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ORIGINAL RESEARCH

Predictive Value of Endometrial Receptivity for Pregnancy Outcomes of In-vitro Fertilization Embryo Transfer for Patients of Different Ages

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ABSTRACT

Context • In recent years, the number of women with unexplained infertility has increased, and clinicians consider poor endometrial receptivity (ER) to be one of the main reasons. ER can have great predictive value for in-vitro fertilization embryo transfer (IVF-ET)-induced pregnancy.

Objective • The study intended to investigate the predictive value of ER—endometrial thickness (EMT) and type and hemodynamic parameters—using color-doppler ultrasound on the pregnancy outcome of IVF-ET for women of different ages.

Design • The research team performed a prospective controlled study.

Setting • The study took place at the Department of Reproductive Medicine at Hebei Reproductive Hospital in Shijiazhuang, China.

Participants • Participants were 841 infertile patients undergoing IVF-ET treatment at the hospital between March 01, 2018 and December 30, 2018. The research team divided participants into two groups: (1) participants diagnosed as having a clinical pregnancy after IVF-ET became the pregnancy group, with 439 participants, and (2) participants who didn't become pregnant became the nonpregnancy group, with 402 participants.

Outcome Measures • The research team: (1) measured EMT, (2) determined endometrium types, (3) classified the intimal and subintimal blood flow, and (4) determined the hemodynamic parameters of the endometrium and subendometrium. The team also measured: (1) the systolic blood flow velocity (VS), (2) diastolic blood flow velocity (VD), and (3) average blood flow velocity (VM) three times and recorded the average value.

Results • Statistically significant differences existed in the pregnancy and implantation rates among the different age groups for the groups with EMTs of <8 mm and 8-13 mm ($P < .05$). The results were similar in the endometrial Type A and endometrial Type B groups as well as between the endometrial blood flow Type 1 and Type 2 groups ($P < .05$). The distribution of endometrial blood flow types was significantly different between the groups ($P = .002$). In addition, statistically significant differences existed in the implantation rates between the <30 years and 30-34 groups in different blood-flow-type groups ($P < .05$). Based on the results of the ROC curve, high-quality embryos (0.566, 95%CI: 0.527-0.605) and endometrial blood flow types (0.554, 95%CI: 0.515-0.593) could not predict clinical pregnancy.

Conclusions • The pregnancy and implantation rates increased between the <30 and 30-34 age groups and them decreased between the age groups as age increased. EMT, endometrial type, and blood flow type can be valuable parameters in predicting the implantation and pregnancy rates of patients of different ages. (*Altern Ther Health Med.* 2023;29(4):210-217).

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The World Health Organization (WHO) indicates that infertility is the third highest disease in incidence, following malignant tumors and cardiovascular diseases, and gradually increases year by year.[1,2] In recent years, the number of patients with unexplained infertility has increased, and clinicians consider poor endometrial receptivity (ER) to be one of the main reasons. ER refers to the endometrium in a state that allows foreign blastocysts to locate, adhere to, and change the endometrial stroma to implant an embryo.

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Endometrial Receptivity

In-vitro fertilization-embryo transfer (IVF-ET) is a common technique for treating infertility, and its success largely depends on embryo quality and ER.[3] Good ER contributes to better outcomes in embryo implantation. Zhang et al found that poor ER could account for two-thirds of failures in embryo implantations, and the remaining one-third was due to embryo defects.[4] Two studies, however, have found that poor endometrial receptivity be the cause of about two-thirds of the failures in embryo transfers.[1,12]

From puberty, ovarian hormones affect the endometrium. Its functional layer changes on the surface periodically, while the endometrial basal layer near the myometrium doesn't. Because of the proliferation, secretion, and shedding of the functional layer, the menstrual cycle consists of menstrual, proliferative, and secretory periods. The middle secretory stage is the main stage for embryo implantation, and the functional layer is implantation's main site.[1,10,12,13]

Many factors affect ER, including endometrial thickness (EMT), volume, morphology, blood supply, local endocrinal changes, and molecular biological mechanisms. The traditional method to evaluate ER is an endometrial-tissue biopsy. The biopsy is invasive in nature, it has low acceptance by patients, and embryo transplantation can't occur until a month after the biopsy. For those reasons, using ER in evaluating the use of IVF-ET has always been tricky in clinical practice because no objective and uniform noninvasive test exists at present.[5-7]

