EVALUATION OF THE ROLE OF ANTIMULLERIAN HORMONE (AMH), FOLLICLE STIMULATING HORMONE (FSH) AND ANTRAL FOLLICLE COUNT (AFC) AS A PREDICTOR FOR CYCLE CANCELLATION IN WOMEN DURING ANTAGONISTIC PROTOCOL FOR ICSI

By

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ABSTRACT

Background: Abnormal ovarian reserve test (ORT) results and, woman age are strong predictors of cycle cancellation during assisted reproductive technique. Use of Anti- Mullerian hormonecan helps to decide cycle cancellation during ICSI at different age groups.

Objectives: To evaluate the role of biomarkers (Anti-Mullerian, FSH hormones) and antral follicle count, as predictors of cycle cancellation in women during antagonistic protocol ICSI.

Participants and Methods: Retrospective study of 491 cases received ovarian stimulation for ICSI by antagonist protocol during the period of 2013-2014, at Misurata National Infertility management center was conducted. Candidate characteristics were collected, endocrine data, collected during early follicular phase (D3) of the stimulating cycle (FSH, AMH). Sonographic data were collected during early follicular phase by counting antral follicles in both ovaries, and after stimulation. An antagonist protocol was applied to all patients of different age groups.

Results: Cycle cancellation occurred in 24.64% of stimulated patients. The mean age for the patients with cancelled cycles was higher than the age of those with completed cycles, and 16.7% got pregnant. The age of the women who got pregnant was lower than the age of non-pregnant women . AMH was a fair test for the discrimination between cancelled and completed cycles with a highly significant value . When investigating the three age groups, AMH was a fair test for the discrimination between cancelled and completed cycles for age group >39 years.

Conclusion: Serum AMH levels can be used as a fair predictor test for cycle cancellation especially in older age group patients. Its use can help to individualize treatments protocols and counselling in different age groups. Counselling plays an important role in addressing psychological issues discussing the risks of cycle cancellation due to costbenefit, and treatment options to ensure maximal therapy benefits and outcomes.

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Key words: Anti-Mullerian hormone, cycle cancellation. different age groups, antagonistic protocol ICSI.

INTRODUCTION

Optimal ovarian response is a key part of controlled ovarian stimulation (COS) procedures. The ability to predict ovarian reserve is crucial to obtain an adequate response and an optimal outcome from assisted reproductive technologies (ART), and offers the possibility of tailoring COS protocols for each individual patient. *(La Marca and Sunkara, 2014).*

It is well acknowledged that some named predictors of ovarian reserve markers including serum basal follicle stimulating hormone (FSH) concentration, antral follicle count (AFC) and serum antimullerian hormone (AMH) concentration can be used as predictors of ovarian responses to gonadotropin stimulation during ICSI treatment *(Li et al., 2013).*

Although, some reports have shown a poor predictive performance of these markers, other reports indicate these predictors can be used accurately for estimation of success rate before initiation of the therapy process *(Broer et al., 2009).* The number of antral follicles as measured by vaginal ultrasound was even superior to basal day 3 FSH and BMI for predicting the number of oocytes retrieved for IVF *(Ng et al., 2000).* Ovarian reserve can be considered normal when stimulation by exogenous gonadotropins will result in development of 5-12 follicles from both ovaries and the retrieval of the same number of healthy oocytes *(Broekmans et al., 2012).*

AMH is specifically expressed in granulosa cells of small growing follicles, and highest expression is observed in pre-antral and small antral follicles. AMH is no longer expressed by mural granulosa cells during the FSH-dependent stages of follicular growth, nor is it expressed in atretic follicles *(Van Houten et al., 2010).* However, expression persists in the cumulus cells of pre-ovulatory follicles. AMH has also been suggested to exert a physiological effect on antral follicles in the human ovary before final selection. It has been suggested that AMH may exert a physiological role in down-regulating the aromatizing capacity of granulosa cells until the time of follicular selection *(Kelsey et al., 2011).* In comparison with other ovarian reserve assessment tests, AMH is characterized by several advantages. AMH levels are stable throughout the menstrual cycle and between cycles andcan be measured at any day of the cycle. AMH levels are not affected by other hormonal variations, including the use of oral contraceptives *(Bentzen et al., 2012).* AMH is not detected in women until puberty and reaches its highest levels at age 24.5 years. With increasing age, the number and quality of oocytes decline. Accordingly, the AMH level also declines and is lowest at menopause; later, it is not detected at all *(Ubaldi et al., 2005).*

