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Original Research

Which Ovarian Reserve Marker is More Reliable in IVF Patients with AMH and AFC Discordance?

Eun Hee Yu[1], Hyun Joo Lee[1], Jong Kil Joo[1,*], Yong Jin Na[1]

[1]Department of Obstetrics and Gynecology, Pusan National University School of Medicine, Pusan National University Hospital Biomedical Research Institute, 49241 Busan, Republic of Korea

*Correspondence: jongkilj@hanmail.net (Jong Kil Joo)

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Abstract

Background: In clinical practice, discordance between anti-müllerian hormone (AMH) and antral follicle count (AFC) presents a recurring challenge. Such discordance can potentially lead to inappropriate clinical decisions, thereby diminishing the clinician's confidence in managing a patient's long-term journey through assisted reproductive technology (ART). This study aims to clarify such discordance and identify the more reliable marker between the two, analyzing ART outcomes among Korean infertility patients with AMH and AFC discordance; furthermore, the study elaborates data to evaluate possible patient-related factors contributing to discordance. **Methods**: This retrospective observational study involved 225 infertile women who underwent their first controlled ovarian stimulation treatment followed by embryo transfer. These patients were categorized into three groups: the congruent (Con) group with predicted AMH according to AFC within 50% prediction interval; the higher-than-predicted (HTP) group with predicted AMH above upper boundary of 50% prediction interval according to AFC; the lower-than-predicted (LTP) group with predicted AMH below lower boundary of 50% prediction interval according to AFC. Variables in the comparative analysis of these three groups focused on ART outcomes. **Results**: The HTP group which had younger patients with lower dose of follicle stimulation hormone (FSH) achieved better ART outcomes than the LTP group. After adjusting for factors affecting ovarian response such as age, body mass index (BMI), AFC, and total dose FSH usage, the HTP group still demonstrated significantly superior results in terms of the oocyte yield, good-quality embryo rates, and pregnancy rate compared to the LTP group. In the logistic regression analysis, age was not a significant patient factor affecting the ART outcomes; however, the patient's status of polycystic ovary syndrome (PCOS) was significantly associated with the AMH-AFC discordance, with an odds ratio (OR) of 1.24. **Conclusions**: Serum AMH provided the more accurate prediction of the patient's ovarian reserve, especially when the discordance between AMH and AFC was present; more favorable ART outcomes were observed in the patients with the higher AMH measurement than the statistically expected value from their AFC. In addition, the presence of PCOS could be considered as one of the significant factors contributing to such discordance between AMH and AFC.

Keywords: anti-müllerian hormone; antral follicle count; discordance; ovarian reserve

1. Introduction

Infertility clinics around the globe are encountering an increasing number of female patients with advanced age and/or diminished ovarian reserve, the majority of whom require assisted reproductive technology (ART) interventions, such as intrauterine insemination (IUI) and *in-vitro* fertilization (IVF) [1,2]. Assessing ovarian reserve before proceeding to controlled ovarian stimulation (COS) is critical since it aids in identifying women at risk of a poor or excessive ovarian response [3–6]. The success of patient counseling and treatment planning heavily relies on this initial yet essential step, leading to the development of numerous markers and methods, along with the refinement of the entire ART process [7,8].

Numerous factors, including age, basal follicle stimulating hormone (FSH), estradiol (E2), anti-müllerian hormone (AMH), ovarian volume, and antral follicle count (AFC), have been used to predict ovarian reserve [9]. Among these factors, both AMH and AFC exhibit superior predictive value compared to other measures [7,10–13]. They are closely correlated and are frequently used interchangeably [14,15]. Indeed, there is mounting evidence that these indicators are associated to the initial and final ovarian response, number of retrieved oocytes, and ultimately even the live birth rate [13,16,17].

