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Review Article

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Physiological and hormonal study of women infertility

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Abstract

Possibility of pregnancy within one year of sexual encounter and contraceptive use. Infertility is classified into two basic types: sterility, which means that there is no possibility of pregnancy at all. Relative infertility or sub-fertility, which means there is an obstacle that prevents pregnancy that should be treated and divides relative infertility into three types, namely primary infertility, secondary infertility, and unexplained infertility. Factors causing infertility associated with females are responsible for (50-40%) of cases, while other factors are attributed to husbands in addition to common causes among females. And males, as well as unexplained causes of infertility. There are multiple reasons causing infertility, including hormonal, hereditary, infectious, anatomical, environmental, etc., these factors have variable affects. The psychological causes of infertility are of great importance as researches have proved that there are many psychological factors that cause women's infertility such as failure of sexual intercourse or to the inability to produce an egg. Failure to fertilize within one year does not mean the women's failure to conceive after this period, since (15-50%) of wives get pregnant after the first year of marriage, and the failure to conceive before the passage of the first year of marriage is not a mark of sterility, so after the first month the pregnancy possibility is (15 -20%) and after the sixth month it is (50-70%), but after the passage of the year, it is (80-90%).

Keywords Sterility, Uterus, Ovaries, Hormonal control, Disorders of the Pituitary Gland

Introduction

Infertility

It is known that it is not possible to become pregnant after at least one year of sexual intercourse without the use of contraceptives, and it occurs in (10-15%) among married people and approximately (50-40% of cases) the woman is responsible for this (Gnothet *al.*, 2005, and infertility may also be known as a disease that has no treatment in cases that are caused by severe congenital and genetic diseases of the reproductive system, such as cryptorchidism, its severe atrophy, the absence of the ovary, anomaly, or other similar cases in which there is a severe defect in the formation of the organ All reproductive causes sterility (Symonds & Symonds, 2004). Infertility is classified into two basic types, which are

absolute sterility, which means an impossible pregnancy for reasons that are not treatable, including lack of formation of the uterus or ovaries, for example. Relative infertility or sub-fertility, which means that there are barriers to pregnancy that can be treated (Al Ras, 2001)

Relative infertility has three types

Primary infertility

It is defined as the woman's inability to conceive after a full year of regular sexual intercourse, and in general, (50%) of husbands will be able to conceive during the second year (Thomas *et al.*, 2007).

Secondary infertility

It is known as the inability of a woman to conceive after one or more successful births, and it's caused by the occurrence of repeated miscarriages, complications of dystocia, endometriosis, or blockage of tubes, and these may occur in women with primary infertility as well (Balasch, 2000).

Unexplained infertility

It affects women without showing hormonal or hereditary reasons, and the true causes behind this type of infertility are not known.

Anatomical and physiological structure female reproductive system

The female reproductive system includes the ovaries, fallopian tubes (tubes), uterus, and vagina, the ovaries of a newborn girl contain approximately two million eggs. However, this number gradually decreases to reach (300,000) at puberty, of which only (300) eggs reach the stage of maturity and ovulation during the fertile period, that is, between puberty and menopause, at the rate of one egg per month. Several glands control the functions of the reproductive system by secreting a group of hormones. At the forefront of these are the pituitary gland, which is located inside the skull, below the brain, and which plays the primary and leading role in controlling most other glands. The pituitary gland, in turn, is controlled by a region in the lower brain called the hypothalamus (Guyton & Hall, 2006).

The reproductive system includes the following parts

Ovaries

They are two oval-shaped glands located on each side of the uterus. The ovary itself consists of an inner layer called the medulla and an outer layer called the Cortex cortex. This cortex surrounds the pulp from all sides except for the Hilar area. These portions are scattered (scattered) throughout the stroma, which contain connective tissues, intercellular cells, blood vessels. The pulp of the ovaries also contains large blood vessels and other connecting parts (Boron & Boulpaep, 2003).

fallopian tubes

These tubes expand from the body of the uterus to the ovaries, and each tube represents the connecting tube from uterus to ovary. Each tube is lined with cells that help push the egg out when it comes out of the ovary and into the inner uterine cavity (Monga, 2008).

Uterus

It is an upside down pear-shaped muscular organ consisting of the fundus, the corpus body, and a narrow part near or facing the back called the cervix, which is lined with a layer of nourishing tissue and blood cells known as the endometrium, which thickens before the onset of period and then falls during

the start of the menstrual cycle, a new layer is formed (Boron & Boulpaep, 2003).

