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Original Research Article

Correlation of uterine scoring system for reproduction with pregnancy rate among infertility patients undergoing intracytoplasmic sperm injection and frozen-thawed embryo transfer

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ABSTRACT

Background: Successful implantation requires presence of a good quality embryo and receptive endometrium. Endometrial receptivity is ability of endometrium to successfully attach embryo, nourish and keep it alive. Sonographic findings are weighed according to uterine scoring system for reproduction (USSR) or uterine biophysical profile (UBP) by Applebaum. It has become absolute necessity to evaluate uterus and endometrium prior to embryo transfer, so that optimum results are obtained in favourable uteri.
Methods: It is a prospective observational study which includes 100 patients undergoing intracytoplasmic sperm injection (ICSI) treatment followed by frozen embryo transfer. The Applebaum scoring system was done on the day of thawing scan, using ultrasonography (USG) and Doppler studies, assessing endometrial thickness, endometrial motion, endometrial layering, myometrial contractions, uterine artery doppler flow, endometrial blood flow in zone 3 and myometrial blood flow – the scores of each parameter was noted, the final score calculated.
Results: Receiver operating characteristic curve **(**ROC) curve total score in Applebaum scoring system for predicting pregnancy has a cut-off- 13 with sensitivity- 90.10%, specificity- 89.5%, positive predictive value (PPV)-97.34%, and negative predictive value (NPV)- 67.95. The above should be incorporated into routine practice. This was suggested by our study results in addition to endometrial patterns.
Conclusions: Applebaum's USSR scoring system is a simple and non-invasive method for prediction of pregnancy rate in ICSI and frozen embryo transfer cycle. Uterine scoring system will help to perform embryo transfers in only favourable uteri and postpone or cancel those cycles in which poor uterine score is demonstrated.

Keywords: Uterine scoring system, Pregnancy, Frozen embryo transfer

INTRODUCTION

Infertility is defined as failure to conceive a clinical pregnancy after 12 months or more of regular unprotected intercourse. Improved stimulation protocol, and lab facilities are available for in vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI). Better ultrasound and Doppler studies of uterus and endometrium have been used.[1] Successful implantation requires presence of a good quality embryo and receptive endometrium. Endometrial receptivity is ability of endometrium to successfully attach embryo, nourish and keep it alive.[2] Endometrium undergoes clinical, morphological and histological changes with typical sonography patterns during different phases of natural as well as stimulated cycles. From the first day of menstrual cycle till mid cycle endometrium progressively thickens and it is sonographically detectable.[1] This appearance can be layered, trilaminar or

five line. A good blood supply to the endometrium is considered essential for implantation and hence assessment of endometrial blood flow in embryo transfer cycle patients has gained importance over years. Endometrial and subendometrial blood flow increases during follicular phase and reach its maximum approximately three days prior to ovulation. Endometrial blood flow can be measured by 2D or 3D ultrasound.[3] Spiral vessels run towards endometrium and penetrate it. These spiral arteries are branches of arcuate artery, radial artery, uterine artery and therefore if resistance in uterine artery is high, evidently resistance in spiral arteries is also high. So, assessment of uterine artery resistance is a clue to implantation potential of endometrium. Estrogen produces vasodilatory effect on uterine artery. So pulsatality index drops with increasing estrogen levels. Transvaginal sonography is a simple, reliable and inexpensive method for evaluation of endometrial receptivity. These sonographic findings are weighed according to uterine scoring system for reproduction (USSR) or uterine biophysical profile (UBP) by Applebaum. It has become absolute necessity to evaluate uterus and endometrium prior to embryo transfer, so that optimum results are obtained in favourable uteri.[1]

Background

USSR is the most commonly used predictor in embryo transfer cycles outcome.

Aim

Aim of the study was to detect whether ultrasonographic parameters and Doppler analysis of uterine blood flow can be of value in the prediction of endometrial receptivity in infertile female patients undergoing embryo transfer.

Objectives

Objectives of the study were: determination of endometrial thickness, endometrial morphology, endometrial vascularity; correlation of endometrial thickness with pregnancy rate; determination of uterine artery PI; and correlation of the above factors with pregnancy rate.

METHODS

It is a prospective observational study which includes 100 patients undergoing ICSI treatment followed by frozen embryo transfer. The Applebaum scoring system was done on the day of thawing scan, using USG and Doppler studies – the scores of each parameter were noted, the final score calculated.

Study place

The study was conducted at ARC Fertility Hospital, Saveetha campus branch, 4 months from October 2021 to January 2022.

Selection criteria

Women between 19-45 years of age, infertility due to tubal factor, male factor, polycystic ovary syndrome (PCOS), unexplained infertility, and those willing to give consent were included in the study.

Statistical analysis done using statistical package for the social sciences (SPSS).

