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Preimplantation Genetic Screening and Its Differential Impact on Live Birth Outcomes Across Heterogeneous IVF Populations

Anindita Kundu (Bio-Technology) Sardar Patel University, Balaghat
Dr. Priyanka Sachan, Associate Professor, Sardar Patel University, Balaghat (M.P.)
Email: sachan.priyanka.1988@gmail.com

Abstract

PGT-A is a new application of preimplantation genetic testing that has become a significant development in the assisted reproductive technologies to advance the embryo selection and augment the in vitro fertilization (IVF) result. The current research is based on the differentiation effect of PGT-A on live births in different groups of IVF populations. The systematic review of the chosen peer-reviewed articles was carried out on the basis of the evaluation of the main reproductive outcomes (live birth rate (LBR), cumulative live birth rate (CLBR), implantation rate, and miscarriage rate) in particular patient groups. The results show that PGT-A has a great effect on increasing live birth rates and decreasing miscarriage in the high-risk group of individuals especially women of advanced maternal age where the occurrence of chromosomal abnormalities is more common. But its advantages are relatively less in younger patients and in poor responders of ovaries, where baseline results are already good or limited by the fact that the number of embryos available is smaller. In addition, PGT-A increases the success of a single cycle, but the effect does not have significant cumulative live birth rates even in the non-risk groups. The research mentions that PGT-A is not universal and highly dependent on the peculiarities of the patient. Thus, the results confirm that individual and selective approach should be used in the clinical practice of PGT-A instead of its universal application in all cases of IVF.

Keywords: Preimplantation Genetic Testing (PGT-A), In Vitro Fertilization (IVF), Live Birth Rate, Cumulative Live Birth Rate, Aneuploidy, Embryo Selection, Assisted Reproductive Technology, Maternal Age, Reproductive Outcomes, Personalized Medicine

1. INTRODUCTION

Assisted reproductive technologies (ART) especially IVF have played a major role in changing the diagnosis and management of infertility in the world. The last several decades have seen a rise of laboratory methodology, ovarian stimulation programs, and embryo culture systems, which have made the clinical outcomes to be more successful. In spite of these changes, the issue of consistent success in terms of live birth rates in reproductive medicine is one of the most pressing issues. Embryonic aneuploidy is one of the main biological limitations of IVF that is well-known as one of the main causes of implantation failure, premature pregnancy loss, and frequent miscarriage. This has led to the enhancement of the accuracy and efficiency of embryo selection becoming one of the priorities of clinicians and researchers in order to increase the rates of reproductive success.

In that regard, preimplantation genetic screening (PGS) now termed PGT-A, has become an important technology in assisted reproduction. Through this method, genetic evaluation of embryos before the process of uterine transfer can be done, thus, allowing the selection and isolation of normal embryos in terms of chromosomes. The rationale behind is that transfer of euploid embryos provides better chances of implantation and less chances of miscarriage thus enhancing the overall live birth rates. Clinical data indicate that PGT-A could be especially useful in some of the high-risk categories, including women of high maternal age or those with a history of frequent pregnancy loss. The degree of PGT-A enhancement in all population of patients is, however, an object of discussion and inquiry.

One of the reasons behind this argument is the heterogeneity that exists within the population of IVF. The patients who are subjected to IVF treatment are a heterogeneous group of patients with different biological, clinical, and demographic features. Age differences in the mother, ovarian reserves, endocrine diseases like polycystic ovary syndrome (PCOS), genetic abnormalities as well as previous abortion history have a role to play in the quality of the embryo as well as the success of the treatment. These differences imply that PGT-A might not be effective in all the patients. Rather, it might be clinically relevant and applicable to particular patient groups, and it is vital to become more patient-centred and evidence-based in its application in IVF cycles.

Preimplantation genetic testing has had a tremendous technological development in the last 20 years. Early screening techniques like the fluorescence in situ hybridization (FISH) could only screen a few chromosomes and in most cases could not do it accurately. By contrast, more recent methods such as next-generation sequencing (NGS) and array comparative genomic hybridization (aCGH) can be used to perform a thorough and accurate analysis of the chromosomes. The process usually includes the biopsy of blastocyst stage embryos, and then genetic assessment to identify aneuploidy, thus allowing embryos with greater implantation capabilities to be chosen.

