ECRONICON OPEN ACCESS

EC GYNAECOLOGY
Research Article

Evaluation of the Anti-Müllerian Hormone as a Predictor of the Ovarian Reserve and its Relation with Outcomes of Assisted Reproduction Treatments in a Latin Population

Héctor Salvador Godoy Morales[1], Germán Gabriel Palacios López[2]*, Griselda Claribel Reyes Torres[3], Pablo Joaquin Cervantes Mondragon[3], Daniel Vieyra Cortés[3], Hilda Sanchez Hernández[3] and Miguel Loyo Guiot[3]

[1]Director of ART Reproduction Center, Head of the Reproductive Medicine Unit of the Hospital Angeles Pedregal, Professor of the Course of Reproductive Endocrinology and Human Reproduction Course, U.N.A.M., Mexico City, Mexico

[2]Resident of the Course of Reproductive Endocrinology and Human Reproduction, U.N.A.M., Master of Health Sciences, Attached to the Military Hospital of Specialties of Women and Neonatology, Mexico City, Mexico

[3]Resident of the Course of Reproductive Endocrinology and Human Reproduction, U.N.A.M., Mexico City, Mexico

***Corresponding Author**: German Gabriel Palacios Lopez, Resident of the Course of Reproductive Endocrinology and Human Reproduction, U.N.A.M., Master of Health Sciences, Attached to the Military Hospital of Specialties of Women and Neonatology, Mexico City, Mexico.

Received: July 13, 2019; **Published:** August 21, 2019

Abstract

Background: The decline in the number of oocytes is reflected in decrease in the AMH, this is used to define the ovarian reserve and low responder criteria.

Objective: To determine the association between AMH and ovarian reserve and if it predicts the response in reproduction treatments.

Methodology: Observational, descriptive, retrospective study between 2010-2018. The number of antral ovarian follicles, follicles on the day of triggering, captured oocytes, metaphase II and final treatment result were analyzed. Statistical analysis was done using ANOVA tests, Mann-Whitney U, linear regression and Pearson/Spearman correlation.

Results: 231 patients, 5% of the AMH variations are related to age (R 2 0.056, Pearson .236, ANOVA p 0.000). Factors such as PCOS (p 0.002) and ovarian surgery (p 0.015) modify AMH levels, but not endometriosis and having only one ovary (p > 0.05). There is a negative, average and linear correlation between AMH and number of antral ovarian follicles (Spearman of -600, p 0.00), same situation for final follicular count. When comparing AMH, PCOS (p 0.168) and ovarian surgery (p 0.261), 42% (R2: .429) of the captured oocytes can be predicted by those factors, being the AMH who predicts them the most (p 0.000), same in metaphase II oocytes. In the AMH group < 0.7 ng/ml we captured fewer oocytes (P 0.000). The distribution of AMH is the same among patients whose treatments did or didn't end in pregnancy (p 0.767).

Conclusions: Determining the values of AMH is still useful and provides data on the ovarian reserve, with a good predictive value on the response to treatments.

Keywords: *Evaluation; Anti-Müllerian Hormone; Ovarian Reserve; Ovarian Response; Assisted Reproduction Treatments*

Abbreviations

AMH: Anti-Müllerian hormone; ICSI: Intracytoplasmic Sperm Injection; IVF: *Invitro* Fertilization; FSH: Follicle Stimulant Hormone; PCOS: Polycystic Ovarian Syndrome;

Introduction

In order to predict the success of Assisted Reproduction Techniques (ART) and also as prognostic factors, markers of ovarian reserve have been widely used, unfortunately these vary considerably between each woman, so this has made difficult, to predict the remaining reproductive life at a given age [1]. These has been of special interest in those patients who have decided to delay their desire to conceive and get pregnant in exchange of their professional development and success [2]. Direct measurement of ovarian reserve markers and a 100% reliable precision in their reports, nowadays, is still impossible, however, the function of antral follicles still represents at least, quantitatively, the aspect of ovarian aging [3].

The older the patient is, the less response she has to the dose of medications used, this has been demonstrated in numerous occasions and has been seen related to other factors such as obesity or various hormonal alterations [4]. Taking in account these aspects and their identification before starting a program of ART has helped both the selection of the appropriate protocol and the relevant advice to the patient, prior to start a treatment. So, over time there have arisen efforts to find the right test or at least the most accurate one, for the correct evaluation of the ovarian reserve [5].

