Araştırma Makalesi
Research Article

Serum Anti-Müllerian hormon düzeyleri yardımcı üreme tedavileri siklus sonuçlarıyla ilişkili mi? Tek bir IVF merkezinden 1544 siklusun retrospektif analizi

DO SERUM ANTI-MULLERIAN HORMON LEVELS ASSOCIATE WİTH ASSISTED REPRODUCTIVE TREATMENT CYCLE OUTCOMES? A RETROSPECTIVE ANALYSİS OF 1544 CYCLES FORM A SINGLE IVF CENTER

Gülnaz ŞAHİN[1], Ferruh ACET[1], Aysin AKDOĞAN[2], Zuhal PARILDAR[3], Aysen DURMAZ GÜVEN[1], Sabahattin Anıl ARI,[4] Ege Nazan TAVMERGEN GÖKER[1], Erol TAVMERGEN[1]

[1]Ege Üniversitesi Aile Planlaması ve İnfertilite Araştırma ve Uygulama Merkezi, İzmir, Türkiye
[2]Tavmergen İnfertilite ve Tüp Bebek Merkezi, İzmir, Türkiye
[3] Ege Üniversitesi Tıp Fakültesi Tıbbi Biyokimya Ana Bilim Dalı
[4] T.C. Sağlık Bakanlığı Menemen Devlet Hastanesi

ABSTRACT

Introduction: To evaluate whether there is a predictive value of serum Anti-Mullerian Hormone (AMH) levels on ovarian response and pregnancy outcomes of infertile women undergoing intracytoplasmic sperm injection (ICSI) cycle.

Methods: A total of 1544 consecutive ICSI cycles of women aged between 18-45 years, performed in a single tertiary In-Vitro Fertilization (IVF) Center between 2015-2018, were retrospectively analyzed. Along with patients' ages and AMH levels, cycle characteristics, clinical pregnancy and live birth outcomes were evaluated. Age and serum AMH levels were categorized. Regression analyses were used to determine the predictive value of AMH on the ovarian response and clinical pregnancy/live birth outcomes.

Results: Among 1544 cycles, 1306 (84.6%) were ended with an embryo transfer cyle. AMH levels were found significantly positively correlated with the numbers of obtained oocytes and 2-pronuclear(2pn) zygotes. AMH value of >1 ng/ml was significantly and independently associated with obtaining more than 5 oocytes (OR: 6.7; 95% CI: 4.9-9.1). The clinical pregnancy and live birth rates per cycle were significantly lower in patients with low AMH for both age <35 and above 35 years groups. However, live birth rates per embryo transfers were not significantly different(25.6% vs 32.8%, p=0.065 for women <35 years age and 17.8% vs 21.8%, p=0.273 for women >=35 years age). Moreover, only age and number of metaphase-2 oocytes were found significant independent predictors for live birth outcome.

Gülnaz ŞAHİN
Ege Üniversitesi Aile Planlaması ve İnfertelite Araştırma ve Uygulama Merkezi, İzmir, Türkiye
E-posta: gsahini@msn.com
https://orcid.org/0000-0002-5520-9229

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Conclusion: Although AMH levels are highly correlated with the oocyte yield in ICSI cycles, the ability to predict clinical pregnancy and live births for fresh embryo transfer cycles seems limited.

Keywords: AMH, ICSI, clinical pregnancy, live birth

ÖZ

Amaç: Serum Anti-Müllerian hormon (AMH) düzeylerinin intrasitoplazmik sperm enjeksiyonu (ICSI) siklusu uygulanan infertil kadınlarda over cevabı ve gebelik sonuçları üzerine öngörücü değeri olup olmadığını değerlendirmek.

Gereç ve Yöntem: 2015-2018 yılları arasında tek bir üçüncü basamak İn-Vitro Fertilizasyon (IVF) Merkezi'nde 18-45 yaş arası kadınlarda gerçekleştirilen toplam 1544 ardışık ICSI siklusu geriye dönük olarak analiz edildi. Hastaların yaşı ve AMH düzeyleri ile birlikte siklus özellikleri, klinik gebelik ve canlı doğum sonuçları değerlendirildi. Yaş ve serum AMH seviyeleri kategorize edildi. AMH'nin ovaryan yanıt ve klinik gebelik / canlı doğum sonuçları üzerine prediktif değerini belirlemek için regresyon analizleri kullanıldı.