Basal follicle stimulating hormone (FSH), provides an indirect marker as its level willincreasewith advanced age. High level of FSH represent small cohort size. Basal FSH levels of less than 10 to 12 milli international units/mL are considered normal *(Kligman, and Rosenwaks, 2001).*

There are not enough studies assessing the predictive value of these markers in different age levels since some ovarian reserve markers may have different accuracy in different ages.

The aim of the current study was to examine the predictive value of AMH, FSH, and AFC to predict cycle cancelation in ICSI cycle in population with different age groups.

PARTICIPANTS AND METHODS

A retrospective cohort study of women (700 cases) receiving treatment during the period of 2013-2014, for ICSI at Misurata national infertility management center, Libya toevaluate the role of biomarkers(Anti-Mullerian, FSH hormones) and antral follicle count, as predictors of cycle cancellation in women during antagonistic protocol ICSI.

Women between the ages of 20-45 years were included in this study. Only 491 cases were involved in the study as women with history of previous ovarian surgeries, polycystic ovarian syndrome and endometriosis were excluded.

Division of women was into three categories according to age, from 20-29 years, 30-39, and older women from 40-45 years. AMH, FSH and AFC can be used as predictors of cycle cancellation.

- AMH measurement was done and quantified in the morning of day 3 of the menstrual cycle by the immunoassay supplied by Diagnostics systems laboratories (DSL) (a Roche Hitachi) that has a sensitivity of 0.043 pmol/l (0.006 ng/ml). AMH in pmol/l units (7.18 pmol/l of AMH is equivalent to 1 ng/ml of AMH).

- FSH was measured in the morning of day 3 of the menstrual cycle. It was reported in mIU/ml, by Electro Cheiluminescence Immuno using Access® technology (Beckman Coulter Inc).

- The AFC and normal anatomy of pelvic organs were determined by performing transvaginal ultrasonography (TVS). The main outcome measures were the number of retrieved oocytes.

STIMULATION PROTOCOL

Antagonist protocol was applied on study population. On day2 of the cycle, the treatment with gonadotropin human menopausal gonadotropin (menogone) was fixed daily in dose of 250 IU HMG (Menogon, Ferring, Kiel, Germany). The ovarian response monitored by transvaginal US from the sixth day of stimulation and repeated every other day.Gonadotropin doses were introduced. Antagonist (Cetrorelix; Serono) started 0.25 mg daily on day 6 of stimulation cycle. When at least three follicles larger than 18 mm or more were observed, 10000 IU of HCG (Pregnyl, Organon UK) was administered intramuscularly. Thirty-six hours later, follicles were collected by transvaginal ultrasonography-guide under general anesthesia. The number of retrieved oocytes was recorded. Ovarian response was defined.

Poor response (Cycle cancellation) in our study: The presence of at least two of the following characteristics: Advanced maternal age ≥ 40 years, three or fewer oocytes on retrieval, low AMH, in the present study we took 2pmol\l as cut off level of AMH according to literature (Calamera et al.,2013). Average response: OCR of 4–15 and hyper response: OCR of >15.

After fertilization of oocytes with sperm in the laboratory, embryos were

transferred. Serum β-hCG levels were measured 12-14 days after transfer to assess conception. All pregnant women received Cyclogest suppository (Alpharma, Barnstaple, UK) 400 mg daily until 12 weeks of gestation to support luteal phase.

