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Female Infertility FAQ

Fertility- Normal fertility is defined as achieving a pregnancy within one year by regular unprotected intercourse. It is estimated that about 90% of couples will achieve pregnancy in the first year & 95% in two years. Therefore, 8 to 15% of couples worldwide experience some form of infertility problem.

Infertility: A couple is usually considered to be infertile when pregnancy has not occurred after one year of unprotected intercourse.

Primary infertility: Inability to conceive within one year of marriage by regular unprotected intercourse.

Secondary infertility: Inability to conceive within one year of regular unprotected intercourse, after having first pregnancy.

Incidence of infertility: Worldwide the incidence of infertility is 10 to 15 % of married couples.

Male factor: 30%

Female factor: 30%

Both factors: 30%

Unexplained infertility: 10%

Causes of female infertility

Female infertility can be caused by any abnormality in reproductive, hormonal (endocrine) system or due to systemic causes.

1. Uterine causes: absent uterus, hypoplastic uterus, septum in uterus, bicornuate uterus, fibroids, intrauterine adhesions, infection, etc.

2. Tubal factors (35 to 45%): Fallopian tube is a very important part of female reproductive system. Infection can cause serious damage to the tube causing infertility. In India, tuberculous infection is an important cause of female infertility. Also repeated curettage of uterus, abortions can cause infection of tubes & their subsequent blockage.

3. Cervical causes: The cervical epithelium secretes important secretions that are necessary for normal passage of sperm through the cervical canal. Disturbance in this process can cause infertility. Cervical stenosis, thick cervical mucus and the presence of sperm antibodies in cervical mucus can cause infertility.

4. Vaginal causes: Hymen is tight membrane that covers the vaginal outlet. Usually this ruptures during first few coital exposures. If this membrane persists, it can cause infertility.

5. Ovarian causes (25 to 40%):

a. Ovulatory dysfunction: This is a condition in which ovulation, the release of an egg from the ovary, does not occur regularly or is absent. These patients usually have irregular cycles.

b. Polycystic ovarian disease (PCOD): PCOD is an endocrine (hormonal) disorder in which the ovaries become enlarged and studded with numerous small cysts. PCOD is usually associated with ovulatory dysfunction, irregular cycles and obesity.

c. Premature ovarian failure (POF): When a female have menopause before the age of 40 years. Ovary is no more able to produce the eggs.

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6. Endometriosis (1 to 10%): In this disease the endometrial tissue spreads to the ovary or elsewhere in the abdominal cavity and cause damage to the organs. The commonest site for endometriosis is ovary.

7. Immunological causes: In this disease antibodies develop in female against the sperms or oocytes. This can result in failure of fertilization, implantation or abortion.

8. Hormonal (endocrine) causes: Endocrine system produces very important hormones that are necessary for normal human reproduction. Abnormal hormonal production can result in infertility. In female FSH, LH, PRL (prolactin) (from pituitary glands), estrogen, progesterone, DHEA (from ovaries), insulin (from pancreas), thyroid hormones (from thyroid gland) & GnRh from hypothalamus are important.

Common endocrine diseases associated with infertility are thyroid disorders (hypothyroidism, hyperthyroidism), diabetes, and Cushing's disease.

9. Genetic causes: Certain genetic diseases cause hormonal imbalance, anovulation, failure of fertilization or implantation or abortion. Common genetic abnormalities are Turner's syndrome, Down's syndrome, etc.

10. Mental Stress: Sound mind is necessary for normal process of hormonal production, ovulation, fertilization, implantation & future pregnancy outcome. Excessive mental stress can cause disturbances in above process of reproduction leading to infertility to some extent.

11. Systemic causes: Obesity, malnutrition, smoking, alcohol intake, kidney disease, sickle cell disease, chemotherapy, HIV/AIDS can lead to infertility.

12. Unexplained infertility: Some couples are unable to conceive in spite of normal reports. In these couples more extensive work up and advanced form of infertility treatment may be necessary.

Risk factors life style issues that affect fertility:

1. Age: the probability of having a baby decreases with increasing age.
2. Alcohol intake & smoking: increases the risk of infertility
3. Prolonged exposure to high temperatures, industrial chemicals and radiation.
4. Depression and stress: may impact the hormones that regulate ovulation.
5. Unprotected sex: may increase the risk of sexually transmitted diseases that can lead to pelvic inflammatory disease.

Investigations:

General & systemic examination: Detailed history of the couple is taken & patient is examined by the infertility specialist. Pulse rate, blood pressure is recorded. Examination of the genital system is done. Couple should inform to the doctor the details of previous treatment taken.

Ultrasonography: Sonography can diagnose the obvious problems related to the uterus & ovaries like fibroid, septum in cavity, ovarian cysts, endometriosis, etc.

Hemogram: Blood tests like hemoglobin, blood grouping, blood cell counts, kidney, and liver function tests are carried out if necessary.

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Hormonal tests: If required hormonal tests like FSH, LH, Prolactin, thyroid tests, estrogen, progesterone, testosterone, DHEAS & insulin are carried out.