Simultaneously, IVF populations are highly diverse, and the key influential factors are the age of the maternal, ovarian reserve (poor versus normal responders), and the presence of such conditions as PCOS, ethnic diversity, and previous IVF failures. The factors do not only affect the reproductive outcomes, but they also define how effective can be PGT-A. Thus, it would be important to understand how patient characteristics and genetic screening results interact to improve the choice of treatment strategies. Against this backdrop, the current research will critically assess the different influence of PGT-A on the birth of living children in various IVF groups with the view to assisting more accurate and individualized clinical judgements in the field of reproductive medicine.

2. REVIEW OF LITERATURE

Brezina and Kutteh (2015) discussed the clinical use of preimplantation genetic testing and emphasized its increased importance in assisted reproductive technologies. The authors indicated that preimplantation genetic screening had enhanced embryo screening because it was possible to detect chromosomally normal embryos before transfer. Their results indicated that such a method had led to improved implantation and decreased risk of miscarriage especially among patients with known genetic defects or recurring reproductive failure. Nevertheless, they also pointed out that the efficiency of the method was conditional on proper patient selection, as well as technological accuracy, which meant that the benefits of the technique were not universal in all IVF populations.

De Vos et al. (2018) examined cumulative live birth rates in patients using IVF therapy with PCOS and found that patient phenotype was a crucial factor in reproductive outcome. The research found out that ovarian response and the difference in hormonal profiles had a significant impact on the quality of embryos and the implantation rates. Authors discovered that some PCOS phenotypes had a higher CLBR than others, thus demonstrating the heterogeneity of this patient group. Their results implied that the intervention like PGT-A could have different results in the light of the clinical nature of the patients.

Dhillon et al. (2015) investigated the influence of ethnicity on the success of IVF and found that the reproductive success of various ethnic groups significantly differed. The research showed that genetic background, socio-economic factors and the availability of healthcare services had determined the outcome of treatments including live birth rates. The authors noticed that these differences could not be attributed only to clinical parameters, which indicated that there were more widespread demographic and biological effects. Their results emphasized the role of taking into account population diversity in the evaluation of the effectiveness of interventions such as PGT-A in enhancing the outcome of IVF.

Kang et al. (2016) warned about the usefulness of preimplantation genetic screening and doubted its universal application in all IVF patients. The research found that although PGT-A had been shown to have definitive benefits in certain subgroups (women of advanced maternal age, in particular), its effect in younger patients with good prognosis was not as extensive. The authors held that the current usage of PGT-A on all patients may not be warranted, because it may be very expensive to provide a treatment with a low likelihood of improving live births. Their results provided a focus on the fact that genetic screening technologies should be used more selectively and individually.

Kasaven et al. (2023) conducted a systematic review and meta-analysis to evaluate the evidence of preimplantation genetic testing of aneuploidy at the blastocyst stage to enhance live birth rates. The researchers reported that PGT-A in comparison to control improved the live birth rates per embryo transfer but did not always enhance cumulative live birth rates per initiated IVF cycle. The authors concluded that although PGT-A increased the short-term clinical outcomes, its general effect still depended on patient-specific factors, including age and ovarian reserve. Their results supported the idea that the PGT-A efficacy was different with heterogeneous IVF groups and could only be used carefully depending on the clinical implications.

3. RESEARCH METHODOLOGY

The current research took a systematic and orderly method to test the varying effects of PGT-A in LBR between heterogeneous IVF groups. Considering the nature of reproductive medicine, which is complex and varied in nature, a multifaceted analysis approach was used to generalize the research findings based on the existing academic literature. The design of the methodology was such that allowed to conduct a rigorous assessment of the evidence that was available and to compare it across various groups of patients. Special focus was made on detecting patterns, trends, and differences in results related to PGT-A to make meaningful and clinically meaningful conclusions.