Currently many indexes are available to objectively evaluate endometrial acceptability, but three techniques—measurement of EMT using ultrasound, assessment of endometrial morphology, and determination of endometrial blood flow type—have the advantage of being noninvasive, simple, and rapid methods. Clinicians generally conduct evaluations to evaluate the endometrial acceptability of a freeze-thaw-cycle embryo transfer. They make evaluations based on endometrial morphology, ultrasound, and biochemistry, and positive evaluation of ER can have great predictive value for IVF-ET-induced pregnancy.[2,5-7]

Endometrial Thickness

EMT is one of the commonly used indicators for ultrasound evaluation of endometrial tolerance, which is positively correlated with pregnancy outcomes for IVF-ET. With an increase in EMT, the pregnancy and implantation rates of patients increase, the spontaneous abortion rate decreases, and the live birth rate increases.

Several studies have shown that a relatively thin endometrium can be difficult for embryo implantation, resulting in pregnancy difficulties.[13-15] Patients with an EMT of ≤7 mm had reduced clinical pregnancy rates, spontaneous abortion rates over 50%, and live birth rates that were significantly lower than those of patients with greater thicknesses.

A relatively thick intima can also have an impact on clinical pregnancy. Zhong et al.[16] found that the pregnancy rate and implantation rate decreased when the intima exceeded 14 mm, while others suggested the opposite.[17] At present, whether clinicians can use EMT as a single predictor of pregnancy outcome is controversial.

Ultrasound

Ultrasound plays a definite role in treatment of gynecological organic diseases and prenatal examinations and is claimed to be the gold standard in the diagnosis of many diseases.[18] Ultrasonography can assess EMT, endometrial type, endometrial volume, and subendometrial blood flow to better understand endometrial receptivity. It's noninvasive, repeatable, and predictable and provides real-time monitoring, which makes ultrasonic diagnosis valuable in clinical application and research.

At present, most reproductive medicine experts use the approach as the first choice to evaluate endometrial receptivity. However, although clinicians widely use ultrasound as a noninvasive method, it can give conflicting results in ultrasonic indicators. [8-10]

Endometrial Morphology

Some studies have found that changes in endometrial morphology can affect pregnancy outcomes after embryo transplantation, including that the Type A endometrium has higher embryo implantation and clinical pregnancy rates than Type B and C endometria. [19-22]

Endometrial Blood Flow

A good blood supply to the endometrium is necessary for embryo implantation, and ultrasound detection of endometrial blood flow can directly reflect the microenvironment of the implantation site for the embryo.

Endometrial blood flow has an important predictive value for endometrial receptivity. Two studies have suggested that an abundance in endometrial blood flow is closely related to successful pregnancy from treatments that use the ovulation induction cycle to induce pregnancy.[7,23]

Two studies found that the clinical pregnancy rate was significantly higher in the group where the researchers could detect both intrauterine and subintimal blood-flow signals than in the group where they could detect no blood-flow signals.[24,25]

Current Study

The current study intended to explore the predictive value of ER— EMT and endometrial type and hemodynamic parameters—using color-doppler ultrasound on the pregnancy outcomes of IVF-ET for women of different ages.

METHODS

Participants

The research team performed a prospective controlled study at the Department of Reproductive Medicine at Hebei Reproductive Hospital in Shijiazhuang, China. Potential participants were infertile patients undergoing IVF-ET treatment at the hospital between March 1 and December 30, 2018.

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The study included potential participants if they had: (1) received transplantations of two high-quality embryos after a first IVF-ET treatment; (2) a regular menstrual cycle; (3) normal results from a routine complete blood count and a normal liver and kidney function; (4) participated in a long program to hyperstimulate ovulation; (5) a follicle-stimulating hormone (FSH) level of <8 IU/mL and a number of basal sinus follicles of ≥8; and (6) no history of uterine or ovarian surgery or endocrinal disorders, such as polycystic ovary syndrome, hyperthyroidism, or other diseases.

The study excluded potential participants if they had: (1) a history of infection within the three months before enrollment; (2) a history of use of hormone drugs or ovulation-induction drugs within the one month before enrollment; (3) adenomyosis or endometriosis of the uterus and ovary; or (4) an ovarian tumor, uterine lesions, or cervical lesions.

Participants signed informed consent forms.