RESULTS

In this study, the endometrial thickness was found to be strongly correlated with successful pregnancy in IVF/ICSI cycles. The most endometrial thickness for pregnancy was 7-9 mm in our study (82.95% of them achieved pregnancy). 76.78% of patients with hazy endometrial appearance, 97.1% endometrial motion (>3 contractions in 2 minutes) have become pregnant, 81.44% patients with homogenous myometrial echogenicity, 84.14% with uterine artery PI-2.2-2.4, 91.48% with multifocal blood flow in zone 3 have become conceived. 80.85% patients with myometrial blood flow have become pregnant. The area under the curve (ROC curves were used) for total score in predicting pregnancy is 0.929 (0.849-1). The cut off of total score for predicting pregnancy is 13 which had a sensitivity of 90.1%, specificity of 89.5%, positive predictive value of 97.34%, negative predictive value of 67.95% and a diagnostic accuracy of 89.99%.

Comparison of endometrial thickness on thawing with the outcome

Comparing the endometrial thickness on thawing with outcome distribution, subjects with 10-14 mm ET had higher proportion of pregnancies with 100% followed by subjects with 7-9 mm ET with 82.95% and least in subjects with <7 mm ET with 50%. The difference in outcome distribution between different endometrial thickness on thawing was statistically significant ($p<0.05$).

Comparison of endometrial layering with the outcome

Comparing the endometrial layering with outcome distribution, 76.78% of the subjects with hazy 5-line endometrial layering had pregnancies which is lower compared to subjects with distinct 5-line endometrial layering of whom 86.36% had pregnancies and the difference was not statistically significant ($p>0.05$).

Comparison of endometrial motion with the outcome

Comparing the endometrial motion with outcome distribution, 45.16% of the subjects with <3 contractions in 2 minutes endometrial motion had pregnancies which is lower compared to subjects with >3 contractions in 2 minutes endometrial motion of whom 97.1% had pregnancies and the difference was statistically significant ($p<0.05$).

Comparison of myometrial echogenicity with the outcome

Comparing the myometrial echogenicity with outcome distribution, 66.66% of the subjects with coarse, inhomogeneous myometrial echogenicity had pregnancies which is lower compared to subjects with relatively homogenous myometrial echogenicity of whom 81.44% had pregnancies and the difference was not statistically significant (p>0.05).

Comparison of uterine artery doppler flow (PI) with the outcome

Comparing the uterine artery doppler flow (PI) with outcome distribution, <2.19 PI had higher proportion of pregnancies with 100% followed by 2.2-2.49 PI with 84.14% and least in 2.5-2.99 PI with 60%. The difference in pregnancies distribution between different uterine artery doppler flow (PI) was statistically significant (p<0.05).

Comparison of endometrial blood flow in zone 3 with the outcome

Comparing the endometrial blood flow in zone 3 with outcome distribution, multifocal blood flow had higher proportion of pregnancies with 91.48% followed by sparse blood flow with 72% and least in absent blood flow with 66.66%. The difference in pregnancies distribution between different endometrial blood flow in zone 3 was statistically significant (p<0.05).

Comparison of myometrial blood flow on gray scale examination with the outcome

Comparing the myometrial blood flow on gray scale examination with outcome distribution, 83.33% of the subjects with absent myometrial blood flow had pregnancies which is higher compared to subjects with myometrial blood flow of whom 80.85% had pregnancies and the difference was not statistically significant (p>0.05).

ROC curve of total score for predicting pregnancy

The area under the curve for total score in predicting pregnancy is 0.929 (0.849-1). The cut off of total score for predicting pregnancy is 13 which had a sensitivity of 90.1%, specificity of 89.5%, positive predictive value of 97.34%, negative predictive value of 67.95% and a diagnostic accuracy of 89.99%.

Table 1: Comparison of endometrial thickness on thawing with the outcome.

Endometrial thickness on thawing (mm)	Outcome (%)		Total (%)	Fisher exact p value
	Pregnant	Not pregnant		
<7	4 (50)	4 (50)	8 (100)	0.017
7-9	73 (82.95)	15 (17.04)	88 (100)	
10-14	4 (100)	0 (0)	4 (100)	
Total	81 (81)	19 (19)	100 (100)	

Table 2: Comparison of endometrial layering with the outcome.

Endometrial layering	Outcome (%)		Total (%)	P value
	Pregnant	Not pregnant		
Hazy 5 line	43 (76.78)	13 (23.21)	56 (100)	0.226
Distinct 5 line	38 (86.36)	6 (13.63)	44 (100)	
Total	81 (81)	19 (19)	100 (100)	

Table 3: Comparison of endometrial motion with the outcome.

Endometrial motion	Outcome (%)		Total (%)	P value
	Pregnant	Not pregnant		
<3 contractions in 2 minutes	14 (45.16)	17 (54.83)	31 (100)	0.001
>3 contractions in 2 minutes	67 (97.1)	2 (2.89)	69 (100)	
Total	81 (81)	19 (19)	100 (100)	

Table 4: Comparison of myometrial echogenicity with the outcome.

Myometrial echogenicity	Outcome (%)		Total (%)	Fisher exact p value
	Pregnant	Not pregnant		
Coarse, inhomogeneous	2 (66.66)	1 (33.33)	3 (100)	0.381
Relatively homogenous	79 (81.44)	18 (18.55)	97 (100)	
Total	81 (81)	19 (19)	100 (100)	

Table 5: Comparison of uterine artery doppler flow (PI) with the outcome.

