THREE -DIMENSIONAL ULTRASOUND MONITORING THE UTERO-OVARIAN RESPONSES IN OF OVULATION INDUCTION IN POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Objective: 3D ultrasound will be used to monitor the response of controlled ovarian stimulation and determination of uterine receptivity in patients of PCOS.

Design : prospective study.

Setting : Suez Canal University & Private clinics

Materials and methods: This study was done for three successive menstrual cycles for each case, including 50 infertile patients with PCOS. The patients had received clomiphene citrate (CC); Follicular growth was monitored by repeated trans-vaginal ultrasound. When lead follicle of ≥18 mm in mean diameter was detected , at this stage 1) Endometrial thickness was measured 2) Determine the presence or absence of three-line appearance of the endometrium. 3) Presence of myometrial contractions 4) Myometrial echogenicity 5) Presence of cumulus oophorus 6) Presence of echolucent space in the endocervical canal. Then, 10000 u of hCG were given intramuscularly to induce ovulation .

Results : In three cycles respectively, pregnancy rate in patients showing triple appearance of the endometrium at the time of hCG administration was 70.6, 71.4, 91.7%, showing homogenous myometrium 73.3, 91.7, 76.9%, showing myometrial contractions 80.0, 84.6, 76.9%, showing the cumulus oophorus 76.5, 73.3, 90.9%, and showing echolucent space in the endocervical canal was 92.9, 73.3, 76.9%.

Conclusion: Folliculometry with 3D ultrasound offers good monitoring and helps in improving cycle fecundity. With 3D folliculometry, it might be possible to time the administration of hCG to coincide with optimal follicle maturity for the release of the highest quality oocytes and optimal uterine receptivity.

Key words: Triple appearance, cumulus oophorus, homogenous myometrium , myometrial contractions

INTRODUCTION

. The polycystic ovary syndrome (PCOS) is the commonest endocrine disturbance affecting women [1]. Polycystic ovaries are commonly detected by ultrasound or other forms of pelvic imaging , with estimates of the prevalence in the general population being in the order of 20-30% [2]. However, not all women with polycystic ovaries demonstrate the clinical and biochemical features which define the PCOS [3]. PCOS accounts for 80% of women with anovulatory infertility [4]. PCOS is usually reserved for those women who exhibit an ultrasound picture of polycystic ovaries, and who display one or more of the clinical symptoms (menstrual cycle disturbances, hirsutism, obesity, hyperandrogensim), and/or one or more of the recognized biochemical disturbances (elevated LH, testosterone, androstenedione, or insulin)[1,2,5]. This definition of PCOS requires the exclusion of specific underlying diseases of the adrenal or pituitary glands (e.g., hyperprolactinemia, acromegaly, and congenital adrenal hyperplasia)

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which could predispose to similar ultrasound and biochemical features [5].

The advent of high resolution ultrasound scanning provided a non invasive technique for the assessment of ovarian size and morphology[6]. Transabdominal and/or transvaginal ultrasound have become the most commonly used diagnostic methods for the identification of polycystic ovaries[6]. The transabdominal ultrasound criteria of Adams et al.[7] defined a polycystic ovary as one which contains, in one plane, at least 10 follicles (usually between 2 and 8 mm in diameter) arranged peripherally around a dense core of ovarian stroma or scattered throughout an increased amount of stroma. Transvaginal ultrasound is a more sensitive method for the detection of polycystic ovaries and that the transvaginal definition of a polycystic ovary should require the presence of at least 15 and usually more than 20 follicles (2-10 mm in diameter) in a single plane [8].

Conventional- two- dimensional (2D) real- time ultrasonography easily provides accurate images of both normal anatomy and pathological findings [6]. 2D ultrasonography however, provides only a linear (length and width) observation of the structure [9]. Although, resolution has increased significantly, these 2D images may be confusing and difficult to construe to some clinicians because they must be interpreted to form a three-dimensional impression of the anatomic structures represented [9]. In addition, accurate volume measurements may not be obtained. With the use of three- dimensional (3D) ultrasonography, three continual different planes representing longitudinal, transverse and horizontal sections and displayed simultaneously[9]. These three planes can be rotated and computer translated to obtain accurate anatomic sections needed for geometric measurements such as distance, area and volume[10]. With the recent advances of 3D ultrasound , its clinical application has been applied in many fields of infertility[10-13]. In this study three- dimensional ultrasound will be used to monitor the response of controlled ovarian stimulation and determination of endometrial receptivity in patients of PCOS.

Clomiphene citrate (CC) is a selective estrogen receptor modulator that primarily works through the hypothalamus to increase pituitary secretion of FSH that in turn stimulates ovulation[14]. Clomiphene citrate has traditionally been used as first line therapy for anovulatory PCOS because it is cheap and given orally[15]. Clomiphene citrate has been available for many years and its use has tended not to be closely monitored. CC induces ovulation in approximately 70-85 % of patients although only 40-50 % conceive [15]. It has been suggested that the most important reason for reduced overall pregnancy rates with CC is discontinuation of therapy, and the antiestrogenic activity may adversely affect the endometrium and can cause thickening of cervical mucus, so may reduce the chance of conception[16]. Recent guidelines advise to stop its use for more than six months[14,16]. So, women who receive CC should be carefully monitored with a combination of endocrine and ultrasonographic assessment of follicular growth and ovulation. However, there is no doubt that the majority of cycles of CC treatment go unmonitored and it is recommended that at least the first cycle of treatment, if not all cycles, should be monitored with a combination of serial ultrasound scans and serum endocrinology.

MATERIALS & METHODS

From January 2003 to March 2006, we studied 50 infertile patients with PCOS, aged from 23-31 years old, who were attending Suez Canal University and some private clinics and agreed to participate in this prospective study. This study was done for three successive menstrual cycles for each case.

All the patients had spontaneous onset of puberty and normal sexual development and all had been affected by oligomenorrhea since puberty. The

duration of infertility was 3-7 years. All the patients were subjected to a thorough history taking and physical examination. For every patient BMI was calculated (body weight in KG divided by square of height in meters). The previous investigations were revised and completed. Base-line serum hormone determinations were performed the month preceding the study including the level of FSH, LH, PRL, TSH, Testosterone, and 17 hydroxy progesterone.

