British Journal of Healthcare and Medical Research - Vol. 12, No. 04
Publication Date: July 17, 2025
DOI:10.14738/bjhr.1204.19056.
Pérez, S. P., Gutiérrez, A. R., Cameselle-Cortizo, L., Varela, M. O., Rodríguez-Fernández, V., & Cameselle-Teijeiro, J. F. (2025). Rare Diseases: Psychological Aspects Related to Preimplantation Genetic Testing in the Detection of Monogenic Diseases. *British Journal of Healthcare and Medical Research*, Vol - 12(04). 87-94.

Rare Diseases: Psychological Aspects Related to Preimplantation Genetic Testing in the Detection of Monogenic Diseases

Susana Portela Pérez
IVI Clinic, Vigo, Spain and ADICAM
Clinical Oncology Research Group, Cangas, Spain

Agustina Ramos Gutiérrez
IVI Clinic, Vigo, Spain

Lucía Cameselle-Cortizo
ADICAM Clinical Oncology Research Group,
Cangas, Spain and Geriatrics Department,
Meixoeiro Hospital, Vigo, Spain

María Ojeda Varela
Clinical Embryologist, IVI Clinic, Vigo, Spain

Vanesa Rodríguez-Fernández
ADICAM Clinical Oncology Research Group,
Cangas, Spain and Department of Obstetrics
and Gynecology, Álvaro Cunqueiro University
Hospital Complex, Vigo, Spain

Jorge F. Cameselle-Teijeiro
ADICAM Clinical Oncology Research Group,
Cangas, Spain and Primary Care, Vigo, Spain

ABSTRACT

Preimplantation Genetic Testing for Monogenic Disorders (PGT-M) offers families affected by rare genetic conditions a powerful tool to prevent the transmission of severe inherited diseases. However, the psychological journey associated with this process is often complex and emotionally intense. This article explores the emotional experiences, ethical dilemmas, and decision-making challenges faced by couples who pursue PGT-M, particularly when there is a known family history of rare disorders. Drawing from clinical experience and current literature, we highlight the importance of clear communication, comprehensive genetic counseling, and continuous psychological support throughout the fertility journey. Addressing issues such as anxiety, guilt, partner dynamics, and expectations management can significantly improve outcomes and emotional well-being. As advances in genetic testing become more accessible, healthcare professionals must be prepared to accompany patients not only through the medical process but also through the emotional and ethical landscape that PGT-M entails.

Keywords: Preimplantation Genetic Testing, Rare Genetic Disorders, Psychological Support, Genetic Counseling.

INTRODUCTION

Rare diseases encompass a group of approximately 5,000 to 8,000 conditions, depending on the classification criteria used. They are defined as low-prevalence disorders (in Europe: <1 in 2,000 newborns) and are characterized by significant genetic and clinical heterogeneity. Although rare individually, collectively they affect a large portion of the population—between 6% and 8%. An estimated 300 million people worldwide are living with a rare disease. The vast majority, more than 80%, have a genetic origin. Children are born with these genetic defects—hence they are also called congenital—and they tend to manifest during childhood, although not always. Typically, they are caused by pathogenic variants in a single gene, hence the term monogenic diseases (1) (e.g., Cystic Fibrosis, Huntington's Disease, Spinal Muscular Atrophy, Sickle Cell Anemia), all of which contribute significantly to early death (fetal, infant, or adolescent) and/or varying degrees of disability (2).

Most rare diseases are inherited from one or both parents, following a Mendelian pattern. Parents carrying a monogenic disorder may transmit the pathogenic variant(s) to their offspring, whether or not they are themselves affected. In a significant percentage of cases—depending on the specific disease—the mutation occurs spontaneously as a "de novo mutation" during embryonic or fetal development, thus making the affected individual the first in their family. However, they may still pass the condition on to their own children. In fact, virtually all people are "mutants"—we are all carriers of one or more mutations associated with hereditary diseases, most of which are recessive.

