BEYOND NUMBERS: UNRAVELING THE COMPLEX RELATIONSHIP BETWEEN AMH AND AFC LEVELS AND EMBRYO QUALITY

Authors

Allison Eubanks[1], Kerry Flannagan[2], Kyle Le[2], Amalia Namath[1], Anupama Rambhatla[3], Jensen Reckhow[4], Atoosa Ghofranian[4], Jerry Wang[2], Kate Devine[2], Matthew Connell[2], Phillip Romanski[4], Micah Hill[1]

1. Walter Reed National Military Medical Center; National Institutes of Health, National Institution of Child Health and Human Development, Bethesda, Maryland
2. Shady Grove Fertility, Rockville, Maryland; Shady Grove Fertility, Washington, D.C.
3. Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Stanford University School of Medicine, Palo Alto, California.
4. Division of Reproductive Endocrinology and Infertility, Department of Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine At Mount Sinai, Reproductive Medicine Associates of New York, New York, NY, USA

Background

Anti-Müllerian hormone (AMH) and antral follicle count (AFC) are traditionally used as indicators of ovarian reserve in women undergoing assisted reproductive technology (ART). While AMH and AFC are reliable markers for assessing oocyte quantity, their utility in predicting embryo quality, particularly euploidy rates, remains controversial.

Objective

To evaluate the association between AMH and AFC levels and embryo euploidy, independent of age and other confounding factors, in patients undergoing in vitro fertilization (IVF) with preimplantation genetic testing for aneuploidy (PGT-A).

Materials and Methods

This retrospective cohort study used data from a large national network of infertility clinics across the United States, including 11,473 women who underwent 13,451 IVF cycles with PGT-A between October 2016 and August 2024. Patients had documented AMH or AFC values within six months of oocyte retrieval. Cycles using donor oocytes or with known genetic disorders were excluded. AMH and AFC were grouped into three clinically relevant categories based on Bologna criteria for diminished ovarian reserve (DOR): AMH <1.1, 1.1-4.0, and >4.0 ng/mL, and AFC <7, 7-16, and >16. Modified Poisson models fitted with generalized estimating equations (GEE), were used to determine adjusted relative risks (RR) for embryo euploidy. Models were adjusted *a priori* for maternal age at retrieval, body mass index (BMI), and diagnosis of polycystic ovary syndrome (PCOS).

Results

Euploidy was similar in each AMH category (56.9%, 54.0%, and 55.8% among cycles with <1.1, 1.1-4.0, and >4.0 ng/mL, respectively) and in each AFC category (56.3%, 54.8%, and 54.9% among cycles with <7, 7-16, and >16, respectively). After adjustment and compared to cycles with AMH 1.1-4.0 ng/mL, euploidy was modestly but statistically significantly higher in the

lowest AMH category (RR, AMH <1.1 vs. 1.1-4.0 ng/mL: 1.08; 95% CI: 1.05, 1.11) and similar in the highest AMH category (RR, AMH >4.0 vs. 1.1-4.0 ng/mL: 1.00; 95% CI: 0.98, 1.02). After adjustment, euploidy was similar among cycles with AFC <7 and 7-16 (RR, AFC <7 vs. 7-16: 1.00; 95% CI: 0.98, 1.03) and slightly but significantly lower among cycles with AFC >16 (RR, AFC >16 vs. 7-16: 0.96; 95% CI: 0.95, 0.98). AMH and AFC levels were not significantly associated with live birth, clinical pregnancy, or implantation outcomes.

Conclusions

Contrary to recent publications,[1,2] lower AMH and AFC levels were not associated with a clinically significant decrease in embryo euploidy or live birth outcomes. These data are reassuring that lower AMH levels are not associated with an increased risk of aneuploidy. These findings suggest that AMH and AFC, while useful for assessing ovarian reserve, may have limited value in predicting embryo quality when used independently of other factors.

Financial Support

This research was not financially supported.