Table 1. Comparison of Demographic and Clinical Characteristics of the Groups at Baseline After IVF-ET (N = 841)

Characteristic	Pregnancy Group n = 439 Mean ± SD n (%)	Nonpregnancy Group n = 402 Mean ± SD n (%)	*t* or χ^2	*P* value
Age, y	31.61 ± 4.42	33.58 ± 5.66	5.593	<.001[a]
BMI, kg/m2	21.99 ± 1.13	22.07 ± 2.03	0.704	.486
Infertility time, y	4.27 ± 3.16	4.54 ± 3.05	1.264	.207
FSH dosage (IU/L)	5.39 ± 1.08	5.51 ± 1.13	1.569	.116
Infertility Type			1.833	.068
Primary infertility	165 (37.6)	176 (43.8)		
Secondary infertility	274 (62.4)	226 (56.2)		
Embryo Transfer Cycle	1.56 ± 0.88	1.62 ± 0.85	0.986	.324
Number of Embryos	1.88 ± 0.33	1.81 ± 0.40	-2.765	.006[a]
Embryo Level			16.748	<.001[a]
A	5 (1.1)	0 (0.0)		
B	49 (11.2)	19 (4.7)		
C	385 (87.7)	383 (95.3)		
High-quality Embryos	1.44 ± 0.72	1.24 ± 0.79	-3.741	<.001[a]

[a]$P < .05$, indicating that the nonpregnancy group's mean age, number of embryos, number of high-quality embryos, and embryo levels were significantly lower than those of the pregnancy group.

Abbreviations: FSH, Follicle-stimulating hormone; Embryo Level A, numerous tightly packed cells; Embryo Level B, several tightly packed cells; Embryo Level C, very few cells.

Procedures

IVF-ET treatment. The research team: (1) selected different superovulation schemes according to participants' ages and ovarian reserve function; (2) collected participants' eggs at 36 h after injection of human chorionic gonadotropin (HCG), and transplanted them 2 days after routine culture; (3) tested three embryos for urinary HCG after 14 days, with the positive ones receiving continued luteal support; (4) two weeks later, if ultrasonography had shown a pregnancy sac and yolk sac, diagnosed participants as having a clinical pregnancy.

Groups. The research team divided participants into two groups: (1) participants diagnosed as having a clinical pregnancy after IVF-ET became the pregnancy group, and (2) participants who didn't become pregnant became the nonpregnancy group.

Ultrasonic detection. The research team performed ultrasound endometrial measurements using the Supersonic AixPlorer SWE ultrasound with a SE12-3 transvaginal probe (Aixplorer, Supersonic Imaging, Aix en Provence). The research team: (1) used the same settings for all participants, with the same surgeon operating on them and (2) performed the detection between 10 and 12 am on the day of the HCG injection.

Outcome measures. The research team compared the relationship between different types of endometrium and between types of "endometrium subendometrium blood flow" and pregnancy rates. The team also compared the differences in hemodynamic parameters and ER between the two groups.

The research team: (1) measured EMT, (2) determined endometrium types, (3) classified the intimal and subintimal blood flow using the Applebaum method,[11] and (4) determined the hemodynamic parameters of the endometrium and subendometrium. The team also measured: (1) the systolic blood flow velocity (VS), (2) diastolic blood flow velocity (VD), and (3) average blood flow velocity (VM) three times and recorded the average value.

Outcome Measures

EMT. The research team measured EMT in the uterus' longitudinal section.

Endometrium types. The types included: (1) Type A—a central hyperechoic line surrounded by two layers; (2) Type B—an isoechoic pattern and indistinct central hyperechoic line relative to the peripheral musculus and (3) Type C—a uniform, hyperechoic endometrium.

Intimal and subintimal blood flow. The types included: (1) Type 1—the blood vessels passed through the lateral, lower, intimal vocal cord but didn't enter the outer edge of the intimal hyperechoic area; (2) Type 2—the blood vessel passed through the endometrium's outer margin with a high echo; and (3) Type 3—the blood vessel

Hemodynamic parameters. The team obtained the Doppler spectrum in the dark zone at the junction of the endometrium and muscle layer in the uterus' sagittal section and the brightest spot of color in the blood flow.