Statistical analysis:

During data analysis, age and biomarkers levels (AMH, FSH, and AFC)were presented as mean, standard deviation, and range. The Mann–Whitney U test was used for comparison of the non-parametric data.Sensitivity was defined by the association of lower hormone level with cancelled cycles, while specificity was defined by the association of higher hormone levels with completed cycles or completed cycles and pregnancy. An area from 0.9 to 1 represents excellent test, from 0.8 to 0.9 good test, from 0.7 to 0.8 fair test, from 0.6 to 0.7 poor test, and from 0.5 to 0.6 fail test. Logistic regression analysis was used to assess the association of AMH and other variables with cycle cancellation. Results of all tests were considered significant if its P value was <0.05.

RESULTS

The mean age of our participants was 37.68 (SD ± 4.73). Out of the 491 cases studied 121 patients (24.64%) were cancelled, and 82 cases were found to be pregnant (16.7%). The mean age for the patients with cancelled cycles is higher than the age of those with completed cycles (p=0.0075) statistically significant. Also, the age of the women who got pregnant is lower than the age of non-pregnant women (p=0.0059) (Table 1).

Table (1): The age in the studied cases

Cases	No.	Mean $\pm$ SD	Range	P value
All cases	491	37.68$\pm$ 4.73	20- 45	
Cancelled	121	38.51$\pm$ 4.84	20-45	0.0075
Completed	370	37.41$\pm$4.67	24-45	
Non-pregnant	288	37.71$\pm$ 4.76	24-45	0.0059
Pregnant	82	36.35$\pm$ 4.18	24-45	

The AMH level shows mean ± SD (2.46 ± 2.36 pmol/l) and the range (0.1–19.4 pmoL/l) of all cases. Cancelled cycles had a lower level than completed cycles (P =0.001), and non-pregnant had non-significant lower level than pregnant (P = 0.0562). The younger age group had higher AMH level (p= 0.001). The FSH level shows mean ± SD (8.24± 3.86 IU/ml) and the range (0.24–33.72) of all cases. Cancelled cycles had a higher level than completed cycles (P =0.005), and

non-pregnant had higher level than pregnant (P = 0.0201). The difference in the FSH level between younger and older age groups is insignificant. The AFC level shows mean ± SD (5.42 ± 3.95) and the range (0-20) of all cases. Cancelled cycles had a lower level than completed cycles (P =0.001), and non-pregnant had lower level than pregnant (P = 0.0084). The younger age group had higher AFC (p= 0.001) (Table 2).

Table(2): The AMH, FSH, and AFC levels in the studied cases

Cases	No.	AMH Mean+SD	Range	P value	FSH Mean+SD	Range	P value	AFC Mean +SD	Range	P value
All cases	491	2.46+2.36	0.1-19.4		8.24+3.86	0.24-33		5.42+3.95	0-20	
Cancelled	121	1.51+1.18	0.1-6.2	0.0001	9.63+5.15	1.6-33	0.0005	4.09+3.22	0-20	0.0001
Completed	370	2.77+2.56	0.3-19.4		7.78+3.21	0.24-26		5.86+4.07	0-20	
Non-pregnant	288	2.70+2.63	0.3-19.4	0.0562	8.02+3.32	0.24-26	0.0117	5.57+4.0	0-20	0.0084
Pregnant	82	3.01+2.3	0.5-11.7		6.92+2.62	1.3-17		6.86+4.18	0-18	
Age 20-29	30	4.32+4.34	0.8-19.4		7.92+3.23	0.24-14		8.33+4.55	0-18	
Age 30-39	266	2.63+2.36	0.2-16		8.09+3.67	0.57-23		5.97+4.16	0-20	
Age 40-45	195	1.95+1.66	0.1-11.7		8.48+4.19	1.6-33		4.23+3.09	0-15	

