Annals of Clinical and Analytical Medicine
Original Research

Autologous ART outcomes and the predictive value of AMH in women with premature ovarian failure

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Abstract

Aim: To compare ovarian response, oocyte quality, embryological development, and clinical outcomes between women with premature ovarian failure (POF) and age-matched controls, and to evaluate the predictive value of basal anti-Müllerian hormone (AMH) and follicle-stimulating hormone (FSH).

Materials and Methods: This retrospective cohort study included 528 women: 249 with POF and 279 age-matched controls. Outcomes included oocyte yield, embryological parameters, live birth, and miscarriage rates. Multivariable linear regression identified independent predictors of oocyte yield.

Results: AMH was significantly lower and FSH higher in the POF group ($p < 0.001$). Women with POF had markedly reduced oocyte yield and impaired embryological outcomes ($p < 0.001$). The live birth rate was lower (10.8% vs. 22.6%; $p < 0.001$), while the miscarriage rate per clinical pregnancy was significantly higher in the POF group (35.7% vs. 19.2%; $p = 0.047$). AMH was an independent predictor of oocyte yield, whereas FSH was not.

Discussion: POF is associated with reduced reproductive potential and increased miscarriage risk. AMH is the most reliable marker for predicting ovarian response and guiding patient counseling.

Keywords

premature ovarian failure, primary ovarian insufficiency, Anti-Müllerian hormone,oocyte quality, assisted reproductive technology

DOI: 10.4328/ACAM.23044 Received: 25/12/2025 Accepted: 25/01/2026 Published Online: 26/01/2026 Printed: 01/02/2026 Ann Clin Anal Med 2026;17(2):168-172
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This study was approved by the Ethics Committee of Harran University Hospital (Date: 2025-03-24, No: HRÜ/25.06.18)

Introduction

Premature ovarian failure (POF), also referred to as primary ovarian insufficiency (POI), is one of the most challenging causes of female infertility in reproductive medicine. It is defined as the cessation of ovarian function before the age of 40, typically characterized by oligo / amenorrhea, hypoestrogenism, and elevated follicle-stimulating hormone (FSH) levels exceeding 25 IU / L on two separate measurements at least one month apart [1]. POF affects approximately 1% of women under 40 and is associated not only with infertility but also with an increased long-term risk of cardiovascular disease, osteoporosis, and psychological morbidity [2].

Unlike natural menopause, ovarian activity in POF can be intermittent. A minority of patients may experience occasional ovulation or even spontaneous conception, but these events are rare and unpredictable [3]. The etiology of POF is heterogeneous and encompasses chromosomal abnormalities (e.g., Turner syndrome, FMR1 premutation), autoimmune oophoritis, environmental exposures, iatrogenic gonadotoxic damage (e.g., chemotherapy, radiotherapy), and idiopathic causes. Despite a comprehensive evaluation, more than 75% of cases remain unexplained. Regardless of its cause, accelerated depletion or dysfunction of the follicular pool ultimately leads to impaired steroidogenesis and infertility [4].

Assisted reproductive technology (ART), particularly in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), remains the primary option for women with POF who wish to conceive using their own oocytes. However, these patients typically exhibit a poor response to ovarian stimulation, reduced oocyte yield, lower oocyte competence, and impaired embryo development [5,6]. Although oocyte donation is associated with high success rates and is frequently proposed as the most effective strategy, it is not universally acceptable due to ethical, religious, cultural, or legal restrictions [7]. Consequently, optimizing autologous IVF strategies and providing realistic counseling for women with POF remain key unmet clinical needs.

Age is a well-established determinant of oocyte competence and ART success. To isolate the impact of POF from the confounding effects of chronological aging, comparisons with age-matched women who have preserved ovarian reserve are essential. Such comparisons allow a clearer understanding of how diminished ovarian reserve per se influences oocyte yield, embryological development, and reproductive outcomes [8]. However, few studies have systematically evaluated both embryological and comprehensive clinical IVF outcomes, including rates of pregnancy loss, in well-defined, age-matched POF and control cohorts. Most available data are limited by small sample sizes, heterogeneous inclusion criteria, or inconsistent laboratory protocols [9]. This gap highlights the need for robust comparative data based on strictly age-matched and clinically homogeneous control groups to fully characterize the reproductive deficit.

