregnant on day 14 of down regulation following transvaginal ultrasound scan. Two patients had no oocyte retrieved from any of their developing 'follicles'. Three patients had no embryo transfer carried out as there was failure to fertilize following incubation for IVF. One patient had no embryo transfer as no spermatozoon was extracted following Percutaneous Epididymal Sperm Aspiration (PESA), Testicular Sperm Aspiration (TESA) and Testicular Sperm Extraction (TESE) on the day of ovum pick up. Twenty one

patients had biochemical pregnancies while 4 had ectopic pregnancies. They were all excluded from the study leaving a total of 251 patients that were subsequently analysed.

The age range of the patients in this study was 20 – 35 years. There was no statistically significant difference in the age of the patients, between the pregnant and the non pregnant groups: 30.22 years (± 3.97) and 30.84 years (± 2.79) respectively ($p = 0.1475$).

One hundred and sixty eight patients (66.9%) had male factor infertility while 73 patients (29.1%) had female factor infertility. Forty patients (15.9%) had unexplained infertility. Overall clinical pregnancy rate was 42.2%.

Table 1 shows that there was no statistically significant difference between the pregnant and non pregnant groups, when age, duration of infertility, number of oocytes retrieved and embryos transferred were analysed; $p = 0.1475$, $p = 0.5224$, $p = 0.5032$ and $p = 0.16$ respectively. Also, the endometrial thickness values between the pregnant and non pregnant women were 11.82 mm (± 1.90) and 11.88 mm (± 3.17) respectively. This difference was not statistically significant ($p = 0.85221$).

In Table 2, the pregnancy rate in women with endometrial thickness < 7 mm was compared with that in women with endometrial thickness 7 – 14mm. No pregnancy occurred at < 7 mm (0%) while 105 pregnancies (50.5%) occurred in the 7 – 14 mm group. This difference was statistically significant ($p = 0.004$).

Furthermore, as shown in Table 3, the pregnancy rate in women with endome-

Table 1: Age, duration of infertility, number of oocytes retrieved, embryos transferred and endometrial thickness in relation to IVF/ICSI outcome

Parameters	Pregnant mean ± SD	Not Pregnant mean ± SD	p value
Age (yrs)	30.22 (± 3.97)	30.84 (± 2.79)	0.1475
Duration of infertility (yrs)	5.13 (± 2.96)	5.39 (± 3.45)	0.5224
Number of oocytes retrieved	6.32 (± 4.1)	5.49 (± 3.66)	0.5032
Embryos Transferred	2.9 (±1.1)	3.2 (±0.8)	0.16
Endometrial thickness (mm)	11.82 (± 1.90)	11.88 (± 3.17)	0.8521

Table 2: Comparison of endometrial thickness < 7 mm and 7 –14 mm in relation to IVF/ICSI outcome

Endometrial thickness (mm)	Pregnant n (%)	Not Pregnant n (%)
< 7	0 (0)	12 (100)
7 – 14	105 (50.5)	103 (49.5)
Total	105 (47.7)	115 (52.3)

p = 0.004

Table 3: Comparison of endometrial thickness < 7 mm and >14 mm in relation to IVF/ICSI outcome

Endometrial thickness (mm)	Pregnant n (%)	Not Pregnant n (%)
< 7	105 (50.5)	103 (49.5)
7 – 14	1 (3.2)	30 (96.8)
Total	106 (44.4)	133 (55.6)

p < 0.0001

trial thickness 7 – 14 mm was compared with the rate in those with thickness >14 mm. The rates were 50.5% and 3.2% respectively and was statistically significant ($p < 0.0001$).

Discussion

Technology with IVF and embryo transfer has improved over the years and most IVF centres report far higher

pregnancy rates than 10years ago when the first cases recording endometrial thickness and echo pattern at the time of hCG injection were documented.³¹

There was no statistically significant difference in the age of the patients, between the pregnant and the non pregnant groups ($p = 0.1475$). Yaman et al²⁶ had found the age of non pregnant women to be significantly higher than in the pregnant group. However unlike in

our study, no upper age limit was set for their patients. Overall 66.9% of all cases had male factor as the sole cause or as a contributor to the infertility. Studies have suggested that male factor accounts for between 20 and 50% of the causes of infertility in different parts of Nigeria.^{32,33}

