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Success Rate of Intra Cytoplasm Sperm Injection (ICSI) among Sudanese Women with Low Serum Anti-mullerian Hormone (AMH)

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Abstract

Background: A lower level of Anti-mullerian Hormone (AHM) is associated with reduced ovarian reserve and reduced chance of pregnancy with IVF treatments. Previous reports indicated that AMH should not be used as the criteria to exclude couples from performing additional IVF treatments.

Aim: The aim of the current study was to assess the outcome of IVF/ICSI in women with low circulating AMH level (< 1.3 ng/ml) and to examine the difference in IVF/ICSI outcome between women with low serum AMH (0.2-1.3ng/ml) and extremely low serum AMH (<0.2ng/ml).

Materials and methods: All patients who underwent an IVF/ICSI treatments with FSH stimulation in DR.Elsir Abu-Elhassan Fertility Center between 2016 and 2017 were between 20 to 49 years of age and had low serum AMH level (<1.3 ng/ml). In total 63 patients were analyzed cross-sectional retrospectively. Statistical analysis was performed with SPSS.

Results: All women underwent IVF/ICSI treatment, the success rate was 20.6% (13 women), among all women understudy serum FSH was significantly affected the success rate (p-value <0.05) women with high serum FSH tend to get not success ICSI.There was a low probability to get success ICSI in women with extremely low AMH (<0.2ng/ml) compared to women with low AMH (0.2-1.3 ng/ml), in women with extremely low AMH there was a lower number of oocytes retrieved , a lower number of fertilized oocytes and a lower number of transferred embryos .

Conclusion: AMH remains a good quantitative marker of the ovarian reserve but is a poor qualitative marker. Women with low (<1.3 ng/ml) AMH levels undergoing IVF/ICSI treatments still have reasonable chances of achieving a pregnancy.

INTRODUCTION

There are numerous markers of ovarian reserve, which are used to prognosticate the chances of success with assisted reproductive techniques (ART), namely, serum follicle-stimulating hormone, estradiol, inhibin B, anti-mullerian hormone (AMH), biophysical tests such as ovarian volume and peak stromal blood flow velocity and antral follicle count (AFC); all the markers apart from the AFC provide an indirect measurement of the antral follicles, which are the resting pool of the follicles ready to be recruited (1).

According to numerous studies, AMH could predict ovarian response better than AFC (2, 3) and it is a more sensitive probe to identify early follicles not visualized by transvaginal ultrasound (4).

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AMH, a glycoprotein of the transforming growth factor – B (TGF – B), is produced by granulosa cells of small and large preantral and small antral follicles (5). AMH levels peak at 25 years of age, gradually declining thereafter and reaching undetectable levels a few years before menopause (6–8). AMH is secreted during the early follicular stage by follicles up to 6 mm in size, is relatively gonadotropin-independent, and remain relatively constant within and between menstrual cycles (9-13).

Since the number of ovarian follicles declines with increasing age, AMH levels might be used as a marker for ovarian aging (14). Human female serum contains measurable amounts of AMH during the reproductive lifespan. (14)Since AMH is solely produced in the growing ovarian follicles, serum levels may be used as a marker for ovarian reserve, representing the quantity and quality of the ovarian follicle pool (14).

Women with serum AMH below the 10th percentile of the general population have been reported to have an overall low global chance of achieving a viable pregnancy (15), and some authors suggested 0.15–0.2 ng/ml as the AMH cutoff value below which a clinical pregnancy may rarely be obtained after in vitro fertilization (IVF) (4, 16). Differently, other studies described ongoing pregnancies after IVF even in patients with low (17, 18) or extremely low AMH levels (<0.1 ng/ml) (19), also including patients older than 40 (20). Obviously, these somehow different results make it difficult to consider circulating AMH as the sole discriminant between women who should be offered IVF treatment and those who should be discouraged.

The current study was designed to determine the success rate of pregnancy in women who have a low AMH level (less than 1.3 ng/ml) undergoing assisted reproduction techniques (ART) IVF – ICSI.

MATERIALS AND METHODS

Ethics Statement

An ethics approval was obtained from Dr.Elsir Abu-Elhassan Fertility Center. For this retrospective study to be carried out using existing patient data in an anonymous manner. The project did not involve any additional intervention or modification from the standard treatment.

Study Population

This retrospective cross-sectional study carried out using existing patient data in an anonymous manner, the study population comprised 63 women who underwent their in vitro fertilization (IVF)/ intracytoplasmic sperm injection (ICSI) treatment at the Dr.Elsir Abu-Elhassan Center of Fertility, between October 2016 to December 2017.

Inclusion and Exclusion Criteria

The women under study were between (20-49) years of age, with low serum AMH levels (< 1.3 ng/ml) , they previously diagnosed as tubal abnormalities (15.9%), sperm abnormalities{male factor} (33.3%), tubal abnormalities with sperm abnormalities (14.3), and hypogonadotropic hypogonadism (3.2%).