Bulgular: 1544 siklusun 1306'sı (%84,6) embriyo transfer siklusu olarak tamamlandı. AMH düzeyleri elde edilen oosit sayıları ve 2-pronükleuslu (2pn) zigot sayıları ile anlamlı düzeyde pozitif korele bulundu. AMH>1 ng/ml düzeyleri, 5'ten fazla oosit elde etmeyle anlamlı ve bağımsız olarak ilişkilendirildi (OR: 6,7; % 95 CI: 4,9-9,1). Siklus başına klinik gebelik ve canlı doğum oranları, hem <35 hem de 35 yaş üstü gruplar için düşük AMH'li hastalarda önemli oranda düşüktü. Fakat embriyo transfer siklusları başına canlı doğum oranları anlamlı düzeyde farklı değildi (% 25,6'ya karşı % 32,8; p: 0.065 <35 yaş grubu- %17,8' e karşı % 21,8; p= 0,273> 35 yaş grubu). Dahası, sadece yaş ve metafaz-2 oosit sayısı, canlı doğum öngörüsü açısından anlamlı bağımsız faktörler olarak bulundu.

Sonuç: AMH düzeyleri ICSI sikluslarında oosit verimi ile yüksek oranda ilişkili olmasına rağmen, taze embriyo transfer siklusları için klinik gebelik ve canlı doğumları tahmin etme gücü sınırlı görünmektedir.

Anahtar Kelimeler: AMH, ICSI, klinik gebelik, canlı doğum

Ovarian reserve defines the oocyte quantity (1). With advancing age, ovarian reserve decreases due to apoptotic loss of primordial follicles. Quantitative ovarian reserve tests are used to manage many fertility-associated situations such as; delaying the plan for childbearing, prediction of ovarian reserve after gonadotoxic treatments and/or ovarian surgeries, prediction of premature ovarian failure or natural menopause, and management of infertility related treatments.

As a result of aging, the number of primordial follicles decreases, oocyte quality deteriorates, implantation rate decreases, and the rate of chromosomal abnormalities increases in the embryo (2). Thereby, evaluating the reproductive potential in women who desire to have children in the late 30s and early 40s, when the age of reproductivity is decreasing, is important. Estimating the ovarian response and the chance of pregnancy allows the physician to inform patients before undergoing a troublesome and expensive infertility treatment program and individualize the treatment protocols for increasing clinical success and preventing economic losses.

Age, antral follicle count, basal serum Follicle-Stimulating Hormone (FSH), and Anti-Mullerian Hormone (AMH) levels are commonly used ovarian reserve markers.

The chronological age is an important factor for predicting individual in-vitro fertilization (IVF) results, as it relates to both the quality and quantity of the oocytes (3). AMH has been proposed in the past decades for this purpose since basal FSH has a moderate/ poor predictive power in terms of cycle outcomes. AMH is a dimeric glycoprotein hormone and reflects the recruited ovarian follicular pool (4). AMH is released from the growing follicles granulosa cells and inhibits the transformation of the primordial follicle into the primary follicle (5). Starting to be synthesized in the primary follicle, AMH peaks in the preantral and small antral follicle stages, and as the follicles grow, its concentration decreases and cannot be detected (5). Throughout the reproductive life, the follicle pool decreases. The levels decrease with reproductive aging and are undetectable after menopause (6-8).

AMH has been demonstrated as a predictive factor for the ovarian response in assisted reproductive technology (ART) treatments by several authors (9-13). However, the association between pregnancy outcomes of ART treatments and serum AMH levels is conflicting. AMH concentrations were associated with the rate of cycle cancellation, ongoing pregnancy, live births (14-17), and even miscarriage rates (18) in several studies. In contrast, the predictive accuracy of AMH level on the pregnancy after ART has not been found or found limited by other studies (10-12, 19). In addition, no association has been reported between AMH levels and fecundity in women attempting natural conception (20, 21). AMH levels were not associated with time to pregnancy in natural conceptions; besides, time to pregnancy was reported shorter in women with low AMH (22).