GENETIC TESTING AND PSYCHOLOGICAL IMPLICATIONS

Preimplantation genetic testing (PGT) is an innovative option that allows for the diagnosis of genetic disorders in embryos before uterine implantation and pregnancy. This specialized procedure can only be performed in conjunction with in vitro fertilization (IVF), which enables access to the developing embryos' genetic material. PGT is designed to identify monogenic diseases (PGT-M), as well as numerical (PGT-A) or structural (PGT-SR) chromosomal abnormalities before embryo transfer (3-5).

The combination of Carrier Genetic Screening and PGT-M represents a paradigm shift in the prevention of hereditary diseases. Several psychological implications must be considered, as appropriate genetic counseling provided to families with at least one member affected by a rare disease can encourage them to have more children without transmitting the same pathogenic variants to future offspring.

Natural human fertility is relatively low, and most couples tend to have unrealistic expectations regarding fertility treatments. The main causes of subfertility include male factor issues, ovulation disorders in women, and tubal-peritoneal factors. In many cases, medical history and physical examination are insufficient to determine the cause, requiring a complete fertility workup. Most diagnostic tests for infertility are easy to perform. Ovulatory disorders often respond to simple treatments that can be safely initiated in primary care. Couples with sperm dysfunction or probable tubal factor infertility should be referred early for specialized

assessment (6). Advanced maternal age is also an indication for early infertility evaluation and treatment.

Medical treatment of infertility can be a significant stressor, particularly when infertility persists for years and is compounded by emotional frustration. The role of the psychologist in assisted reproduction clinics is to support and guide patients throughout their reproductive treatments. In recent years, psychological support during these treatments has proven highly beneficial. Psychological support is associated with lower dropout rates and higher pregnancy and live birth rates (7, 8), compared to patients who undergo routine medical care without psychological intervention.

PSYCHOLOGICAL COUNSELING IN FERTILITY TREATMENTS

According to the Spanish Fertility Society (SEF), between 25% and 65% of patients undergoing assisted reproduction treatment experience symptoms consistent with anxiety and/or depression at some point during the process. Additionally, feelings of guilt, anger, hopelessness, and low self-esteem may also arise.

Patients often arrive with high expectations about treatment success. Scientific evidence indicates that the actual probability of pregnancy per menstrual cycle, even in the most fertile couples, does not exceed 33%. Therefore, it is unrealistic to expect higher probabilities with assisted reproduction treatments (6). From the beginning, clear and compassionate communication is essential to align the expectations of patients and medical professionals throughout the treatment, ensuring informed and realistic decision-making (9, 10). Addressing expectations early in the process can shape patient perspectives and reduce stress (11). It is important to note that, unlike most families seeking assisted reproduction due to fertility problems, families requesting PGT-M who have at least one member affected by a rare disease typically do not present with fertility issues.

The goal of psychological intervention in fertility treatments is to prevent emotional distress during the process, provide adaptive coping strategies at each stage, and offer long-term follow-up. Sometimes, expectations must be adjusted, as frustration can be high when results are not as desired. A multidisciplinary approach, including psychologists from the start of the assisted reproduction process, is recommended. There is a positive association between psychological interventions—especially long-term ones—and pregnancy rates in infertile women and couples undergoing assisted reproduction (12).

DECISION-MAKING AND THE ROLE OF EDUCATION AND SUPPORT

Lin Cheng and colleagues analyzed the factors influencing patients' decision-making regarding PGT-M, emphasizing the importance of effective patient education and the need to provide high-quality, patient-centered information. Patients benefit from information that specifically addresses their concerns about PGT-M. From women's perspectives, the support of their partners is essential, so their involvement in all decision-making stages should be encouraged. Factors such as perceived coherence and satisfaction with the information provided, individual self-efficacy (belief in one's ability to make informed decisions), actual knowledge of PGT-M, and social support from partners all play a significant role (13). Attachment dimensions in one partner can directly affect the infertility-related stress experienced by the other (14). Tara Hughes and collaborators (15) reviewed the motivations, decision-making factors,

URL: http://dx.doi.org/10.14738/bjhr.1204.19056.

attitudes, and experiences of couples using PGT for inherited conditions. The main motivations were the desire to have a healthy child and avoid pregnancy termination. Families with a sick child or a history of miscarriages were more likely to use PGT-M. Patients often felt compelled to use the available technology.

