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## A review on triggering factors and causes of infertility

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### Abstract



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### Keywords:

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Emotional support.

Infertility affects approximately 10-15% of men and women worldwide, and it is influenced by a variety of factors. These include age, family history, nutrition, body weight, exercise habits, psychological stress, hormonal imbalances, and environmental factors. While infertility is often viewed as a physical condition, it also has profound emotional and psychological implications, impacting overall well-being. Individuals struggling with infertility, especially women, are more likely to experience mental health challenges, such as depression, anxiety, and stress. Infertile women often report a significantly lower quality of life compared to their fertile counterparts, with many experiencing feelings of inadequacy, grief, and isolation. About 23% of women facing infertility are diagnosed with anxiety disorders, highlighting the emotional toll the condition takes. The psychological impact is further intensified after failed fertility treatments like in vitro fertilization (IVF). Unsuccessful IVF attempts can lead to a sense of hopelessness, deepening depression, and anxiety, complicating the emotional landscape. Because of the mental health challenges associated with infertility, it is crucial to provide comprehensive care that includes emotional support. Addressing the psychological aspects of infertility alongside physical treatment can improve patients' well-being, making it a vital part of holistic infertility management. Supporting emotional health is essential to help individuals cope with the emotional burden infertility brings.

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### INTRODUCTION

Infertility is a failure condition that may cause physical, mental, and psychological detriments to the patient. It is unable to conceive after a year (12 months) of actively trying to become pregnant. Infertility affects 48.5 million globally. Based on statistical data, 60–80 million couples worldwide experience infertility each year. Infertility is a severe social and medical issue that affects both men and women globally. The inability to conceive following frequent, unprotected intercourse is known as infertility [1]. The World Health

Organization (WHO) acknowledges the worldwide health concern of infertility. Regrettably, emotional and psychological issues are among the clinical consequences of infertility. The most common psychological co-existing conditions with infertility are depression and anxiety (distress), which impact roughly 25–35% of women and 40–75% of women undergoing reproductive medical treatment [2].

It has been established that psychological therapy is the most successful in addressing the emotional and psychological effects of an infertility diagnosis. One of the earliest meta-analyses of psychological therapies' effectiveness was carried out by Boivin (2003).

The research, which included 25 trials, supported the psychological impacts of infertility but did not affect the likelihood of conception. The emotional effects of infertility have been demonstrated to be lessened by psychological therapies. The majority of individuals receiving treatment for infertility use assisted reproductive technology (ART) [3].

**EPIDEMIOLOGY :**

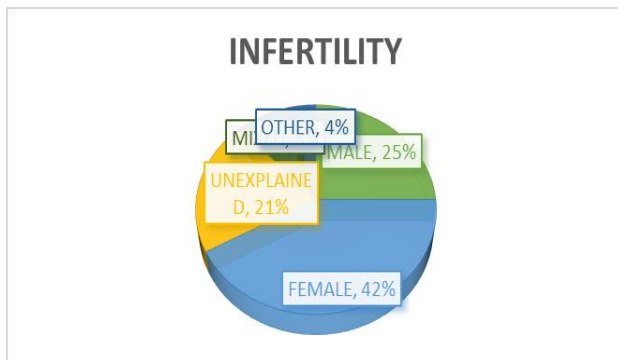
Around 15% of infertility globally (varies in different populations).

According to INDIA,

- approximately 18% - 20% of men and women are causing infertility.

According to the USA,

- 20% of cases are causing infertility due to men.
- 40% - 50% of cases are causing infertility due to women.
- 30% of cases are causing infertility (men and women).[4]



**Figure 1 Epidemiology of Infertility**

**ETIOLOGY OF INFERTILITY IN MEN AND WOMEN:**

**IN MEN:**

**Less sperm count:** Less than 10 million sperm/ml of semen. Average value(20 million sperm/ml semen or more).

**Hypogonadism:** Failure of gonads and testes in men.

**Hypospadias:** It is a congenital disability in men. A condition in which the opening of the penis is on the underside rather than the tip.

