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A RETROSPECTIVE STUDY ON INFERTILITY, ITS RISK FACTOR AND TREATMENT TRENDS AT AKANSHA HOSPITAL AND RESEARCH INSTITUTE, ANAND

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INTRODUCTION

A condition of the male or female reproductive system, infertility is characterized by the inability to conceive after 12 months or more of consistent, unprotected sexual activity.[2]

Some doctors analyse and treat women of 35 years of age or older, and other women having 6 months of unprotected intercourse, because it is well-known that fertility in women declines significantly with age.[1]

Millions of people experience infertility, which impacts them as well as their families and communities. Roughly one in six individuals globally who are of reproductive age may become infertile at some point in their lives.

Infertility in the male reproductive system is primarily brought on by issues with semen ejection, a lack of sperm or a low concentration of sperm, or aberrant sperm morphology and motility.

Infertility in the female reproductive system can result from a variety of conditions affecting the uterus, fallopian tubes, ovaries, and endocrine system, among other places.[2]

TYPES OF INFERTILITY

Infertility can be primary, secondary, unexplained infertility

- **Primary infertility –** when a person who has never before conceived finds it difficult to conceive.
- **Secondary infertility –** when a person has previously given birth to one or more children but is having difficulty getting pregnant again.[3]
- **Unexplained infertility:** Fertility testing has not identified a cause for an individual's or couple's infertility.[4]

CAUSES

In the female,

Ovulation disorders includes, Polycystic ovarian syndrome, High level of prolactin hormone, Hyperthyroidism, Hypothyroidism, Conditions of uterus like Uterine polyps, Fibroids, Fallopian tube damage or blockage, Pelvic inflammatory disease, Swelling of fallopian tube(salpingitis)Tumor in fallopian tube, Endometriosis, Primary ovarian insufficiency, Ovaries stop working and menstrual periods end before age 40Turner syndrome, Radiation or chemotherapy treatment, Pelvic adhesions, Cancer and its treatment, Chemotherapy, Radiation, Smoking, Alcohol, Obesity, Being underweight.

In the male

Undescended testicles, Hormone problems, Diabetes, Chlamydia, Gonorrhea, Mumps or HIV, Varicocele, Premature ejaculation, Cystic fibrosis, Blockage in the testicles, Damage or injury to the reproductive organs, Exposure to pesticides, other chemical or radiation, Testicles often exposed to heat, they may affect the ability to make sperm, Chemotherapy, Radiation, Smoking, Alcohol, Obesity, Being underweight.

DIAGNOSIS

For Female infertility

First, your healthcare provider will get your full medical and sexual history. Those who have uterus must ovulate healthy eggs in order to be fertile. In order for an egg to

be released from your ovary, travel via your fallopian tube, and land on your uterine lining, your brain must transmit hormonal signals to your ovary. Identifying a problem with any of these procedures is the goal of fertility testing.
These tests can also help diagnose or rule out problems:

Pelvic exam: To look for structural issues or disease indicators, your doctor will do a pelvic exam.

Transvaginal ultrasound: To check for problems with your reproductive system, your doctor will introduce an ultrasound wand into your vagina.

Hysteroscopy: To inspect your uterus, your doctor will introduce a thin, lighted tube, or hysteroscope, into your vagina.

Saline sonohysterogram (SIS): A Transvaginal ultrasound is performed while your uterus is filled with sterile salt water.

Sono hysterosalpingogram (HSG): During a SIS procedure, your healthcare professional will flood your fallopian tubes with saline and air bubbles to look for tubal obstructions.

X-ray Hysterosalpingogram (HSG): An injected dye is captured by X-rays as it passes through your fallopian tubes. This test searches for obstructions.

Laparoscopy: A tiny abdominal incision is made, and your doctor inserts a laparoscope a thin tube with a camera into it. It aids in the detection of issues such as scar tissue, uterine fibroids, and endometriosis.

