Uterine Artery and Endometrial Vascularity Doppler Indices and Pregnancy Outcome in ICSI

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Abstract

Background: Good blood flow within uterine arteries and endometrium is important for implantation this study was conducted to determine the role of Doppler indices in prediction of pregnancy outcome during evaluation of ICSI women .Material and Method: It was case control study. 60 infertile women were included in the study and prepared for IVF-ET/ICSI, . All the patients underwent controlled ovarian stimulation, and evaluated by Transvaginal ultrasound and measurements performed on day oocyte retrieval and on day embryo transfer. Assessment of endometrial thickness, pattern and grade of vascularity zones, peak systolic velocity (PSV), end diastolic velocity (EDV), systolic/diastolic ratio, resistance index (RI), and pulsatility index for both uterine arteries and endometrial vessles.

Result: 30 women are pregnant and 30 women, there was significant differences at a cut value of endometrial thickness of ≥ 8 mm between pregnant and non pregnant groups(27 (90 %) versus 20 (66.7 %) with 0.015 p value at day of oocyte retrieval and (27 (90 %) versus 20 (66.7 %) with P value of 0.28 at day of embryo transfer), pregnant women are limited to zone II and III with mainly zone III while non pregnant are mainly zone II. four cases has absent endometrial vascularity at day of embryo transfer, no one of them get pregnancy, there is significant difference in day of embryo transfer regarding endometrial RI being lower in pregnant. Significant differences in uterine PSV and high significant difference in uterine EDV at embryo transfer day.

Conclusion: Endometrial thickness of 8 mm., with vascularity zone III at day of oocyte retrieval and embryo transfer are significant for positive pregnancy outcome, absent endometrial and sub endometrial vascularity at day of embryo transfer predict poor outcome of pregnancy .

Keywords: *Doppler indices, uterine blood flow .endometrial vascularity.*

Introduction

In vitro Fertilization and Embryo Transfer (IVF-ET) were currently the most selective and readily available management method for treatment of infertility weather its explained or unexplained. In spite of development in this technique over the last forty years, success has been limited to 15-45 % as a result of implantation failure.(1) implantation of human embryo only occurs in a receptive uterus at a time of functional changes of the window of implantation, during the mid secretory phase in the menstrual cycle (19-23 days)(2), during that time profound molecular changes occurs in the stromal component create the state of receptivity(3), these changes include specialized natural killer cells recruitment, remodeling of vascular bed and decidualization of stromal fibroblast.(4)

This state of endometrial receptivity is a result although not well understood harmony between ovarian

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hormones, growth factors, cytokines, and adhesion molecules[5]. And it reflect the end resulting effect of cooperation of the hypothalamic pituitary ovarian axis in preparing endometrium for embryo implantation. The awareness of endometrial receptivity and the presence of window of implantation has been proposed for the first time by scholarly work of Hertig and RocK in 1956[6]. clinically Determination of receptive endometrial remains a challenge. In clinical practice the ultrasound has a great and important role in the evaluation and treatment of subfertile women. It is a non invasive efficient and cost-effective method for assessing female reproductive organs.[7]

Ultrasound assessment of endometrial morphology may reveal "readiness",state of endometrium by endometrial blood flow, pattern and thickness, all have been used as markers for endometrial receptivity and subsequent implantation and pregnancy in IVF.[8] Uterine impedance and perfusion has been linked to subsequent success of implantation[9] further more abnormal uterine artery velocimetry has been associated with unexplained sub-fertility, poorer uterine receptivity to implantation, and recurrent miscarriages.[10] Uterine blood flow is an important factor contributing to uterine receptivity[11] and can be studied by means of two-dimensional (2D)-power color doppler (PCD) ultrasound.[12] in this study ultrasound assessment of anatomical changes include,thickness, pattern and grade of vascularity in addition to assessment physiological 2 D vascular flow indices includes both endometrial and uterine vessels both at day of oocyte retrieval and day of embryo transfer, in ICSI cycle with antagonist down regulation, to determine which time of ultrasound assessment is more predictive for receptivity and pregnancy outcome .

Subjects material and method: This is a case control study includes 60 patient, under the age of 39 years have undergone ICSI cycle because of different causes of sub fertility in the high institute of infertility and assisted reproductive technique in Al-Nahrain university in Baghdad between September 2018-february 2019, outcome all patient has written informed consent about their acceptance for participating in this study .

