Since 1983
EPITHEORESE KLINIKES FARMAKOLOGIAS KAI FARMAKOKINETIKES | 42(Sup1): 37-45 (2024)

Received: 28 July 2024 | **Accepted**: 15 December 2024 | **Published**: 27 December 2024

Open Access | **RESEARCH**

Low serum anti-Müllerian hormone levels, ovarian stimulation protocol, oocyte number, antral follicle count, age, ICSI outcome, and pregnancy rate in Iraqi women

Ruqaya Bashar Al-Smak[1,*], Rana R. Al-Saadi[2], Ban Thabit[2]

[1]Faculty of Medicine, Ibn Sina University for Medical and Pharmaceutical Sciences, Baghdad, Iraq
[2]High Institute of Infertility Diagnoses and Assisted Reproductive Technologies, Al-Nahrain University, Baghdad, Iraq

***Corresponding author:** Rana R. Al-Saadi, High Institute of Infertility Diagnoses and Assisted Reproductive Technologies, Al-Nahrain University, Baghdad, Iraq; Tel.: +964-7731290013; e-mail: drranaa2018@gmail.com

ABSTRACT

Background: The anti-Müllerian hormone (AMH), secreted by granulosa cells in the preantral and the small antral ovarian follicles, is a predictor of the ovarian oocyte reserve. *Aim:* To investigate the correlation between low serum AMH levels (≤1.5 ng/mL), ovarian stimulation protocols, oocyte number, antral follicle count, age, and pregnancy outcomes in Iraqi women undergoing intracytoplasmic sperm injection (ICSI). *Methodology:* This study was conducted at the Rooh Al Hayat IVF Centre in Baghdad, Iraq, from September 2022 to May 2023. Two hundred infertile women with low serum AMH levels participated in the ICSI program. Women with polycystic ovarian syndrome were excluded. The mean patient age was 28.98 years, and the mean serum AMH levels were 0.96 ng/mL. Blood samples were collected on cycle day 2 or 3. Serum AMH levels were measured using a Roche Cobas e 411 analyzer. Patients were divided into groups based on their ovarian stimulation protocol into those receiving a gonadotropin-releasing hormone (GnRH) agonist and those receiving a GnRH antagonist as well as based on pregnancy outcome. *Results:* The pregnancy rate was higher in patients under a GnRH antagonist protocol, although there were no statistically significant differences (p=0.053) in the pregnancy rates between the short GnRH agonist and the GnRH antagonist protocols. There were no significant differences between pregnant and non-pregnant women regarding their mean serum AMH levels and mean age. However, there were significant positive correlations between the serum AMH levels and both the total oocyte count (r=0.870, p<0.001) and the antral follicle count (r=0.859, p<0.001). *Conclusion:* In assisted reproductive techniques, the pregnancy rate was higher in patients treated with GnRH antagonist protocols among women with low serum AMH levels. There were insignificantly higher AMH levels in women aged less than 20 years old, although the pregnancy rates were lower in this age group. Positive correlations were observed between the serum AMH levels and both the total oocyte count and the antral follicle count.

KEYWORDS

AMH, GnRH, ICSI, oocyte count, ovarian reserve

How to cite this article: Al-Smak R. B., Al-Saadi R. R., Thabit B.: Low serum anti-Müllerian hormone levels, ovarian stimulation protocol, oocyte number, antral follicle count, age, ICSI outcome, and pregnancy rate in Iraqi women *Epitheorese Klin. Farmakol. Farmakokinet.* 42(Sup1): 37-45 (2024).
DOI: 10.61873/FZMY1367

Publisher note: PHARMAKON-Press stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. INTRODUCTION

Infertility is defined as the inability to achieve a clinical pregnancy after 12 months or more of regular

unprotected sexual intercourse, with no other identifiable reason such as postpartum amenorrhea. It may be primary or secondary and can be attributed to female factors, male factors, both, or remain unexplained [1]. Among the various risk factors for infertility, including lifestyle, environment, and body weight, age is considered the most crucial. Women's fertility gradually declines with age as both the number and quality of oocytes decrease [2].