Blood test: This examination of hormone levels can determine whether you are ovulating or whether an imbalance in hormones is the cause.[4]

Thyroid function test: If your medical team believes that a thyroid issue could be the cause of your infertility, they can order this blood test. An insufficient or excessive production of thyroid hormone by the gland may contribute to difficulties with conception.

Ovarian reserve testing: This helps your care team in determining the number of eggs you have available for ovulation. Testing for hormones early in the menstrual cycle is a usual initial phase in the process.[7]

For Male Infertility
Diagnosing infertility in people with a penis typically involves making sure a person ejaculates healthy sperm. Most fertility tests look for problems with sperm.

These tests can help diagnose or rule out problems
General physical examination and medical history: Examining your genitals and inquiring about any hereditary disorders, long-term health issues, diseases, traumas, or operations that may impact fertility are all part of this process. Your doctor may also inquire about your sexual preferences and the sexual development of your during puberty.[7]

Semen analysis: This test looks for decreased sperm motility and count. For diagnostic purposes, some individuals require a needle biopsy to extract sperm from their testicles.

Blood test or hormone test: Hormone levels, such as thyroid, can be checked using a blood test. Blood tests with genetics search for chromosomal abnormalities.

Scrotal ultrasound: An ultrasound of your scrotum identifies varicocele or other testicular problems.[4]

Trans rectal ultrasound: In your rectum, a tiny, lubricated wand is inserted. It enables your physician to examine your prostate and search for semen-transporting tube blockages.

Post-ejaculation urinalysis: A urine sample containing sperm may be a sign that your sperm are retrograde ejaculating—that is, going backward into your bladder instead of coming out of your penis.

Genetic tests. There may be a hereditary explanation for very low sperm concentrations. If there are minor alterations in the Y chromosome, which could indicate a genetic disorder, a blood test can detect them. A variety of congenital or hereditary syndromes may require genetic testing to be diagnosed.

Testicular biopsy: In this process, a little portion of testicle tissue is removed for microscopic examination in the lab. In rare cases, it could be carried out to determine whether the reproductive system is blocked, preventing sperm from exiting the body as semen.

Specialized sperm function tests. To find out how well your sperm survive after ejaculation, how effectively they can penetrate an egg, and whether they have any issues adhering to the egg, a variety of tests can be performed. These tests are rarely performed and typically have little effect on therapy recommendations.

PREVENTION
General steps to protect your fertility,
Eat a well-balanced diet and maintain a weight that's healthy for you. Don't smoke, misuse drugs or drink alcohol. Get treated for sexual transmitted disease or infection. Limit exposure to environmental toxins. Stay physically active, but don't overdo exercise. Don't delay conception until an advanced age. Undergo fertility preservation procedures (freezing eggs or sperm).

Prevention for Men
Although the majority of male infertility issues cannot be avoided, the following techniques may be useful like,

Avoid using hot tubs and hot baths as their high temperatures can momentarily impair sperm motility and production. Limit prescription and over-the-counter medications that could affect fertility. If we frequently use any prescriptions, we should discuss them with our doctor; nevertheless, we should never cease using prescription drugs without first consulting a doctor.

Prevention for Women

Several tactics for women may raise their chances of getting pregnant like, avoiding extremes in weight; our hormone production might be impacted by being overweight or underweight, which can lead to infertility. Limiting our caffeine intake: Caffeine consumption may need to be restricted for women attempting to get pregnant. For advice on how to take caffeine safely, we should consult our physician.

MANAGEMENT AND TREATMENT

Treatment for infertility depends mostly on the cause and your goals. Your age, how long you've been trying to conceive and your personal preferences are factors in deciding on a treatment. Sometimes, one person needs treatment, but other times, treatment involves both partners.

In most cases, people and couples with infertility have a high chance of pregnancy. Things like medication, surgery or assisted reproductive technology (ART) can help. Often, lifestyle changes or improving the frequency and timing of intercourse can improve your chances of pregnancy. Treatment can also include a combination of methods.[10]

Infertility treatment for women

Lifestyle modification: Gaining or losing weight, stopping smoking or using drugs, and improving other health conditions can improve your chance of pregnancy.

