The role of anti-Müllerian hormone in prediction of pregnancy in young and older women with unexplained infertility undergoing intrauterine insemination

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Abstract

Background: Serum anti-Müllerian hormone (AMH) level is considered to be a reliable marker of ovarian reserve. However, there are conflicting reports on the role of AMH level in predicting pregnancy after intrauterine insemination (IUI) cycles. The aim of this study is to investigate the clinical value of AMH in predicting pregnancy in younger and older women with unexplained infertility undergoing gonadotropin stimulation and IUI.

Methods: The medical records of 84 women who underwent first gonadotropin-stimulated IUI cycle owing to unexplained infertility were retrospectively evaluated. The relation of AMH levels with clinical pregnancy rate was analyzed.

Results: The overall clinical pregnancy rate was 19%. There was no significant difference in AMH levels between the pregnant and nonpregnant women (2.0 ± 1.0 vs 2.8 ± 2.0 ng/mL, respectively, $p = 0.250$). A further analysis according to age also failed to reveal significant differences in AMH levels between pregnant and nonpregnant women for both the younger (<35 years, n = 61) and the older (≥35 years, n = 23) subgroups ($p = 0.714$ and 0.532, respectively). Post-hoc power analysis showed a power of 0.80 with a 5% level of significance and a 0.8 effect size.

Conclusion: These findings indicate that AMH levels cannot predict pregnancy in women with unexplained infertility undergoing gonadotropin-stimulated IUI cycle. In addition, AMH is not a strong predictive factor for pregnancy either in younger or older women.

Keywords: Anti-Müllerian hormone; Controlled ovarian stimulation; Intrauterine insemination; Pregnancy; Unexplained infertility

1. INTRODUCTION

Unexplained infertility is one of the most common forms of infertility, affecting an estimated 15% to 30% of infertile couples.[1] Controlled ovarian stimulation (COS) is widely used in conjunction with intrauterine insemination (IUI) as the first line of treatment for unexplained infertility.[2] It has been reported that gonadotropin stimulation with IUI is an effective treatment in infertile couples with no identifiable etiology.[2,3] Gonadotropin combined with IUI may correct subtle problems of ovulation and increase the number of oocyte and motile spermatozoa with a higher percentage of normal morphology at the right place at the right time, around the time of fertilization.[4] Additionally, this form of therapy is less expensive and invasive than in vitro fertilization (IVF).

Various prognostic factors such as female age, duration of infertility, and semen parameters have been studied in predicting treatment outcomes in COS–IUI cycles.[5] According to recent data from the extant literature, female age is the most important factor affecting COS–IUI success rates.[6] It is well known that advancing female age is associated with diminished ovarian reserve. However, some relatively young women with a diminished ovarian reserve might have a poor response to COS.

Serum concentrations of the anti-Müllerian hormone (AMH) have been considered a valuable predictive marker of ovarian reserve.[7] Circulating AMH is produced by granulosa cells of preantral and small antral follicles, and it plays an important role in folliculogenesis.[8] Serum AMH levels reflect the size of the resting ovarian primordial follicle pool.[9] The clearest data on the clinical utility of AMH are related to IVF outcomes. It has been demonstrated that serum AMH measurements can predict both poor and hyper-ovarian response in women treated with IVF,[9,10] and AMH levels at the start of stimulation are correlated with the number of oocytes retrieved.[11]

A limited number of studies have evaluated the prognostic value of AMH in COS–IUI cycles, with inconsistent results.[12–22] Moreover, many of these investigative studies have included couples with various causes of infertility. Therefore, in light of the heterogeneity of the published studies, we sought to assess the role of serum AMH concentrations in predicting pregnancy outcomes of gonadotropin-stimulated IUI cycles in both younger and older women with unexplained infertility.

2. METHODS

A retrospective cohort study was carried out in the Department of Reproductive Endocrinology, Zekai Tahir Burak Women's

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Health Education and Research Hospital, Ankara, Turkey, from January 2016 to June 2018. Data were collected from the records of women with unexplained infertility undergoing their first gonadotropin-stimulated IUI cycle.