However, within this interrelated status of AMH and AFC, discordance is commonly encountered in clinical practice. IVF specialists often confront situations in which the serum AMH level is either higher or lower than expectations based on the AFC, even when the AMH measurement and AFC are performed at the same clinical center during the early follicular phase of the same menstrual cycle [18,19]. The observed discordance cannot be solely attributed to technical issues in antral follicle counting or the analytical variability of the AMH assays [3]. This incongruity poses challenges and uncertainties in the pretreatment patient counseling and COS planning, which is

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particularly critical in older patients where even a single oocyte retrieval result can lead to significant difference in cascade to IVF pregnancy outcome.

Undoubtedly, while a single IVF procedure does not guarantee a successful pregnancy, when the discordance between AMH and AFC is present, improper management can undermine the clinician's confidence in the patient's long-term ART journey. This can have enduring negative implications for subsequent procedures. Although there have been limited studies on this discordance, even these studies have not provided a consistent answer regarding which ovarian reserve marker is reliable in such cases [18–21]. Therefore, the objective of this study is to determine which marker is more reliable in infertility patients with the AMH and AFC discordance by comparing their ART outcomes between different patient groups with congruent or discordant values of AMH and AFC, as well as evaluating possible patient-related factors that could contribute to such discordance in ovarian reserve markers.

2. Methods

2.1 Patient Characteristics

The present study was a retrospective observational analysis of 225 infertile women who sought treatment at the Pusan National University Hospital Infertility Centre between January 2017 and December 2020. The hospital's electronic medical record system was used for the retrospective review of patient information. Inclusion criteria required that patients had completed their first COS treatment followed by subsequent embryo transfer (ET). Clinical and demographic data were collected for all patients, including age at COS, gravida, height, weight, body mass index (BMI), cause and duration of infertility, AFC, serum FSH, and AMH levels. A single expert determined the COS procedure, dose, and duration of gonadotropin stimulation based on patients' age, BMI, serum FSH and AMH, and AFC. Exclusion criteria included the patients who had undergone oocyte donation for IVF or oocyte freezing cycles, those with severe male factors, abnormal natural killer cell levels or activity, thrombophilia, uterine anomalies or synechiae, smokers, alcohol consumers, and those who had undergone unilateral oophorectomy or chemotherapy.

2.2 Classification of Patient Groups

Fig. 1 illustrated the distribution of the AFC and AMH in all patients, and the patients' AFC was strongly correlated to their AMH (R = 0.72, $p < 0.001$). To describe the association between AMH and AFC, this study utilized predicted values derived from Pearson's correlation analysis and linear regression analysis. Patients were categorized into three groups based on the 50% prediction interval of linear regression model comparing the relationship between AMH and AFC. The concordant (Con) group included patients falling within the 50% prediction interval, the higher-than-predicted (HTP) group consisted of patients with AMH levels surpassing the upper boundary of the 50% prediction interval, and the lower-than-predicted (LTP) group encompassed patients with AMH levels falling below the lower boundary of the 50% prediction interval. In other words, the three patient groups could be statistically interpreted as follows:

(1) HTP group: patients with higher AMH levels than those predicted based on AFC.

(2) Con group: patients with AMH levels that match the predictions based on AFC.

(3) LTP group: patients with lower AMH levels than those predicted based on AFC.