The anti-Müllerian hormone (AMH) levels have emerged as a marker for ovarian aging [3,4]. AMH is secreted by the granulosa cells of pre-antral and small antral ovarian follicles with diameters less than 8 mm. Researchers have demonstrated a positive correlation between AMH levels and the antral follicle count, which represents the number of follicles with diameters between 2 and 9 mm [5]. AMH is used as a biological marker for evaluating the ovarian reserve as it reflects the follicular pool [6]. Throughout a woman's lifespan, the AMH levels are very low at birth and in female newborns, rise gradually until adolescence, and then reach a plateau until 25 years of age [7]. After the age of 25, the AMH levels are negatively correlated with the age of adult women [8]. Sherman *et al.* (1976) have recognized AMH as an early marker of decline in the follicular pool compared to follicle-stimulating hormone (FSH), which increases only after the age of 35 due to the decreased ovarian reserve [9]. The AMH is a predictor of ovarian response used to select appropriate gonadotropin-releasing hormone (GnRH) agonist and antagonist protocols, potentially maximizing success rates in assisted reproductive techniques and enhancing the safety of ovarian stimulation practices [10]. The selection of an appropriate ovarian stimulation strategy can improve the assisted reproductive technique outcomes. Although the two common ovarian stimulation protocols (GnRH agonist and GnRH antagonist) exhibit similar implantation and pregnancy rates, each protocol has specific characteristics.

Several ovarian stimulation protocols are used in order to increase ovarian production of follicles. Without these protocols, only one mature follicle would typically be produced and released by the ovaries in each menstrual cycle. In stimulation regimens, injectable FSH or human menopausal gonadotropin (hMG) is used so as to stimulate the development of multiple follicles, by using medications such as Gonal-F, Follistim, Bravelle, and Menopur. Final maturation is induced by using human chorionic gonadotropin (hCG). The ovaries are typically stimulated with FSH drugs for 7 to 12 days until an appropriate number of mature-size follicles (≥17 mm) have developed [11].

The AMH levels have been reported to be valuable in predicting ovarian response in *in vitro* fertilization (IVF) cycles [12]. An AMH level below 1.1 ng/mL has been associated with total fertilization failure [13]. Dose adjustment of gonadotropins used for ovarian stimulation, accompanied by either GnRH agonists or antagonists, is important in preventing under- or over-stimulated cycles. The European Society of Human Reproduction and Embryology recommends the use of either the antral follicle count or the AMH levels for predicting high and poor responses to ovarian stimulation, with serum AMH level measurement being recommended over other hormonal ovarian reserve tests [14]. Several factors can contribute to low AMH levels, which are indicative of a reduced ovarian reserve. Some of the main causes include genetics [15] and previous ovarian surgery, such as cyst removal or treatment for endometriosis, which can reduce the number of follicles and result in significant declines in the AMH levels [16]. In previous studies, GnRH antagonists have been found effective for ovarian stimulation by directly binding to GnRH receptors, thereby blocking receptor activity in a competitive manner [17].

The aim of this study was to investigate the correlation between low serum AMH levels (≤1.5 ng/mL) and ovarian stimulation protocols, oocyte number, antral follicle count, age, and pregnancy outcomes in Iraqi women undergoing intracytoplasmic sperm injection (ICSI) cycles.

2. METHODOLOGY

2.1. Study design and participants

This study was conducted at the Rooh Al Hayat IVF Centre in Baghdad, Iraq, from September 2022 to May 2023. The study protocol was approved by the Institutional Review Board of the High Institute of Infertility Diagnosis and Assisted Reproductive Technologies at the Al-Nahrain University (approval number: 0702-MF-2024B39; date: 2-1-2022). All participants provided written informed consent before enrolling in the study. Two hundred infertile Iraqi women with low serum AMH levels were selected from those attending the IVF Centre for ICSI treatment. Participants were divided into groups based on their ovarian stimulation protocol (GnRH agonist or GnRH antagonist) as determined by their treating gynaecologist, and further subdivided based on pregnancy outcome. The mean (± standard error of the mean) patient age was 28.98 ± 0.31 years, with serum AMH levels of 0.96 ± 0.03 ng/mL. The mean oocyte count was 4.42 ± 0.12, and the mean antral follicle count was 6.24 ± 0.17 (Table 1).

The study included women aged 18 to 35 years undergoing ICSI treatment, with low serum AMH levels (≤1.5 ng/mL). The exclusion criteria included a diagnosis of polycystic ovary syndrome, diabetes mellitus (as assessed by glucose tolerance test), hyperprolactinemia (as determined by prolactin measurement), and severe male factor infertility. All participants underwent a complete physical examination, serial ultrasound scans until the day of the oocyte retrieval, and assessment of serum hormone levels on cycle days 2 to 3. Hormones measured included AMH, FSH, luteinizing hormone, prolactin, estradiol (E2), and testosterone.