The Institutional Review Board approved the use of the patients' medical records. The study protocol was conducted in accordance with the principles of the Declaration of Helsinki. Because this was a noninterventional, retrospective study, formal consent was not required.

Unexplained infertility was defined as the lack of pregnancy with no definite reason among couples after one year of unprotected sexual intercourse. Patients with regular ovulatory menstrual cycles, patent tubes on hysterosalpingography and/or laparoscopy, normal uterine cavities, and husbands with normal semen analysis according to World Health Organization criteria[23] were included. The exclusion criteria were as follows: women with basal follicle stimulating hormone (FSH) >12 mIU/mL, age of >40 years, body mass index (BMI) ≥30 kg/m^2, antral follicle count (AFC) <6, endocrinopathies (including hyperprolactinemia, thyroid dysfunction, and diabetes mellitus), endometriosis, a fibroid uterus, and previous ovarian surgery.

Blood AMH samples were obtained during the initial infertility investigation before treatment, irrespective of the day of the menstrual cycle. Samples were separated by centrifugation at 4000 rpm for 10 minutes. Serum AMH measurements were performed using the electrochemiluminescence immunoassay (Elecsys Cobas e analyzers, Roche Diagnostics GmbH, Mannheim, Germany). The AMH concentration range was determined as 0.01 to 23 ng/mL, and the minimum detectable dose was 0.01 ng/mL. Inter- and intra-assay coefficients of variation were <1.8% and <4.4%, respectively.

Before each course of treatment, patients were evaluated using basal serum hormone tests for FSH, luteinizing hormone (LH), and estradiol (E_2). Baseline transvaginal ultrasound scanning was performed to assess AFC and to exclude the presence of ovarian cysts. To calculate total AFC, the number of follicles measuring 2 to 9 mm in both ovaries was evaluated. All sonographic examinations were performed with the 7.5-mHz endovaginal probe of a General Electric Medical Systems, Logic 200 Pro ultrasound device. The COS was done using an initial dose of 75 IU of recombinant FSH (rFSH) (Gonal-F, Merck Serono, Modugno, Bari, Italy) from day 3 of menses. Ovarian follicular response was monitored by serum E_2 level and transvaginal ultrasonography starting on day 6 of stimulation and every 2 to 3 days thereafter. If no follicle ≥12 mm had developed, the rFSH dosage was increased. Ovulation trigger was planned when the leading follicle reached ≥17 mm in diameter using a subcutaneous injection of 250 μg recombinant human chorionic gonadotropin (hCG) (Ovitrelle, Merck Serono, Modugno, Bari, Italy). To avoid multiple pregnancies, hCG was withheld if more than two follicles ≥16 mm in diameter were present. A single IUI was done 36 hours after hCG administration.

Semen samples were prepared with the swim-up technique. On the day of IUI, all patients were instructed to start 90 mg/d vaginal progesterone gel (Crinone 8%, Merck Serono, Bedford, UK) for luteal support until a pregnancy test or 12 weeks of gestational age if the patient conceived. A serum βhCG test was done 14 days after insemination. Clinical pregnancy was defined as the presence of a gestational sac with fetal heart activity on ultrasound performed at the 7th week of gestation.

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 22.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were expressed as numbers (percentages), and differences between categorical data were evaluated using the χ^2 test. Continuous variables were shown as mean ± SD or median and interquartile range (25th-75th percentile) where applicable. The normality of continuous variables and the homogeneity of variances were tested using the Shapiro–Wilk test and the Levene's test, respectively. The mean differences and median values between the groups were compared using the Student's *t* test and the Mann–Whitney *U* test, respectively. The correlation coefficients between serum AMH levels and the other ovarian reserve parameters, including FSH, E_2, and AFC, were estimated using Spearman's rank correlation. A p-value <0.05 was considered statistically significant. Post-hoc power analysis was carried out using G-power software (G-power v3.1.9.2, Universitat Kiel, Kiel, Germany).