Statistical Analysis

The research team used SPSS 19.0 for statistical analysis. The team: (1) expressed counting data as numbers and percentages (%) and used the Chi-square test for comparisons between groups, (2) expressed measurement data as means and standard deviations (SDs) and used the independent

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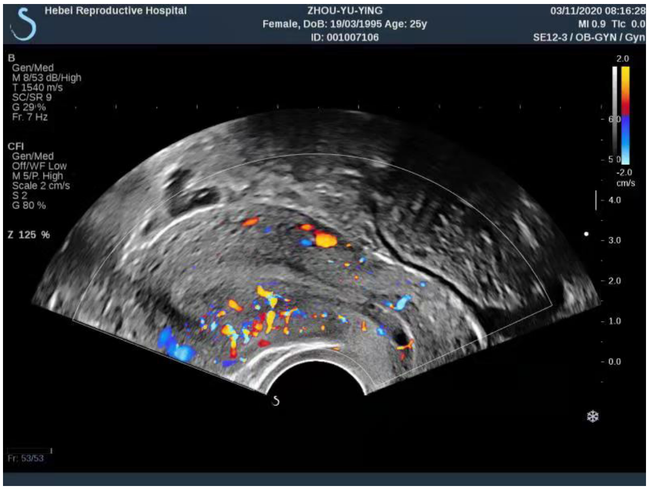
Table 2. Comparison of Uterine Conditions of the Groups (N = 841)

Conditions	Pregnancy Group n = 439 Mean ± SD n (%)	Nonpregnancy Group n = 402 Mean ± SD n (%)	*t* or χ^2	*P* value
Endometrial Thickness, cm	0.92 ± 0.17	0.92 ± 0.17	-0.170	.865
Endometrium Types			5.249	.072
A	250 (56.9)	200 (49.8)		
B	155 (35.3)	158 (39.3)		
C	34 (7.7)	44 (10.9)		
Endometrial blood flow types			12.710	.002[a]
1	15 (3.4)	23 (5.7)		
2	313 (71.3)	315 (78.4)		
3	111 (25.3)	64 (15.9)		
Uterine Position			0.504	.777
Anterior	262 (59.7)	243 (60.4)		
Horizontal	90 (20.5)	75 (18.7)		
Posterior	87 (19.8)	84 (20.9)		

[a]$P < .05$, indicating that the nonpregnancy group's mean age, number of embryos, number of high-quality embryos, and embryo levels were significantly lower than those of the pregnancy group.

Figure 1. Color Doppler Ultrasound Imaging of Endometrial Blood Flow Type 2



sample *t* test for comparisons, and (3) applied multivariate logistic regression analysis to determine the factors influencing the pregnancy outcomes of IVF-ET and drew an ROC curve of the pregnancy outcomes based on the relevant parameters. $P < .05$ indicates statistically significant results.

RESULTS

Participants

The study included 841 participants, 439 in the pregnancy group and 402 in the nonpregnancy group (Table 1). The pregnancy group had: (1) a mean age of 31.61 ± 4.42, (2) a mean body mass index (BMI) of 21.99 ± 1.13 kg/m2, (3) a mean infertility time of 4.27 ± 3.16 years, and (4) a mean FSH dosage of 5.39 IU/L. The nonpregnancy group had: (1) a mean age of 33.58 ± 5.66, (2) a mean body mass index (BMI) of 22.07 ± 2.03 kg/m2, (3) a mean infertility time of 4.54 ± 3.05 years, and (4) a mean FSH dosage of 5.51 ± 1.13 IU/L.

In the pregnancy group: (1) 165 participants had primary infertility (37.6%), and 274 had secondary infertility (62.4%); (2) the embryo transfer cycle was 1.56 ± 0.88; (3) the number of embryos was 1.88 ± 0.33; and (4) the number of high-quality embryos was 1.44 ± 0.72. In the nonpregnancy group: (1) 176 participants had primary infertility (43.8%), and 226 had secondary infertility (56.2%); (2) the embryo transfer cycle was 1.62 ± 0.85; (3) the number of embryos was 1.81 ± 0.40; and (4) the number of high-quality embryos was 1.24 ± 0.79.

In the pregnancy group, the embryo levels of 5 participants were level A (1.1%), 49 were level B (11.2%), and 385 were level C (87.7). In the non-pregnancy group the embryo levels of no participants were level A, 19 were level B (4.7%), and 383 were level C (95.3%).

At baseline after IVF-ET, the nonpregnancy group's mean age ($P < .001$), number of embryos ($P = .006$), number of high-quality embryos ($P < .001$), and embryo levels ($P < .001$) were significantly lower than those of the pregnancy group. No statistically significant differences existed in the other characteristics of the two groups (all $P > .05$).

Uterine Conditions

In the pregnancy group and nonpregnancy group, the EMT was 0.92 ± 0.17 cm and 0.92 ± 0.17 cm, respectively (Figure 1 and Table 2).

For the pregnancy group, the endometrium type of 250 participants was Type A (56.9%), 155 was Type B (35.3%), and 34 was Type C (7.7%). For the nonpregnancy group, the endometrium type of 200 participants was Type A (49.8%), 158 was Type B (39.3%), and 44 was Type C (10.9%).

