Chelonian Conservation And Biology

Vol. 17No.2 (2022) | https://www.acgpublishing.com/ | ISSN - 1071-8443

DOI:doi.org/10.18011/2022.04(1) 1087-1089

COMPREHENSIVE ANALYSIS OF ENVIRONMENTAL FACTORS CONTRIBUTING TO HIGH INFERTILITY RATES

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ABSTRACT

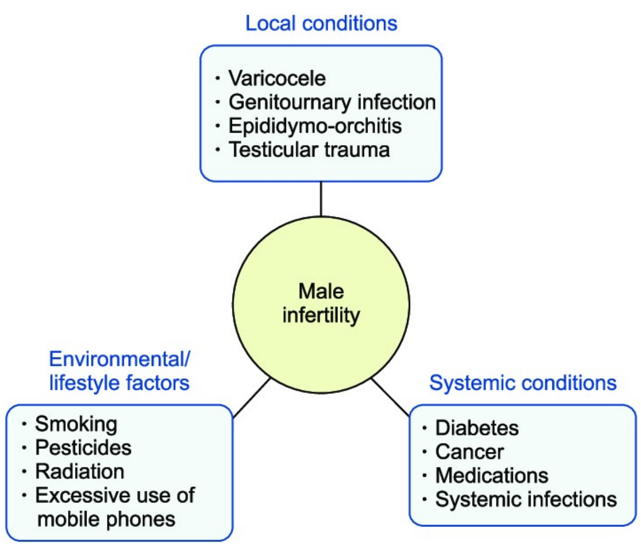
According to medical definitions, infertility is a condition that is present when a couple doesn't get pregnant after a year of unprotected sex in which both partners are active and sexually healthy; personal samples indicate that around 10-15% of couples are facing infertility(Kamiński et. al 2020). According to the latest WHO statistics, it is estimated that 50–80 million men and women in the world are referred to infertility cases, and one in three of them is due to male factors. Most of the men's infertility diagnoses rely on semen analysis. Human sperm's constituents are divided into two main fractions: a) density, b) appearance, and c) motility. Male infertility may be caused by multiple conditions, such as body abnormalities, hormone imbalances, lifestyle problems, psychological issues, poor sexual practices, chromosomal abnormalities, and even single gene errors. In essence, for about 70% of men who are proven to have infertility, scientists have failed to unravel their origins.

Keywords: male infertility, spermatogenesis, azoospermic-obstructive azoospermia.

INTRODUCTION

Infertility is the inability of a couple to conceive after one year of regular, unprotected intercourse, although the rate of this reaches 10–15%. The most recent WHO data indicated that significantly more than 50–80 million humans suffer from fertility issues. Research-based results state that between 50 cases of female infertility for every 100 cases of infertility, 20–30 cases for the male factor, and 20–30 cases for both factors, the gender-related causes each account for (Kamiński et. al 2020). According to the most recent studies and those conducted by specialists, in 20–70% of infertility cases, males have some problem with their reproductive ability (Kamiński et. al 2020). Given a definitive male contribution to the factors that cause infertility in a couple, in addition to a quite commonly unknown cause that male infertility is characterized by, it is an apparent lack of knowledge about the underlying mechanisms that highlights the most critical problem in trying to solve this problem (Kamiński et. al 2020).

Fig. 1, Risk factors of male factor infertility.



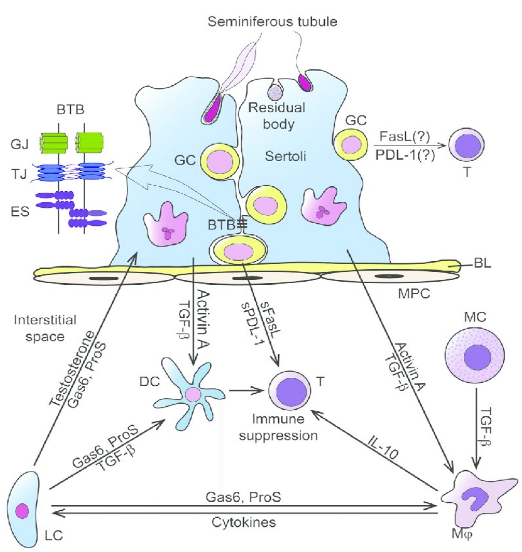
(Kamiński et. al 2020).

Males's reproductive organs

To get an idea regarding the worries of a man related to infertility, we will discuss the main aspects of male fertility in the beginning. Biphasically and secondaryly, they are also found in the human reproductive organs. In male mammals, gonads serve as primary organs (which are in charge of spermatozoa and hormone production). At the same time, ducts and glands are secondary organs that assist in spermatozoa development and its transmission. Testes might be regarded as the main male reproductive organs that the testicles bask in, and they are kept safe by the tunica albuginea capsule in the testicle sack. The testis comprises two sections—one sectional and one sectional—which do very different activities.