None of the women had received hormonal therapy in the previous 3 months. Women with an ovarian cyst (> 3 cm in diameter), PCOS, endometriosis, a history of ovarian surgery or endocrine disorders were excluded from entering the study.

Hormonal Measurement

During the follicular phase of the menstrual cycle and prior to treatment, blood samples for assay of AMH, FSH, and luteinizing hormone (LH) were collected by venipuncture. The serum was separated and frozen in aliquots

at -80 C for future analysis with the measurement being performed by enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions.

Statistical Analysis

Data were analyzed using Statistical Program for Social Sciences (SPSS) version 21 the results were expressed as mean, SD, frequency and percentage(%). The statistic tests used in this study were paired test, Pearson correlation, P-value <0.005 considered significant correlation, one sample, and Chi-squared test.

RESULTS

Table (3-1) show the age group of the women in the study; 20 women (31.7%) were between 20 – 34 years and 43 women (68.3%) were between 35 – 49 years. Table (3-2) show that the study group was divided into two subgroups according to the type of infertility. Women never had been pregnant previously were considered had primary infertility whereas women had been pregnant previously were considered had secondary infertility, 48 women (76%) had primary infertility while 15 women (24%) had secondary infertility.

Table (3-3) show the success rate of the ICSI was underwent to the women in the present study; ICSI treatment succeeded in 13 women(20.6%) but did not succeed in 50 women (79.4%).

Table (3-4) explain the comparison between the mean of study parameters with the mean of the reference values, there was a statistically significant difference (P<0.05) in the mean concentration of both FSH and LH compared with the mean of their reference value. LH was significantly lower than the reference value but FSH was significantly higher than the reference value.

Table(3-1). *age group*

Age	Frequency	Percentage (%)
20-34 Years	20	31.7
35-49 Years	43	68.3
Total	63	100.0

Table (3-2). *Type of infertility*

Type	Frequency	Percentage (%)
Primary	48	76.0
Secondary	15	24.0
Total	63	100.0

Table (3-3). *comparison between the mean of study parameters with the mean of the reference values:*

Parameters	Mean±SD	Mean (R.V)	*P-value*
FSH (mIU/L)	9.93±5.19	7.75 (4.5-11)	0.001
LH (mIU/L)	5.51±2.45	7.8 (1.7-13.9)	0.000
LH/FSH ratio	0.68±0.44		

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Table(3-4). *frequency and percentages of the Success and failure rate of the ICSI:*

ICSI	Frequency	Percentage (%)
Success	13	20.6
Failed	50	79.4
Total	63	100.0

Table (3-5) show that in present study 21 of patients(33.3%) had male factor ,10 of patients(15.9%) had tube damage , 9 of patients(14.3%) had male factor& low AMH, 7 patients(11.1%) had tube damage& low AMH, 2 of patients(3.2%) had hypogonadotropic hypogonadism , 9 of patients(14.3%) had male factor& tube damage, while 5 of patients(7.9%) had low AMH .

Table (3-6) shows a significant difference (P<0.05) between ICSI Success and ICSI not Success as regard FSH but no significant difference (P>0.05) between ICSI Success and ICSI not Success as regard LH, LH/FSH ratio and AMH.

Table (3-7) explain the distribution of ICSI Success and ICSI, not Success according to AMH groups, the women were divided into two groups according to their AMH levels including women with extremely low AMH levels (<0.2 ng/ml) and women with low AMH levels (0.2–1 ng/ml), there were 11 women with Extremely low AMH levels (<0.2 ng/ml){ (4.8%) gave positive ICSI &12.7% gave negative ICSI }and 52 women with low AMH level (0.2–1 ng/ml) {15.9 % gave positive ICSI and 66.7% gave negative ICSI}, the odds ratio (>1) indicate there was low probability to get success ICSI in women with extremely low AMH than women with low AMH.

Table (3-8) show no significant difference (P>0.005) between Primary infertility and secondary infertility as regard FSH, LH, LH/FSH ratio and AMH.