2.2. Blood sampling

Blood samples were collected in gel tubes and were allowed to clot at 37ºC for 30 min before centrifugation at 5,000 rpm for 10 min in order to isolate the serum. Serum samples were stored at -40ºC until the undertaking of the AMH assay. AMH levels were measured using a Roche Cobas e 411 analyzer with an AMH assay kit. Based on the obtained AMH results, patients were divided into two groups: (i) group 1 that included 100 women with low AMH serum levels and positive pregnancy tests and (ii) group 2 that included 100 women with low AMH serum levels and negative pregnancy tests.

2.3. Controlled ovarian stimulation

Patients were stimulated using either a GnRH agonist or a GnRH antagonist protocol, based on their age, medical history, and underlying conditions. The short GnRH agonist protocol, also known as the flare protocol, started with GnRH agonist administration on day 1 to 2 of the stimulation cycle. The GnRH agonist was given once daily from the first or second day of the menstrual cycle, along with FSH or hMG, until the day of the hCG trigger. Ovarian stimulation with gonadotropins typically began on cycle day 2. The GnRH antagonist was administered when the leading follicles reached approximately 14 mm in diameter (as determined by ultrasound) [18,19]. FSH was started on day 2 of the menstrual cycle, followed by GnRH antagonist administration through a flexible method based on the size of the largest follicles (13–14 mm). For both protocols, serial transvaginal ultrasound scans were performed in order to monitor the follicular size and number, along with serum E2 level measurements until the time of the hCG trigger. Gonadotropin doses were individualized based on the obtained serum E2 measurements and the transvaginal ultrasound monitoring of developing follicles.

Oocyte pickup was performed *via* transvaginal ultrasound-guided aspiration approximately 36 h after the hGG injection under general anesthesia. Mature metaphase II oocytes were retrieved from cumulus-oocyte complexes and were inseminated using an ICSI technique according to clinical indications. After 36 h, one or two embryos were transferred into the uterus by using an embryo transfer catheter. Intravaginal progesterone was used for the luteal phase support, starting on the day of the embryo transfer and continuing for 15 days. Pregnancy tests were performed 14 to 15 days after the embryo transfer.

2.4. Statistical analysis

Data were analyzed using SPSS v.23 and Microsoft Office 2010. Descriptive statistics, including frequency, range, mean, and standard error of the mean, were calculated. Groups were compared using chi-square tests (for non-continuous variables or percentages) and independent sample *t*-tests (for unpaired comparisons between two groups). The degree of association between continuous variables was calculated by using the Pearson's correlation coefficient (*r*). Results were considered as statistically significant when the *p* value was less than or equal to 0.05.

3. RESULTS

3.1. Baseline characteristics

Two hundred infertile women were enrolled in this study. The mean patient age was 28.98 years, and the mean serum AMH levels were 0.96±0.03 ng/mL. The mean oocyte count was 4.42, and the mean antral follicle count was 6.24 (Table 1). Of the 200 study participants, 148 (74.0%) were treated with the short GnRH agonist protocol, and 52 (26.0%) were placed under the GnRH antagonist protocol. The overall pregnancy rate was 50.0% (100 out of 200 patients). Participants were divided into four age groups: 10 patients (5.0%) were younger than 20 years old, 21 patients (10.5%) were between 20 and 24 years of age, 66 patients (33.0%) were between 25 and 29 years of age, and 103 patients (51.5%) were 30 years old or older.

3.2. Clinical parameters

The total oocyte count and the antral follicle count were significantly higher in pregnant women compared to non-pregnant women: 4.76 ± 0.16 *vs*. 4.07 ± 0.17 (p=0.003) and 6.75 ± 0.22 *vs*. 5.72 ± 0.24

(*p*=0.002), respectively (Table 2). There were no significant differences between pregnant and non-pregnant women regarding their mean serum AMH levels (0.97 ± 0.03 *vs.* 0.96 ± 0.03 ng/mL; *p*=0.916) and their mean age (29.31 ± 0.41 *vs.* 28.64 ± 0.45 years; *p*=0.283), as also show in Table 2. Patients treated with the GnRH antagonist protocol showed insignificantly higher values for the following parameters compared to those treated with the GnRH agonist protocol (Table 3): (i) AMH levels (1.04 ± 0.04 *vs.* 0.93 ± 0.03 ng/mL; *p*=0.062), (ii) total oocyte count (4.54 ± 0.15 *vs.* 4.37 ± 0.14; *p*=0.538), and (iii) antral follicle count (6.42 ± 0.29 *vs.* 6.17±0.20; *p*=0.504).