The seminiferous tubules are in the germinal layer, while the interstitial spaces are between them. The intratubular border of seminiferous tubules provides a blood supply for the tissue and immunological defense against viruses and other infections that try to gain access. Leydig cells constitute the most essential testicular cells, generating testicular testosterone and the inulin-like 3 factor. The other crucial components of the intercellular elements are Tousch-Leidig cells, immune cells, arteries and lymph vessels, neurons, connective tissue, and fibroblasts. The seminiferous tubules are the functional working units in the testis, which have a 60–80% volume of this structure. These tubes are surrounded by epithelial tissue containing two types of cells. These cells act as supporting roles that assemble and organize the spermatogenic cells within the seminiferous tubules. Sertoli cells feed growing sperm and give them needed support during all the stages of spermatogenesis. In addition, they keep sperm in formation during various reshaping and rearrangement processes. There are two classes of cells in the anterior pituitary, which are the source of inhibin and activin hormones, where inhibin functions as positive feedback and activin functions as negative feedback to FSH.

Figure 2: Schematic of the Blood Test Barriers.

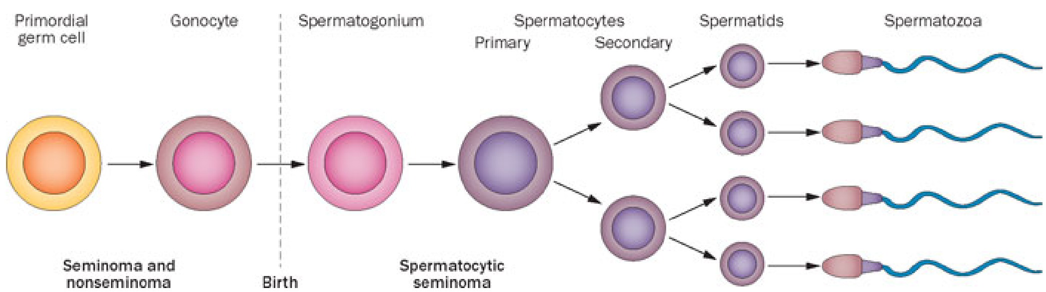


(Kamiński et. al 2020).

Spermatogenesis

Spermatogenesis is the phenomenon of the smallest in male fertility, which we all need to know about. Sperm male infertility can sometimes manifest itself in the absence of significant deviations from the norm hyperoperation of spermatogenesis. Spermatogenesis is the process that allows the formation of male gametes, and the haploid germ cells arrive in the seminiferous tubules from the diploid spermatogonia within the seminiferous epithelial tissue, thus being released. Each rung of spermatogenesis takes 16 days in the human body, and the adult sperm's differentiating and maturing take about 4.6 cycles and a total of 74 days.

Figure 3 depicts the spermatogenesis process.



(Kamiński et. al 2020).

Spermatogoniogenesis

The germ cell lines, upon further differentiation, behave similarly to embryos. Their primary germ cell (PGC), from which they are derived, would help trace their development. The cells called the PGCs of humans start forming by the end of the third week, when they are among the cells of the endoderm inside the genital tract, and they continue until the fifth week when the presence of the Y chromosome causes the proliferation and conversion into the primary sexual organs of males. PGCs adhere to the first trimester of the cell cycle and are referred to as gonocytes when the name PGCs is given to these oocytes or tests. Nevertheless, they stop at the G3 phase of the cell cycle (the end of the formation of zygotes) and remain silent until delivery (when they are taken for the formation of spermatogonia). Spermatogonia is now adaptive without activity until puberty begins.

Meiotic Division

Meiosis, as well as mitosis, involves DNA replication, chromosomal condensation, and cell division. However, meiosis allows sexual reproduction across species. Meiosis makes haploid gametes by having diploid cells as starting materials. The DNA replication cycle happens twice, with the cell returning to meiosis during the nuclear division in mammalian meiosis.

Spermatogenesis

Sperm formation, or spermatogenesis (minus sign period), forms the ultimate product of spherical spermatids resulting from meiosis II into specialized spherical spermatids and does not separate the cells. This process necessitates the growth of cytoplasm and nucleus regeneration, which can occur in four stages: the liquid phase, the solid phase, the thermophilic phase, and the denaturation phase(Okonofua et. al 2022).