It will be difficult to comment on the contribution of the female partners to infertility in this study. This is because the centre usually starts its investigation of the infertile couple with a seminal fluid analysis. This generally will determine the extent to which the female partner is investigated. Cases in which there is mild oligozoospermia, result in the female partner having the full complement of investigations including a tubal patency test to determine the suitability or otherwise for intrauterine insemination (IUI). Those with severe oligozoospermia or azoospermia do not usually have a tubal patency test done, except where this had been done previously before presentation. Notwithstanding however, 29.1% of the patients had female factor as a sole cause or as a contributor to the infertility and as expected all were tubal in origin. 15.9% of the cases had unexplained infertility. It is known that about 5 – 15% of adult couples in African countries have unexplained infertility.³⁴

Overall, endometrial thickness ranged between 5.6 mm and 21mm. The average endometrial thickness in the pregnant and non pregnant groups was 11.82 mm (± 1.90) and 11.88 mm (± 3.17) respectively. This was not statistically different ($p = 0.8521$). No pregnancy

occurred in the 12 patients who had endometrial thickness below 7mm. When this was compared to the 50.5% pregnancy rate in the 7 – 14 mm group, it was statistically significant ($p=0.004$). This finding is consistent with that of Oliviera et al¹⁷ where no pregnancy was found in patients with endometrial thickness less than 7mm. The number of patients in this group was rather small as many patients (14 or 53.8%) had their treatment cycles cancelled for poor follicular response. This finding would suggest that follicular response could determine endometrial thickness. However, Okonofua et al³⁵ in their study concluded that serum estradiol showed a better positive correlation with endometrial thickness than with total number of developing follicles. They also showed that estradiol value per follicle and estradiol/progesterone ratio both weakly correlated respectively with endometrial thickness.

Patients who had endometrial thickness between 7 – 14 mm had 105 (50.5%) pregnancies. This was significantly greater than the 1 (3.2%) pregnancy in the group of patients with endometrial thickness greater than 14mm ($p < 0.0001$).

Previous studies in support of a role for endometrial thickness in determining pregnancy outcome concluded that “increased endometrial thickness was significantly associated with higher pregnancy rates”.^{1,10-12} Other studies which did not show a statistically significant difference in endometrial thickness between pregnant and non pregnant patients had equally concluded

that measuring endometrial thickness on the day of hCG injection had “no predictive value for conception in IVF/ICSI cycles”¹⁸⁻²⁰ or “not useful in predicting IVF outcome”.²⁶ From our study even though there was no statistically significant difference in the endometrial thickness between those who achieved pregnancy and those who did not, we found that a critical endometrial thickness has to be attained for pregnancy to occur.¹⁴⁻¹⁷ Similar to Weissman,²⁴ we found that patients with endometrial thickness greater than 14 mm on the day of hCG administration had significantly reduced chances of conception ($p < 0.0001$).

The above findings have important clinical implications. On the day of hCG administration, less than 7mm or greater than 14mm from our study would mean reduced chances of pregnancy occurring in that treatment cycle. Some studies have shown that there is no statistically significant difference in pregnancy rate following single or double embryo transfer.^{36,37} A case could therefore be made for either transferring one embryo and freezing the others when such “unfavourable” endometrial thickness is encountered or totally avoiding any transfer during that cycle and freezing all the embryos. Later embryo transfer could be done preferably using a natural cycle, for this age group, to avoid the discomfort of repeated injections during another attempt at down regulation. This is practicable as there are reports that pregnancy and live birth rates following natural cycle frozen embryo transfer and a down regulated cycle frozen embryo

transfer in regularly menstruating women are statistically the same.³⁸ This is more so considering studies done by Wada et al which showed that birth characteristics of babies conceived from cryopreserved/thawed embryos were similar to those from fresh embryos with significantly fewer congenital malformations in the cryopreserved group.³⁹

In conclusion while there was no statistically significant difference in the endometrial thickness between pregnant and non pregnant patients following IVF/ICSI, pregnancy would likely not occur in patients with endometrial thickness less than 7 mm. Significantly less pregnancies are likely to occur in those with endometrial thickness greater than 14 mm.