3.3. Serum AMH levels by protocol

Pregnant women treated with the GnRH antagonist protocol had significantly higher serum AMH levels than pregnant women treated with the short GnRH agonist protocol (1.07 ± 0.05 *vs.* 0.92 ± 0.04 ng/mL; *p*=0.041) (Table 4). In non-pregnant women, there was no significant difference with regard to the serum AMH levels between the two protocols (0.95 ± 0.04 *vs.* 0.99±0.08 ng/mL; *p*=0.604; Table 4).

Table 1. Baseline characteristics of the participants of this study.

Parameters	Range	Mean ± standard error of the mean
Age (years)	17–35	28.98 ± 0.31
Serum anti-Müllerian hormone levels (ng/mL)	0.01–1.49	0.96 ± 0.03
Total oocyte count	1.0–8.0	4.42 ± 0.12
Antral follicle count	1.0–11.0	6.24 ± 0.17

Table 2. Comparison of the mean (± standard error of the mean) age, serum anti-Müllerian hormone levels, total oocyte count, and antral follicle count between the pregnant and the non-pregnant women included in this study.

Parameters	Pregnant women (N=100)	Non-pregnant women (N=100)	*p* value
Age (years)	29.31 ± 0.41	28.64 ± 0.45	0.283
Serum anti-Müllerian hormone levels (ng/mL)	0.97 ± 0.03	0.96 ± 0.03	0.916
Total oocyte count	4.76 ± 0.16	4.07 ± 0.17	0.003
Antral follicle count	6.75 ± 0.22	5.72 ± 0.24	0.002

Table 3. Comparison of the mean (± standard error of the mean) serum anti-Müllerian hormone levels, total oocyte count, and antral follicle count between women under gonadotropin-releasing hormone (GnRH) agonist and antagonist protocols.

Parameters	Short GnRH agonist protocol (N=148)	GnRH antagonist protocol (N=52)	*p* value
Serum anti-Müllerian hormone levels (ng/mL)	0.93 ± 0.03	1.04 ± 0.04	0.062
Total oocyte count	4.37 ± 0.14	4.54 ± 0.15	0.538
Antral follicle count	6.17 ± 0.20	6.42 ± 0.29	0.504

Table 4. Comparison of the mean (± standard error of the mean) serum anti-Müllerian hormone levels between pregnant and non-pregnant women under gonadotropin-releasing hormone (GnRH) agonist and antagonist protocols.

Group	Short GnRH agonist protocol (N=68)	GnRH antagonist protocol (N=32)	*p* value
Pregnant women	0.92 ± 0.04	1.07 ± 0.05	0.041
Group	**Short GnRH agonist protocol (N=80)**	**GnRH antagonist protocol (N=20)**	***p* value**
Non-pregnant women	0.95 ± 0.04	0.99 ± 0.08	0.604

Table 5. Distribution of pregnancy rates and serum anti-Müllerian hormone levels across different age groups.

Age group	Pregnancies and pregnancy rate in age group (%)	Serum anti-Müllerian hormone levels (ng/mL)
Less than 20 years	1 (10.0%)	1.08 ± 0.08
20–24 years	13 (61.9%)	0.93 ± 0.08
25–29 years	32 (48.5%)	0.92 ± 0.05
>30 years	54 (52.4%)	0.99 ± 0.04
p value	0.048	0.487

3.4. Pregnancy rates

The pregnancy rate was higher in patients treated with the GnRH antagonist protocol when compared to that of patients treated with the GnRH agonist protocol (61.5% *vs.* 45.9%). However, this difference was not statistically significant (p=0.053).

3.5. Correlation analysis

There was no significant correlation between the serum AMH levels and the patient age (r=0.015, p= 0.836). However, significant positive correlations were observed between the serum AMH levels and the total oocyte count (r=0.870, p<0.001; Figure 1) and between the serum AMH levels and the antral follicle count (r=0.859, p<0.001; Figure 2). The serum AMH levels were insignificantly higher in women younger than 20 years (1.08 ± 0.08 ng/mL, p=0.487); however, the pregnancy rate was significantly lower in this age group (10.0%, p=0.048) compared to other age groups (Table 5).