For the pregnancy group, the endometrial blood flow type of 15 participants was Type 1 (3.4%), 313 was Type 2 (71.3%), and 111 was Type 3 (25.3%). For the nonpregnancy group, the endometrial blood flow type of 23 participants was Type 1 (5.7%), 315 was Type 2 (78.4%), and 64 was Type 3 (15.9%).

For the pregnancy group, the uterine position of 262 participants was anterior (59.7%), 90 was horizontal (20.5%), and 87 was posterior (19.8%). For the nonpregnancy group, the uterine position of 243 participants was anterior (60.4%), 75 was horizontal (18.7%), and 84 was posterior (20.9%).

The distribution of endometrial blood flow type was significantly different between two groups ($P = .002$). No statistically significant differences existed in EMT, endometrium types or uterine position between the groups (all $P > .05$).

EMT and Pregnancy Rates

For all thicknesses, the pregnancy rate increased from the <30 group to the 30-34 group and then decreased for all thicknesses between each group older than 30-34 (Table 3).

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Table 3. Pregnancy Rates of Participants in Different Age Groups by Endometrial Thickness (N = 841)

	All Groups		<8 mm Group		8-13 mm Group		≥ 14 mm Group	
Age, y	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)
<30	252	143 (56.7)	52	35 (67.3)	198	107 (54.0)	2	1 (50.0)
30-34	313	189 (60.4)	70	40 (57.1)	241	147 (61.0)	2	2 (100.0)
35-38	159	77 (48.4)	28	12 (42.9)	127	61 (48.0)	4	4 (100.0)
39-41	72	23 (31.9)	13	5 (38.5)	59	18 (30.5)	-	-
≥42	45	7 (15.6)	11	2 (18.2)	33	5 (15.2)	1	0 (0.0)
Total	841	439 (52.2)	174	94 (54.0)	658	338 (51.4)	9	7 (77.8)

Table 4. Pregnancy Rates of Participants With Different Endometrial Thicknesses by Age Group (N = 841)

	<30 Group		30-34 Group		35-38 Group		39-41 Group		≥42 Group	
Endometrial Thickness	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)
< 8mm	52	35 (67.3)	70	40 (57.1)	28	12 (42.9)	13	5 (38.5)	11	2 (18.2)
8-13 mm	198	107 (54.0)	241	147 (61.0)	127	61 (48.0)	59	18 (30.5)	33	5 (15.2)
≥ 14 mm	2	1 (50.0)	2	2 (100.0)	4	4 (100.0)	-	-	1	0 (0.0)
Total	252	143 (56.7)	313	189 (60.4)	159	77 (48.4)	72	23 (31.9)	45	7 (15.6)

Table 5. Implantation Rates of Participants in Different Age Groups by Endometrial Thickness (N = 841)

	All Groups		<8 mm Group		8-13 mm Group		≥ 14 mm Group	
Age, y	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)
<30	252	160 (63.5)	52	39 (75.0)	198	120 (60.6)	2	1 (50.0)
30-34	313	214 (68.4)	70	47 (67.1)	241	165 (68.5)	2	2 (100.0)
35-38	159	85 (53.5)	28	12 (42.9)	127	69 (54.3)	4	4 (100.0)
39-41	72	36 (50.0)	13	8 (61.5)	59	28 (47.5)	4	-
≥42	45	12 (26.7)	11	2 (18.2)	33	10 (30.3)	1	0 (0.0)
Total	841	507 (60.3)	174	108 (62.1)	658	392 (59.6)	9	7 (77.8)

Table 6. Implantation Rates of Participants With Different Endometrial Thicknesses by Age Group

	<30 Group		30-34 Group		35-38 Group		39-41 Group		≥42 Group	
Endometrial Thickness	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)
< 8mm	52	39 (75.0)	70	47 (67.1)	28	12 (42.9)	13	8 (61.5)	11	2 (18.2)
8-13 mm	198	120 (60.6)	241	165 (68.5)	127	69 (54.3)	59	28 (47.5)	33	10 (30.3)
≥ 14 mm	2	1 (50.0)	2	2 (100.0)	4	4 (100.0)	-	-	1	0 (0.0)
Total	252	160 (63.5)	313	214 (68.4)	159	85 (53.5)	72	36 (50.0)	45	12 (26.7)

Table 7. Pregnancy Rates of Participants in Different Age Groups by Endometrial Type (N = 841)