AMH was a fair test for the discrimination between cancelled and completed cycles with a highly significant value (ROC–AUC 0.7103, 95% CI 0.65624-0.76434). When investigating the three age groups, AMH was a fair test for the discrimination between cancelled and completed cycles for age group >39(age group 3) (ROC–AUC 0.7434, 95% CI 0.66980-0.81696) but a poor test for the discrimination for the age group 1 (ROC–AUC 0.6118, 95% CI 0.38846-0.83514) and age group (ROC–AUC 2 0.6761, 95% CI 0.59038- 0.76185) (Fig.1).
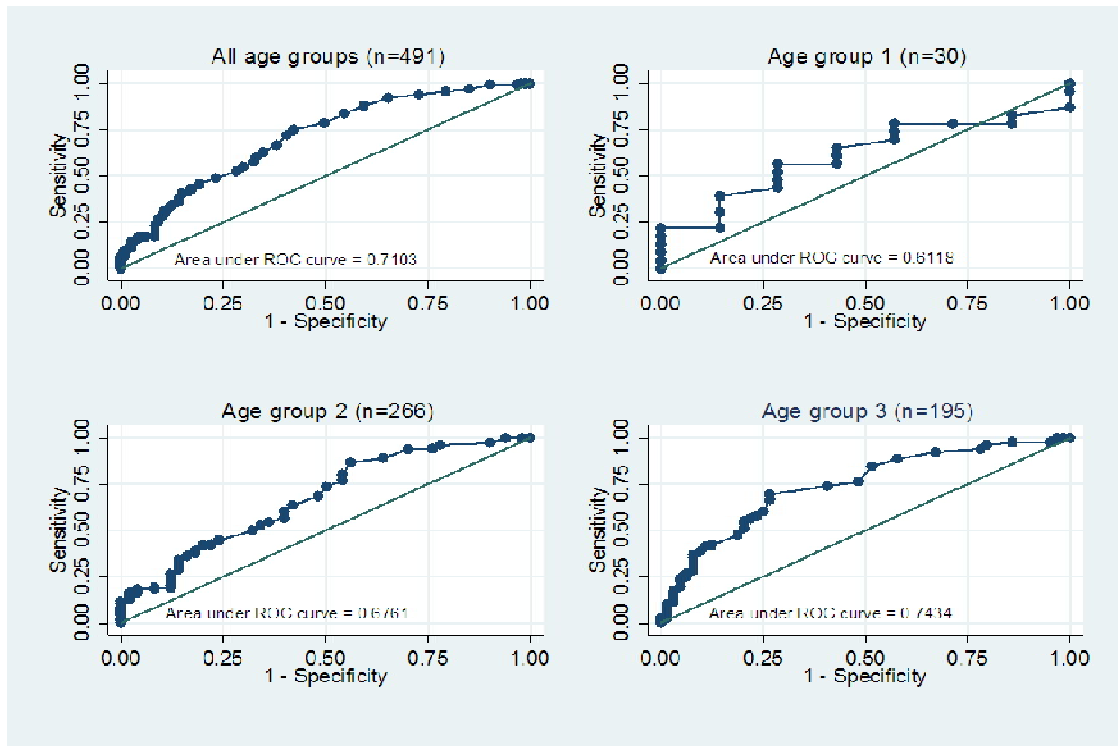
Figure(1): ROC–AUC for AMH prediction of cancelled and completed cycle

In the present study, we examined biomarkers and antral follicular count under each age group according to the quartiles of AMH. Table 3 shows the lowest and highest quartiles. We observed that, in all age groups, AMH and AFC tended to increase with increasing quartiles of AMH and FSH level tends to decrease. Also, women in advanced age group (age group 3)showed the lowest AMH level and antral follicular count, and showed the highest FSH level relative to the other age groups. The women in the advanced age group with the highest AMH quartile showed significantly higher AMH and AFC than those in women in the lowest AMH quartile (Table 3).

