ISSN: 1343-4292
Volume 140, Issue 09, December, 2022

The value of ultrasound examination at day of trigger in determining endometrial thickness and its role in predicting positive pregnancy test in a group of Iraqi infertile couples subjected to "intracytoplasmic sperm injection (ICSI)"

Khaleel Kareem Alomari[1], Saba Shamran Alomari[2]

M.B.Ch.B / FICMS (radiology), Assistant professor, Department of surgery, College of Medicine, University of Al-Qadisiyah, consultant radiologist[1]
M.B.Ch.B.D.O.G, Women's and Children's Teaching Hospital[2]

ABSTRACT— Ultrasound examination at day of triggering is preferred to assess endometrial thickness since it's a non invasive procedure. It has been found in various studies that thin endometrium is correlated to poor results in cycles of "intracytoplasmic sperm injection". Nevertheless, the issue that endometrial thickness greater than certain cutoff value association with better ICSI outcome is still controversial and need further deep research work both clinically and experimentally. The goal of the current research is to evaluate the correlation of endometrial thickness evaluated by ultrasound examination to the outcome of ICSI cycles in a sample of Iraqi infertile women. The current cross sectional study included 290 infertile women undergoing ICSI cycles in a single fertility center in Iraq. We retrieved the clinical reports of those women from the archival pool present in this center. The following variables were reported: age of women, infertility duration, body mass index (BMI), type of infertility and thickness of endometrium estimated by ultrasound at day of trigger and result of pregnancy test. At the end of the study, positive pregnancy test was reported in 98 women out of 290 participants making the pregnancy rate at 33.8 %. Type of infertility, duration of infertility, body mass index and age were not significantly associated with pregnancy outcome ($p > 0.05$). Mean endometrial thickness in those with a pregnancy test that is positive was higher significantly than that of those with pregnancy test that is negative. The analysis of Receiver operating characteristic has been utilized to determine endometrial thickness cutoff value, figure 2 and table 3. The cutoff value was > 9.3 mm with 74.4 % accuracy level. Our study revealed that ultrasound examination at day of trigger of women undergoing ICSI is a valuable mean in determining positive pregnancy outcome by defining the thickness of endometrium and that endometrium thickness greater than 9.3 mm is the best predictor of positive ICSI outcome.

KEYWORDS: ultrasound, endometrial thickness, ICSI

1. INTRODUCTION

When couples fail to possess clinical childbearing following single year of unprotected intercourse that is regular, the problem is designated as infertility [1], [2]. Globally it affects about 8 -12 % of couples within reproductive age [3]. The reasons behind infertility might be attributable to male factors, female factors, combined factors or unexplained factor [4], [5]. In general, males account for about 20-30 % of cases [3]. Female factors account for approximately 47 % [4]. These female factors may be categorized into a variety of causes such as hormonal problems, genital tract anatomical problems, ovarian related factors and other

causes [4].

The introduction of assisted reproductive techniques had substantially raised the chance of clinical childbearing in infertile individuals and these techniques included “in vitro fertilization (IVF)” and “intracytoplasmic injection (ICSI)” [6], [7]. The factors that determine the primary outcome of ICSI, namely clinical pregnancy, are multiple and include age of women, age of male partner, hormonal levels, oocyte count and quality and embryo count and quality in addition to other factors [8- 11]. One of these important predictors is endometrial thickness assessed by ultrasound examination. Ultrasound examination at day of triggering is preferred to assess endometrial thickness since it’s a non invasive procedure [12].

It has been found in various studies endometrium which is thin is correlated to poor outcome in cycles of ICSI [13], [14]. Nevertheless, the issue that endometrial thickness greater than certain cutoff value association with better ICSI outcome is still controversial and need further deep research work both clinically and experimentally [15]. Some authors reported that thicker endometrium is associated with better clinical pregnancy outcome [16], whereas, other authors reported that endometrium that is thick is correlated to more rate of miscarriage or failure of implantation [17].