Key factors considered when deciding to use PGT-M included the requirement for IVF, technological acceptability, economic cost, and ethical views on embryo creation and manipulation. There was broad agreement that PGT-M should be applied in severe or lethal childhood diseases, while there was less consensus regarding adult-onset or variably expressed conditions. There was general agreement against using PGT-M to select aesthetic traits and frustration over societal opinions about its use. Couples often find it difficult to fully assess the benefits and costs of PGT-M, resulting in ambivalence and prolonged indecision. Once the decision is made, the process is often found to be highly impractical and psychologically demanding.

CARRIER SCREENING AND PREVENTIVE STRATEGIES

Carrier Genetic Screening is now a reality. Thanks to technological advances based on next-generation sequencing (NGS), it is possible to study a large number of mutations simultaneously, in record time and at costs unimaginable just a few years ago. This opens the door to a promising future in terms of disease prevention. In the 21st century, the progress of both molecular and clinical genetics enables couples to consider PGT-M as a tool to prevent the transmission of pathogenic genetic variants to the next generation.

Although eradicating most hereditary rare diseases globally is still not feasible, it is now realistic to aim at reducing the incidence of some of the more prevalent rare diseases—such as Cystic Fibrosis or Spinal Muscular Atrophy—among healthy individuals with no known family history. It may even be possible to nearly eradicate others, such as Huntington's Disease. This new preventive strategy could also apply to certain monogenic hereditary diseases that are not classified as rare due to their high prevalence, such as idiopathic or familial hypertrophic obstructive cardiomyopathy, which follows an autosomal dominant inheritance pattern. Therefore, clinical situations in this context can be very diverse.

When a family member is already affected by a rare disease, regardless of the type of Mendelian inheritance or specific disorder, PGT-M should be employed. This prenatal diagnostic tool allows for the genetic study of a specific condition in the embryo before uterine transfer.

Of course, when there is already a family member affected by a rare disease, regardless of the type of Mendelian inheritance or specific disease, PGT-M should be used. This prenatal diagnostic tool enables the genetic study of a specific condition in the embryo before it is transferred to the uterus.

A fundamental requirement for "drastically reducing the incidence of certain rare hereditary diseases" is that the percentage of de novo mutations must be very low or practically nonexistent, as is the case with Huntington's Disease, a hereditary neurodegenerative disorder with motor, cognitive, and neuropsychiatric symptoms, caused by the expansion of a CAG trinucleotide repeat on chromosome 4p16.3. CAG repeat lengths are defined as fully penetrant at ≥40, reduced penetrance at 36–39, high-normal at 27–35, and normal at ≤26. Most cases are

inherited from an affected parent, but approximately 10% appear de novo. Even these de novo (sporadic) cases could be prevented, as they typically result from the expansion of intermediate alleles.

Being an autosomal dominant disease, the risk of transmission is 50%. Therefore, when a family member is affected, appropriate genetic counseling must be provided. Only in this way can we break the chain of transmission and prevent more family members from being affected. These interventions do not infringe upon the reproductive rights of individuals with Huntington's Disease (or others) who wish to remain unaware of their carrier status. In such cases, it is possible to have mutation-free offspring through PGT-M without the parents knowing their own CAG repeat number. The process can be done anonymously.

When intermediate alleles range from 27 to 35 CAG repeats, the higher the number, the greater the risk of expansion into the disease range, especially via paternal transmission. Fathers—but not mothers—with high-normal alleles (27–35 CAG repeats) are at risk of transmitting potentially pathogenic Huntington's Disease alleles (≥36) to their offspring. The estimated risk for a man with a high-normal allele to have a child with a fully penetrant expanded allele ranges from 1 in 6,241 to 1 in 951. These estimates are useful in genetic counseling for men carrying high-normal alleles. Carrier Screening is essential to identify asymptomatic individuals at risk of transmitting Huntington's Disease alleles to their children.

ETHICAL CONSIDERATIONS AND EMOTIONAL IMPACT

When reviewing fertility-related psychological aspects, it is also important to address the reasons influencing young women's decisions to accept or decline fertility preservation after a cancer diagnosis. The central issue is whether to prioritize cancer survival or future biological motherhood.

