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Infertility – A Global Critical Issue in reproductive system

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Abstract

Infertility is defined as a "disease of the reproductive system" and results in disability. Despite the high burden, couples and individuals, who desire but are unable to achieve and maintain a desired pregnancy, have needs which are not being addressed, especially in lower resource settings worldwide. Yet, the field of reproductive medicine and endocrinology is rapidly growing, with success stories that have resolved infertility and fertility problems – from the most simple fertility awareness methods to more advanced innovations. WHO has calculated that over 10% of women are inflicted – women who have tried un successfully, and have remained in a stable relationship for five years or more. Estimates in women using a **two** year time frame, result in prevalence values 2.5 times larger. The burden in men is unknown. However, in most cases, women are held responsible for the same without proper diagnosis. Statistically, female factors contribute to about 40–60% of infertility cases, whereas 20–40% of infertility cases are due to factors contributed by males, of which, deficiency in semen quality is the major cause which accounts for 40–50% of infertility cases. A decrease in semen quality has been reported which can be due to lifestyle changes, occupational exposures to chemicals, heat, and stress.

Keywords: Infertility, Fertility, Reproductive System, Diagnosis, WHO, Embryonic, Miscarriage.

Introduction

Infertility means not having children after one year of regular sexual life without usage contraception techniques. Infertility is one of the major health care problems in all societies worldwide. The average prevalence of infertility in developed countries is 3.5-16.7% and in developing countries is 6.9-9.3%. Causes of infertility are numerous such as anatomical, physio

logical and genetic factors. Many environmental and acquired factors also influence fertility and may lead to infertility. Menstrual and ovulation dysfunction and uterine factors are the most common causes of impairment in fertility. Etiology of infertility prevalence and patterns of causes of infertility in different regions are diverse. This discrepancy is due to existence of differences in environmental conditions associated with reproductive behaviors, such as age at marriage, environ mental pollution, smoking and alcohol abuse, changing in lifestyle and diet.

Possible Causes of Infertility in Women are

Ovulation failure

It may happen due to primary ovarian insufficiency or polycystic ovary syndrome.

Endocrine disorders

Hormonal problems like thyroid (production of less or more hormones which are not required).

Lifestyle

It is also one of the causes of infertility. Smoking, excess eating of junk, too much of exercises, age are the causes.

Environmental factors

It is also one of the causes of infertility.

Infections

Infections also cause infertility in both men and women like STIs (Sexually Transmitted Infections), chronic infections (Human papilloma virus)

Egg mature failure

An immature egg may not release in the right time, may not make it down to the fallopian tubes, or may not be able to be fertilized.

Implantation failures

Failures like Genetic defects in the embryo, thin endometrium Embryonic defects, Endometriosis, Progesterone resistance, Scar tissue in the endometrial cavity.

Endometriosis

Research has found a connection between infertility and endometriosis. Studies proposed that women 30%-40% of women with endometriosis are infertile. This cause is not yet known.

Uterine fibroids

Non-cancerous cells growth in the uterus causes infertility.

Autoimmune disorders

In this condition reasons are yet known properly for the cause. But the antibodies which make in men and women attack the sperms or other reproductive organs.

Irregular menstrual cycles

This condition may have several reasons. But irregular periods cause infertility.

A woman is having more possibilities fertile in her early 20s. The chance a woman can get pregnant drops drastically after age 35. The age of fertility starts to decline which varies from woman to woman. Miscarriage, infertility problems rates increase after 35 years of age.

Possible causes of infertility in men are

- Decreased number of sperm
- Blockage that prevents the sperm from being released
- Defects in the sperm
- Birth defects
- Cancer treatments, including chemotherapy and radiation
- Exposure to high heat for prolonged periods • Heavy use of alcohol, marijuana, or cocaine
- Hormone imbalance
- Impotence
- Infection

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- Medicines such as cimetidine, spironolactone, and nitrofurantoin
- Obesity
- Older age
- Retrograde ejaculation
- Scarring from sexually transmitted infections (STIs), injury, or surgery
- Smoking
- Toxins in the environment
- Vasectomy or failure of vasectomy reversal
- History of testicular infection from mumps.

