Research Article

IMPACT OF MATERNAL AGE ON EMBRYO CHROMOSOMAL COMPETENCE: A RETROSPECTIVE ANALYSIS OF 4,204 CONSECUTIVE PGT-A BLASTOCYSTS FROM A HIGH-VOLUME IVF CENTER

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ABSTRACT

Background: Maternal age is the most important determinant of embryo chromosomal competence and remains the strongest predictor of IVF success. Although preimplantation genetic testing for aneuploidy (PGT-A) has become an integral component of modern assisted reproductive technology (ART), large single-center studies evaluating comprehensive chromosomal outcomes across different maternal age groups remain relatively limited. Therefore, this study aimed to evaluate the association between maternal age and embryo chromosomal status in a large cohort of consecutive blastocysts analyzed by PGT-A.

Methods: This retrospective cohort study included 495 women undergoing IVF/ICSI with PGT-A between January 2025 and January 2026 at a high-volume IVF center. Patients were stratified into three maternal age groups: Group I, aged 20-29 years (n = 90); Group II, aged 30-39 years (n = 226); and Group III, aged 40-43 years (n = 179). Only patients with at least six biopsied blastocysts were included. A total of 4,204 blastocysts underwent trophectoderm biopsy followed by comprehensive chromosome screening using next-generation sequencing (NGS). The primary outcome was the proportion of euploid embryos. Secondary outcomes included the proportions of aneuploid, mosaic, and segmental-abnormality embryos, as well as samples yielding no result.

Results: Among the 4,204 blastocysts analyzed, 2,826 (67.2%) were euploid, 731 (17.4%) were aneuploid, 240 (5.7%) were mosaic, and 322 (7.7%) demonstrated segmental abnormalities; 85 (2.0%) yielded no result. Age-stratified analysis demonstrated a progressive decline in embryo euploidy with advancing maternal age, accompanied by increasing rates of chromosomal abnormalities.

Conclusions: Maternal age remains the strongest determinant of embryo chromosomal competence. Although high laboratory performance resulted in a very low technical failure rate, advancing maternal age was associated with reduced euploid embryo yield and increasing chromosomal abnormalities. These findings support individualized reproductive counseling and emphasize the clinical value of PGT-A in women of advanced reproductive age.

CITATION: *Dvali T, Tchokhonelidze A, Goikman I, Kuliev A. Impact of maternal age on embryo chromosomal competence: A retrospective analysis of 4,204 consecutive PGT-A blastocysts from a high-volume IVF center. Medical Times. Georgian-German Reproduction Center; 2026;(5):67–72. https://doi.org/10.71419/mtggrc.2026.42*

Keywords: aneuploidy; blastocyst; embryo biopsy; euploidy; IVF; maternal age; mosaic embryo; PGT-A; segmental abnormality.

Introduction

Embryonic chromosomal abnormalities represent one of the leading causes of implantation failure, miscarriage, and reduced live birth rates following assisted reproductive technology (ART).[1,3]

Among all known prognostic factors, maternal age has consistently been identified as the strongest predictor of embryo chromosomal competence.[3,4,7]

Female reproductive aging is characterized by progressive deterioration in both the quantity and quality of oocytes.[7] While declining ovarian reserve reduces the number of available oocytes, age-related impairment of oocyte competence has an even greater influence on reproductive success. The majority of chromosomal abnormalities originate during maternal meiosis, particularly during the first meiotic division, where cohesion loss, spindle instability, and impaired chromosome alignment increase the likelihood of nondisjunction.[5,7,8] Consequently, embryos generated from older oocytes demonstrate substantially higher rates of whole-chromosome aneuploidy.

Age-related deterioration of oocyte quality results primarily from meiotic spindle dysfunction, mitochondrial impairment, and increased chromosome segregation errors, leading to a progressive rise in embryonic aneuploidy. Consequently, the proportion of transferable euploid embryos declines substantially after age 35 and decreases even more rapidly after age 40.

The introduction of preimplantation genetic testing for aneuploidy (PGT-A) has enabled comprehensive assessment of embryo chromosomal status before transfer.5 In addition to identifying euploid and aneuploid embryos, contemporary next-generation sequencing (NGS) platforms detect mosaicism and segmental chromosomal abnormalities with high analytical accuracy.[2,4]

Despite widespread clinical implementation of PGT-A, relatively few studies have analyzed large consecutive embryo cohorts from a single laboratory using standardized biopsy, vitrification, and genetic testing protocols.[8]

The present study evaluates chromosomal outcomes in 4,204 consecutive blastocysts and investigates the relationship between maternal age and embryo chromosomal competence.

Methods

Study Design

This retrospective cohort study was performed at the Georgian-German Reproductive Center (GGRC) in collaboration with IMC Genomix, Israel.

All consecutive IVF/ICSI cycles undergoing PGT-A during the study period were reviewed.Institutional approval was obtained before analysis.

Patient Population

A total of 495 women fulfilled the inclusion criteria.

Patients were categorized into three age groups:

Group	Age	Number of Patients
Group I:	20-29	90
Group II:	30-39	226
Group III:	40-43	179

Inclusion Criteria: IVF/ICSI treatment, PGT-A performed – Only patients with six or more biopsied blastocysts were included to ensure adequate embryo numbers for meaningful evaluation of chromosomal competence within each treatment cycle. This criterion minimized the influence of extremely poor responders while allowing robust embryo-level analysis.