This study aimed to evaluate whether there is a predictive value of serum AMH for ovarian response and pregnancy outcomes after intracytoplasmic sperm injection (ICSI) cycle in infertile females from a single tertiary IVF center. Our primary aim was to analyze the value of AMH on clinical pregnancy and live birth outcomes. The secondary aims were; i) to investigate the association between the oocyte yield and AMH levels, ii) to evaluate the predictive factors for live births after ICSI in women whose AMH levels ≤1ng/ml.

MATERIALS AND METHODS

A total of 1544 consecutive fresh ICSI/embryo transfer (ET) cycles of women aged 18-45 years performed in a tertiary IVF Center between January 2015 and December 2017 were included in this retrospective cohort study. The first cycles of these women were analyzed. All freeze cycles that were performed aiming preimplantation genetic diagnosis or fertility preservation were excluded from the analyses. Baseline characteristics, AMH levels, and ICSI cycle parameters were obtained from the IVF database and patients' medical records. AMH measurements were performed by using the electrochemiluminescence immunoassay method (ECLIA) (AMH assay, Roche Diagnostics International Ltd. Switzerland) in cases whom measurements performed in our institution. AMH results obtained outside from our institution were also included to the study. Institutional ethics committee approval (21-2.1T/64; 18.02.21) was obtained for the study.

The majority of controlled ovarian stimulation was performed using exogenous gonadotropins (recombinant or urinary, 100-450 IU, based on ovarian reserve status) with an antagonist protocol. In a limited cycle, a long agonist protocol was also used. When at least one follicle reached 18 mm diameter, human chorionic gonadotropin (hCG) was implemented for ovulation triggering. Following 35-36 hours of hCG injection, oocyte pick-up procedure was performed. Embryo transfer was performed on the second to fifth day of embryo culture, with a maximum of two embryos being transferred under transabdominal ultrasound guidance. Vaginal micronized natural progesterone was used for the luteal phase supplementation.

The following data were evaluated; serum AMH, basal FSH levels, infertility etiologies, age at oocyte retrieval, the dose of total gonadotropin used, peak estradiol (E2) (pg/ml) levels, numbers of obtained total and metaphase-2 oocytes, numbers of 2-pronuclear (2pn) zygotes , clinical pregnancy (CP) and live birth (LB) rates. Observation of a gestational sac by transvaginal ultrasonography 4 weeks after embryo transfer was considered as a clinical pregnancy. Delivery of an infant after 24th weeks of gestation was defined as a live birth.

Descriptive statistics for continuous variables were calculated and presented as mean, standard deviation (SD). Spearman correlation analysis was used to evaluate possible associations between serum AMH levels and baseline patient/cycle characteristics. Female age and serum AMH levels were categorized as; age<35 and >=35, AMH levels ≤1.0 and >1 ng/ml for comparing the groups. The number of obtained oocytes ≤5 was accounted as low oocyte yield. Continuous variables were compared with the Student-t test. Pearson Chi-square test was used for the comparison of the categorical variables. Univariate and multivariate regression analyses were used to evaluate the value of AMH on ovarian response as low or normal oocyte yield, clinical pregnancies and live births. The Odds ratios (OR) are determined with 95% confidence intervals. SPSS 22.0 (Statistical Package for Social Sciences ver. 22.0, Inc, Chicago, IL) IBM software was used for the statistical analyses. A two-tailed p-value of <0.05 was considered statistically significant.