3. RESULTS

Ninety-one patients were initially recruited into the study. Of these, five had cycles with more than bi-follicular growth, and two had low follicular growth in response to gonadotropin stimulation. Therefore, these patients were excluded from the analysis, leaving a total of 84 cycles for evaluation. The mean age of the participants was 31.4 ± 4.7 years (range 20-40 years), and the mean infertility period was 3.8 ± 2.2 years (range 1-12 years). The mean BMI, serum AMH, and basal FSH concentrations of the subjects were 23.2 ± 2.6 (range 18.0-29.9) kg/m^2, 2.6 ± 1.8 (range 0.7-8) ng/mL, and 7.4 ± 1.8 (range 4-11.7) mIU/mL, respectively. Among the subjects, 16 (19%) had achieved clinical pregnancy. There were no cases of ectopic and multiple pregnancies. Ovarian hyperstimulation syndrome did not develop in any of the patients.

When women compared according to achievement of clinical pregnancy, no statistically significant differences were observed in terms of average age, duration of infertility, BMI, basal FSH, LH and E_2 levels, total AFC, and basal total motile sperm count. Serum AMH concentrations were similar in pregnant and nonpregnant women (2.0 ± 1.0 vs 2.8 ± 2.0 ng/mL, p = 0.250) (Table 1).

There were also no significant differences with respect to the duration of the stimulation, total rFSH dose used, serum E_2 levels, endometrial thickness, and number of intermediate-sized (12-15 mm) and dominant follicles (≥16 mm) on the day of hCG injection (Table 2). The correlations of serum AMH levels with age, E_2, FSH, and AFC were as follows: r = –0.182, p = 0.097; r = –0.025, p = 0.23; r = –0.327, p = 0.002; and r = 0.377, p < 0.001.

To further analyze the role of AMH in predicting clinical pregnancy as it relates to age, participants were placed into subgroups of younger (<35 years, n = 61) and older (≥35 years, n = 23) women. No significant differences in serum AMH concentrations were found between pregnant and nonpregnant women in both the younger and the older subgroups (Table 3).

According to our post-hoc power analysis, we achieved a power of 0.80 with a 5% level of significance and a 0.8 effect size by using a two-sample comparison.

4. DISCUSSION

In this study, we assessed the clinical value of AMH to predict pregnancy in patients with unexplained infertility undergoing

Table 1

Demographics and laboratory characteristics of pregnant and nonpregnant women

	Pregnant (n = 16)	Nonpregnant (n = 68)	*p*
Age, y[a]	31.6 ± 5.5	31.3 ± 4.4	0.781
Duration of infertility, y	3.6 ± 1.5	3.9 ± 2.3	0.946
Primary infertility n, %[b]	6 (62.5)	52 (76.5)	0.253
BMI, kg/m^2	23.8 ± 3.6	23.0 ± 2.4	0.266
Basal FSH, mIU/mL	7.4 ± 1.3	7.4 ± 1.9	0.864
Basal LH, mIU/mL	5.3 ± 2.0	6.1 ± 3.5	0.851
Basal E_2, pg/mL	40.3 ± 17.6	41.0 ± 14.5	0.703
Antral follicle count (total)	11.4 ± 2.7	11.5 ± 2.9	0.913
Basal sperm count, 10^6/mL	28.0 ± 10.7	30.8 ± 11.9	0.393
AMH, ng/mL[c]	2.0 ± 1.0 2.1 (1.2-2.6)	2.8 ± 2.0 2.3 (1.1-3.4)	0.250

AMH = anti-Müllerian hormone; BMI = body mass index; E_2 = estradiol; FSH = follicle stimulating hormone; LH = luteinizing hormone.

[a]Mean ± SD.

[b]Number with (percentage).

[c]Mean ± SD with median (inter quartile range, 25th-75th); p < 0.05 is significant.

first rFSH-stimulated IUI cycles. The results demonstrate that serum AMH concentration is not a strong predictive factor for clinical pregnancy after the first IUI cycle. In addition, AMH does not predict the chance of pregnancy either in younger or older women.