3.1 Research Design

The study adopted a systematic narrative review research design, comprising both qualitative synthesis and comparative analytical understanding. This design was deemed suitable because it would enable the combination of the results of various peer-reviewed studies and contribute to differences in the populations of the studies, methods, and the results they reported. This methodology, as opposed to a strictly quantitative meta-analysis, allowed one to gain a larger picture of how PGT-A affected the live birth rates of various subgroups of IVF.

3.2 Data Sources and Selection Criteria

Peer reviewed journal articles that were chosen in the reference list were used to derive the data of this study. Fifteen studies were taken into analysis, all of which were published between 2015 and 2023. Inclusion criteria were that the studies had to involve PGS, had to report pertinent reproductive outcomes (LBR, CLBR) and had to have separate IVF populations. Articles that lacked outcome specific data, were not peer reviewed or studies that were not directly related to IVF and genetic screening were eliminated to ensure the quality and relevance of the analysis.

3.3 Data Extraction and Variables

The selected studies were systematically searched to extract relevant data that would be used in the comparative analysis. The most important variables were as follows: LBR, CLBR, rate of implantation, and rate of miscarriage. Moreover, individual factors, including maternal age, status of the ovarian reserves, occurrence of the PCOS, and past IVF records were also taken into account. These variables were chosen because they have a direct effect on reproductive outcomes and they were necessary to determine the heterogeneous population effects of PGT-A.

3.4 Population Stratification

The study divided the population of IVF in subgroups depending on clinically relevant characteristics to address the heterogeneity of the population. These were women of old maternal age (more than 35 years), younger patients (less than 35 years), poor ovarian responders, PCOS patients, and the general population of IVF. This stratification allowed conducting a more focused assessment regarding the effect of PGT-A on the outcomes in each subgroup and make meaningful comparisons between patients of various categories.

3.5 Analytical Approach

Comparative analytical method was used in the study to assess the effect of PGT-A in various IVF populations. The analysis of data in the chosen studies was synthesized and interpreted in terms of descriptive and logical analysis, but not statistics pooling. The comparison was made and trends in the LBR, implantation success, and miscarriage reduction were identified and compared in the subgroups. The results were also presented in analytical tables and conceptual illustrations to make them easier to understand and interpret. This method helped to have a thorough insight on how much PGT-A helped to enhance better reproductive outcomes in different clinical settings.

4. RESULTS AND DISCUSSION

The results of the chosen studies showed that the quality of PGT-A depended greatly on various populations of IVF. The findings showed that patient-specific factors were significant in the outcome of live births especially the maternal age and reproductive risk profile.

The table below gives a comparative analysis of LBR with and without the use of PGT-A in various populations of IVF.

Table 1: Comparative Live Birth Rate (LBR) Across IVF Populations

Patient Group	LBR with PGT-A (%)	LBR without PGT-A (%)
Advanced Age (>35)	50	30
Younger Patients (<35)	60	55
Poor Responders	25	23
PCOS Patients	55	48
General IVF Population	53	45

Table 1 indicates that PGT-A led to significant increase in LBR among women of advanced maternal age (50% vs 30%), whereas the difference was insignificant in younger patients (60% vs 55%), and poor responders (25% vs 23%). This shows that patient risk profile is a critical factor in the clinical benefit of PGT-A.

Figure 1 displays a bar graph of the relative contribution of key factors that affect success in IVF, and these include maternal age, embryo quality, ovarian reserve, genetic screening, and other variables.