Along the way we have found, for example, the Anti-Müllerian Hormone (AMH), a member of the β transforming factor family that is produced in the granulosa cells in the ovary [6]. The highest levels of AMH have been observed in follicles of up to 6 mm (pre antral follicles) in the puberty and they decrease as age advances, being undetectable at menopause, although with the limitation that this marker can vary in each menstrual cycle, and that its normal levels vary between populations and different studies, but are related to a level between 0.7 to 3.5 ng/ml [7-10].

This means that a woman with a low AMH level (< 0.7 ng/dl) has a low ovarian reserve and therefore is closer to menopause, compared to another woman with higher levels of the same age; although there have been studies that do not support this argument, every time that the vast majority of the time they AMH is measured in a single time only [11]. Also, its values rise in patients with Polycystic Ovarian Syndrome (PCOS) where the average value of AMH to predict the disease is 7.76 ng/ml, due to the high number of antral follicles [12]; and can also be modified by the body mass index [13]. Because of all these variations, the use of the AMH is still controversial.

In our population in addition its little extended use by its cost, have done that for years it was not profitable; however nowadays and after the evidences accumulated in many centers of fertility treatments, it's use has been increased and is a tool that is not missed, for example in our Reproductive Medicine Unit, where it is part of the initial protocol to patients who seek attention for infertility, especially in those that are going to be subjected to ART. In the present study, all the patients who have been sampled for this hormone were analyzed and we value their relationship in the results of these treatments and its usefulness as a marker of the ovarian reserve.

Materials And Methods

Observational, descriptive, retrospective and cross-sectional study, where we analyzed data collected from patients who received medical consultation at the Reproductive Medicine Unit in the Angeles del Pedregal Hospital, Mexico City from 2010 to 2018. We used medical records taken from clinical files. We included patients with any type of infertility diagnosis and with complete records, with any risk factor and without age limit. Incomplete files or patients that weren't treated by ART were excluded, there was also no exceptions by protocol or medications taken during the Controlled Ovarian Stimulation.

The variables studied per case were: age, basal hormonal study (AMH, FSH, estradiol), antral follicles count, follicles at the end of stimulation, captured oocytes, mature oocytes (metaphase II), fertilized oocytes, fertilization technique, type of transference (fresh vs frozen), number of stimulation days and the final result of the treatment (if she got pregnant or not and how many of these pregnancies finished with a new born).

The sample used was non-probabilistic and conventional; observation and data collection were the investigation methods, we recollected all data obtained in an information form. The statistical analysis was performed with data base programs (Microsoft Excel© and IBM SPSS Statistics© version 23), using descriptive statistics with measures of central tendency and dispersion for quantitative variables and frequency and proportions for qualitative ones.

To evaluate associations between variables we used Pearson's correlation index for quantitative and normal distribution variables and Spearman correlation index for the rest of variables. To study independent variables, the tests we used to compare independent variables was ANOVA one way to quantitative variables of normal distribution or Mann-Whitney in the other case. Finally, to predict the associated success factors of the treatment of ART we used linear regression to obtain the coefficient determination (r2) values.

Angles del Pedregal Hospital´s investigation committee authorized this study and is strictly attached to current guidelines of the General Law of health in the chapter I, etic aspects at research of human body at article 17 (Mexican normative). The authors manifest there aren't any interest conflicts in the present research.

Results

We analyzed 653 clinical records at the Angeles del Pedregal Hospital in the Reproductive Medicine Unit, performing the research with the key word: "infertility"; 450 clinical records had both AMH levels and age, it is important to mention that not all of these patients were treated by ART, so we decided to exclude those who didn't received this treatment (we only included patients treated with own oocytes and homologous embryo transfers and discarded embryo and oocyte donations), so the final number of patients included in the study was 231. The most frequent kind of infertility was primary (58%), the causes of infertility are summarized on table 1 and the main characteristics of the patients and antecedents are summarized on tables 2 and 3. It's important to point out that when we analyzed the AMH and its association with the body mass index (using the Pearson correlations index) we didn't find a statistic significance between both (p = 0.742).