Basic pelvic ultrasound examination was performed for each patient by the same investigator on day two or three of her menstrual cycle prior to starting the treatment with CC.

PCOS patients were diagnosed according to :

- Clinical criteria; a history of oligomenorrhea/ amenorrhea, clinical evidence either of acne, alopecia, obesity (BMI >25 Kg / m2) or hirsutism [3].
- Biochemical data, of elevated concentration of serum testosterone or an LH/FSH ratio > 1 [5].
- Vaginal ultrasound, the presence of >15 peripherally oriented cysts in one ultrasonographic plane, each measuring 2-8 mm in diameter and arranged around a dense, ultrasonically bright ovarian stroma, and/or increased ovarian volume > 10ml [6].

Patient to be diagnosed as PCOS must have at least one of the abnormal clinical findings and at least one abnormally elevated laboratory value.

The inclusion criteria were:

1) No pelvic factors of infertility (diagnosed by hysterosalpingography and laparoscopy in some cases).
2) Normal values of semen analysis according to WHO criteria.
3) Normal post-coital test.
4) Euthyroid.
5) Normal prolactin level.

The exclusion criteria were:

1) Other factors of infertility with anovulation.
2) Patients who have an ovarian cyst > 12mm in diameter in first basic ultrasonographic examination.

The patients received CC: The initial dose of CC was 50 mg per day for 5 consecutive days, Starting on the third day of spontaneous or induced bleeding. If no response was obtained, the dose of CC was successively increased in subsequent cycles until 100 or 150 mg per day were given. The smallest effective CC dose continued for the next cycles. Transvaginal ultrasound monitoring of folliculogenesis, starting on day 8 of each cycle was performed. All ultrasound examinations were performed using a scanner designed with both 2D and 3D imaging capabilities (Voluson 530 D) with the use of a motor-driven 5-7.5 MHz transvaginal volume probe for transvaginal scanning, and 3.5 MHz volume transducer used for transabdominal examination. Before the 3D examination, a standard 2D real time scan was obtained. After this conventional ultrasonographic examination, a satisfactory image of the desired anatomic field was obtained and a 3D sample box was defined on the screen. All examinations were performrd by two investigators. In first basic examination, both ovaries were measured for three-dimensional diameters, and detailed echographic slicing of the ovaries was performed by a single investigator within 10 minutes. Many sectional images were automatically scanned and reviewed *simultaneously in three planes*: a frontal section , a median sagital section , and a horizontal section (Figure 1). The complete data set was then stored in the scanners random access memory. The system thus allows for the recording and storage of the data for immediate or later diagnosis. Three basic modes of acquired images were mode : volume mode; transparent maximum/ minimum mode, which provides a transparent image of the anatomic structure studied; and surface-

rendering mode, which allows study of the surface of the region under consideration. Estimation of follicle size was performed by measuring the maximum transverse (D1), anterior-posterior (D2), and longitudinal (D3) diameters of the largest follicles, the measurements were taken from the outmost limits of the follicle in all planes. Follicular growth was monitored by repeated transvaginal ultrasound every other day from day 8 of the cycle. If a lead follicle of > 18 mm in mean diameter was detected, at this stage endometrial assessment was performed as follows (Figures 2-5) :

A) Endometrial thickness was measured; the maximum endometrial thickness was measured in the central longitudinal axis from the junction of the stratum basale and the inner myometrium on the anterior side of endometrium to the same plane on the posterior side of endometrium (endometrial thickness). Full thickness measured from myometrial end junction to endometrium, in the A-P dimension, in absence of contractions. Also the measurement is taken when both endometrial and cervical canal appear continuous and recorded as permanent photographic image.

B) Determine the presence or absence of three-line appearance of the endometrium. (endometrium pattern, multi-layered or non multi- layered).

C) Myometrial echogenicity, course inhomogeneous, or relatively homogeneous (Figure 2).

D) Myometrial contractions , in the inner third of the myometrium-the slightly hypoechoic junctional zone of the myometrium immediately adjacent to the endometrial lining exhibits wavelike contractions with a frequency of one to two per minute. This contractility can be appreciated if the endometrium is recorded on videotape during TVS and then played back at a faster speed. (Figure 3).

E) The cumulus oophorus is seen on the wall of the clear spherical follicle as 1-3mm belb, may appear as an ultrasonically echo- dense area in the follicular perimeter, it is found to be better and more obvious in 3 D by adding the coronal plane. (Figure 4).

F) Presence of echolucent space in the endocervical canal (The mucus in the endocervical canal is highly viscous and echogenic in its interface with cervical mucosa, except at the time of ovulation. when it has a higher water content and may be seen as an echolucent space on ultrasound) (Figure 5).

Cumulus oophorus, echolucent space in the endocervical canal were found to be better in 3D by adding the coronal plane, which is really a good plane to look at all these items.

Having completed the ultrasound examination 10.000 u of hCG (Pregnyl ; Organon) were given intramuscularly to induce ovulation. Transvaginal ultrasound scan was obtained on the second day after hCG administration to establish whether ovulation had occurred, or not. For evidence of ovulation we used the following criteria: the follicle disappeared. the follicle filled in with low level echoes and the collapsed follicle was later replaced by a corpus luteum[14]. The fresh corpus luteum usually appears as a hypoechoic structure with an irregular wall and may contain some internal echoes. In addition to delineation of changes in follicle size and structure . transvaginal ultrasound examination can depict the presence of intra peritoneal fluid. It is normal to have approximately 1 to 3 ml of intra peritoneal fluid in the cul-de-sac through out the cycle; when ovulation occurs, there typically is between 4 to 5 ml within the cul-de-sac[14].

On the ninth day after hCG administration , serum progesterone level was determined. Also on the same day an ultrasound examination was performed to detect the presence OHSS. In this study ovulation was considered to have occurred if the serum progesterone level was > 5ng / ml on the ninth day

after hCG administration. Vaginal micronized progesterone (300 mg / day,Uterogestan) twice daily were prescribed as luteal support. A urine pregnancy test was performed 17 days after ovulation. If the pregnancy test was positive, luteal support was continued until transvaginal ultrasonography, which was performed 2 weeks later to confirm the presence of intrauterine pregnancy. All patients with a clinically viable pregnancy on ultrasound scan continued luteal support with progesterone until 10 weeks gestation.