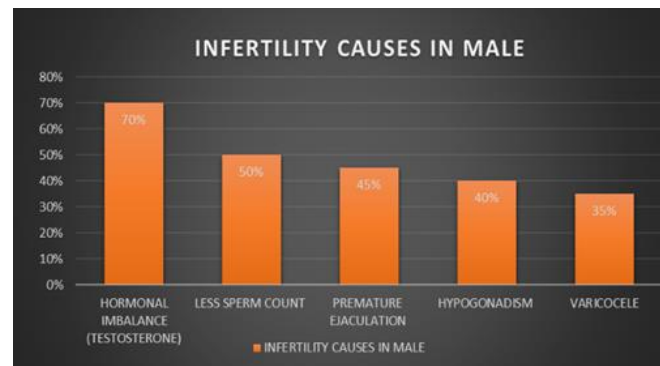
**Varicocele:** A varicocele is an enlargement or swelling of veins that drains the testicle and leads to male infertility [5].

**Ejaculation Causes:** Premature ejaculation occurs in men when semen is released into the body. It is the most common sexual complaint.

**Hormone Imbalances:** The hypothalamus, pituitary, thyroid, and adrenal glands are among the numerous hormonal systems that might exhibit abnormalities leading to infertility. Numerous underlying factors may contribute to low testosterone and other hormonal issues.

Infertility can result from issues with sustaining an erection, early ejaculation, painful sex, anatomical abnormalities, psychological problems, or relationship issues that interfere with sex [6].

**MEDICATION:** Cancer medications, certain antifungal medications, testosterone replacement therapy, long-term anabolic steroid use, and some ulcer drugs, among other medications, can impair sperm production and decrease male fertility [7].



**Figure 2 Causes of Male Infertility**

**IN WOMEN:**

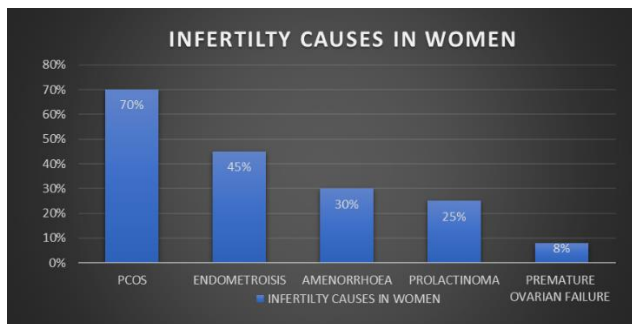
**Polycystic ovary syndrome (PCOS):** PCOS is a primary cause of infertility in women, as it induces a hormone imbalance that inhibits ovulation. Around 70 percent of women experience infertility.

**Hypothalamic dysfunction:** The pituitary gland secretes two chemicals, progesterone and estrogen, which trigger ovulation each month. A disturbance in the synthesis of these hormones may impact ovulation and lead to infertility in women [8].

**Premature ovarian failure:** Either an autoimmune reaction or an early loss of ovarian eggs are the causes. The ovary is responsible for female infertility, reduces estrogen production in women under 40, and does not generate eggs [9].

**Prolactinoma:** Infertility in women may result from the pituitary gland's overproduction of prolactin, which also lowers estrogen production.

**Endometriosis:** Another essential factor is endometriosis, which damages the uterine lining and prevents the fertilized egg from implanting properly. The sperm or egg is harmed by the condition [10].