Medications: Fertility drugs stimulate your ovaries to ovulate more eggs, which increases your chance of getting pregnant.

Fertility medications typically stimulate ovulation by acti ng similarly to the body's own follicle-stimulating hormone (FSH) and luteinizing hormone (LH).

In an effort to induce a better or additional egg or eggs, t hey are also utilized by women who ovulate.

Fertility drugs

Citrate clomiphene: Taken orally, this medication induces the pituitary gland to release more luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which promote the development of an ovarian follicle that contains an egg. This is typically the initial course of treatment for women under the age of 39 without polycystic ovarian syndrome (PCOS)

Gonadotropins The ovary is stimulated to generate many eggs by these injectable treatments. Human menopausal gonadotropin, or hMG (Menopur) and FSH (Gonal-F, Follistim AQ, Bravelle) are examples of gonadotropin-containing drugs.

Human chorionic gonadotropin, also known as Ovidrel or Pregnyl, is another gonadotropin that is used to develop eggs and cause their release during ovulation. There are concerns that using gonadotropin increases the chance of getting multiples and preterm birth.

Metformin: When insulin resistance—usually in women with a diagnosis of PCOS—is a known or suspected cause of infertility, this medication is taken. By reducing insulin resistance, metformin (Fortamet) can increase the chance of ovulation.

Letrozole: Letrozole, also marketed as Femara, functions similarly to clomiphene and is a member of the class of medications known as aromatase inhibitors. Letrozole is typically prescribed for PCOS in women under 39.

Bromocriptine: A dopamine agonist called bromocriptine (Cycloset, Parlodel) may be used if the pituitary gland's excessive synthesis of prolactin (hyperprolactinemia) is the cause of ovulation issues.[7]

Antibiotics: Antibiotics can help remove an infection from your reproductive organs.[4]

Surgery: Surgery can open blocked fallopian tubes and remove polyps, fibroids or scar tissue.

Hysteroscopy surgery: Use to treat polyps, scar tissue and some fibroids.

Laparoscopic surgery: In this a small cuts or traditional surgery with a large cut in the stomach area may be needed to treat conditions such as endometriosis, pelvic adhesions and larger fibroids.[7]

Assisted Reproductive Technology (ART)

IUI

INTRA-UTERINE INSEMINATION. In this, healthy sperms are collected, concentrated and directly in the uterus around the timing of ovulation.[10]

IVF

IN-VITRO FERTILIZATION. In this multiple mature eggs from a woman are retrieved and fertilized with a man's sperm outside the womb. Then, fertilized embryos are implanted in the uterus.[9]

ZIFT

ZYGOTE INTRA-FALLOPIAN TRANSFER. In this, fertilized egg is directly transferred into the fallopian tube.

GIFT
GAMETE INTRA FALLOPIAN TRANSFER. In GIFT, a mixture of sperms and eggs is placed in the fallopian tube and fertilization occurs here.[11]

ICSI
INTRACYTOPLASMIC SPERM INJECTION. In this, a single healthy sperm is injected into a mature egg. ICSI is used when there is a problem with the quality of the semen or there are few sperm.

ASSISTED HATCHING
Through this technique, implantation of the embryo into the uterus is assisted by breaking the outer covering of the embryo, this helps embryo to smoothly implant.

DONOR EGGS AND SPERMS
This technique mostly uses the married couple's eggs and sperms, but when there are severe issues with the eggs and sperm then donor sperms or even embryo is taken to enhance fertility.

GESTATIONAL CARRIER
Some may decide to use a gestational carrier for IVF if they are unable to conceive or if pregnancy offers a significant danger to their health. Here, the individual who consents to bear the pregnancy gets the couple's embryo implanted in her uterus.