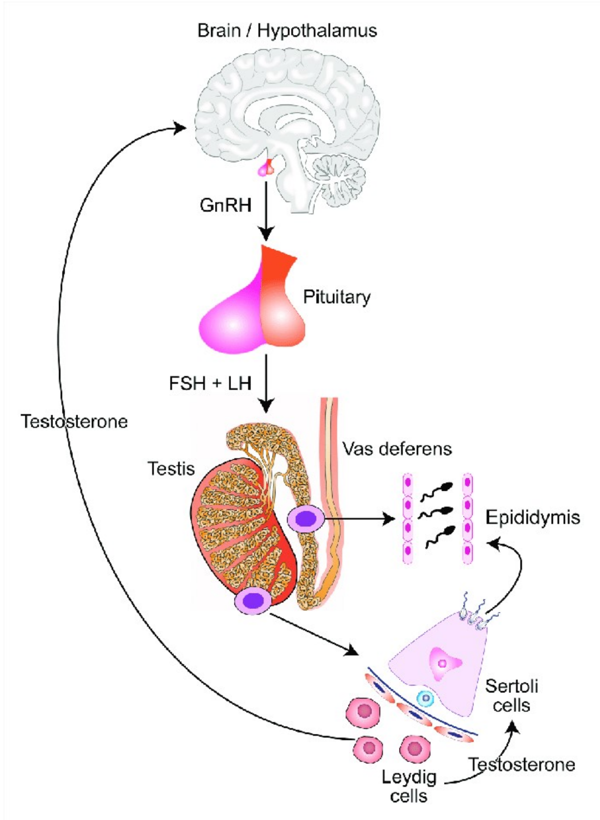
The leading causes of infertility

Hormonal Defects

The other, known as the hypothalamic-pituitary-gonadal or hormonal axis for males, is the male reproductive hormone axis. The hypothalamus and its associated organs, such as the pituitary and testis glands, comprise the three hypothalamus-pituitary-gonadal axes (Figure 4). This pin is a favorite part of this axis because it has adequate hormones for male sexual growth and function. A couple can be sterile because of any condition afflicting the entire system. Lifelong amenorrhea develops if the brain cannot produce GnRH (gonadotropic releasing hormone), a condition induced by the decrease of testosterone in men and the prevention of sperm production—a deficiency of GnRH results in the occurrence of dysfunction in the reproductive system. Hypogonadal hypogonadism, as it is called, is a general term covering several health problems characterized by deficient levels of gonads-dependent hormones, such as testosterone in males and estrogen and progesterone in females. Among these numerous symptoms, we have the main one, Kallmann syndrome, which is a change of smell and immaturity(Okonofua et. al 2022).

LH and FSH levels increase with the amount of testosterone in low production. This thus results in spermatogenic deficiencies. Therefore, using elevated amounts of testosterone and estrogen can be a successful method for preventing LH and FSH because they already suppress LH and FSH production. Enhanced prolactin levels may result in low sperm count and libido and can also hurt impotence. Marked by hyperprolactinemia, in 11% of cases with oligospermia, infertility is observed as a consequence. In many cases, adding a dopamine agonist can be a potent pharmacotherapy.

Figure 4 depicts the brain-pituitary-testicular axis.



(Assidi, 2022).

Sexual Problems

Problems cause many sexual issues to be both physical and psychological. Sexual difficulties broadly fall under the lines of erectile dysfunction (otherwise known as impotence), early ejaculation, and being unable to ejaculate (Borumandnia et. al 2022).

Environment and Lifestyle

Working men with hazardous substances like solvents, pesticides, glue, silicon, and radiation are susceptible to fertility problems and disabilities. Following radiation exposure, a loss in efficiency in the production of sperm and complete infertility caused by extreme levels of exposure are often reported. The overexposure to sunlight might be harmful to the sperm count and may temporarily decrease its level. Such occupations as long driving (e.g., long-haul trucking), in which circumstances there is straining of the back, or in which prolonged standing is required (e.g., bakeries), may negatively impact fertility rates. How much drinking and smoking may influence either sperm parameters or reproductive results makes no such agreement (Babakhanzadeh et. al 2020).

Genetic factors

Genetic causes are discovered in 15% of male infertility cases and are divided into two categories: syndromes that are brought about by chromosomal aberrations and single-gene mutations. Chromosomal abnormalities, chromosomal modifications, and non-uniform shuffling of genetic materials at the chromosomal level are some of the major genetic causes of male infertility. Approximately 14% of the cases of azoospermia are caused by chromosomal abnormalities. In oligospermia, they are found in 2% of cases, while the corresponding statistic of the general population is equal to 0.6%. In some cases, there is inheritance; in others, they are acquired. Klinefelter syndrome leads to a majority of genetic anomalies, primarily through sex chromosomes, accounting for about 14% of the aneuploid sex chromosome cases of male infertility.