Table 2

Stimulation cycle characteristics of pregnant and nonpregnant women

	Pregnant (n = 16)	Nonpregnant (n = 68)	*p*
Duration of stimulation, d[a]	11.3 ± 3.6	10.8 ± 3.1	0.741
Amount of total FSH used, IU	660.6 ± 349.5	633.3 ± 282.3	0.693
E_2 on hCG day, pg/mL	401.2 ± 220.7	386.2 ± 261.4	0.645
Endometrial thickness on hCG day, mm	8.8 ± 1.9	9.1 ± 1.8	0.517
No. of intermediate-sized follicles (12-15 mm)	0.9 ± 1.0	0.8 ± 0.7	0.961
No. of dominant follicles (≥16 mm)	1.0 ± 0.6	1.0 ± 0.6	0.928

E_2 = estradiol; FSH = follicle stimulating hormone; hCG = human chorionic gonadotropin.
[a]Mean ± SD; $p < 0.05$ is significant.

Table 3

Comparison of serum AMH levels (ng/mL) with regard to age in pregnant and nonpregnant women

Characteristics	Pregnant (n = 16)	Nonpregnant (n = 68)	*p*
Age <35 y	2.3 ± 1.1[a] 2.2 (1.6-3.0) (n = 9)	2.8 ± 1.9 2.5 (1.2-3.4) (n = 52)	0.714
Age ≥35 y	1.5 ± 0.8 1.2 (0.9-2.4) (n = 7)	2.5 ± 2.3 1.7(0.8-3.5) (n = 16)	0.532

AMH = anti-Müllerian hormone.
[a]Mean ± SD with median (inter quartile range, 25th-75th); $p < 0.05$ is significant.

For physicians treating infertile patients prior to the IUI cycle, it is crucial to assess ovarian reserve and the potential to achieve pregnancy. Serum AMH concentrations have been found to correlate with AFC and ovarian response, and this represents a better marker than age, basal FSH, and E_2 in IVF patients.[10] Despite evidence of its role as a predictor of ovarian response, AMH is not a strong marker in predicting pregnancy outcomes in IVF.[24] Recently, it has been suggested that AMH measurements may also be useful in predicting IUI outcomes.[12,13] In a retrospective study, Li et al.[12] evaluated the performance of AMH in predicting pregnancy outcomes in COS–IUI cycles and found significantly higher serum AMH concentrations in patients with a live birth. They revealed that AMH concentration has a modest predictive value in terms of successful pregnancy. Similarly, various studies[15,17-20,22] have identified higher AMH levels in women who became pregnant after IUI treatment. Wang et al.[18] also detected an association between low AMH levels and a decreased chance of pregnancy, regardless of age. Nevertheless, some of these previous studies have also suggested that in spite of the association between AMH concentration and pregnancy rates, the predictive ability of AMH is not sufficient for use as the sole predictor of clinical pregnancy in patients undergoing COS–IUI.[19,22]

Contrary to these reports, Freisleben et al.[13] found that AMH levels were not significantly correlated with ovarian responses and pregnancy rates in ovulatory patients undergoing IUI. According to these investigators, AFC and FSH appear to be more closely related to ovarian response when compared to AMH. In other studies, Tremellen and Kolo[14] and Hansen et al.[21] both found that although serum AMH is an effective measure of ovarian reserve, it does not predict live births or miscarriages in patients undergoing COS–IUI. Table 4 summarizes the data from previous studies on serum AMH levels and pregnancy outcomes in IUI cycles.

In the present study, serum AMH levels were not related to the likelihood of clinical pregnancy after IUI. Our findings are consistent with the suggestion that AMH is a strong marker of quantitative ovarian reserve, but it is not an accurate determinant of oocyte quality.[14] Hansen et al. proposed that serum

Table 4

Summary of data from previous studies on serum AMH levels and pregnancy outcomes in IUI cycles