Menstrual cycle

The menstrual cycle begins when the girl reaches the puberty phase, and it repeats every (26-32) day, and the 28-day cycle is the typical cycle for a woman, and the cycle continues until the woman reaches menopause. This is why the menstrual cycle is known as the series of events that are repeated in the female once Almost every month.

The characteristics of a regular menstrual cycle are

- The delivery of only one single egg that is naturally released from one of the ovaries every month, so it is normal for a single embryo to begin its development in the event of pregnancy.
- The inner lining of the uterus is prepared in a direction that serves the implantation of the fertilized egg within the required time of the month, and the moment a normal girl reaches puberty until the menstrual cycle begins, and the hypothalamus, pituitary, ovaries and endometrium interfere in organizing this cycle (Guyton & Hall, 2006).

The phases of the menstrual cycle are divided into

1. According to the stages that occur in the ovary on

The follicular phase is in days (1-8) of the cycle and during which the ovarian follicles mature (Reyftmann & Ovtchmikoff, 2003)).

- The ovulation phase takes place on the day (14) of the cycle, in which the egg is thrown from the ovarian follicle (Grazul *et al.*, 1996).
- The luteum phase occurs on days (15-28) of the cycle, and the luteum is formed (Nader, 2010).

2. According to the phases that occur in the womb

The proliferative phase or Preovulatory phase happens during the follicular phase of the ovaries where the endometrium is under the release of the estrogen hormone (E2), which causes the proliferation of glands in the endothelium (Molitch, 1995).

Secretory phase or postovulatory phase: occurs after ovulation, when the endometrium is under the influence of the hormone progesterone, which stimulates the production of secretions in the endometrial gland (Nader, 2010).

- Menstrual phase: occurs after the luteum ceases to secrete the hormones estrogen and progesterone at the end of the luteal phase of the ovaries, which leads to the death of cells of the surface layer of the endometrium as a result of a shortage or stopping of blood flow, which causes bleeding and spotting (Montgomery, 1998).

Hormonal control of the menstrual cycle

The process of secreting hormones from the brain begins in an area called the hypothalamus that secretes the hormone (GnRH) that stimulates the pituitary gland to secrete the hormones FSH and LH in pulses. The estrogen hormone declines at the start of the cycle, as shown in GnRH secretes the hormone (GnRH), which in turn stimulates the production of the hormones FSH and LH, which stimulate the ovaries to start producing eggs. When the egg is formed, the hormone estrogen is secreted, and this hormone begins to rise gradually in the blood. During this period, one of the eggs is ready to mature more than the others and begins to grow rapidly and secrete the hormone estrogen in a greater amount. The high level of this hormone reduces the secretion of FSH and stimulates the rush of LH and FSH, as well as inhibits the inhibin that is secreted from granulosa cells (Hohmann *et al.*, 2005; Chandramouli, 2003).

The raise in the level of the hormone estrogen helps the egg maturation more and also helps the growth of the uterine lining, and the raise of the estrogen hormone continues until it reaches a stage where it leads to a sudden raise in the concentration of LH approximately in mid-cycle, and this raise in the concentration of LH helps the final maturation of the egg inside the vesicle After (36) hours of this increase in the concentration of LH, ovulation takes place and the egg is ready for fertilization, and in the regular natural cycle the date for the increase in the concentration of the hormone LH is day (12) and ovulation per day (14) and after the egg is released, the vesicle shrinks to form a luteal body On the outside of the ovary, which continues to secrete the hormones estrogen and progesterone, which work together to reduce the secretion of FSH and LH from the pituitary gland, If fertilization of the egg occurs, the corpus luteum continues to grow and secrete the hormones estrogen and progesterone to prepare the lining of the uterus to receive the fertilized egg, and after the first trimester of pregnancy the corpus luteum disappears and the placenta begins to secrete estrogen and progesterone, but if pregnancy does not occur, the luteum disappears after ten days of ovulation and begins The concentration of the hormones estrogen and progesterone falls, and two weeks the endometrium shears and menstrual circulation occurs (Gillmer & Hurley, 1999; Seeley *et al.*, 1998). The decrease in the concentration of the hormones estrogen and progesterone leads to an increase in the concentration of hormone (GnRH) and a new menstrual cycle begins.