Method

Baseline evaluation include medical history,clinical examination and baseline hormonal evaluation and basal antral follicle count by ultrasound at cycle day 2 with gonadotrohin started at a dose determined according to the age and previous cycle response, on cycle day 5 assessment for number and follicular growth rate,till three follicles reach 18 mm at that time trigger of final maturation, at that day just before oocyte retrieval time ultrasound evaluation for endometrial receptivity parameters by 2 D ultrasound using transvaginal probe (5-9 MHz, Voluson P8 GE health care ultrasound machine,) after emptying urinary bladder,by US asses endometrial thickness (the thickest distance between the outer hyper echogenic lines of endometrium .Endometrial pattern, indicating echogenicity of the endometrium relative to the nearby myometrium visualized on a longitudinal ultrasound scan,the endometrium achieves the triple line appearance during the proliferative phase of the menstrual cycle while the endometrium acquires a hyper echogenic appearance(at the secretory phase of the menstrual cycle, which is due to stromal oedema .After activation of color Doppler the endometrial vascularity zones are assessed,then pulsed Doppler is activated to measure the indices which includes: peak systolic velocity,end diastolic velocity,systolic to diastolic ratio, resistance index, pulsatility index for both uterine arteries and sub-endometrial and uterine arteries. All these parameter are calculated electronically

Results

Demographic Factors: In this case control study,during ICSI cycles 30 patients with positive clinical pregnancy outcome and 30 patients with negative clinical pregnancy outcome,there were no difference in the baseline demographic parameters .There was no significant difference in mean age BMI and type of infertility,primary or secondary between pregnant women and non pregnant women .

Women were also categorized according to causes of infertility as male factor, female factor, combined and unexplained; the difference in the distribution of women according to cause of infertility was not significant (P = 0.129), as shown in figure 1.

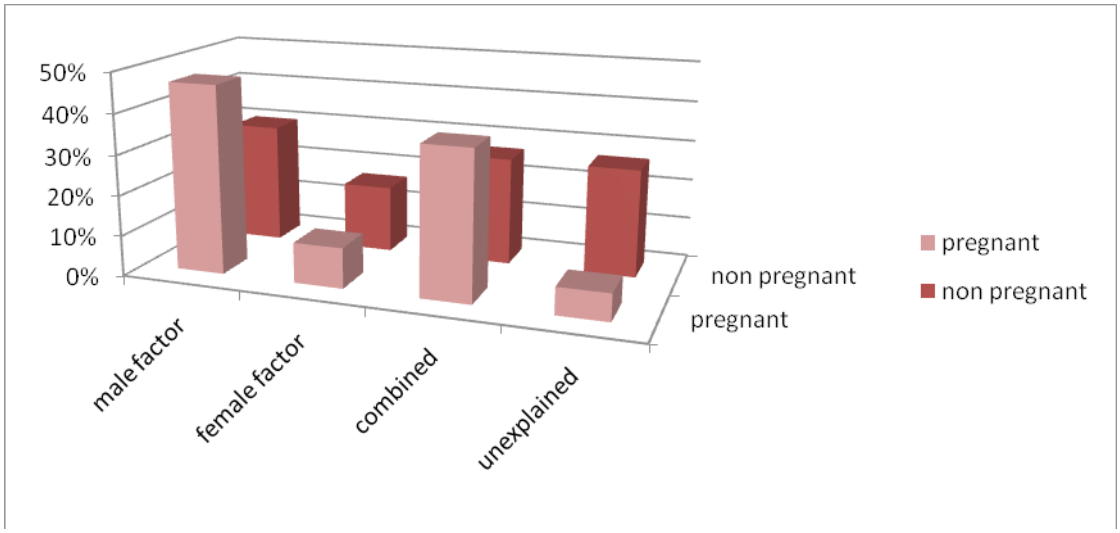

Figure 1. Distribution of causes of sub infertility in pregnant and non pregnant groups

Ultrasound assessment for endometrial receptivity at day of oocyte retrieval: There was no significant difference in mean Endometrial thickness between pregnant and non pregnant ladies However, considering a cutoff value of 8 mm revealed that the frequency of pregnant ladies with an endometrial thickness ≥ 8 mm was significantly higher than non pregnant ladies with an endometrial thickness ≥ 8 mm, there no was significant difference in the frequency distribution of subfertile women according to endometrial pattern, trilaminar versus echogenic, between pregnant and non pregnant groups .There was significant difference in the frequency distribution of subfertile women according to vascular pattern, zone I versus II versus III versus IV, between pregnant and non pregnant groups in such a way that zone I was limited to non pregnant women, Zone II was less frequent and Zone III was more frequent in pregnant ladies, table 1.