Uterine artery Doppler flow (PI)	Outcome (%)		Total (%)	Fisher exact p value
	Pregnant	Not pregnant		
2.5-2.99	9 (60)	6 (40)	15 (100)	0.019
2.2-2.49	69 (84.14)	13 (15.85)	82 (100)	
<2.19	3 (100)	0 (0)	3 (100)	
Total	81 (81)	19 (19)	100 (100)	

Table 6: Comparison of endometrial blood flow in zone 3 with the outcome.

Endometrial blood flow in zone 3	Outcome (%)		Total (%)	Fisher exact p value
	Pregnant	Not pregnant		
Absent blood flow	2 (66.66)	1 (33.33)	3 (100)	0.004
Sparse blood flow	36 (72)	14 (28)	50 (100)	
Multifocal blood flow	43 (91.48)	4 (8.51)	47 (100)	
Total	81 (81)	19 (19)	100 (100)	

Table 7: Comparison of myometrial blood flow on gray scale examination with the outcome.

Myometrial blood flow on Gray scale examination	Outcome (%)		Total (%)	Fisher exact p value
	Pregnant	Not pregnant		
Absent	5 (83.33)	1 (16.66)	6 (100)	0.409
Present	76 (80.85)	18 (19.14)	94 (100)	
Total	81 (81)	19 (19)	100 (100)	

Table 8: Area under curve of total score for predicting pregnancy.

Test result variable(s)	Area under the curve	95% confidence interval		P value
		Lower bound	Upper bound	
Total Score	0.929	0.849	1.000	0.001

Table 9: Total score for predicting pregnancy.

Parameters	Total score (%)
Cut off	13
Sensitivity	90.10
Specificity	89.50
PPV	97.34
NPV	67.95

DISCUSSION

The assessment of endometrial receptivity is mandatory for the success of IVF/ICSI procedures. Angiogenesis plays an important role in various female reproductive processes s maturation of dominant follicle, endometrial growth and implantation process.[1-3]

Hence there was no difference in all demographic features or details of ovarian stimulation between pregnant and non-pregnant women.

In this study, the endometrial thickness was found to be strongly correlated with successful pregnancy in IVF/ICSI cycles. The most endometrial thickness for pregnancy was 7-9 mm in our study (82.95% of them achieved pregnancy), followed by endometrial thickness of 10-14 mm (100% of them achieved pregnancy – only 4 of them had this). The least of them is when the endometrial thickness was less than 7 mm (only 8% of them achieved pregnancy). No pregnancy was achieved when endometrial thickness was less than 5 mm. According to the fisher p exact test results, ET on thawing was statistically significant, p=0.017 (p<0.05). Singh et al reported that largest number of pregnancies occurred when endometrial thickness is 8-10 mm he also postulated that no pregnancies is less than 5-8 mm.[4] Weissman et al reported the lowest percentage of conception when endometrial thickness is more than 14 mm.[5]

In our research study most of the patients who achieved pregnancy had a hazy five-line appearance of endometrium on the day of thawing. However almost equal had distinct 5-line appearance - 2 conceived. El Zenneni et al stated that the triple layer of endometrial pattern was the most suitable for conception.[6]

Singh et al proved that triple layer endometrium was a good prognostic factor for occurrence of pregnancy.[4] Ng et al reported, no relationship between endometrial thickness, morphology and pregnancy outcomes.[7]

Regarding the endometrial blood flow zone 3, in this study 50% of pregnant women had sparse blood flow in zone III of endometrial blood flow, 47% had multifocal blood flow in zone III of endometrial blood flow. While only 3% of the pregnant women had absent blood flow in zone III. Ng et al found that the endometrial and subendometrial blood flow was not a good predictor of pregnancy.[8] In this study clinical pregnancy rate reached 81%, Fisher exact p, test p=0.004, hence statistically significant.

Sardana et al suggested that a combination of ET and Doppler analysis of endometrial blood flow was a simple and effective tool to improve the outcome of IVF/ICSI ET.[9] In our study all were frozen embryo transfer. ROC curve total score in Applebaum scoring system for predicting pregnancy has a cut off -13 with sensitivity-90.10%, specificity -89.5%, PPV-97.34%, and NPV-67.95. The above should be incorporated into routine practice. This was suggested by our study results in addition to endometrial patterns.

CONCLUSION

Applebaum's USSR scoring system is a simple and non-invasive method for prediction of pregnancy rate in ICSI and frozen embryo transfer cycle. Endometrial receptivity including endometrial thickness, Endometrial morphology and vascularity are predominant in predicting the outcome of pregnancy. Average endometrial thickness of 7-10 mm and triple line (good morphological texture) are good prognostic values if good embryos of grade 5AA, 5AB are transferred. The endometrial blood flow is used as predictor for implantation rate in IVF/ICSI cycles. It requires further studies to explore the potential benefit of improving the IVF/ICSI FET outcomes by intervening in circumstances of poor endometrial vascularity or freezing embryos until endometrial vascularity is good enough for ICSI-FET. Uterine scoring system will help to perform embryo transfers in only favourable uteri and postpone or cancel those cycles in which poor uterine score is demonstrated.

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