Among ovarian reserve markers, anti-Müllerian hormone (AMH) and basal FSH are widely used in clinical practice. AMH, secreted by granulosa cells, is considered a relatively stable, cycle-independent marker of the growing follicular pool [10]. Numerous studies have demonstrated strong associations between AMH levels and ovarian response to stimulation, oocyte yield, and ART outcomes [11]. In contrast, basal FSH is subject to substantial inter-cycle variability and may be less reliable as a standalone predictor [6,12]. Given that POF inherently represents a state of extremely diminished reserve, it is critical to assess whether AMH and FSH retain predictive value in this specific context and how they relate to actual embryological and clinical outcomes.

We hypothesized that women with POF would exhibit significantly poorer ovarian response, impaired embryological development, and reduced reproductive outcomes—including a higher risk of pregnancy loss—than age-matched women with tubal factor infertility and preserved ovarian reserve. Accordingly, this study aimed to comprehensively compare ovarian response, oocyte quality, embryological parameters, and clinical outcomes between women diagnosed with POF and age-matched women with tubal factor infertility undergoing IVF / ICSI, and to evaluate the independent predictive performance of AMH and basal FSH for ovarian response in this challenging population. By integrating hormonal markers with detailed IVF performance metrics in a large, age-matched cohort, this study seeks to provide clinically relevant data to support individualized counseling and evidence-based treatment planning for women with POF.

Materials and Methods

Study Design and Participants

This retrospective cohort study included 528 women who underwent IVF / ICSI at a tertiary clinic between January 2018 and December 2024. The study flow and participant stratification are detailed in Supplementary Figure S1. Participants were divided into two groups: the Premature Ovarian Failure (POF) group (n = 249) and an age-matched (± 1 year) control group with tubal factor infertility (n = 279).

POF was defined as age < 40 years, oligo / amenorrhea for ≥ 4 months, and elevated FSH (> 25 IU / L on two occasions) with low AMH (< 1.1 ng / mL). The control group consisted of women with regular cycles, normal FSH (< 10-12 IU / L), age-appropriate AMH, and confirmed tubal factor infertility.

Exclusion criteria included uterine anomalies, stage III–IV endometriosis, prior chemo/radiotherapy, severe male factor infertility, known chromosomal abnormalities, and incomplete data. Only the first autologous fresh cycle for each patient was analyzed; donor cycles were excluded.

Ovarian Stimulation and ART Procedures

Controlled ovarian stimulation (COS) was performed using either a GnRH antagonist or a long GnRH agonist protocol, with the former generally preferred for the POF group. Recombinant FSH and/or highly purified hMG were used for stimulation. Initial daily doses (225–300 IU) were individualized based on age, BMI, and ovarian reserve markers, with subsequent adjustments made via serial ultrasound and estradiol monitoring. Ovulation was triggered with hCG when at least two follicles reached ≥ 17 mm. Oocyte retrieval was performed 34–36 hours post-trigger. Fertilization was achieved via IVF or ICSI, and embryo transfer occurred on day 3 or day 5, followed by vaginal progesterone

for luteal phase support.

Data Collection and Outcome Measures

Baseline characteristics included age, BMI, and infertility duration. Early follicular phase (day 2–4) hormonal levels (AMH, FSH, LH, and E_2) were recorded. Embryological outcomes assessed were the total oocytes retrieved, MII oocyte rate, fertilization rate (2PN zygotes per inseminated oocytes), and blastocyst formation rate (blastocysts per fertilized oocytes).

Clinical outcomes were defined as biochemical pregnancy (β-hCG > 25 IU / L), clinical pregnancy (intrauterine sac with fetal heartbeat at 6–7 weeks), and live birth (delivery ≥ 24 weeks). Miscarriage was defined as a spontaneous loss before 24 weeks. Failure to achieve pregnancy was recorded as the absence of biochemical or clinical evidence of pregnancy.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics v25.0. Data normality was assessed with the Shapiro–Wilk test. Continuous variables are presented as mean ± SD and compared using the independent samples t-test or Mann–Whitney U test. Categorical variables were analyzed using the chi-square or Fisher's exact test. Multivariable linear regression, adjusted for age and BMI, was used to identify independent predictors of oocyte yield. Results are reported as unstandardized coefficients (B) with 95% CIs and R^2. Statistical significance was set at $p < 0.05$.

Ethical Approval

This study was approved by the Ethics Committee of Harran University Hospital (Date: 2025-03-24, No: HRÜ/25.06.18).

Results

Baseline Characteristics and Embryological Outcomes

A total of 528 women were included in the study: 249 in the POF group and 279 age-matched controls. The mean age was 31.83 ± 5.82 years in the POF group and 30.10 ± 5.91 years in the control group ($p = 0.052$). As expected, serum AMH levels were significantly lower in the POF group, while FSH, LH, and estradiol levels showed significant alterations compared with controls ($p < 0.001$ for all).

