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IVF AND AMH LEVELS

The cutoff values of serum AMH levels and starting recFSH doses for the individualization of IVF treatment strategies

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Abstract

Objective: The main purpose of our study is to categorize starting doses of recombinant follicle-stimulating hormone (recFSH) based on various cutoff values of anti-Mullerian hormone (AMH) and to determine the effectiveness of serum AMH levels in the prediction of poor ovarian response.

Material and methods: Prospective data analysis was conducted at IVF center. A total of 323 patients were included. All patients were divided into four groups according to the patients' serum AMH concentrations: Group 1 (AMH $<$ 1 ng/ml; 450 IU/day $n = 157$); Group 2 (AMH 1–2 ng/ml; 375 IU/day, $n = 55$); Group 3 (AMH 2–3 ng/ml; 225 IU/day, $n = 48$); and Group 4 (AMH $>$ 3 ng/ml; 150 IU/day, $n = 63$). Collected data included age, total gonadotropin dosage, duration of stimulations, the total number of oocytes retrieved, ovarian response, cancelation rate, and cPRs.

Results: As serum AMH levels increased, there were significant decreases in the starting recFSH dose and total gonadotropin dosage, and a significant increase in the total number of oocytes retrieved. There was a significant trend toward increasing cycle cancelation rates and decreasing cPRs with decreasing serum AMH levels. Although there were no significant differences with regard to the proportion of cycles with hypo-response between all groups. A result of $\leq$0.83 was considered the cutoff value of AMH to predict a hypo-response to ovarian stimulation.

Conclusions: AMH is a useful marker in selecting the starting dose of recFSH and prediction of poor ovarian response. Our protocol may allow clinicians to modulate the starting dose of recFSH according to these cutoff values for serum AMH levels.

Keywords

AMH, assisted reproduction technology, IVF, ovarian response, ovarian stimulation, poor response

History

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Introduction

Ovarian stimulation (OS) is an important step in assisted reproduction technology (ART). The main goal of OS is to stimulate multiple follicle development for achieving the optimum number of oocytes in a single cycle [1,2]. The reason behind this is that the number of oocytes is a good predictor for the likelihood of achieving successful pregnancy rates with IVF treatments [3]. However, OS has some complications including abnormal ovarian responses. IVF cycles are frequently canceled due to an abnormal response to OS, which can include either a poor ovarian response or a hyper-ovarian response. Therefore, to reduce cycle cancelations, dropout rates, and costs, while maximizing success, optimizing the OS strategy with individualization of IVF treatment should be a focus.

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The selection of an optimal starting gonadotropin dose is an extremely critical step in OS to achieve the optimal ovarian response. It is generally modified according to the woman's age, ovarian reserve, and body mass index (BMI). The starting gonadotropin dose is individualized to avoid low or excessive doses since the standard starting dose may not be reasonable for all women undergoing IVF treatments [4]. The correct prediction of ovarian reserve can provide more accurate information related to the selection of an optimal starting gonadotropin dose.

Anti-Mullerian hormone (AMH) is a dimeric glycoprotein and a member of the transforming growth factor-β family. AMH is synthesized by granulosa cells located on ovarian follicles. AMH has been demonstrated to be the most reliable predictor of ovarian reserve and therefore, it is commonly used for individualization of OS strategies during IVF treatment and optimizing treatment success [5–7]. AMH has also been identified as a useful marker for the prediction of poor and excess ovarian responses to stimulation. Some studies have focused on AMH based on OS, and various AMH cutoff values and starting gonadotropin doses have been used in these studies but show conflicting results.

The main purpose of this study was to categorize starting doses of recombinant follicle-stimulating hormone (recFSH) based on

various cutoff values of AMH, the most recently identified marker of ovarian reserve. We also aimed to determine the effectiveness of serum AMH levels in the prediction of poor ovarian response for individualization of IVF treatment.