RESULTS

A total of 1544 ICSI cycles performed over 3 years in our single IVF center were analyzed. The mean patient's age was 32.7±5.0 (min.-max:19-45), the mean serum AMH level was 2.46±2.5 ng/ml (min-max: 0.1-19 ng/ml). Their infertility etiologies were; 30.8 % male factor, 5.1 % tuboperitoneal, 21.4 % unexplained, 25.8 % diminished ovarian reserve, 6.7 % other ovulatory, 8.7 % combined (both male and female) and 1.5% other etiologies. Of those total group, 34.4% of patient's AMH levels were ≤1 ng/ml. A mean 1983±856 IU dose of gonadotropin was used, and average 7.7±6.5 oocytes were retrieved. Those ovulation induction cycles were performed mainly with an antagonist protocol (89.6%, n=1384), and for the remaining (10.4 %, n=160) long agonist protocol was used. Of those 1544 cycles, 1306 cycles (84.6%) ended with an embryo transfer cycle. The reasons for the cancellation of embryo transfer were; 3.8 % (n=58 cycle) failed to obtain any mature oocyte, 7.4 % (n=115) fertilization or cleavage failure, 2.6 % (n=40) freezing all embryos due to ovarian hyperstimulation_syndrome (OHSS) prevention, or 1.6 % freezing embryos for other reasons.

The peak E2 levels (r:0.555, p<0.001), number of obtained oocytes (r:0.662, p<0.001), and number of 2pn's (r:0.500, p<0.001) were significantly positively correlated with AMH levels. Whereas the age (r:-0.432, p<0.001) and the total dose of gonadotropin used (r:-0.540, p<0.001) were in a significant negative correlation with the AMH levels. Moreover, these associations were found similar for both long agonist (n=160) and antagonist protocols (n=1384), when the data analyzed separately for those protocols.

Patients were stratified according to their age (<35 years of age or >=35 years) and AMH levels (<=1 or >1 ng/ml) to evaluate the effect of AMH levels on the cycle outcomes (Table1). The mean ages of the patients were slightly older (1.5 years) in the low AMH groups for both age <35 and >=35 years, although this difference was not clinically significant. Total gonadotropin used was significantly higher for patients with low AMH (<=1 ng/ml); on the other hand, their peak E2 levels, total oocyte yield, numbers of mature oocytes, and 2pn embryos were significantly lower compared to AMH>1 ng/ml in both age groups (p<0.001). In addition, the percentages of cycles that lead to obtaining any transferrable embryos significantly decreased in the group of patients whose AMH levels≤1 ng/ml (p<0.001) because of failure to obtain any oocyte or fertilization/cleavage failure.

The clinical pregnancy and live birth rates per cycle were significantly lower in patients with low AMH for both age groups. Although clinical pregnancy rates per embryo transfer cycle were lower in women with low AMH, the live birth rates per embryo transfers were not significantly different between the AMH groups (25.6% vs 32.8%, p=0.065 for women aged <35 years and 17.8% vs 21.8% , p=0.273 for women aged >=35 years) (Table1). The miscarriage rates in patients ages>=35 and serum AMH levels >1 ng/ml were higher than in the same age group with low AMH levels. Moreover, this unexpected finding was statistically significant (p=0.002). (Table 1)