Infertility factor	Frequency
Age (> 40 years)	25.2%
Uterine factor	10.4%
Cervical factor	0.4%
Tubal factor	12.6%
Low reserve (< 5 antral follicles)	15.6%
Low responder (< 3 oocytes captured in an IVF cycle prior to conventional doses in patients without low responder characteristics)	3.5%
Ovarian factor	7%
Male factor	16.1%
Others (Not specified)	10.9%

Table 1: *Main reasons for consulting the reproductive medicine unit.*

Characteristics of patients	Minimum level	Maximum level	Mean	SD
Age	18	47	36.14	5.34
Basal AMH	0.023	12	2.37	2.55
Basal FSH	1.2	19.2	6.61	19.2
Basal Estradiol	4	88	32.05	18.28
Infertility time (months)	12	168	41.64	35.16
Body mass index	18	34.5	23.78	3.60

Table 2: *Main characteristics of the patients.*

Background of patients	Yes	No	Non specified
Previous low complex, assisted reproductive techniques (Scheduled Coitus or Intrauterine Insemination)	33.9%	64.8%	0.9%
Previous pregnancy (newborn 13.5%, abortion 19.1%, ectopic pregnancy 2.2%, fetal death 0.4%)	34.3%	65.5%	0.4%
Previous surgery (miomectomy 6.1%, C-Section 15.2%, H-Scope 21.3%, L-Scope 10%, Uterine curetagge 3.1%, Salpingectomy 0.9%)	54%	43%	3%
Inmunologic diseases	3.9%	94.8%	1.3%
Uterine malformations (except endometrial polips y myomas, includes mullerian malformations)	3.5%	95.2%	1.3%
Ovarian Cyst	15.2%	96.5%	1.3%
Poliquistyc Ovarian Syndrome	13%	86.5%	0.4%
Uterine myomas	30.9%	68.7%	0.4%
Endometrial polyps	14.3%	85.2%	0.4%
Regular menses	86.1%	10.9%	3%
Parents with multiple pregnancy	15.2%	83.5%	1.3%
Parents with infertility	10%	88.7%	1.3%
Hipotiroidism	18%	82%	0
Ovarian Surgery	12.2%	87.4%	0
Endometriosis	27.8%	72.2%	0

***Table 3**: Main background of patients attended at the reproductive medicine unit.*

All patients were seen in day 2 or 3 of the menstrual cycle to start the Controlled Ovarian Stimulation and to get samples for basal hormonal levels, these two actions are indicated as part of the treatment protocol in this Reproductive Medicine Unit and in the case of AMH, the serum study was send to one reference laboratory called LabCorp® (CENAREM) to be analyzed. We also made a graph of the AMH distribution within the pass of the time (AMH levels by age group) showing that with increase of age, decreases AMH levels. This is represented on figure 1.

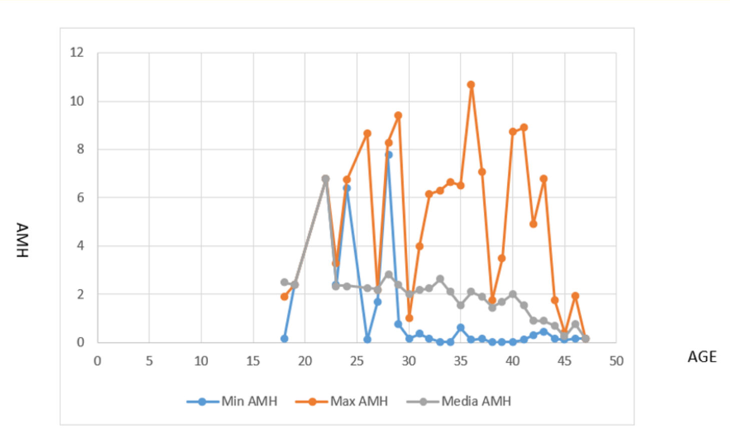

***Figure 1:** Minimum, maximum and mean levels of AMH (ng/ml) distributed by age.*

To assess if age predicts or not the AMH levels, we performed a lineal regression analysis which reported a R^2 or determination´s coefficient of 0.056 (R^2 corrected of 0.52) and a standard error of the determination of 2.48, which indicates that just about 5% of the variations of the AMH can be explained or predicted by age, with a Pearson's correlation index of 0.236, which symbolizes that there exists association but in a low correlation in this study group between variables, but with a lineal association according to the ANOVA test (p = 0.000). There was an annual decrease of AMH levels of 0.113 ng/ml per year approximately.

Analyzing by separate, some of the diseases already described, that can modify the AMH levels, we found the distribution by cases shown in table 4. To perform the analysis if these factors were related with AMH levels, first we preformed normality tests in all the cases using the Kolmogorov-Smirnov test, showing that data hadn`t normal distribution, so we had to perform the Mann-Whitney U test, to compare means in independent samples resulting the next findings:

- Polycystic ovarian syndrome (PCOS) group: the distribution of AMH is different between the patients that present or not the syndrome (p = 0.002).
- Previous ovarian surgery group: the distribution of AMH is different between the patients that present or not ovarian surgery (p = 0.015).
- One ovary group: the distribution of AMH is the same between the patients that have one or two ovaries (p = 0.180).
- Endometriosis group: the distribution of AMH is the same between the patients that had or hadn't endometriosis (p = 0.077).