Material and methods

Participants

We prospectively analyzed the database of clinical and laboratory information conducted at our IVF center in Yeditepe University Hospital, Istanbul, Turkey, from January 2013 through May 2015. There were 323 patients that met the inclusion criteria and were included in this study. Written informed consent was then obtained from all patients. The study protocol was approved by the Ethical Committee of the Medical Faculty of Yeditepe University. Inclusion criteria included the following: (1) women undergoing IVF due to primary infertility with their first IVF/intracytoplasmic sperm injection (ICSI) attempt; (2) BMI $\leq 25\,kg/m^2$; (3) 18–41 years of age; (4) FSH levels on cycle day 3 of ≤ 12 mIU/ml; (5) treatment with an antagonist (Cetrotide; Serono, Geneva, Switzerland) protocol and stimulation with recFSH (Gonal F; Serono, Geneva, Switzerland) using fresh embryos; (6) nonsmoker; (7) both ovaries were identified with a transvaginal ultrasound scan; (8) no previous exposure to cytotoxic drugs or pelvic radiation; (9) no history of ovarian surgery; and (10) no hormonal therapy in the preceding 6 months. Exclusion criteria consisted of polycystic ovary syndrome (PCOS) and other endocrinological diseases such as diabetes mellitus and thyroid disease. Collected data included age, serum AMH levels, starting recFSH dose, total gonadotropin dosage, duration of stimulations, the total number of oocytes retrieved, ovarian response, cancelation rate, and clinical pregnancy rates (cPRs). All patients were divided into four groups according to the patients' serum AMH concentrations to determine the starting recFSH dose. The groups were as follows: Group 1 (AMH <1 ng/ml; $n=157$); Group 2 (AMH 1–2 ng/ml; $n=55$); Group 3 (AMH 2–3 ng/ml; $n=48$); and Group 4 (AMH >3 ng/ml; $n=63$). The starting recFSH dose was 450, 375, 225, and 150 IU/day in groups 1, 2, 3, and 4, respectively. Ovarian responses were defined according to the total number of oocytes retrieved (≤ 3 = hypo-response; ≥ 20 = hyper-response; and 3–20 = normo-response).

Assisted reproduction procedures

The gonadotropin-releasing hormone (GnRH) antagonist protocol and stimulation with recFSH were used for controlled ovarian stimulation (COS). After determination of the starting recFSH dose (150–450 IU/day) based on the serum AMH level, OS was commenced with recFSH on day 2 after the baseline transvaginal scan and recFSH was continued throughout the stimulation period. Transvaginal scans were performed for the measurements of follicular development. A daily dose of cetrorelix (0.25 mg) was initiated after two or more follicles reached 13–14 mm in diameter and cetrorelix was continued until the day of human chorionic gonadotropin (hCG) administration. A single dose of recombinant hCG (Ovitrelle, 250 mg; Serono) was administered for the triggering of the final oocyte maturation when there were at least two follicles ≥ 17 mm. Transvaginal ultrasound-guided oocyte retrieval was performed 36 h after hCG administration. The standard ICSI technique was applied to all oocytes for fertilization. According to age, indication for IVF, and the number and quality of embryos available, one, or a maximum of two, embryos were transferred on day 3 or 5 after oocyte retrieval. All embryo transfers were performed by the same physician (C.F.) under transabdominal ultrasound guidance. Luteal phase support was provided by daily vaginal Crinone gel (Crinone 8%, 90 mg; Merck Serono, Central Pharma Ltd., Bedfordshire, UK) and it was started on the day of retrieval. Serum quantitative β-hCG levels were obtained 12 days after embryo transfer. Clinical pregnancy was defined as the presence of a fetal heart beat visualized by transvaginal ultrasound examination.

AMH measurement

Serum AMH hormone levels were measured by an ultrasensitive enzyme-linked immunosorbent assay (ELISA) using Beckman-Coulter at a single reference laboratory as described elsewhere on day 2 or 3 of a cycle and within 3 months of commencing OS [8]. The collection and handling of all AMH samples were conducted according to the standards set by the manufacturer. Serum samples were transported immediately to the Department of Clinical Biochemistry of our hospital. Samples were frozen at $-20\,^{\circ}C$ until analysis, normally within 1 week of receipt [9]. Basal serum AMH values are presented in concentrations of ng/ml. The assay range for AMH was 0.16–20 ng/ml, functional sensitivity was 0.08 ng/ml, and intra-assay and inter-assay coefficients of variation were 5.4% and 5.6%, respectively.