In addition to clinical pregnancy outcome, it had been shown that endometrium that is thin may be correlated to adverse maternal outcome such as hypertensive disorder [18] or adverse fetal outcome such as small for gestational age [19].

Therefore, assessment of endometrial thickness using ultrasound in women undergoing ICSI is mandatory for predicting pregnancy outcome as well as fetal and maternal outcomes. The target of the current research is to evaluate the correlation between endometrial thickness evaluated by ultrasound examination and the outcome of ICSI cycles in a sample of Iraqi infertile women.

2. Patients and methods

The current cross sectional study included 290 infertile women undergoing ICSI cycles in a single fertility center in Iraq. We retrieved the clinical reports of those women from the archival pool present in this center. The following variables were reported: age of women, infertility duration, body mass index (BMI), type of infertility and thickness of endometrium estimated by ultrasound at day of trigger and result of pregnancy test.

The research approval has been issued by the authority of ethical approval belonging to the “college of medicine / University of Al-Qadisiyah”. Formal agreement was issued by the health directorates belonging to governorates at which the study was carried out.

The data were transferred into a spread sheet of the software: statistical package for social science (USA, Chicago, IBM, SPSS, version 16) and statistical analysis was done using this software in addition to Microsoft Office Excel 2007 and Mecalc statistical software. Quantitative variables were presented using range, mean and standard deviation. Nominal information was shown as percentage and count. Student t-test has been utilized to compare mean differences of quantitative variables. Chi-square test has been used to study association between nominal data and pregnancy outcome. The analysis of Receiver operating characteristic (ROC) has been utilized to figure out endometrial thickness cutoff value. The significance level was considered at $p \leq 0.05$.

3. Results

ISSN: 1343-4292
Volume 140, Issue 09, December, 2022

When the research was finished, positive pregnancy test was reported in 98 women out of 290 participants making the pregnancy rate at 33.8 %, figure 1. Demographic characteristics of infertile women categorized according to results of pregnancy test are shown in table 1. Type of infertility, duration of infertility, body mass index and age were not significantly associated with pregnancy outcome ($p > 0.05$). Comparison of mean endometrial thickness measured by ultrasound at day of trigger between positive pregnancy group and negative pregnancy group is shown in table 2. Mean endometrial thickness in those with a pregnancy test that is positive was higher significantly than that of those with pregnancy test that is negative. The analysis of Receiver operating characteristic has been utilized to determine endometrial thickness cutoff value, figure 2 and table 3. The cutoff value was > 9.3 mm with 74.4 % accuracy level.