References

1. Jaswa EG, McCulloch CE, Simbulan R, Cedars MI, Rosen MP. Diminished ovarian reserve is associated with reduced euploid rates via preimplantation genetic testing for aneuploidy independently from age: evidence for concomitant reduction in oocyte quality with quantity. Fertil Steril. 2021 Apr;115(4):966-973. doi: 10.1016/j.fertnstert.2020.10.051. Epub 2021 Feb 12. PMID: 33583594.
2. Li HJ, Seifer DB, Tal R. AMH independently predicts aneuploidy but not live birth per transfer in IVF PGT-A cycles. Reprod Biol Endocrinol. 2023 Feb 4;21(1):19. doi: 10.1186/s12958-023-01066-w. PMID: 36739415; PMCID: PMC9898926.
3. Franasiak JM, Forman EJ, Hong KH, Werner MD, Upham KM, Treff NR, Scott RT Jr. Aneuploidy across individual chromosomes at the embryonic level in trophectoderm biopsies: changes with patient age and chromosome structure. *J Assist Reprod Genet.* 2014;31(11):1501-1509. doi:10.1007/s10815-014-0333-x
4. Venetis CA, Kolibianakis EM, Papanikolaou EG, Bontis J, Devroey P. Is AMH a significant predictor of oocyte quality and pregnancy outcome in IVF? Results from a meta-analysis. *Hum Reprod Update.* 2013;19(5):483-502. doi:10.1093/humupd/dmt010
5. Stovezky YR, Romanski PA, Bortoletto P, Spandorfer SD. Antimüllerian hormone is not associated with embryo ploidy in patients with and without infertility undergoing in vitro fertilization with preimplantation genetic testing. Fertil Steril. 2023 Mar;119(3):444-453. doi: 10.1016/j.fertnstert.2022.11.018. Epub 2022 Nov 21. PMID: 36423663.
6. 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**:1489–1498. doi: 10.1093/humrep/dey238.

Table 1: Demographics

Characteristic	Total Population	AMH <1.1 ng/mL (DOR)	AMH 1.1-4.0 ng/mL (normal)	AMH >4.0 ng/mL (high)
Number of Patients	11473	1971	5945	3504
Number of IVF cycles	13451	2291	6884	3960
Age (years), mean (SD)	36.4 (3.7)	37.9 (3.3)	36.7 (3.5)	35.1 (3.8)
BMI (kg/m²), mean (SD)	26.7 (5.5)	26.9 (5.6)	26.6 (5.5)	26.7 (5.6)
Race/Ethnicity, N (%)				
Asian	1813 (13.5)	253 (11)	962 (14)	566 (14.3)
Black/African American	1254 (9.3)	218 (9.5)	629 (9.1)	385 (9.7)
Hispanic/Latino	731 (5.4)	167 (7.3)	359 (5.2)	186 (4.7)
White	6672 (49.6)	1143 (49.9)	3450 (50.1)	1932 (48.8)
Other race or multiracial	778 (5.8)	143 (6.2)	395 (5.7)	227 (5.7)
Unknown	2203 (16.4)	367 (16)	1089 (15.8)	664 (16.8)
PCOS Diagnosis, N (%)	1655 (12.7)	43 (1.9)	460 (6.9)	1101 (28.6)
Smoking History, N (%)	159 (1.6)	23 (1.4)	86 (1.7)	45 (1.6)
Nulliparious, N (%)	9426 (70.1)	1538 (67.1)	4794 (69.6)	2872 (72.5)
AMH, median (IQR)	2.6 (1.4, 4.6)	0.7 (0.5, 0.9)	2.2 (1.6, 3)	6.1 (4.9, 8.4)
Baseline AFC, median (IQR)	16 (10, 23)	10 (7, 13)	15 (10, 20)	25 (17, 34)
Number of FET cycles per patient, m	1.4 (0.8)	1.2 (0.5)	1.4 (0.7)	1.6 (0.9)

Table 2: AMH vs Euploidy

		Euploid embryos		Total Biopsied Embryos				
Exposure	**N (Cycles)**	**N, total**	**N, median (IQR) per cycle**	**N, total**	**N, median (IQR) per cycle**	**Euploidy Rate (%)**	**Adjusted RR (95% CI)*, euploidy**	**Adjusted euploidy rate (95% CI)****
DOR<1.1 ng/mL	2291	4914	2 (1, 3)	10040	4 (2, 6)	56.9 (28.5)	1.08 (1.05, 1.11)	54.6 (53.5, 55.7)
Normal 1.1-4.0 ng/mL	6884	20224	2 (1, 4)	41733	5 (3, 8)	54 (26.2)	Ref	50.6 (50.1, 51.2)
High >4.0 ng/mL	3960	17242	4 (2, 6)	32259	7 (4, 11)	55.8 (23.1)	1 (0.98, 1.02)	50.7 (49.9, 51.4)
P for trend							0.004670894	