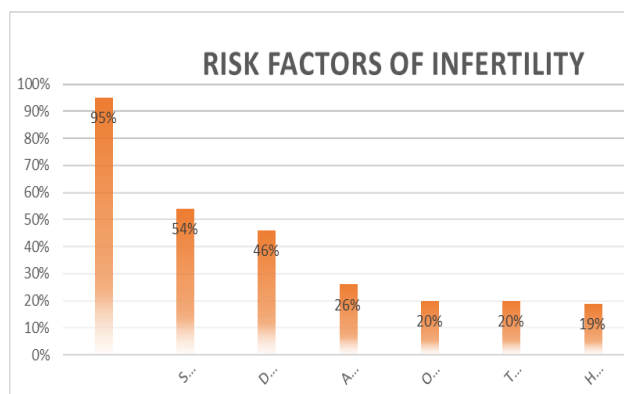


**Figure 3 Causes of Women's Infertility**

**RISK FACTORS:**

Some of the risk factors that cause the infertility such as age, nutritional deficiency (vit D3, vit B12), obesity (females above 80kgs, males above 100kgs), lack of physical exercises, alcohol consumptions, cigarette smoking, psychological stresses, recreational drug use, usage of OPIODS and tobacco (EX- over usage of marijuana that causes abnormal reproductive function), dietary changes, usage of anti psychiatric drugs ( such as anti-anxiety, depression, sedatives, hypnotics) [11], environmental changes (some type of toxic agents like silicones, chemical dust, volatile

organic solvents, pesticides these agents may affect the testes, sperm quality and quantity), urinary tract infections (most of the women are affecting when compare to men), sexually transmitted diseases (STD transmitted through sexual activity with an infected partner which cause the infertility, several physical factors (hyperthermia, radiation and electro magnetic fields) occupational factors (occupational hazards such as industrial toxins like dioxin and poly chlorinated biphenyls and exposed to heavy metals) [12].



**Figure 4 Risk Factors of Infertility**

**IN-VITRO FERTILIZATION (IVF):**

In vitro fertilization involves fertilization in a laboratory and then the transfer of embryos into the uterus. This was first used for humans in 1977 at Bourne Hall in Cambridge,(England), and tens of thousands of babies have been delivered worldwide as a result of IVF treatment [13].



**Figure 5 In-Vitro Fertilization**

**Table 1 Diagnostic Tests and Values**

S. No	Name of the test	Normal values	In case of infertility
1.	Urine analysis	-	It indicates the presence of infection. Light yellow – dark yellow indicates the infertility.
2.	Semen analysis	15 million – 200 million sperms/ml of semen.	Assess the sperm count, motility, or movement (sperm shape and maturity of sperm). Less than 14million/ml.
3.	Hormone test	300-1000/dl (testosterone levels) 1.4-18.1 U/ml (FSH values)	Evaluate the levels of testosterone and FSH (follicle-stimulating hormone). It determines the overall balance of the hormonal system and sperm production. An FSH level of less than 4.5 IU/ml leads to infertility. Below 300/dl leads to infertility.
4.	Seminal fructose test :	1200-4500 ug/ml	Fructose is a resource for the metabolism and motility of sperm. Values below 1200ug/ml indicate the infertility.
5.	Semen leukocyte analysis :	Less than 1 million/ml	To identify the white blood cells in the semen. If it contains greater than 1 million/ml of WBC, it may affect the sperm and lead to infertility.

**TREATMENT:****Table 2 Treatment and the effect of a drug on Reproductive Function**

DRUG	DOSE	EFFECT ON REPRODUCTIVE FUNCTION
ANTIBIOTICS : Gentamycin Cotrimoxazole Nitrofurantoin	80mg 100mg	Impairment of spermatogenesis.
ANTI-EPILEPTICS : Phenytoin	50mg/ml	Impairment of sperm motility.
ANTIHYPERTENSIVES : Nifedipine Prazosin	30mg 2.5mg	Fertilization failure Erectile dysfunction
ANTI-OESTROGENS : Clomiphene citrate	50mg	Impairment of endometrial development.
ANTI-PSYCHOTICS : Phenothiazine Butyrophenones	25mg/ml 1-100mg	Increased prolactin concentration that may leads to sexual dysfunction.
H2 BLOCKERS : Ranitidine Cimetidine	150mg 200mg	Loss of libido and erectile dysfunction.

