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Going against the guidelines: patient decisions following preimplantation genetic testing

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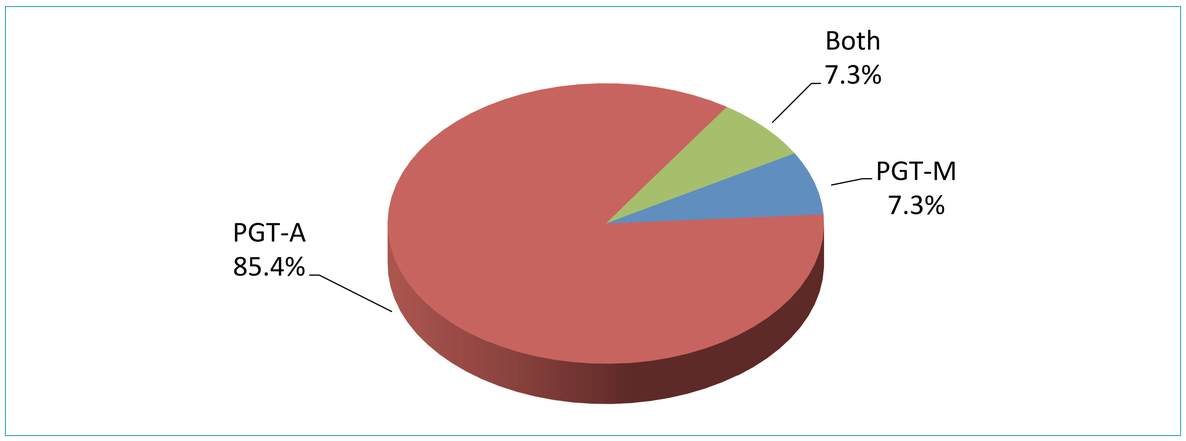
I. Introduction and Purpose

The Society for Assisted Reproductive Technologies recently documented the continued and "steady increase" of the use of assisted reproductive technologies (ART) with over 70,000 babies born in 2016. At the same time, the use of preimplantation genetic testing (PGT) for aneuploidy screening (PGT-A) and for specific single gene testing (PGT-M) has also become more mainstream. A 2007 ASRM committee opinion on PGT recommended that patients undergoing PGT-M have genetic counseling and confirmatory testing while patients undergoing PGT-A receive education and discussion of screening and diagnostic options. The purpose of this study is to evaluate prenatal testing decisions in prenatal patients who have undergone PGT.

The study population included 137 patients who received genetic counseling in a pregnancy conceived using ART with PGT from 2015-2017. Overall, 85.4% of patients (n=117) had PGT-A testing, 7.3% of patients (n=10) had PGT-M, and 7.3% of patients (n=10) had both (**Figure 1**). The majority of the patients in the overall cohort were advanced maternal age with 84% of the PGT-A patients and 60% of both the PGT-M and combination patients being 35 years or older at delivery.

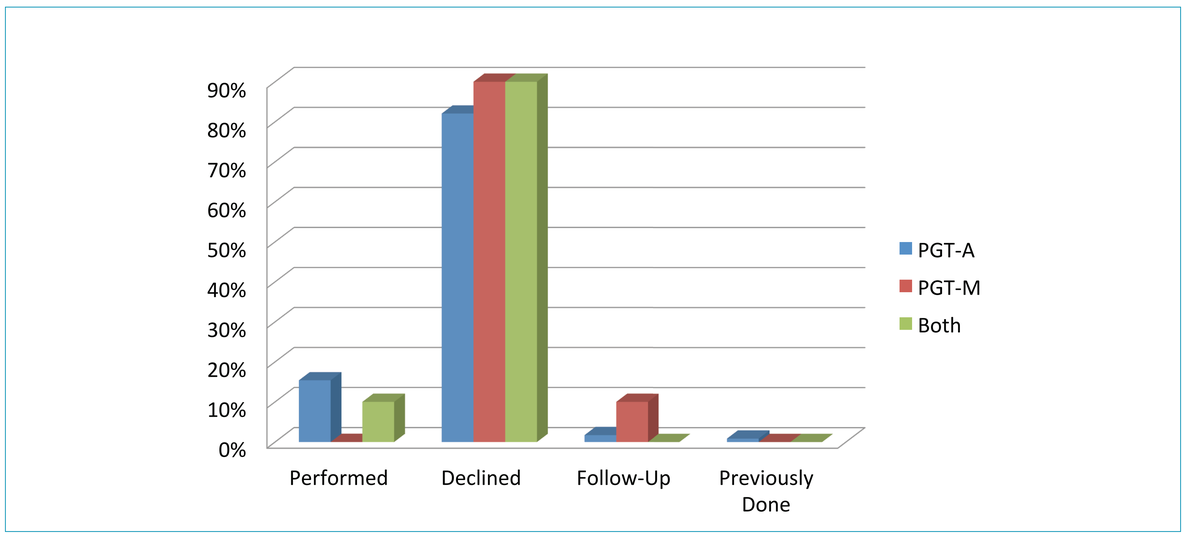
Figure 1: Overall Distribution of Preimplantation Methodologies