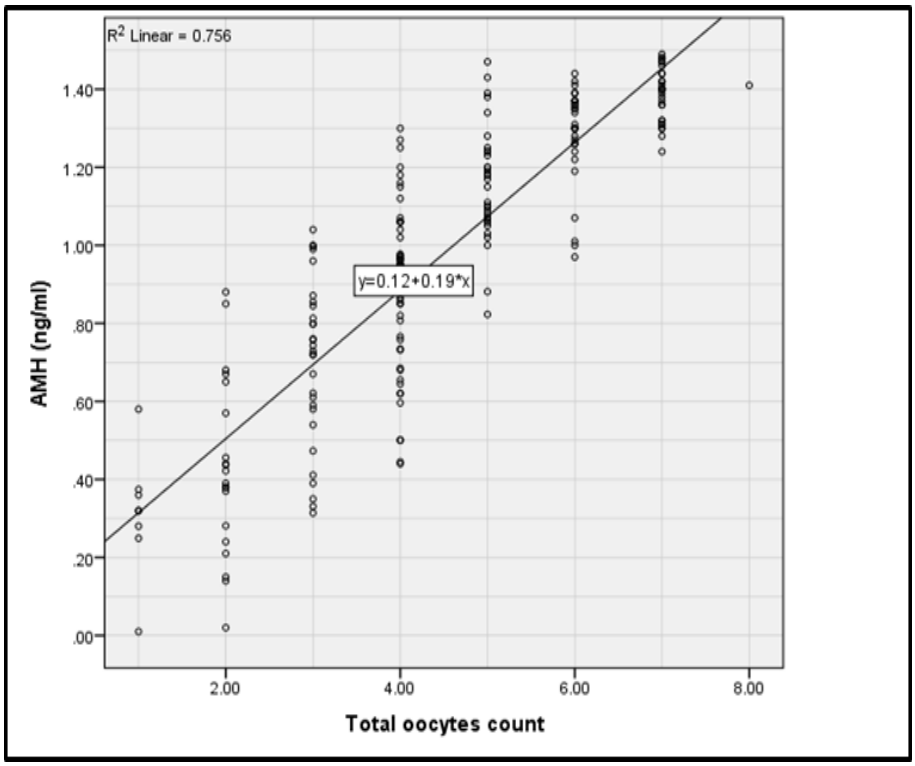

Figure 1. Correlation between the serum anti-Müllerian hormone (AMH) levels and the total oocyte count in the participants of this study.

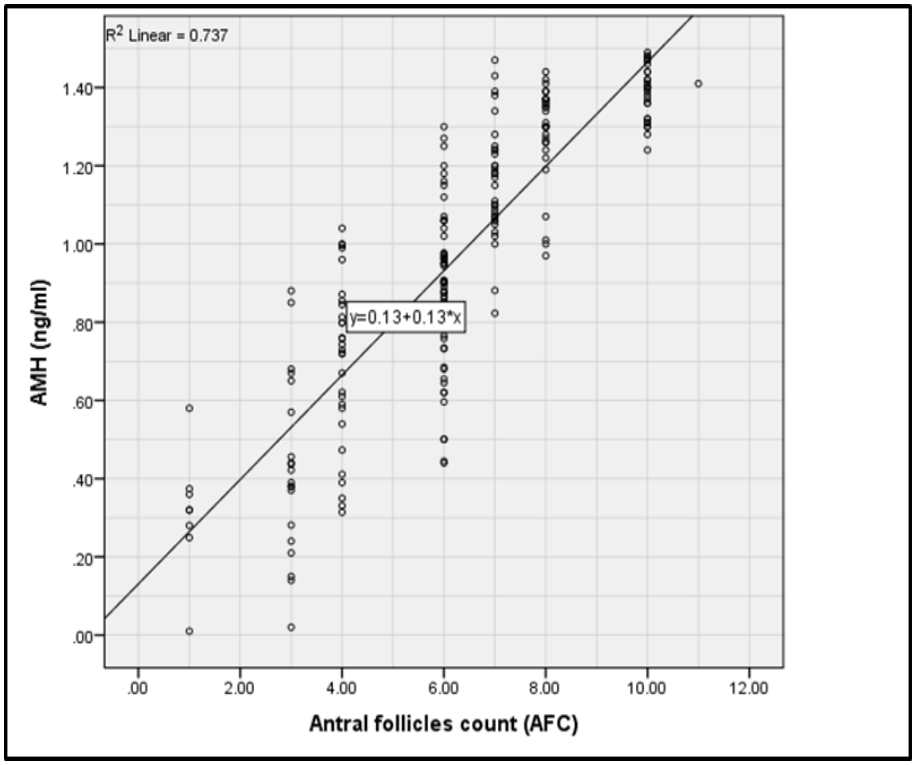

Figure 2. Correlation between the serum anti-Müllerian hormone (AMH) levels and the antral follicle count in the participants of this study.