GENETIC TESTING
IVF embryos can be examined for genetic issues. We refer to this as preimplantation genetic testing. It is possible to implant embryos in the uterus that don't appear to have a genetic issue. As a result, there is less chance that a parent will pass on a genetic disease to their offspring.[7]

Infertility treatment for men
Male fertility treatment can range from medical therapies and surgeries to advanced ART (Assisted Reproductive Technology) for infertile men.

Lifestyle changes
Bringing healthy changes in the day-to-day lifestyle can help to improve fertility conditions in men. A few highly suggested improvements include; Avoiding the use of any recreational substance, Avoid consuming alcohol, Stopping habits like smoking, taking marijuana, etc., Exercising or dietary changes to maintain an optimum body weight, Manage stress, staying away from using sexual lubricants (lubber) during sexual activity.

Medication treatment
Medicines are normally the first line of treatment administered to patients with less severe infertility issues. This can include prescribing medications for –

Treatment of Reproductive Tract Infections
Controlling Sexual Health Problems e.g., premature ejaculation, erectile dysfunction, etc.
Restoring Hormonal Balance (for abnormally high or low levels of hormones), etc.
Men with fertility issues generally have low sperm counts. Some prescription-based medications stimulate certain hormone-releasing organs in the body that in turn work to increase sperm production in the male partner. The drugs should be taken in the manner instructed by the doctor.[14]

Clomiphene citrate
Clomiphene citrate is an estrogen blocker. It causes the pituitary gland to produce more luteinizing hormone (LH) and follicular stimulation hormone (FSH) when males take it orally. Increased levels of these two hormones can enhance motility, morphology, and sperm count. Moreover, clomiphene citrate raises natural testosterone levels.

HCG(Human chorionic-gonadotropin) and HMG(Human menopausal gonadotropin)
Your doctor may recommend HCG or hMG injections if you are one among the few males who does not respond to clomiphene citrate. These have the same advantages and disadvantages as clomiphene citrate, but because they are injectable drugs, handling and administration are more complicated, thus they are only recommended when necessary.

Anastrazole (Arimidex)
When anastrozole was first developed, it was intended to treat estrogen-sensitive breast cancer in both men and women (stimulated by estrogen). It keeps too much testosterone from inside the body's tissues from turning into estradiol. When a man's testosterone and estradiol levels are not what they should be, anastrozole is usually prescribed. Anastrazole can enhance sperm production, morphology, and motility after reversing this initial hormone imbalance.[16]

Assisted Reproductive Technology (ART) for Male Infertility
ART or Assisted Reproductive Technology provides men and women with pre-existing infertility issues to get additional help to conceive easily. These techniques also come to use when the cause of delayed pregnancy is difficult to identify.

IVF (In Vitro Fertilization)
ICSI (Intracytoplasmic Sperm Injection)
IUI (Intrauterine Insemination)
Sperm Donation
Through the Sperm Donation program, a female partner's eggs can be fertilized by sperm from a different person than the male spouse. Any sperm bank or storage facility can provide healthy sperm for this treatment. Following an IVF process, they are utilized for artificial insemination. This method can assist males with severe sperm morphology, poor sperm counts, or women who wish to conceive without a male companion.[14]

Surgical Treatment for Male Infertility

Some men with infertility problems may also be suggested to undergo certain surgeries if needed. A few common lines of surgical treatments are mentioned below:

Vasectomy reversal

Vasectomy involves surgically cutting, obstructing, or sealing the ducts in the scrotum that carry sperm, so stopping their flow from the testicles to the penis. When they ejaculate, their semen lacks of sperm as a result. The vas deferens is expertly rebuilt and rejoined during vasectomy reversal.

Varicocelectomy

Male infertility can result from varicocele in a number of ways, including low sperm production and quality. This results from varicose vein swelling in the scrotum. Effective treatment for this problem involves surgery, such as varicocelectomy, which lowers testicular pain and improves fertility.

