Anti-Mullerian Hormone Role in In Vitro Fertilization Outcome

Chiman Khudhur Mawlood*

Abstract

Background and objectives: The in vitro fertilization plays a significant role for human development in last decades. Anti-müllerian hormone level evaluation is indicator of ovarian reserve. The aim of this study was to assess the role of anti-müllerian hormone in assessing the quality of in vitro fertilization outcomes.

Methods: It was a retrospective study implemented at in vitro fertilization center of private hospital in Erbil city, Kurdistan region-Iraq in duration of one year from 1st of October, 2022 to 30th of September, 2023 on sample of 50 infertile women underwent in vitro fertilization. The biochemical pregnancy was diagnosed through serum recognition of human chorionic gonadotrophin, while the clinical pregnancy was diagnosed by ultrasonography. The in vitro fertilization outcome was assessed in relation to anti-mullerian hormone level and other variables like demographic and hormonal status.

Results: Biochemical pregnancy was positive in 80% of infertile women, while clinical pregnancy was positive in 72% of them; 24 women with ongoing pregnancy and 12 women ended with live birth pregnancy. Mean anti-mullerian hormone level was not significantly different in regard to clinical pregnancy outcome (p=0.4). The means of oocyte retrieved and embryo transferred were significantly higher among infertile women with positive clinical pregnancy (p≤0.05). The anti-mullerian hormone level was positively correlated to the count of oocyte retrieved and embryo transferred.

Conclusions: The serum anti-mullerian hormone level is not a predictor for in vitro fertilization quality.

Keywords: Anti-mullerian hormone, Infertility, In vitro fertilization

*MBChB, MD (Obs. & Gyne), PhD (Reproductive Medicine), Lecturer at College of Medicine-Hawler Medical University-Erbil city-Kurdistan region/Iraq,Corresponding author: E-mail: Chimankhudhur1964@gmail.com

Introduction

The assisted reproductive technology (ART) played a fundamental role in treatment of infertility and building of different families with birth of millions of infants all over the world. In vitro fertilization (IVF) which the most common central medical ART procedure referring to outside fertilization of eggs that returned back to uterus for development.[1] The IVF results in 1-3% of new live births every year and succeeded in about half of infertile younger than 35 years age.[2] Exploring the outcomes of IVF is essential in prioritizing the infertile cases, maintenance of IVF cycles and adoption of other ART techniques in addition to cost-effectiveness.[3] Different predictors of IVF outcomes were reported especially those reflecting the ovarian reserve like women's age, infertility duration, follicular stimulating hormone, number of oocytes, in addition to luteinizing hormone (LH) and estradiol (E2) levels with ultrasonography monitoring of antral follicular count.[4] Nowadays, the anti-müllerian hormone (AMH) was evaluated as a predictor of ovarian response to IVF technology.[5] Anti-müllerian hormones are glycoproteins related to super family of transforming growth factors-β (TGF-β) that is produced by small antral follicles of females and helps in follicular maturation and gradually declined after menopause.[6] Disturbances of AMH levels are related various gynecological disorders like polycystic ovaries syndrome and ovarian tumors.[7] Clinically, the AMH is useful in assessing fertility, pediatric endocrinology and early menopause.[8] However, the fundamental role of AMH recently was checked in IVF as the serum AMH among infertile women helps in prediction of ovarian stimulation, quality of embryo quality and sometimes the pregnancy outcomes.[9] The anti-müllerian hormone is secreted by small antral follicles (gonadotropin-independent) and highly related to antral follicular count, reflecting continuous growth and maturation of non-cyclic preantral and small antral follicles with demonstration of small intra and inter-cycles variations. For that, the AMH was considered as a cohesive and valid predictor of ovarian reserve.[10] Additionally, the serum AMH had the same efficacy of antral follicular count and ultrasonography in prediction of ovarian reserve among infertile women.[11] Generally, the AMH level of less than 1 ng/ml was a marker of reduced ovarian reserve. Consequently, measuring serum levels of anti-müllerian hormones is marked as an important element of ovarian reserve monitoring characterized by high sensitivity and acceptable specificity that motivated physicians to use it as a predictor for in vitro fertilization outcomes.[12] Although AMH significance in prediction of ovarian reserve, different authors have been reported the failure of AMH in prediction of pregnancy outcome of IVF. The pregnancy favorable outcomes may be related factors other than ovarian reserve such as the sperm and oocyte quality, endometrial thickness and age of involved infertile women.[13, 14] On other hand, many literatures showed a direct link between anti-müllerian hormones and successful pregnancy outcomes of in vitro fertilization, with role of anti-müllerian hormones in controlled ovarian stimulation in predicting declined ovarian reserve, cycle's withdrawal and hyperresponse.[15,16] However, the role of anti-müllerian hormones in prognosis of in vitro fertilization among infertile women is still controversial issue.[16, 17] The aim of present study was to assess the role of anti-müllerian hormone in assessing the quality of in vitro fertilization outcomes in Erbil city-Kurdistan region.

