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The correlation of AMH with clinical outcomes of patients with IVF-ICSI failures according to the ovarian response

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Abstract

Anti-Mullerian Hormone (AMH) is considered as the most important biomarkers of ovarian reserve, its response and even as predictor of IVF outcomes. However, until now, the correlation of AMH to IVF outcomes is still debated depending on AMH cut-off. Couples with IVF failures are representing the most critic population to understand using different biomarkers in order to predict the results and suggest wisely a personalized management algorithm for them, especially those with low and high AMH. For this reason, our retrospective cross-sectional study, 147 patients were included with women's mean age of 35 years old (22-40 years) with at least 2 IVF-ICSI failures and undergoing IVF-ICSI fresh cycle, representing an idiopathic infertility, who were divided into 3 groups: Group PR (Poor Response; Patients with less than 5 retrieved oocytes (n=47)), Group NR (Normal Response; Patients presenting between 5 and 10 retrieved oocytes (n=55)), and Group HR (Hyper-Response; Patients with more than 10 retrieved oocytes (n=45)). Then, each group was studied based on the female age. As results, AMH differences were significant between the 3 groups PR, NR and HR respectively (0.54 ± 0.76, 2.13±2.10, 4.03 ± 2.82). The PR showed 16% for pregnancy rate while NR and HR could have 53% and 39% respectively. Even the group with extreme low AMH (<0.5ng/ml) could to reach 17% of pregnancy rate. AMH showed significant correlation with AFC (r=0.67) but non-significant with the number of IVF failures (r=-0.03). Those results could to show the correlation of AMH to clinical outcomes especially the pregnancy rate whatever is the ovarian response, while even the category with extreme low AMH could succeed the IVF process clinically while it is generally ignored. Those results are calling in need to develop more the predictive model of AMH and AFC correlated to ovarian response, of clinical outcomes for patients with IVF failures for deeper understanding of risk factors.

Keywords: Anti-müllerian hormone, IVF-ICSI failures, Antral follicle count, Poor responders, High responders, Ovarian reserve.

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1. Introduction

Anti-Mullerian Hormone (AMH) has emerged as a valuable prognostic marker for predicting the outcome of assisted reproductive technology (ART). Many studies showed the importance of AMH as biomarker and predictor of clinical pregnancy outcomes in infertile couples [1-2]. However, it is still unclear the assessment of AMH level based on serum or follicular fluid (FF) to predict IVF-ICSI success rates linked to oocyte quality and ovarian response to the controlled ovarian stimulation (COS), due to the heterogeneity of FF AMH compared to serum AMH [1]. Infertile women with low AMH levels may still have a chance of successful pregnancy through IVF/ICSI treatments. However, lower AMH levels could compromise pregnancy outcomes, even though it does not impair embryo developmental competence [3].

In contrast, higher AMH levels are positively correlated with higher chances of pregnancy, the number of obtained embryos, high-quality embryos, and transferred embryos [3].

The correlation between AMH and pregnancy is more dependent on the number of oocytes and embryos available for transfer than embryo quality [3]. Consequently, AMH levels can aid in counselling patients undergoing IVF/ICSI treatments about the chances of success and risk of early miscarriage [2-3]. Although AMH has potential as a predictor of pregnancy in IVF/ICSI, its role in predicting early miscarriage is inconclusive [2]. Overall, serum AMH is positively correlated with pregnancy outcome in IVF/ICSI but is not enough to alter a clinical decision. Hence, further research is needed to reduce heterogeneity and calculate the cut-off value of AMH to improve its accuracy as a predictive model [1].