Polycystic Ovarian Syndrome

Polycystic ovary syndrome, or PCOS, is the most common cause of female infertility related to the infertility anovulation. It is well known that many of the symptoms of PCOS are present before a girl has her first menstrual period and 5-10% of females age 18 to 44 are affected by PCOS in some way. PCO syndrome results from a combination of factors, including genes and environmental features. Many women are not aware that they have PCOS until they follow a diagnostic procedure on infertility or menstrual and ovulation irregularities such as amenorrhea or oligomenorrhea, heavy and anovulatory periods. The PCOS symptoms at 70% is hirsutism, severe acne, that does not respond to conventional treatments or that remains in spite of treatment, very oily skin and patches of thickened, dark brown or black skin, and 70-95% cysts on the ovaries. The hormone levels are out of balance in women with PCOS and they have, in fact, higher than normal levels of androgens and may have lower than normal levels of Estrogen. The high levels of androgens can cause problems with ovarian follicle growth and development, make immature follicles on the ovaries forming large lumps or cysts. The current treatments for PCOS includes lifestyle changes, such as eating a lower calorie diet, losing weight, and getting more physical activity, oral contraceptives, antiandrogens and insulin sensitizing agents. Women with PCOS to succeed pregnancy are treated with clomiphene citrate, metformin, gonadotropins and can also try other forms of assistive reproductive technology, such as egg donation and in vitro fertilization.

Obesity in Early Adolescence Alters Sex-Specific Hormone Production

Research shows that obesity is associated with increased production of androgens in adult women and during late female puberty or adolescence. Androgens are often called "male hormones" because males' bodies make more of them than do women's bodies, but both males and females need certain levels of androgens for normal health. Changes in hormone levels, including increases in androgens, can disrupt female reproductive cycles and lead to infertility.

In research funded by the NICHD Reproductive Sciences (RS) Branch, investigators studied whether obesity prior to and during early puberty also increased androgen hormone production. Researchers compared androgen levels in normal-weight and obese girls between ages 8 and 14 years. Girls who were obese had higher androgen levels throughout puberty compared with normal-weight girls. The results of this study demonstrate that childhood obesity affects normal hormone production and that these early hormone level changes could influence fertility later in life. [Obesity and sex steroid changes across puberty: evidence for marked hyperandrogenemia in pre- and early pubertal obese girls.

High Dietary Fiber Intake Reduces Fertility in Women

Increased fiber intake has been a recent focus of women's health efforts because research findings showed

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that high-fiber diets were connected to lower breast cancer rates. The effect may be the result of fiber reducing levels of the hormone Estrogen, which is an important factor not only in breast cancer, but also in reproduction. DESPR researchers aimed to determine the effects of such high-fiber diets on women's reproduction. The researchers evaluated data from the BioCycle Study, a prospective cohort study conducted from 2004 to 2006 that included 250 women. The participants were between 18 and 44 years old, and they contributed daily data over two menstrual cycles.

The researchers found that dietary fiber intake lowered reproductive hormone levels and was associated with ovulation failure. Absence of ovulation is a leading cause of female infertility. This study suggests that diet could be one factor that contributes to infertility in some women.

Cigarette Smoking Affects Women's Reproductive Hormones

Research has implicated cigarette smoking in lower fertility in women, specifically in delayed conception, but the reason that this occurs is unknown. In another analysis of data from the Bio-Cycle Study, DESPR researchers examined the effect of cigarette smoking on women's reproductive health. Researchers measured women's reproductive hormones, including estradiol, progesterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH), across the menstrual cycle. The levels of these hormones, which vary during the menstrual cycle, are critical for a woman's reproductive health. In the study, researchers found that smokers had abnormal increases in FSH and LH. High levels of these hormones are common during menopause and are associated with reduced fertility. This research points to a possible explanation for the adverse effect of smoking on women's fertility and reproductive health.

Effects of the Environment on Men's and Women's Fertility

Higher blood levels of cadmium in females, and higher blood levels of lead in males, delayed pregnancy in couples trying to become pregnant, according to a study by researchers at the National Institutes of Health and other academic research institutions.