**Table 2 Treatment and the effect of a drug on Reproductive Function (continued)**

DRUG	DOSE	EFFECT ON REPRODUCTIVE FUNCTION
ANTI-PROGESTINS : Emergency contraceptive pills	100mcg	Impairment of both implantation and tubal function.
ANTI-ANDROGENS : Finasteride Ketoconazole Danazol	10mg 200mg 200mg	Impairment of spermatogenesis and erectile dysfunction.
ANTI-INFLAMMATORY 5-ASA AND DERIVATIVES : Sulfasalazine	500mg	Impairment of spermatogenesis and sperm motility.
ANTIMITOTICS: Colchicine cyclophosphamide	0.6mg 25mg	Arrest of spermatogenesis; Azoospermia.
ANTIMALARIALS: Quinine and its derivatives	100mg	Impairment of sperm motility.

**INTRACYTOPLASMIC SPERM INJECTION (ICSI):**

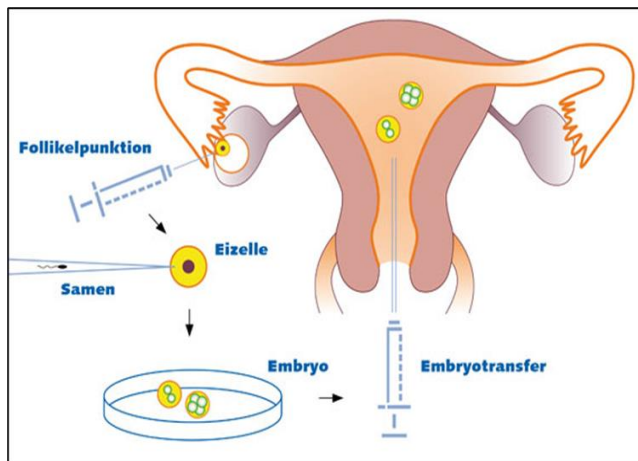
The sperm sample is surgically extracted from the testicles or in semen.

Eggs are surgically collected from women's ovaries.

An excellent hollow needle injects the sperm cell into the egg.

The fertilized egg is observed in the laboratory for signs of growth and development.

Once the egg starts to show development, it is reinserted into the woman's uterus and developed as a fetus [14].

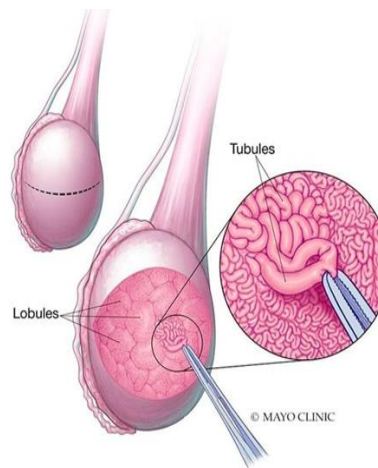


**Figure 6 Intra-Cytoplasmic Sperm Injection**

**TESTICULAR SPERM EXTRACTION (TESA):**

Duration (15 min)

This procedure is done to get sperm directly from the testicle. TESA involves percutaneous aspiration of sperm by inserting a needle directly into the testicular parenchyma [15].

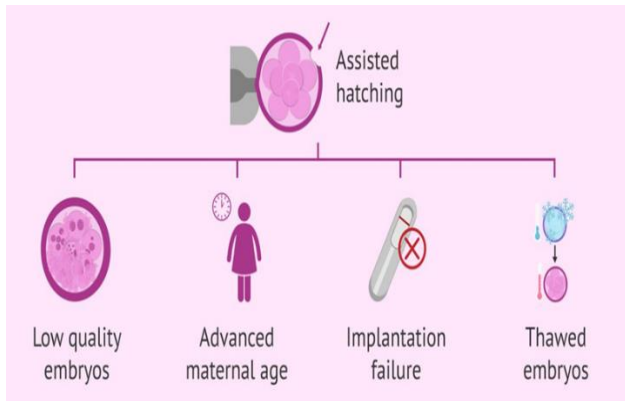


**Figure 7 Testicular Sperm Extraction**

**ASSISTED HATCHING:**

A laser is used to thin the wall of the embryo. Making a small hole in the layer. It allows us to escape. The hatched embryo is then transferred to the parent's womb. It is usually recommended for patients who obtained poor-quality embryos in previous treatments (IVF or ICSI)[16].

