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Research Article

Assessment of Chromosomal Aneuploidy in PGT-A Embryos

G Shiva Krishna[1], Sanjeev Krishna Gupta[2]

[1]Senior Embryologist, Laxmi Narasimha Hospital, Warangal, India.
[2]Professor, OPJS University, Rajasthan, India.
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I N F O

Corresponding Author:
G Shiva Krishna, Laxmi Narasimha Hospital, Warangal, India.
E-mail Id:
shiva.g5621@gmail.com
Orcid Id:
https://orcid.org/0000-0003-2946-6632
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A B S T R A C T

Introduction: Preimplantation genetic testing is a procedure to evaluate genetically normal embryos and take them for embryo transfer. It helps in identifying chromosomal aneuploidies, mosaicism, and euploid embryos.

Aim: To assess chromosomal aneuploidy through PGT-A in IVF embryos.

Methods: A retrospective study was done from January 2021 to June 2022. 55 blastocysts were assessed for PGT-A through Comparative Genomic Hybridisation (CGH).

Results: Among the 55 blastocysts included in the study, 19 embryos showed euploidy and 7 embryos showed multiple aneuploidies. Autosomes were normal but sex chromosomes were abnormal in 3 embryos. Multiple mosaic gain/ loss was reported in 4 embryos. Sex chromosomes abnormality was seen in 8 embryos.

Conclusion: 19 embryos showed euploidy. More than half of the embryos showed aneuploidy. Mosaicism seems to be a more common phenomenon in IVF embryos as compared to other kinds of aneuploidy like syndromes, triploidy, monosomy, and other genetic abnormalities. Sex chromosome abnormality was reported in 8 embryos.

Keywords: PGT-A, Embryo Biopsy, Aneuploidy, Mosaicism

Introduction

Preimplantation genetic testing for aneuploidy PGT-A has been widely applied today in IVF (in vitro fertilisation) units to select the healthy euploid embryo for transfer and to enhance clinical outcomes such as embryo implantation, clinical pregnancy, and live birth rates. Traditionally, morphology-based grading had been the primary technique used in IVF to assess and select the most competent embryos for transfer. Technologies have emerged in the fields of genomics, transcriptomics, proteomics, metabolomics, and time-lapse imaging to try to assist in the selection of the best embryos. However, the focus has been on the analysis of 24-chromosome copy number for evaluation and transfer of only diagnosed euploid embryos, also known as preimplantation genetic testing for aneuploidy (PGT-A). PGT-A is a test done on embryos obtained through IVF. It is done for patients who have had previous miscarriages, advanced maternal age, and previous child anomalies. It helps in identifying chromosomal aneuploidies, mosaicism, and euploid embryos.[1,2] Chromosomal mosaicism has become a common phenomenon, and high-level mosaicism has shown lower implantation rates.[3-5]

Objective

To assess chromosomal aneuploidy through PGT-A in IVF embryos.

Materials and Methods

A retrospective study was conducted from January 2021 to June 2022 at Laxmi Narasimha Fertility Centre, Hanamkonda. We evaluated the associations of aneuploidy and mosaicism with maternal age and the chromosome abnormalities present in individual chromosomes. 12 Indian couples underwent IVF and opted for PGT-A. Female patients between 35 and 39 years of age and male patients between 38 and 42 years of age were included in the study. The mean age of female patients was 37 ± 1 years and most of them had a previous miscarriage and the mean age of male patients was 40 ± 2 years (Table 1). Male patients with severe oligoasthenoteratozoospermia and female patients aged more than 39 years and cases in which less than 5 oocytes were retrieved during the IVF procedure were excluded from the study. 9 patients had normozoospermia and 3 patients had oligozoospermia. Ovarian stimulation was done with antagonist protocol, human chorionic gonadotropin (HCG) trigger was given and ovum pick-up was done after 34 hours. Embryos were cultured in a single-step medium (Vitrolife, 6% CO_2). Morphological assessment and embryo biopsy were done on days 5 and 6 based on morphological criteria. 55 blastocysts were obtained and subjected to embryo biopsy and PGT-A analysis by Comparative Genomic Hybridisation (CGH-Agilent technologies). 5-10 cells were removed from the trophectoderm of the embryo and were sent for PGT-A analysis.

Ethical approval for the study was taken from the Institutional Ethics Committee (ECR/1301/Inst/TG/2019) and informed consent was obtained from the participants.

Table 1.Demographics (Age and Gender) of the Patients

	Gender	Mean Age (Years)
1.	Female	37 ± 1
2.	Male	40 ± 2

Results

In our study, 55 embryos from 12 patients were analysed for PGT-A and 4 embryos were excluded from the study due to failed amplification. 19 embryos showed euploid with no aneuploidy. 7 embryos showed multiple aneuploidies. Autosomes were normal but sex chromosomes were abnormal in 3 embryos. Multiple mosaic gain/ loss was reported in 4 embryos, and sex chromosome abnormality was shown in 8 embryos. Chromosomes 19 and 8 showed mosaicism in 4 embryos which seemed to be the most affected chromosomes among all other chromosomes (Table 2).