Patients and methods

A retrospective cross-sectional study implemented at in vitro fertilization center of Erbil International hospital in Erbil city, Kurdistan region-Iraq in duration of one year

from 1st of October, 2022 to 30th of September, 2023. All infertile women presented for IVF were study population. Adult women with primary or secondary infertility underwent ovarian stimulation and complete cycles of in vitro fertilization with completed data of IVF process and outcomes were the inclusion criteria. Exclusion criteria were congenital anomalies of uterus, Cushing syndrome, congenital adrenal hyperplasia, cancer, missing or incomplete data and not reached embryo transfer. Ethical issues were subjected to Ethical Committee of Kurdistan Higher Council of Medical Specializations by approval of hospital authorities and confidentiality of data. A sample of 50 infertile women underwent in vitro fertilization was selected after eligibility to inclusion and exclusion criteria. The data of women were collected and reviewed retrospectively by researchers and filled in a prepared questionnaire that included infertile women's general characteristics (age, body mass index, gravidity history, parity history, infertility type, duration of infertility and duration of infertility), laboratory investigations findings (basal luteinizing hormone level, day 2 estradiol hormone level, antral follicles count, day 2 progesterone hormone level, progesterone hormone level at human chorionic gonadotropin administration, endometrial thickness at ovulation, duration of ovulation stimulation, number of oocyte retrieved, number of embryo transferred and anti-müllerian hormone level) and IVF outcomes (biochemical pregnancy, clinical pregnancy, termination, miscarriage, ongoing pregnancy and live birth). The diagnosis of infertility and types were done by the researcher. The biochemical pregnancy was diagnosed through serum recognition of human choriononic gonadotrophin, while the clinical pregnancy was diagnosed by ultrasonography. Assessing other outcomes of IVF was done through reviewing data of

women which some of them ended in live birth, termination, miscarriage still pregnant. All investigations were done at Laboratory of Erbil International hospital. The selected infertile women underwent antagonist IVF protocol for ovarian stimulation included stimulating of gonadotrophin at 2nd or 3rd day of cycle. The women's data were entered and analyzed statistically by statistical package of social sciences program-26 with suitable tests like chi square and fishers' exact tests for statistical relationships, while independent sample t-test was used for continuous variables. Significance level was ≤0.05.
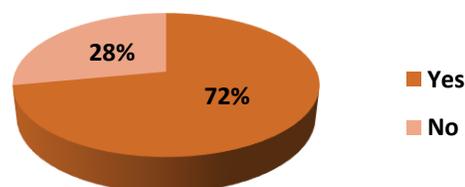
Results

Current study included 50 infertile women underwent in vitro fertilization (IVF). Biochemical pregnancy was positive in 80% of infertile women, while clinical pregnancy was positive in 72% of them; 24 women with ongoing pregnancy and 12 women ended with live birth pregnancy. Figures (1-3).
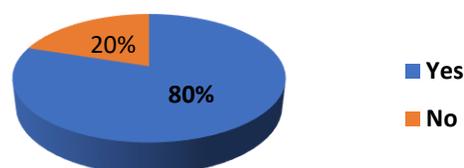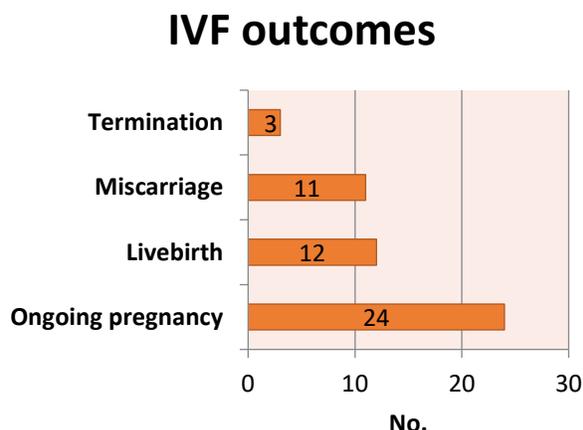

Figure (1): Biochemical pregnancy outcome of IVF.

