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Reproductive outcome of Ovulation Induction for Polycystic Ovary Syndrome Patients according To Edessy Ovarian Reserve Score

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Abstract:

Objective: to assess the reproductive outcome (ovulation rate and pregnancy rate) in relation to a proposed Edessy ovarian reserve score after different methods of ovulation inductions.

Patients and Methods: 200 primary infertilitywomen due to PCOS were recruited for the study that conducted in Obstetrics and Gynecology Department Of Al-Azhar university hospital at Assiut from October 2015 to June 2016..Patients were classified into four groups according to methods of ovulation induction (50 patients for each): Group I: clomide, Group II: metformin +clomid, Group III:letrozole and Group IV: laparoscopic ovarian drilling. Patients included in this study wereevaluated according to Edessy Ovarian Reserve Score(EORS).

Results: ovulation rate was 76.9%, 75%,61.5% and 71.2% for group I, II, III and IV respectively. Pregnancy rate was 42.3%, 59.6%, 28.8% and 38.5% for group I, II, III and IV respectively.There were significant negative correlations between ORS and FSH, E2. There were significant positive correlation between ORS and AMH, AFC and MOV. Also, there were significant positive correlation between ORS and ovulation and pregnancy rate. In our study There is significant positive relationship between pregnancy rate and ORS (37% 0f pregnancy in all subgroups were EORS ≥ 5 while 6.5%of pregnancy in all subgroups were EORS <5)

Conclusionsand Recommendations: This study suggests that ORS that used in this study is useful for prediction of poor response to controlled ovarian hyperstimulation (COH), prediction of pregnancy rate and counseling the couples regarding their performance during ovarian stimulation.Our results suggest that AFC and AMH are better than age, FSH, E2 and MOV as regard prediction of response to COH and also in prediction of pregnancy rate.We recommend using AFC and AMH as routine markers of ovarian reserve and for prediction of poor responders for COH.

Keyword: Letrozole- Clomiphene Citrate- PCOs.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is an endocrine disorder that affects approximately 5% to 10% of all women. It occurs amongst all races and nationalities, is the most common hormonal disorder among women of reproductive age, and is a leading cause of infertility (Goldenberg, 2008).

Traditional methodology used to assess ovarian reserve has consisted of baseline serum levels of hormones such as FSH, estradiol and chronological age. Also, a number of provocative tests have been devised to indirectly

assess ovarian reserve and identify patient who might not be detected by basal hormone screening alone. Thus, despite the validity of all these tests, there still remain patients who respond poorly to stimulation despite having normal tests of ovarian reserve. This support the idea that ovarian reserve is not a simple static anatomic number of follicles but rather a dynamic process, the mechanism of which is not yet fully understood (Abha et al., 2005).

AIM OF THE WORK

The aim of this work is to evaluate the reproductive outcome of polycystic ovarian syndrome (PCO) women according to Edessy ovarian reserve score (EORS) after different modalities of ovulation induction (clomidealone ,clomide plus metformin, letrazole and laparoscopic ovarian drilling).

MATERIALS AND METHODS

200 primary infertilityAnovulatorywomen with polycystic ovary syndrome (PCOS) were selected from outpatient Infertility Clinic, Department of Obstetrics and Gynecology, Assuit Hospital, Al-Azharuniversity from October 2015 to June 2016. Women were diagnosed as PCOS based on. the ESHRE/ASRM criteria including presence of two of the following three criteria 1) oligomenorrhea or amenorrhea 2) hyperandrogenism (e.g., hirsutism, acne, alopecia) or hyperandrogenemia (elevated levels of total or free testosterone) and 3) polycystic ovaries on ultrasonography after exclusion of other endocrinopathies (The Rotterdam ESHRE/ ASRM. 2004).

Inclusion criteria: Primary infertility not less than one year.With Patent fallopian tubes by hysterosal pingography, Normal semen analysis of the husband.

Exclusion criteria: Male factors of infertility, Secondary infertility, Tubal, uterine, cervical factors of infertility, Coital problems or Hyperprolactinemia.