II. Findings

When patient decisions about prenatal diagnosis are stratified by PGT methodology, 15.4% of patients with PGT-A elected to undergo diagnostic testing while none of the PGT-M patients pursued diagnostic testing. 10% of the patients who used both PGT-A and PGT-M pursued diagnostic testing. There was no statistically significant difference regarding the uptake in these groups. When all patients were combined, 86.1% of patients utilizing any PGT methodology declined diagnostic confirmation (**Figure 2**).

Figure 2: Patient Decisions Distributed by Preimplantation Methodology



Of the total cohort, 19 patients underwent a diagnostic procedure, accounting for 13.9%. Upon further investigation as noted in **Table 1**, the majority (73.7%) of the patients who had diagnostic testing had new findings in pregnancy including abnormal ultrasound findings and positive biochemical screen results. Another 15.8% of patients were either confirming a known diagnosis or checking for an issue known to be undetectable by PGT-A technology. The final 10.5% of patients who pursued prenatal diagnosis did not have any additional risk factors. The majority of the prenatal diagnosis results were available for review (18/19, 94.7%). They revealed two unexpected findings including a single gene disorder and a case of common descent.

Table 1: Information regarding the patients undergoing prenatal diagnosis and those testing outcomes

N	%	Presumed Factors Contributing to Prenatal Diagnosis Decision	Prenatal Diagnosis			
			Normal	Abnormal	N/A	Abnormal Results
12	63.2%	Abnormal US	83%	17%	0%	1 case Noonan syndrome, 1 case common descent with AR disorder risk
2	10.5%	MMS +DS	50%	0%	50%	
2	10.5%	Chromosomal issue in family undetectable by PGT-A	100%	0%	0%	
1	5.3%	Positive PGT-M results	0%	100%	0%	Positive for Huntington's disease as expected
2	10.5%	No additional factors	100%	0%	0%	

III. Discussion

Regardless of the type of PGT performed or the indication for the PGT, patients overwhelmingly declined prenatal diagnostic confirmation during the subsequent pregnancy. Despite the guidelines from the ASRM specifically recommending diagnostic confirmation in pregnancies following PGT-M, only 5% of patients who had PGT-M had diagnostic testing. It is not clear that these patients pursued prenatal diagnostic testing for reasons related to the preimplantation testing. When looking at patients who pursued prenatal diagnosis there appear to be additional findings in pregnancy that were presumably unrelated to the PGT testing, such as abnormal ultrasound. This suggests that factors beyond PGT may have influenced their decision making regarding prenatal diagnosis. While small in number, the abnormal findings detected by the prenatal diagnostic testing performed would not have been reliably detected by traditional PGT-A technology.

IV. Conclusion

This study reveals that the vast majority of PGT patients choose not to pursue diagnostic testing, despite the recommendations for confirmatory testing following PGT-M. While the reasons for patient decisions were not specifically evaluated, these findings suggest that patients are not having prenatal diagnosis unless additional risk factors are identified. This is in line with an overall shift away from prenatal diagnostic testing. Given this tendency, it is even more important that patients receive genetic counseling to discuss the inherent limitations of PGT and the testing options available during pregnancy.

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