All data were entered into a computer using a statistical package for Social Sciences 10.0 for Windows (Chicago, IL, USA). $P < 0.05$ was considered statistically significant. Results are presented as mean ± SD. The data were analyzed by *two-way analysis of variance. Correlation analysis* was performed using Pearson's correlation test. Standardized Descriminant function coefficients (DFC) reflect importance of the 3D variables, while unstandardized DFC used for calculation of discriminant score for each case by adding the constant to the products of multiplying each coefficient by the value of its variable for the cases tested. Discriminant scores are compared with group centroid and pregnancy is predicted. Differences between means were assessed by Student's t-test.

RESULTS

A total of 112 treatment cycles were performed in 50 couples within the study period. Clear morphology of ovaries was obtained in 50 women of reproductive age with polycystic ovary syndrome (Figure 1). The images obtained are far superior to those from 2D examination. This increases the accuracy of measurements of the follicular diameter and allows much more detail of the follicle to be seen. In 3D the cumulus oophorus appears as an ultrasonically echo-dense area in the follicular perimeter (it was seen on the wall of the clear spherical follicle as 1 to 3 mm bleb) (Figure 4). Also the triple morphology of the myometrium, the myometrial contractions and myometrial echogenicity appear more in 3D than in 2D examinations.

The patients were divided retrospectively into two groups: those who got pregnant during the study cycles (*pregnant group*) and those who didnot get pregnant (non pregnant group). These groups were compared with respect to age, BMI, duration of infertility, number of preovulatory follicles > 18 mm, mean endometrial thickness, and endometrial morphology.

The follicular diameter range at ovulation was 18-25 mm. No apparent change in the relative position of follicle within the ovary has been detectable. In 25% of the cycles more than one dominant follicle appeared to develop. When multiple follicles coexist, ovulation occurs simultaneously rather than sequentially. The range of the endometrial thickness at the time of ovulation was 10-13mm.

DISCUSSION

Ultrasound offers a simple, reliable, quick and non-invasive method of assessing the female pelvic region, especially follicular and endometrial growth [17].

There are definitive changes of the endometrium throughout the menstrual cycle. Early in the menstrual cycle the endometrium is thin and is hypoechoic compared with the surrounding myometrium. As the follicular phase progresses, the endometrial thickness increases and takes on a characteristic trilaminar appearance. Following ovulation, the endometrium becomes more heterogenous with a hyperechoic appearance compared to the surrounding myometrium [18].

Endometrial receptivity is a qualitative term used to describe a favorable situation with respect to

implantation potential. This can be assessed during ultrasound examination by a combination of appearance and thickness, as well as estimating the uterine artery blood flow with Doppler ultrasound[19]. Typically, during the late proliferative phase of the menstrual cycle, the following factors are regarded as markers of endometrial receptivity: (1) minimum thickness of 7 mm (2) trilaminar appearance (3) uterine artery pulsatility index values (PI) 3.0 [18].

According to Applebaum[20], certain sonographic qualities of the uterus are noted during the normal mid-cycle (Applebaum called them the Uterine Biophysical Profile) determined using trans-vaginal colour Doppler sonography. Applebaum undertook the project of attempting to predict the outcomes of conception cycles during both IVF and medically stimulated non- IVF attempts. Applebaum noticed some sonographic findings which may be useful in foretelling the outcome. These findings have been compiled into an examination called the Uterine Biophysical Profile (UBP). The UBP are weighed according to the Uterine Scoring System for Reproduction (USSR). The USSR comprises evaluation of the following parameters and each parameter is scored as follows: Endometrial thickness < 7mm has score 0, 7-9 mm has score 2, 10-14 mm has score 3, > 14 mm has score 1.

Endometrial layering appearance (no layering has score 0, hazy 5-line appearance has score 1, distinct 5-line appearance has score 3).

Endometrial motion (the number of mymetrial contractions in 2 minutes < 3 has score 0, if it is > 3 has score 3).

Myometrial echogenicity (course, inhomogeneous has score 1, relatively homogeneous has score 2).

Uterine artery Doppler flow (PI), 2.99-3 has score 0, 2 - 2.49 has score 1, < 2 has score 2.

Endometrial blood flow in zone 3, absent has score 0, present but sparse has score 2, present multifocally has score 5.

Myometrial blood flow (Gray scale), absent has score 0, present has score 2.

In Applebaum's study with this system, a USSR "perfect score" of 20 has been associated with conception 100% of the time. The number of patients in which they predicted successful conception cycles based upon the UBP and USSR perfect score was 5. This group included 2 spontaneous cycles (non- IVF, non-IUI), 2 IUI and 1 IVF. Scores 17- 19 (10 patients) have been associated with conception 80 % of the time. Scores of 14-16 (10 patients) had a 60% chance, while scores of 13 or less (25 patients) have resulted in no pregnancies.

In this study our findings are in agreement with the results of Applebaum's study. In this study, based upon these 3D variables, the overall percent of correctly predicted cases was 98 % in the first cycle, 94.3 % in the second cycle, 95.7 % in the third cycle.

In this study, pregnancy rates were 70.6% in patients of the first cycle showing the triple appearance versus 9.1% in patients who didn't show triple appearance ($P < 0.001$); in the second cycle (71.4% versus 9.5% $P < 0.007$), in the third cycle (91.7% versus 0% $P < 001$). This can be explained by a multilayered endometrial pattern, due to glandular edema, may be associated with higher pregnancy rate. Its absence indicate suboptimal condition for implantation.

