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TRANSVAGINAL DOPPLER ASSESSMENT OF OVARIAN AND ENDOMETRIAL BLOOD FLOW DURING OVULATION

By

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ABSTRACT

Background: Infertility is customarily defined as the inability to conceive after 1 year of regular unprotected intercourse. Assessment of the pelvis is greatly facilitated by the use of color Doppler imaging, which allows the simultaneous display of anatomic (gray scale) and flow (color) information. Quick and reproducible blood flow measurements are possible with transvaginal color Doppler.

Objective: To assess the uterine and ovarian perfusion during ovulation assessed by transvaginal color Doppler.

Patients and methods: Patients enrolled in this study were 180, which was done at October 6 University hospital during the period between September 2019 to September 2020, between 20 - 30 years old, with a previous duration of infertility ranging between 1 - 5 years and with BMI lying between 20 - 25. The patients were allocated to four groups: (group II) receiving clomiphene citrate (CC) induction alone, (group III) receiving human menopausal gonadotrophin (HMG), (group IV) receiving CC with HMG and (group I) control group receiving no medication.

Results: The deleterious effects of CC induction on endometrial thickness and pattern were clear especially in the (group II) that showed the least ratio of trilaminar endometrium among the four groups. The study showed the apparent reversing power of both spoteneous and HMG on endometrial thickness and pattern, although patients of the (Group IV) showed the highest ratio of trilaminar endometrium among the four groups. The mean day of appearance of dominant follicle was not significantly different among the 4 groups. However, it was slightly lower in the group that received CC + HMG. The three groups that received induction showed a statistically significant higher number of dominant follicles when compared with the control group, and the group that received CC+HMG showed the largest number of dominant follicles and largest diameter of the dominant follicles.

Conclusion: Use of combined transvaginal ultrasound together with color Doppler indices gave the best detection rate of ovulation than any of them alone.

Keywords: Infertility, Transvaginal Doppler, Ovarian, Endometrial Blood Flow during Ovulation.

INTRODUCTION

Infertility is defined as failure to conceive after one year of practicing sexual intercourse without any contraceptive measures. Primary infertility means that pregnancy has never occurred. While, secondary infertility means that the couple had a previous conception (irrespective of its outcome), but is unable to conceive again after one year of trying *(Biswas et al., 2016)*.

Clomiphene citrate (CC) is a selective estrogen receptor modu-lator (SERM) that binds to the estrogen receptors at multiple sites throughout the reproductive tract, and can act as an estrogen agonist or as an antagonist. Gonadotrophins are glycoprotein hormones that can be extracted from urine of postmenopausal women or can be manufactured by recombinant technology. They stimulate follicular growth by acting directly on ovarian follicle-stimulating hormone (FSH) receptors, and have no anti-estrogenic effect on cervical mucus or endometrium like clomiphene *(Peeraer et al., 2015).*

Adequate perfusion to the endometrium is essential requirement for implantation of the embryo and therefore assessment of endometrial blood flow using color Doppler ultrasound is believed to be useful in assessing endometrial receptivity *(Rai et al., 2017).* A healthy endometrium is essential for reception of the fertil-ized blastocyst. An adequate endometrial blood supply is a crucial requirement for implantation *(Zeng et al., 2013).*

Trans-vaginal color Doppler ultrasonography is a non-invasive and efficient method for visualizing small vessels and study of blood flow changes *(Qiu et al., 2016).* Doppler ultrasound has been used for several years to study the pattern of blood flow in fetal and maternal vessels. Color Doppler imaging had been used to diagnose various gynaecological disorders. Transvaginal color flow Doppler gives us an accurate tool to study the female reproductive system *(Sinha et al., 2017).*

Transvaginal color Doppler imaging facilitates the detection of small vessels in the utero-ovarian circulation and measurement of impedance to flow in this vascular tree *(Sinha et al., 2017).* Transvaginal sonography (TVS) can be safely used as an initial investigation in the management of abnormal uterine bleeding as it is a non-invasive procedure for the detection of endometrial pathology. The incidence of detection of an abnormal pathology by TVS is high when focal lesions as fibroids or polyps are concerned *(Noyes et al., 2010).*

The aim of this study was to assess the uterine and ovarian perfusion during ovulation assessed by transvaginal color Doppler.