Anti-Müllerian hormone (AMH) is an established marker of ovarian reserve predicting ovarian response after controlled ovarian stimulation (COS) in *in vitro* fertilization (IVF) cycles as a part of the gold standard for modern fertility tests [4-6]. AMH known as a Müllerian inhibiting substance (MIS), is a member of Transforming Growth Factor (TGF) beta family of glycoproteins that are involved in the regulation of growth and differentiation. AMH produced by cells in ovarian follicles presenting a positive correlation with the number of oocytes retrieved after COS. AMH acts as a natural follicular gatekeeper limiting follicle growth initiation and maintains the primordial follicle pool throughout the reproductive age. Currently, age, antral follicle count (AFC), and AMH level are generally acknowledged as the best predictors for ovarian reserve [7]. The value of the AMH level in the prediction of pregnancy has been investigated in various studies, but the results have been inconsistent. Several studies showed the AMH prediction power of oocyte quality, fertilization rate, blastocyst development, embryo quality, pregnancy outcome, and live birth rate, but were not confirmed in other studies [5-12]. Though AMH level has an association with predicting IVF outcomes, its specificity is still depending on age and other factors including lifestyle calling in need to establish a real consensus [4,13-14]. The poor ovarian response rate (cycle cancellation or ≤ 3 oocytes) is approximately 10% between 30 and 35 years of age or sometimes-higher reaching 24% of young women with poor response [15-16]. This issue enhanced the importance of management strategy to design especially for poor responders in IVF presenting a challenge for clinicians with high risk not to achieve clinical pregnancy after IVF with high cancelled cycles rate. Whatever, few studies could be interested on these women profiles especially those with extremely low AMH values with limited size studied population [17-18]. This study aims to evaluate the predictive power of AMH as well as AMH with AFC as markers of ovarian reserve in IVF-ICSI failures for couples with idiopathic infertility, by studying their correlation with the duration of hormonal stimulation and the total dose of the FSH in the context of ovarian stimulation. However, the main objective can be summarized in evaluation of the interval of AMH values on the one hand according to the ovarian response of the patient in IVF and on the other hand according to the maternal age in order to predict the IVF-ICSI results.

2. Material and Methods

2.1. Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All patients who participated in this study signed an informed consent after being informed about the terms and issues of study.

2.2. Patients' selection

This is a retrospective study design collecting data from January 2018 to November 2022 selecting infertile couples with at least 2 previous repeated IVF-ICSI failures in Fertility Center Ghandi, Casablanca, Morocco. 147 patients were included with women's mean age of 35 years old (22-40 years) with at least 2 IVF-ICSI failures and undergoing IVF-ICSI fresh cycle, representing an idiopathic infertility (Table 1). Among all the patients undergoing the antagonist protocol, we excluded those treated with another specific stimulation protocol or those with other adjuvant treatments and those included in frozen cycles. In one hand, the inclusion criteria included repeated IVF-ICSI cycle, Fresh IVF-ICSI cycle, idiopathic infertility and fixing female and male age cut-off for infertile couples at 40 years old (according to previous published studies, primary infertility, endometrial thickness more than 6mm in ovulation induction, regular menstrual cycles, BMI <30, absence of uterine pathology and infectious negative balance.

In the other hand, the exclusion criteria included IOP, PCOS, endometriosis, a partner with a poor-quality sperm (OATS, non-obstructive azoospermia), or improvement sperm quality with specific selective protocols as MACS, PGS, and antioxidant treatments. Thus, we proceeded to follow a first distribution based on the ovarian response presented by the number of oocytes retrieved after hormonal stimulation, in order to determine the AMH and AFC threshold for each type of response and to evaluate their degree. prediction at this level: Group PR (Poor Response; Patients with less than 5 retrieved oocytes (n=47)), Group NR (Normal Response; Patients presenting between 5 and 10 retrieved oocytes (n=55)), and Group HR (Hyper-Response; Patients with more than 10 retrieved oocytes (n=45)). Then, each group was studied based on the female age. Serum AMH concentrations (ng/ml) evaluated by ELISA (Elecsys AMH® assay, Cobas, Roche, Germany), were included as a standard measure in the IVF program. Written informed consent was obtained from each included couple to perform ICSI on at least some of the retrieved oocytes. Moreover, informed consent to present our data in any publication was obtained as long as confidentiality was maintained.

2.3. IVF/ intra-cytoplasmic spermatozoa injection (ICSI) protocol

In order to eliminate the effect of protocol and better align the sample and follicular cohort, it is preferable to use the antagonist protocol using the r-FSH (Orgalutran 0.25 and Gonal-F). The ultrasound examination was performed

endovaginally to analyze the antral follicle count (AFC) on the third day of the cycle. Follicles were measured in both dimensions. All follicles larger than 2mm were taken into account. At the day of oocyte pick-up, the semen sample is obtained by masturbation after 3-5 days of sexual abstinence into sterile, non-toxic plastic vials, which have been incubated for 30 minutes to facilitate liquefaction. In the self-controlled group, the sperm was treated by double density gradient centrifugation (DGC) (PureSperm: Nidacon, International AB, Gothenburg, Sweden). All semen samples were loaded onto a 40% and 80% discontinuous gradient and centrifuged at 1600 rpm for 20 min.