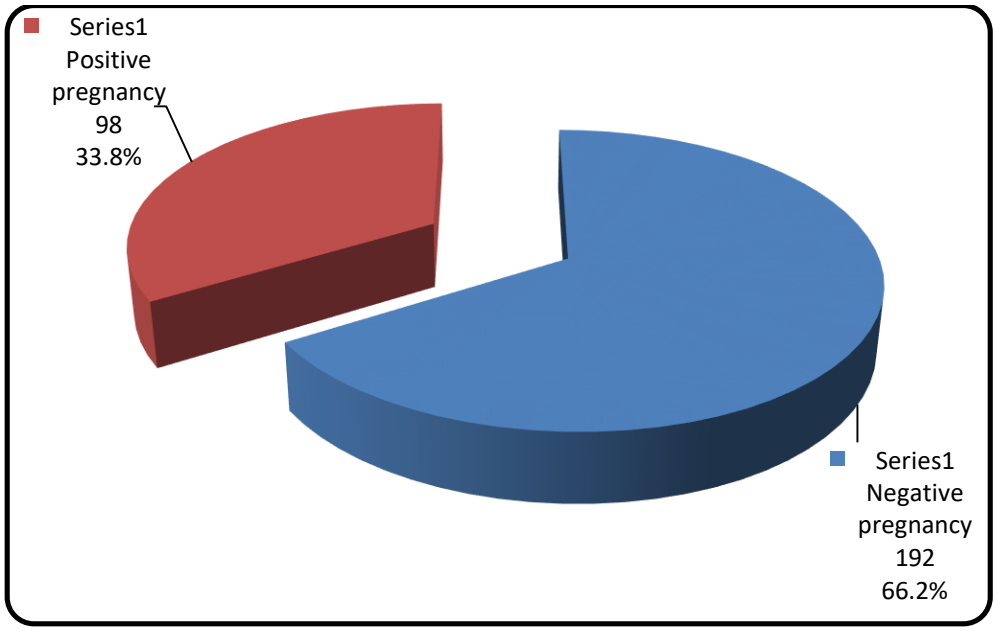

Figure 1: Pie chart showing the rate of positive pregnancy according to biochemical pregnancy test

Table 1: Demographic characteristics of infertile women categorized according to results of pregnancy test

Characteristic	Total *n* = 290	Positive pregnancy *n* = 98	Negative pregnancy *n* = 192	*p*
Age (years)				
Range	18 -44	18 -44	18 -44	0.577 I NS
Mean ±SD	31.24 ±6.14	30.96 ±6.02	31.39 ±6.21	
≤ 35 years, *n* (%)	214 (73.8 %)	76 (77.6 %)	138 (71.9 %)	0.298 C NS
> 35 years, *n* (%)	76 (26.2 %)	22 (22.4 %)	54 (28.1 %)	
BMI (kg/m^2)				
Range	17.57 -48.8	18.59 -43.1	17.57 -48.8	0.801 I NS
Mean ±SD	28.60 ±4.58	28.51 ±4.34	28.65 ±4.70	
Normal weight, *n* (%)	62 (21.4 %)	21 (21.4 %)	41 (21.4 %)	0.943 C NS
Overweight, *n* (%)	125 (43.1 %)	41 (41.8 %)	84 (43.8 %)	

Obese, *n* (%)	103 (35.5 %)	36 (36.7 %)	67 (34.9 %)	
Duration of infertility (years)				
Range	1 -23	2 -23	1 -21	0.561 I NS
Mean ±SD	7.63 ±4.41	7.84 ±4.62	7.52 ±4.30	
Type of Infertility				
Primary, *n* (%)	210 (72.4 %)	64 (65.3 %)	146 (76.0 %)	0.053 C NS
Secondary, *n* (%)	80 (27.6 %)	34 (34.7 %)	46 (24.0 %)	

NS: not significant; C: chi-square test; I: independent samples t-test; BMI: body mass index; SD: standard deviation; n: number of cases

Table 2: Comparison of mean endometrial thickness measured by ultrasound at day of trigger between positive pregnancy group and negative pregnancy group

Characteristic	Total *n* = 290	Positive pregnancy *n* = 98	Negative pregnancy *n* = 192	*p*
Endometrial thickness (mm)				
Range	4 -14.5	6 -14.5	4 -12.2	< 0.001 I***
Mean ±SD	8.87 ±1.58	9.74 ±1.43	8.42 ±1.46	