PATIENTS AND METHODS

This was a prospective randomized control study which done at October 6 University hospital during the period between September 2019 to September 2020, and the study included 180 patients.

Women were divided into 4 groups:

Group (I) (90 women) control group with normal menstrual cycles. They were selected according to clinical and ultrasonographic findings of normal uterus and ovaries with documented ovulation and menstrual cycle length of 21-35 days for at least the previous 3 cycles.

Group (II) (30 women) were prescribed clomiphene citrate (clomid tablets, 50 mg, Aventis co, Cairo) administered orally, starting on the third day of the menstrual cycle. Treatment began with a 50 mg tablet daily for 5 consecutive days, increasing by 50 mg in subsequent cycles

until ovulation is induced for at least 3 Consecutive cycles.

Group (III): (30 women) were prescribed human meoupasal gonadotrophin (EPIGONAL, epico Co, Cairo) containing (fsh +lh) 75 IU. It was taken in the form of intramuscular injection format at least 3 Consecutive cycles.

Group (IV): (30 women) were prescribed clomiphene citrate (clomid) combined with human menopausal gonadotropin (EPIGONAL ampule, Epico Co, Cairo) containing 75 IU FSH+75 IU LH. It was taken in the form of intramuscular injection, administered daily from day 3 to day 7 of menstrual cycle in a daily dose of 2 ampoules for at least 3 Consecutive cycles.

Inclusion Criteria: Age between 18-40 years old, unexplained infertility, and no hormonal contraception.

Exclusion Criteria: Infertility due to ovarian factor, infertility due to tubal disease, infertility due to uterine or cervical cause, infertility due to male factor, pregnant woman, and patient who refuse to participate in the study.

Baseline vaginal ultrasound at the start of the cycle was to provide information on uterine and ovarian morphology and to delineate pelvic structures.

Transvaginal ultrasound folliculometry: Monitoring was started on the 10th day of the cycle on an every other day basis after we started induction of ovulation by different drug protocols as mentioned above. The woman was placed in the supine position with flexed legs and an empty bladder. The vaginal probe was covered with coupling gel and introduced into one of the digits of a sterile surgical glove that was lubricated with coupling gel, vaginal probe (Sonoscape, SSI 6000, 7.5 MHz, China). Using the B-mode transvaginal sonography, morphology of the uterus, endometrial thickness and ovaries were explored (folliculometry). The dominant follicle was measured in three planes: after obtaining the roundest possible image using B-mode gray-scale transvaginal ultrasound, in two perpendicular dimensions at the center; cranio-caudal and transverse. All measurements were expressed in mm. The mean follicular diameter was then calculated by taking the mean of three serial measurements of the three follicular diameters. The monitoring was started on the 10th day of the cycle on an every other day basis till the dominant follicle reached 14 mm diameter when daily follow up was then performed. Human chorionic gonadotropin injection 10,000 IU IM (Pregnyl Ampoule 5000 IU, Nile Co, Cairo) was given to the patient when the dominant follicle reached 18mm in diameter. At that time, the endometrium was evaluated as regards both endometrial thickness and pattern.

Color Doppler ultrasound was done using the transvaginal transducer with pulsed and color Doppler. The Doppler studies were better done at the same time every day as circadian rhythm is seen in uterine artery flow in periovulatory phase. The pulsatility index (PI) and resistance index (RI) of the uterine and ovarian arteries were calculated electronically when similar consecutive waveforms of good quality are obtained. Doppler flow parameters of uterine and ovarian vessels were then measured. Flow waveforms were obtained from the ascending main

branch of uterine artery on the right and left side of the cervix in a longitudinal plane before it entered the uterus.

