Research Article

The Predictive Value of Anti-Mullerian Hormone on Pregnancy Rate After IVF

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Abstract

Introduction: The role of AMH in the ovary is to participate in the regulation of ovarian function, especially in follicle development and selection. It inhibits the initiation of human primordial follicle growth and prevents multiple selection of a dominant follicle by reducing the sensitivity of follicles to follicle stimulating hormone (FSH). Several reports suggest that AMH might be a better predictor of ovarian responses to controlled ovarian hyperstimulation (COS) than traditional parameters such as age, FSH, estradiol (E_2) and inhibin B (INH-B). So, the objective of this study was to investigate the predictive value of anti-Mullerian hormone (AMH) on fertilization rate (FR), implantation rate, blastocyst development, embryo quality, chemical pregnancy, clinical pregnancy and ongoing pregnancy after ICSI. **Method:** In this prospective clinical trial outcomes were followed in 60 women undergoing cycles of IVF/ICSI within El-Minia university hospital. AMH concentration was estimated in pooled FF on day of oocyte pickup. Cycles were sorted into low and high groups according to median (50 th centile) values of measurement. The fertilization rate (FR), implantation rate, blastocyst development, embryo quality, chemical pregnancy, clinical pregnancy and ongoing pregnancy after ICSI were counted as the main outcomes. **Results:** Low FF AMH group shows significantly higher percentage of top-quality oocytes (67.1±24.3 vs. 49.6 ± 30.3 %, P =0.014), fertilization rate (83.9±20.9 vs. 72.4 ±21.4%, P =0.021), clinical pregnancy (57.57 vs. 16.67%, P >0.0001), and embryo implantation rates (57.7 vs. 16.7% , P =0.001) compared to high FF AMH group. FF AMH shares an inverse correlation with FF E2 (Pearson r = −0.409, p <0.001) and clinical pregnancy (Pearson r = −0.618, p<0.001). Threshold value of FF AMH for pregnancy is >1.75 ng/mg protein. Receiver operating characteristic analysis showed that the sensitivity of FF AMH at predicting CPR was 73.1 %; the specificity was 85.3 % and ROC_{AUC} was 0.715 (P < 0.0001). **Conclusion:** FF AMH is a plausible specific indicator of functional viability and quality of oocyte in IVF cycles.

Key words: ICSI, FF AMH, clinical pregnancy, implantation rate, oocyte quality

Introduction

Antimullerian hormone (AMH), also referred to as mullerian inhibiting substance (MIS), may be a dimeric glycoprotein member of the reworking growth factor-β family. AMH is secreted by granulosa cells within preantral and early antral follicles, less than 4 mm in diameter. Its secretion decreases because the antral follicles begin to grow, and stops when the follicles are larger 8 mm in diameter, or when atresia occurs (Durlinger et al., 2002). A previous study has showed that the performance of AMH as a predictor of poor ovarian response was very almost like that achieved with antral follicle counts (AFC) (Broer et al., 2009). However AFC was tested within the early stage of the cycle and was evaluated using ultrasound (Broekmans et al., 2006).

Thus the accuracy and stability of AFC testing is inferior thereto achieved with serum AMH. Previous studies have found associations between AMHs (including serum AMH and follicle fluid AMH), fertilization rate, blastocyst development, embryo quality, pregnancy outcome and birth rate (LBR). Some studies showed that prime serum AMH levels on Day 3 were correlated with high numbers of mature oocytes, leading to more embryos and ultimately a better clinical pregnancy rate (Lekamge et al., 2007).

Other workers found no associations between basal serum AMH levels and embryo quality (Lie Fong et al., 2008). An association has also been found between follicle fluid AMH (FF AMH) levels and therefore the quality of embryos in

patients with polycystic ovary syndrome (PCOS) (Mashiach et al., 2010). However, during this study population there was no correlation between FF AMH and therefore the degree of maturation of retrieved oocytes, or the success of fertilization.