***: significant at $p \leq 0.001$; I: independent samples t-test; SD: standard deviation; n: number of cases

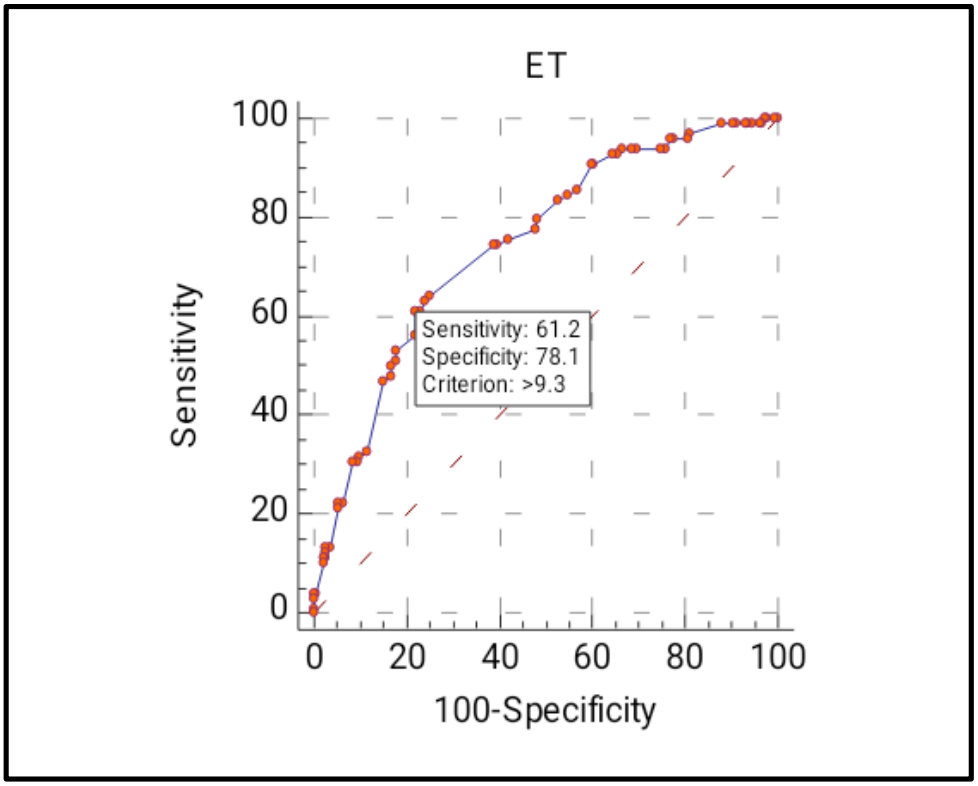

Figure 2: Curve analysis of "Receiver operating characteristic (ROC)" to find the ideal value of cutoff of endometrial thickness in terms of sensitivity and specificity that can predict positive pregnancy test

ISSN: 1343-4292
Volume 140, Issue 09, December, 2022

Table 3: Characteristic of ROC analysis

Characteristic	Results
Cutoff	>9.3 mm
AUC	0.744
95 % CI	0.690 - 0.794
p-value	< 0.001 ***
Sensitivity %	61.2
Specificity %	78.1
Accuracy %	74.4

AUC: are under curve; CI: confidence interval; ***: significant at $p \leq 0.001$

4. Discussion

Infertility is one of the major health issues worldwide and in our country. Treatment of infertility requires improvement of number of predictors of ICSI outcomes including endometrial thickness that can be easily determined using ultrasound examination at day of trigger. In the current study we were able to show that endometrial thickness assessed by ultrasound can be a significant predictor of positive pregnancy test in a group of Iraqi couples subjected to ICSI. In addition we showed that age of mother, body mass index, type of infertility and duration of infertility lacks the predictive capability of thickness of endometrium in determining positive pregnancy test since the association between these parameters and pregnancy test was not significant.

Some authors have previously defined certain cutoff values of endometrial thickness to be associated with ICSI outcomes such as 7, 6.5 and 14 mm [3]. However, in our study we found that a cutoff value of > 9.3 mm was the ideal predictor of positive pregnancy outcome with an acceptable accuracy level.

According to one previous meta-analysis, it has been shown that thin endometrium, thickness below pre-define cutoff value, was associated with significantly lower pregnancy outcome in ICSI cycles [3]. This finding is indeed in agreement with our finding and is also supported by the finding of several previous studies [20], [21].

The possible mechanism of thin endometrium development is not clear but it has been linked to oxygen level in basal layer and to differential expression of a number of transcriptional factors [22- 24], but this issue is somewhat away from the target of the current research.

In addition, to raising chance of pregnancy in women underlying ICSI when the endometrial thickness is increased by a number of medical interventions, maternal and fetal outcomes can also be improved. As we said previously it had been shown that endometrium that is thin may be correlated to adverse fetal as well as maternal outcomes [18], [19].