The resulting pellets were washed with 2 ml of (HTF Irvine Scientific, Santa Ana, CA, USA) and centrifuged at 1200 rpm for 10 min. For the test group, sperm was treated with DGC. Subsequently, the oocytes of the patients were injected with the treated spermatozoa by ICSI, evaluating eventually the embryological outcomes including fertilization, and embryo development (cleavage at day 3, blastulation at day 5 and embryo quality according to the Gardner classification). Depending on the patient, one or two embryos were transferred in utero using a Frydman catheter (CCD Laboratories, Paris, France). Clinical pregnancy was defined as the presence of an intrauterine gestational sac as visualized by transvaginal ultrasonography.

2.4. Statistical analysis

Data are presented as mean ± standard deviation (SD) or standard number representing the total. Thus, these data are analyzed by the student's t-test for comparison of mean values or chi squared test for comparison of percentages using the Statistical Package, Statistica (version 6.0) to compare a significantly different populations: $p < 0.05$ shows the significant difference.

3. Results and Discussion

This study investigated the IVF-ICSI outcomes in women with repeated IVF-ICSI failures with idiopathic infertility based on AMH and AFC for couples under 40 years old, to exclude the real impact of age. The ovarian response is represented clinically by the number of oocytes retrieved after ovarian stimulation from which the weak ovarian response is judged by a poor retrieved oocyte number less than 5 (PR), normal between 5 and 12 oocytes (NR) whereas a hyper-response such is generally the case for women with PCOS who have a retrieval of more than 12 oocytes (HR) knowing that we excluded the PCOS cases (Table 2). Indeed, according to several studies, especially by La Marca et al. (2007; 2013; 2014) showed that this ovarian response can be predicted by AMH or AFC [19-21]. This led to the consensus suggestion based on ESHRE reports that a poor response can be predicted by an AMH less than or equal to 1.5 while a hyper-response starts from an AMH of 3.5 ng/ml or even in the case of a PCOS patient with an AMH from 2.8 ng/ml and an average of 4.2 ng/ml.

However, these values remain debatable, discriminating any patient with an AMH less than 1.5, which prompted us to carry out this statistical analysis on a total of 147 patients in order to analyse our determining values of AMH and AFC according to the response. Thus, for a poor ovarian response, we found an average AMH of 0.5 ng/ml with an interval of 0.03 going up to a value of 5. Such a result challenges the presence of special cases of patients involving well other factors including BMI, patient lifestyle, maternal age, and rank of IVF attempt. Indeed, sometimes even a woman with an AMH of 5 ng/ml could however have a poor ovarian response despite the key role of AMH in predicting the number of oocytes to be retrieved in IVF. On the other hand, for patients with a normal response after hormonal stimulation, according to ESHRE recommendations in 2013, the AMH interval should be limited 1.5 and 3.5 ng/ml with an average of 2.5. Furthermore, although the average AMH of a normal response is 2 ng/ml, which is part of the interval accepted by the ESHRE [1.5 ng/ml; 3.5 ng/ml], our results reveal a tolerance of the AMH interval including even low AMH of 0.5 ng/ml up to high AMH of 9 ng/ml characterizing PCOS. This encourages us to recommend to clinicians on the one hand to avoid discrimination of patients with a low AMH knowing that a patient with AMH at 0.5 could ensure a good response likely for the success of IVF and on the other hand, better management of PCOS patients and ovarian hyper-response would however remain a pre-judgment for this category which is not always true. Concerning the ovarian hyper-response with an oocyte retrieval on average 15 oocytes, our results revealed that sometimes even a patient with an AMH of 0.7 ng/ml could therefore develop an excessive ovarian response with a risk of hyperstimulation recommending to clinicians not to rush to prescribe to patients with a low AMH a high dose of FSH (starting dose) from the start, requiring several parameters to be taken into consideration. But generally, the total dose of FSH decreases significantly with the increase of the two markers of ovarian reserve "AMH and AFC". Since AMH correlates with IVF clinical outcomes in a non-linear function with a peak at AMH exhibiting the normal response (on average 1.5 ng/ml) as demonstrated by several studies [19-21]. A cut-off AMH value of ≤ 1.2 ng/ml was chosen according to Gnoth et al. (2008) and Weghofer et al., (2011) while the normal range of AMH considered as control was limited between 1.3 and 2.6 ng/ml, while HR was considered when AMH bypassed 2.6 ng/ml [18-20].