Hysteroscopy & laparoscopy: These are minimally invasive procedures which are usually done on outpatient basis under suitable anesthesia. These procedures can be done for diagnostic or therapeutic purpose depending on the patient's profile. Hysteroscopy is used for viewing the uterine cavity, openings of fallopian tubes inside the uterus & other abnormalities of cavity. Laparoscopy is done to see the uterus from outside, fallopian tubes, ovaries, other pelvic & abdominal organs. These procedures are gold standards in the diagnosis & management of female infertility.

Hysterosalpingography: This test is done for visualizing the uterine cavity & patency of fallopian tubes. X- Ray is taken after instilling radio-opaque dye through the cervical canal inside uterus & tubes under light sedation or anesthesia. Tubal patency on HSG does not necessarily indicate normal tubal function and when there is any history of pelvic infection or surgery, laparoscopy is recommended.

Genetic karyotyping: These are done to diagnose the genetic diseases in suspected couples. Also these tests necessary before undergoing IVF, ICSI

Treatment: To treat female partner various treatment options are available. Usually multimodal treatment is useful.

Changing the lifestyle:

a. Stress management: Excessive mental & physical stress leads to hormonal imbalance that can lead or contribute to infertility. Therefore couple should try to reduce the stress. Stress relaxation exercises like YOGA, meditation, swimming; outdoor games, etc are helpful.

b. Weight reduction: Obesity also causes hormonal imbalance & other associated problems. These patients are also at high risk for polycystic ovaries (30% more risk). In many obese patients simple weight reduction can improve the outcome. Weight reduction also improves the response to medicines & other assisted reproductive techniques.

c. Stop addiction: stop using tobacco, alcohol.

Fertility drugs: These are given to cause the growth of oocytes in ovary or to improve the hormonal imbalance.

Hystero-laparoscopy: These minimally invasive surgeries are useful to diagnose and treat the disease in uterus, tubes or ovary. These are called fertility enhancing endoscopic surgeries. **(Refer to section on endoscopy)**

IUI (Intrauterine insemination of husband semen): This treatment is used when patient fails to respond to the fertility enhancing drugs, in patients with unexplained infertility or before IVF-ICSI.

In this assisted reproductive technique the semen of male partner is washed with semen washing media in centrifuge machine at specific speed. By this procedure the good quality sperms are separated from the poor quality sperms & cell debris in the semen. These good quality sperms are then placed in culture media in incubator for some time and these sperms are then inseminated in uterine cavity. This technique improves sperm motility & increase the pregnancy rate. Success rate of IUI is 8 to 10% worldwide.

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Donor IUI (Intrauterine insemination of donor semen): When the male partner is azoospermic or has some transmissible genetic diseases, with the consent of the couple, donor IUI is done. The donor semen is taken from authorized semen bank. Complete matching of donor is done with male partner i.e. blood group, color of skin, eye & hair, ethnic & intellectual background, built of bones & height, etc. The donors are screened for HIV, hepatitis, syphilis, and other sexually transmitted diseases.

IVF (In vitro fertilization):

This is most advanced form of assisted reproductive techniques (ART). In this procedure the oocytes are aspirated from the ovary of female partner & fertilized with the sperms of male partner & kept in incubator for certain period of time. After fertilization embryo grows and when it reaches optimal stage for transfer to uterus, it is transferred with the help of catheter in uterine cavity. After that the embryo grows as that of normal pregnancy. After embryo transfer hormonal support is given to the female partner to have a favorable outcome. Pregnancy test is done after 15 days of embryo transfer. Success rate of IVF treatment worldwide is 20 to 40%.

ICSI (Intracytoplasmic sperm injection):

This form of treatment is used for couple with low sperm count or motility or in patients with previous IVF failure or as a routine method of IVF. This technique is also used when sperms are surgically retrieved from male partner (TESA, MESA, and PESA).

In this technique with the help micromanipulator a single sperm is injected directly in the oocyte. This increases the fertilization rate. Success rate of ICSI worldwide is 35 to 55%.

Embryo freezing:

In IVF or ICSI procedure usually 4 to 6 embryos are formed. In a given treatment cycle usually one to three embryos are transferred depending on the quality of embryos and condition of uterus. The remaining embryos can be frozen with help of embryo freezer instrument and kept in liquid nitrogen for hundreds of years for future use to the same couple or can be donated to other recipients with their consent. This tremendously reduces the cost of future treatment. Similarly semen sample can be frozen for future use.

Our IVF center provides facilities to freeze semen and embryos. Optimum freezing procedures are carried out in the laboratory before adding the cryoprotectants. Specimens are processed in laminar flow hoods for protection from contamination of the specimen during processing. Specimens are mixed before freezing with cryoprotectants to protect the specimen from cryoinjury during freezing, storage and thawing process. Aliquots of semen are packed in vials and labeled with thorough identification of patient's name and the date of freezing. Each embryo is stored in special embryo freezing straws again with identification of patient's name and the date of freezing. Identity of the patient is distinctly recorded on the vials and straws before storing them at -196° C in liquid nitrogen. Initial freezing is done in the machine having computerized programmes to lower the temperature gradually and steadily, followed by storing at -196° C in liquid nitrogen in vial or straw. At this temperature the specimen can be stored for decades.