The sample size in our study was 290 and in our opinion this relatively large sample size in such an Iraqi study is sufficient to make solid evidence about the role of ultrasound examination in predicting pregnancy outcome in women undergoing ICSI cycles. It appears that adopting strategy of increasing the thickness of endometrium should be a routine step in assisted reproductive technology institutes in Iraq.

5. Conclusion

Our study revealed that ultrasound examination at day of trigger of women undergoing ICSI is a valuable

mean in determining positive pregnancy outcome by defining the thickness of endometrium and that endometrium thickness greater than 9.3 mm is the best predictor of positive ICSI outcome.

Acknowledgment
We feel that deep appreciations and thanks must be expressed to all women participating in this study in order to improve the outcome of future ICSI cycles in Iraqi infertile women.

6. References

[1] Carson SA, Kallen AN. Diagnosis and Management of Infertility: A Review. JAMA. 2021;326(1):65-76. doi:10.1001/jama.2021.4788

[2] Walker MH, Tobler KJ. Female Infertility. In: StatPearls. Treasure Island (FL): StatPearls Publishing; December 28, 2021.

[3] Vander Borght, M., & Wyns, C. (2018). Fertility and infertility: Definition and epidemiology. Clinical biochemistry, 62, 2–10.

[4] Deshpande PS, Gupta AS. Causes and Prevalence of Factors Causing Infertility in a Public Health Facility. J Hum Reprod Sci. 2019;12(4):287-293. doi:10.4103/jhrs.JHRS_140_18

[5] Öztekin Ü, Caniklioğlu M, Sarı S, Selmi V, Gürel A, Işıkay L. Evaluation of Male Infertility Prevalence with Clinical Outcomes in Middle Anatolian Region. Cureus. 2019;11(7):e5122. Published 2019 Jul 10. doi:10.7759/cureus.5122

[6] Farquhar C, Marjoribanks J. Assisted Reproductive Technology: An Overview of Cochrane Reviews. Cochrane Database Syst Rev (2018) 8. doi: 10.1002/14651858.CD010537.pub5

[7] Liao Z, Liu C, Cai L, et al. The Effect of Endometrial Thickness on Pregnancy, Maternal, and Perinatal Outcomes of Women in Fresh Cycles After IVF/ICSI: A Systematic Review and Meta-Analysis. Front Endocrinol (Lausanne). 2022;12:814648. Published 2022 Feb 11. doi:10.3389/fendo.2021.814648

[8] Kdous M, Chaker A, Zhioua A, Zhioua F. Qualité ovocytaire et embryonnaire et issue des cycles d'ICSI chez les patientes porteuses d'un syndrome des ovaires polykystiques (SOPK) versus normo-ovulantes [Oocyte and embryo quality and outcome of ICSI cycles in patients with polycystic ovary syndrome (PCOS) versus normo-ovulatory]. J Gynecol Obstet Biol Reprod (Paris). 2009;38(2):133-143. doi:10.1016/j.jgyn.2008.12.001

[9] Wu Y, Kang X, Zheng H, Liu H, Huang Q, Liu J. Effect of Paternal Age on Reproductive Outcomes of Intracytoplasmic Sperm Injection. PLoS One. 2016;11(2):e0149867. Published 2016 Feb 22. doi:10.1371/journal.pone.0149867

[10] Mai Z, Liu M, Pan P, et al. Comparison of Cumulative Live Birth Rate Between Aged PCOS Women and Controls in IVF/ICSI Cycles. Front Endocrinol (Lausanne). 2021;12:724333. Published 2021 Sep 28. doi:10.3389/fendo.2021.724333

[11] Mai Z, Liu M, Pan P, et al. Comparison of Cumulative Live Birth Rate Between Aged PCOS Women and Controls in IVF/ICSI Cycles. Front Endocrinol (Lausanne). 2021;12:724333. Published 2021 Sep 28.