Causes of female infertility

Hypothalamic Disorder

Hypothalamic disorder leads to disturbance of the pituitary glands functions, and this disorder could be resulted from diseases affecting the middle brain region such as meningitis, tumors, or a fracture of the base of the skull as a result of an accident, and the reason might be due to a woman's mental state disorder or her taking some medications used to treat high blood pressure (Leos, 2003).

Pituitary gland disorders

Small tumors may form in or near the pituitary gland that could lead to a defect in the functions of this gland, the severity of the damage depends on the location and size of the tumor and on the number of hormones it secretes. (75%) of cases may be accompanied by menopause or significant weight gain (Leos, 2003).

Uterine disorders

The most important disorders that occur in the womb are:

1. The presence of tumors, polyps, or adhesions as a result of infections, previous surgical interventions, or congenital anomalies, and all of this hinder the implantation of the fertilized egg in the endometrium to grow and enlarge. Michel, 2002).

2. A defect in the cervix is estimated to be the reason (5%) of female infertility cases, as the cervix is the first barrier that sperm must pass its secretions to reach the uterus, and any change in the order of these cervical secretions or cervical mucus may It hinders the entry of sperm, prevents them, or even kills them, due to the presence of previous infections or surgeries in the cervix or the influence of hormonal disorders or even birth defects which are few and rare (Speroff & Fritz, 2005; Haile, 1990)

3. Endometriosis: Endometriosis: Endometrial proliferation is characterized by the emergence of the endometrial glands and stroma glands outside the uterus in the pelvis and lower part of the abdomen, accompanied by pelvic pain and infertility (Speroff & Fritz, 2005). Other than the body (Trickey, 2003).

Approximately (10%) of couples are infertile by endometriosis and (30-40%) of cases with endometriosis are infertile (D'Hooghe *et al.*, 2003; Cramer & Missmer, 2002). Although it affects women at any time from puberty to menopause, it is more frequent during a woman's sexual activity. And pelvic pain is the most common symptom, as it intensifies during the menstrual cycle, specifically in the last days, with blood in the urine, back pain, and abdominal pain accompanied by painful intestinal cramps (Chehval & Purcell, 1992).

4. Fibroids: They are tumors in the uterine muscle that may cause a protrusion in the uterine gap depending on their location, and they are not a reason of infertility in most cases unless they greatly affect the uterine cavity, or if there are many fibroids (Leos, 2003 Mukhatar, 2006; -A1).

5. Fibrosis of the uterus: This occurs after a woman has had Endometriosis, and the diagnosis is made by H.S.G. hysteroscopy, and a Hysteroscope may be useful in treating this condition (Leos, 2003) (Mustafa, and AL-Samarraie, 2020).

Fallopian tube disorders

If a defect occurs in the fallopian tube, this may lead to infertility, as the fallopian tube is the way that connects the ovary to the uterus, and in this channel, the first step of pregnancy takes place as every month an egg moves from the ovary to the uterus and during its trip through the fallopian tube is fertilized from Before the sperm and when there is any obstruction or narrowing of the fallopian tubes, this is an important reason of infertility (Leos, 2003; AL-Mukhtar, 2006).

It is most likely the result of:

1. Infection caused by both bacteria and viruses, usually transmitted through sexual contact and these infections usually lead to damage to the fallopian tubes (Shevell *et al.*, 2005).
2. The most common abdominal diseases are appendicitis and colitis, which lead to inflammation in the abdominal cavity that may affect the fallopian tubes and lead to scarring and blockage (Healy *et al.*, 1994).
3. Previous surgeries This is one of the most important causes of diseases that affect the fallopian tubes, as surgery of the pelvis or abdomen can lead to adhesions in the canal, preventing the passage of eggs through it (Belker *et al.*, 1991).
4. An ectopic pregnancy is a pregnancy that occurs in the canal itself and may cause harm to her and may threaten a woman's life. Morgan & Siddighi, 2005; Steptoe *et al.*, 1980).
5. Birth defects In rare cases, women may be born with abnormalities of the fallopian tubes that are occasionally associated with the uterus (Visscher, 1994).

Folliculitis disorders

These include

- Follicle non-burst syndrome and this condition occur in females who produce normal follicles that contain the egg every month, but these follicles do not burst and remain inside the ovarian follicle (Beaker, 2001).
- The scarring that occurs in the ovaries as a result of physical factors such as heat or as a result of repeated surgeries leads to incomplete growth of the Kraff follicle and ultimately failure to complete the ovulation process (Peterson, 2002).