References

1. Kovacs P, Matyas S, Boda K, Kaali SG. The effect of endometrial thickness on IVF/ICSI outcome. *Hum Reprod* 2003; 18(11):2337-41
2. Malhotra N, Malhotra J. Transvaginal sonography in infertility. In: Rao K. eds. *The infertility manual* 2nd ed. 2004. pp 19 – 41.
3. Parihar M, Potdar R, Modi S. Enigma of implantation. In: Rao K. eds. *The infertility manual* 2nd edn. 2004. pp 274 – 81.
4. Psychoyos A. Hormonal control of uterine receptivity for nidation. *J Reprod Fertil* 1976; 25(suppl):17 – 28.
5. Develioglu OH, Hisiu JG, Nikas G, Toner JP, Oehniger S. Endometrial estrogen and progesterone receptor and pinopode expression in stimulated cycles in oocyte donation. *Fertil Steril* 1999; 71:1040 – 47.
6. Dietterich C, Check JH, Choe JK, Nazari A, Lurie D. Increased endometrial thickness on the day of human chorionic gonadotrophin

- injection does not adversely affect pregnancy or implantation rates following in vitro fertilization – embryo transfer. *Fertil Steril*. 2002; 77(4):781 – 6
7. Randall JM, Templeton A. Transvaginal sonographic assessment of follicular and endometrial growth in spontaneous and clomiphene citrate cycles. *Fertil Steril* 1991; 56:208-212
 8. Dickey RP, Olar TT, Taylor SN, Curole DN, Matulich EM. Relationship of endometrial thickness and pattern to fecundity in ovulation induction cycles: Effect of clomiphene citrate alone and with human menopausal gonadotropin. *Fertil Steril* 1993; 59:756-760
 9. Cohen BM, Berry L, Roethemeyer V, Smith D. Sonographic assessment of late proliferative phase endometrium during ovulation induction. *J Reprod Med* 1992; 37:685-690
 10. Gonen Y, Casper RF, Jacobson W, Blankier J. Endometrial thickness and growth during ovarian stimulation: A possible predictor of implantation in invitrofertilization. *Fertil Steril* 1989; 52: 446-450
 11. Yakin L, Bustilo M, Krysa LW. Uterine receptivity in an oocyte donation programme *Hum Reprod*. 1995; 10:442 – 45.
 12. Zhang X, Chen CH, Confino E, Barnes R, Milad M, Kazer R. Increased endometrial thickness is associated with improved treatment outcome for selected patients undergoing in vitro fertilization – embryo transfer. *Fertil Steril*. 2005; 83(2):336 – 40
 13. Sher G, Herbert C, Maassarani G, Jacobs MH. Assessment of the late proliferative phase endometrium by ultrasonography in patients undergoing in vitro fertilization and embryo transfer (IVF/ET). *Hum Reprod* 1991; 6:232–237
 14. Zeynep C, Serap Y . The effect of endometrial thickness and pattern to pregnancy outcome in IVF cycles. *Turk J Fertil* 2003; 11:27–34
 15. Gonen Y, Casper RF. Prediction of implantation by the sonographic appearance of the endometrium during ovarian stimulation for IVF: *J Invitro Fert Embryo Transf* 1990; 7(3):146 – 52.
 16. Bergh C, Hillensjo T, Nilsson L. Sonographic evaluation of the endometrium in invitrofertilization cycles. A way to predict pregnancy?: *Acta Obstet Gynecol Scand*. 1992; 71(8):624 – 8.
 17. Oliveira JB, Baruffi RL, Mauri AL, Petersen CG, Borges MC, 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.
 18. Glissant A, Mouzon J, Frydman R. Ultrasound study of the endometrium during invitro fertilization cycles. *Fertil Steril*. 1985; 44:786 – 90
 19. Fleicher AC, Herbert CM, Sacks GA, Wentz AC, Entman SS, James AE. Sonography of the endometrium during conception and non-conception cycles of in vitro fertilization and embryo transfer. *Fertil. Steril*. 1986; 46: 442–447.
 20. Welker BG, Gembuch U, Dietrich K, al-Hasani S, Krebs D. Transvaginal sonography of the endometrium during ovum pick up in stimulated cycles in invitrofertilization. *J Ultrasound Med* 1989; 8:549 – 53
 21. Eichler C, Krampfl E, Reichel V, Zegermacher G, Obruca A, Strohmer H, Feldner- Busztin M. The relevance of endometrial thickness and echo patterns for the success of in vitro fertilization evaluated in 148 patients. *J Assist Reprod Genet* 1993; 10:223-227
 22. Khalifa E, Brzyski RG, Oehninger S, Acosta AA, Muasher SJ. Sonographic appearance of the endometrium: The predictive value for the outcome of IVF in stimulated cycles. *Human Reprod* 1992; 7(5):677 –80.
 23. Bassil S. Changes in endometrial thickness, width, length and pattern in predicting pregnancy outcome during ovarian stimulation in IVF. *Ultrasound Obstet Gynecol* 2001; 18(3):258 – 63.