The head of the transducer was directed into the lateral fornix of the vaginal vault and rotated 90 degrees. Therefore, a coronal section could be obtained and we were able to scan the ovaries. Lateral to and below the ovaries, a shape of a longitudinal vessel could be identified, the internal iliac artery. Thereafter, color Doppler equipment was added for monitoring ovarian blood flow on the dominant side. 10,000 IU of HCG was given to the patient IM when the dominant follicle reached 18mm in diameter.

All patients were advised to have a sexual intercourse 36 & 48 hours after the HCG injection to detect pregnancy outcome.

Statistical analysis:

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). For statistical analysis of categorical data, the Fisher exact test or the Chi2 test was used. Continuous data were analyzed with the unpaired (two sample) student's t test where appropriate. A probability value (P value) less than or equals 0.05 was considered significant. Accuracy was represented using the terms sensitivity, specificity, +ve predictive value and –ve predictive value.

RESULTS

A total of 180 infertile patients were included in the study, 90 of them are infertile with normal semen analysis of the husband, free HSG, normal size and shape of the pelvic organs assessed by transvaginal ultrasound and 90 patients with no history of fertility problem used as control group.

There was a statistically significant difference between group (I) and the other three groups concerning the mean age of the patients who participated in the study, but; fortunately this significant difference is in favor of the benefit of using clomid for super induction as the control group has the youngest mean age of the four groups so they have the best probability of regular and proper ovulation when compared to the older mean age of the rest of the groups i.e they have a better chance of ovulation than patients receiving treatment. At the same time, the P value for the other groups together i.e P (1#2) =1.0, P (1#3) =0,729, P (2#3) =0,746 was statistically non-significant which means that there is no special preference of patients enrolled.

Concerning the body mass index (BMI) of the patients, the only statistically significant difference was between group (I) and group (IV); it was noted that the higher mean BMI of patients in group (IV) compared to the lower one of group (I) gave them better chance of ovulation success. At the same time, there was no significant difference between the other groups which gave them equal chances to respond to induction of ovulation. There was no statistically significant difference concerning the duration of infertility

among different groups and this indicates that there is no special preference of one of groups than the others.

Concerning the endometrial thickness, there was a statistically significant difference between group B1 and B2 (P =0.001) and, between group 1 and B 3 (P =0.006) and between group B1 and A (P =0.006). This indicates that induction of ovulation with the use of CC seriously affects the endometrial thickness and also indicates that the use of FSH or HMG can partially reverse this effect. However, the P value for group B2 and B3 (P =0.547) was statistically insignificant which indicates non superiority of either mode of treatment upon the other **(Table 1)**.

Table (1): The age, BMI, duration of infertility and endometrial thickness of the study groups

Parameters	Groups	Mean ± SD	P value
Age	**Group I: (Control)**	24.42 ± 2.59	
	Group II: (on clomid)	26.2 ± 2.5	P(1#4)=**0.009**
	Group III: (on HMG)	26.2 ± 2.86	P(2#4)=**0.014**
	Group IV: (on clomid + HMG)	25.9 ± 2.7	P(3#4)=**0.027**
BMI	**Group I: (Control)**	22.75 ± 1.45	
	Group II: (on clomid)	23.75 ± 1.33	P(1#4)=;0.101 P(1#2)=0.807
	Group III: (on HMG)	23.65 ± 1.79	P(2#4)=0.075; P(2#3)=0.717
	Group IV: (on clomid + HMG)	24.85 ± 1.63	P(3#4)= 0**.023**; P(3#1)=0.479
Duration of infertility	**Group I: (Control)**		
	Group II: (on clomid)	4.12 ± 1.14	P(1#2)=0.735
	Group III: (on HMG)	4.02 ± 1.13	P(2#3)=0.707
	Group IV: (on clomid + HMG)	3.01 ± 1.25	P(3#1)=0.957
Endometrial thickness	**Group I: (Control)**	10.27 ± 1.58	
	Group II: (on clomid)	9.17 ± 1.38	P(1#4)=**0.006**; P(1#2)=**0.001**
	Group III: (on HMG)	10.37 ± 1.22	P(2#4)=0.785; P(2#3)=0.547
	Group IV: (on clomid + HMG)	10.17 ± 1.33	P(3#4)=0.792; P(3#1)=**0.006**

S.D = Standard deviation,

Although the mean day of appearance of dominant follicle was slightly lower in patients receiving HMG than the rest groups; which is probably due to increased blood flow to the pelvic region and subsequently to the ovaries; yet there was no statistically significant difference that can point to the value of using HMG to achieve an earlier ovulation day in different protocols of ovulation induction.