Reasons for choosing fertility preservation relate to four theoretical dimensions: Cognitive, Emotional Responses, Moral Judgments, and Decision Associations. Women who declined often cited cognitive evaluations, including financial costs and human risks. Most who accepted did so based on emotional responses and a strong desire for biological motherhood, while those who declined prioritized surviving cancer. A minority declined for moral reasons. Most decisions were influenced by partners, including spouses, boyfriends, parents, and clinicians. Family members with Hereditary Cancer Syndromes often express concern about passing on genetic risks. PGT-M allows identification of embryos with mutations that increase hereditary disease risk. Surveys among women with Hereditary Breast and Ovarian Cancer Syndromes showed that over half had negative attitudes toward using PGT-M. However, those who supported its use viewed it as a new option for motherhood, especially if they had previously decided against biological children. Many respondents had never heard of PGT-M and supported broader education and access.

Social media and the internet are widely used by individuals with infertility to learn about PGT. Conversations with healthcare professionals about fertility concerns and satisfaction with those interactions are linked to reduced distress, greater understanding of cancer's effects on fertility, informed decision-making, and satisfaction with care. Training and empowering primary care professionals to provide information about assisted reproduction, Carrier Screening, and PGT-M would be highly effective.

URL: http://dx.doi.org/10.14738/bjhr.1204.19056.

A review of 25 articles analyzing patient experiences and attitudes toward PGT found five main points: 1) couples are motivated by the hope of having a healthy child, 2) PGT demands time, money, energy, and emotions, 3) there are ethical and logistical concerns about discarding embryos, 4) there is a sense of responsibility to use new technology, and 5) PGT decisions are complex for both individuals and couples. More research is needed to support clinical counseling and fill gaps in the literature on decision-making. The use of PGT to select genetically 'normal' embryos for transfer remains controversial, involving concerns about sex selection, embryo manipulation, and eugenics. Generally, PGT is widely accepted under a shared decision-making model where couples maintain autonomy. Disagreements arise over criteria for embryo transfer, PGT use restrictions, and embryo disposal. Factors encouraging PGT use include infertility, recurrent miscarriage, having a child with a rare disease, or lack of other options. Having a living child with a rare disease reduced PGT use. Inheritance type and clinical impact did not influence the decision. The cost of PGT generates high anxiety. Still, couples prioritize the opportunity to avoid passing on a genetic disorder over the financial burden, even as they recognize it as a major barrier. When comparing two groups—those with prior counseling for a known risk of fetal defects or genetic diseases and those who learned of major anomalies during routine ultrasound—the latter group experienced shock, denial, and guilt after pregnancy termination. One-third of both groups felt pressured to terminate. More women in the prior counseling group sought psychiatric help and viewed future pregnancies as replacements for the lost one. Adequate staff training, nursing support, respectful environments, anticipatory grief counseling, and long-term follow-up are essential to ensure proper psychological care and future pregnancy counseling.

Ensuring proper genetic counseling and specialized psychological support throughout assisted reproduction is vital. Couples value respectful, empathetic communication from healthcare professionals. This emotional recognition must also extend to patients navigating PGT-M decisions.

Gameiro et al. recommend that fertility clinics follow ESHRE guidelines for routine psychosocial care in infertility and assisted reproduction. Adherence improves stress management, fertility awareness, lifestyle outcomes, patient well-being, and treatment compliance.

CONCLUSIONS

In summary, counseling for women and their partners considering PGT-M must be comprehensive. The decision is often difficult, requiring consideration of relationship dynamics, reproductive history, belief systems, economic factors, and healthcare interactions—covering personal, interpersonal, and clinical dimensions. Virtually everyone is a carrier of one or more mutations associated with hereditary diseases. We must look to the future with hope. Advances in genetics require the integration of Carrier Screening and PGT-M to reduce the incidence of as many hereditary monogenic diseases as possible, most of them rare or ultra-rare. Health education and psychological support are fundamental to any strategy. Much work remains to be done.

References

1. Korf BR, Pyeritz RE, and Grody WW, “Nature and Frequency of Genetic Disease,” in Emery and Rimoin's Principles and Practice of Medical Genetics and Genomics, Seventh ed., eds. Pyeritz RE, Korf BR, and Grody WW (Amsterdam, The Netherlands: Academic Press, 2019), 47–51.