The aim of this work is to know the predictive value of anti-Mullerian hormone (AMH) on fertilization rate (FR), implantation rate, blasto-cyst development, embryo quality, chemical pregnancy, clinical pregnancy and ongoing pregnancy after ICSI .

Materials and methods

This quasi-experimental study was conducted in the Department of Obstetrics and Gynecology, El-Minia Infertlity center Faculty of Medicine, El-Minia University and two private centers during the period from June, 2016 to June, 2018 after being approved by the department ethical Committee. The study population included60 women who had their first cycles of intracyto-plasmic sperm injection (ICSI) treatment .

Inclusion criteria:

The women with age ≤38 years ,The body mass indexes (BMI between 18 and 29 kg/m2,Day 3 serum FSH levels <12 IU/L ,The women with a history of regular, ovulatory menstrual cycles (every 24 to 35 days)&The women with no previous history of ovarian surgery.

Exclusion criteria:

Women with ovarian cyst (> 3 cm in diameter), Women with PCOS, Women with endometriosis & Women with a history of ovarian surgery or endocrine disorders.

Methods:

- All Patients were subjected on Day 3 of the menstrual cycle and prior to treatment, blood samples for assay of AMH, FSH, E2 and luteinizing hormone (LH) were collected by venipuncture.
- Ultrasound scanning with a 6.5-MHz transva-ginal probe was used to count the number of antral follicles in each ovary that had a mean diameter of 3 to10 mm.
- Anti-Mullerian hormone was measured using the Immunotech Enzyme Immune Assay kit consistent with the handbook. On the day of ovum pick-up (dOPU), under transvaginal ultrasound guidance, fluid from three to 5 dominant follicles was gently and thoroughly aspirated employing a 10 mL syringe. The fluid was maintained at 37 °C until the oocyte were found and isolated.
- The level of AMH in FF was measured as described above.
- All patients received standard ovarian stimulation protocol with recombinant FSH (r-FSH) under pituitary suppression with a GnRH agonist.
- Briefly, the GnRH agonist (Decapeptyl, 3.75 mg Ferring, Kiel, Germany) was administered subcutaneously in the mid-luteal phase of the previous menstrual cycle.
- Stimulation commenced two weeks later, when the circulating E2 level was less than 150 pmol/L, the thickness of endometrium was less than 5 mm, serum LH was less than 5 IU/L and a vaginal ultrasonographic scan showed an absence of follicles more than 10 mm in diameter.
- The criteria for human chorionic gonado-tropin (HCG) administration is the presence of three or more follicles ≥17-18 mm in diameter with a consistent rise in serum estradiol concentration.
- Oocyte aspiration was performed using vagi-nal ultrasound, 34 to 36hr after human chori-onic gonadotropin injection.
- Egg quality: metaphase II oocyte collected from the patient varying in qualities, both nuclear and cytoplasmic maturation have to be comleted in aco-ordinate mode to ensure opitimal condition for subsequent fertili-zation. Disturbances of these processesmay result in different morpholigical abnor-malities, depending on wether nuclear or cytoplasmic maturation has been affected
- Intracytoplasmic sperm injection (ICSI) was performed using standard procedures and the embryos were transferred two or three days

later. The luteal phase was supported with 40 mg progesterone administration by daily injection.

- A pregnancy test was carried out on Day 14 after embryo transfer.
- After two weeks, a transvaginal ultrasound was performed to confirm pregnancy
- Study endpoints were: Fertilization rate (FR), the good quality embryos, clinical pregnancy and biochemical pregnancy.
- Then follow up of the pregnant women by serial ultrasound was done.

Ethical consent:

The nature of the study was clearly explained to each patient. An informed written consent was obtained. Also, an approval from the local committee was taken.

Results

Results were analyzed using SPSS (ver. 25.0; IBM, Chicago, IL, USA). Quantitative data was displayed in the form of mean ± standard deviation (SD). Qualitative data was demonstrated through figures of frequency and percentage.