Disease	Age range (years)	Minimum AMH level	Maximum AMH level	Mean
PCOS (n = 30)	19 - 42	0.1	12	4.15
Previous ovarian surgery (n = 28)	18 - 43	0.023	6.74	1.48
1 ovary (n = 12)	18 - 43	0.032	2.4	1.16
Endometriosis (n = 64)	18 - 46	0.023	9.4	1.84

Table 4: *Diseases that modify AMH levels.*

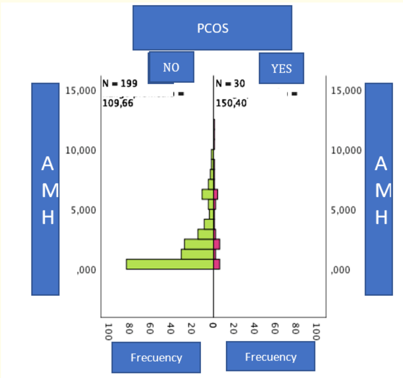

Figure 2: *Distribution of AMH levels in patients with PCOS.*

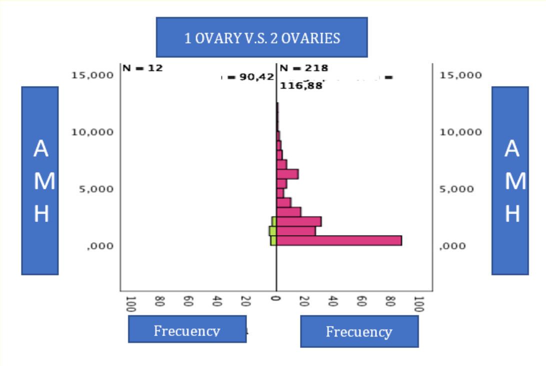

Figure 3: *Distribution of AMH levels in patients with 1 or 2 ovaries.*

To analyze the correlation between the AMH and the antral follicles, both ovarian reserve markers, we observed by realizing normality tests, that they hadn't a normal distribution, so we decided to obtain the Spearman correlation index which reported a correlation coefficient of -600, this means that there is correlation between the AMH and the level of antral follicles, in this case negative (medium correlation) but lineal (p = 0.00).

All patients went on treatment with antagonist protocol cycles, where the most frequent ovarian stimulation treatment was done by using recombinant FSH (60%), or with recombinant LH (30%) and finally Hormonal Menopause Gonadotropin (17.3%), depending of the case, and patient. All were followed up after 5 days of treatment to check dosage of medications(which was with conventional doses protocols) and then adjusted if necessary and then followed up every 48 hours, and when we observed a diameter of 16mm in any follicle we started the antagonist medication, being Cetrotid® the most common in 93% cases and Orgalutran® in the rest; ovulation induction was done when the follicle reached at least 20 mm or more in diameter, the most common medication used to do the triggering was Gonadotropic Corionic Hormone (Gch) (45%), recombinant Gch (35%) and the rest received a Gonadotropin hormone releasing (GnRH) analogue (in patients with hyper response or with risk of ovarian hyper stimulation syndrome) at a dosage of 0.2 mg (20%). The mean of days of use of the medications at cycles was 10.83 days with ED 2.43, the most frequent number of cycles was 1 (45.7%), most of the patients could get pregnant in the first cycle but one patient needed 9 cycles to get pregnant (including endometrial preparations and frozen transfer) in this last case, the pregnancy was achieved by embryo-donation. When we analyzed the correlation between the AMH levels and the antral follicles count at the end of the stimulation, day when we decided to do the triggering, we observed that data didn`t follow a normal distribution, so we decided to get the Spearman correlation index, which reported a correlation coefficient of -676, which means that there is relation between AMH and the antral follicles level like in the last case negative and medium, but lineal (p = 0.00).

To evaluate if AMH value could predict the number of mature and captured oocytes and based on the previous analysis of diseases that could change the AMH levels, we proceeded to perform a lineal logistic regression analysis (Figure 4) including the next variables: AHM, PCOS (p 0.168) and ovarian surgery (p 0.261). In the first case (captured oocytes number) we found a R^2 of 0.429, which indicate 42% of the captured oocytes could be predicted by this variable, with a constant of 6.22, showing that PCOS has a negative value in relation with captured oocytes (-1737) and AMH is the factor that could predict the most number of captured oocytes (p 0.000). It signifies that having these two diseases didn't predict the number of retrieved oocytes, at least in this study.