AMH concentrations were measured prior to the start of each cycle. Indeed, based on AMH concentrations, the groups were divided into 5 groups to evaluate the IVF-ICSI outcomes (Table 3). Indeed, our distribution of the population followed the same strategy but even taking into account two critical categories of patients, one with an AMH less than 0.5 ng/ml and a second with an AMH between 0.5 and 1.2 ng/ml, being generally discriminated by clinicians. Indeed, these two categories could give rise to a non-negligible clinical pregnancy rate of 17% (AMH<0.5) and 29% (AMH (0.5-1.2)) for women with low AMH. In addition, women with an AMH greater than 2.6 ng/ml might include PCOS patients even if we excluded them based on Rotterdam criteria (2008). This group show a clinical pregnancy rate 35% lower than the rate of the reference series (49%) including women with normal AMH (1.5- 2.6). But generally, it should be noted that the clinical results for each category of AMH could however be influenced by the effect of the age of the patient. In the past, many studies have concluded that AMH concentrations could predict pregnancy success [22-23]. However, only a

few large studies have shown the relationship between AMH concentrations and IVF outcomes [4-5,9,24-25]. A current diagnostic issue for clinicians is the treatment of women with extremely low AMH concentrations. In that group of patients can be expected poor ovarian response, which can lead to cancelled cycle, consequently decreasing the probability to achieve pregnancy [4].

It seems clear that clinicians should communicate the probability of IVF outcomes when the woman has extremely low AMH concentrations under 0.5 ng/ml to allow both the couples and clinicians to begin either treatment or prescribe other alternatives including aromatase inhibitors treatments or Estrogenic pre-treatment. Probability of success with IVF cycle largely depends on a woman's ovarian reserve and her ability to produce a large number of high-quality mature oocytes in a cycle after HR. Average serum AMH is approximately 4 ng/ml in healthy young women with normal ovarian reserve, while recent consensus reported in La Marca et al (2016) considered poor response at AMH under 1ng/ml and high response when AMH is over 3 ng/ml [14,26]. Nikmard et al. (2016) considered normal AMH range at 1.3-2.6 ng/ml obtaining good ovarian response and clinical outcomes after ART [20]. Since AMH is produced only in small ovarian follicles, levels of this substance in the blood have been used to try to measure the size of the reservoir of developing follicles in women. Several studies showed us that the size of the reservoir of developing follicles is heavily influenced by the size of the reservoir of remaining primordial follicles (the microscopic "deeply sleeping" follicles) [27].

Thus, AMH levels in the blood are thought to reflect the size of the remaining egg stores - or ovarian reserve. As the woman ages, the size of her reserve of remaining microscopic follicles decreases. Likewise, her blood levels of AMH and the number of ultrasound-detectable ovarian antral follicles drop. Women with many small follicles, such as those with polycystic ovaries, have high AMH values, and women with few remaining follicles and those nearing menopause have low anti-Mullerian hormone levels [27]. Women with higher AMH values will tend to have a better response to ovarian stimulation for in vitro fertilization and will have more eggs retrieved. In general, having more eggs for in vitro fertilization gives a higher success rate. We don't yet have a lot of data to inform couples who practice in vitro fertilization about their AMH results and their chances of conceiving. AMH levels probably don't reflect egg quality, but having more eggs at retrieval gives us more material to work with - so we're more likely to have at least one embryo. of very good quality available for transfer to the woman's uterus. Women who have had an ART attempt, their AMH dosages on the 3rd day of the cycle. 28 women with fewer than 6 retrieved oocytes had an AMH of 1.0 + 0.4 ng/mL, while 79 women with more than 11 retrieved oocytes had an AMH 2 to 2.5 times higher (2.5 + 0.3 ng/mL) [28].

There are certain issues that come into play in the interpretation of AMH levels. Since the test has not been in common use for many years, the levels considered "normal" are not clarified and experts do not all agree on it. In addition, current commercial analyses do not all give equivalent results. Our results (Table 3 and 4) give an idea of the interpretation in relation to the scientific literature and our own experience of fertility. Do not focus on the limit values indicated here. For example, the difference between a test result of 0.6 and 0.7 ng/ml. puts the woman in a "different box" of this table - but there is very little real difference in terms of fertility potential. In reality, it is a continuum - not something that is easily categorized. AMH less than 0.2 – 0.5ng/ml presents an increased risk of a cancelled IVF cycle and a decrease in oocytes retrieved. While an AMH exceeding the value of 2.5 ng/ml can be considered as a good indicator of the oocyte pool with a good potential for fertility. Indeed, a simple dosage of AMH by comparing it to the dosage of FSH can predict the ovarian reserve, the quality of retrieved oocytes and embryos and even the possibility of having a clinical pregnancy, hence an AMH cut-off of 2.8 ng/ml is a more sensitive and specific value to predict a weak ovarian response to lead to 18% clinical pregnancy compared to normal responders having 35% pregnancy [23,29-30]. Thus, it is necessary to test the ovarian reserve first for some cases such as Sills et al. (2009) described, especially in women over the age of 30, with previous exposure to gonadotoxins (tobacco, chemotherapy, radiotherapy), a family history of early menopause or premature ovarian failure or even ovarian surgery (cystectomy, unilateral oophorectomy).