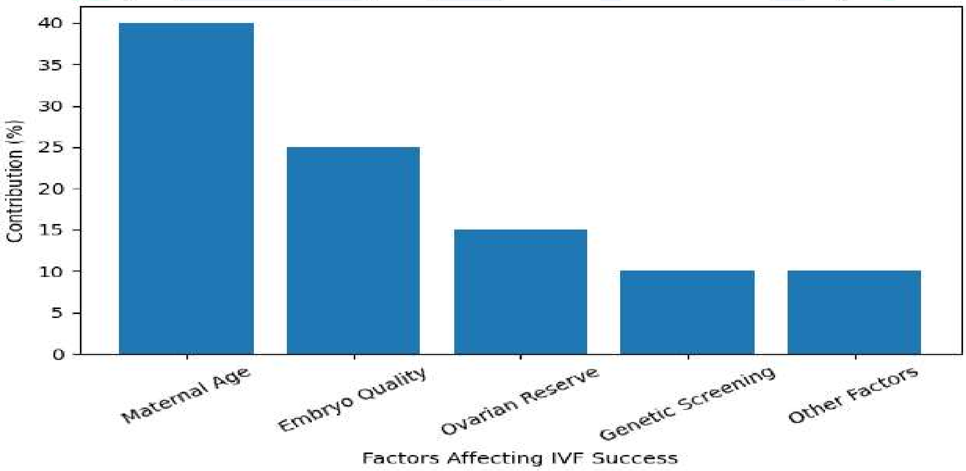

Figure 1: Bar Graph Showing Contribution of Key Factors to IVF Success

The figure 1 indicates that the highest percentage (40%) of IVF success is attributed to the mother age, and then the embryo quality (25%) and then the ovarian reserve (15%). The genetic screening takes into consideration a relatively smaller proportion (10%), which means that

despite the significance of PGT-A, the final reproductive outcomes are more significantly influenced by the inherent biological factors.
Table 2 gives CLBR which give a more detailed measure of IVF success.

Table 2: Cumulative Live Birth Rate (CLBR) Across Patient Groups

Patient Group	CLBR with PGT-A (%)	CLBR without PGT-A (%)
Advanced Age	65	50
Younger Patients	75	72
Poor Responders	35	32
PCOS Patients	70	65

Table 2 demonstrates that PGT-A had a greater impact on CLBR in more advanced age patients (65% vs 50%), with a small difference in younger patients (75% vs 72%), demonstrating that it did not bring much extra benefit to the low-risk populations.
Figure 2 shows a bar graph of the relationship between maternal age and the risk of embryonic aneuploidy, using representative percentage values of the various age groups.

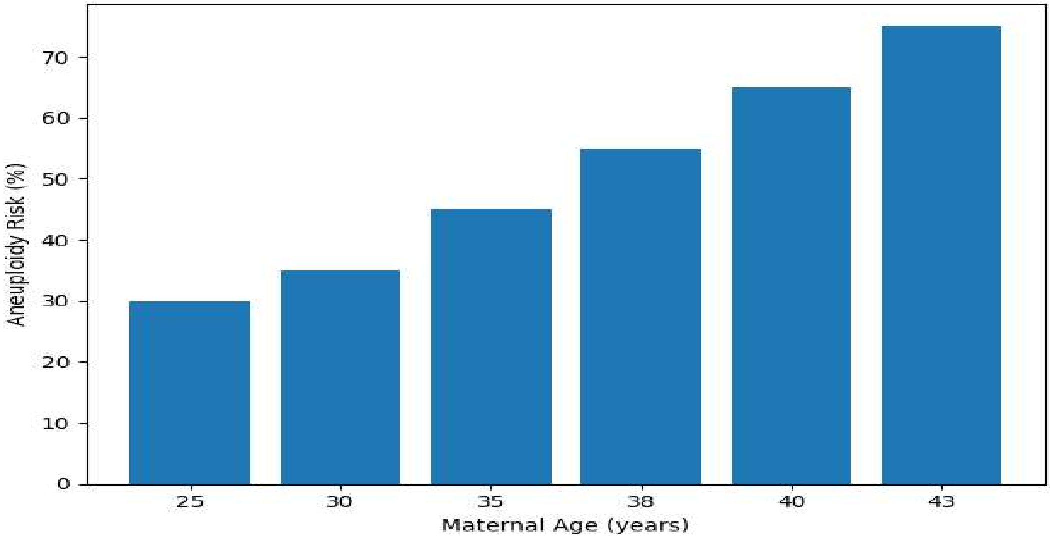

Figure 2: Bar Graph Showing Aneuploidy Risk Across Maternal Age Groups

Figure 2 demonstrates that aneuploidy risk increases gradually with maternal age, with a percentage of about 30% at the age of 25 and about 75% at the age of 43. The trend explains the effectiveness of PGT-A in older patients whereby the risk of the abnormality of the chromosomes increases with age.
Table 3 below dwells on miscarriage rates in the various populations under IVF.