Table (3-5). *indication for ICSI:*

Diagnosis	Frequency	Percentage (%)
Male Factor	21	33.3
Male Factor & Low AMH	9	14.3
Tube damage	10	15.9
Tube damage & Low AMH	7	11.1
Hypogonadotropic hypogonadism	2	3.2
Male factor and Tube damage	9	14.3
Low AMH	5	7.9
Total	63	100.0

Table (3-6). *Comparison between ICSI Success and ICSI not Success as regard FSH, LH, LH/FSH ratio and AMH:*

Parameters	ICSI Success (Mean±SD)	ICSI not Success (Mean±SD)	P-value
FSH (mIU/L)	8.98±3.29	10.18±3.58	0.023
LH (mIU/L)	5.86±3.09	5.42±2.28	0.568
LH/FSH ratio	0.79±0.56	0.65±0.40	0.304
AMH (ng/mL)	0.64±0.37	0.62±0.37	0.847

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Table (3-7). *Distribution of ICSI Success and ICSI not Success according to AMH levels:*

AMH group	ICSI	
	Positive	**Negative**
Extremely low AMH levels (<0.2 ng/ml)	3 (4.8%)	8 (12.7%)
Low AMH levels (0.2–1 ng/ml)	10 (15.9%)	42 (66.7%)
Total	13 (20.6%)	50 (79.4%)
P-value	0.123	
Odds ratio	1.575	
CI Lower	0.353	
CI Upper	7.026	

Table (3-8). *Comparison between Primary infertility and secondary infertility as regard FSH , LH , LH/FSH ratio and AMH :*

Parameters	Primary (Mean±SD)	Secondary (Mean±SD)	*P-value*
FSH (mIU/L)	10.09±5.71	9.39±3.11	0.650
LH (mIU/L)	5.39±2.46	5.88±2.47	0.510
LH/FSH ratio	0.67±0.44	0.71±0.43	0.765
AMH (ng/mL)	0.59±0.37	0.73±0.34	0.206

DISCUSSION

AMH has become a prominent tool for the evaluation of ovarian reserve. Recent studies have shown a strong correlation between AMH levels and pregnancy rates (21,4,22–24) where it is expected that the lower the AMH level, the lower the pregnancy rate.

Our study aimed to measure the pregnancy rate in women with low AMH levels (< 1.3ng/ml) who underwent IVF/ICSI treatment.

In this study 63 women underwent IVF/ICSI in assisted reproductive technology center of Dr.Elsir Abu-Elhassan.

The study shows that there is a chance to get pregnancy (success ICSI) in women with low serum AMH levels (< 1.3ng/ml), there were 13 women (20.6%) gave success ICSI whereas 50 women (79.4%) did not get pregnancy (not success ICSI). In agreement with our results Weghofer et al. reported in a large retrospective study, reasonable pregnancy and live birth rates in women with AMH levels ranging from 0.1–0.4 ng/ml (25). By contrast, Nelson and colleagues could not establish any pregnancies in 26 women up to 44 years of age with AMH concentrations <0.15 ng/ml using a range of different treatment approaches (4).

More recently, the accuracy of AMH in predicting live birth was tested by independent groups: some data showed that AMH could be used as a prognostic factor (26,21,27)but its predictive value at low or very low concentrations was not clearly clarified.

On the other hand our study examined the difference in IVF outcome in women with low (< 1,3ng / ml) and extremely low (<0.2 ng / ml) AMH levels, the women were divided into two groups according to their AMH levels including women with extremely low AMH levels (<0.2 ng/ml) and women with low AMH levels (0.2–1 ng/ml). According to our statistical analysis (odds ratio > 1) we found that there was low probability to get

pregnancy (success ICSI) in women with extremely low AMH than women with low AMH , 3 women (4.8%) have extremely low AMH and gave success ICSI whereas 10women (15.9%)have low AMH and gave success ICSI, the explanation that there was a lower number of oocytes retrieved, a lower number of fertilized oocytes and a lower number of transferred embryos in cycle of women with extremely low AMH levels.

In similar to our result La Marca et al. (2010) found that, for women with very low AMH concentrations(5), either cycle termination or poor response could be anticipated, also Muttukrishna et al. (2004) found that women with very low AMH concentrations are at very high risk for cycle termination(28), and La Marca et al. (2010) proposed that these patients should be refused treatment(5).

Some authors reported acceptable results in terms of clinical pregnancies even in patients with very low AMH levels whereas others suggested their exclusion from IVF treatment due to a very poor prognosis (17, 25).

On contrary to our results, other studies showed no significant effect of low AMH level on pregnancy rate and discouraged using AMH level as an indicator for ongoing pregnancy or as prerequisite for infertility treatment (29,30).

This work also shows that there was a significant difference between women gave success ICSI and women gave not success ICSI as regard to serum FSH(p0.023), the explanation that the women with low AMH levels and having high serum FSH results in giving not success ICSI due to poor ovarian response or ovarian failure.

Other studies were documented that higher FSH level was found to be correlated to low AMH level in women expected to have a poor ovarian response (31,20,32,33).

CONCLUSION

Our data indicate, AMH remains a good quantitative marker of the ovarian reserve but is a poor qualitative marker, it is one of the best available tools for the detection of low ovarian reserve and its role as a clinical test is clear. However, it also appears that reducing the AMH cut-off level below1.3 ng/ml by itself does not improve the predictive capacity of pregnancy occurrence following IVF. Therefore, extremely low cut-off AMH values should not be used to exclude couples from IVF treatment.

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