GIFT (Gamete intrafallopian transfer):

GIFT involves transfer of oocytes and washed spermatozoa in the fallopian tube in cases of non-tubal infertility including unexplained infertility, endometriosis, oligospermia and immunological or cervical

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factor. As fertilization and embryonic development occurs in natural conditions i.e. in the fallopian tube, the chances of conception are theoretically higher in GIFT than IVF-ET. However, the chances of an ectopic pregnancy could be higher in GIFT than in IVF-ET. If there is failure of procedure, we do not know whether failure is due to failure of fertilization or implantation.

ZIFT (Zygote intra-fallopian transfer, PROST):

This involves the fertilization of oocytes in vitro and transfer of fertilized oocytes (zygote) containing two pronuclei or cleaved embryos into the fallopian tube. In this procedure the fertilization takes place outside the body and further development of zygote takes place in the fallopian tube. This is also an invasive procedure, so usually not done now days. The indications of ZIFT or PROST are similar to that of GIFT.

Oocyte donation (OD): This treatment method is useful when the female partner is having absent ovary, when she is not able to produce the oocytes, she is having premature menopause or has some transmissible genetic diseases. The oocyte donor is usually a close relative or friend or taken from a patient who is undergoing the IVF treatment with her consent. The oocyte is fertilized with her male partner's sperm & the embryo is transferred in her uterine cavity.

Embryo Donation (ED): This treatment is useful in couple who is unable to have child due to genetic diseases or not able to produce sperms & oocytes. The embryo is taken from embryo donor or from a couple who has extra embryos after completion of their IVF treatment cycle in an IVF center with both couples consent. This embryo is transferred in the uterus of a recipient female.

Surrogate motherhood (IVF Surrogacy): In this condition a female partner has ovaries that produce the oocytes, but absent uterus. Here the oocyte of female partner is fertilized with male partner's sperm and the embryo is then transferred in the uterus of surrogate mother. The pregnancy grows as natural pregnancy and after delivery the surrogate mother gives the child to the genetic parents.

Adoption: A child can be adopted from relatives, friends, governmental institutes or legal non-governmental organizations (NGO's). This can be an initial option for the infertile couple or after failure of above assisted reproductive techniques.

Assisted Hatching (Zona drilling): This new technique is sometimes helpful for women who have undergone IVF previously and have not conceived, or for older women undergoing IVF. Assisted hatching is a technique performed after fertilization in which the zona pellucida (which is the covering of the fertilized egg or embryo) is thinned, lysed or interrupted either chemically or mechanically with laser beam under microscopic guidance to facilitate the release of the embryo from the zona. This technique may improve embryo implantation in the uterus.

Pre-implantation Genetic Diagnosis (PGD, polar body or blastomere biopsy):

Preimplantation Genetic Diagnosis (PGD) is a very early form of prenatal diagnosis aimed at eliminating embryos carrying serious genetic defects before implantation, thereby allowing only unaffected embryos to be selected for transfer to the patient. It has an advantage over currently available prenatal diagnosis methods like amniocentesis or chorionic-villus sampling, which suffer from the drawback that if the fetus

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is diagnosed to be affected, the couple has a choice of either terminating the pregnancy or carry on with the knowledge that their child will be affected by genetic disease.

In this procedure a single or few cells (polar bodies or blastomeres) from the fertilised oocyte or embryo are taken for genetic karyotyping to know whether the embryo is having normal genotype or have some genetic abnormalities. If the embryo has some genetic disease then that embryo is not transferred.

Several groups of patients in whom PGD is a preferred option include:

- Couples with past history of previously affected genetically abnormal child.
- Women with advanced maternal age.
- Couples with repeated miscarriages due to unbalanced chromosome arrangements in the fetus.
- Male factor infertility patients.
- Patients with family history of genetic abnormality.
- Patients with history of sex-linked disease.

PGD covers several fields that include IVF, genetics, embryo biopsy and single cell diagnosis using fluorescent in-situ hybridization (FISH) for the determination of ploidy status of the chromosomes. PGD, would thus, be a boon for the couples at high genetic risk, thereby increasing the chance of pregnancy and reducing the risk of producing offspring with genetic aberration.

Karyotyping

Genetic aberration is the most common cause of pregnancy wastage affecting a number of couples. Structural and numerical abnormalities of the chromosomes are the predisposing factors in most of the cases. This has led to a great expansion of the diagnostic cytogenetic services.

Karyotyping is the ideal method to examine the chromosomes of a cell. This enables the study of chromosomal aberrations like aneuploidy, balanced translocations, inversions, insertions, deletions, marker and ring chromosomes and sex chromosome abnormalities including mosaicism.

Indications for karyotyping include:

- Advanced maternal age
- Primary amenorrhea
- Primary infertility
- Secondary infertility
- Unexplained infertility
- Male factor infertility
- Previous aneuploid pregnancy
- Missed abortion
- Recurrent abortion