Studies	No. of couples	Study type (protocol)	Infertility cause	Results
Li et al.[12]	243	Retrospective (gonadotropin)	Unexplained, male factor, anovulation	Serum AMH levels are positively correlated with successful pregnancy ($p = 0.002$). AMH has a modest predictive value for live birth (AUC = 0.668)
Freiesleben et al.[13]	123	Prospective, multicenter, randomized (gonadotropin)	Unexplained, male factor	AMH levels are not significantly correlated with ovarian response and pregnancy outcome
Tremellen and Kolo[14]	244	Retrospective (gonadotropin)	Unexplained, male factor, anovulation	AMH levels are not significantly correlated with pregnancy outcome independent of age
Speyer et al.[15]	352	Retrospective (clomiphene citrate or gonadotropin)	Unexplained, male factor, endometriosis, other	AMH levels are positively correlated with live birth ($p = 0.001$); AMH is a good predictive factor for pregnancy outcome
Aanesen et al.[17]	245	Prospective cohort (clomiphene citrate or gonadotropin)	Unexplained, male factor	AMH levels are significantly higher in the pregnant group ($p < 0.05$)
Wang et al.[18]	204	Retrospective (GnRH agonist followed by gonadotropin or sequential clomiphene citrate/ gonadotropin)	Unexplained, anovulation, advanced age, endometriosis	Low AMH levels are associated with a decreased chance of a clinical pregnancy regardless of age (OR = 0.895, $p = 0.026$)
Bakas et al.[19]	195	Retrospective (gonadotropin)	Unexplained, male factor, tubal factor	AMH levels are positively correlated with pregnancy rate. But the ability of AMH is not enough to be used as a sole predictor of pregnancy success (AUC = 0.53 at first cycle and 0.76 for cumulative pregnancy rate)
Moro et al.[20]	276	Retrospective (gonadotropin)	Unexplained	AMH levels are positively correlated with ongoing pregnancy rate (AUC = 0.70)
Hansen et al.[21]	900	Prospective, multicenter, randomized, (clomiphene citrate or gonadotropin)	Unexplained	AMH levels are not significantly associated with pregnancy outcomes
Dondik et al.[22]	209	Retrospective (natural or stimulated cycles)	Unexplained, male factor, anovulation, other	AMH levels are significantly higher in women achieving pregnancy ($p = 0.02$). But the predictive value of AMH for pregnancy is not good (AUC = 0.64)

AMH = anti-Müllerian hormone; AUC = area under the curve; GnRH = gonadotropin releasing hormone; IUI = intrauterine insemination; OR = odds ratio.

AMH concentrations do not reflect oocyte genetic competence.[21] As it is well known, pregnancy rates are affected by oocyte and therefore embryo quality; nonetheless, a correlation between serum AMH levels and embryo quality has not been observed in IVF treatment.[25]

According to the extant literature, there is a strong positive correlation between serum AMH levels and AFC.[26] Consistent with these reports, we found that serum AMH levels were more strongly correlated with total AFC ($r = 0.377$, $p < 0.001$) than other ovarian reserve markers, including basal serum E_2, FSH levels, and age.

It has been demonstrated that the significance of AMH levels in predicting clinical pregnancy during IVF treatment is lower in young women. However, their predictive value appears to gradually increase in older women.[27] In a recent study, Gomez et al.[28] suggested that AMH can be used as a prognostic factor in women older than 36 years of age before performing an IVF/intracytoplasmic sperm injection (ICSI) treatment. According to Park et al.,[27] older women with higher ovarian reserve quantitatively compensate for the age-related decrease in the quality of oocytes, and as a result, these women may demonstrate better pregnancy outcomes compared with women of the same age. In terms of IUI cycles, the role of AMH in predicting pregnancy for different age groups has not been sufficiently examined. By conducting further analysis, we found that AMH levels did not predict pregnancy after IUI, irrespective of age.

Some have considered whether IVF observations are relevant to IUI treatments. In IUI cycles, as a more physiological model, the gonadotropin dose used for ovarian stimulation does not exceed the serum FSH threshold concentration that will induce growth of the two or three follicles most sensitive to FSH.[13] Hence, it has been postulated that treatment outcomes after IUI cycles are less dependent on ovarian reserve than IVF.[21]

In our current study, only couples with unexplained infertility were selected for analysis. The majority of the earlier studies that have investigated the role of AMH in the prediction of IUI success included patients with different causes of infertility. It is well established that the type of infertility, the sperm count in the initial analysis, the number of mature follicles on the day of hCG administration, female age, and the presence of endometriosis and obesity may influence IUI success rates.[5] We assumed that reporting the results of a select study population including unexplained infertility and favorable fertility characteristics would be more informative regarding the prognostic value of AMH in relation to clinical pregnancy rates following IUI. In addition, some data have suggested that the pregnancy rate per cycle is highest in the first COS–IUI cycle.[29] Thus, we only evaluated the results of initial IUI cycles.