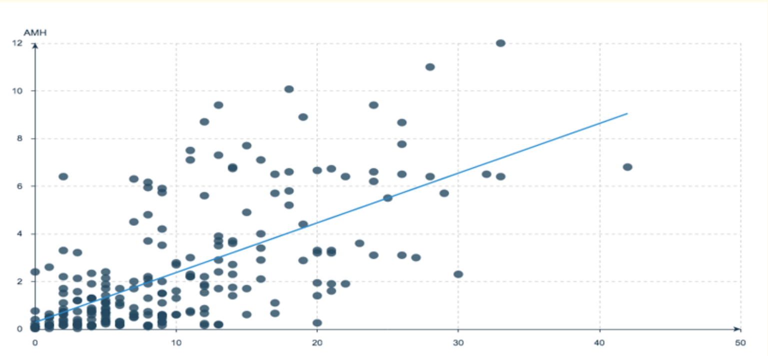

Figure 4: *Dispersion graphic between AMH and number of retrieved oocytes.*

Results in the second group had little variation, we found a R^2 of 0.425, which means that 45% of metaphase II oocytes could be predicted by this variables with a constant of 6.22, marking that the PCOS has a negative value in relation with the number of metaphase II oocytes (-1720) and AMH is the one that can predict in most of cases, the number of metaphase II oocytes (p = 0.000). This means that with these two diseases we can't predict the number of retrieved oocytes (PCOS p 0.120, ovarian surgery p 0.693).

Table 5 shows the number of metaphase II oocytes in 3 different groups, the first, with low reserve with an AMH of 0.7 ng/ml [16], the second with normal reserve and the third in patients who are in risk of develop ovarian hyper stimulation syndrome with more than

3.36 ng/ml (sensitivity 90.5%, specificity 81.3%) [14]. In this case to decide if there were difference between groups we performed the test of variance homogeneity, performing one way ANOVA test, to determinate the difference between means, getting between and intra group differences, with statistical significance values (p = 0.000).This symbolizes that at lower levels of AMH, there are less retrieved oocytes and less metaphase II oocytes especially in the AMH < 0.7 group. After the ovular retrieval, the most common type of insemination technique in this study was ICSI (28.7%), followed by FIV (22.2%) FIV/ICSI (128.3%), IMSI (6.5%), PICSI (3.9%), IMSI/ICSI (.9%), being impossible to get the information in 8% of the cases. The rest of the 11.9% patients represent those who had cancelled cycles, either by poor response or that in the day of the retrieval, didn't get oocytes retrieved that could be inseminated (cancelation rates) or because they were patients that wanted fertility preservation (6.1%); the 62.7% of the cases when transferred were done in fresh and the rest 19% were by frozen transfers. Finally, we can mention that the rate of pregnancy in these cycles was 33%, the new born rate was 22%. To compare if AMH level could have influenced in getting or not a pregnancy, we determined that the distribution of AMH is the same between the patients who achieved or not pregnancy (p 0.767)

Level of AMH	Oocytes Retrieved (mean)	Metaphase II oocytes (mean)
< 0.7	5.16	3.85
0.7 - 3.36	9.33	8.37
> 3.36	10.04	8.42

Table 5: *Oocytes retrieved and Oocytes in Metaphase II according to groups based by AMH levels.*

Discussion

Although the first *Invitro* Fertilization treatment was carried out in a natural cycle and without highly advanced techniques or resources to predict success, over the years, more information has been collected on all the tests that can be used before a controlled ovarian stimulation cycle, these tests help us to inform patients about their prognosis and predict the response according to the ovarian reserve. In our country, we were the first Reproductive Medicine Unit to use these ovarian reserve tests as part of our initial diagnostic and treatment protocol, and today, 8 years later, we can perform the second evaluation with a greater number of cases, with information of the results and usefulness of this test in our group of patients, and reporting at this time the most complete study that has been carried out in our country.

As the first important point in our research objectives, we demonstrate the demographic characteristics, which are peculiar characteristics of a private Reproductive Medicine Center, where many of the patients have complex diseases and also have ages that exceed 35 years and that, in the first instance, despite their reserved prognosis (especially those over 42 years old), they decide to start treatments with their own oocytes instead of accepting oocyte donation directly. The behavior of AMH through age, shows an interesting decrease over time, although this relationship is weak in our study (at least statistically), these findings are consistent with what was observed in studies conducted in China [15] and with another performed in patients healthy in the United States [16]; the last study cited has the advantage that it includes healthy patients and excludes adolescent girls, concluding that the usefulness of the study is applicable for 25-year-old women or more. And not for the youngest.