Cigarette smoke is the most common source of exposure to cadmium, a toxic metal found in the earth’s crust, which is used in batteries, pigments, metal coatings and plastics. Smokers are estimated to have twice the levels of cadmium as do non-smokers. Exposure also occurs in workplaces where cadmium-containing products are made, and from the air near industrial facilities that emit cadmium. Airborne cadmium particles can travel long distances before settling on the ground or water. Soil levels of cadmium vary with location. Fish, plants, and animals absorb cadmium from the environment, and all foods contain at least low levels of the metal.

Lead, a toxic metal also found in the earth’s crust, is used in a variety of products, such as ceramics, pipes, and batteries. Common sources of lead exposure in the United States include lead-based paint in older homes, lead-glazed pottery, contaminated soil, and contaminated drinking water. Exposure to these metals is known to have a number of effects on human health, but the effects on human fertility have not been extensively studied, especially when studying both partners of a couple.

Perspectives on the Biological Role of Human Prostasomes

Prostasomes are extracellularly occurring organelles which are secreted in human semen by the prostate gland. Prostasomes have several known biological activities, but their physiological function is still unclear. The motility-stimulatory effect of prostasomes on

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cryopreserved spermatozoa was further studied by supplementing the swim-up medium with seminal prostasomes, and with prostasomes purified from a PC-3 prostate cancer cell line (PC-3 prostasomes), on fresh spermatozoa. The recovery of motile spermatozoa after swim-up increased by 50% when the swim-up medium was supplemented with prostasomes. The PC-3 prostasomes bore a functional resemblance to seminal prostasomes as regards various expressions of sperm motility promotion. Prostasomes proved to have potent antibacterial effects. The effects were not strictly confined to Bacillus megaterium since a few other bacteria were also sensitive. The high percentage of patients with anti-prostasome antibodies showed that prostasomes could be one of the major targets for antispam antibodies (ASA). The results demonstrate that ASA in serum of infertile men and women recognize prostasomes as antigens, and that polyclonal antibodies raised against prostasomes agglutinate human sperm to zoa. This suggests that prostasomes contribute at least partly to immunological infertility.

Chlamydia trachomatis as a risk factor for infertility in women and men, and ovarian tumor development

Chlamydia trachomatis in women is a risk factor for tubal factor infertility and extra uterine pregnancies, but the impact of a C. trachomatis infection on male fertility is unclear. It is also hypothesized that persistent infection with C. trachomatis, or other microorganisms, might initiate/promote ovarian tumor development. The aims of the thesis were to study whether C. trachomatis serum antibodies in women and men had an impact on infertility diagnoses, semen characteristics, pregnancy rates and pregnancy outcomes; furthermore, to explore associations of C. trachomatis, and Mycoplasma cancer and borderline ovarian tumors, as well as the presence of C. trachomatis bacteria, and other microorganisms, in ovarian tissues. C. trachomatis IgG and IgA antibodies in the man substantially decreases the chances of the infertile couple to achieve pregnancy and are associated with subtle negative changes in semen characteristics. C. trachomatis IgG and cHSP60 IgG antibodies in the woman are risk factors for tubal factor infertility. Prospective plasma cHSP60-1 IgG antibodies are associated with type II ovarian carcinomas, but C. trachomatis bacteria, or the other microorganisms studied, could not be detected in benign, borderline or malignant ovarian tissues. Lifestyle and Reproductive Health among Women prior to Conception

Health and lifestyle is of great importance when women intend to become pregnant, as well as during pregnancy. It is crucial that people seeking for infertility are aware of which lifestyle changes they can undertake to enhance the likelihood of treatment success. The overall aim of this project was to investigate the extent to which women comply with recommendations for lifestyle changes during the time they try to conceive and during early pregnancy and the impact of lifestyle risk factors on treatment results in sub-fertile women.