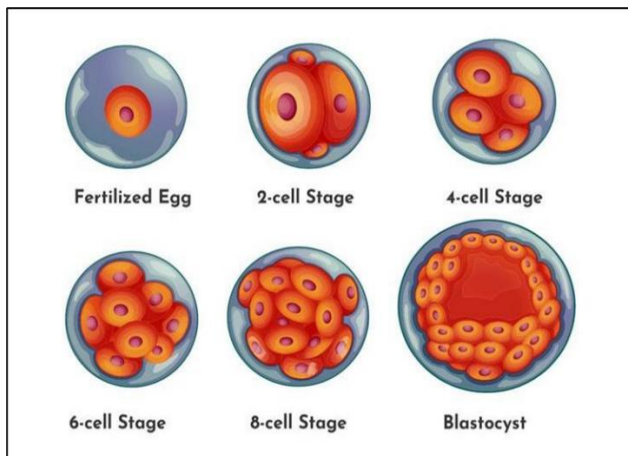




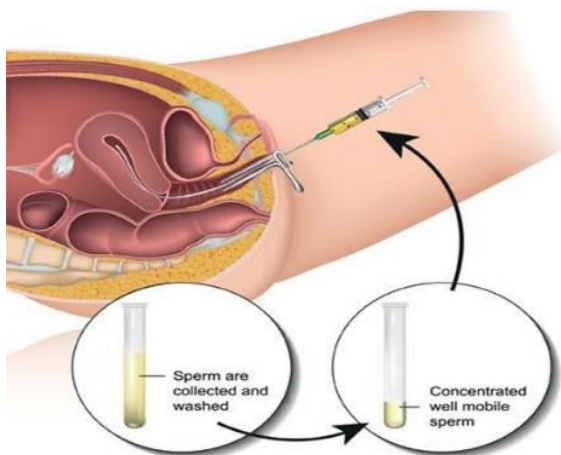
**Figure 8 Assisted Hatching**

**BLASTOCYST CULTURING:**

Blastocyst culturing is used to grow the embryos beyond the third day of culturing, done outside the body. Once fertilization occurs, an embryo is formed. Embryonic cells divide and multiply over one week to become a blastocyst [17].



**Figure 9 Culturing of Blastocyst**



**Figure 10 Artificial Insemination**

**INTRA UTERINE INSEMINSTION (IUI):**

It is also called artificial insemination. In the procedure, sperm is placed directly into the uterus using a small catheter [18].

**CONCLUSION:**

Infertility is a significant problem faced by many young couples worldwide. By this, we studied that the majority of the cases causing infertility are mainly due to PCOS faced by women as well as psychological anxiety and depression. Many of the causes, like premature ejaculation in men, hypogonadism, and low sperm count, were causing infertility in men. These infertility risks in both men and women were mainly due to triggers like anti-psychiatric drugs, smoking, dietary changes, alcohol consumption, opiates, tobacco, and HIV.

This study also gives equal importance to both men and women in infertility studies. Considerably, women are playing a major in infertility. Apart from women, Men who are taking medications like opiates or anti-psychiatric and who are consuming alcohol, tobacco, and HIV patients are susceptible to infertility. So, both men and women and health and other environmental factors play a vital role in infertility. Apart from pharmacological treatments and surgical procedures the, psychological health is more important. When the patient is psychologically healthier it will be helpful in the success of the pharmacological and other surgical procedures. Infertility treatment is more successful with psychological support.

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**Conflict of Interest**

The authors declare no conflict of interest, financial or otherwise.

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