4. DISCUSSION

The present study investigated the relationship between low serum AMH levels, ovarian stimulation protocols, and various clinical parameters in Iraqi women undergoing ICSI treatment. Our findings contribute to the ongoing discussion about the optimal management of patients with diminished ovarian reserve [15-25]. The observed higher pregnancy rate in patients treated with the GnRH antagonist protocol, although not statistically significant, aligns with the findings of Pu *et al.* [20]; they proposed the antagonist protocol as the frontline treatment for women with low serum AMH levels. This preference for the GnRH antagonist protocol is further supported by Zhu *et al.* [19], who have concluded that the GnRH antagonist protocol was comparable to the GnRH agonist protocol in terms of clinical outcomes and obstetric and perinatal outcomes, with a lower risk of developing ovarian hyperstimulation syndrome. The significant positive correlations we found between serum AMH levels and the total oocyte count as well as between the serum AMH levels and the antral follicle count corroborate the findings of previous studies. Kotanidis *et al.* [24] and Lie Fong *et al.* [26] have reported that the AMH levels appear to be a valuable marker for ovarian reserve and the response to IVF treatment. They noted strong associations between AMH levels and the number of retrieved oocytes, which in turn may influence pregnancy rates. However, it is important to note that Takahashi *et al.* [27] have found a negative relation between AMH levels and the oocyte number, thereby highlighting the complexity of this relationship.

Interestingly, our study has found no significant correlation between the serum AMH levels and the age of the patients. This contrasts with the findings of Belloc *et al.* [2], who have reported a decline in AMH levels with increasing age. This discrepancy might be due to our study's focus on women with already low AMH levels, potentially obscuring age-related trends observed in the general population. The insignificantly higher AMH levels observed in women younger than 20 years, coupled with significantly lower pregnancy rates in this age group, present an intriguing finding. This seemingly paradoxical result aligns with the observations of van Loendersloot *et al.* [28], who have suggested that relatively young patients with reduced ovarian reserve may still have favorable

IVF outcomes due to preserved oocyte competence. Our findings underscore the complex interplay between age, ovarian reserve, and fertility outcomes. Nikmard *et al.* [29] have suggested that high-dose gonadotropin and GnRH agonist protocols are not associated with improved outcomes in patients with low AMH levels; they have proposed that the GnRH antagonist protocol might be a more ideal ovarian stimulation strategy for these patients, given the higher pregnancy rates. Our results, showing a trend towards higher pregnancy rates with the employment of the GnRH antagonist protocol, support this recommendation.

The limitations of using AMH as a sole predictor of IVF success are highlighted by our finding of no significant difference in terms of the serum AMH levels between pregnant and non-pregnant women. This aligns with the conclusions of Umarsingh *et al.* [30], who have demonstrated only weak positive relationships between AMH levels and the number of oocytes, mature oocytes, and fertilized oocytes. These findings collectively suggest that while AMH is a valuable marker of ovarian reserve, it should not be used in isolation for the prediction of IVF outcomes.

Our study is characterized by some limitations, including its single-center design and the focus on a specific population of women with low AMH levels. Future multicenter studies with larger sample sizes and longer follow-up periods could provide more comprehensive insights into the optimal management of patients with diminished ovarian reserve.

5. CONCLUSION

This study provides insights into managing women with low serum AMH levels undergoing assisted reproduction. Our findings suggest a potential benefit of GnRH antagonist protocols for these patients, as indicated by a trend towards higher pregnancy rates. While we confirmed significant positive correlations between AMH levels and both oocyte and antral follicle counts, the lack of difference in AMH levels between pregnant and non-pregnant women highlights the limitations of using AMH levels alone to predict IVF success. The unexpected finding of lower pregnancy rates in younger women despite slightly higher AMH levels underscores the complex interplay between age, ovarian reserve, and fertility outcomes. These results emphasize the need to consider AMH levels alongside other clinical factors when predicting IVF outcomes and selecting treatment strategies.

ACKNOWLEDGMENTS

We are grateful to Dr Salim Abd Mohammed Ghanim for performing all of the statistical analysis of the present study. Special acknowledgement for the Rooh Al Hayat IVF Centre for helping us in collecting the data.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

REFERENCES

1. Elhussein O. G., Ahmed M. A., Suliman S. O., Yahya L. I., Adam I.: Epidemiology of infertility and characteristics of infertile couples requesting assisted reproduction in a low-resource setting in Africa, Sudan. *Fertil. Res. Pract.* 5: 7 (2019).
DOI: 10.1186/s40738-019-0060-1