Figure (2): Clinical pregnancy outcome of IVF.

IVF outcomes

Figure (3): Outcomes of IVF.

No statistically significant differences were observed between infertile women positive and negative clinical pregnancy regarding age (p=0.7), body mass index (p=0.1), gravidity history (p=0.9), parity history (p=0.7), infertility type (p=0.9) and infertility duration (p=0.7). There was a significant association between infertile women with unexplained etiology and positive clinical pregnancy (p=0.009), Table (1).

Table (1): Distribution of women's general characteristics according to clinical pregnancy.

Variable	Clinical pregnancy				P
	Yes		No		
	No	%	No	%	
Age					0.7 NS
20-29 years	14	38.9	4	28.6	
30-39 years	17	47.2	5	35.7	
≥40 years	5	13.9	5	35.7	
BMI mean±SD (Kg/m²)	27.1±2.1		28.5±1.2		0.1 NS
Gravidity					0.9 NS
Primi	16	44.4	6	42.9	
1-2 gravida	14	38.9	5	35.7	
3-4 gravida	6	16.7	3	21.4	
Parity					
Nulliparous	20	55.6	7	50.0	0.7 NS
1-2 para	12	33.3	6	42.9	
3-4 para	4	11.1	1	7.1	
Infertility type					0.9 NS
Primary	21	58.3	8	57.1	
Secondary	15	41.7	6	42.9	
Infertility duration					0.7 NS
<5 years	9	25.0	3	21.4	
5-10 years	16	44.4	8	57.1	
>10 years	11	30.6	3	21.4	
Infertility etiology					0.009 S
Unexplained	13	36.1	2	14.3	
Low ovarian reserve	3	8.3	6	42.9	
Uterine abnormalities	11	30.6	2	14.3	
Genetic abnormalities	0	-	1	7.1	
PCO	0	-	1	7.1	
Tubal	0	-	1	7.1	
Ovarian hyperstimulation syndrome	7	19.4	1	7.1	
Male factor	2	5.6	0	-	

S=Significant, NS=Not significant.

No statistically significant differences were observed between infertile women positive and negative clinical pregnancy regarding basal LH (p=0.2), day 2 estradiol level (p=0.3), antral follicle count (p=0.1), day 2 progesterone level (p=0.1) and progesterone level at HCG administration (p=0.4). The mean endometrial thickness was significantly higher among infertile women with positive clinical pregnancy (p=0.01). The mean duration of ovulation stimulation was significantly shorter among infertile women with positive clinical pregnancy (p=0.05). The means of oocyte retrieved and embryo transferred were significantly higher among infertile women with positive clinical

pregnancy (p≤0.05). Mean anti-mullerian hormone level was not significantly different in regard to clinical pregnancy outcome (p=0.4), Table (2).

Table (2): Distribution of investigations findings according to clinical pregnancy.

Variable	Clinical pregnancy		P
	Yes	No	
	Mean±SD	Mean±SD	
Basal LH (IU/ml)	7.3±4.1	5.8±4.1	0.2 NS
Day 2 estradiol (pg/ml)	36.7±18.9	55±114.4	0.3 NS
AFC	8.2±2.6	6.5±2.2	0.1 NS
Day 2 progesterone (ng/ml)	0.38±0.32	0.25±0.23	0.1 NS
Progesterone at HCG administration (ng/ml)	11.7±0.8	11.5±1	0.4 NS
Endometrial thickness at ovulation (mm)	14.3±2.8	11.6±3.7	0.01 S
Duration of ovulation stimulation (days)	9±1	9.8±1.5	0.05 S
Number of oocytes retrieved	11.3±6.9	6.5±4.8	0.02 S
Number of embryos transferred	2.4±0.7	1.9±1	0.05 S
AMH (ng/ml)	2±1.6	1.5±2	0.4 NS

S=Significant, NS=Not significant.

No statistically significant differences were observed between infertile women positive and negative clinical pregnancy regarding IVF metaphase (p=0.6). There was a highly significant association between infertile women with positive biochemical pregnancy and positive clinical pregnancy (p=0.009), 71.4% of women with negative biochemical pregnancy had negative clinical pregnancy, Table (3).

Table (3): Distribution of IVF process outcomes according to clinical pregnancy.