Table 1. Baseline characteristics and cycle outcomes

	Age <35 years (n=967)			**Age >=35 years (n=577)**		
	AMH<=1 ng/ml (n=214)	**AMH>1 ng/ml (n=753)**	***P* value**	**AMH<=1 ng/ml (n=317)**	**AMH>1 ng/ml (n=260)**	***P* value**
Age	30.8(3.0)	29.3(3.3)	<0.001	38.5(2.8)	37.3(2.1)	<0.001
AMH (ng/ml)	0.5(0.3)	3.8(2.7)	<0.001	0.4(0.3)	2.7(1.8)	<0.001
Basal FSH (IU/L)	10.6(5.7)	6.5(2.3)	<0.001	11.4(6.3)	7.3(3.5)	<0.001
Total gonadotropin used (IU)	2374(1032)	1637(552)	<0.001	2600(1019)	1913(630)	<0.001
Peak E2	687(420)	1429(922)	<0.001	637(415)	1260(787)	<0.001
No. of oocytes	4.1(2.9)	10.7(6.9)	<0.001	3.1(2.5)	8.1(6.1)	<0.001
No. of m2 oocytes	3.2(2.4)	7.8(5.0)	<0.001	2.5(2.3)	6.3(4.4)	<0.001
Low oocyte yield(<6 oocyte)%	75.2	21.0	<0.001	85.5	37.3	<0.001
No. of 2pn	2.5(1.7)	5.4(3.7)	<0.001	2.3(1.7)	4.4(3.3)	<0.001
Obtaining any transferable embryos (%)	84.6	94.7	<0.001	73.5	93.8	<0.001
Reason for ET cancellation (%)			<0.001			<0.001
No oocyte	7.0	0.8		10.7	1.2	
Fertilization or cleavage failure	8.4	4.5		15.8	5.0	
All freeze	2.3	6.1		2.5	2.3	
(%) of patients underwent ET	82.2	88.6	0.014	71.0	91.5	<0.001
Single ET (%)	89.2	86.5	0.368	48	18.5	<0.001
Pregnancy/cycle (%)	26.6	35.9	0.012	17.7	36.2	<0.001
Clin.Preg/cycle (%)	25.2	34.4	0.011	16.7	33.5	<0.001
Miscarriage/cycle (%)	4.2	5.3	0.515	4.1	13.5	<0.001
Live birth/cycle (%)	21.0	29.1	0.020	12.6	20.0	0.016
Pregnancy/et (%)	32.4	40.5	0.050	24.9	39.5	<0.001
Clin. Preg/et (%)	30.7	38.8	0.047	23.6	36.6	0.002
Miscarriage/et (%)	5.1	6	0.656	5.8	14.7	0.002
Live birth/et (%)	25.6	32.8	0.065	17.8	21.8	0.273

Continuous variables were expressed as mean and standard deviation (SD)
Categorical variables were expressed as percentages (%)
χ^2 or student-t test used for the comparison

Logistic regression analyses were used to evaluate the association between AMH levels and ovarian response, clinical pregnancy/live births. To assess the predictive capacity of AMH on the ovarian response (obtaining more than 5 oocytes), adjustments were made for female age, basal FSH, total dose of gonadotropins. AMH was found as a significant independent predictor for the ovarian response as with both age and basal FSH levels (Table2). As expected, increase in age and basal FSH levels were independently associated with decreased chance of a good ovarian response, whereas the AMH value of >1 ng/ml was significantly and independently associated with obtaining more than 5 oocytes (OR:6.7; 95% CI: 4.9-9.1) (Table2).

Table 2. Predictors for obtaining more than 5 oocytes

	Adjusted p-value	OR	95% CI	
			Lower	Upper
Basal FSH (IU/L)	.000*	0.853	0.817	0.891
Gonadotropin dose (IU)	.240	1.000	1.000	1.000
Age>35	.000*	0.550	0.418	0.723
AMH>1 ng/ml	.000*	6.724	4.945	9.145

OR: Odds' Ratio, CI: Confidence Interval, *donates statistically significance

To determine the predictive value of baseline and cycle characteristics on clinical pregnancy and live birth outcomes, the univariate and multivariate regression analyses were performed. The female age, AMH level, basal FSH level, total gonadotropin doses, number of metaphase-2 oocytes and number of transferred embryos (double vs. single) were included to the analyses as possible predictive factors on the cycle outcomes. Concerning to the univariate analyses; female age, AMH levels, basal FSH levels, total gonadotropin doses and number of metaphase-2 oocytes were found as significantly associated factors for the clinical pregnancy and live birth outcomes. However, when the adjustments for these confounders were made by multivariate regression analysis, only the female age (OR: 0.960, 95% CI; 0.930-0.990, p=0.01), number of metaphase-2 oocytes (OR:1.091, 95% CI;1.054-1.129, p<0.001) and number of transferred embryos (double vs. single, OR: 1.417, 95% CI; 1.048-1.925, p=0.024) were found to be statistically significant factors to achieve a clinical pregnancy (Table 3).