Embryological outcomes were significantly impaired in the POF group. The mean total number of oocytes retrieved was markedly lower (4.53 ± 2.96 vs. 9.18 ± 5.23; $p < 0.001$). Furthermore, the metaphase II (MII) oocyte rate, fertilization rate, and blastocyst formation rate were all significantly reduced in women with POF compared to the control group ($p < 0.001$). The mean number of day 3 embryos was also substantially lower in the POF cohort (2.08 ± 1.15 vs. 5.94 ± 2.57; $p < 0.001$). Detailed baseline and embryological data are summarized in Supplementary Table S1.

Clinical Outcomes

Clinical outcomes differed significantly between the groups (Supplementary Table S2). While biochemical pregnancy (8.4% vs. 11.8%; $p = 0.462$) and clinical pregnancy rates (16.9% vs. 28.0%; $p = 0.082$) did not reach statistical significance, the live birth rate was significantly lower in the POF group (10.8% vs. 22.6%; $p < 0.001$). Notably, the miscarriage rate per clinical pregnancy was significantly higher in the POF group (35.7% vs. 19.2%; $p = 0.047$). Failure to achieve pregnancy was more common in the POF cohort (57.8% vs. 32.3%; $p < 0.001$). The distribution of these clinical outcomes is illustrated in Supplementary Figure S2.

Predictors of Ovarian Response

Analysis of hormone levels by outcome confirmed that AMH levels were consistently lower and FSH levels higher in the POF group across all categories ($p < 0.001$). A multivariable linear regression model was constructed to evaluate predictors of total oocyte yield. AMH emerged as the only significant independent positive predictor ($B = 0.610$; 95% CI: 0.52–0.70; $p < 0.001$). In contrast, FSH, age, and weight were not significant independent predictors ($p > 0.35$). The regression analysis results are integrated into Supplementary Table S2.

Discussion

This study demonstrated that women with premature ovarian failure (POF), despite being age-matched to controls, exhibited significantly lower oocyte yield, impaired embryo development, and reduced reproductive outcomes during ART cycles. These findings confirm that diminished ovarian reserve, rather than chronological age, is the primary determinant of reproductive competence in this population.

Consistent with prior literature, anti-Müllerian hormone (AMH) emerged as a strong and independent predictor of ovarian response, whereas basal FSH did not retain significance in multivariable analysis. After adjusting for age and weight, AMH showed a robust positive association with total oocyte yield, supporting its role as a comprehensive marker of both follicular quantity and functional competence [13]. These results align with meta-analytic evidence showing that AMH outperforms FSH in predicting poor or excessive ovarian response during controlled ovarian stimulation, and with studies linking low AMH values to reduced fertilization, suboptimal embryo development, and poorer ART outcomes [14,15].

By selecting women with tubal factor infertility—who possess normal endocrine profiles—as controls, confounding related to other infertility etiologies was minimized. Although mean age did not differ significantly between groups, the POF cohort displayed markedly poorer embryological and clinical outcomes, reinforcing the concept that biological ovarian age may diverge substantially from chronological age [16].

A key and clinically important finding of this study is the significantly elevated miscarriage rate observed in POF patients who achieved clinical pregnancy. When calculated correctly per clinical pregnancy, the miscarriage rate in the POF group was nearly double that of controls (35.7% vs. 19.2%). This suggests that diminished ovarian reserve not only limits implantation potential but may also compromise post-implantation embryo viability. Elevated FSH levels and severely reduced ovarian reserve have been previously linked to meiotic errors and increased aneuploidy, providing a biologically plausible mechanism for the higher pregnancy loss observed in our cohort [17,18].

Despite these challenges, it is notable that a subset of women with POF successfully achieved live birth. Once pregnancy was established, the likelihood of carrying to term was comparable to that of controls, suggesting that viable and developmentally competent oocytes may still be present in selected POF patients.

This finding challenges the assumption of universal impairment in this group and underscores the importance of individualized treatment planning rather than automatic referral to donor-oocyte programs, particularly in regions where donation is restricted or culturally unacceptable [19].

Embryologically, the POF group exhibited significantly fewer cleavage-stage embryos and blastocysts, consistent with evidence that AMH correlates not only with oocyte yield but also with embryo development and quality. The reduced blastocyst formation rate may further reflect compromised oocyte competence, cumulative effects of accelerated follicular depletion, or reduced granulosa cell functionality [6,20].