As regards the number of dominant follicles in patients treated by clomid, the mean was 1.83 ± 0.59 SD, while in patients treated by HMG it was 2.10 ± 0.67 SD, and this showed a highly statistically significant difference (P value= 0.001). Also, there was a statistically significant difference between groups II and III (P value= 0.005), between groups II and I (P value= 0.006), between groups III and IV (P value= 0.017) and between groups IV and I (P value= 0.002). However, the greatest number of dominant follicles was obtained in patients treated with clomid+HMG.

As regards the diameter of dominant follicles in patients treated by clomid, the mean was 18.05±0.83 SD, while in patients treated by clomid + HMG it was 19.09 ± 0.67 SD, and this showed a highly statistically significant difference (P value= 0.001). Also, there was a statistically significant difference between groups II and III (P value= 0.005), between groups II and IV (P value= 0.006) and between groups III and IV (P value= 0.017). However, there was no statistically significant difference between groups II and I (P value= 0.444). The largest diameter of dominant follicles was obtained in patients treated with clomid +HMG **(Table 2)**.

Table (2): The day of appearance, mean number and diameter of dominant follicle

Parameters	Groups	Mean ± SD	P value
Day of appearance	**Group II: (clomid)**	13.53 ± 1.55	P(1#4)=0.550; P(1#2)=0.925
	Group III: (HMG)	13.57 ± 1.17	P(2#4)=0.559; P(2#3)=0.674
	Group IV: (clomid + HMG)	13.43 ± 1.28	P(3#4)=0.350; P(3#1)=0.786
	Group I: (Control)	13.77 ± 1.45	
Mean number	**Group II: (clomid)**	1.83 ± 0.59	P(1#4)=**0.006**; P(1#2)=**0.005**
	Group III: (HMG)	2.10 ± 0.67	P(2#4)=**0.004** P(2#3)=**0.017**
	Group IV: (clomid + HMG)	2.30 ± 0.65	P(3#4)=**0.002**; P(3#1)=**0.001**
	Group I: (Control)	1.00±0.02	
Diameter	**Group II: (clomid)**	18.05±0.83	P(1#4)=**0.006**; P(1#2)=**0.005**
	Group III: (HMG)	19.01 ± 1.56	P(2#4)=**0.025** P(2#3)=**0.017**
	Group IV: (clomid + HMG)	19.09 ± 0.67	P(3#4)=0.444; P(3#1)=**0.001**
	Group I: (Control)	18.01 ± 0.84	

S.D = Standard deviation.

Regarding the pulsatility index (PI) of the uterine artery, a statistically significant difference was obtained when we compared the pulsatility indices of different groups with each other. First, comparing the PI of groups II and I (P value=0.004) showed a significant increase in the PI of group II which indicates the deleterious effect of CC induction of ovulation on the uterine blood flow. And more importantly, comparing the other groups together showed that group IV had the lowest PI among all groups which indicates sure correction of deleterious effects of CC on uterine blood flow. In addition, although both groups III and IV showed improvement of the PI with the addition of HMG, respectively, yet the upper hand and the best improvement remains related to the use of HMG rather than Clomid. It is the effect CC induced changes in uterine pulsatility index more or less to be close to that of the control group or slightly increased. A statistically significant difference was obtained when we compared the pulsatility indices of groups II and III (P value=0.003), groups III and IV (P value=0.001), groups II and IV (P value=0.005) and groups I and IV (P value=0.003).

There was no statistically significant difference between the different groups concerning the RI of the uterine artery although the lowest mean RI 0.65 ± 0.02 SD remained for those patients who used HMG indicating better blood flow to uterine artery.