Table 3. Regression Analyses for the Predictors of Clinical Pregnancy Outcome

	Univariate LRA				Multivariate LRA			
	Unadjusted *P*-value	OR	95% CI		Adjusted *P*-value	OR	95% CI	
			Lower	Upper			Lower	Upper
Age	0.000*	0.946	0.925	0.967	0.010*	0.960	0.930	0.990
AMH (ng/ml)	0.000*	1.102	1.054	1.152	0.433	0.976	0.919	1.037
Basal FSH (IU/L)	0.000*	0.926	0.898	0.955	0.385	0.984	0.949	1.020
Gonadotropin dose (IU)	0.001*	1.0	1.0	1.0	0.831	1.0	1.0	1.0
Number of M2 oocytes	0.000*	1.135	1.105	1.166	0.000*	1.091	1.054	1.129
Number of transferred embryos=2	0.407	1.108	0.869	1.413	0.024*	1.417	1.048	1.915

LRA: Logistic Regression Analysis

OR: Odds' Ratio CI: Confidence Interval,*donates statistically significance

The multivariate regression analysis for the live birth outcome showed after adjustment for potential confounders that only the female age and number of metaphase-2 oocytes were significantly associated factors for the live birth outcome (Table 4). Increase in age was significantly associated with decreased probability of live birth (OR:0.937, 95% CI;0.906-0.969, p<0.001), whereas increase in number of metaphase-2 oocytes was significantly associated with increase in probability of a live birth (OR:1.075, 95 % CI; 1.038-1.113, p<0.001) after embryo transfer. However, AMH levels were not significantly associated with probability of clinical pregnancy and live birth outcomes after the adjustment of confounders.
(Table 4)

When cycles with AMH≤1 ng/ml were considered (n=531); only the female age was found as a significant predictive factor for live birth outcome (P=0.001).

Table 4. Regression Analyses for the Predictors of Live Birth Outcome

	Univariate LRA				Multivariate LRA			
	Unadjusted *P*-value	OR	95% CI		Adjusted *P*-value	OR	95% CI	
			Lower	Upper			Lower	Upper
Age	0.000*	0.923	0.901	0.946	0.000*	0.937	0.906	0.969
AMH (ng/ml)	0.000*	1.093	1.044	1.144	0.379	0.972	0.912	1.036
Basal FSH (IU/L)	0.000*	0.923	0.892	0.955	0.336	0.981	0.944	1.020
Gonadotropin dose (IU)	0.007*	1.0	1.0	1.0	0.322	1.000	1.000	1.000
Number of M2 oocytes	0.000*	1.124	1.093	1.155	0.000*	1.075	1.038	1.113
Number of transferred embryos=2	0.222	0.84	0.65	1.10	0.220	1.225	0.886	1.695

LRA: Logistic Regression Analysis,

OR: Odds' Ratio CI: Confidence Interval, *donates statistically significance

DISCUSSION

Granulosa cells in small follicles continuously produce AMH during the menstrual cycle. Thereby, in determining the ovarian reserve, AMH is a better marker than periodically produced gonadotropins (FSH, LH) and ovarian steroids (E2, Progesterone). Many studies and meta-analyses indicate that decreased AMH levels are associated with poor IVF outcomes (14-18). In addition, low AMH levels are thought to associate with decreased pregnancy outcomes by a lower rate of euploid embryos (23). But there are studies that do not support the results of these publications by reporting the AMH results do not predict pregnancies in IVF cycles (10-12, 19). These incompatible data in the literature possibly due to the heterogeneity of the study methods, and the results are still conflicting. In the present study, we found that AMH values were associated with ovarian response to stimulation; however, did not predict pregnancy results in women who underwent embryo transfer. AMH has been one of the most important biomarker in the evaluation of ovarian reserve for infertile women. Predictive capacity of AMH levels for ovarian response to gonadotropin stimulation in ART treatments have been shown in numerous studies previously (9-13,19). A significant positive correlation between AMH levels with numbers of obtained oocytes and peak E2 levels were shown in our study results, in accordance with these previous studies. Higher AMH levels were associated with higher peak E2 levels and higher oocyte yield after ovarian stimulation including both long agonist and antagonist protocols in our study results. In addition, AMH level >1ng/ml was found as an independent predictor for obtaining more than five oocytes in the present study. Although total gonadotropin used (IU) for ovarian stimulation was significantly higher in the group of patients with low AMH (<=1 ng/ml), their peak E2 levels and total oocyte yield were significantly lower compared to patients with AMH>1 ng/ml, in our study cohort. Since AMH levels reflect the quantity of the early antral follicles which have growing potential after gonadotropin stimulation, our study findings and previous reports are supporting that AMH testing prior to the ART treatments is an effective tool for the prediction of ovarian response.