Statistical analysis

The results were analyzed using the Statistical Package for the Social Sciences, version 22 (SPSS, Chicago, IL). Data were reported as mean ± SD or number and percentage. Kolmogorov–Smirnov tests were used to determine whether the variables were normally distributed. The Levene test was used to assess the homogeneity of the variances. An analysis of variance (ANOVA) was used to test for differences in normally distributed variable means with homogenous variances between the groups, and the Bonferroni correction was used to test the significance of pairwise differences for multiple comparisons. The Welch test was used to test for differences in normally distributed variable means with non-homogenous variances between the groups, and Dunnet's T3 test was used to test the significance of pairwise differences for multiple comparisons. Non-normally distributed metric variables were analyzed by Kruskal–Wallis tests and dual comparisons between groups with significant values were analyzed by Mann–Whitney U tests. Chi-square tests were used to compare categorical variables in the form of frequency tables. $p<0.05$ was considered statistically significant. ROC analysis was used to analyze the predictive value of AMF and the sensitivity and specificity of differences cutoffs values of AMH for ovarian response.

Results

There were a total of 323 patients included in the present study. Characteristics of patients and IVF cycles are shown in Table 1. According to the evaluation of different cutoff values of AMH, there were significant differences with regard to the distributions of age, starting recFSH doses, total gonadotropin doses, the total number of oocytes retrieved, cancelation rates, and cPRs between the four groups (all $p<0.01$) (Table 1). As serum AMH levels increased, there were significant decreases in the starting recFSH dose and total gonadotropin dosage, and a significant increase in the total number of oocytes retrieved. There was a significant trend toward increasing cycle cancelation rates and decreasing cPRs with decreasing serum basal AMH levels. Only four cycles in Group 4 (the highest AMH group) were canceled because of hyper-responses to OS and the other 35 cycles were canceled because of hypo-responses to OS. Of the 35 cancelations, 32 were in Group 1 (the lowest AMH group). The lowest cPRs (19.1%) and highest cancelation rates (20.4%) were also in Group 1. Although there were no significant differences with regard to the

Table 1. Characteristics of patients and IVF cycles.

Variables	Group 1 (AMH <1) ($n = 157$)	Group 2 (AMH 1–2) ($n = 55$)	Group 3 (AMH 2–3) ($n = 48$)	Group 4 (AMH >3) ($n = 63$)	p
Age	37.49 ± 4.65	34.13 ± 4.41	33.48 ± 4.49	31.43 ± 4.85	<0.01*a
AMH (ng/ml)	0.59 ± 0.82	2.01 ± 3.06	3.14 ± 3.10	5.74 ± 2.50	<0.01*b
Starting dose of recFSH (IU/day)	450 ± 0.00	375 ± 0.00	229.69 ± 32.48	152.38 ± 13.25	<0.01*b
Total dosage of gonadotropins (IU)	4228.85 ± 429.74	3500 ± 371.45	2239.06 ± 390.17	1471.43 ± 220.70	<0.01*b
Duration of stimulations	9.38 ± 1.06	9.38 ± 1.05	9.79 ± 1.13	9.62 ± 1.10	0.29
Ovarian response					
Hypo	54 (34.4%)	17 (30.9%)	15 (31.2%)	19 (30.2%)	0.83
Normo	100 (63.7%)	38 (69.1%)	30 (62.5%)	44 (69.8%)	0.7
Hyper	0	0	0	3 (4.76%)	0.5
No. of oocytes retrieved	3.34 ± 2.69	6.45 ± 2.60	9.60 ± 3.71	10.25 ± 4.85	<0.01*b
Clinical pregnancy rates	30 (19.1%)	27 (49.1%)	21 (43.8%)	23 (36.5%)	<0.01*b
Cancellation rate	32 (20.4%)	1 (1.8%)	2 (4.2%)	4 (6.3%)	<0.01*b

All values are expressed as mean ± SD, number and percentage.
*$p < 0.05$, significant difference.
[a]Analysed by Welch test.
[b]Analysed by Kruskal–Wallis test.