Lifestyle factors and mental health at baseline and lifestyle changes women made while they were trying to conceive were assessed by a study-specific questionnaire. Both pregnant women and nonpregnant sub-fertile women in the mid-Sweden region were included. The level of pregnancy planning was associated with planning behavior. Only one-third of all pregnant women took folic acid one month prior to conception, 17% used tobacco daily and 11% used alcohol weekly three months before conception. In the sub-fertile non-pregnant women cohort, 13.2% used tobacco daily, 13.6% drank more than three cups of coffee per day, and 11.6% consumed more than two glasses of alcohol weekly. Among sub-fertile women,

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one-third were overweight or obese. Pregnant women who conceived with Assisted Reproductive Technology (ART) reported lower rates of anxiety and depression symptoms compared to sub-fertile women. They also showed no difference in depression and anxiety symptoms compared to women who conceived naturally. Among sub-fertile women undergoing their first IVF treatment cycle, an independent as well as a cumulative effect of smoking and BMI on the number of aspirated oocytes and the proportion of mature oocytes was observed, especially among women with low ovarian reserve. In conclusion, approximately half of the women in our studies retained habits with negative effects on fertility. This is worrying because the harmful consequences of negative lifestyle factors are well established. These negative lifestyle factors are easy to detect and adjust at an early stage in the assessment process and might allow for optimization of fertility treatment and pregnancy outcomes.

Strategies for infertility treatment in men with azoospermia

Treatment of severe male infertility has been restricted. With the introduction of intracytoplasmic sperm injection (ICSI), infertile men have been given new hope of achieving genetic fatherhood.

Method-The relationship between sperm recovery following percutaneous epididymal sperm aspiration (PESA), TESA and testicular sperm extraction (TESE), as related to testicular volumes, serum levels of FSH and chromosome analysis was analyzed retrospectively in men with obstructive and non-obstructive azoospermia (NOA). Predictive factors for sperm recovery were investigated utilizing ultrasonography and Doppler flow imaging, by which intratesticular echogenicity and blood flow resistance were evaluated. Additionally, Fluore scence in situ hybridization (FISH) of lymphocytes and buccal cells was used to detect possible 47, XXY/ 46, XY mosaicism in 19 men with non-mosaic Klinefelter's syndrome. Sperm recovery and fertilization/pregnancy rates were analyzed retrospectively in 56 men with obstructive azoospermia and NOA after 3-6 repeated TESA procedures. Physio logical consequences were investigated pro spectively in 35 azoospermia men following TESA. Serum levels of FSH, testosterone and antispam antibodies (ASA) were analyzed preoperatively, as well as 3- and 6-months post TESA. Intratesticular texture was compared before and 3 months after TESA. The outcome of the 1293 resulting pregnancies was investigated in 6 subgroups divided according to sperm origin, sperm quality and the use of cryopreservation of pre-embryos.

Results

In all men with obstructive azoospermia and 39% of men with NOA, sperm retrieval was successful following the completed diagnostic sperm recovery work-up. An increased frequency of chromosomal aberrations (8%) was seen in patients with NOA. His to pathology seemed to be the best predictor of successful sperm recovery in men with NOA, including men with Klinefelter's syndrome. TESA can be repeated several times in azoospermia men, with the recovery of mature spermatozoa resulting in pregnancies. The time interval between procedures seems to be of little importance. Postoperative hematomas occurred in 6.6% of testes and 11.4% of patients following TESA, with no tendency toward persistence. Hormone profiles were not affected and formation of ASA was not observed subsequent to TESA. Neither sperm origin nor sperm quality had any influence on obstetric outcome after ICSI.

Conclusions

Diagnostic sperm recovery and histopathology seem to be the best predictors of successful sperm recovery in

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subsequent ICSI cycles in patients with azoospermia. No azoospermia men should be denied an infertility work-up based on clinical or laboratory findings. Karyotyping of all men with NOA is recommended before ICSI treatment. TESA seems to be a safe method of sperm retrieval, resulting in minimal physiological con sequences. Neither sperm origin nor sperm quality seem to influence the obstetric outcome following ICSI. Multiple births are still the main concern.

Female infertility is the major cause of lack of reproducibility and conception. 25% of the couples are tracing this problem. Many reasons are sorted out for female infertility but through proper diagnosis and counseling for treatment of female infertility can be only ray of hope. Review reveals extensively all the major reasons and causes for infertility. All these problems can surely be sorted out to come out this problem. Female infertility can surely be treated with medicines, minor surgical operations, laparoscopic procedures, hormonal therapy and prevention of preconception failure. The review is helpful to all the scientific, medical researchers who can put efforts to put end to female infertility.

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