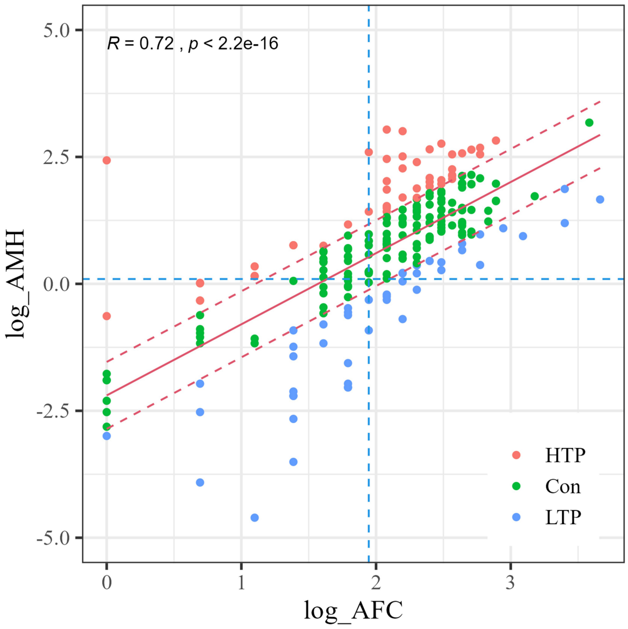

Fig. 1. The relationship between serum AMH (ng/mL) and AFCs. Linear regression line equation: log AMH = –2.197 + 1.401 × log AFC. Red dotted line: 50% prediction interval. HTP, higher-than-predicted; Con, Concordant; LTP, lower-than-predicted; AMH, anti-müllerian hormone; AFC, antral follicle count.

2.3 COS, Oocyte Retrieval and Embryo Transfer

All patients received with either a gonadotropin releasing hormone (GnRH) agonist long protocol or GnRH antagonist protocol, followed by IVF or intracytoplasmic sperm injection (ICSI). The treatment involved medical injections, including recombinant FSH (rFSH) (Gonal-F; Merck Serono, Darmstadt, Germany), human menopausal gonadotrophins (hMG) (Menopur; Ferring, NJ, USA), and/or either GnRH agonist (Lorelin; DongKook, Seoul, Republic of Korea) or GnRH antagonist (Orgalutran; Organon, Quebec, Canada).

All patients were closely monitored during COS with serial transvaginal ultrasonographic measures of follicle

Table 1. Comparison of clinical and biochemical characteristics of the study population.

	Overall	HTP	Con	LTP	p-value
n (%)	225	46 (20.4)	133 (59.0)	46 (20.4)	
Age (years)	35.20 (4.42)	33.39 (4.06) †	35.48 (4.27)	36.20 (4.75) ‡	0.004
Gravida	0.76 (1.25)	0.50 (0.96)	0.79 (1.32)	0.96 (1.28)	0.121
BMI (kg/m^2)	22.81 (3.80)	23.56 (3.75)	22.67 (4.05)	22.48 (2.97)	0.286
Infertility duration (month)	40.09 (32.32)	34.50 (23.72)	43.74 (35.81)	35.11 (27.93)	0.095
Infertility type (%)					
Primary	141 (62.7)	33 (71.7)	84 (63.2)	24 (52.2)	0.162
Secondary	84 (37.3)	13 (28.3)	49 (36.8)	22 (47.8)	
Ovarian pathology history (%)					
None	154 (68.4)	25 (54.3) †	98 (73.7)	31 (67.4) ‡	
Endometriosis	32 (14.2)	2 (4.3) †	19 (14.3)	11 (23.9) ‡†	0.000
PCOS	38 (16.9) †	18 (39.1) †	16 (12.0)	4 (8.7) ‡†	
Both	1 (0.4)	1 (2.2)	0 (0.0)	0 (0.0)	
FSH (mIU/mL)	7.21 (5.52)	6.41 (2.75)	6.89 (4.90)	8.94 (8.34)	0.142
AMH (ng/mL)	3.64 (3.98)	7.88 (5.43) †	3.06 (2.69)	1.07 (1.34) ‡†	0.000
AFC	9.24 (5.52)	8.65 (4.43)	9.38 (4.89)	9.41 (7.84)	0.639

Data are presented as the mean (SD, standard deviation) or number of patient (%). A value of $p < 0.05$ was considered as statistically significant. For post hoc analysis, ‡ indicates a statistically significant comparison between HTP and LTP, while † signifies statistical significance in the comparisons between HTP *vs.* Con or Con *vs.* LTP.

HTP, higher-than-predicted; Con, concordant; LTP, lower-than-predicted; BMI, body mass index; PCOS, polycystic ovarian syndrome; FSH, follicle stimulation hormone; AMH, anti-müllerian hormone; AFC, antral follicle count.

Table 2. Comparison of COS protocols and ART outcomes of the study population.