Besides , the current study has several limitations that must be considered when interpreting our results. The primary limitations are its retrospective design and limited sample size. As mentioned earlier, the analysis was restricted to a selective group of patients who underwent their first rFSH-stimulated IUI cycle. Also, according to our clinical policy, we aimed to develop a maximum number of two mature follicles at the time of hCG administration. For this reason, we could not investigate the relationship between serum AMH levels and follicular response in our study population.

In conclusion, our data suggest that serum AMH measurement cannot predict clinical pregnancy in patients with unexplained infertility undergoing their initial gonadotropin-stimulated IUI cycle. Moreover, the value of AMH in predicting pregnancy is not dependent on age in these patients. Additional large-scale, prospective studies should be undertaken to confirm these results.

REFERENCES

1. Gelbaya TA, Potdar N, Jeve YB, Nardo LG. Definition and epidemiology of unexplained infertility. *Obstet Gynecol Surv* 2014;**69**:109–15.
2. Aboulghar MA, Mansour RT, Serour GI, Al-Inany HG. Diagnosis and management of unexplained infertility: an update. *Arch Gynecol Obstet* 2003;**267**:177–88.
3. Zeyneloglu HB, Arici A, Olive DL, Duleba AJ. Comparison of intrauterine insemination with timed intercourse in superovulated cycles with gonadotropins: a meta-analysis. *Fertil Steril* 1998;**69**:486–91.
4. Fritz M, Speroff L. *Induction of ovulation*. In: Lippincott Williams & Wilkins, editors. *Clinical gyneocology endocrinology and infertility*. 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2011, p. 1137–90.
5. Merviel P, Heraud MH, Grenier N, Lourdel E, Sanguinet P, Copin H. Predictive factors for pregnancy after intrauterine insemination (IUI): an analysis of 1038 cycles and a review of the literature. *Fertil Steril* 2010;**93**:79–88.
6. Sicchieri F, Silva AB, Silva ACJSRE, Navarro PAAS, Ferriani RA, Reis RMD. Prognostic factors in intrauterine insemination cycles. *JBRA Assist Reprod* 2018;**22**:2–7.
7. van Disseldorp J, Lambalk CB, Kwee J, Looman CW, Eijkemans MJ, Fauser BC, et al. Comparison of inter- and intra-cycle variability of anti-Mullerian hormone and antral follicle counts. *Hum Reprod* 2010;**25**:221–7.
8. Weenen C, Laven JS, Von Bergh AR, Cranfield M, Groome NP, Visser JA, et al. Anti-Müllerian hormone expression pattern in the human ovary: potential implications for initial and cyclic follicle recruitment. *Mol Hum Reprod* 2004;**10**:77–83.
9. Grynnerup AG, Lindhard A, Sørensen S. Recent progress in the utility of anti-Müllerian hormone in female infertility. *Curr Opin Obstet Gynecol* 2014;**26**:162–7.
10. La Marca A, Sighinolfi G, Radi D, Argento C, Baraldi E, Artenisio AC, et al. Anti-Mullerian hormone (AMH) as a predictive marker in assisted reproductive technology (ART). *Hum Reprod Update* 2010;**16**:113–30.
11. Seifer DB, MacLaughlin DT, Christian BP, Feng B, Shelden RM. Early follicular serum müllerian-inhibiting substance levels are associated with ovarian response during assisted reproductive technology cycles. *Fertil Steril* 2002;**77**:468–71.
12. Li HW, Yeung WS, Lau EY, Ho PC, Ng EH. Evaluating the performance of serum antimullerian hormone concentration in predicting the live birth rate of controlled ovarian stimulation and intrauterine insemination. *Fertil Steril* 2010;**94**:2177–81.
13. Freiesleben Nl, Rosendahl M, Johannsen TH, Løssl K, Loft A, Bangsbøll S, et al. Prospective investigation of serum anti-Müllerian hormone concentration in ovulatory intrauterine insemination patients: a preliminary study. *Reprod Biomed Online* 2010;**20**:582–7.
14. Tremellen K, Kolo M. Serum anti-Mullerian hormone is a useful measure of quantitative ovarian reserve but does not predict the chances of live-birth pregnancy. *Aust N Z J Obstet Gynaecol* 2010;**50**:568–72.
15. Speyer BE, Abramov B, Saab W, Doshi A, Sarna U, Harper JC, et al. Factors influencing the outcome of intrauterine insemination (IUI): age, clinical variables and significant thresholds. *J Obstet Gynaecol* 2013;**33**:697–700.
16. Kim JY, Yi G, Kim YR, Chung JY, Ahn JH, Uhm YK, et al. Association between serum anti-Müllerian hormone level and ovarian response to mild stimulation in normoovulatory women and anovulatory women with polycystic ovary syndrome. *Clin Exp Reprod Med* 2013;**40**:95–9.
17. Aanesen A, Westerbotn M. Prospective study of a Swedish infertile cohort 2005–08: population characteristics, treatments and pregnancy rates. *Fam Pract* 2014;**31**:290–7.
18. Wang MH, Chen CH, Wang CW, Hsu MI, Tzeng CR. A higher anti-Müllerian hormone level is associated with an increased chance of pregnancy in patients undergoing controlled ovarian stimulation and intrauterine insemination. *J Obstet Gynaecol* 2015;**35**:64–8.
19. Bakas P, Boutas I, Creatsa M, Vlahos N, Gregoriou O, Creatsas G, et al. Can anti-Mullerian hormone (AMH) predict the outcome of intrauterine insemination with controlled ovarian stimulation? *Gynecol Endocrinol* 2015;**31**:765–8.
20. Moro F, Tropea A, Scarinci E, Leoncini E, Boccia S, Federico A, et al. Anti-Müllerian hormone concentrations and antral follicle counts for the prediction of pregnancy outcomes after intrauterine insemination. *Int J Gynaecol Obstet* 2016;**133**:64–8.
21. Hansen KR, He AL, Styer AK, Wild RA, Butts S, Engmann L, et al. Eunice Kennedy Shriver National Institute of Child Health and Human Development Reproductive Medicine Network. Predictors of pregnancy and live-birth in couples with unexplained infertility after ovarian stimulation-intrauterine insemination. *Fertil Steril* 2016;**105**:1575–83.e2.
22. Dondik Y, Virji N, Butler TS, Gaskins JT, Pagidas K, Sung L. The value of anti-Müllerian hormone in predicting clinical pregnancy after intrauterine insemination. *J Obstet Gynaecol Can* 2017;**39**:880–5.
23. World Health Organization, Department of Reproductive Health and Research: *WHO laboratory manual for the examination and*