2. Blencowe H, Moorthie S, Petrou M, Hamamy H, Povey S, Bittles A, Gibbons S, Darlison M, Modell B; Congenital Disorders Expert Group. Rare single gene disorders: estimating baseline prevalence and outcomes worldwide. J Community Genet. 2018 Oct; 9(4):397-406.
3. Basille C, Frydman R, El Aly A, Hesters L, Fanchin R, Tachdjian G, et al. Preimplantation genetic diagnosis: State of the art. European Journal of Obstetrics &Gynecology and Reproductive Biology. 2009; 145(1):9-13.
4. Hershberger PE, Schoenfeld C, Tur-Kaspa I. Unraveling preimplantation genetic diagnosis for high-risk couples: implications for nurses at the front line of care. Nursing for Women's Health. 2011b; 15(1):36-45.
5. Simpson JL. Preimplantation genetic diagnosis at 20 years. Prenatal Diagnosis. 2010; 30(7):682-695.
6. Cahill D J, Wardle P G. Management of infertility BMJ 2002; 325:328.
7. Domar, A. D., Clapp, D., Slawsby, E., Kessel, B., Orav, J., & Freizinger, M. (2000). The impact of group psychological interventions on distress in infertile women. Health Psychology 2000; 19(6): 568–575.
8. Dolz, P. y García, A. Incidencia positiva de los Programas de Apoyo Psicológicos en los Tratamientos de Reproducción Asistida. Revista Iberoamericana de Fertilidad y Reproducción Humana. Número especial del 24 Congreso de la Sociedad Española de Fertilidad, 2002; 233.
9. Mertes H, Harper J, Boivin J, Ekstrand Ragnar M, Grace B, Moura-Ramos M, Rautakallio-Hokkanen S, Simopoulou M, Hammarberg K, International Reproductive Health Education Collaboration Irhec OBOT. Stimulating fertility awareness: the importance of getting the language right. Hum Reprod Open. 2023; (2):hoad009.
10. Rosenzweig MQ. Breaking bad news: a guide for effective and empathetic communication. Nurse Pract. 2012; 37(2):1-4.
11. Childress KJ, Lawson AK, Ghant MS, Mendoza G, Cardozo ER, Confino E, Marsh EE. First contact: the intersection of demographics, knowledge, and appraisal of treatment at the initial infertility visit. Fertil Steril. 2015; 104(1):180-187.
12. Katyala N., Poulsena C.M., Knudsen U.B., Frederiksend Y. The association between psychosocial interventions and fertility treatment outcome: a systematic review and meta-analysis. Eur. J. Obstet. Gynecol. Reprod. Biol. 2021;259:125-132.
13. Cheng L, Meiser B, Kirk E, Kennedy D, Barlow-Stewart K, Kaur R. Factors influencing patients' decision-making about preimplantation genetic testing for monogenic disorders. Hum Reprod. 2022; 37(11):2599-2610.
14. Donarelli Z, Lo Coco G, Gullo S, Marino A, Volpes A, Allegra A. Are attachment dimensions associated with infertility-related stress in couples undergoing their first IVF treatment? A study on the individual and cross-partner effect. Hum Reprod. 2012; 27(11):3215-3225.
15. Hughes T, Bracewell-Milnes T, Saso S, Jones BP, Almeida PA, Maclaren K, Norman-Taylor J, Johnson M, Nikolaou D. A review on the motivations, decision-making factors, attitudes and experiences of couples using pre-implantation genetic testing for inherited conditions. Hum Reprod Update. 2021; 27(5):944-966.
16. Tabrizi SJ, Flower MD, Ross CA, Wild EJ. Huntington Disease: New Insights into Molecular Pathogenesis and Therapeutic Opportunities. Nat Rev Neurol2020;16:529–546.
17. Warby SC, Montpetit A, Hayden AR, et al. CAG expansion in the Huntington disease gene is associated with a specific and targetable predisposing haplogroup. Am J Hum Genet 2009; 84:351–366.
18. Semaka A, Collins JA, Hayden MR. Unstable familial transmissions of Huntington disease alleles with 27-35 CAG repeats (intermediate alleles). Am J Med Genet B Neuropsychiatr Genet 2010; 153B:314–320.
19. Hendricks AE, Latourelle JC, Lunetta KL, Cupples LA, Wheeler V, MacDonald ME, Gusella JF and Myers RH. Estimating the probability of de novo HD cases from transmissions of expanded penetrant CAG alleles in the Huntington disease gene from male carriers of high normal alleles (27–35 CAG). Am J Med Genet 2009; 149A: 1375-1381.