Table 2.Abnormality/ Aneuploidy of the Chromosome

Embryo Number	Abnormality/ Aneuploidy	Chromosome Number																						
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	Sex Chrm0
E1																		SG		SG				SG
E2	No aneuploidy																							
E3	Multiple aneuploidy																							
E4	No aneuploidy																							
E5		M							M	M					M				M					
E6							SG																	SG
E7	Autosomes normal																							ABN
E8									M															
E9	No aneuploidy																							
E10	No aneuploidy																							
E11	No aneuploidy																							
E12	No aneuploidy																							

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E13	Multiple aneuploidy																						
E14	No aneuploidy																						
E15	No aneuploidy																						
E16	Multiple aneuploidy																						
E17	No aneuploidy																						
E18	No aneuploidy																						
E19	Autosomes normal																						ABN
E20																			SL				
E21												ML											
E22		ML									SL							SL					
E23	Multiple mosaic gains and losses								SL														
E24																	SL			SL			
E25							ML																
E26																		SG					SG
E27	Multiple aneuploidy																						
E28	No aneuploidy																						
E29																			AN				
E30		ML																					
E31	No aneuploidy																						
E32	No aneuploidy																						
E33	No aneuploidy																						
E34																	MA						
E35	Multiple aneuploidy																						
E36	Multiple aneuploidy																						
E37	Multiple mosaic gains and losses																						
E38	Multiple mosaic gains and losses																						
E39	No aneuploidy																						
E40	No aneuploidy																						
E41						MSG/ L								ML/ G	ML/ G	ML/ G	ML/ G						ML/ G	

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E42		MSG						MSG	MSG					MSG	MSG						MSG			MSG
E43		MSG	MSG			MSG				MSG					MSG		MSG							MSG
E44	Failed amplification																							
E45	Failed amplification																							
E46									DEL					DEL										
E47	Multiple aneuploidy																							
E48	Multiple segmental gains/ loss																							
E49	No aneuploidy																							
E50	No aneuploidy																							
E51	autosomes normal																							
E52	No aneuploidy																							ABN
E53													MG											
E54	Failed amplification																							
E55	Failed amplification																							

Table 3.Number of Embryos showing a Particular Kind of Abnormality

S. No.	Abnormality	No. of Embryos
1.	Euploidy	19
2.	Multiple aneuploidy	7
3.	Autosomes normal, but sex chromosomes abnormal	3
4.	Multiple mosaic gain/ loss	4

Discussion

55 embryos were subjected to PGT-A analysis. 4 embryos were excluded from the study due to failed amplification. 37% of the embryos showed euploidy (Table 3). This is similar to a study done by Lang-liu et al. which showed that 36% of the embryos were euploid. PGT-A by Lang-liu et al. showed that abnormalities of chromosomes 22, 21, 16, and 15 were the most frequently observed, but in our study, chromosomes 8 and 22 were the most frequently involved. 15% of the embryos showed sex chromosomes aneuploidy which is a concern as abnormality in sex chromosomes leads to infertility. 19 embryos showed euploidy which implied that more than half of the embryos are aneuploidy. 10 embryos were reported with mosaicism. Mosaicism contributes to 1/3rd of the abnormal embryos.

Mosaicism is defined as two or more cell populations with different chromosomal complements being present within the same embryo. It was first identified as a common phenomenon in cleavage-stage embryos, although the exact cause of mosaicism in embryos is unknown. Embryonic mosaicism is believed to be a confounding factor when trying to interpret PGT-A results, as mosaic embryos are currently categorised as either aneuploid mosaic or diploid-aneuploid mosaic, the latter of which is influenced more by early cleavage of the embryo when chromosomal segregation occurs. Trophectoderm biopsy, in which 4-10

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cells are removed from the embryo for chromosomal analysis, has provided several advantages over cleavage-stage biopsy as it includes more numbers of cells than cleavage stage, including the purported improved detection of mosaicism. Numerous studies have demonstrated the utility of Array Comparative Genomic Hybridisation (aCGH) for use in PGT-A. However, the efficiency of aCGH to detect mosaicism is dependent on the percentage of aneuploid cells in the trophectoderm biopsy.

Assessment of PGT-A analysis of embryos showed that only 19 embryos were normal and 32 embryos showed aneuploidy. Aneuploidy has been reported mostly in the form of segmental loss/ gain of chromosomes and mosaicism gain/ loss of chromosomes in our study by Comparative Genomic Hybridisation (CGH). More than half of the embryos were abnormal in our study. Apart from our study, there are many studies which report more than half of the IVF embryos to be abnormal. Complex mosaicism was reported in 4 embryos.[1,3]

Limitations

The limitations of the study include less sample size and the need for a larger study. In addition, it includes the inability to detect balanced chromosomes, including translocations, inversions and polyploidy, and DNA sequence changes (point mutations) or other types of mutations such as epigenetic changes.

Conclusion

Assessment of PGT-A analysis of embryos showed that more than half of the embryos were abnormal and 37% of the embryos showed euploidy in our study. Complex mosaicism has been reported in 4 embryos. Our results showed that fewer than half of the embryos in this cohort (mean maternal age - 39 years) were euploid. An association of aneuploidy with maternal age is also seen in this study. Embryonic mosaicism is better detected in trophectoderm biopsy than cleavage stage biopsy due to the availability of more cells (4-10 cells) for analysis.

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Conflict of Interest: None

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