processing of human semen. 5th ed. Geneva, Switzerland: World Health Organization; 2010.
24. Tal R, Tal O, Seifer BJ, Seifer DB. Antimüllerian hormone as predictor of implantation and clinical pregnancy after assisted conception: a systematic review and meta-analysis. *Fertil Steril* 2015;**103**:119–30.e3.
25. Lie Fong S, Baart EB, Martini E, Schipper I, Visser JA, Themmen AP, et al. Anti-Müllerian hormone: a marker for oocyte quantity, oocyte quality and embryo quality? *Reprod Biomed Online* 2008;**16**:664–70.
26. Barbakadze L, Kristesashvili J, Khonelidze N, Tsagareishvili G. The correlations of anti-mullerian hormone, follicle-stimulating hormone and antral follicle count in different age groups of infertile women. *Int J Fertil Steril* 2015;**8**:393–8.
27. Park HJ, Lee GH, Gong du S, Yoon TK, Lee WS. The meaning of anti-Müllerian hormone levels in patients at a high risk of poor ovarian response. *Clin Exp Reprod Med* 2016;**43**:139–45.
28. Gomez R, Schorsch M, Hahn T, Henke A, Hoffmann I, Seufert R, et al. The influence of AMH on IVF success. *Arch Gynecol Obstet* 2016;**293**:667–73.
29. Nuojua-Huttunen S, Tomas C, Bloigu R, Tuomivaara L, Martikainen H. Intrauterine insemination treatment in subfertility: an analysis of factors affecting outcome. *Hum Reprod* 1999;**14**:698–703.