Vasoepididymostomy

Any further obstruction in the vas deferens or epididymis that may have developed over time due to trauma, infections, or other factors is surgically removed during the vasoepididymostomy surgery. The ends of the vas deferens tubes are reconnected when the obstruction is cleared using this technique.

Sperm Retrieval

To remove semen from the testicles, a sperm retrieval method is used. Men who are unable to ejaculate or produce any sperm or semen can benefit from this therapy.

RESULT

The patient with infertility were categorized into three types (i.e primary infertility, secondary infertility, unexplained infertility). Among this type, major case were of primary infertility followed by secondary infertility and unexplained infertility are in proportion of 61%, 28% and 11%, respectively.

Age criteria	Primary infertility	Secondary infertility	Unexplained infertility	Total %
18-22	5	0	0	3.28 %
23-27	15	2	1	11.84%
28-32	29	8	10	30.92%
33-37	18	12	3	21.71%
38-42	16	13	2	20.39%
>43	10	7	1	11.84%
TOTAL	93	42	17	152(≅100%)

On further analysis it was found that Primary infertility was highest 31.18% (29) in 28-32 Year age group which was followed by 19.35% (18) in 33-37 year age group and 17.20%(16) in 38-42 year age group where as it was found that the lowest case 5.37%(5),10.75%(10) and 16.19%(15) were found in the age group of 18-22, >43 and 23-27 year age group respectively. It was also noticed that patient suffering from secondary infertility were highest in age group 38-42year 30.95% (13), 28.57% (12) in 33-37year age group, 19.04%(8) in 28-32 year age where as lesser cases were found in 18-22, 23-27 and >43 year age group which was 0%,4.76%(2) and 16.66(7) respectively. It was found that the lowest cases were found in unexplained type of infertility which were 58.82%, 17.64%, 11.76%, 5.88%, 5.88% and 0 in the age group 28-32,33-37, 38-42,23-27,>43 and 18-22 respectively.

It was found that the single female were affected more in all the types of infertility where more female were affected by the primary causes 63.6% followed by 21.2% affected by the secondary type of infertility and 13.1% were affected by unexplained causes. It was noted that single male and Both male and female ratios were found to be almost similar that is single male affected by primary infertility were 66.6% and both male and female were 46.8%. The secondary and unexplained cause show more variation in single male and both male and female. Both male and female affected by the secondary cause are 50% and only 1.3% were affected by the unexplained causes. The single males affected by the secondary causes are 20.8% and unexplained were 12.5%.

CAUSES OF INFERTILITY

There are many different causes for primary infertility in females such as polycystic Ovary Syndrome, obesity, endometriosis, hypothyroidism, swelling of fallopian tubes, Hyperthyroidism, fibroids and many more.

For primary infertility in female we found many different types of causes out of which polycystic Ovary Syndrome, Obesity was found to be 12.4% (14), Endometriosis, Hypothyroidism, Swelling of fallopian tubes 11.5% (13), 8.8%(10), 5.3%(6) respectively the other causes which cause primary infertility are of less affected but it causes infertility which are Hyperthyroidism, Fibroids and Ovaries stop working and menstrual periods end before age 14 were 4.4%(5), Being underweight and Cyst in ovary were 3.5%(4), and others.

There are many different causes for primary infertility in males such as undescended testicles, varicocele, premature ejaculation and many more.

For primary infertility in male we found many different types of causes out of which Sperm quality decrease and Undescended testicles 10.3%(4), Hormonal problems,

Exposure to pesticide ,other chemical or radiation, Premature ejaculation and Vericocele7.7%(3), diabetes, sperm count decrease, sperm motility and age 5.1%(2) and the other causes which cause primary infertility are of less affected but it causes infertility which are blockage of testis, alcohol, smoking, hypertension and other 2.6%(1) receptively.