A statistically significant difference was obtained when we compared the pulsatility indices of the ovarian arteries of different groups with each other. First, comparing the PI of groups II and I (P value=0.001) showed a significant increase in the PI of group II indicates the deleterious effect of CC induction of ovulation on the ovarian blood flow. And more importantly, comparing the other groups together showed that group III had the lowest PI among all groups which indicates correction of deleterious effects of CC on ovarian blood flow. In addition, although both groups II and IV showed improvement of the PI with the addition of HMG, yet the upper hand and the best improvement remains related to the use of HMG than use of clomid alone.

As regards the resistance index (RI) of the ovarian artery, there was no statistically significant difference between the different groups except concerning the statistically significant difference which was obtained when we compared the resistance index between group IV and group I (P value=0.002). The lowest mean RI of the ovarian artery 0.43 ± 0.03 SD remained for those patients who used HMG indicating better blood flow to the ovarian artery **(Table 3)**.

Table (3): The pulsatility index, resistance index of the uterine and ovarian artery.

Parameters	Groups	Mean ± SD	P value
Pulsatility index of the uterine artery	**Group II: (clomid)**	2.57 ± 0.05	P(1#4)=**0.004;** P(1#2)=**0.003**
	Group III: (HMG)	2.29 ± 0.07	P(2#4)=0.212; P(2#3)= **0.001**
	Group IV: (clomid + HMG)	2.13 ± 0.03	P(3#4)=**0.003**; P(3#1)=**0.005**
	Group I: (Control)	2.24 ± 0.07	
Resistance index of the uterine artery	**Group II: (clomid)**	0.64 ± 0.03	P(1#4)=0.282; P(1#2)=0.522
	Group III: (HMG)	0.65 ± 0.01	P(2#4)=0.635; P(2#3)= 0.242
	Group IV: (clomid + HMG)	0.63 ± 0.02	P(3#4)=0.095; P(3#1)=0.699
	Group I: (Control)	0.65 ± 0.02	
Pulsatility index of the ovarian artery	**Group II: (clomid)**	1.06 ± 0.1	P(1#4)=**0.001;** P(1#2)=0.124
	Group III: (HMG)	0.91 ± 0.1	P(2#4)=0.199; P(2#3)= 0.114
	Group IV: (clomid + HMG)	0.96 ± 0.13	P(3#4)=0.130; P(3#1)=0.054
	Group I: (Control)	1.03 ± 0.13	
Resistance index of the ovarian artery	**Group II: (clomid)**	0.49 ± 0.8	P(1#4)=0.273; P(1#2)=0.497
	Group III: (HMG)	0.51 ± 0.07	P(2#4)=0.612; P(2#3)= 0.234
	Group IV: (clomid + HMG)	0.43 ± 0.03	P(3#4)=**0.002**; P(3#1)=0.683
	Group I: (Control)	0.49 ± 0.07	

Table (4): The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of transvaginal sonography in detection of ovulation at cut off value of 18 mm follicular diameter

Cut off value of follicular diameter in mm	Sensitivity	Specificity	(+)ve PV	(-)ve PV	Accuracy
18 mm	39.4%	28.6%	72.2%	9.1%	37.5%

As regards using the 4 Doppler indices used in detection of ovulation, they gave better results regarding the sensitivity, specificity, positive predictive value, negative predictive value and accuracy than using any one of them alone or transvaginal ultrasound alone as the figures were 62.9%, 83.3%, 98.2%, 44.5%, 65% respectively **(Table 5)**.

Table (5): The overall sensitivity, specificity, positive predictive value, negative predictive value and accuracy of the 4Doppler indices alone used in detection of ovulation

Sensitivity	62.9%
Specificity	83.3%
Positive predictive value	98.2%
Negative predictive value	44.5%
Accuracy	65%

The best results were obtained when we used combined TVS and the 4 Doppler indices in detection of ovulation as the best findings regarding the sensitivity, specificity, positive predictive value, negative predictive value and accuracy were evident than using any one of them alone or transvaginal ultrasound alone as the figures were 69.5%, 88.9%, 95.4%, 55.6%, 77% respectively **(Table 6)**.