URL: http://dx.doi.org/10.14738/bjhr.1204.19056.

20. Hershberger PE, Sipsma H, Finnegan L, Hirshfeld-Cytron J. Razones por las que las mujeres jóvenes aceptan o declinan la preservación de la fertilidad después del diagnóstico de cáncer. J Obstet Gynecol Neonatal Nurs 2016; 45(1):123-134.

21. Rubin LR, Werner-Lin A, Sagi M, Cholst I, Stern R, Lilienthal D, Hurley K. 'The BRCA clock is ticking!': negotiating medical concerns and reproductive goals in preimplantation genetic diagnosis. Hum Fertil (Camb). 2014, 17(3):159-164.

22. Quinn GP, Vadaparampil ST, King LM, Miree CA, Friedman S. Conflict between values and technology: perceptions of preimplantation genetic diagnosis among women at increased risk for hereditary breast and ovarian cancer. Fam Cancer. 2009; 8(4):441-449.

23. Hurley K, Rubin LR, Werner-Lin A, Sagi M, Kemel Y, Stern R, Phillips A, Cholst I, Kauff N, Offit K. Incorporating information regarding preimplantation genetic diagnosis into discussions concerning testing and risk management for BRCA1/2 mutations: a qualitative study of patient preferences. Cancer; 2012: 118(24):6270-6277.

24. Rubin LR, Pastore LM, Subramony S, Lobel M, Stelling J. Navigating preimplantation genetic testing decisions in the age of social media: a qualitative study. Fertil Steril 2018; 110:e146.

25. Ussher JM, Parton C, Perz J. Need for information, honesty and respect: patient perspectives on health care professionals communication about cancer and fertility. Reprod Health. 2018; 15(1):2.

26. Genoff Garzon MC, Rubin LR, Lobel M, Stelling J, Pastore LM. Review of patient decision-making factors and attitudes regarding preimplantation genetic diagnosis. Clin Genet 2018; 94:22-42.

27. Katz MG, Fitzgerald L, Bankier A, Savulescu J, Cram DS. Issues and concerns of couples presenting for preimplantation genetic diagnosis (PGD). PrenatDiagn 2002; 22:1117–1122.

28. van Rij MC, Gielen M, Lulofs R, Evers JL, van Osch L, Muntjewerff N, Geraedts JP, de Die-Smulders CE. Profiles and motives for PGD: a prospective cohort study of couples referred for PGD in the Netherlands. Hum Reprod 2011; 26:1826–1835.

29. Karatas JC, Barlow-Stewart K, Meiser B, McMahon C, Strong KA, Hill W, Roberts C, Kelly P. Psychological adjustment, knowledge and unmet information needs in women undergoing PGD. Hum Reprod 2010; 25:1481–1489.

30. Drazba KT, Kelley MA, Hershberger PE. A qualitative inquiry of the financial concerns of couples opting to use preimplantation genetic diagnosis to prevent the transmission of known genetic disorders. J Genet Couns. 2014; 23(2):202-211.

31. Dallaire L, Lortie G, Des Rochers M, Clermont R, Vachon C. Parental reaction and adaptability to the prenatal diagnosis of fetal defect or genetic disease leading to pregnancy interruption. PrenatDiagn. 1995; 15(3):249-259.

32. Gameiro S, Boivin J, Dancet E, de Klerk C, Emery M, Lewis-Jones C, Thorn P, Van den Broeck U, Venetis C, Verhaak CM, Wischmann T, Vermeulen N. Oracción de ESHRE: atención psicosocial rutinaria en infertilidad y reproducción asistida médicamente - una guía para el personal de fertilidad. Hum Reprod. 2015 Nov; 30(11):2476-85.