The strength of that study is the large number of patients with different AMH concentrations representing IVF-ICSI failures and with couple’s cut-off age at 40 years old as previously demonstrated. Moreover, excluding PCOS patients from HR group will give us a clear vision about the impact of AMH and AFC independently to other factors. Thus, as far as is known, this is the first study to evaluate the correlation of AMH and AFC for idiopathic infertile patients with previous IVF-ICSI failures, excluding PCOS for hyper response. We have to believe that low AMH levels by themselves should not exclude a woman as a good candidate for IVF, even in case of extreme AMH low levels as shown in our previous study [31]. In some cases, women with low AMH levels may have reduced oocytes quantity but still have good oocytes quality and chance to obtain clinical pregnancy. Recently women with low ovarian reserve could be pre-treated with AMH prior to COS and is intended to improve follicular synchrony, oocyte yield and pregnancy rates with fertility treatments programming AMH starting dose of 4-8ng/ml daily for 90 days [32-33]. Moreover, this current study offers reliable background information to counsel young women presenting low ovarian reserve before treatment.

Table 1: Characteristics of the included patients in the study.

Parameter	Results of included patients (n=147)
Patient age (years)	34,63 ± 2,80 (22-40)
Partner age (years)	38,46 ± 3,38 (27-40)
Number of IVF-ICSI failures	2,87 ± 1,19
Estradiol at day 2 (pg/ml)	46,13 ± 27,92
Progesterone at day 2 (ng/ml)	0,48 ± 0,33
AMH (ng/ml)	2,20 ± 2,48
AFC	9,15 ± 5,37
Endometrium thickness (mm)	10,02 ± 1,83
Duration of stimulation (days)	9,87 ± 2,06
Total dose of gonadotropines (UI)	2886 ± 1377
Number of retrieved oocytes	8,08 ± 6,06 (n=1188)
Maturation rate (%)	5,22 ± 4,43 (n=768; 65%)
Fertilization rate (%)	4,43 ±3,89 (n=651; 85%)
Cleavage rate (%)	4,20 ± 3,86 (n=618; 88%)
Number of transferred embryos	1,02 ± 0,53
Clinical pregnancy per patient (%)	35%
Clinical pregancy per transfer (%)	44%
Miscarriage rate (%)	11%
Empty follicle rate (%)	5%

Results are expressed as n, n (%) or mean ±standard deviation (SD). A statistic significant difference is considered when $P<0.05$ (n). $P\geq0.05$ is not significant (ns). AFC: Antral Follicle Count, AMH was measured on day 2 of the cycle and the endometrial thickness was evaluated in day of oocyte retrieval. Cleavage rate was calculated relatively to embryos at day 3 by 2 pronucleus. The miscarriage rate is expressed relative to the number of clinical pregnancies.

Table 2: Comparison of IVF-ICSI outcomes between PR, NR and HR groups.

	PR- group (n=47)	**NR- group (n=55)**	**HR- group (n=45)**
Number of retrieved oocytes	2.21 ± 1.41[b,c]	7.18 ± 1.69[a,c]	15.31 ± 3.2[a,b]
AMH (ng/ml)	0.54 ± 0.76 (0.03-5.1)[b,c]	2.13±2.10 (0.5-9.63)[a,c]	4.03 ± 2.82 (0.8-11.8)[a,b]
AFC	3.94 ± 2.21 (1-12)[b,c]	9.13 ± 3.56 (4-25)[a,c]	14.62 ± 3.90 (6-23)[a,b]
Estradiol at day 2 (pg/ml)	55.56 ± 39.19	46.44 ± 19.02	35.89 ± 8.31
Progesterone at day 2 (ng/ml)	0.38 ± 0.18	0.49 ± 0.26	0.56 ± 0.47
Endometrium thickness (mm)	9.55 ± 1.76	10.32 ± 1.92	10.14 ± 1.74
Maturation rate (%)	61% [a]	71%[b,c]	62%[a]
Fertilization rate (%)	86%	86%	84%
Cleavage rate (%)	97%	94%	95%
Top embryo quality rate (%)	72%[a,b]	74%[c]	76%[c]
Clinical pregnancy rate (%) (per transfer)	16%[a,b]	53%[b,c]	39%[a,c]
Miscarriage rate (%)	9%	7%	11%