After stratifying for diseases that have been shown to alter AMH levels, in our study we could only demonstrate that PCOS and previous ovarian surgery alter AMH levels, and that it is not altered by endometriosis or by having a single ovary. Despite our small sample size, the cases were specific to determine this situation, according to what was determined in a study, where AMH levels affected predict PCOS; there they observed the ages most likely to suffer from the disease were 25 to 30 years, and levels higher than 10.25 ng/ml predicted the disease with an OR of 16.8 [17]. In our study we did not determine this odds ratio but we observed variations of up to 12 ng/ml and we may even have difficulties so that these patients also have the disadvantage of a poor response during ovarian stimulation cycles.

When we correlating the AMH level with the other frequently used ovarian reserve marker, the count of antral follicles by ultrasonography (with the disadvantage that was taken by different doctors), we observed a low correlation, but in a linear way, in the case of both antral follicles and in the follicle count at the end of stimulation. There is a meta-analysis of 13 published studies to evaluate this relationship where the conclusion was the level of AMH is at least as good as the follicular count, to predict the response but not to predict whether a woman can achieve pregnancy, one of the points to highlighting this meta-analysis was the prospective nature of the studies [18]. In our case, the retrospective nature of the study is a point against our study and may also have influenced the outcome of the statistical analysis. However, we can agree that the follicular antral count, due to its low cost and increased availability, at least for now, will be the first option to measure ovarian reserve even before hormonal measurement, as others have already suggested. studies in Latin America [19]. Bearing in mind also that there are no fluctuations demonstrated at the time of the study of the count of antral follicles during the menstrual cycle and that their levels are parallel and also predictive in a pair [20].

When we analyzed the prediction rate of the number of retrieved and mature oocytes after ovarian stimulation cycles, we have the disadvantage that this situation can be influenced by several factors and some definitely could not be controlled in the analysis, these aspects can remove weight in our findings but it are worth to mention, first, for example, are the type of medications and protocols used, which were variable in all the patients, and individualized according to the particular case and that could only have been controlled by a prospective study. To remove the other situations that could interfere, we performed the analysis taking into account factors such as age, PCOS and ovarian surgery that we had already shown that in these patients, they modified AMH values, reaching the result that the level of AMH predicts both the quantity of retrieved oocytes and metaphase II oocytes, these findings coincide with those of a study, where 238 patients were evaluated, divided into 2 groups of norm responders if 8 oocytes were captured, and hypo responders if less than 4 were captured, determining that the level of AMH was higher than the measurement of FSH as a predictor of ovarian reserve [21].

There is another study where in addition to take the basal hormonal levels, they measured levels of AMH in the day of triggering, to evaluate if there was a relationship with the number of retrieved oocytes (what we routinely do in this and all centers is to take Estradiol) as a test of research, finding interesting results, since a positive correlation was found in both times, although there was no correlation with the rate of aneuploidy, a point that will be discussed later [22]. We settled cut-off points according to what has already been described in the literature as hypo, normo and hyper responders patients, based in AMH cut-off points, finding that the group with AMH < 0.7 ng/ml was the one that was related to a lower number of retrieved oocytes, in the study previously mentioned there was no cut point, but we agreed with what was already published in criteria of low ovarian reserve [23]. In our country however there is a single study that analyzes the cut off value of the AMH in Mexico and found it at an AMH level of 1 ng/ml [24].

Finally, because of the retrospective nature of the study, we compared means to determine if AMH levels influenced pregnancy or not (not as a predictor, since other tests would have been necessary), finding that there was no relationship between the AMH levels and having achieved the pregnancy, this in some way coincides with reports from other studies where they observed that AMH does not predict the time in which a normoevolutive pregnancy will be obtained in healthy women planning their pregnancy [24], but not with the findings of other studies where they claim that it serves as a predictor of pregnancy (gestational capability), examples are studies, performed in women between 30 and 42 years, who concluded that after 35 years and with AMH levels < 0.7 ng/ml the pregnancy is decreased [25]. This is controversial, since another study states that although it serves as a predictor of ovarian response, its usefulness is limited (although it does not rule out) to predict pregnancy [26]. To end that point, most agree that with low AMH levels a low pregnancy rate can be expected, as described in a review where it is mentioned that although the AMH guides us to predict the ovarian response, a low level doesn't mean in the majority of cases that pregnancies won't achieved, moreover AMH by itself, does not exclude the possibility of such, because with adequate protocols and treatments, pregnancies can be achieved [27], similar situation with a meta-analysis where [19] studies were evaluated, they found a weak predictive relationship, but at the end they argued AMH values are useful for counseling of women seeking pregnancy [28]. Finally the rate of aneuploidy predicted by AMH, which has been also a matter of study, we did not analyze this factor in ours, there are studies, however, that say that although AMH sometimes predicts pregnancy, it does not work to predict embryo quality or rate of aneuploidy, with controversial results among the studies [29,30].