Our study results indicated that the most important factor in predicting live birth seems to be female age and the number of metaphase two oocytes. Although the AMH levels were found to be associated with the oocyte yield, the direct association with pregnancy

outcome was not found for the first fresh embryo transfer cycles of these women.

Female age is a simple way to have knowledge about the ovarian reserve of a woman. However, it is necessary to discriminate women who have reduced or sufficient ovarian reserve in between similar age groups. Recently, Zhao et al. reported a total of 1281 IVF cycle outcomes from 999 women, according to their age-specific AMH values. In their study, age-specific reference intervals for AMH values were calculated by regression analysis. They reported significantly lower clinical and ongoing pregnancy rates with higher miscarriage rates in women aged <35 years with low AMH levels (below 10th centile for their age) compared to women with normal AMH group (24). In our study, we observed higher CP and LB rates per cycle in women both age<35 and >=35 years groups with AMH levels>1 ng/ml, however, the differences in LB rates per embryo transfers did not reach the statistically significant level. Additionally, higher miscarriage rates were noticed in women aged>35 years and with serum AMH>1 ng/ml group. This finding may be explained by the dominant effect of the female age on oocyte quality rather than the effect of AMH on quantitative oocyte yield and suggesting that AMH levels may not directly be correlated with oocyte quality.

Reproductive potential includes both oocyte quality and quantity. Oocyte quality is a complex phenomenon, and it is well known that chromosomal abnormalities of the oocytes and thereby embryos increase with advancing maternal age (25-28). Also, oocyte quantity associates with female age. Therefore, female age has been found as a significant predictor for ART outcomes (29-31). Although the predictive capacity of ovarian response to stimulation has been clearly shown for AMH levels, no added value to the age on the prediction of ongoing pregnancy after IVF has been found in an individual patient data meta-analysis including 28 studies (10). Similar results were also reported by several other studies (11, 12, 19, 32). In another two meta-analyses, a weak association between AMH levels and pregnancy outcomes has been shown in women undergoing IVF (15, 33). Tal et al. (2018) evaluated SART (Society for Assisted Reproductive Technology) national database from the USA, including 85,000 autologous fresh and frozen cycles with AMH values over the two years (34). Although the AMH has been found an independent predictor of live birth after controlling potential confounders, they reported that it is a weak predictor for this outcome.

Although there are many related publications in the literature, the results are still contradictory. Taken together with previous studies, this study supports that AMH is a valuable predictor for the ovarian response to gonadotropin stimulation; however, its predictive capacity on pregnancy outcomes after ART treatments is limited. When combined with female age, AMH levels have a value in evaluating ART outcomes, particularly in quantitative oocyte yield, and thus indirectly on pregnancy outcomes.

The strength of our study is the availability of detailed information in a large number of cycles included from a tertiary single IVF center. However, the retrospective design of the study is a limitation. Secondly, AMH measurements were not all centralized and heterogeneity of the measurement of the AMH is a limitation for the present study. However, the inclusion of a large number of cycles from recent 5-year period and the AMH value categorization as ≤1 ng/ml and >1 ng/ml allowed us to evaluate the AMH levels on the ART outcomes of women for daily practices. Thirdly, the evaluation of cumulative pregnancy rates per patient, including frozen-thawed embryo transfer cycles, might give more clear answers.

In conclusion, although AMH levels are highly correlated with the oocyte yield in ICSI cycles, the ability to predict clinical pregnancy/live births seems limited. The effect of female age seems more dominant on the success of ART treatments as it reflects oocyte quality better than AMH levels.

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