	Overall	HTP	Con	LTP	p-value
n (%)	225	46 (20.4)	133 (59.0)	46 (20.4)	
Protocol (%)					
Long	125 (55.6)	18 (39.1) †	76 (57.1)	31 (67.4) ‡	0.022
Antagonist	100 (44.4)	28 (60.9)	57 (42.9)	15 (32.6)	
Total FSH usage	4827.04 (2338.56)	4185.52 (2062.78)	4726.13 (2237.73)	5760.33 (2633.99) ‡†	0.008
Pre-ovulatory follicles	14.11 (10.66)	19.46 (14.11) †	13.76 (9.02)	9.76 (8.85) ‡†	0.001
FOI	1.04 (0.80)	1.62 (1.13) †	0.97 (0.64)	0.66 (0.44) ‡†	0.000
FORT	1.66 (1.21)	2.50 (1.64) †	1.57 (1.06)	1.06 (0.48) ‡†	0.000
Total oocytes retrieved	9.22 (7.66)	13.13 (10.14) †	8.88 (6.46)	6.30 (6.49) ‡†	0.001
Germinal vesicle	0.81 (1.19)	1.24 (1.65)	0.74 (1.03)	0.57 (0.98) ‡	0.066
Metaphase I	0.83 (1.07)	0.80 (1.09)	0.84 (1.07)	0.80 (1.09)	0.968
Metaphase II	7.10 (6.51)	10.41 (8.40) †	6.80 (5.77)	4.63 (5.04) ‡†	0.001
Total embryos	6.93 (5.76)	9.74 (7.23) †	6.73 (5.15)	4.70 (4.66) ‡†	0.001
Blastocyst	2.36 (3.12)	3.63 (3.73) †	2.32 (3.01)	1.24 (2.26) ‡†	0.001

Data are presented as the mean (SD) or number of patient (%). A value of $p < 0.05$ was considered as statistically significant. For post hoc analysis, ‡ indicates a statistically significant comparison between HTP and LTP, while † signifies statistical significance in the comparisons between HTP *vs.* Con or Con *vs.* LTP.

COS, controlled ovarian stimulation; ART, assisted reproductive technology; HTP, higher-than-predicted; Con, concordant; LTP, lower-than-predicted; FSH, follicle stimulation hormone; FOI, follicle-to-oocyte index; FORT, follicular output rate.

growth and endometrial thickness in order to optimize rFSH and hMG dosages (Voluson E6 General Electric, Milwaukee, Wauwatosa, WI, USA). When the dominant follicle achieved a diameter of 17 mm, human chorionic gonadotropin (hCG) and/or GnRH agonist were administered to induce oocyte maturation. Oocyte retrieval was performed using ultrasound-guided aspiration 35 hours after the trigger was given. For fresh ET, the procedure was carried out three days following the oocyte retrieval, while frozen ET was performed with the proper endometrial preparations. Most of the endometrial preparation was performed using an artificial protocol, and luteal phase sup-

Table 3. Binary logistic regression analysis to validate the correlation between patient groups and the outcomes of ART.