doi:10.3389/fendo.2021.724333

[12] Liao Z, Liu C, Cai L, et al. The Effect of Endometrial Thickness on Pregnancy, Maternal, and Perinatal Outcomes of Women in Fresh Cycles After IVF/ICSI: A Systematic Review and Meta-Analysis. Front Endocrinol (Lausanne). 2022;12:814648. Published 2022 Feb 11. doi:10.3389/fendo.2021.814648

[13] Lv H, Li X, Du J, et al. Effect of endometrial thickness and embryo quality on live-birth rate of fresh IVF/ICSI cycles: a retrospective cohort study. Reprod Biol Endocrinol. 2020;18(1):89. Published 2020 Aug 21. doi:10.1186/s12958-020-00636-6

[14] Bu Z, Hu L, Yang X, Sun Y. Cumulative Live Birth Rate in Patients With Thin Endometrium: A Real-World Single-Center Experience. Front Endocrinol (Lausanne). 2020;11:469. Published 2020 Sep 4. doi:10.3389/fendo.2020.00469

[15] Li W, Cao Z, Yu X, Hu W. Effect of growth hormone on thin endometrium via intrauterine infusion. Ann Transl Med. 2021;9(16):1325. doi:10.21037/atm-21-3583

[16] Zhang X, Chen CH, Confino E, Barnes R, Milad M, Kazer RR. Increased Endometrial Thickness Is Associated With Improved Treatment Outcome for Selected Patients Undergoing In Vitro Fertilization-Embryo Transfer. Fertil Steril (2005) 83:336–40. doi: 10.1016/j.fertnstert.2004.09.020

[17] Weissman A, Gotlieb L, Casper RF. The Detrimental Effect of Increased Endometrial Thickness on Implantation and Pregnancy Rates and Outcome in an In Vitro Fertilization Program. Fertil Steril (1999) 71:147–9. doi: 10.1016/s0015-0282(98)00413-0

[18] Liu X, Wang J, Fu X, Li J, Zhang M, Yan J, et al.. Thin Endometrium Is Associated With the Risk of Hypertensive Disorders of Pregnancy in Fresh IVF/ICSI Embryo Transfer Cycles: A Retrospective Cohort Study of 9,266 Singleton Births. Reprod Biol Endocrinol (2021) 19:55. doi: 10.1186/s12958-021-00738-9

[19] Guo Z, Xu X, Zhang L, Zhang L, Yan L, Ma J. Endometrial Thickness Is Associated With Incidence of Small-for-Gestational-Age Infants in Fresh In Vitro Fertilization-Intracytoplasmic Sperm Injection and Embryo Transfer Cycles. Fertil Steril (2020) 113:745–52. doi: 10.1016/j.fertnstert.20619.12.014

[20] Kasius A, Smit JG, Torrance HL, Eijkemans MJ, Mol BW, Opmeer BC, et al.. Endometrial Thickness and Pregnancy Rates After IVF: A Systematic Review and Meta-Analysis. Hum Reprod Update (2014) 20:530–41. doi: 10.1093/humupd/dmu011

[21] Tomic V, Kasum M, Vucic K. Impact of Embryo Quality and Endometrial Thickness on Implantation in Natural Cycle IVF. Arch Gynecol Obstet (2020) 301:1325–30. doi: 10.1007/s00404-020-05507-4

[22] Zong L, Zheng S, Meng Y, Tang W, Li D, Wang Z, et al.. Integrated Transcriptomic Analysis of the miRNA-mRNA Interaction Network in Thin Endometrium. Front Genet (2021) 12:589408. doi: 10.3389/fgene.2021.589408

[23] Maekawa R, Taketani T, Mihara Y, Sato S, Okada M, Tamura I, et al.. Thin Endometrium Transcriptome Analysis Reveals a Potential Mechanism of Implantation Failure. Reprod Med Biol (2017) 16:206–27. doi: 10.1002/rmb2.12030

[24] Casper RF. It's Time to Pay Attention to the Endometrium. Fertil Steril (2011) 96:519–21. doi: 10.1016/j.fertnstert.2011.07.1096