Table (3): Patients' characteristics according to age and AMH level

Groups Parometers	Group 1: age 20-29 (n=30)			Group 2: age 30-39 (n=266)			Group 3: age 40-45 (n=195)		
AMH	Low AMH (n=8)	High AMH (n=6)	P-value	Low AMH (n=73)	High AMH (n= 6)	P-value	Low AMH (n=73)	High AMH (n=45)	P-value
Age(years)	25.5	26.3	NS	36.2	35.2	0.0141	42.43	41.95	NS
AMH	1.41	10.43	0.0019	0.86	5.88	0.0001	0.63	4.22	0.0001
FSH	8.26	6.85	NS	9.71	6.77	0.0001	9.84	7.73	NS
AFC	6.25	12.67	0.0233	3.71	9.15	0.0001	2.6	6.51	0.0001

Low AMH =Lowest AMH quartile for the age group
High AMH= Highest AMH quartile for the age group

The logistic regression, the odd ratio of having a cycle cancellation for young patients (20-39) with level of AMH of 2pmoL/l or less was double the odds for those with AMH level more than 2 pmoL/l in the same age group (age group 1 &2)(p=0.018). The odds of having a cancelled cycle for women of advanced reproductive age (40-45) with AMH (2 pmoL/l or less) is 5 times was more than those with AMH level more than 2 pmoL/l in the same age group (age group 3). When adding FSH and AFC to the logistic regression, the prediction of cycle cancellation is only significant for women of advanced reproductive age (i.e. group 3). Patients with AMH level of 2pmoL/l or less are 4 times more likely to have a cancelled cycle and patients with FSH level more than 10 are 3 times more likely to have a cancelled cycle for patients who are 40-45 years old(Table 4).

Table (4): Logistic regression analysis of the variables, for the prediction of cycle cancellation

Groups / Parameters	Group 1&2: age 20-39 (n=296)			Group 3: age 40-45 (n=195)		
	Odd ratio	95% CI	P-value	Odd ratio	95% CI	P-value
Univariate analysis						
AMH	2.06	1.131-3.759	0.018	5.06	2.235-11.479	0.0001
Multivariate analysis						
AMH	1.83	0.945-3.551	NS	4.35	1.801-10.538	0.001
FSH	1.42	0.365-1.343	NS	3.31	0.149-0.608	0.001
AFC	1.09	0.480-1.740	NS	1.29	0.314-1.887	NS

AMH, anti-müllerian hormone; FSH, follicle stimulating hormone; AFC, antral follicle count .
Statistically significant: P<0.05, NS: not significant.

The AMH cut off point of 2 pmoL/l was chosen to be consistent with the literature which defines this point as a point of absolute poor response *(Calamera et al., 2013)*. Similarly, the cut off point for FSH is 10 *(Le et at., 2013)* and the cut off point for AFC is 12 *(Ng et al., 2000* and *Broekmans et al., 2012)*.

DISCUSSION

In this study, we investigated the use of AMH and other biomarkers in the detection of cycle cancellation during ART treatments (ICSI). ART are expensive for healthcare systems or private practices and represent a stressful situation for the couple, therefore, the necessity exists for optimization of the evaluation of the ovarian reserve to minimize the uncertainty of the outcome of ART procedures *(Calamera et al., 2013)*.

Broekmans stated that female age is considered the main predictor of ovarian aging, there is a decline in fertility after the age of thirty years which will accelerates thereafter. The rate of decline in fertility may vary considerably between women of the same age. The availability of a test capable of providing reliable information regarding a woman's individual ovarian reserve within certain age category would enable to individually tailor treatment protocols *(Broekmans et al., 2012)*.

La Marca stated that the correlation with oocyte yield and AMH is better than the association observed for the age of the patient, day3FSH, estradiol, or inhibin B *(La Marca et al., 2010)*.Hendriks and Broer stated that the number of antral follicles represents a good estimator of the primordial follicle pool and, therefore, of the quantitative aspect of the ovarian reserve *(Hendriks et al., 2007*, and *Broer et al., 2009)*.