Body mass index (BMI) was slightly higher in the POF group; however, BMI was not an independent predictor of ovarian response in our multivariable model. This suggests that ovarian reserve markers, particularly AMH, remain the dominant determinants of oocyte yield and developmental potential in this population [21].

Overall, these findings indicate that POF patients should not be categorically excluded from attempts at autologous IVF / ICSI. Rather, they should receive counseling that integrates both the markedly reduced likelihood of achieving pregnancy and the significantly increased risk of miscarriage [22]. Future research should aim to identify molecular, cytogenetic, or morphological predictors of embryo viability in low-oocyte-yield populations, which may improve patient stratification and optimize individualized treatment strategies.

Clinical Implications

AMH measurement should be incorporated early in the fertility evaluation of women with menstrual irregularities, unexplained infertility, or suspected ovarian insufficiency. Beyond conventional counseling regarding low pregnancy and live birth rates, clinicians should also inform patients of the significantly elevated risk of miscarriage due to likely compromised oocyte quality. Early interventions such as embryo banking and individualized stimulation regimens may help optimize outcomes, while donor oocyte strategies should be discussed when acceptable and feasible.

Limitations

This study is limited by its retrospective design and single-center nature, which may affect generalizability. Variations in stimulation protocols and unmeasured genetic contributors, such as FMR1 premutation status, were not assessed in subgroup analyses. Although the miscarriage finding reached statistical significance, the number of events was relatively small. Larger multicenter prospective studies, incorporating embryo ploidy testing, are warranted to further elucidate the mechanisms underlying compromised embryo viability in POF.

Conclusion

This study confirms that women with POF experience significantly diminished reproductive potential, characterized by lower oocyte yield, impaired embryo development, and reduced live birth rates compared to age-matched controls. A critical finding is the significantly higher miscarriage rate in the POF cohort (35.7% vs. 19.2%), suggesting compromised post-implantation embryo viability. AMH was identified as a strong, independent predictor of oocyte yield, reinforcing its role as the definitive marker for ovarian reserve assessment over FSH. These findings mandate individualized counseling for POF patients, specifically addressing the dual risks of low oocyte yield and increased pregnancy loss.

References

1. Ishizuka B. Current understanding of the etiology, symptomatology, and treatment options in premature ovarian insufficiency (POI). Front Endocrinol (Lausanne). 2021;12:626924. doi:10.3389/fendo.2021.626924.

2. Tsiligiannis S, Panay N, Stevenson J. Premature ovarian insufficiency and long-term health consequences. Curr Vasc Pharmacol. 2019;17(6):604-9. doi:10.2174/1570161117666190122101611.

3. Zhang W, Wang H, Deng C. Intermittent spontaneous ovulation in patients with premature ovarian failure: three case reports and review of literature. World J Clin Cases. 2023;11(31):7647-55. doi:10.12998/wjcc.v11.i31.7647.

4. Jin M, Yu Y, Huang H. An update on primary ovarian insufficiency. Sci China Life Sci. 2012;55(8):677-86. doi:10.1007/s11427-012-4355-2.

5. Sun B, Li L, Zhang Y, Wang F, Sun Y. Pregnancy outcomes in women with primary ovarian insufficiency in assisted reproductive technology therapy: a retrospective study. Front Endocrinol (Lausanne). 2024;15:1343803. doi:10.3389/fendo.2024.1343803.

6. Zeng Y, Zhang Y, Cao Q, et al. Independent predictors and thresholds of in vitro fertilization outcomes in patients with diminished ovarian reserve. Sci Rep. 2025;15(1):18875. doi:10.1038/s41598-025-01937-9.

7. Preisler L, Samara N, Kalma Y, et al. Stringent regulations of oocyte donation among Jewish women in Israel: characteristics and outcomes of the national oocyte donation program in one central IVF unit. J Relig Health. 2024;64(1):124-47. doi:10.1007/s10943-024-02200-7.

8. Morin SJ, Patounakis G, Juneau CR, Neal SA, Scott RT, Seli E. Diminished ovarian reserve and poor response to stimulation in patients <38 years old: a quantitative but not qualitative reduction in performance. Hum Reprod. 2018;33(8):1489-98. doi:10.1093/humrep/dey238.

9. Liu F, Ming H, Huang K, et al. Clinical pregnancy outcomes in young women with diminished ovarian reserve undergoing frozen embryo transfer: a comprehensive analysis with exploratory insights into endometrial aging. Front Endocrinol (Lausanne). 2025;16:1608200. doi:10.3389/fendo.2025.1608200.