2. Belloc S., Hazout A., Zini A., Merviel P., Cabry R., Chahine H., *et al.*: How to overcome male infertility after 40: Influence of paternal age on fertility. *Maturitas* 78(1): 22-29 (2014).
DOI: 10.1016/j.maturitas.2014.02.011

3. Josso N., Rey R. A., Picard J. Y.: Anti-Müllerian hormone: a valuable addition to the toolbox of the pediatric endocrinologist. *Int. J. Endocrinol.* 2013: 674105 (2013).
DOI: 10.1155/2013/674105

4. Shembekar C. A., Upadhye J. J., Shembekar M. C., Welekar S. H.: Anti-Mullerian hormone (AMH) as predictor of ovarian reserve. *Int. J. Reprod. Contracept. Obstet. Gynecol.* 6(9): 4006-4010 (2017).
DOI: 10.18203/2320-1770.ijrcog20174053

5. 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.* 8(4): 393-398 (2015).
DOI: 10.22074/ijfs.2015.4179

6. de Vet A., Laven J. S., de Jong F. H., Themmen A. P., Fauser B. C.: Antimüllerian hormone serum levels: a putative marker for ovarian aging. *Fertil. Steril.* 77(2): 357-362 (2002).
DOI: 10.1016/s0015-0282(01)02993-4

7. Lie Fong S., Visser J. A., Welt C. K., de Rijke Y. B., Eijkemans M. J., Broekmans F. J., *et al.*: Serum anti-Müllerian hormone levels in healthy females: a nomogram ranging from infancy to adulthood. *J. Clin. Endocrinol. Metab.* 97(12): 4650-4655 (2012).
DOI: 10.1210/jc.2012-1440

8. Moolhuijsen L. M. E., Visser J. A.: Anti-Müllerian hormone and ovarian reserve: update on assessing ovarian function. *J. Clin. Endocrinol. Metab.* 105(11): 3361-3373 (2020).
DOI: 10.1210/clinem/dgaa513

9. Sherman B. M., West J. H., Korenman S. G.: The menopausal transition: analysis of LH, FSH, estradiol,

and progesterone concentrations during menstrual cycles of older women. *J. Clin. Endocrinol. Metab.* 42(4): 629-636 (1976).
DOI: 10.1210/jcem-42-4-629

10. Aflatoonian A., Oskouian H., Ahmadi S., Oskouian L.: Prediction of high ovarian response to controlled ovarian hyperstimulation: anti-Müllerian hormone versus small antral follicle count (2-6 mm). *J. Assist. Reprod. Genet.* 26(6): 319-325 (2009).
DOI: 10.1007/s10815-009-9319-5

11. Orvieto R.: Triggering final follicular maturation -- hCG, GnRH-agonist or both, when and to whom? *J. Ovarian Res.* 8: 60 (2015).
DOI: 10.1186/s13048-015-0187-6

12. Hamdine O., Eijkemans M. J., Lentjes E. W., Torrance H. L., Macklon N. S., Fauser B. C., *et al.*: Ovarian response prediction in GnRH antagonist treatment for IVF using anti-Müllerian hormone. *Hum. Reprod.* 30(1): 170-178 (2015).
DOI: 10.1093/humrep/deu266

13. Tian T., Chen L., Yang R., Long X., Li Q., Hao Y., *et al.*: Prediction of fertilization disorders in the *in vitro* fertilization / intracytoplasmic sperm injection: a retrospective study of 106,728 treatment cycles. *Front. Endocrinol. (Lausanne)* 13: 870708 (2022).
DOI: 10.3389/fendo.2022.870708

14. Ovarian Stimulation TEGGO, Bosch E., Broer S., Griesinger G., Grynberg M., Humaidan P., *et al.*: ESHRE guideline: ovarian stimulation for IVF/ICSI. *Hum. Reprod. Open* 2020(2): hoaa009 (2020).
DOI: 10.1093/hropen/hoaa009

15. Schneiderman M., Dahan M. H.: GnRH agonist protocols. In: Allahbadia G. N., Ata B., Lindheim S. R., Woodward B. J., Bhagavath B. (editors): Textbook of Assisted Reproduction. Singapore: *Springer*, 79-88 (2020).
DOI: 10.1007/978-981-15-2377-9_9

16. Cheung L. P., Lam P. M., Lok I. H., Chiu T. T., Yeung S. Y., Tjer C. C., *et al.*: GnRH antagonist *versus* long GnRH agonist protocol in poor responders undergoing IVF: a randomized controlled trial. *Hum. Reprod.* 20(3): 616-621 (2005).
DOI: 10.1093/humrep/deh668