	All Groups		Type A Group		Type B Group		Type C Group	
Age, y	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)
<30	252	143 (56.7)	146	86 (58.9)	88	49 (55.7)	18	8 (44.4)
30-34	313	189 (60.4)	169	106 (62.7)	120	69 (57.5)	24	14 (58.3)
35-38	159	77 (48.4)	80	43 (53.8)	63	27 (42.9)	16	7 (43.8)
39-41	72	23 (31.9)	40	13 (32.5)	20	6 (30.0)	12	4 (33.3)
≥42	45	7 (15.6)	15	2 (13.3)	22	4 (18.2)	8	1 (12.5)
Total	841	439 (52.2)	450	250 (55.6)	313	155 (49.5)	78	34 (43.6)

No significant differences existed in pregnancy rates among participants with different thicknesses in any of the age groups ($P > .05$).

Significant differences existed in the pregnancy rates for the different age groups ($P < .05$).

EMT and Implantation Rates

For all thicknesses, the implantation rate increased from the <30 group to the 30-34 group and then decreased for all thicknesses between each group older than 30-34 (Table 5). No significant differences existed in implantation rates

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Table 8. Pregnancy Rates of Participants With Different Endometrial Types by Age Group

	<30 Group		30-34 Group		35-38 Group		39-41 Group		≥42 Group	
Endometrial Type	**Total n**	**Pregnancy Rate n (%)**	**Total n**	**Pregnancy Rate n (%)**	**Total n**	**Pregnancy Rate n (%)**	**Total n**	**Pregnancy Rate n (%)**	**Total n**	**Pregnancy Rate n (%)**
Type A	146	86 (58.9)	169	106 (62.7)	80	43 (53.8)	40	13 (32.5)	15	2 (13.3)
Type B	88	49 (55.7)	120	69 (57.5)	63	27 (42.9)	20	6 (30.0)	22	4 (18.2)
Type C	18	8 (44.4)	24	14 (58.3)	16	7 (43.8)	12	4 (33.3)	8	1 (12.5)
Total	252	143 (56.7)	313	189 (60.4)	159	77 (48.4)	72	23 (31.9)	45	7 (15.6)

Table 9. Implantation Rates of Participants in Different Age Groups by Endometrial Type (N=841)

	All Groups		Type A Group		Type B Group		Type C Group	
Age, y	**Total n**	**Implantation Rate n (%)**	**Total n**	**Implantation Rate n (%)**	**Total n**	**Implantation Rate n (%)**	**Total n**	**Implantation Rate n (%)**
<30	252	160 (63.5)	146	93 (63.7)	88	58 (65.9)	18	9 (50.0)
30-34	313	214 (68.4)	169	118 (69.8)	120	80 (66.7)	24	16 (66.7)
35-38	159	85 (53.5)	80	47 (58.8)	63	30 (47.6)	16	8 (50.0)
39-41	72	36 (50.0)	40	19 (47.5)	20	9 (45.0)	12	8 (66.7)
≥42	45	12 (26.7)	15	3 (20.0)	22	8 (36.4)	8	1 (12.5)
Total	841	507 (60.3)	450	280 (62.2)	313	185 (59.1)	78	42 (53.8)

Table 10. Implantation Rates of Participants With Different Endometrial Types by Age Group

	<30 Group		30-34 Group		35-38 Group		39-41 Group		≥42 Group	
Endometrial Type	**Total n**	**Implantation Rate n (%)**	**Total n**	**Implantation Rate n (%)**	**Total n**	**Implantation Rate n (%)**	**Total n**	**Implantation Rate n (%)**	**Total n**	**Implantation Rate n (%)**
Type A	146	93 (63.7)	169	118 (69.8)	80	47 (58.8)	40	19 (47.5)	15	3 (20.0)
Type B	88	58 (65.9)	120	80 (66.7)	63	30 (47.6)	20	9 (45.0)	22	8 (36.4)
Type C	18	9 (50.0)	24	16 (66.7)	16	8 (50.0)	12	8 (66.7)	8	1 (12.5)
Total	252	160 (63.5)	313	214 (68.4)	159	85 (53.5)	72	36 (50.0)	45	12 (26.7)

among participants with different thicknesses in any of the age groups ($P > .05$).

Significant differences existed in the implantation rates for the different age groups (Table 6).

Endometrial Types and Pregnancy Rates

For all endometrial types, the pregnancy rate increased from the <30 group to the 30-34 group and then decreased for all types between each group older than 30-34 (Table 7). No statistically significant differences existed in pregnancy rates among participants with different endometrial types in any of the age groups.