24. Weissman A, Gotlieb L, Casper RF. The detrimental effect of increased endometrial thickness on implantation and pregnancy rates and outcome in an IVF programme. *Fert Steril*. 1999; 71(1):147 – 9.
25. Yoeli R, Ashkenazi J, Orvieto R, Shelef M, Kaplan B, Bar-Hava I. Significance of increased endometrial thickness in ART treatments. *J Assist Reprod Genet* 2004; 21(8):285 – 9.
26. Yaman C, Ebner T, Jesacher K, Sommergruber M, Radner G, Tews G. Sonographic measurement of endometrial thickness as a predictive value for pregnancy through IVF: *Ultraschall Med*. 2002; 23(4):256 – 9.
27. De Geyter C, Schmitter M, De Geyter M, Nieschlag E, Holzgreve W, Schneider HP. Prospective evaluation of the ultrasound appearance of the endometrium in a cohort of 1,186 infertile women. *Fert Steril*. 2000; 73(1):106 – 13.
28. Wada I, Matson PC, Macnamee MC, Brinsden PR, Lieberman BA. High ovarian response in Yoruba African women during ovulation induction for assisted conception. *Hum Reprod*. 1994; 9(6):1077 – 80.
29. Baruffi RL, Contart P, Mauri AL, Petersen C, Felipe V, Garbellini E. A uterine ultrasonographic scoring system as a method for the prognosis of embryo implantation. *J Assist Reprod Genet*, 2002; 19(3):99 – 102.
30. Taylor DW. The calculation of sample size and power in the planning of experiments. *Dept. Clin. Epid. Biostat. McMaster University. Hamilton Ontario, Canada*. 1994; 1 – 23.
31. Check JH, Dietterich C, Lurie D. Non homogenous hyperechogenic pattern 3 days after embryo transfer is associated with lower pregnancy rates. *Hum Reprod* 2000; 15(5):1069 – 74.
32. Chukwudebelu WO, Esege N, Megafu U. Etiological factors in infertility in Enugu, Nigeria. *Infertility*, 1979; 193 – 200.
33. Esimai OA, Orji EO, Lasisi AR. Male contribution to infertility in Ile – Ife, Nigeria. *Niger J Med* 2002; 11(2):70 – 2.
34. Giwa – Osagie OF. ART in developing countries with particular reference to sub - Saharan Africa. In: *Current practices and controversies in assisted reproduction. Report of a WHO meeting*. Vayena E, Rowe PJ, Griffin PD (eds) 2002. pp 22 – 27.
35. Okonofua FE, Onwudiegwu U, Smith W, Thomas N, Craft I, Dandona F. Correlation of ultrasound assessment of endometrial growth and plasma steroid concentration during superovulation for IVF. *Afr J Med Sci* 1993; 22(1):89 – 93.
36. Giorgetti C, Chabert Orsini V, Barry B, Chinchole JM, Franquebalme JP, Hans E, Glowaczower E. Elective single embryo transfer, a justified policy for selected patients. *Gynecol Obstet Fertil* 2006; 34(4):317 –322.
37. Criniti A, Thyer A, Chow G, Lin P, Klein N, Soules M. Elective single blastocyst transfer reduces twin rates without compromising pregnancy rates. *Fert Steril* 2005; 84(6):1613 – 9.
38. Gelbaya TA, Nardo LG, Hunter HR, Fitzgerald C, Horne G, Pease E, Briston D, Lieberman B. Cryopreserved thawed embryo transfer in natural or down regulated hormonally controlled cycles: a retrospective study. *Fert Steril* 2006; 85(3):603 – 9.
39. Wada I, Macnamee MC, Wick K, Wick K, Bradfield JM, Brinsden PR. Birth characteristics and perinatal outcome of babies conceived from cryopreserved embryos. *Hum Reprod* 1994; 9(3):543 – 6.