17. Daya S.: Gonadotropin releasing hormone agonist protocols for pituitary desensitization in *in vitro* fertilization and gamete intrafallopian transfer cycles. *Cochrane Database Syst. Rev.* 2000(2): CD001299 (2000).
DOI: 10.1002/14651858.CD001299

18. Griesinger G., Venetis C. A., Marx T., Diedrich K., Tarlatzis B. C., Kolibianakis E. M.: Oral contraceptive pill pretreatment in ovarian stimulation with GnRH antagonists for IVF: a systematic review and meta-analysis. *Fertil. Steril.* 90(4): 1055-1063 (2008).
DOI: 10.1016/j.fertnstert.2007.07.1354

19. Zhu J., Xing W., Li T., Lin H., Ou J.: GnRH antagonist protocol *versus* GnRH agonist long protocol: a retrospective cohort study on clinical outcomes and maternal-neonatal safety. *Front. Endocrinol. (Lausanne)* 13: 875779 (2022).
DOI: 10.3389/fendo.2022.875779

20. Pu D., Wu J., Liu J.: Comparisons of GnRH antagonist *versus* GnRH agonist protocol in poor ovarian responders undergoing IVF. *Hum. Reprod.* 26(10): 2742-2749 (2011).
DOI: 10.1093/humrep/der240

21. Mochtar M. H.; Dutch Ganirelix Study Group: The effect of an individualized GnRH antagonist protocol on folliculogenesis in IVF/ICSI. *Hum. Reprod.* 19(8): 1713-1718 (2004).
DOI: 10.1093/humrep/deh334

22. Hoseini F. S., Noori Mugahi S. M., Akbari-Asbagh F., Eftekhari-Yazdi P., Aflatoonian B., Aghaee-Bakhtiari S. H., *et al.*: A randomized controlled trial of gonadotropin-releasing hormone agonist *versus* gonadotropin-releasing hormone antagonist in Iranian infertile couples: oocyte gene expression. *Daru* 22(1): 67 (2014).
DOI: 10.1186/s40199-014-0067-4

23. Sun H. G., Lee K. H., Park I. H., Kim H.J., Kim Y.Y., Jo J.D.: In low AMH level, which protocol is best on IVF? *Fertil. Steril.* 100(3): S521 (2013).
DOI: 10.1016/j.fertnstert.2013.07.255

24. Kotanidis L., Asimakopoulos B., Nikolettos N.: Association between AMH, oocyte number and availability of embryos for cryopreservation in IVF. *In Vivo* 27(6): 877-880 (2013).

25. La Marca A., Sighinolfi G., Radi D., Argento C., Baraldi E., Artenisio A. C., *et al.*: Anti-Mullerian hormone (AMH) as a predictive marker in assisted reproductive technology (ART). *Hum. Reprod. Update* 16(2): 113-130 (2010).
DOI: 10.1093/humupd/dmp036

26. Lie Fong S., Baart E. B., Martini E., Schipper I., Visser J. A., Themmen A. P., *et al.*: Anti-Müllerian hormone: a marker for oocyte quantity, oocyte quality and embryo quality? *Reprod. Biomed. Online* 16(5): 664-670 (2008).
DOI: 10.1016/s1472-6483(10)60480-4

27. Takahashi C., Fujito A., Kazuka M., Sugiyama R., Ito H., Isaka K.: Anti-Müllerian hormone substance from follicular fluid is positively associated with success in oocyte fertilization during *in vitro* fertilization. *Fertil. Steril.* 89(3): 586-591 (2008).
DOI: 10.1016/j.fertnstert.2007.03.080

28. van Loendersloot L. L., van Wely M., Limpens J., Bossuyt P. M., Repping S., van der Veen F.: Predictive factors in *in vitro* fertilization (IVF): a systematic review

and meta-analysis. *Hum. Reprod. Update* 16(6): 577-589 (2010).
DOI: 10.1093/humupd/dmq015

29. Nikmard F., Aflatoonian B., Hosseini E., Aflatoonian A., Bakhtiyari M., Aflatoonian R.: A comparative study on the results of agonist and antagonist protocols based on serum AMH levels in patients undergoing intracytoplasmic sperm injection. *Int. J. Reprod. Biomed.* 14(12): 769-776 (2016).

30. Umarsingh S., Adam J. K., Krishna S. B. N.: The relationship between anti-Müllerian hormone (AMH) levels and pregnancy outcomes in patients undergoing assisted reproductive techniques (ART). *PeerJ* 8: e10390 (2020).
DOI: 10.7717/peerj.10390