Within the limitations of the study we can mention for example its retrospective nature, it influenced that we could not have a stricter control of the factors that influence the level of the hormone and that all cases were selected including the diseases that alter its parameters. Collect more patient data, perform more extensive studies, according to each particular situation (the different diseases already mentioned) in addition to performing randomized and prospective controls, is the goal for future studies.

Conclusions

With this study, we confirm that if there is an association between AMH levels and ovarian reserve and it predicts the response in reproduction treatments, which supports previous findings that determined, that values of AMH, are useful in the evaluation of patients who are treated in fertility clinics [31]. Conducting studies in specific populations will serve as a basis for epidemiological studies, make personalized advice to specific population patients and will provide specific data in our patients who share different characteristics from those of other countries in various areas already known, both genetic and environmental. Performing measurements of this marker, serves to assess the ovarian reserve, has good predictive value on the response to Controlled Ovarian Stimulation treatments and correlates with others such as the antral follicle count, surpassing FSH and Estradiol in both situations. The decrease in AMH through age provides evidence for a group of women who are increasingly seeking professional self-realization and delayed motherhood, which should be advised in time and form on their reproductive future with real data and in accordance with women who share these same characteristics, because they are part of the same population to make timely decisions in favor of their reproductive future.

Individualized treatment protocols and tools that provide us an overview of what we expect with our interventions, is one of the goals of the medicine of the future, which seeks to be "personalized". This hormonal study does not predict who will be pregnant or not, or if they manage to have pregnancies without malformations, but it helps to know what medications and dose should be given, to initiate their treatment according to the ovarian reserve and possible response that will be shown. This study symbolizes the largest of its kind so far in Mexico and should serve as a reference for future investigation of the subject, in order to make recommendations according to our population.

Bibliography

1. Te Velde ER and Pearson PL. "The variability of female reproductive aging". *Human Reproduction Update* 8.2 (2002): 141-154.

2. Leridon H. "Demographic effects of the introduction of steroid contraception in developed countries". *Human Reproduction Update* 12.5 (2006): 603-616.

3. Broekmans FJ., *et al*. "A systematic review of tests predicting ovarian reserve and IVF outcome". *Human Reproduction Update* 12.6 (2006): 685-718.

4. De Koning CH., *et al*. "The distribution of FSH receptor isoforms is related to basal FSH levels in subfertile women with normal menstrual cycles". *Human Reproduction* 21.2 (2006): 443-446.

5. Hendriks DJ., *et al*. "Antral follicle count in the prediction of poor ovarian response and pregnancy after in vitro fertilization: a meta-analysis and comparison with basal follicle-stimulating hormone level". *Fertility and Sterility* 83.2 (2005): 291-301.

6. Lee MM., *et al*. "Müllerian inhibiting substance in humans: normal levels from infancy to adulthood". *The Journal of Clinical Endocrinology and Metabolism* 81.2 (1996): 571-576.

7. Weenen C., *et al*. "Anti-müllerian hormone expression pattern in the human ovary: potential implications for initial and cyclic follicle recruitment". *Molecular Human Reproduction* 10.2 (2004): 77-83.

8. Gruijters MJ., *et al*. "Anti-müllerian hormone and its role in ovarian function". *Molecular and Cellular Endocrinology* 211.1-2 (2003): 85-90.

9. Hehenkamp WJ., *et al*. "Anti-müllerian hormone levels in the spontaneous menstrual cycle do not show substantial fluctuation". *The Journal of Clinical Endocrinology and Metabolism* 91.10 (2006): 4057-4063.

10. Eifer DB., *et al*. "Early follicular serum müllerian-inhibiting substance levels are associated with ovarian response during assisted reproductive technology cycles". *Fertility and Sterility* 77.3 (2002): 468-471.