Table 1: Endometrial parameters with vascularity zone.

Character	Oocyte retrieval pregnant	Oocyte retrieval Non pregnant	oocyte retrieval P-value	Embryo transfer Pregnant	Embryo transfer Non pregnant	Embryo transfer P-value
mean Endometrial Thickness	9.39±1.39	8.98±2.61	0.451 NS	10.27 ±2.04	9.81 ±2.60	0.446 † NS
Endometrial thickness <8	3 (10.0 %)	11 (36.7 %)	0.015 S	3 (10.0 %)	10 (33.3 %)	0.028 ¥ S
Endometrial thickness ≥8mm	27 (90.0 %)	19 (63.3 %)		27 (90.0 %)	20 (66.7 %)	
Endom. Pattern trilaminar echogenic	28 (93.3 %) 2 (6.7 %)	27 (90.0 %) 3 (10.0 %)	1.000 NS	0 (0.0 %) 30 (100.0 %)	5 (16.7 %) 25 (83.3 %)	0.052 € NS
Vascularity grade						
absent	0	0		0 (0.0 %)	4 (13.3 %)	0.003 ¥ HS
ZI	0(0.0%)	2(6.7 %)	0.014 ¥ S	0	0	
ZII	14 (46.7 %)	22 (73.3 %)		10 (33.3 %)	18 (7 0.0 %)	
ZIII	16 (53.3 %)	5 (16.7 %)		20 (66.7 %)	8 (26.7 %)	
ZIV	0(0.0 %)	1(3.3%)		0	0	

There was also no significant difference in mean Endometrial Peak systolic velocity (PS), mean Endometrial End diastolicvelocity (ED) ., mean Endometrial S/D ratio between pregnant and non pregnant ladies. Table 2. There was significant difference in mean Endometrial Resistance index (RI) being lower in pregnant ladies, No significant difference in mean Endometrial Pulsatility Index (PI) between pregnant and non pregnant ladies . No significant difference in mean Uterine Peak systolic velocity (PS), mean Uterine end diastolic velocity (ED) .mean uterine S/D ratio, Uterine Resistance index (RI),mean Uterine Pulsatility Index (PI) between pregnant and non pregnant ladies. Table 2.

Table 2. Pulsed power Doppler of endometrial and uterine vascularity at day of oocyte retrieval

Pulsed power Doppler of endometrial and uterine vascularity at day of oocyte retrieval

Characteristics	Pregnant	Non-pregnant	P
E Peak systolic velocity (PS)	6.09±1.56	6.23±1.23	0.700† NS
E End diastolic velocity (ED)	3.09±0.67	2.70±1.04	0.085† NS
E S/D ratio	2.24±0.62	2.74±1.30	0.065† NS
E. Resistance index (RI)	0.51±0.11	0.60±0.16	0.013† S
E. Pulsatility Index (PI)	0.90±0.33	0.94±0.36	0.683† NS
U Peak systolic velocity (PS)	37.92±11.78	31.77±14.69	0.079† NS
U End diastolic velocity (ED)	6.76±3.58	5.51±3.70	0.189† NS
U S/D ratio	6.16±2.06	7.38±6.16	0.310† NS
U Resistance index (RI)	0.82±0.06	0.83±0.09	0.620† NS
U Pulsatility Index (PI)	1.92±0.49	2.19±0.55	0.052† NS

Comparison of subfertile women characteristics at day of embryo transfer between pregnant and pregnant ladies: There was also no significant difference in mean Endometrial Peak systolic velocity (PS) (P = 0.065),and mean Endometrial End diastolic velocity (ED) between pregnant and non pregnant ladies (P = 0.660).

Moreover, there was significant difference in mean Endometrial S/D ratio between pregnant and non pregnant ladies (P = 0.032), Table 3.