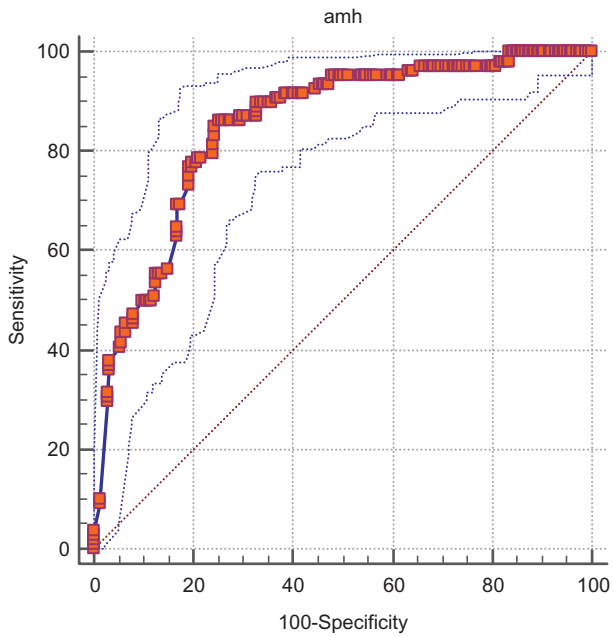

Figure 1. The cutoff value of serum basal AMH for predicting hyporesponse to ovarian stimulation (AUC = 0.84; 95% CI 0.80–0.88; sensitivity 85.1% and specificity 75.5%).

proportion of cycles with hypo-response between all groups, the proportion of cycles with hypo-response to OS was highest in Group 1 (34.4%), however, this was not significant. We analyzed the cutoff value of AMH by using the ROC curve to predict a poor response. A result of ≤0.83 was considered the cutoff value of serum AMH levels to predict a hypo-response to OS (Figure 1) (AUC = 0.84; 95% CI 0.80–0.88; sensitivity 85.1% and specificity 75.5%).

Discussion

Most studies have focused on the individualization of IVF treatment strategies in women undergoing their first IVF cycles. The determination of ovarian reserve and the selection of starting gonadotropin doses are clearly two important steps for the individualization of IVF treatment strategies. Therefore, several models have been described to accurately estimate the starting FSH dose with patient characteristics such as age and ovarian reserve, which are strongly linked with IVF success. In these studies, there was a high level of heterogeneity in ovarian reserve markers, the cutoff value of serum AMH levels, the starting FSH dose, and the treatment protocols. Most authors believe that the maximum number of oocytes retrieved in a cycle is strongly associated with the pool of recruitable antral follicles within the ovaries. Therefore, it would obviously not be effective to increase the maximum FSH dose for avoiding a negative ovarian response [10]. In light of the above-mentioned studies, the starting FSH dose varies between 150–375 IU per day, but the maximum starting FSH dose is generally 300–375 IU in the studies that have evaluated starting FSH doses in women younger than 40 years of age [11].

AMH is currently the most commonly used serum biomarker to predict ovarian reserve because it is the best current available measure in terms of sensitivity, specificity, and low intra-cycle and inter-cycle variability. It is a first choice ovarian reserve test for various clinical conditions including management of women with cancer, prediction of ovarian dysfunctions such as PCOS and primary ovarian failure (POF), fecundity, menopause prediction in the general population, and management of women undergoing IVF [12,13]. Additionally, AMH can be considered as a reliable predictor for a woman's ability to respond to OS because of the strong relationships between AMH and the size of the primordial follicle pool and follicular recruitment rates. Therefore, AMH allows for a good prediction of ovarian response and the number of oocytes retrieved by choosing the optimal starting FSH dose in IVF treatment; however, the criteria to determine the optimal starting gonadotropin dose have not yet been clearly identified [3]. Several studies described below were recently designed for the identification of AMH based on the prediction of optimal starting FSH doses in the individualization of IVF cycles.

In a retrospective study that investigated the possible benefits of AMH-tailored stimulation, 769 women undergoing a long or short flare-up of GnRH agonist or GnRH antagonist protocol were divided into a basal FSH (conventional) group and an AMH-tailored stimulation group [14]. A total of 423 women in the AMH-tailored stimulation group were classified according to four cutoff values of serum AMH levels and starting gonadotropin doses (<2.2 pmol/L-exclude; 2.2–15.6 pmol/L–300 IU/day hMG + GnRH antagonist; 15.7–28.6 pmol/L–200 IU/day recFSH or 225 hMG + long down-regulation GnRH agonist protocol; and >28.6 pmol/L–150 IU/day hMG + GnRH antagonist). This study demonstrated that AMH-tailored stimulation protocols significantly provide improvements in positive clinical outcomes, as well as reductions in complication rates and costs. However, this study did not analyze further subgroup evaluations in the AMH-tailored stimulation group. Another retrospective analysis of 461