All patients included in this study were exposed to complete clinical and investigatory assessment as follow

CLINICAL ASSESSMENT

History: Age, duration of infertility. Menstrual history (age of menarche, presence of irregularly, type, duration of irregularly).Previous medical or surgical treatment.Family history for (PCOS, DM, Cushing's syndrome).

Clinical examination: Body weight (Kg), height (m) and Body mass index (BMI)(Kg/m^2).Normal weight is defined by a body mass index 19-24 Kg/m^2 , overweight is BMI 25-30 kg/m^2, while obesity is BMI over 30 kg/m^2, and underweight is a BMI less than 18 kg/m^2 (Redmond. 2005).Hyperandrogenism: presence of hirsutism either typical or atypical (Lobo, Carmina. 2000), and or acne.

Sonographic assessment: Transvaginalsonography was performed for all cases using transvaginal probe (6 MHZ angle 60) early in the cycle (day 3 3 to 7) in oligomenorrheic patients and randomly in amenorrheic ones forCalculation of ovarian volume using the simplified formula for a prolate ellipsoid (0.5 × length × ×width × thickness) (Swanson et al., 1981).Calculating mean follicle number per ovary of both ovaries (by scanning each ovary from the inner to the outer margin in longitudinal section) (Michael et al., 2006).

Laboratory investigations: Before the treatment, the following hormones are assayed once early in 2nd

or 3rd day of cycle in regular, oligomenorrheic ,or after progesterone withdrawal bleeding in amenorrhoeic patients: Luteinizing hormone(LH) ,Follicle stimulating hormone (FSH), Prolactin, Androstenedione, Estradiol (E2) and Anti-mullarian hormone (AMH).

All patients included in this study were given a score according to the following proposed Edessy Ovarian Reserve Score(EORS) (Table 1).

Table1. *Edessy Ovarian Reserve Score*

Score Variable	0	1	2
AMH (ng/ml)	<1	1-5	>5
FSH (mlU/ml)	>10	5-10	<5
E2 (pg//ml)	>50	20-50	<20
AFC	<3	3-9	>9
MOV (Cm^3)	< 6	6-10	>10

MOV: *mean ovarian volume.*   **AFC:** *antral follicle count*

AMH: *antimullerian hormone*

Then the patients are randomized intofour groups after obtaining a written consent and approval of the study from the ethical approval committee of Azhar Assiut faculty of medicine.

Group I: Included 50 patients received clomide 100mg daily from 3rd day to 7th day of menstrual cycle.

Group II: Included 50 patients received metformin orally (500 mg three times daily) given from the 1st to 28th day and(clomid)orally 100mg /daily from 3 to day 7 of cycle.

Group III: Included 50 patients received aromatase inhibitor letrozole 5 mg/day for 5 days starting on day 3 of a spontaneous or induced menstrual cycle.

Group IV: Included 50 patients for whomlaparoscopic ovarian drilling. Using electrocautarywas performed just after the end of menstruation using Storzlaparosopic equipment. Drilling by monopolarcautery for 4seconds using 40 watt and number of drills for each ovary range from 4 -6 according to the size of the ovary.

Patients were followed up for six months to evaluate the following:

- Ovulation rate (by ultrasoundfolliculometry and/or midluteal progesterone).
- Pregnancy rate.

Statistical analysis: Data were collected, registrated and statistically analyzed using SPSS program version 22.Student's t test and chi square tests were used. P <0.05 is considered statistically significant.