Treatment trend

There are many type of infertility treatment (i.e medicational, art procedure, etc.). Medicational treatment like progesterone, Estradiol valerate, Dydrogesterone and many more. There are lots of medication use to treat and prevent infertility. On analysis, it was found that to treat primary infertility the highly use medicine or drug are progesterone, estradiol valerate, aspirin, L-methyl folate, enoxaparin ,prednisolone and other in 15.03%, 13.80%, 9.82%, 5.83%, 5.52%, 4.29% and other respectively. For secondary infertility the highly use medication are estradiol valerate, progesterone, dyhrogestrone, enoxaparin, prednisolone and other in 15.49%, 15.47%, 11.27%, 7.03%, 6.34% and other respectively. For unexplained infertility mostly drug treatment are same as primary and secondary, highly use medicine are progesterone, dydrogestrone, estradiol valerate, aspirin, hydroxychloroquine and other are in 16.28%, 12.79%, 11.63%, 6.98%, 4.65% and other respectively.

ART procedure

There are many type of art procedure used to treat and prevent infertility (i.e. IVF, IUI and many more).

Infertility patient differentiation according to type of ART treatment taken

Art procedure	Primary cases	Secondary cases	Unexplained cases	% Total
IUI	15	9	5	17%
IVF	60	26	9	56%
ZIFT	0	0	0	0%
GIFT	0	0	0	0%
ICSI	6	2	2	6%
SURROGACY WITH OWN EGG	3	3	0	4%
SURROGACY WITH SURROGATE EGG	8	6	3	10%
GAMATE DONNER	3	9	0	7%

CONCLUSION

From the collected 152 cases 98.02% infertility cases are females & other 1.97% infertility cases are males. Primary infertility majorly found age group between 28 – 32 years, secondary infertility majorly found in age group between 38 – 42 years and unexplained infertility majorly found in age group between 28 – 32 years. In our study, 63% cases are primary infertility, 28% secondary infertility and 9% unexplained infertility. Among 152 cases 60% patients are infertile due to female factors, 21% patients are infertile due to both male and female factors, 16% patients are infertile due to male factors and 3% patients are infertile without causes. In male undescended testicles, decreased sperm quality, premature ejaculation, hormonal problems, varicocele and exposure to pesticide, chemical or radiation are major factors for causing primary infertility. Alcohol, undescended testicles, smoking, hormonal problems are major factors for causing secondary infertility. Diabetes, hormonal problems and small testis are major factors for causing unexplained infertility. In female, obesity, endometriosis, hypothyroidism, swelling of fallopian tube, fibroids are major factors for causing primary infertility. Polycystic ovary syndrome, obesity, hypothyroidism, endometriosis, swelling of fallopian tube, ovary stop working, cyst in ovary are major factors for causing secondary infertility. Obesity, endometriosis, PCOS and diabetes are major factors for causing unexplained infertility. Majority patients prefer IVF as treatment of infertility. it was found that to treat primary infertility the highly use medicine or drug are progesterone, estradiol valerate, aspirin, L-methyl folate, enoxaparine, prednisolone and other in 15.03%, 13.80%, 9.82%, 5.83%, 5.52%, 4.29% and other respectively. For secondary infertility the highly use medication are estradiol valerate, progesterone, dyhrogestrone, enoxaparine, prednisolone and other in 15.49%, 15.47%, 11.27%, 7.03%, 6.34% and other respectively. For unexplained infertility mostly drug treatment are same as primary and secondary, highly use medicine are progesterone, dydrogestrone, estradiol valerata, aspirine, hydroxychloroquine and other are in 16.28%, 12.79%, 11.63%, 6.98%, 4.65% and other respectively. This data can be helpful to the physician and the society as it shows that females are at the higher risk of getting infertile by the risk factor such as PCOS, obesity, Endometriosis, vaginitis, diabetes etc which can be diagnosed at the early stages and can be cured so that it can treat or prevent infertility in future. Also few male who are working on the laptops the radiation of which can reduce the production of the sperms or can produce defective sperms and get infertility such as (low sperm count, motility decrease, quality of sperm decrease etc) which can diagnosed and can be treated or prevented at the early stages.

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