In this study pregnancy occured in 80.0 % of patients of the first cycle showing myometrial contractions versus 8.6% in patients who didn't show myometrial contractions; and in the second cycle (84.6 % versus 4.5 % $P < 0.001$), in the third cycle (76.9% versus 10.0% $P < 0.001$). This can be explained by that these contractions can help propel sperm to the fallopian tubes before ovulation and later perhaps to ensure that the embryo upon reaching the uterine cavity, remained in the upper part of the uterus for implantation. In agreement with this study also, Anderson and colleagues[21] recorded

endometrial motion in 378 transvaginal follicle scans on 137 women undergoing frozen embryo transfer cycles. The video recordings taken on days 5, 8, 11, 15, and 21 were assessed later by different observers who were unaware of the circumstances in which the recordings had been made. They found that the amplitude of the contractions increased slightly from the early to the late follicular stage and then fell after ovulation until it was almost gone by the mid-luteal phase. The frequency of contractions showed a similar pattern of change throughout the cycle. The direction in the follicular phase was not specific. In the early luteal phase, the contractions were directed toward the fundus, presumably to ensure that the embryo, upon reaching the uterine cavity, remained in the upper part of the uterus.

As regard to the homogenous myometrium, pregnancy occurred in 73.3% of the patients of the first cycle showing homogenous myometrium versus 11.4% in the patients who didn't showing homogenous myometrium. In the second cycle (91.7 % versus 4.5 % $P < 0.001$), in the third cycle 76.9 % versus 10.0% $P < 0.001$).

In this study, we didn't depend on colour Doppler study because endometrial blood flow is of low velocity; if the sweep through the endometrium is too rapid, flow may not be seen. Additionally, endometrial blood is somewhat "mercurial" -it may seem to"come and go", and appear in some areas and not in others. Also, endovaginal scans, both coronally and sagittally there may be difference in how well the blood flow is imaged [22]. Also there is ongoing debate about the role of Doppler ultrasound assessment of uterine or endometrial blood flow in predicting likelihood of implantation. There have been a number of studies that have shown differences in the uterine PI between women who conceived and those who did not following IVF treatment. More recently, interest has focussed on sub endometrial blood flow [23]. The most promising application of color Doppler could be in assisted conception to improve the pregnancy rate per embryo transfer [24, 25].

In this study we measured endometrial thickness in a total of 112 cycles. The range of the endometrial thickness in both groups was 10-13 mm. There were no significant differences between the patients who did not conceive and those who conceived in terms of mean endometrial thickness (in the first cycle 10.8 versus 10.9, in the second cycle 10.9 versus 10.7, in the third cycle 10.6 versus 10.7). This is similar to the study done by Schild et al.[26] and that done by Yaman et al [27]. Schild et al measured endometrial thickness and volume in a total of 47 IVF cycles on the day of oocyte retrieval. There were no significant differences between the group of fifteen patients that conceived (31.9%) and the remaining 32 non-pregnant women in terms of the mean endometrial thickness (10.8 + 2.3 mm versus 11.8 + 3.4mm) or volume (4.9+2.2 cm^3 versus 5.8+3.4 cm^3) respectively. Yaman et al. reported similar findings with no differences in thickness (11+2mm versus 11+2mm) in 21pregnant and 44 non-pregnant women on the day of hCG administration. Conventional measurement of endometrial thickness is already known to have a similar negative predictive value with conception less likely in patients with an endometrium measuring less than 5mm in diameter. In the study done by Kovacs et al[28], a retrospective analysis was conducted of 1228 IVF- ICSI cycles. Stimulation with CC + hMG in one- third of the cycles, and ultrashort GnRH agonist stimulation in two-thirds. Cycle parameters were compared between pregnant and non-pregnant patients. They noted an improved pregnancy rate in cycles when endometrium was ≥ 10 mm; rates further improved between 10-14 mm. with additional increases in endometrial thickness. Zhang et al. study [29] included 897 IVF-embryo transfer cycles. Endometrial thickness was recorded on the day of hCG injection, 2 days before oocyte retrieval.

Treatment outcome (clinical pregnancy) after IVF-embryo transfer was positively associated with increased endometrial thickness and peak E2 concentration in serum, and negatively associated with advanced age. Thin endometrium (< 9 mm) reduced pregnancy rates in relatively young patients (< 38 years old), in patients who required more than 10 days of gonadotropin stimulation, or in patients whose embryo transfers consisted of poor quality embryos.

Considering the relatively wide range of follicular diameter on the day of ovulation, depnding on the diameter provide only an imprecise indication of when the follicle will rupture [30]. The attainment of follicular maturity can be difficult to predict by follicular size alone. In this study there was no significant difference in size of the largest follicles of the two groups. Our results show a high significant difference in percentage of pregnancies occurring when the patients cumuli had been visualized within their follicles (in the first cycle from the patients in whom cumuli were visualized 82.0% conceived versus 0.0% in patients in whom cumuli were not visualized ($P < 0.001$), in the second cycle 73.3 % versus 5% ($P < 0.001$), in the third cycle 90.9% versus 8.3 % ($P < 0.001$). This is similar to the study of Poehl et al.(31). They used the spatial appearance of intrafollicular cumulus-like structures with the number and maturity of information provided by the multiplanar display to correlate the oocytes retrieved from 50 women undergoing IVF treatment. All follicles measuring 16 mm or more were carefully examined for the presence of cumuli in all three perpendicular planes or in a reconstructed three-dimensional composite image. A total of 296 mature oocytes were eventually retrieved from 318 follicles and 218 of these fertilized successfully. In all, 262 cumuli had been visualized within these follicles and this correlated well with the number of retrieved oocytes ($r2 = 0.78$; $P < 0.0001$) and fertilization rate ($r2 = 0.65$; $P < 0.0001$).

When the cervix is demonstrated sonographically the internal and the external os should be included in the image. The fibrous part of the cervix uteri is of intermediate echo texture. The cervix changes in appearance during the menstrual cycle. During menstruation, a hypoechoic area due to blood may be seen. The appearance of the cervix does not change until the midfollicular phase. Initially, the anterior and posterior walls are adjacent, appearing as an echogenic line. Around the time of ovulation, the cervical canal is of reduced echogenicity, due to mucus accumulation in the cervical canal. This reaches a maximum thickness of 5 mm by ovulation and disappears by second post ovulatory day. These changes are seen in spontaneous cycles and in induced cycles [32]. Estrogenic-type cervical mucus secretions are known to increase in volume about 5-6 days prior to ovulation stimulated by an increase in estrogen. Women can reliably identify amount and type of cervical mucus based on feeling and observation of vaginal discharge (33). In addition, estrogenic-type mucus serves not only as a marker of the fertile days, but also as a direct predictor of conception success, because sperm are incapable of survival and transport to the ovum in the absence of sufficient levels estrogenic-type mucus[34]. In different studies of many cycles evaluation of cervicovaginal fluid changes is an accurate indicator of the ovulation.