RESULTS

A total of 200 patients with an ovulatory infertility associated with PCOS were included in this study. The characteristics of this of women are shown in (Table 2) and according to a proposed EORS score are shown in (Table 3). The reproductive outcome (ovulation rate and pregnancy rate) of the studied groups are as following:

Table 2: *Socio-demographicand clinical characteristics of the study groups*

	Group I	Group II	GroupIII	GroupIV	ANOVA	p-value
Age (years)						
Mean±SD	30.02±3.30	30.85±3.27	30.65±3.06	30.23±3.22	0.724	0.539
Range	25-35	25-35	25-35	25-35		
BMI						
Mean±SD	28.49±4.47	29.02±4.56	28.56±4.78	28.57±4.13	0.149	0.93
Range	19.8-35	18.6-35	18.3-35	20.4-35		
Duration of infertility						
Mean±SD	3.74±1.81	4.02±1.9	3.7±1.38	4.04±2.49	0.429	0.733
Range	1.2-9	1.2-9.2	1.2-6.4	1-11		

Table3. *Comparison between groups according toEORS score*

	GroupI	Group II	Group III	Group IV	ANOVA	p-value
AMH						
Mean±SD	3.59±1.59	3.88±1.47	3.49±1.61	3.43±1.49	0.867	0.459
Range	0.59-6.5	0.7-6.5	0.67-6.4	0.86-6.4		
F S H						
Mean±SD	8.11±2.50	7.97±2.77	7.93±2.63	7.88±2.66	0.076	0.973
Range	2.7-13.4	2.9-13.4	2.4-13.3	2.9-13.4		
E2						
Mean±SD	54.42±36.53	54.96±33.14	56.31±34.72	53.88±31.51	0.049	0.986
Range	15-172	15-166	13-177	17-166		
MOV						
Mean±SD	8.23±2.15	8.49±2.33	8.71±2.23	9.18±2.11	1.759	0.156
Range	4.5-13	4.3-13	4.4-13	4.8-13		
AFC						
Mean±SD	11.29±7.00	11.23±6.19	11.94±6.84	11.46±6.16	0.126	0.945
Range	1-23	2-23	2-23	1-22		
ORS						
Mean±SD	5.33±1.42	5.48±1.26	5.42±1.36	5.42±1.38	0.115	0.951
Range	2-8	3-8	2-8	2-8		
BMI: Body mass indes			**ORS:** Ovarian reserve score			
MOV: Mean ovarian volume			**AFC:**Antral follicle count			
			AMH: Anti-mullerian hormone			

Table4. *Ovulation and pregnancy according to EORS*

Groups		Group I			Group II			Group IIII			Group IV	
EORS	No. %	Ov.	Preg	No.%	Ov	Preg	No.%	Ov	Preg	No. %	Ov	Preg
≥5	38 (76)	29 (58)	14 (28)	40 (80)	32 (64)	28 (56)	38 (76)	29 (58)	17 (34)	39 (78)	37 (74)	18 (36)
<5	12 (24)	2 (4)	1 (2)	10 (20)	7 (14)	4 (8)	12 (24)	6 (12)	2 (4)	11 (22)	4 (8)	3 (6)

OV: *ovulation rate – PREG: pregnancy rate=*

Table5. *Significance differences of Ovulation and pregnancy according to EORS*

	I Vs II	I Vs III	IVs IV	IIVsIII	II Vs IV	III VsIV
Ovulation	0.698	0.968	0.759	0.958	0.852	0.045
Pregnancy	0.018	0.593	0.048	0.038	0.021	0.687