Epigenetic factor

Acetylation and methylation are two regulatory parts of epigenetic changes that depict gene expression. Gene mutation is the leading cause of male fertility control, and epigenetic mechanisms associated with it have been the primary study area. Throughout spermatogenesis, the germ cells go through a pivotal structural transformation that includes reprogramming the sex-specificity of sperm's organization—one such change being the replacement of histones with protamines. Many studies have reported deviations in the sperm's epigenetic functioning, especially among men with oligozoospermia and oligoastheno-toliquozoospermia (Kumar & Singh 2022).

Procedures for Identifying Genes That Bind with Infertility

There are two general approaches to infertility research for identifying genes involved in infertility: candidate genes and the entire genome. The candidate gene approach consists of identifying genes that harm fertility efficiency in model animals (mainly mice), selecting those genes, and studying their action and outcomes in reducing fertility efficiency in humans.

One has to pay attention to this strategy; the function and expression profile of candidate genes in model animals have been identified before, and these could be used to deduce the gene involved in morphological infertility in humans. C) Whole-genome technique: the latest in the whole-genome studies field, like SNP microarrays and similar advanced genome or exome sequencing technologies, has been looked into to identify genes beneficial to infertility (Bala et. al 2021).

In an SNP or single nucleotide polymorphism, one nucleotide differs from the immediate base and causes diverse phenotypes. SNPs grouped as standard or not common are concerned with the frequency of different alleles. The sequencing platform empowers multilayered sequencing, which can read several millions of DNA parts simultaneously. In addition, exome sequencing is one of the emerging fields that has shaped the understanding of several diseases, such as infertility.

The exome that takes up 1% of the DNA is responsible for 85% of all genetic mutations that may be harmful. Unlike whole genome sequencing, which is a comprehensive analysis of an entire genetic code, exome sequencing is more focused since it only involves analysis of the protein-coding area. While whole-genome sequencing can pick up detrimental mutations throughout the genome, it cannot determine which genes are predisposed to certain diseases. Investigations by GWAS have unraveled SNP variants, which are considered to have a role in spermatogenesis anomalies (Bala et. al 2021).

Fertility Assistance Techniques

The number of definitions that have been issued did not exclude assisted reproductive technologies; they describe a group of procedures that are intended to be used for treating infertility disorders in humans and helping infertile couples have healthy children. This area will go through three stages of progressive processes. An orgasm triggered by sex might help the woman develop more mature eggs, which is an advantage as well; hence, to conceive, you might want to try to time your intercourse correctly. B) The second strategy is to induce ovulation and, using the sperm, inject it into the woman's reproductive system. C) In vitro fertilization: the processive egg and sperm fertilization occurs outside the body, and the embryo transfers to the uterus. Therefore, the outline of this article is given in the subsequent lines (Bala et. al 2021).

DISCUSSION

Presently, approximately 10–15% of all marriages on our planet find themselves dealing with infertility (between 60 and 80 million people). Female infertility can be caused by a hormonal imbalance, anatomical abnormalities, or congenital illnesses, whereas the underlying male factor, according to the research, accounts for 50% of the cases. Male infertility, in the majority of cases, is triggered by spermation disruption, and genetic mutations that are involved in spermatogenesis are among the top causes of the observed cases of idiopathic male infertility. Therefore, I think highlighting the predictive changes and advancing non-invasive treatment strategies looks promising based on the above assessment. The micro-TESE method is precisely the desired gadget for hormonal studies, as FSH will be a biomarker with the highest diagnostic accuracy of sperm production at all testis levels. Due to variation in the testicular tissue, the micro-TESE procedure is aimed at improving the chances of viable sperm retrieval despite the low FSCH levels by collecting small pieces of testicular tissue(Skakkebæk et. al 2022)..

CONCLUSION

Because male infertility is common and not well understood, some instances are a complete mystery in this light. Consequently, the invention of crucial parts and diagnostic and non-intrusive biomarkers is a primary need. It is possible to talk about the tremendous progress scientists have made in identifying noncoding RNAs and studying their interactions about the infertility issue as a problem that has grown over the past couple of years. Nevertheless, these are not enough; it is essential to find other domains of pregnancy flows based on a better comprehension of the complex stages of a human being pregnancy to increase the efficiency of treatments by reducing waste of resources and risks. It might be the time in not the so remote future when causes of male infertility will be diagnosed and then successfully treated as technology advances, and consequently, new treatment plans and treatments are put into place.

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