In this study, pregnancy occurred more when cervical mucus plug is seen. In the first cycle, from the patients in whom the cervical mucus plug was seen 92.9% conceived versus 5.6% patients in whom cervical mucus was not seen, in the second cycle 73.3% versus 5%, in the third cycle 76.9 % versus 10%. In the present study, we relied on ultrasound detection of mucus plug in the cervix. It is an interesting area for future research is the development of methods for better quantifying mucus characteristics, and for removing potential subjectivity in classifying mucus symptoms.

This can explain why some cases do not conceive In the non conception group may be the result of inappropriately timed exposure to hCG, which if injected at other than the peak of follicular maturity can induce atresia rather than ovulation. Conversely, correctly synchronized hCG exposure ensures ovulation between 24 and 48 hours after injection. Greater success has been achieved when hCG administration was carried out with suitable thickness and morphology of the endometrium.

CONCLUSION

Folliculometry with 3D ultrasound offers good monitoring and helps in improving cycle fecundity. With 3 D folliculometry, it might be possible to time the administration of hCG to coincide with optimal follicle maturity for the release of the highest quality oocytes and optimal uterine receptivity. Ovulation must be triggered when all available utero-ovarian parameters are optimized.

RECOMMENDATION

Our results are preliminary and substantially more patients need to be evaluated.

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Table I : Clinical data of both non pregnant and pregnant groups in the three cycles of the study.

First cycle	Age	BMI	Daration of infertility	Second cycle	Age	BMI	Daration of infertility	Third cycle	Age	BMI	Daration of infertility
No. Pregnancy (n=35)				No. Pregnancy (n=23)				No. Pregnancy (n=12)			
Mean	25.4	26.3	3.6	Mean	25.0	26.3	3.6	Mean	25.2	26.2	3.6
S.D	2.4	1.3	1.4	S.D	2.3	1.2	1.4	S.D	1.5	1.2	1.4
Pregnancy (n=15)				Pregnancy (n=12)				Pregnancy (n=11)			
Mean	25.4	26.2	3.7	Mean	25.4	26.2	3.3	Mean	25.2	26.3	3.7
S.D	2.5	1.3	1.4	S.D	2.4	1.3	1.4	S.D	1.4	1.3	1.4
P	0.9	0.7	0.8	P	0.8	0.8	0.6	P	0.9	0.7	0.8

Table (I) shows a non significant difference between the clinical data of both groups in the three cycles of the study.

Table II : Hormonal data of both non pregnant and pregnant groups in the three cycles of the study.

	First Cycle						Second Cycle						Third Cycle					
No. Pregnancy	PRL	TSH	FSH	*Test	#OH17	LH	PRL	TSH	FSH	Test	OH17	LH	PRL	TSH	FSH	Test	OH17	LH
Mean	27.4	2.1	3.8	2.5	10.6	9.7	27.3	1.8	3.5	2.5	10.2	9.0	27.5	1.8	3.5	2.6	10.3	10
S.D	1.6	1.9	1.0	0.6	1.5	1.3	1.8	0.8	0.9	0.6	1.4	1.3	1.8	0.7	0.9	0.7	1.5	1.2
Pregnancy																		
Mean	27.2	1.9	3.9	2.5	10.4	9.6	27.5	2.0	3.4	2.5	10.3	9.1	27.2	1.8	3.5	2.5	10.4	10
S.D	1.5	0.8	1.2	0.6	1.5	1.3	1.3	0.9	0.8	0.6	0.6	0.9	1.8	0.9	1.0	0.5	1.4	1.7
P	0.9	0.9	0.8	0.7	0.7	0.8	0.7	0.7	0.7	0.6	0.7	0.8	0.6	0.7	0.9	0.7	0.8	0.9

Table II shows a non significant difference between the hormonal profile of both groups in the three cycles of the study.
* testosterone, # 17 hydroxy progestrone

Table III : Standard parameters of typical folliculometry of both non pregnant and pregnant groups in the three cycles of the study.

First cycle	* Endom. thickness	No of Preovula follicles	Diameter Largest Follicle	Second cycle	* Endom. thickness	No of Preovula follicles	Diameter Largest Follicle	Third cycle	* Endom. thickness	No of Preovula follicles	Diameter Largest Follicle
No. Pregnancy (n=35)				No. Pregnancy (n=23)				No. Pregnancy (n=12)			
Mean	10.8	1.4	19.0	Mean	10.9	1.5	18.7	Mean	10.6	1.5	18.8
S.D	1.3	0.6	4.8	S.D	1.3	0.5	4.7	S.D	1.4	0.4	3.6
Pregnancy (n=15)				Pregnancy (n=12)				Pregnancy (n=11)			
Mean	10.9	1.6	20.0	Mean	10.7	1.6	19.2	Mean	10.7	1.5	19.2
S.D	1.2	0.8	1.0	S.D	1.3	0.5	2.1	S.D	1.2	0.6	2.6
P	0.6	0.6	0.8	P	0.8	0.7	0.8	P	0.9	0.8	0.7

Table (III) shows non significant difference in the data of the typical folliculometry of both groups.
* Endometrial Thickness, No. of mature Preovulatory Follicles

Table IV : Frequency of pregnancy after the first cycle in relation to three- dimensional ultrasound findings.