Table (1): This table showed that age, BMI, baseline AMH and E2d HCG showed statistical insignificant difference between both groups while, FF E2 was significantly higher among low than high group (p=0.001).

Table (2): This table showed significantly higher rates of fertilization, more number of top-quality oocytes, and higher clini-cal pregnancy and embryo implant-tation rates than high FF AMH group. However, the twin pregnancy rates were comparable and did not differ significantly between the two groups.

Figure (1): This figure showed that Clinical pregnancy had significant indirect correlations with AMH.

Figure (2): ROC curve showed that AMH had 73.1% sensitivity and 85.3% specificity for predication of clinical pregnancy.

Table (1): Hormone data in low vs. high FF AMH groups**:**

	Low FF AMH (≤1.720 ng/mg protein) (n=30)	High FF AMH (>1.720 ng/mg protein) (n=30)	Test value	p-value
Age (years)	32.6±1.09	32.5±1.04	0.482	0.631[1]
BMI (kg/m^2)	27.6±1.4	28.03±1.4	1.196	0.231[1]
Baseline (d3) serum AMH(ng/mL)	1.73±0.21	2.24±0.30	2.120	0.195[1]
E2 d hCG (pg/mL)	1221.9±21.11	1185.3±17.8	0.921	0.420[1]
FF E2 (pg/mL)	262628.5±155320	164853.8±52411	29.04	0.001*[1]

1. Independent t-test used

*Statistical significant when p-value <0.05.

Table (2): Embryology data in low vs. high FF AMH groups:

	Low FF AMH (≤1.720 ng/mg protein) (n=30)	High FF AMH (>1.720 ng/mg protein) (n=30)	Test value	p-value
No. of oocytes retrieved	416	402	1.23	0.731[1]
Top-quality oocytes (%)	67.1±24.3	49.6±30.3	23.81	0.014*[1]
Fertilization rate (%)	83.9±20.9	72.4±21.4	18.56	0.021*[1]
Total no. of embryos transferred (mean)	140 (1.98±0.87)	159 (2.29±0.91)	31.34	0.016*[1]
No. of clinical pregnancies (%)	17 (56.7)	5 (16. 7)	10.34	0.001*[2]
No. of twin pregnancies (%)	3 (10)	2 (6.7)	0.220	0.884[3]
Embryo implantation rate (%)	10 (33.3)	5 (16.7)	17.89	<0.001*[2]

1. Man-Whitney test 2. Chi-square test 3. Fisher exact test

*Statistical significant when p-value <0.05.

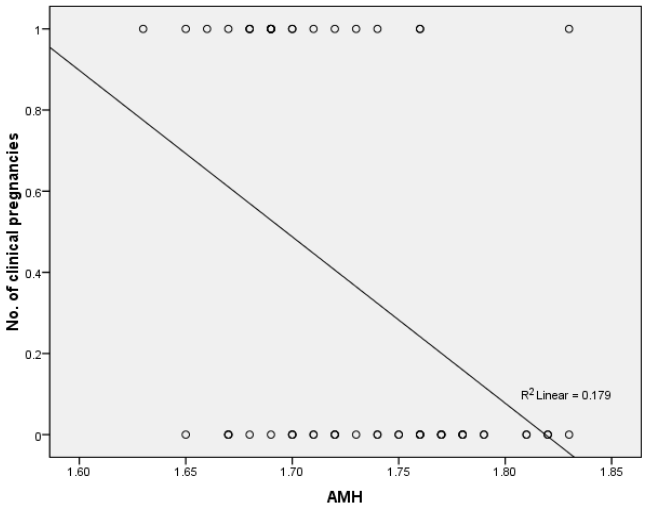

Figure (1): Correlation clinical pregnancy and AMH.