	Group	n	Event (%)	Crude		Adjusted (1)		Adjusted (2)	
				OR [95% CI]	*p*-value	OR [95% CI]	*p*-value	OR [95% CI]	*p*-value
Outcomes: event: >median									
Pre-ovulatory follicles	LTP	46	14 (30.4%)	Ref.		Ref.		Ref.	
	HTP	46	27 (58.7%)	3.248 [1.375, 7.673]	0.007	5.565 [1.652, 18.746]	0.006	4.484 [1.250, 16.084]	0.021
	Con	133	65 (48.9%)	2.185 [1.070, 4.463]	0.032	2.378 [0.855, 6.615]	0.097	2.214 [0.776, 6.321]	0.137
FOI	LTP	46	12 (26.1%)	Ref.		Ref.		Ref.	
	HTP	46	34 (73.9%)	8.028 [3.165, 20.361]	0.000	7.980 [3.145, 20.251]	0.000	7.732 [2.948, 20.283]	0.000
	Con	133	63 (47.4%)	2.550 [1.216, 5.350]	0.013	2.553 [1.216, 5.359]	0.013	2.477 [1.171, 5.239]	0.018
FORT	LTP	46	11 (23.9%)	Ref.		Ref.		Ref.	
	HTP	46	37 (80.4%)	13.081 [4.837, 35.373]	0.000	13.193 [4.845, 35.926]	0.000	13.011 [4.648, 36.424]	0.000
	Con	133	63 (47.4%)	2.864 [1.342, 6.112]	0.007	2.942 [1.367, 6.333]	0.006	2.943 [1.362, 6.360]	0.006
Total oocytes retrieved	LTP	46	14 (30.4%)	Ref.		Ref.		Ref.	
	HTP	46	29 (63.0%)	3.899 [1.637, 9.285]	0.002	7.396 [2.200, 24.857]	0.001	6.844 [1.920, 24.400]	0.003
	Con	133	68 (51.1%)	2.391 [1.171, 4.884]	0.017	2.744 [1.003, 7.507]	0.049	2.685 [0.967, 7.458]	0.058
Germinal vesicle	LTP	46	14 (30.4%)	Ref.		Ref.		Ref.	
	HTP	46	28 (60.9%)	3.556 [1.500, 8.429]	0.004	4.700 [1.754, 12.597]	0.002	6.033 [2.112, 17.237]	0.001
	Con	133	57 (42.9%)	1.714 [0.838, 3.507]	0.140	1.791 [0.780, 4.115]	0.169	1.973 [0.839, 4.640]	0.119
Metaphase I	LTP	46	7 (15.2%)	Ref.		Ref.		Ref.	
	HTP	46	11 (23.9%)	1.751 [0.612, 5.013]	0.297	2.373 [0.742, 7.586]	0.145	2.242 [0.653, 7.704]	0.200
	Con	133	27 (20.3%)	1.419 [0.572, 3.521]	0.450	1.727 [0.622, 4.795]	0.294	1.818 [0.632, 5.229]	0.268
Metaphase II	LTP	46	13 (28.3%)	Ref.		Ref.		Ref.	
	HTP	46	30 (65.2%)	4.760 [1.968, 11.512]	0.001	8.726 [2.772, 27.470]	0.000	6.686 [2.032, 22.002]	0.002
	Con	133	64 (48.1%)	2.355 [1.139, 4.868]	0.021	2.747 [1.057, 7.139]	0.038	2.619 [0.978, 7.012]	0.055
Total embryos	LTP	46	13 (28.3%)	Ref.		Ref.		Ref.	
	HTP	46	30 (65.2%)	4.760 [1.968, 11.512]	0.001	9.651 [2.911, 31.996]	0.000	8.120 [2.329, 28.312]	0.001
	Con	133	68 (51.1%)	2.656 [1.285, 5.490]	0.008	3.328 [1.230, 9.003]	0.018	3.231 [1.164, 8.968]	0.024
Blastocyst	LTP	46	13 (28.3%)	Ref.		Ref.		Ref.	
	HTP	46	28 (60.9%)	3.949 [1.649, 9.456]	0.002	5.592 [2.016, 15.511]	0.001	4.612 [1.618, 13.149]	0.004
	Con	133	58 (43.6%)	1.963 [0.948, 4.064]	0.069	2.153 [0.907, 5.112]	0.082	1.968 [0.831, 4.657]	0.124

A value of $p < 0.05$ was considered as statistically significant. Adjusted (1) for "AFC", Adjusted (2) for "age", "BMI", "AFC", "total FSH usage".

ART, assisted reproductive technology; HTP, higher-than-predicted; Con, concordant; LTP, lower-than-predicted; FOI, follicle-to-oocyte index; FORT, follicular output rate; AFC, antral follicle count; BMI, body mass index; FSH, follicle stimulation hormone; OR, odds ratio; 95% CI, 95% confidence interval.

port was continued until 8 to 10 weeks from the day of ET. No more than two cleavage-stage embryos were transferred, and the same policy applied to frozen ETs.