In the current study, we investigated the value of morphometric and basal endocrine parameters during the follicular phases as predictors of cycle cancellation. We found significant evidence that AMH is a reliable predictor of cycle cancellation in advanced age women (>40 years old). In the present study, the patients were divided into three groups based on their age. AMH was found to be a fair test to discriminate between completed and cancelled cyclesin advanced age women (>40 years old). Also, we found significant relationship between low level of AMH and cycle cancellation in advanced age women (>40 years old).Our results are in line with those previously reported by other author (Kailasam)

showing that AMH is a useful marker for predicting cycle cancellation, and poor response to ovarian stimulation *(Kailasam et al., 2004)*.Broerstated that AMH represents a better predictor than the other classically associated parameters such as FSH, estradiol and age *(Broer et al., 2009)*. Interestingly, our data shows the special importance of serum AMH in women aged >40.The chance of cycle cancellation in young patients (20-39) with low level of AMH aretwo times more likely than other women in the same age group. For the women in advanced age group, the likelihood of having a cancelled cycle for women with low AMH is five times more than other women in the same age group. When having other predictors (FSH and AFC) in the analysis, the AMH still predicts cycle cancellation for women in advanced age group. High FSH level also shows significant prediction of cycle cancellation but only for women in advanced age group.

CONCLUSION

According to results observed in this study, serum AMH levels can be used as a fair predictor test for cycle cancellation especially in older age group patients. Its use can help to individualize treatments protocols and counselling in different age groups.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

REFERENCES

1. **Bentzen G, Forman L, Pinborg A, Lidegaard ? , Larsen C, Friis-Hansen L, Johannsen T and Nyboe A. (2012):** Ovarian reserve parameters: a comparison between users and

non-users of hormonal contraception. Reprod. Biomed Online, 25(6): 612-19.

2. **BroekmansF,BroerS,FauserB andMacklonN (2012):** Prognostic testing for ovarian reserve. Textbook of assisted reproductive techniques. 4th edition. Ed, Gardner, D. Weissman, A. Informa Healthcare, 2: 40-8.

3. **Broer L, Mol B, Hendriks Dand BroekmansF (2009):** The role of antimullerian hormone in prediction of outcome after IVF: comparison with the antral follicle count. FertilSteril.;91:705–14. [PubMed].

4. **Calamera P, Mariano G, Buffone G, De Vincentiis S, Rey R and Olmedo S (2013):** Serum AMH level can predict the risk of cycle cancellation and the chances of good ovarian response independently of patient's age or FSH. JBRA Assisted Reproduction, 17 (2):101-8.

5. **Hendriks J, Kwee J, MolW, Velde Rand Broekmans J (2007):** Ultrasonography as a tool for the prediction of outcome in IVF patients: a comparative meta-analysis of ovarian volume and antral follicle count. FertilSteril., 87:764-75.

6. **Kailasam S, Keay P. Ford W and Jenkins M (2004):** Defining poor ovarian response during IVF cycles, in women aged <40years, and its relationship with treatment outcome. Hum Reprod., 19: 1544–7.

7. **Kelsey W, WrightP, Nelson M, Anderson Aand Wallace H (2011):** A validated model of serum anti-Müllerian hormone from conception to menopause. PLoS One, 6(7): e22024.

8. **Kligman I and Rosenwaks Z (2001):** Differentiating clinical profiles: predicting good responders, poor responders, and hyperresponders. FertilSteril., 76:1185–90.

9. **La Marca A and Sunkara SK (2014):** Individualization of controlled ovarian stimulation in IVF using ovarian reserve markers: from theory to practice. Hum Reprod. Update, 20: 124-40.

10. **La Marca A, Sighinolfi G, Radi D, Argento C, Baralchi e, Artenisio A, Stabile G and Valope A (2010):** Anti- Mullatian hormone (AMH) as a predictive marker in assisted reproductive technique (ART). Hum Reprod Update, 16: 113-30.

11. **Li W, Lee C, Lau Y, Yeung S, Ho C and Ng H (2013):** Role of baseline antral follicle count and anti-Mullerian hormone in prediction of cumulative live birth in the first in vitro fertilization cycle: a retrospective cohort analysis. PLoS One, 8: e61095. [PMC free article] [PubMed].

12. **Ng H, Tang S and Ho C (2000):** The significance of the number of antral follicles prior to stimulation in predicting ovarian responses in an IVF programme. Hum Reprod., 15:1937–42. [PubMed].

