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# FACTORS ASSOCIATED WITH LOW OR HIGH ANEUPLOIDY RATES AT THE EXTREMES OF AGE

Devora Aharon, MD[1], Kelsey Martin, MD[1], Dmitry Gounko, MA[2], Joseph A. Lee, BA[2], Erkan Buyuk, MD[2], Tanmoy Mukherjee, MD[2], Alan B Copperman, MD[2] and Rachel S. Gerber, MD[2]

1. Icahn School of Medicine at Mount Sinai, New York, NY
2. Reproductive Medicine Associates of New York, New York, NY

**OBJECTIVE:**
Evaluating patients who are outliers in their rate of embryonic aneuploidy may improve our understanding of drivers of success and failure in assisted reproduction. Our study assesses young patients who produce a high percentage of aneuploid embryos and older patients with low percentages of aneuploid embryos. We aim to identify factors associated with aneuploidy rates above or below age-expected values.

**MATERIALS AND METHODS:**
This study included patients who underwent controlled ovarian stimulation cycles with preimplantation genetic testing for aneuploidy (PGT-A) from September 2016-December 2019 who had ≥3 embryos biopsied. The mean aneuploidy rates (AR) and distribution among patients <35 years old (yo) and in those >40yo were determined. In patients <35yo, those with AR greater than the 90$^{th}$ percentile were compared to those with AR below the 90$^{th}$ percentile. Among patients >40yo, those with AR <10$^{th}$ percentile were compared to those with AR above the 10$^{th}$ percentile. Baseline demographics and cycle characteristics were compared among the groups using Chi-square, Student's t-test, and multivariable logistic regression.

**RESULTS:**
A total of 1298 cycles in patients <35yo and 562 cycles in patients >40yo were identified and included in the study. In the <35yo cohort, the mean AR was 34.9%, and >90%ile corresponded to a rate of 66.7% and included 86 patients. The mean AR in the >40yo cohort was 33.3%. The <10%ile corresponded to a rate of 70.2% and included 74 patients. In patients <35yo, those with >90%ile AR were similar in age to patients <90%ile (32.2±3.5 vs. 31.9±2.6, p=.19) but had a significantly lower serum AMH (3.22±2.40 vs. 4.80±4.81, p=.008). BMI, BAFC, day 3 FSH, male partner age, male factor diagnosis, and gravidity were similar between the groups, while patients >90%ile had lower parity (0.11±0.36 vs. 0.27±0.66, p=.048). Cycle characteristics including stimulation protocol and duration and estradiol and progesterone at surge were similar. Patients with >90%ile AR had fewer eggs (17.4±7.4 vs. 20.5±9.9, p=.008) and mature oocytes (MII) (12.9±6.1 vs. 16.1±8.0, p<.0001) retrieved but similar MII/oocyte ratio (0.76±0.17 vs. 0.80±0.14, p=.08). Controlling for age, BMI, parity, and eggs retrieved revealed that lower AMH was significantly associated with AR >90%ile (aOR=1.23, 95% CI 1.02-1.25, p=.02). Among women >40yo, those <10%ile AR were significantly younger than those >10%ile (41.0±0.9 vs. 41.8±1.4, p<.0001). No differences were seen in any of the other variables assessed.

**CONCLUSIONS:**
Young patients with lower AMH levels demonstrated an increased AR, suggesting evidence of both quantitative and qualitative aging in this population. However, even those <35yo with elevated AR consisted of good prognosis patients in terms of ovarian reserve testing and cycle outcome. In

patients >40yo, aneuploidy rate is related to age alone, most likely due to the high incidence of meiotic errors in older women.

**IMPACT STATEMENT:**
This data confirms that in all age groups the strongest predictor of AR is female age, and only genetic testing of embryos can confirm patient-specific risk for aneuploidy.

**REFERENCES:**

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