2.4 Assessment of AMH and AFC

Peripheral blood samples of the patients were collected on any day during the follicular phase of the menstrual cycle, and AMH was measured using the MIS/AMH ELISA kit from Beckman Coulter (High Wycombe, Buckinghamshire, UK). The assay kit has intra- and inter-assay coefficients of variation of less than 12.3% and 14.2% respectively. Total number of AFCs was measured on the same day of AMH measurement, on the menstruation day 2 or 3 by transvaginal ultrasonography using with 5–9 MHz transvaginal probe. All measurements were assessed by a single investigator.

2.5 Main Outcome Measurements

Ovarian response evaluation included the count of retrieved oocytes, metaphase II oocytes, total embryos, and blastocysts, along with the determination of the follicular output rate (FORT) and the follicle-to-oocyte index (FOI). FORT, initially introduced by Gallot *et al*. [22] measures the ratio of pre-ovulatory follicles, sized 16–22 mm in diameter, to pre-antral follicles, measuring 3–8 mm in diameter. FOI, which builds upon the concept of FORT, was introduced as a novel marker by Alviggi *et al*. [23]. It specifically represents the ratio of the total number of collected oocytes at the end of COS to the number of antral follicles available at the beginning of COS.

Table 4. Binary logistic regression analysis conducted to identify factors affecting discordance.

Outcome	Group	n	Event (%)	Crude	
				OR [95% CI]	p-value
Outcome: event = discordant (HTP or LTP)					
Age (years)	>35	105	41 (39.0%)		
	≤35	120	51 (42.5%)	1.035 [0.910, 1.178]	0.601
Ovarian pathology history (%)	None	154	56 (36.4%)		
	Endometriosis	32	13 (40.6%)	1.044 [0.867, 1.257]	0.653
	PCOS	38	22 (57.9%)	1.240 [1.043, 1.475]	0.016
	Both	1	1 (100.0%)	1.890 [0.724, 4.932]	0.195

A value of $p < 0.05$ was considered as statistically significant.

HTP, higher-than-predicted; LTP, lower-than-predicted; PCOS, polycystic ovarian syndrome.

2.6 Statistical Analysis

To examine the correlation between AFC and AMH, we employed Pearson's correlation analysis and linear regression analysis. To assess differences between patient groups, we utilized either the Chi-squared test or Fisher's exact test for categorical variables and the one-way analysis of variance (ANOVA) or Kruskal-Wallis test for continuous variables. Subsequently, post hoc tests were conducted for multiple comparisons. Binary logistic regression models were employed to provide odds ratios (OR) while adjusting for covariates. Statistical analysis was conducted using R version 4.3.1 (The R Foundation for Statistical Computing, Vienna, Austria), in conjunction with additional packages (ggplot2, ggpubr, http://cran.r-project.org). A p-value of <0.05 was considered as statistically significant.

3. Results

The clinical and biochemical characteristics of all patients were presented in Table 1. The mean age of the entire patient was 35.20 ± 4.42 years, ranging from 23 to 47 years. The mean AMH level was 3.64 ± 3.98 ng/mL, and AFC was 9.24 ± 5.52, indicating the inclusion of patients with a diverse range of ovarian reserve markers across various age groups in the study. The HTP group (n = 46) was younger than the LTP group (n = 46), while there were no statistically significant differences between the two groups in terms of gravida, BMI, infertility duration, infertility type, or FSH. Regarding the history of ovarian pathology, the HTP group exhibited the higher prevalence of polycystic ovary syndrome (PCOS), while the LTP group predominantly had cases of endometriosis.

Table 2 compared COS protocols and ART outcomes among the patient groups. In the HTP group, 61% of patients used the antagonist protocol in COS, while the LTP group predominantly utilized the long protocol (67%). The mean total FSH usage in the HTP group was lower than that in the LTP group, with the LTP group having the highest mean total FSH usage among the three groups. The HTP group displayed significantly higher numbers of pre-ovulatory follicles, total oocytes retrieved, metaphase II oocytes, total embryos, and blastocysts, along with higher FOI and FORT values when compared to the LTP group.