	Pregnancy		χ^2	P
	N	%		
Triple appearance				
No (n = 33)	3	9.1%	20.2	< 0.001
Yes (n = 17)	12	70.6%		
Myometrial contraction				
No (n = 35)	3	8.6%	25.5	< 0.001
Yes (n = 15)	12	80.0%		
Homogenous myometrium				
No (n = 35)	4	11.4%	19.2	< 0.001
Yes (n = 15)	11	73.3%		
Ovulation				
No (n = 20)	0	0.0%	41.6	< 0.001
Yes (n = 30)	15	82.0%		
Cumulus				
No (n = 33)	2	6.1%	26.5	< 0.001
Yes (n = 17)	13	76.5%		
Cervical mucus				
No (n = 36)	2	5.6%	36.6	< 0.001
Yes (n = 14)	13	92.9%		

N =number of pregnant cases. Table IV shows high significant difference in number and % of pregnancy between patients showing these variables and the patients not showing these variables at the time of hCG administration.
Table IV shows that 17 patients showing triple appearance , 12 of them got pregnant and 33 patients did not show triple appearance, 3 of them got pregnant
15 Patients showing myometrial contractions , 12 of them got pregnant . 35 did not show myometrial contractions 3 of them got pregnant.

Table V : frequency of pregnancy after the second cycle in relation to three- dimensional ultrasound findings (parameters) .

	Pregnancy		χ^2	P
	N	%		
Triple appearance				
No (n = 21)	2	9.5	7.304	0.007
Yes (n = 14)	10	71.4		
Myometrial contraction				
No (n = 22)	1	4.5	23.252	< 0.001
Yes (n = 13)	11	84.6		
Homogenous myometrium				
No (n = 23)	1	4.3	26.686	< 0.001
Yes (n = 12)	11	91.7		
Ovulation				
No (n = 10)	0	0.0	14.287	< 0.001
Yes (n = 25)	12	48.0		
Cumulus				
No (n = 20)	1	5.0	17.764	< 0.001
Yes (n = 15)	11	73.3		
Cervical mucus				
No (n = 20)	1	5.0	17.764	< 0.001
Yes (n = 15)	11	73.3		

N= number of pregnant casess. Table V shows high significant difference in number and % of pregnancy between patients showing these variables and the patients who don't show these variables at the time of hCG administration. 12 patients showed homogenous myometrium, 11 of them got pregnant. 23 patients did not show homogenous myometrium, 1 of them got pregnant.

Table VI : Frequency of pregnancy after the third cycle in relation to three-dimensional ultrasound findings.

	Pregnancy		χ^2	P
	N	%		
Triple appearance				
No (n = 11)	0	0.0	19.326	< 0.001
Yes (n = 12)	11	91.7		
Myometrial contraction				
No (n = 10)	1	10.0	10.145	0.001
Yes (n = 13)	10	76.9		
Homogenous myometrium				
No (n = 10)	1	10.0	10.145	0.001
Yes (n = 13)	10	76.9		
Ovulation				
No (n = 8)	0	0.0	11.244	0.001
Yes (n = 15)	11	73.3		
Cumulus				
No (n = 12)	1	8.3	15.683	< 0.001
Yes (n = 11)	10	90.9		
Cervical mucus plug				
No (n = 14)	1	10.0	10.145	0.001
Yes (n = 11)	10	76.9		

N = number of pregnant cases. Table VI shows high significant difference in number and % of pregnancy between patients showing these variables and the patients who did not show these variables at the time of hCG administration. 11 patients showed cumulus oophorus, 10 of them got pregnant. 12 patients did not show cumulus oophorus, 1 of them got pregnant. 11 patients showed cervical mucus plug, 10 of them got pregnant. 14 patients did not show cervical mucus plug, 1 of them got pregnant.

Table VII : Classification results of pregnancy predicted from discriminant analysis.

The first cycle actual group	N	Predicted pregnancy	
		No pregnancy	Pregnancy
No pregnancy	35	35 100.0%	0 0.0%
Pregnancy	15	1 6.7 %	14 93.3 %

98 % of grouped cases correctly classified

The second cycle actual group	N	Predicted pregnancy	
		No pregnancy	Pregnancy
No pregnancy	23	22 95.7%	1 4.3%
Pregnancy	12	1 8.3 %	11 91.7 %

94.3% of grouped cases correctly classified

The Third cycle actual group	N	Predicted pregnancy	
		No pregnancy	Pregnancy
No pregnancy	12	11 91.7%	1 8.3%
Pregnancy	11	0 0 %	11 100%

95.7% of grouped cases classified

TableVII shows results of pregnancy predicted from discriminant analysis compared with the actual results reported. In the first cycle 35 non-pregnant cases were 100% correctly predicted and 14 (93.3%) of the 15 pregnant were correctly predicted while one pregnant case (6.7%) was incorrectly predicted as non-pregnant. The overall percent of correctly predicted cases was 98%. In the second cycle the overall percent of correctly predicted cases was 94.3%. In the third cycle the overall percent of correctly predicted cases was 95.7%.

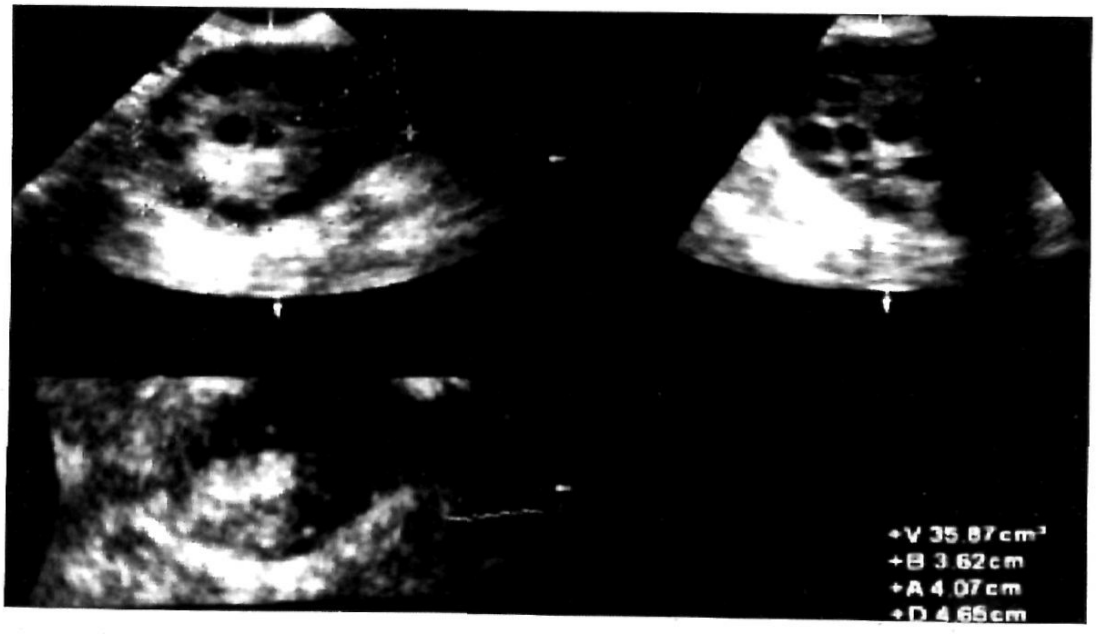

Fig. 1. TV 3D US: measurement of ovarian volume in three orthogonal planes showing increased size of the ovary in a case of PCO.