IVF cycles with a long or short flare-up GnRH agonist or GnRH antagonist protocol investigated the predictor value of AMH levels for ovarian response and IVF cycle outcomes. The results indicated a significant correlation between serum AMH levels and the number of retrieved oocytes [15]. In this study, Choi et al. used three cutoff values of serum AMH levels (low: <1.05 ng/ml; middle: 1.05 ng/ml–3.55 ng/ml; and high: >3.55 ng/ml) and found significant differences in cPRs between groups. This study also indicated that the cutoff value of serum AMH levels to predict a poor response was 1.05 ng/ml (ROC AUC = 0.85, sensitivity 74%, specificity 87%).

La Marca et al. aimed to develop a nomogram based on patient characteristics and AMH and to determine an appropriate starting gonadotropin dose in IVF cycles with a long GnRH agonist protocol. The maximum starting FSH dose of 225 IU/day was used in this study. They indicated that age and serum AMH levels are the most significant predictors of ovarian response and daily FSH dose [16]. Furthermore, this study showed that the number of oocytes retrieved per unit of FSH would be reduced with decreasing serum basal AMH levels in women of similar ages. A recent randomized, parallel, and open-label study including 348 cycles evaluated the efficacy and safety of two different algorithms based on antral follicle count (AFC) and AMH to determine the starting recFSH dose [17]. It demonstrated that the effectiveness of AMH and AFC for determination of the starting recFSH dose is similar. In the AMH arm, three cutoff values of serum AMH levels and starting recFSH doses (<0.7 ng/ml, 375 IU/day; 0.7–2.1 ng/ml, 225 IU/day; and >2.1 ng/ml, 150 IU/day, respectively) were evaluated. Total and daily FSH doses significantly decreased with increasing serum AMH levels, and the proportion of poor ovarian response (70.6%) was significantly higher in women with AMH < 0.7 ng/ml. Although not achieving a statistically significant difference, the lowest AMH group had the lowest cPRs (14.3%). The AUC and 95% CI for AMH to predict a hypo-response were 0.88 and 0.81–0.95, respectively.

Our study demonstrated that lower serum AMH levels were related to significantly greater cancelation rates, total and starting recFSH doses, and lower numbers of retrieved oocytes and cPRs. In especially women with serum AMH level > 1 ng/ml, our results suggest an increase in the the number of oocytes retrieved and cPRs (at least 40%) and there was also a general reduction in the cancelation rates (<5%) in the AMH based on the starting recFSH dose with the GnRH antagonist protocol that optimized OS, especially in women with serum AMH level > 1 ng/ml. The cPRs were higher in women with serum AMH levels > 1 ng/ml with the lowest hyper-ovarian response. However, even in the lowest AMH group (<1 ng/ml), cPRs reached almost 20%. In light of these results, these cutoff values of serum AMH levels and starting doses of recFSH may be useful for clinical practice. However, the starting recFSH dose may be increased to 450 IU/day in women with serum AMH levels of < 1 ng/ml in order to achieve higher cPRs while decreasing the poor ovarian response rates.

When comparing the results of all AMH groups, although there was no statistically significant difference between groups in terms of hypo-ovarian response, more than half (51.4%) of the women with hypo-ovarian responses were in the lowest AMH group (<1 ng/ml). The proportion of hypo-ovarian responses and the cancelation rates due to a hypo-response were the highest in the lowest AMH group; however, this rate was lower than those reported in previous studies. In our previous study, we demonstrated an AMH cutoff value of ≤1 ng/ml may predict poor ovarian reserve and poor ovarian response to OS and IVF outcomes [18]. The current study determined that a cutoff value of serum AMH levels of ≤0.83 ng/ml may predict a poor response (sensitivity 85.1%, specificity 75.5%). Our results indicate that increasing the starting recFSH dose to 450 IU/day was not able to overcome all hypo-response cases, but it may have provided some reduction in the incidence of hypo-response to OS and promote cPRs.

In conclusion, the current study demonstrated that AMH is a useful marker in selecting the starting dose of recFSH in IVF cycles with a GnRH antagonist and recFSH. Moreover, our protocol may allow clinicians to modulate the starting dose of recFSH according to these cutoff values for serum AMH levels to reach the optimal number of retrieved oocytes necessary for achieving maximal IVF success. It may also be easily adopted into daily clinical practice. The introduction of these protocol outcomes could provide further information on the individualization of IVF treatment strategies with AMH based on the starting recFSH dose and to improve ovarian response and IVF outcomes. Further prospective randomized trials are needed to confirm our cutoff values of serum AMH levels and starting recFSH doses as markers based on IVF protocols.