The results of logistic regression analysis for correlation between patient groups and ART outcomes were presented in Table 3. Events that exceeded the median values for ART outcomes in the entire patient were considered as the outcomes. When comparing the HTP group to the LTP group, the OR [95% confidence interval (95% CI)] were found to be 3.248 [1.375–7.673] for pre-ovulatory follicles, 8.028 [3.165–20.361] for FOI, 13.081 [4.837–35.373] for FORT, 3.899 [1.637–9.285] for total oocytes retrieved, 4.760 [1.968–11.512] for metaphase II oocytes, 4.760 [1.968–11.512] for total embryos, and 3.949 [1.649–9.456] for blastocysts. These ORs remained statistically significant even after adjustments for AFC alone and when adjusting age, BMI, AFC and total FSH usage together. Table 4 described the results of logistic regression analysis aimed at identifying factors influencing discordance. While age did not exhibit statistical significance, presence of PCOS was associated with OR of 1.24 with 95% CI of 1.043–1.475.

4. Discussion

Infertility specialists frequently encounter clinical situations where a patient's AMH and AFC do not align, and most of them tend to consider such discordance as a technical limitation [18,19]. However, in 2018, a study was published indicating that when such discordance occurs, pregnancy rates were lower in concordant patients [20]. Furthermore, in real clinical settings, healthcare providers face challenges when they encounter discordance, particularly in the pre-treatment patient counseling and COS planning processes. Alebic *et al.* [3] suggested that this discordance goes beyond being a mere technical constraint and instead reflects patient-specific differences in the production of AMH within the follicles. When the actual measurement of AMH was higher than what could have been expected from the AFC, it might indicate an up-regulation of AMH secretion, which was a typical clinical feature of PCOS. Conversely, when AMH was lower than what could have been expected from the AFC, it might suggest down-regulated AMH secretion, which could be an early indication of diminished ovarian reserve and premature ovarian insufficiency. In other terms, when challenged against AFC, the serum AMH level could not only a quantitative but also a qualitative follicle marker, in relation with clinical and endocrine parameters [3].

The aim of the current study did not focus on exploring any underlying mechanisms of the discordance between AMH and AFC. Nevertheless, several patient-related clinical factors influencing the discordance were confirmed in the study; it was noted that patients with higher AMH in comparison to their AFC were more inclined to have PCOS, and the presence of PCOS increased the discordance rate among the infertility patients. This implies that PCOS could be regarded as one of the factors contributing to the observed discordance. Moreover, the group with higher AMH levels compared to the expected values from AFC had the lowest mean age and the lowest total FSH dosage among the groups, and their ART outcomes were more favorable than those of the group with lower AMH compared to AFC. In contrast, the group with lower AMH compared to AFC turned out to have the highest mean age and highest total FSH usage, also having less favorable ART outcomes than the other groups. Even after adjusting for factors known to affect ovarian response, such as age, BMI, AFC, and total FSH usage, the group with higher AMH compared to AFC demonstrated superior results in terms of oocyte yield and good-quality embryo rate compared to the group with lower AMH compared to AFC. This suggests that AMH might be a more robust predictor of ovarian response than AFC when the discordance is present.

In the study conducted by Li *et al.* [21] which involved 1046 patients of various age groups, in the presence of discordance between AMH and AFC, the group with higher AMH compared to AFC exhibited a higher number of retrieved oocytes and a greater cumulative live-birth rate. Similarly, Guo *et al.* [24] confirmed that in the group with higher AMH compared to AFC, there was a greater yield of oocytes and favorable embryos. Furthermore, in a recent investigation by Aslan *et al.* [25] involving 662 Turkish diminished ovarian reserve patients, when discordance between AFC and AMH was present, those with normal AMH and low AFC showed a better ovarian response than the patients with low AMH and normal AFC. This led to the conclusion that serum AMH possess higher predictive value for stimulation success in cases of discordance with AFC [25].