10. Ufnal J, Wolff A, Morawska M, et al. Ovarian reserve: a critical indicator of female reproductive health. J Educ Health Sport. 2025;77:56916. doi:10.12775/jehs.2025.77.56916.

11. Huang J, Lin J, Gao H, et al. Anti-müllerian hormone for the prediction of ovarian response in progestin-primed ovarian stimulation protocol for IVF. Front Endocrinol. 2019;10:325. doi:10.3389/fendo.2019.00325.

12. Lensen S, Wilkinson J, Leijdekkers J, et al. Individualised gonadotropin dose selection using markers of ovarian reserve for women undergoing in vitro fertilisation plus intracytoplasmic sperm injection (IVF/ICSI). Cochrane Database Syst Rev. 2018;2(2):CD012693. doi:10.1002/14651858.cd012693.pub2.

13. Nardo L, Gelbaya T, Wilkinson H, et al. Circulating basal anti-Müllerian hormone levels as predictor of ovarian response in women undergoing ovarian stimulation for in vitro fertilization. Fertil Steril. 2009;92(5):1586-93. doi:10.1016/j.fertnstert.2008.08.127.

14. Salemi F, Jambarsang S, Kheirkhah A, et al. The best ovarian reserve marker to predict ovarian response following controlled ovarian hyperstimulation: a systematic review and meta-analysis. Syst Rev. 2024;13(1):303. doi:10.1186/s13643-024-02684-0.

15. Tsai H, Liao P, Li C, et al. High serum anti-Müllerian hormone concentrations have a negative impact on fertilization and embryo development rates. Reprod Biomed Online. 2021;44(1):171-6. doi:10.1016/j.rbmo.2021.08.016.

16. Li S, Hu L, Zhang C. Effect of chronological age of patients with diminished ovarian reserve on in vitro fertilization outcome. J Obstet Gynaecol. 2021;42(4):654-7. doi:10.1080/01443615.2021.1922996.

17. Busnelli A, Somigliana E, Cirillo F, Levi-Setti P. Is diminished ovarian reserve a risk factor for miscarriage? Results of a systematic review and meta-analysis. Hum Reprod Update. 2021;27(6):973-88. doi:10.1093/humupd/dmab018.

18. Sun L, Zhang C, Yin B, et al. Low anti-müllerian hormone levels increased early pregnancy loss rate in patients undergoing frozen-thawed euploid single blastocyst transfer: a retrospective cohort study. Reprod Biol Endocrinol. 2025;23(1):112. doi:10.1186/s12958-025-01445-5.

19. Zhu X, Ye J, Fu Y. Premature ovarian insufficiency patients with viable embryos derived from autologous oocytes through repeated oocyte retrievals could obtain reasonable cumulative pregnancy outcomes following frozen-embryo transfer. Ann Transl Med. 2021;9(7):539. doi:10.21037/atm-20-1112.

20. Carnesi E, Castellano S, Albani E, et al. Diminished ovarian reserve is associated to euploidy rate: a single center study. Front Endocrinol (Lausanne). 2025;15:1535776. doi:10.3389/fendo.2024.1535776.

21. Guo Z, Ishizuka B, Itakura A, Kawamura K. A highly sensitive Anti-Müllerian hormone test as a promising tool for follicle growth prediction in primary ovarian insufficiency patients. Sci Rep. 2025;15(1):14005. doi:10.1038/s41598-025-98808-0.

22. Lebovitz O, Haas J, Mor N, et al. Predicting IVF outcome in poor ovarian responders. BMC Womens Health. 2022;22(1):395. doi:10.1186/s12905-022-01964-y.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content, including study design, data collection, analysis and interpretation, writing, and some of the main line, or all of the preparation and scientific review of the contents, and approval of the final version of the article.

Animal and Human Rights Statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Data Availability Statement
The datasets used and/or analyzed during the current study are not publicly available due to patient privacy reasons but are available from the corresponding author on reasonable request.

Funding: *None*

Conflict of Interest
The authors declare that there is no conflict of interest.

Ethics Declarations
This study was approved by the Ethics Committee of Harran University Hospital (Date: 2025-03-24, No: HRÜ/25.06.18)

How to cite this article:
Mehmet İncebıyık, Muhammet Erdal Sak*. Autologous ART outcomes and the predictive value of AMH in women with premature ovarian failure. Ann Clin Anal Med 2026;17(2):168-172*