Table 8 shows that the Type A, Type B, and Type C groups' pregnancy rates were the highest for participants in the 30-34 age group, and statistically significant differences occurred among the different age groups ($P < .05$).

Endometrial Types and Implantation Rates

For all endometrial types, the implantation rate increased from the <30 group to the 30-34 group and then decreased for all types between each group older than 30-34 (Table 9). No statistically significant differences existed in pregnancy rates among participants with different endometrial types in any of the age groups.

Table 10 shows that the Type A, Type B, and Type C groups' implantation rates were the highest for participants in the 30-34 age group, and statistically significant differences occurred among the different age groups ($P < .05$).

Endometrial Blood Flow Type and Pregnancy Rates

For all endometrial blood flow types, the pregnancy rate increased from the <30 group to the 30-34 group and then decreased for all types between each group older than 30-34 (Table 11). No statistically significant differences existed in pregnancy rates among participants with different endometrial blood flow types in any of the age groups.

Table 12 shows that the Type 1, Type 2, and Type 3 groups' pregnancy rates were the highest for participants in the 30-34 age group. Statistically significant differences in pregnancy rates among the different age groups ($P < .05$).

Endometrial Blood Flow Type and Implantation Rates

For all endometrial blood flow types, the implantation rate increased from the <30 group to the 30-34 group and then decreased for all types between each group older than 30-34 (Table 13). No statistically significant differences existed in pregnancy rates among participants with different endometrial blood flow types in any of the age groups.

Table 14 shows that the Type 1, Type 2, and Type 3 groups' implantation rates were the highest for participants in the 30-34 age group. Statistically significant differences in implantation rates among the different age groups ($P < .05$).

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Table 11. Pregnancy Rates of Participants in Different Age Groups by Endometrial Blood Flow Types (N = 841)

	All Groups		Type 1 Group		Type 2 Group		Type 3 Group	
Age, y	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)
<30	252	143 (56.7)	6	3 (50.0)	193	108 (56.0)	53	32 (60.4)
30-34	313	189 (60.4)	7	5 (71.4)	238	135 (56.7)	68	49 (72.1)
35-38	159	77 (48.4)	8	4 (50.0)	117	52 (44.4)	34	21 (61.8)
39-41	72	23 (31.9)	8	2 (25.0)	47	13 (27.7)	17	8 (47.1)
≥42	45	7 (15.6)	9	1 (11.1)	33	5 (15.2)	3	1 (33.3)
Total	841	439 (52.2)	38	15 (39.5)	628	313 (49.8)	175	111 (63.4)

Table 12. Pregnancy Rates of Participants With Different Endometrial Blood Flow Types by Age Group

Endometrial Blood Flow Type	<30 Group		30-34 Group		35-38 Group		39-41 Group		≥42 Group	
	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)	Total n	Pregnancy Rate n (%)
Type 1	6	3 (50.0)	7	5 (71.4)	8	4 (50.0)	8	2 (25.0)	9	1 (11.1)
Type 2	193	108 (56.0)	238	135 (56.7)	117	52 (44.4)	47	13 (27.7)	33	5 (15.2)
Type 3	53	32 (60.4)	68	49 (72.1)	34	21 (61.8)	17	8 (47.1)	3	1 (33.3)
Total	252	143 (56.7)	313	189 (60.4)	159	77 (48.4)	72	23 (31.9)	45	7 (15.6)

Table 13. Implantation Rates of Participants in Different Age Groups by Endometrial Blood Flow Type (N=841)

	All Groups		Type 1 Group		Type 2 Group		Type 3 Group	
Age, y	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)
<30	252	160 (63.5)	6	3 (50.0)	193	120 (62.2)	53	37 (69.8)
30-34	313	214 (68.4)	7	6 (85.7)	238	154 (64.7)	68	54 (79.4)
35-38	159	85 (53.5)	8	5 (62.5)	117	59 (50.4)	34	21 (61.8)
39-41	72	36 (50.0)	8	5 (62.5)	47	23 (48.9)	17	8 (47.1)
≥42	45	12 (26.7)	9	3 (33.3)	33	8 (24.2)	1	1 (33.3)
Total	841	507 (60.3)	38	22 (57.9)	628	364 (58.0)	175	121 (69.1)

Table 14. Implantation Rates of Participants With Different Endometrial Blood Flow Types by Age Group