Variable	Clinical pregnancy				P
	Yes		No		
	No.	%	No.	%	
Metaphase					0.6 NS
MI	1	2.8	0	-	
MII	3	8.3	2	14.3	
MI & MII	32	88.9	12	85.7	
Biochemical pregnancy					<0.001 S
Yes	36	100.0	4	28.6	
No	0	-	10	71.4	

S=Significant, NS=Not significant.

There was a negative significant correlation between age of infertile women and their anti-mullerian hormone level (r=-0.35, p=0.01). A highly positive significant correlation was observed between anti-mullerian hormone level of infertile women and number of oocytes retrieved (r=-0.53, p<0.001). There was a positive significant correlation between anti-mullerian hormone level of infertile women and number of embryos transferred (r=-0.3, p=0.03), Table (4).

Table (4): AMH correlation with different variables.

Variable	AMH
Age	r=-0.35
	P=0.001
Number of oocytes retrieved	r=0.53
	P<0.001
Number of embryos transferred	r=0.3
	P=0.03

Discussion

Assessing quality of in vitro fertilization in specialized centers regularly is important in evaluating the IVF techniques used and experience of workers in addition to determine the best markers used to predict the pregnancy outcomes quantitatively and qualitatively.[18] This study found a successful biochemical pregnancy rate reaching to (80%), while the clinical pregnancy rate of infertile women was reaching to (72%). These IVF outcome rates are better than findings of recent Iraqi study which reported positive biochemical pregnancy rate of (45%) and positive clinical pregnancy rate of (38%) for infertile women following IVF.[19] Present study outcomes are also better than results of previous study conducted in Erbil city-Kurdistan region/Iraq that reported IVF outcomes as biochemical pregnancy rate of (37%) and clinical pregnancy rate of (32%).[20] In general our study pregnancy outcome rates are within expected clinical pregnancy rate of 30-70% after IVF treatment worldwide. [21] The live birth rate of IVF in our study was (24%). This rate is close to live birth rate of (29.5%) reported by previous study carried out by Smith et al.[22]The current study showed that mean anti-mullerian hormone level was not significantly different in regard to clinical pregnancy outcome. Similarly, Pacheco et al, retrospective cohort study found no significant difference in mean anti-mullerian hormone level with regard to clinical pregnancy outcome of IVF. [23]Inconsistently, Park et al, retrospective study documented a significant association between high anti-mullerian hormone level and successful clinical pregnancy of IVF. [24] This discrepancy in results might be attributed to fact that IVF quality is only dependable on ovarian reserve, but affected by age of women, IVF technology, infertility duration, endometrial thickness, etc. Some authors reported that anti-mullerian hormone level is useful in small antral follicles quantity and

might not be applicable for quality evaluation of IVF. One study documented infertility in women with high levels of anti-mullerian hormone, while pregnant women were detected with very low levels of this hormone.[25] Karkanaki et al stated that measurement of intrafollicular anti-mullerian hormone could be helpful in assessing prognosis of IVF quality.[26]This study found a significant relationship between infertile women with unexplained etiology and positive clinical pregnancy following IVF. This finding coincides with different literatures.[27, 28] In our study, mean endometrial thickness was significantly higher among infertile women with positive clinical pregnancy following IVF. This finding is consistent with results of Momeni et al meta-analysis study.[29] Our study showed that mean duration of ovulation stimulation was significantly shorter among infertile women with positive clinical pregnancy after IVF. Ryan et al revealed that longer duration of ovulation stimulation was accompanied by poor prognosis of IVF.[30] In our study, means of oocyte retrieved and embryo transferred were significantly higher among infertile women with positive clinical pregnancy following IVF. Consistently, different authors revealed that both numbers of oocyte retrieved and embryo transferred are significant markers of clinical pregnancy of IVF.[31, 32] In same direction, our study showed that both numbers of oocyte retrieved and embryo transferred were positively correlated to anti-mullerian hormone level of infertile women, while the anti-mullerian hormone level was negatively correlated to age of infertile women. These findings are in agreement with results of Sun et al retrospective study.[33] The main limitations of present study were missing or incomplete data, single center study and small sample size.This study concluded that serum anti-mullerian hormone level is not a predictor for in vitro fertilization quality; however, this

hormone is a good predictor for ovarian reserve that predicts the in vitro fertilization outcomes. The pregnancy outcome of in vitro fertilization is affected by infertility etiology, endometrial thickness, duration of ovarian stimulation, number of oocytes retrieved and number of embryos transferred. This study recommended the use of anti-mullerian hormone as a marker in prediction prognosis of in vitro fertilization.

Conflicts of interest
None

Acknowledgment

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