Added to that, there was highly significant difference in mean Endometrial Resistance index (RI) between pregnant and non pregnant ladies (P = 0.037). Table 3 .Furthermore, there was highly significant difference in mean Endometrial Pulsatility Index (PI) between pregnant and non pregnant ladies (P = 0.005). Table 3. In addition, there was highly significant difference in mean Uterine Peak systolic velocity (PS) (P = 0.004). There was also significant difference in mean Uterine End diastolic velocity (ED) between pregnant and non pregnant ladies (P = 0.048. Table 3.There was also no significant difference in mean Uterine S/D ratio .No significant difference in mean Uterine Resistance index (RI) (P = 0.731), No significant difference in mean Uterine Pulsatility Index (PI) between pregnant and non pregnant ladies (P = 0.924 table 3.

Table 3. Pulsed power Doppler of endometrial and uterine vascularity at day of embryo transfer.

Pulsed power Doppler of endometrial and uterine vascularity at day of embryo transfer.

Characteristics	Pregnant (n=30)	Non pregnant (n=30)	P
E Peak systolic velocity (PS)	8.04±2.06	6.57±3.77	0.065† NS
E End diastolic velocity (ED)	2.99±1.31	2.81±1.84	0.660† NS
E S/D ratio	3.03±1.01	2.31±1.34	0.023† S
E. Resistance index (RI)	0.63±0.12	0.52±0.25	0.037† S
E. Pulsatility Index (PI)	1.09±0.26	0.81±0.45	0.005† HS
U Peak systolic velocity (PS)	43.73±9.04	34.00±15.18	0.004† HS
U End diastolic velocity (ED)	7.29±2.93	5.89±2.42	0.048† S
U S/D ratio	6.68±2.66	5.67±1.82	0.093† NS
U Resistance index (RI)	0.82±0.05	0.82±0.05	0.731† NS
U Pulsatility Index (PI)	2.21±0.48	2.23±0.57	0.924† NS

Discussion

The endometrial receptivity has long been linked to successful implantation[6], the endometrium is the key factor in reproduction,and many method have been used for evaluation other than ultrasound,which in non invasive and effective in monitoring controlled ovarian hyperstimulation and has many different studies with different predictors at different cycles days.

In our study, pregnant women had higher mean endometrial thickness than non pregnant at day of oocyte retrieval although this was not statistically significant .this goes with many studies which found no significant difference in the mean endometrial thickness between pregnant and non pregnant women at that day such as schild et al 2001[13] and even a study by Kumbak et al. 2009[14]. By using a cut off value of 8 mm and more,in the current study,there was significant differences with higher number of pregnant women than non pregnant with significant effect of endometrium of 8 mm and more,on pregnancy outcome, similar to observational study by Tao Zhanget al. 2018[15] how found a higher pregnancy rate with higher endometrial thickness . At day of embryo transfer our study at a cut of 8 mm and more give significant difference between pregnant and non pregnant groups as in a study by, Kovacs et al. [16]. On the other hand there was no significant difference with higher thickness in pregnant group, this is similar to other studies like that of kinay et al 2010[17], Kovachev et al. at 2005[18] suggest that assessment of endometrial volume is better in prediction of pregnancy outcome at day of embryo transfer . This controversy of endometrial thickness as predictor of pregnancy outcome is contrasted with a well known role at day of hCG administration explained in many studies as by Richter et al. 2007[19], Traub et al. 2009 [20], chen et al. 2010[21], Yu We et al. 2014 [22] and Yuan et al. 2016 [23] .

Triple line appearance was detected in all the studied pregnant women,while most pregnant cases shows ecchogenic endometrium,these detected differences were statistically not significant similar result obtained from a study, by Bassil et al. 2001 [24] while a study by Jarvela et al. 2005[25] shows statistically significant.

Vascularity grade shows significant relation in prediction of pregnancy in our study as in many other at day of oocyte studies as Khan et al. 2016 [26], Endometrial and uterine vascularity indices at day of oocyte retrieval has non-significant difference regarding pregnancy rate between pregnant and non-pregnant group(Bassilet

al. 2001 and Yuval et al. 1999)[13,27] only in case of resistance index,as a lower mean resistance indices were found in pregnant group which was statistically significant,in a study by Elham Pourmatroud et al.[28].

Conclusion

In our study,endometrial thickness of 8 mm and triple line appearance,s vascularity grade of III is correlated with good pregnancy outcome and absence of endometrial vascularity has a poor pregnancy outcome

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq.

Conflict of Interest: Non

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