Endometrial Blood Flow Type	<30 Group		30-34 Group		35-38 Group		39-41 Group		≥42 Group	
	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)	Total n	Implantation Rate n (%)
Type 1	6	3 (50.0)	7	6 (85.7)	8	5 (62.5)	8	5 (62.5)	9	3 (33.3)
Type 2	193	120 (62.2)	238	154 (64.7)	117	59 (50.4)	47	23 (48.9)	33	8 (24.2)
Type 3	53	37 (69.8)	68	54 (79.4)	34	21 (61.8)	17	8 (47.1)	3	1 (33.3)
Total	252	160 (63.5)	313	214 (68.4)	159	85 (53.5)	72	36 (50.0)	45	12 (26.7)

Table 15. Area Under the ROC Curve

Test Variables	Area	Standard Error	Gradual Sig.	95%CI	
				Lower	Upper
Age	0.404	0.020	0.000*	0.336	0.443
Embryo level	0.462	0.020	0.056	0.423	0.501
High-quality embryo	0.566	0.020	0.001*	0.527	0.605
Endometrial blood flow types	0.554	0.020	0.007*	0.515	0.593

ROC Curve

Table 15 and Figure 2 area show that the under the ROC curve by age and embryo level were 0.404 (95%CI: 0.336-0.443), with $P = .000$, and 0.462 (95%CI: 0.423-0.501), with $P > .05$, respectively, so the two indexes appear to have no predictive value for clinical pregnancy. The area under the ROC curve for high-quality embryos was 0.566 (95%CI: 0.527-0.605), with $P = .001$, and for endometrial blood flow types 0.554 (95%CI: 0.515-0.593), with $P = .007$, suggesting that high-quality embryos and endometrial blood flow types may predict clinical pregnancy, but with low accuracy for predicting the clinical-pregnancy rate by a single indicator. The above results were presented in 15 and Figure 2.

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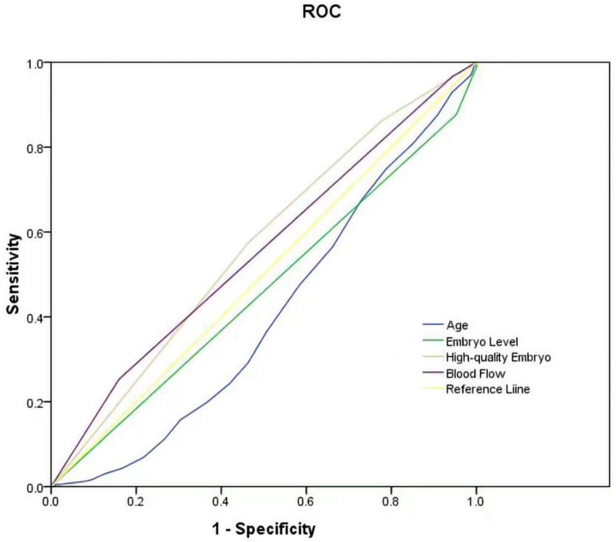
Figure 2. Receiver Operating Characteristic (ROC) Curves for Clinical Pregnancy



DISCUSSION

The current study found that the number of participants with an EMT of 8-13mm was the highest, followed by EMT<8mm, and the lowest number was in the EMT≥14mm group. Because the size of the EMT≥14mm was too small, the comparison between groups wasn't meaningful.

The current study found that the number of participants with the endometrial type of Type A was the highest, followed Type B, and the lowest number was in the Type C group. The implantation and pregnancy rates of Type A participants were higher than Type B and Type C patients.

The current study found that the number of participants with the endometrial blood flow type of Type 2 was the highest, followed by Type 3 and Type 1. The pregnancy and implantation rates were the highest in the 30-34 groups, with statistically significant differences in pregnancy and implantation rates among the different age groups ($P < .05$). The pregnancy and implantation rate of Type 3 were significantly higher than Type 2 and Type 1 ($P < .05$). The area under the ROC curve of endometrial blood flow types was 0.554 (95% CI: 0.515-0.593), with P with $P = .007$, indicating that endometrial blood flow types may have limited predictive value for clinical pregnancy.

At present, the field needs more studies with large sample sizes to confirm and identify more predictors of endometrial receptivity, s to further improve the success rate of embryo transfer in freeze-thaw cycles.

CONCLUSIONS

The pregnancy and implantation rates increased between the <30 and 30-34 age groups and them decreased between the age groups as age increased. EMT, endometrial type, and blood flow type can be valuable parameters in terms of predicting implantation and pregnancy rates of patients of different ages.

AUTHORS' DISCLOSURE STATEMENT

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