Table (6): The overall sensitivity, specificity, positive predictive value, negative predictive value and accuracy of combined TVS and the 4Doppler indices used in the study in detection of ovulation

Sensitivity	69.5%
Specificity	88.9%
Positive predictive value	95.4%
Negative predictive value	55.6%
Accuracy	77%

DISCUSSION

In the present work, we studied the role of vaginal ultrasonography and color Doppler in examination of the endometrium, uterine and ovarian vasculature in infertile patients treated with clomiphene citrate alone or with addition of human menopausal gonadotrophin (HMG) to evaluate their effects on different endometrial parameters, comparing them with other patients not receiving induction and taken as control. Color Doppler studies were performed when vaginal ultrasonography demonstrate optimum diameter of the leading follicle, i.e at the time of HCG administration.

Although there were no preferences upon classifying the patients among the different groups, the patients chosen to receive CC+HMG induction were those with younger age groups and more or less shorter duration of infertility. This coincidence gave those patients the best chances concerning ovulation and possible pregnancy, as, according to *Cai et al. (2011)*, the younger the patient and the shorter the duration of infertility, the better the results during ICSI. This ensures that if there are any benefits of

adding HMG to CC induction, it would be the more power of the drugs to revert the changes of CC rather than a better patient profile.

In the present study, the administration of either drug had a reversing power on the unfavorable changes in endometrial thickness due to CC induction.

Omran et al. (2018) described that administration of clomiphene citrate resulted in reduction of endometrial thickness. In contrary, *Ernest et al. (2010)* found no decrease in endometrial thickness or affection of the implantation window in clomiphene citrate treated cycles.

In this study, it was clear that the best pregnancy rate was achieved with the concomitant use of HMG rather than with the use of clomid and HMG and the mean endometrial thickness with HMG use was greater than with HMG and clomid.

Kovacs et al. (2010) concluded that increased endometrial thickness is associated with higher pregnancy rates. However, neither attainment of pregnancy nor pregnancy outcome was predicted by endometrial thickness alone.

Kasius et al. (2014) described that, the probability of pregnancy was significantly lower in the group with thin EMT ≤ 7 mm. This matched with *Chen et al (2010)* who reported that pregnancy rates ranged from 11.1% among patients with an endometrial thickness of ≤ 6 mm to 59.1% among patients with an endometrial thickness of 14-15 mm.

The endometrium must be sufficiently thick (6-8 mm) to enable embryonic implantation *(Tropea et al., 2010)*.

This did not match with the result of *Noyes et al. (2010)* who found endometrial thickness of ≥ 14 mm in 9.6 % of IVF-ET cycles which was associated with a normal rate of pregnancy but with a higher rate of biochemical pregnancies, Noyes et al. (2010) also noted that endometrial thickness of ≥ 15 mm was found in 11.6% of IVF-ET cycles and resulted in high implantation rates and clinical pregnancies.

In our study, definite affection of the endometrial triple layer appearance occurred in patients receiving CC alone. The percentage ratio of those with triple layered endometrium to non-triple layer was 15:85%. The use of clomid and HMG corrected this ratio to be 60:40%. Whereas; the use of HMG produced a ratio of 30:70% exactly. The net result was that the addition of HMG produced the best ratio of trilaminar endometrium which believed by many authors to be associated with better pregnancy rates than non trilaminar pattern *(Kuc et al., 2011* and *Zhao et al., 2012)*. Other studies showed no significant correlation *(Bozdag et al., 2010* and *Singh et al., 2011)*.

As regards Doppler study of the uterine artery, in the current study, PI was statistically significant between the group that received clomid only and both groups in which (clomid and HMG) and HMG were added and also a statistically significant difference was found between the group that received clomid only and the control group. However, the difference was statistically non-significant between (clomid+ HMG) group and the control group.