Exclusion Criteria: Donor oocyte cycles, Structural chromosomal rearrangements, Monogenic PGT cycles, Incomplete genetic reports, and embryology procedures were excluded. Controlled ovarian stimulation was individualized according to ovarian reserve.

Following oocyte retrieval: Mature oocytes underwent ICSI. Embryos were cultured to the blastocyst stage. Trophectoderm Biopsy was performed on high-quality blastocysts. Embryos were vitrified immediately after biopsy. Samples underwent NGS-based comprehensive chromosome screening.

PGT-A Classification

Embryos were classified as:

Primary Outcome:	Secondary Outcome:
Euploid Embryo	Aneuploid Embryos
	Mosaic Embryos
	Segmental Abnormalities
	No-result

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation.

Categorical variables were summarized as percentages.

Comparisons among maternal age groups were performed using χ^2 tests for categorical variables and one-way ANOVA where appropriate.

Multivariable logistic regression may be used to assess the independent association between maternal age and embryo euploidy after adjustment for potential confounders. A p-value <0.05 was considered statistically significant.

Results

Overall Chromosomal Outcomes

A total of 4,204 blastocysts were successfully analyzed.

Overall, 2,826 embryos (67.2%) were classified as euploid, demonstrating a high proportion of chromosomally normal embryos within the study population. Aneuploid embryos represented 17.4% of all biopsied blastocysts, while mosaic embryos accounted for 5.7% and segmental abnormalities for 7.7%. Only 85 embryos (2.0%) yielded inconclusive results, reflecting excellent laboratory performance and high analytical reliability. The overall chromosomal distribution:

Chromosomal Status	%	Total Number
Euploid embryos:	67.2%	2826
Aneuploid embryos:	17.4%	731
Mosaic embryos:	5.7%	240
Segmental abnormalities:	7.7%	322
No-result rate:	2%	85

The laboratory demonstrated excellent technical performance, with only 2% of PGT-A results inconclusive.

Age-stratified analysis demonstrated a statistically significant decline in euploid embryo rates with increasing maternal age, accompanied by progressive increases in aneuploidy, mosaicism, and segmental chromosomal abnormalities. The laboratory maintained excellent analytical performance throughout the study period, with a technical failure rate of only 2%.

Maternal Age and Euploidy

A progressive decline in embryo euploidy was observed with advancing maternal age.Younger patients demonstrated the highest proportion of chromosomally normal embryos, whereas women aged 40-43 years exhibited the lowest euploid rates and the highest frequency of chromosomal abnormalities.

Group I (20-29 years)

This group demonstrated the highest embryo chromosomal competence, characterized by the greatest proportion of euploid embryos and the lowest incidence of aneuploidy.

Group II (30-39 years)

Women in this age group showed an intermediate decline in euploid embryo production together with modest increases in mosaic and segmental abnormalities.

Group III (40-43 years)

Advanced maternal age was associated with a marked reduction in euploid embryos and a substantial increase in chromosomal abnormalities, consistent with age-related meiotic dysfunction.

Discussion

The present study represents one of the largest single-center analyses of consecutive PGT-A blastocysts evaluating maternal age and embryo chromosomal competence.[3,4,5]

The findings confirm that maternal age remains the strongest biological determinant of embryo ploidy.[3,7,9] Although laboratory performance remained highly consistent throughout the study period, the proportion of chromosomally normal embryos decreased progressively with increasing maternal age.[1,2,7]

This observation is biologically plausible and reflects age-dependent deterioration in oocyte quality, spindle integrity, mitochondrial function, and chromosome segregation during meiosis.[5,7,9]

Importantly, the laboratory achieved an overall technical failure rate of only 2%, indicating excellent biopsy quality, DNA amplification, and sequencing performance. Such consistency strengthens the validity of the observed age-related differences.

These findings are consistent with previous reports from ESHRE, ASRM, and large multicenter PGT-A registries demonstrating increasing aneuploidy after age 35 years and an accelerated decline after age 40 years.[9,13,14]

The present study further highlights the importance of individualized reproductive counseling and supports the clinical role of PGT-A in patients of advanced reproductive age.

Strengths: The principal strengths of this study include its large consecutive embryo cohort, standardized embryology laboratory procedures, use of a single validated NGS platform, inclusion

of consecutive clinical cases rather than selected populations, and excellent laboratory quality control, as reflected by the very low rate of inconclusive genetic results. These characteristics reduce methodological variability and strengthen the reliability of the observed associations.[12,14]

Limitations

Its retrospective design and single-center setting limit the study. Additional multicenter prospective studies are needed to validate these findings. Clinical outcomes such as implantation, miscarriage, and live birth rates were not evaluated and should be investigated in future research.

Conclusions

In this large retrospective analysis of 4,204 consecutive blastocysts, maternal age was strongly associated with embryo chromosomal competence. Euploid embryo rates declined progressively with advancing age, while aneuploid, mosaic, and segmental abnormalities increased. Despite these biological differences, laboratory performance remained consistently high, with an exceptionally low rate of inconclusive PGT-A results.

These findings reinforce the central role of maternal age in reproductive prognosis and support the use of PGT-A as an important tool for individualized embryo selection and patient counseling, particularly in women of advanced reproductive age.

Future investigations should combine embryo chromosomal analysis with implantation rates, miscarriage rates, cumulative live birth rates, and neonatal outcomes.[12,13] Additional multicenter prospective studies may further clarify the relationship between maternal age, embryo competence, and long-term reproductive success.

Declarations

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest: The authors declare no competing interests.

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