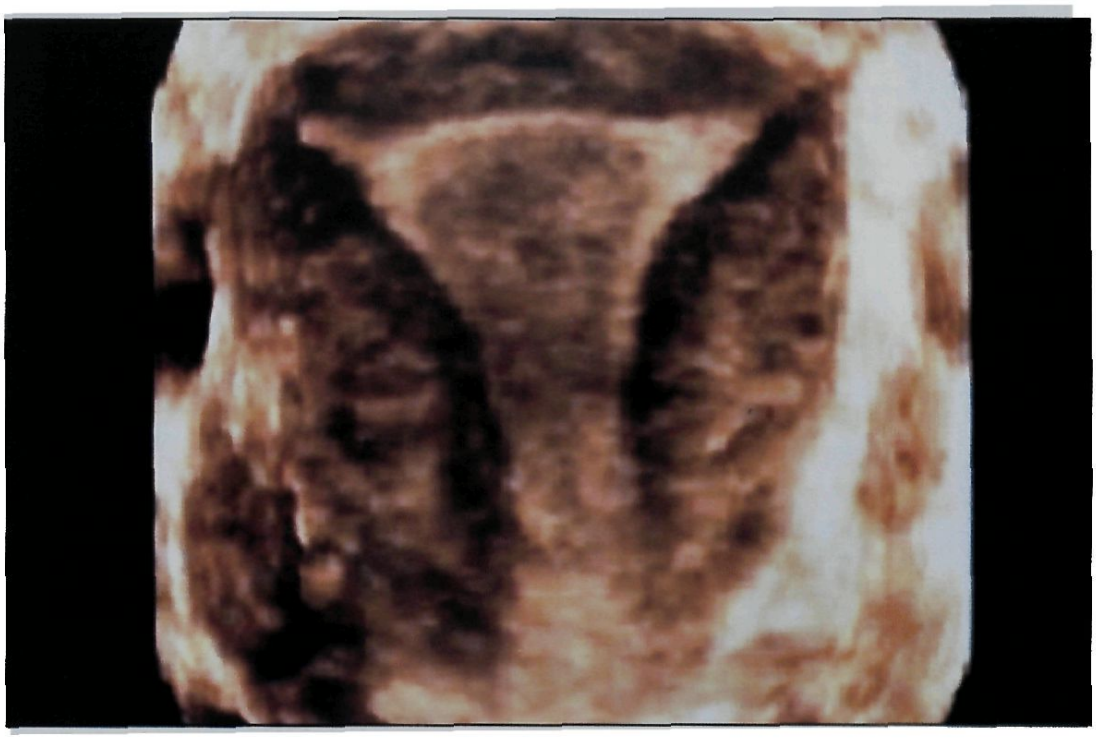

Figure 2. Normal endometrium and homogenous myometrium in 3D Ultrasound

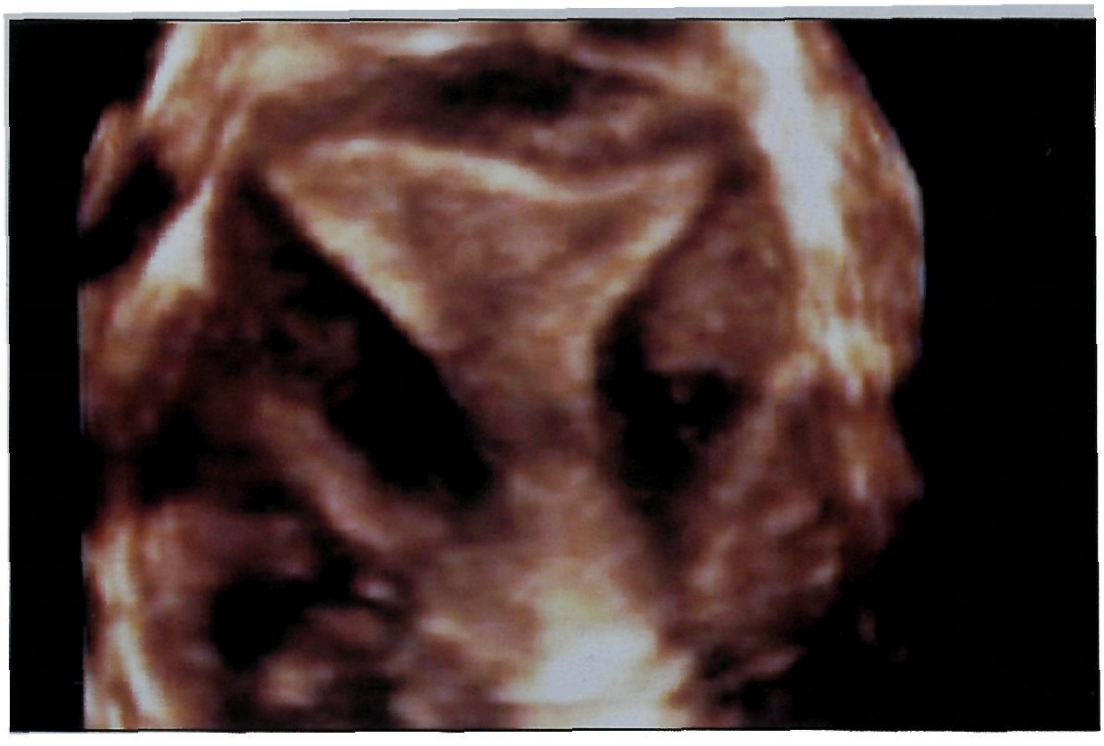

Figure 3. Focal uterine contractions (white arrows) causing indentations on the endometrium seen by 3D TV US.