From these results, it was clear that vascular impedance is lower in the control

group rather than patients receiving induction specially those receiving clomiphene citrate. This matched with *Takasaki et al. (2013)* who gave one possible explanation for the lower uterine perfusion seen in the induced ovarian cycles is that clomiphene citrate is shown to deplete estrogen receptors in estrogen-sensitive tissues influencing both endometrial growth and pattern show that administration of estradiol can improve uterine response in cases of poor uterine perfusion.

In the present study, the mean PI of the uterine artery in the third group (clomid+ HMG) had the lowest value of PI of uterine artery.

Omran et al. (2018) studied the effect of CC on uterine hemodynamics, found that uterine perfusion was better in natural cycles than stimulated ones.

These results match with the results of *Khan et al. (2016)* who performed a valuable study to evaluate the prognostic value of uterine perfusion on the day of human chorionic gonadotrophin administration in patients who were undergoing intrauterine insemination. No pregnancy occurred when the pulsatility index (PI) of the ascending branch of the uterine arteries was more than 2.8. This data suggests that measurement of uterine perfusion on the day of human chorionic gonadotrophin administration may have predictive value regarding fecundity and the continuation of pregnancy.

In the present study, the RI of the uterine artery value was statistically non-significant among different groups. The lowest mean RI was for those patients who used HMG + clomid indicating better blood flow to the uterine artery. *Omran et al. (2018)* found that uterine artery RI in stimulated cycles with CC was 0.84+/-0.19 and in natural cycles was 0.78+/-0.15.

In this study, the mean serum progesterone level in all groups that received induction of ovulation was higher than 10 ng/ml, and the highest value was obtained with the addition of HMG to clomid.

The study done by *Warne et al. (2011)* to patients who were treated with human follicle-stimulating hormone (FSH) concluded that a midluteal progesterone level <10 ng/mL may represent an appropriate threshold for inducation of ovulation resulting in live birth. Multiple pregnancies were associated with higher mean midluteal progesterone levels.

In this study, all groups that received induction of ovulation showed a higher number of dominant follicles than the control group and the difference was statistically significant. Again, addition of HMG to clomid gave the highest mean number of dominant follicles when compared with the group that received clomid.

This keeps with the results of the study of *Chang et al. (2010)* who reported that the dominant follicle number increased with total antral follicle number in women who received CC plus HMG. The pregnant group had a higher number of antral follicles and dominant follicles in comparison with the non-pregnant group. The pregnancy rate was low in women aged older than 35 years regardless of the number of antral follicles and the extent of HMG administration. Women aged older than 35 also produced fewer dominant follicles.

Chien et al. (2012) found that women with unexplained subfertility demonstrated significant changes with time in the indices of vascularity within the endometreium during the menstrual cycle characterized by a pre-ovulatory peak and post-ovulatory fall. These changes were significantly reduced in the endometrium during the mid-late follicular phase and early luteal phase. There were no differences in endometrial thickness or volume between the groups or in the plasma concentrations of estradiol or progesterone and they concluded that endometrial and subendometrial vascularity are significantly reduced in women with unexplained subfertility during the mid-late follicular phase irrespective of estradiol or progesterone concentrations and endometrial morphometry.

In the current study, using the 4 Doppler indices used in detection of ovulation gave better results regarding the sensitivity, specificity, positive predictive value, negative predictive value and accuracy than using any one of them alone or transvaginal ultrasound alone. These findings were consistent with those of *Farrag et al. (2010)* addressing the better detection and assessment of ovulation using Doppler indices.

In this study, the best results were obtained when we used combined TVS and the 4 Doppler indices in detection of ovulation as the best findings regarding the sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 69.5%, 88.9%, 95.4%, 55.6%, 77% respectively. This is in accordance with other previous stories *(Brannstorm et al., 2010, Lunenfeld et al., 2010* and *Winer et al., 2011)* suggesting the potential adventitious role of color Doppler imaging of ovarian blood flow in assessment of ovulation in stimulated cycles.

CONCLUSION

The use of combined transvaginal ultrasound together with color Doppler indices gave the best detection rate of ovulation than any of them alone.