13. **Ubaldi M, Rienzi L, Ferrero S, Baroni E, Sapienza F, Cobellis Land Greco E (2005):** Management of poor responder in IVF. Reprod Biomed Onlin,10:235–46.

14. **Van HoutenL,Themmen Pand VisserA (2010):** Anti-Mullerian hormone: regulator and marker of ovarian function Ann. Endocrinol., 71: 191–7.

تقييم دور هرمونات كدليل موثوق به لإلغاء الدوره التحفيزيه خلال بروتوكول المعادية ICSI للنساء في سن الإنجاب المتقدمة

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**باحثه احصائيه جامعه كاليدونيا جلاسكو ـ جامعه جلاسكو – المملكه المتحدة

خلفية البحث : يمكن أن يساعد استخدام المؤشرات (FSH, LH and Anti- Mullerian) مـع احتياطي المبيض (ORT) و عمر المراه علي اتخاذ قرار إلغاء استكمال الدورة التحفيزيـه خـلال بروتوكول الحقن المجهري في الفئات العمرية المختلفة.

الهدف من البحث: لتقييم دور هرمون مضـاد موللريـان كمؤشر لإلغاء الدوره التحفيزيـه في النسـاء خلالبروتوكول عدائيه الحقن المجهري.

المشاركات والأساليب: دراسه استعاديه وصفيه لعدد ٤٩١(حالـه) . الحـالات تلقت تحفيز المبيض استعدادا للحقن المجهري بواسطة البروتوكول المعادي خلال الفتره (٢٠١٣-٢٠١٤) ، في المركز الوطني لمعالجه العقم بمصراته- ليبيا . تم تقشيم المشاركات لثلاثه فئات عمريه . وجمعت خصائص المرشحين ، وبيانات الغدد الصماء ، خلال مرحله البصيلات المبكرة (D3) للدورة المحفزة (FSH، amh). كـذلك جمعـت البيانـات السوكسـوغرافيه خـلال مرحلـه البصيـلات المبكـرة مـن خـلال عـد البصيـلات الطيفيـة في كـلا المبيضـين ، و كـذلك بعـد التحفيـز. وطبق بروتوكول المعاديـة ICSI علـي جميع المرضي من مختلف الفئات العمرية.

النتائج: اوضـحت نتـائج هـذه الدراسـه انـه حـدث إلغـاء (٢٤,٦٤ ٪) مـن المرضـي المحفـزات وكـان متوسط العمر بالنسبة للمريضات الذين يعانون من إلغاء الدورات اعلي من عمر أولئك مع الانتهاء من دورات (p = 0.0075) ، وحدث حمل في (١٦,٧ ٪) من الحالات. ويقل عمر المراه الحامل عـن سن المـراه غير الحامل (p = 0.0059). وكانت المبـادرة اختبـارا عـادلا للتمييز بين الدورات الملغيـة والمكتملـة ذات القيمـة البالغـة الاهميـه (ROC-0.7103، 0.65624-0.76434 CI 95%). وعنـد التحقيق في الفئات العمرية الثلاث ، كانت الحركة اختبارا عادلا للتمييز بين الدورات الملغيـة والمكتملـة للفئات العمرية < ٣٩ سنهمن العمر و كان هرمون AMH هو الاكثراهميه في المؤشرات الثلاثه.

الاستنتاج: هرمون Anti-Mullerian مؤشر موثوق به لإلغاء الدوره التحفيزيه خلال بروتوكول ICSI المعادية

التوصيات: يمكن استخدام مستويات هرمون AMH كاختبار التوقع العادل لإلغاء الدوره التحفيزيه خاصه في فئات النساء الاكبر سنا. كما ان يساعد لإضفاء الطابع الفردي علي بروتوكولات العلاج وتقديم المشورة في مختلف الفئات العمرية. وتؤدي المشورة دورا هاما في معالجه القضايا النفسانية ومناقشه امكانيه إلغاء الدورة التحفيزيه وذلك للمساعدة في تخفيف التكلفه العلاجيه.