Declaration of interest

The authors report no declarations of interest

References

1. Macklon NS, Stouffer RL, Giudice LC, Fauser BC. The science behind 25 years of ovarian stimulation for *in vitro* fertilization. Endocr Rev 2006;27:170–207.
2. Ji J, Liu Y, Tong XH, et al. The optimum number of oocytes in IVF treatment: an analysis of 2455 cycles in China. Hum Reprod 2013; 28:2728–34.
3. La Marca A, Sunkara SK. Individualization of controlled ovarian stimulation in IVF using ovarian reserve markers: from theory to practice. Hum Reprod Update 2014;20:124–40.
4. Nardo LG, Fleming R, Howles CM, et al. Conventional ovarian stimulation no longer exists: welcome to the age of individualized ovarian stimulation. Reprod Biomed Online 2011;23:141–8.
5. Fiçicioglu C, Kutlu T, Baglam E, Bakacak Z. Early follicular antimüllerian hormone as an indicator of ovarian reserve. Fertil Steril 2006;85:592–6.
6. Loh JS, Maheshwari A. Anti-Mullerian hormone-is it a crystal ball for predicting ovarian ageing? Hum Reprod 2011;26:2925–32.
7. Nelson SM, Yates RW, Lyall H, et al. Anti-Müllerian hormone-based approach to controlled ovarian stimulation for assisted conception. Hum Reprod 2009;24:867–75.
8. Long WQ, Ranchin V, Pautier P, et al. Detection of minimal levels of serum anti-Mullerian hormone during follow-up of patients with ovarian granulosa cell tumor by means of a highly sensitive enzymelinked immunosorbent assay. J Clin Endocrinol Metab 2000; 85:540–4.
9. Rustamov O, Smith A, Roberts SA, et al. Anti-Mullerian hormone: poor assay reproducibility in a large cohort of subjects suggests sample instability. Hum Reprod 2012;27:3085–91.
10. Oudendijk JF, Yarde F, Eijkemans MJ, et al. The poor responder in IVF: is the prognosis always poor? A systematic review. Hum Reprod Update 2012;18:1–11.
11. Sterrenburg MD, Veltman-Verhulst SM, Eijkemans MJ, et al. Clinical outcomes in relation to the daily dose of recombinant follicle-stimulating hormone for ovarian stimulation *in vitro* fertilization in presumed normal responders younger than 39 years: a meta-analysis. Hum Reprod Update 2011;17:184–96.
12. Practic Committee ASRM. Testing and interpreting measures of ovarian reserve: a committee opinion. Fertil Steril 2012;98:1407–15.
13. Broer SL, Broekmans FJ, Laven JS, Fauser BC. Anti-Müllerian hormone: ovarian reserve testing and its potential clinical implications. Hum Reprod Update 2014;20:688–701.
14. Yates AP, Rustamov O, Roberts SA, et al. Anti-Mullerian hormone-tailored stimulation protocols improve outcomes whilst reducing adverse effects and costs of IVF. Hum Reprod 2011;26:2353–62.
15. Choi MH, Yoo JH, Kim HO, et al. Serum anti-Müllerian hormone levels as a predictor of the ovarian response and IVF outcomes. Clin Exp Reprod Med 2011;38:153.
16. La Marca A, Papaleo E, Grisendi V, et al. Development of a nomogram based on markers of ovarian reserve for the

individualisation of the follicle-stimulating hormone starting dose *in vitro* fertilisation cycles. BJOG 2012;119:1171–9.
17. Lan VT, Linh NK, Tuong HM, et al. Anti-Müllerian hormone versus antral follicle count for defining the starting dose of FSH. Reprod Biomed Online 2013;27:390–9.
18. Ficicioglu C, Cenksoy PO, Yildirim G, Kaspar C. Which cut-off value of serum anti-Müllerian hormone level can predict poor ovarian reserve, poor ovarian response to stimulation and *in vitro* fertilization success? A prospective data analysis. Gynecol Endocrinol 2014;30:372–6.