P<0.05 is considered significant

DISCUSSION

Our study was performed to assess the reproductive outcome (ovulation rate and pregnancy rate) in relation to a proposed Edessy ovarian reserve score and polycystic ovary score through evaluation the effectiveness of clomiphene citrate therapy alone compared to laparoscopic ovarian drilling alone, clomiphene+metformin and letrazole inducing ovulation and pregnancy rate. In our study total of 87 patients out of 200 patients got pregnant (43.5%). In the our study there was no significant difference in women age, BMI, duration of infertility and all subgroups; The results of Group 1 were consistent with the results of Col SK Rath et al, 2006 who found that pregnancy rate42.9%. and similar to results of Eledessy M.S et al 2008 ovulation occurred in (65%) and pregnancy occurred in (30%).Group 2: Women included were subjected to CC+metformin. 64% got pregnant, this is similar to Ayaz A etal;.2013 who recorded 66.6% pregnancy rate. Group 3: Women subjected to Letrozole.70% ofpatient get ovulation this results are less than result of Eledessy M.S et al.,2014 who report ovulation 75% ,and 38% of patients of this group got pregnant, that's more than Mostafa I et al;. 2012 who reported 23.7% pregnancy in patients treated with Letrozole. And also more than Richard s et al;.2014 who showed 27.5% pregnancy rate in patients treated with Letrozole. Group 4: 42% of the patients were pregnant this is less than the results of Api et al, 2005 who reported pregnancy in 64.4%.but this results similar to Eledessy M.S et al 2008 ovulation occurred in(85%) and pregnancy occurred in (45%).As As regard correlation between pregnancy rate and different ovarian reserve tests,.In our study 48% of case had ovulated AMH between 2-5ng/dl while only 7% of ovulation >5 this confirmed with Mhran A et al in our study we found that 46.5% in all groups had ovulation have the AFC above 9(group1 34%;group 2 54%; group3; 50%; group4 48%) versus 23.5% less than 9 (group 1 28% group2 26% group3 26% group4 14%) while pregnancy occurred in 35% AFC above 6 (group1 26% group2 36% group3 54% group4 24%) versus 8.5% less than 6(group1 4% group2 6% group3 10% group4 14%) . Our results suggests that AFC is better than age and FSH as regard prediction of poor response to COH This was concluded by other investigators (Chang et al., 1998, Ng et al., 2000, Nahum et al., 2001).There is significant positive relationship between pregnancy rate and MOV in our study ovulation

in all groups 85% had MOV above 6 cm (group1 60% group2 78% group3 68% group4 66%) vesus 5% had MOV less than 6cm (group1 3% group2 4% group3 10% group4 0%) while pregnancy occurred in 36.5 % in all groupshad MOV above 6cm (group1 28% group2 78% group3 68% group4 66%) versus 3% had MOV less than 6cm (group1 2% group2 4% group3 4% group4 2%) Erdem et al., 2004, concluded that ovarian volume alone was better than age and basal.In our study in all subgroup ovulation occurred in 63% in women basal FSH <10 versus 10.5% in women basal FSH >10 however , in all subgroup pregnancy occurred in 33.5% in women basal FSH <10 (group1 26% group2 28% group3 48% group4 32%) while in women basal FSH >10 was 10% (group1 4% group2 14% group3 16% group4 6%) so there was no correlation between bFSH and ongoing pregnancy this supported by Van Rooij et al., 2004 concluded that bFSH of limited value in predicting ongoing pregnancy rate and Abha et al., 2006 suggested Combined with other markers, such as age and antral follicle count (AFC), FSH can be useful. In the present study, basal E2 showed there is no significant correlation between E2 and both of FSH and MOV or pregnancy outcome The value of cycle day 3 estradiol levels in the prediction of ovarian reserve is still debatable (Bukulmez and Arici, 2004). In the present study every patient was given a score according to the value of FSH, E2, AMH, AFC and MOV as prescribed in patient and method. There were significant negative correlations between ORS and FSH, E2. There were significant positive correlation between ORS and AMH, AFC and MOV. Also, there were significant positive correlation between ORS and ovulation and pregnancy rate. In our study There is significant positive relationship between pregnancy rate and ORS (37% 0f pregnancy women in all sub groups were EORS ≥ 5 while 6.5%of pregnancy in all subgroups were EORS <5) the results showed that all patients with ORS < 3 are poor responders. Patient with ORS 3 are borderline (55% are poor responders and 45% optimal responders). Patient with ORS with ORS <3 are good responders. This suggests that we can use this ORS for prediction of poor response to controlled ovarian hyper stimulation (COH) .this result supported by another prospective study Edessy M et al; 2013.

CONCLUSIONS AND RECOMMENDATIONS

We recommend using AFC and AMH as routine markers of ovarian reserve and for prediction of poor responders for COH Also use of such EORS for prediction of pregnancy rate and counseling the couples regarding their performance during ovarian stimulation. Further researches are suggested to be done on a larger patient cohort of wider age limits to compare the value of different ovarian reserve markers.

Conflict of interest: authors declare that no conflict of interest is present

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