11. Doroftei B., *et al*. "It's never over until it's over: how can age and ovarian reserve be mathematically bound through the measurement of serum AMH-A study of 5069 Romanian women". *PLOS ONE* 10.4 (2015): e0125216.

12. Homburg., *et al*. "The relationship of serum anti-Mullerian hormone with polycystic ovarian morphology and polycystic ovary syndrome: a prospective cohort study". *Human Reproduction* 28.4 (2013): 1077-1083.

13. Kriseman M., *et al*. "Anti-müllerian hormone levels are inversely associated with body mass index (BMI) in women with polycystic ovary syndrome". *Journal of Assisted Reproduction and Genetics* 32.9 (2015): 1313-1316.

14. Ballesteros A and Izquierdo A. "Guía 23 REGO prevención y manejo del síndrome de hiperestimulación ovárica". IVI Barcelona.

15. Xiaofang Du., *et al*. "Age-Specific Normal Reference Range for Serum Anti-Müllerian Hormone in Healthy Chinese Han Women: A nationwide Population-Based Study". *Reproductive Sciences* 23.8 (2016): 1019-1027.

16. Lie Fong., *et al*. "Serum Anti-Müllerian Hormone Levels in Healthy Females: A Nomogram Ranging from Infancy to Adulthood". *The Journal of Clinical Endocrinology and Metabolism* 97.12 (2012): 4650-4655.

17. Quinn M., *et al*. "Age-stratified thresholds of anti-Müllerian hormone improve prediction of polycystic ovary syndrome over a population-based threshold". *Clinical Endocrinology* 87.6 (2017): 733-740.

18. Broer S., *et al*. "The role of anti-müllerian hormone in prediction of outcome after IVF: comparison with the antral follicle count". *Fertility and Sterility* 91.3 (2009): 705-714.

19. N Lonegroa N and Napoli. "Recuento de folículosantrales como predictor de la respuesta ovárica". *Revista Argentina de Radiología* 80.4 (2016): 252-257.

20. Depmann M., *et al*. "Fluctuations in anti-Müllerian hormone levels throughout the menstrual cycle parallel fluctuations in the antral follicle count: a cohort study". *Acta Obstetricia et Gynecologica Scandinavica* 95.7 (2016): 820-828.

21. Tremellen K and Kolo M. "Anti-müllerian hormone as a marker of ovarian reserve". *Australian and New Zealand Journal of Obstetrics and Gynaecol* 45.1 (2005): 20-24.

22. Ferraretti La Marca., *et al*. "ESHRE consensus on poor ovarian response definition" *Human Reproduction* 26.7 (2011): 16-24.

23. S Lie Fong., *et al*. "Anti-Müllerian hormone: a marker for oocyte quantity, oocyte quality and embryo quality?". *Reproductive BioMedicine Online* 16.5 (2008): 664-670.

24. Mendoza J., *et al*. "Correlation of the serum levels of Anti-müllerian Hormone and woman age with the rate of ovular recovery and Pregnancy". *Ginecología y Obstetricia de México* 87.8 (2019): 535-542.

25. Depmann M., *et al*. "Anti-Müllerian hormone does not predict time to pregnancy: results of a prospective cohort study". *Gynecological Endocrinology*33.8 (2017): 644-648.

26. Steiner Anne Z and Amy H. Herring "Antimullerian Hormone as a Predictor of Natural Fecundability in Women Aged 30-42 Years". *Obstetrics and Gynecology* 117.4 (2011): 798-804.

27. Simone L., *et al*. "The role of anti-Mullerian hormone assessment in assisted reproductive technology outcome". *Current Opinion in Obstetrics and Gynecology* 22.3 (2010): 193-201.

28. Pacheco A., *et al*. "Impact of very low anti-Mullerian hormone on pregnancy success". *Current Opinion in Obstetrics and Gynecology* 29.3 (2017): 131-135.

29. Reshef Tal and Oded Tal. "Antimullerian hormone as predictor of implantation and clinical pregnancy after assisted conception: a systematic review and meta-analysis". *Fertility and Sterility* 103.1 (2015): 119-130.

30. Jesper M and J Smeenk. "Antimüllerian hormone predicts ovarian responsiveness, but not embryo quality or pregnancy, after in vitro fertilization or intracyoplasmic sperm injection". *Fertility and Sterility* 87.1 (2007): 223-226.

31. Itai Gat., *et al*. "Significant correlation between anti-müllerian hormone and embryo euploidy in a subpopulation of infertile patients". *Reproductive BioMedicine Online* 35.5 (2017): 602-608.

Volume 8 Issue 9 September 2019