Table 3: Miscarriage Rate Comparison Across IVF Populations

Patient Group	Miscarriage Rate (PGT-A %)	Without PGT-A (%)
Advanced Age	12	30
Younger Patients	10	13
PCOS Patients	15	22
Poor Responders	20	25

Table 3 indicates that, miscarriage was higher in patients who were in advanced age (12% vs 30%), and moderately higher in PCOS patients (15% vs 22%), thus proving that PGT-A plays a role in reducing chromosomal abnormalities that result in pregnancy termination.
Implantation rates are found in table 4 and they have a direct effect on IVF success.

Table 4: Implantation Rate Comparison Across IVF Populations

Patient Group	Implantation Rate (PGT-A %)	Without PGT-A (%)
Advanced Age	60	40
Younger Patients	70	65

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PCOS Patients	65	55
Poor Responders	35	30

Table 4 shows that PGT-A increased the rates of implantation significantly in patients of advanced age (60% vs 40%), and the increase was inconspicuous in younger patients (70% vs 65%).

Figure 3 shows a comparative bar chart of the relative cost and clinical benefit of PGT-A among various patient risk groups such as high-risk, moderate-risk, and low-risk groups.

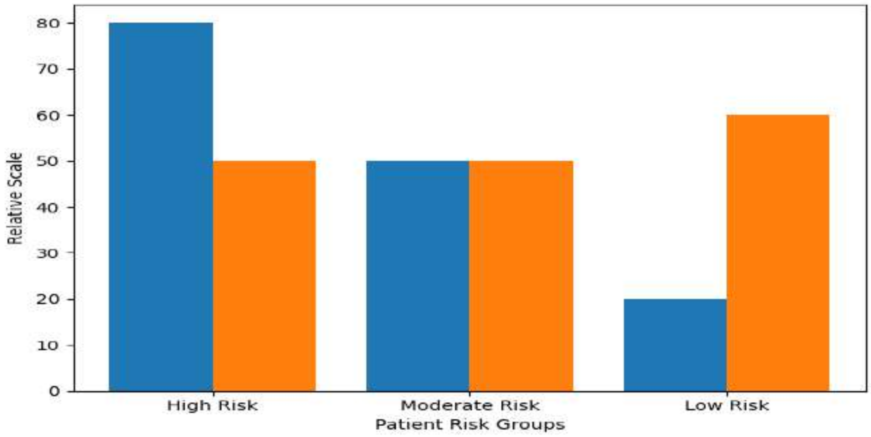

Figure 3: Bar Graph Showing Cost–Benefit Comparison of PGT-A Across Risk Groups

Figure 3 indicates that high-risk patients benefit most in PGT-A compared to cost, but low-risk patients benefit less despite a relatively high cost. This implies that the PGT-A is most cost-effective in high-risk groups and less in low-risk groups.

5. CONCLUSION

This study concludes that PGT-A has a selective influence on the live birth rates among heterogeneous IVF patients and the efficacy of this testing largely relies on patient-specific factors including maternal age, ovarian reserve, and underlying clinical conditions. The results have shown that high-risk populations such as those with advanced maternal age are highly influenced by PGT-A in improving live birth rates, implantation rates, and the rate of miscarriages due to the increased chances of chromosomal abnormalities. Nonetheless, its advantages are relatively small in younger patients and in poor responders in the ovary, where inherently good success rates prevail or low embryo supply limits the approach. Moreover, PGT-A positively affects the outcomes of each embryo transfer, but its effect on the cumulative live birth rates is less significant in low-risk groups, which brings up the question of whether PGT-A is cost-effective and should be used regularly. This study generally emphasizes the need of a tailored and evidence-based practice, as it can be argued that PGT-A must not be used in all IVF cases but should be selectively applied to those patients who are likely to respond.

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