Results are expressed as n, n (%) or mean ±standard deviation (SD). A statistic significant difference is considered when $P<0.05$ (n). $P\geq0.05$ is not significant (ns). AFC: Antral Follicle Count, AMH was measured on day 2 of the cycle and the endometrial thickness was evaluated in day of oocyte retrieval. Cleavage rate was calculated relatively to embryos at day 3 by 2 pronucleus. The miscarriage rate is expressed relative to the number of clinical pregnancies

Table 3: Comparison of IVF-ICSI outcomes between patients based on AMH.

	AMH (<0.5) (n=39)	**AMH (0.5-1.2) (n=20)**	**AMH (1.3-1.5) (n=24)**	**AMH (1.5-2.6) (n=29)**	**AMH (>2.6) (n=35)**
Patient age (years)	37.05 ± 2.83	37.90 ± 2.34	33.59 ± 3.69	33.97 ± 3.90	30.92 ± 5.51
AMH (ng/ml)	**0.27 ± 0.12**[b.c]	**0.65 ± 0.15**[b.c]	**1.38 ± 0.14**[b.c]	**1.99±0.41**[a.c]	**5.82 ± 2.02**[a.b]
AFC	**4.41 ± 2.81**[b.c]	**6.85 ± 4.39**[b.c]	**8.05 ± 3.18**[b.c]	**11.31 ± 3**[a.c]	**14.35 ± 5.08**[a.b]
Number of retrieved oocytes	2.85 ± 2.92	5.50 ± 3.66	7.41 ± 3.94	10.45 ± 4.26	13.54 ± 6.40
Maturation rate (%)	**51%**[b.c]	**72%**[b.c]	**75%**[b.c]	**64%**[a]	**63%** [a]
Fertilization rate (%)	77%	85%	86%	85%	85%
Cleavage rate (%)	84%	94%	92%	93%	95%
Top embryo quality rate (%)	**75%**[c]	**76%**[c]	**78%**[c]	**79%**[c]	**85%**[a.b]
Clinical pregnancy rate (%) (per transfer)	**17%**[b,c]	**29%**[b,c]	**39%**[b,c]	**49%**[a,c]	**35%**[a,b]
Miscarriage rate (%)	10%	9%	9%	8%	10%

Results are expressed as n, n (%) or mean ±standard deviation (SD). A statistic significant difference is considered when P<0.05 (n). P≥0.05 is not significant (ns). AFC: Antral Follicle Count, AMH was measured on day 2 of the cycle and the endometrial thickness was evaluated in day of oocyte retrieval. Cleavage rate was calculated relatively to embryos at day 3 by 2 pronucleus. The miscarriage rate is expressed relative to the number of clinical pregnancies

Table 4: Correlation between AMH and AMH/AFC with IVF-ICSI failure and the maternal age.

	AMH	**AFC**	**Number of IVF-ICSI failures**	**E2**	**P4**	**Maternal age (years)**
AMH	-	**0.67 (s)**	-0.03 (ns)	-0.13 (ns)	**0.14 (s)**	**-0.31 (s)**
AMH/AFC	-	**-**	-0.04 (ns)	**-0.67 (s)**	**0.31 (s)**	**-0.51 (s)**

A statistic significant difference of r correlation is considered when P<0.05 (s) while is represented with P≥0.05, it is not significant (ns). AFC: Antral Follicle Count, AMH was measured on day 2 of the cycle

4. Conclusions

AMH is known as good and powerful biomarker of ovarian response and clinical outcomes after IVF-ICSI program. However, studies focused on patients with repeated IVF failures are rarely linked to AMH concentrations. AMH level showed significant correlation with AFC in our study whatever is the ovarian response. Those results could to show the correlation of AMH to clinical outcomes especially the pregnancy for poor, normal and high responders. Nevertheless, the category with extreme low AMH who is generally misjudged in IVF, could succeed the IVF process clinically. Indeed, there is a real need to develop more the predictive model of AMH and AFC correlated to ovarian response, of clinical outcomes to understand clearly the risk factors of patients with repeated IVF failures.

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