CAUSES OF FEMALE AND MALE INFERTILITY

DITER ATASIE

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Abstract: *Infertility is defined as the inability of a couple to achieve pregnancy, irrespective of the cause, after a year of unprotected, well-timed intercourse and affects almost 15% of the couples of fertile age. The paper approaches the multiple causes of sterility in both genders.*

Keywords: *sterility, causes*

Rezumat: *Infertilitatea este definită ca şi incapacitatea unui cuplu de a obţine o sarcină, indiferent de cauză, după 1 an de act sexual fără a folosi mijloace contraceptive şi afectează circa 15% din cuplurile de vârstă fertilă. Lucrarea abordează cauzele multiple ale sterilităţii la ambele sexe.*

Cuvinte cheie: *sterilitatea, cauze*

Infertility is defined as the inability of a couple to achieve pregnancy, irrespective of the cause, after a year of unprotected, well-timed intercourse and affects almost 15% of the couples of fertile age. The average time necessary for conception is of about 3 months. 25% of the normal couples conceive on the first menstruation, while 75% during a period of one year.

The reproduction process is a complex mechanism which supposes:

- Monthly release of an egg by the ovaries, process which is called ovulation;
- Spermatozoa of corresponding aspect and quality produced by the male's testicle (*spermatogenesis*)
- Egg fertilization by the spermatozoon, with the formation of the zygote in the fallopian tube;
- Zygote transportation through the fallopian tube to the uterus, its attachment to endometrium (*implantation*) and its subsequent development.

Any affection of the above-mentioned processes may lead to infertility. Infertility may be of female (30%) or male cause (30%). In the rest of the cases, both male and female factors are involved *(couple or mixed infertility)* or, there are cases in which the cause cannot be detected *(idiopathic infertility).* Infertility has a strong emotional charge and should be looked as a problem that affects the couple.

Sterility in female gender may have multiple causes:

Anomalies of the reproductive tract:

I .**<u>uterine anomalies</u>**

- Uterus bicornis, bipartite uterus
- Plurimalformative syndromes (for example: McKusick/Kaufman syndrome with cardiac, renal, digital anomalies)
- MURCS association (uterine, renal anomalies, anomalies of the cervical spinal column) Rokitansky sequence (uterine, renal anomalies)

II. **<u>anomalies of the cervix, vagina</u>** – cervix aplasia, septate vagina

Ovarian dysfunction:

- Disorders in the sexual hormones synthesis – suprarenal congenital hyperplasia, type I (excess of androgens, lack of cortisol and aldosterone)
- Ovarian dysplasia - Stein-Levinthal syndrome (polycystic ovary, hirsutism)
- Other endocrine diseases – hypophisary deficiency (FSH, LH deficiency)
- Systemic diseases, chronic affections – cerebral dysfunction, infections, autoimmunity that perturbs the hypophysary stimulation of the ovaries.

Ovarian dysgenesis:

Chromosomal anomalies:

- Turner syndrome (small waist, palmate neck, reduced secondary sexual characters, primary amenorrhea)
- Mixed gonadic dysgenesis 45,x / 46,xy
- Certain cases of trisomy x or polysomy x
- Deletions or autosome-x translocations

Inflammations of the reproductive tract:

- infections (gonorrhoea, syphilis, Chlamydia) that produce tubal obstruction
- endometrioses (endometrial tissue outside the uterus) that may produce abnormal menstruations, pelvic pains

Out of the above-mentioned causes, dysgenesis or the ovarian dysfunction represent a percentage of 40% of infertility causes, tubular obstruction – 40% and the anomalies or the diseases that affect the reproductive tract - 20%. Genetically speaking, the critic regions correlated to the ovarian dysgenesis are: POF 1 (Xq 26-q28) and POF 2 (Xq13.3-q22), where the genes necessary for the normal development of the ovaries could be found (for example: the gene DIAPH2 in the region POF2).

The causes that lead to male sterility, in terms of frequency, are represented by:

Anomalies of the reproductive tract (48%):

- varicocele (abnormal dilatations of the veins of the spermatic cord that may compress the deferent ducts)
- cystic fibrosis (absence of the deferent ducts, pulmonary and gastro-intestinal affection)
- more malformative syndromes with hipospadias or urethra stenosis (for example: McKusick/Kaufman syndrome)

Testicular dysgenesis (18%):

I. chromosomal anomalies – Klinefelter syndrome (47,xxy)-high waist, reduced secondary sexual characters, non-functional small testicles

II. inadequate masculinization (masculine pseudohermaphroditism)

- gonadic dysgenesis 46,xy through mutations of the gene SRY with feminine phenotype.
- feminized testicle (feminine phenotype, androgen receptors deficit)

III. congenital anomalies – many chromosomal and mendelian syndromes (criptorhidism, micropenis, normal spermatogenesis).

Testicular dysfunction (9%):

I. disorders in the sexual hormones synthesis

- Reifenstein syndrome (partial deficit of androgen receptors)
- Suprarenal congenital hypoplasia (deficit of androgen, cortisol, androgen)

II. other endocrine anomalies – Kallman syndrome (hypophysary dysfunction, anosmy)

III. environment agents – mumps, hyperthermia (intraabdominal testicles), radiations that may produce hypoplasic testicles, spermatogenesis blocking

IV. abnormal spermatogenesis

– Kartagener syndrome (azoospermia, bronchial dilatations, situs inversus)

– Structural chromosomal anomalies (oligo-azoospermia)

Inflammations of the reproductive tract (25%):

- infections (gonorrhoea, syphilis, Chlamydia, TBC) which produce the obstruction of the deferent ducts.

The genetic causes are relatively frequent in male sterility. Chromosomal anomalies affect 15% of the individuals with azoospermia and 6% of those with severe oligospermia. Chromosomal anomalies in terms of number, which affect the testicular structure and function are represented especially by Klinefelter syndrome (47,xxy). The only trisomies that may reach the reproductive age are trisomy 21 and trisomy 8, both of them being associated to male sterility. An important part in establishing male infertility is played by the unbalanced structural anomalies of the Y chromosome and by the balanced structural anomalies of the autosomes.

The most frequent unbalanced anomalies of the Y chromosome are the microdeletions Yq. The majority of them are de novo and were identified in 3-18% of the men with azoospermia and in 5-10% of those with severe oligospermia. The presence of a microdeletion of the Y chromosome brings about testicular anatomopathological alterations that vary from the complete absence of the germinal cells (Sertoli cell-only syndrom) up to spermatogenesis blocking. The presence of the microdeletions of the Y chromosome may be emphasized through FISH technique (fluorescence in situ hybridization) or through PCR technique (polymerase chain reaction).

Balanced structural chromosomal anomalies represented by inversions, translocations (mutual, Robertsoniene), insertions determine the male sterility, affecting the formation of the sex vesicle, because of the presence of the derivative chromosome (chromosomes). The inversions of chromosomes 1, 2, 3, 5, 6, 7 and 9 were associated to male sterility, their incidence being 8 times higher than in normal people. The mutual translocations and the insertions may be encountered in 1% of male sterilities, producing spermatogenesis blocking, through the alteration of the fertility configuration. Therefore the cytogenetic exploration is necessary for each man with abnormal spermogramme, in which case an infectious etiology is eliminated.

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