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Cauzele genetice ale infertilității

REZUMATUL TEZEI DE ABILITARE

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In this paper titled **"The Genetic Causes of Infertility"** I present the main results of my research in the field of medical genetics, focusing on how genetic factors contribute to infertility in both men and women. My studies focus on elucidating the role that genetic mutations and chromosomal abnormalities play in infertility, providing a detailed view of the molecular mechanisms involved. These studies have a major impact on clinical practice in reproductive medicine and are essential for improving the treatments available for patients dealing with this condition.

Since the beginning of my medical career, I have been drawn to the complexity of the human body and how genetics influence reproductive health. My choice to dedicate my clinical and research activities to medical genetics was inspired by the desire to contribute to improving the quality of life of patients, especially those who face difficulties in conception. Infertility is a global problem that affects approximately 10-15% of couples of reproductive age, and identifying the genetic causes of this condition is crucial for improving therapeutic interventions.

My paper addresses three main areas: the genetic causes of male infertility, the genetic causes of female infertility, and future research and intervention perspectives in this field.

The first part of my research focuses on identifying and analyzing the genetic causes of male infertility, one of the most complex and frequent issues encountered in medical practice. Klinefelter syndrome is one of the main chromosomal causes of male infertility. This condition is characterized by the presence of an extra X chromosome, which leads to a 47,XXY karyotype, severely affecting testicular function and sperm production. Men with Klinefelter syndrome suffer from hypogonadism, and their testes do not produce enough testosterone, contributing to oligospermia or even azoospermia. In my studies, I have analyzed multiple cases of patients with this condition, focusing on ways to improve the available hormonal and fertility treatments for them.

Y chromosome microdeletions are another major genetic cause of male infertility. The Y chromosome contains essential genes for spermatogenesis, and microdeletions in the azoospermia factor (AZF) regions can lead to the disruption of the sperm production process. I have investigated the impact of these microdeletions and demonstrated that they are associated

with azoospermia and severe oligospermia. My studies have shown that the frequency of these deletions varies by population, with higher rates in certain ethnic groups, underscoring the need for detailed genetic investigations for infertile patients.

Additionally, I explored the role of CFTR gene mutations in male infertility. The CFTR gene, traditionally associated with cystic fibrosis, can cause infertility through congenital absence of the vas deferens, structures essential for sperm transport. Men with CFTR mutations, even without the classic symptoms of cystic fibrosis, may present infertility due to this anatomical abnormality. My research has demonstrated the importance of early diagnosis of these mutations to offer appropriate treatment options for affected patients.

A significant portion of my research also focuses on female infertility, where I have investigated the genetic causes underlying ovarian insufficiency and other reproductive dysfunctions. Turner syndrome, characterized by the absence of an X chromosome (45,X0), is one of the most common genetic causes of female infertility. This chromosomal anomaly leads to premature ovarian failure, which causes most affected women to be infertile. In my studies, I have analyzed cases of women with Turner syndrome and emphasized the importance of early diagnosis and genetic counseling for these patients.

Another important syndrome I studied is triple X syndrome (47,XXX), which, although not always presenting obvious symptoms, can lead to ovarian insufficiency and infertility. Women affected by this syndrome may have irregular menstrual cycles and an increased risk of spontaneous miscarriage. My research has shown that this genetic condition should be considered in the evaluation of women facing conception difficulties, even in the absence of other obvious clinical signs. I also analyzed mutations in the FMR1 gene, associated with fragile X syndrome, a well-known cause of intellectual disability and female infertility. Women who are carriers of FMR1 gene mutations have an increased risk of developing premature ovarian failure, limiting their ability to have children. In my studies, I highlighted the need for specific genetic testing for these patients to identify the risk of infertility early and offer appropriate assisted reproduction options.

Another important genetic factor I addressed is hereditary thrombophilia, a condition that can negatively affect pregnancy and fertility in women. Thrombophilia, characterized by

an increased tendency for blood clot formation, can affect embryo implantation and lead to recurrent miscarriages. My research has shown that women with mutations in coagulation genes (such as the factor V Leiden mutation) have an increased risk of infertility and pregnancy complications. I have proposed personalized treatment approaches for these patients, including anticoagulant therapy to increase the chances of pregnancy success.

Based on these studies, I concluded that genetics play a crucial role in infertility, and correctly diagnosing the genetic causes can significantly improve the success rates of assisted reproduction treatments. Infertility is a multifactorial condition, and combining advanced genetic screening methods with modern fertility treatments can offer personalized solutions for patients facing this issue. In the future, I aim to continue researching these genetic causes and exploring new biomarkers that could be used in the diagnosis and treatment of infertility. I am committed to developing and implementing new genetic screening techniques to identify genetic abnormalities that affect fertility more quickly and accurately.

Another important goal of my future research is to collaborate with experts from various fields, such as embryology and immunology, to better understand the interaction between a patient's genetics and their environment. I also intend to study in more detail the effect of genetic polymorphisms on women's immune response to embryo implantation, a field that may offer new solutions for preventing spontaneous miscarriages and improving the success rate of in vitro fertilization.

Research in the field of genetic infertility is still in its infancy, but its potential is enormous. I hope that my contributions to this field, both through research and clinical activity, will bring significant improvements to the lives of patients who wish to become parents. I hope that, through my continued efforts, I can contribute to the creation of a relevant genetic database for infertility in Romania and help develop more efficient and personalized treatment protocols.

My work represents an important step in understanding the genetic causes of infertility and offers practical solutions for diagnosing and treating this condition. I have explored both male and female infertility and emphasized the importance of a genetic approach in treating patients. I have also identified clear directions for future research, focusing on developing

more efficient genetic screening methods and interdisciplinary collaboration to find solutions to this complex problem. My clinical and research activities will continue to focus on supporting couples dealing with infertility, by correctly diagnosing genetic causes and providing the best available therapeutic solutions. I am committed to contributing to the progress of this field through rigorous research and interdisciplinary collaborations, always with the final goal of improving reproductive health and supporting patients on their path to forming a family.