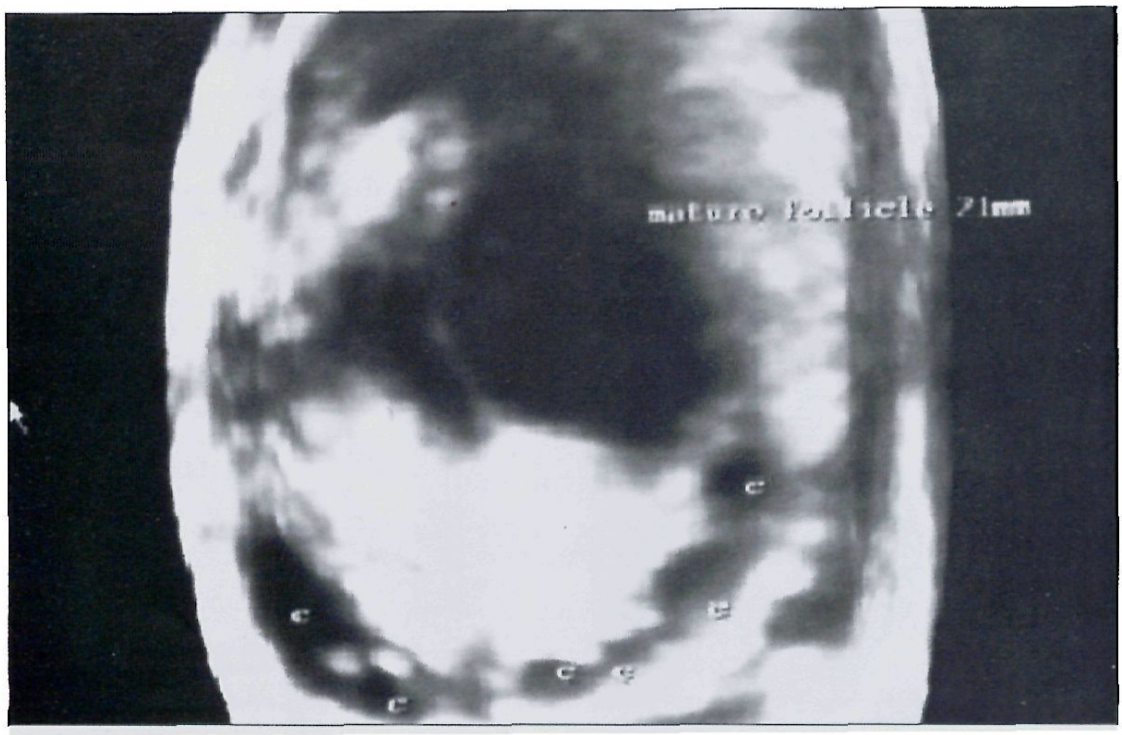

Figure 4. A mature follicle containing cumulus oophorus (white arrow) as it is seen by 3D TV US. In a case of PCO

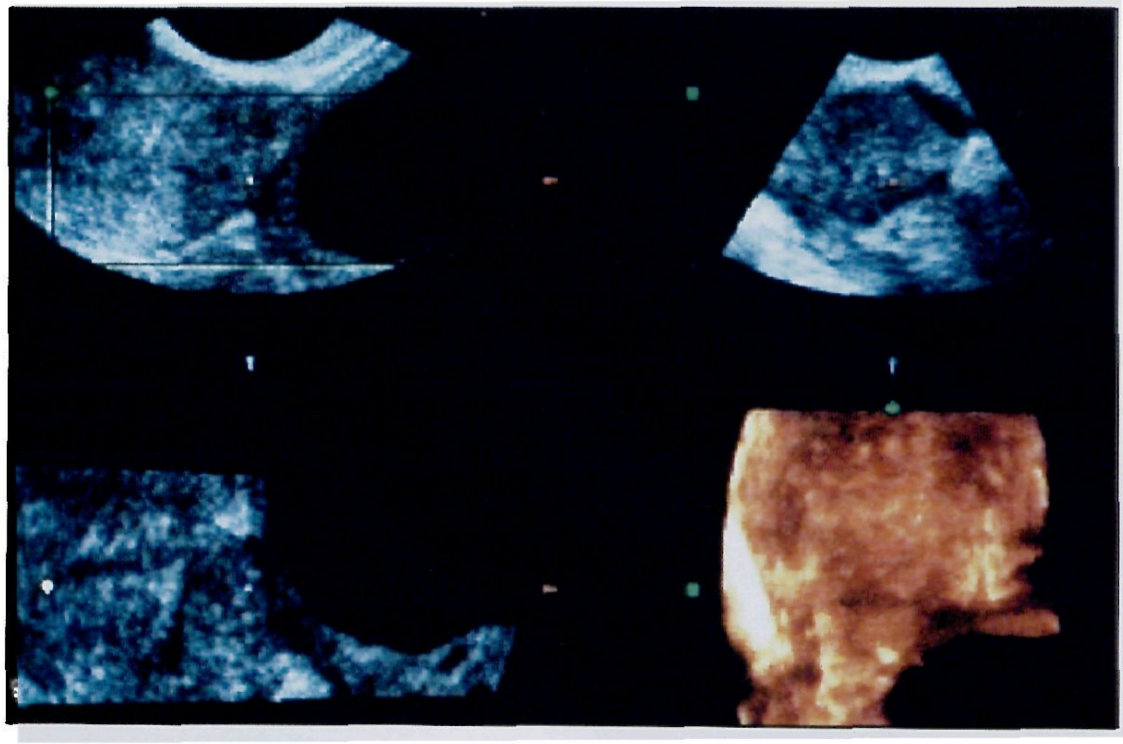

Figure 5. TV 3D US of the uterus showing a wide cervical canal containing sonolucent mucus.