Disturbances in the ovulation process

It is a group of pathological factors that inhibit the ovulation process or hinder the release of a mature egg, which reduces the possibility of pregnancy, including:

Polycystic Ovary Syndrome

Polycystic ovary syndrome (PCOS) is one of the biggest health problems in women, resulting from the disturbance of the hormonal system in the woman's body, and it is a

common cause of anovulation and sterility (Alaf, 2000 Adolescent Medicine, 2000; Silva *et al.*, 2001; Gurnee *et al.*, 2009). Besides, it is considered one of the most common diseases that women are exposed to, so that (30%) of the world's women are infected with it (Desloover& Ernst, 2001). Hirsutism, polycystic ovaries, obesity, and infertility are hallmarks of the disease (Chabbert *et al.*, 2006). As the outer layer of the ovary coheres in this disorder, preventing the ripe egg from emerging from the ovarian layer, without this egg being released, the pregnancy process does not take place (Dahlgren *et al.*, 1992), as well as enlargement of the ovary as it increases in size, and it can reach three Times of its size, an increase in the concentration of ovarian tissue in the center of the ovary around the cysts is observed (Scholes *et al.*, 2002). The severity of this condition varies among patients, in some patients, the symptoms are almost not noticeable, and in others, the symptoms are severe and clear and have an effect on fertility (Sturt&Ashmong, 2000).

P.O.F, Premature ovarian failure

It is the loss of ovarian fertility before the age of (40) years in affected women, and it is also called hyper gonadotropinism (Hubayter, 2009).

The main ovarian function in providing eggs for women is until the age of (51) years. As for ovarian failure, it becomes unable to produce eggs and this happens as a result of a physiological defect, and some cases of infertility are resulting from these signs as some women with infertility do not have ovulation and This is called primary ovarian failure, and the phenomenon of osteoporosis in women may be due to premature ovarian failure due to the loss of estrogen, and there is also the possibility of an increased risk of heart disease.

Amenorrhea

This term refers to the interruption of menstrual bleeding (Thibodeau& Patton, 2003). It is a trait in females before puberty, pregnant women, and after menopause or old age (Al-Jabouri, 2006) (Mustafa, and AL-Samarraie,2020).

Menopause is one of the main problems in females at the age of reproduction or reproduction, as about (10-20%) of women who suffer from infertility have a state of menopause (Aldo, 2001). It is one of the dangerous diseases that impede the reproductive process that occurs due to genetic abnormalities, imbalances in the endocrine system, and psychological and environmental conditions. To facilitate accurate and immediate work, obtaining a complete history and a detailed physical examination is an important necessity (Jacobs, 1996).

Anovulation

It is one of the most common causes of female infertility, and it is found in almost (40%) of them. It is easily diagnosed by the date of the menstrual cycle, which is an effective screening tool for assessing ovulation.

An absence of menstruation is indicative of a lack of ovulation (Hamilton-Fairley, 2004).

Ovulation-related disorders were classified based on the 2003 World Health Organization (WHO) classification (2003) into three groups:

Group I: Includes women who have a dysfunction between the pituitary gland and the hypothalamus, caused by menopause-related to stress, dietary disorders, and strenuous exercise, in addition to Kallmann's Syndrome.

Group II: Includes women who have an organizational defect between the ovaries, the pituitary gland, and the hypothalamic-pituitary-Ovarian body, and who suffer from impaired Eugonadotropic ovarian dysfunction with various degrees of anovulation and oligomenorrhea such as polycystic ovary syndrome.

Group III: includes women who have an organic deficiency, ovarian immaturity, or ovarian resistance, and those patients respond in a simple way to the possibility of inducing ovulation (Abdul Razzaq, 2010).

Conclusion

The psychological causes of infertility are of great importance as researchers have proved that many psychological factors affect women and lead to the failure of sexual intercourse or to the inability to produce an egg. Failure to fertilize within one year does not mean the wife's inability to conceive after this period, since (15-50%) of wives get pregnancy after a year of marriage, and the failure to conceive before the passage of the first year of marriage is not evidence of sterility, so after the first month the rate of pregnancy is (15-20%) and after the sixth month it is (50-70%), but after the passage of the year, it is (80-90%).

Authors' contributions

Aseel Ahmed Mustafa, Ansam Hussein Ali, Mohammed Ahmed Mustafa and Marwan Q.AL-Samarraie have contributed significantly to the conception and design of the study, the interpretation of data, and the drafting and revision of the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

The authors hereby declare no conflict of interest.

Consent for publication

The authors declare that the work has consent for publication.

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