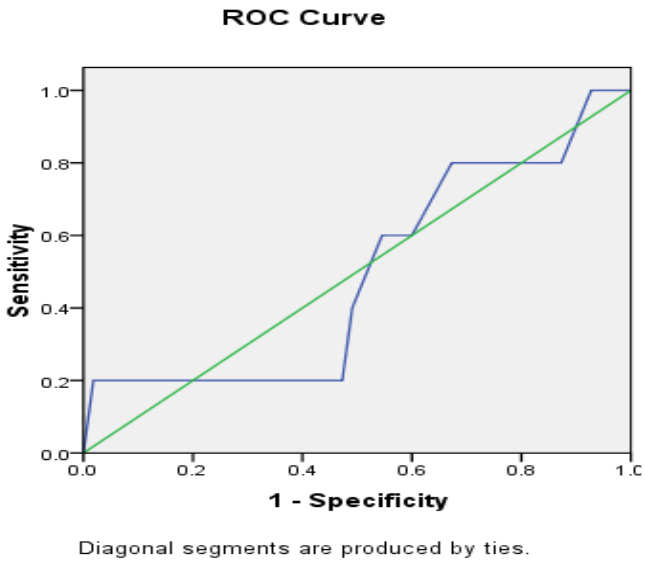

Figure (2): ROC curve for AMH.

Discussion

The role of AMH within the ovary is to participate within the regulation of ovarian function, especially in follicle development and selection. It inhibits the initiation of human primordial follicle growth and prevents multiple selection of a dominant follicle by reducing the sensitivity of follicles to FSH (Hamdine et al., 2015).

Several reports suggest that AMH could be a far better predictor of ovarian responses to controlled ovarian hyperstimulation (COS) than traditional parameters like age, FSH, estradiol (E2) and inhibin B (INH-B) (Massin et al., 2017). Our results, associating lower follicular fluid (FF) AMH levels on day of OPU with conception cycles and indicating an inverse correlation of follicular fluid AMH with clinical pregnancy,

completely conform to and are in conjunction with earlier reports of a progressive decline in AMH levels during ovarian stimulation, hence confirming the decreased ability of maturing follicles to supply AMH (Bakas et al., 2015). Similar to Mehta et al., (2013) study in which FF AMH shares an inverse correlation with FF E2 (Pearson r =−0.43, r^2 =0.18) and clinical pregnancy (Pearson r = −0.46, r^2 = 0.21).

Another study administered in monofollicular fluid (FF obtained from each individual follicle) of stimulated cycles by Takahashi et al., (2008) reported correlation of upper FF AMH levels with higher rates of fertilization. However, they might not associate it with pregnancy outcome. Moreover, their study involved comparison of FF AMH between two broad groups namely fertilization success versus fertilization failure. Wunder et al., (2008) correlated higher FF AMH with reproductive outcome in IVF-ICSI cycles.

some other observe done by using Fanchin et al., (2007) in monodominant follicles (single lead follicle) of unstimulated cycles, mentioned correlation of FF AMH with implantation rates and pregnancy outcome but not with fertilization costs. In another have a look at, Aflatoonian et al., (2010) correlated FF AMH with fertilization and embryo excellent. concerning AMH validity, our take a look at consequences determined that AMH >1. seventy five ng/mg had 73.1% sensitivity and eighty five.3% specificity for predication of medical being pregnant.

also Mehta et al., (2013) have a look at located that AMH >1.75 ng/mg had eighty% sensitivity and sixty three.1% specificity for predication of medical being pregnant. regarding bad reaction, the AMH cutoff price is 1.26 ng/mL with a sensitivity of 72.0% and a specificity of 86. Four %.

patients with AMH underneath this threshold have to be knowledgeable earlier in their fantastically low opportunity of reaching being pregnant because of a substantially higher rate of no available embryos (36.9 vs. 7. three%, P <zero.001). nevertheless, it must now not be utilized in isolation as the criterion for with holding fertility treatment (Seckin et al., 2019). A major strength of the current study stems from its prospective and randomized design.

Conclusion and Recommendations

Our study demonstrates that FF AMH is an adequate predictor of clinical pregnancy after ICSI. Further studies are urgently needed to investigate the efficiency, safety and cost-effectiveness of individualized gonadotropin dosing based on the AMH level prior to IVF.

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