Various patient factors have been examined to understand their possible influence on such discordance between AMH and AFC. In the study of Zhang *et al.* [26], patients were classified according to Bologna criteria, and the length of the menstrual cycle was observed as a possible discordant factor. When the discordance arose, the group with higher AFC to detected AMH had significantly higher oocyte yield, embryo quality, and clinical pregnancy rates than the group with lower AFC to AMH. They concluded that the AFC should be the preferable marker for predicting ovarian response in order to design the most effective personalized COS regimen in this group of patients [26]. Their conclusions are contrasting to ours, probably due to the difference in the adopted study design; Zhang's study [26] excluded women who had undergone ovarian surgery and/or been diagnosed with PCOS, whereas in the current study, more than one-third of the patients were diagnosed with endometriosis or PCOS. Regarding endometriosis and PCOS, as they have been widely known as the leading causes of infertility, the current study tends to more practically reflect the real-world clinical data of poor ovarian response (POR) patients, thus being more clinically appropriate in deciding ART management of POR patients. Yet, despite the varying results, previous literature has commonly considered the age and PCOS history of a patient as possible discordant components. These studies do agree that discordance is not merely a technical issue; when discordance exists, the COS outcome and clinical pregnancy rate can be reduced. When possible discordant factors are observed, careful analysis of AMH and AFC might enhance the success of the ART treatment [21,24–26].

To our knowledge, the current study is the first analysis of Korean infertility patients investigating the discordance between AMH and AFC among ethnically and racially homogenous study groups. Also, while most of the previous studies related to discordance primarily focused on ART outcomes, specifically the number of oocytes, FOI, and FORT, our study employed a comprehensive approach by not only evaluating the quantity but also the quality of oocytes and embryos, as well as FOI, and FORT. Moreover, it is noteworthy that previous studies addressing discordance typically categorized patients using criteria such as the Bologna or Poseidon classification, which might have not effectively accounted for the diverse range of ages and values for AMH and AFC observed in clinical practice. On the other hand, we employed an AMH prediction model based on actual AFC from the study groups when classifying the patients, thereby overcoming such limitation.

Several limitations still exist and should be thoroughly considered in the current study. Firstly, the study's retrospective nature imposed constraints on addressing potential heterogeneity in COS protocols; the adjustment of these protocols was not feasible within the current framework. It is important to emphasize that the primary focus of the study did not involve evaluating the specific protocols themselves; nevertheless, the selection of the most appropriate stimulation protocols was consistently made by the same experienced reproductive endocrinologist and embryologists within a tertiary hospital setting throughout the study. Secondly, the sample size was relatively small due to the study being conducted at a tertiary infertility clinic in a single center, and it did not include the assessment of live birth rates as one of the outcome measures. Thus, there is a compelling need for a multi-centered study design with a more diverse population that incorporates live birth rate data. Despite these limitations, the findings of this study can serve as a foundational step towards improving effective treatment plans for infertility patients and providing valuable guidance to specialized clinicians faced with the challenge of discordance between AMH and AFC.

5. Conclusions

Serum AMH provided a more accurate prediction of the patient's ovarian reserve, especially in the presence of discordance between AMH and AFC, resulting in more favorable ART outcomes in the patients with higher AMH compared to their AFC. Regarding the discordance between AMH and AFC, the presence of PCOS could be considered as one of the significant factors contributing to this observed discordance; special clinical attention should be given to this specific patient group when tailoring ART management plans in order to magnify their chances of a successful pregnancy.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

EY and HL designed the research study. EY performed the research. JJ and YN provided help and advice on data gathering and analysis. HL analyzed the data. EY, HL, JJ, and YN wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

This study was submitted to the Institute Review Board (IRB) with the assigned number 2209-006-118, granted ethical approval by the IRB of Pusan National University Hospital. Given its retrospective observational nature, informed consent was not required.

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Conflict of Interest

The authors declare no conflict of interest.

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