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إستخدام الموجات فوق الصوتيه والدوبلر في تقييم تدفق الدم فى بطانة الرحم والمبيض وقت التبويض

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خلفيــة البحــث: يُعــرَّف العقــم عــادةً علــى أنــه عــدم القــدرة علــى الحمــل بعــد عــام واحـد مـن الجمـاع المنـتظم غيـر المحمـي. يـتم تسـهيل تقيـيم الحـوض إلـى حـد كبيـر مــن خــلال اســتخدام تصــوير دوبلــر الملــون، والــذي يســمح بــالعرض المتــزامن للمعلومـــات التشـــريحية (المقيـــاس الرمـــادي) والتـــدفق (اللـــوني). يمكـــن إجـــراء قياسات سريعة وقابلة للتكرار لتدفق الدم باستخدام دوبلر اللون عبر المهبل.

الهــدف مــن البحــث: تقيـيم نضـح الـرحم والمبـيض أثنـاء التبـويض بواسـطة دوبلـر اللون عبر المهبل.

المريضـــات وطـــرق البحـــث: بلـــغ عـــدد المريضـــات المســـجلات فـــي هـــذه الدراســـة 180 مريضـــا، والتـــي أجريـــت فـــي مستشـــفى جامعـــة 6 أكتـــوبر مـــن الفتـــرة مـــا بـــين ســـبتمبر 2019 إلـــى ســـبتمبر 2020، بـــين 20 - 30 عامـــا، مـــع فتـــرة ســـابقة مـــن العقـــم تتـــراوح مـــا بـــين 1 - 5 ســـنوات و مـــع مؤشـــر كتلـــة الجســـم بـــين 20 - 25. وقـــد تـــم تقســـيم المريضـــات إلـــى أربـــع مجموعـــات. وقـــد تلقـــت (المجموعـــة B1) تحـــريض ســـيترات الكلـــوميفين وحـــده، (المجموعـــة B2) الغـــدد التناســـلية البشـــرية بعـــد انقطـــاع الطمـــث، (المجموعـــة الثالثـــة) ســـيترات الكلـــوميفين مـــع الغـــدد التناســـلية بعـــد انقطـــاع الطمـــث البشـــري , و (المجموعـــة الاولـــى) هـــى المجموعة الضابطة لم تتلقى أي دواء.

نتـــائج البحـــث: كانـــت التـــأثيرات الضـــارة لتحـــريض ســـيترات الكلـــوميفين علـــى ســـمك ونمـــط بطانـــة الـــرحم واضـــحة خاصـــة فـــي المجموعـــة (B1) التـــي أظهـــرت أقـــل نســـبة لبطانـــة الـــرحم ثلاثيـــة الطبقـــات بـــين المجموعـــات الأربـــع. وأظهـــرت

الدراسة قوة الانعكاس الواضحة لكل من الغدد التناسلية سبوتينيوس والإنسان بعد إنقطاع الطمث على سمك ونمط بطانة الرحم، على الرغم من أن المريضات من (B3) أظهرن أعلى نسبة لبطانة الرحم ثلاثية الصفائح بين المجموعات الأربع. ولم يكن متوسط يوم ظهور الجريب السائد مختلفًا بشكل كبير بين المجموعات الأربع؛ ومع ذلك، كان أقل قليلاً في المجموعة التي تلقت عقار كلوميفين سترات + موجهة الغدد التناسلية البشرية بعد إنقطاع الطمث. وقد أظهرت المجموعات الثلاث التي تلقت الاستقراء عددًا ذا دلالة إحصائية أعلى من البصيلات السائدة مقارنة بالمجموعة الضابطة، وأظهرت المجموعة التي تلقت عقار كلوميفين سترات + الغدد التناسلية بعد إنقطاع الطمث البشري أكبر عدد من البصيلات السائدة وأكبر قطر للبصيلات السائدة.

الاستنتاج: إستخدام الموجات فوق الصوتية عبر المهبل مع مؤشرات دوبلر الملونة تعطي أفضل معدل للكشف عن الإباضة من أي منهما بمفرده.

الكلمات الدالة: العقم، دوبلر عبر المهبل، المبيض، تدفق الدم في بطانة الرحم أثناء الإباضة.