

## Causes of Female Infertility: A Systematic Review

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### ABSTRACT

*Infertility is generally defined as the inability of a couple to conceive even after two or more years of unprotected sexual intercourse. It affects approximately 60 million to 168 million people and 13% to 15% of couples worldwide. MEDLINE, Scopus, EMBASE, PUBMED and Science Direct database were searched for this study. Thirty one research articles were examined in the overall review. The aim of the present study was a systematic review of the literature to ascertain the risk factors of female infertility. The risk factors for infertility include smoking, obesity, and alcohol consumption, advanced maternal age, sexually transmitted infection, ovarian factors, tubal and peritoneal factors, hormonal disorders, genetic factors, life style and many others. There have been numerous factors associated with the causes of infertility. Changes of lifestyle, controlling and identifying of chronic diseases, rapid and suitable treatments for sexually transmitted diseases can increase the chance of women fertility process. This research article is useful and beneficial for all medical and scientific researchers who want to uproot infertility.*

**Keywords:** Infertility causes, Female infertility, Systematic review

### INTRODUCTION

Reproduction is one of the most important biological functions of all life forms. For most couples having children feels like a primal need and inability is considered as devastating. Infertility is generally defined as the inability of a couple to conceive even after two or more years of unprotected sexual intercourse. Primary infertility defines as the couples who have not become pregnant after at least one year having sex without using any contraceptive methods. Secondary infertility refers to couples who have been able to get

pregnant at least once and now unable to conceive. This constrains the relationship of the couples resulting in divorces. Even if the couple seeks treatment, women are often blamed for childlessness and she alone is expected to undergo the diagnostic procedures to know the cause of infertility. All couples undergoing infertility treatment experienced life changes which includes lifestyle changes, various physical and emotional changes, and changes in their relationships. There was a perceived loss of control over many aspects of their lives.

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During the last decade, advances in medicine and technology have expanded the range of infertility treatment options available which has contributed to an increased demand for infertility treatment. According to WHO, the overall prevalence of primary infertility in India to be between 3.9 to 16.8 percent. It affects approximately 60 million to 168 million people and 13% to 15% of couples worldwide. There are exists a core group of couples, approximately 3 to 5 percent, who are infertile due to unknown or unpreventable conditions. Infertility rates vary amongst countries from less than 5% to more than 30%. Infertility is a universal barrier affecting people all over the world and its causes and importance of infertility may vary with geographical location and influenced by socioeconomic, demographic and anthropometric factors. The risk factors for infertility include smoking, obesity, alcohol consumption, advanced maternal age, sexually transmitted infection, ovarian factors, tubal and peritoneal factors, hormonal disorders, genetic factors, life style and many others. There have been numerous factors associated with the causes of infertility. Identification of the burden of infertility in each country has a crucial role in evidence based decision making. Approximately only 5% of the infertility incidence due to endocrinological, anatomical, genetic and immunological problems leaving about 95% of the infertility preventable. These preventable conditions including STD, parasitic diseases, health services and exposure to environmental toxic substances. The factors that contribute to these conditions vary from region to region. Lack of access for primary infertility and precise methodology to determine infertile women and the population exposed to the risk of fertility have a great impact on the estimated infertility prevalence and its influencing factors. Infertility awareness is the first step in maintaining pregnancy power in lifestyle modification. Changes of lifestyle, controlling and identifying of chronic diseases, rapid and suitable treatments for sexually transmitted diseases can increase the chance of women fertility process. A global survey of almost

17,500 women from 10 countries revealed that knowledge regarding fertility biology of reproduction was poor. Increasing the level of knowledge of the risk factors may help to decrease the incidence of infertility by allowing couples to avoid certain risk factors that might lead to it. This study reviews the causes of female infertility with the various factors including primary and secondary risk factors. There are various causes of female infertility. A huge number of investigations have been done to rule out the exact cause of infertility in female. This attempt was made to update and circulate the information on female infertility which could act as guideline in the evaluation of female infertility.

### MATERIALS AND METHODS

This study reviews some research articles on female infertility related risk factors. This article mainly aims to find the risk factor that causes female infertility. The primary and secondary infertility factors are discussed in the results from the scientific research article which were published in various journals. There were some studies conducted on database of MEDLINE, Scopus, EMBASE, PubMed and Science Direct and thirty one research articles were evaluated with similar subject to know the different risk factors that causes female infertility.

### RESULTS

Some major risk factors of female infertility include smoking, obesity, alcohol consumption, age, sexually transmitted infection, ovarian factors, tubal and peritoneal factors, hormonal disorders, residency, family history, cell phone use, stress, nutrition, unknown factors and any chronic disease reducing the chance of successful pregnancy.

#### Age:

Age may be the higher risk of infertility. The quality and quantity of woman's eggs is declining with the Increasing age. The rate of follicle loss speeds after the age 30, resulting in lesser and poorer quality eggs. This makes conception more difficult and increases the chance of miscarriage.

**Endometriosis:**

Endometriosis is a gynecological disorder that affecting menstruating women and it's declared as ectopic implantation of endometrial glands and stroma outside the uterine cavity. These endometrial implants may reperussion like normal endometrium to cyclic hormones and may manifest in pain and bleeding. Research suggesting that endocrine disrupting chemicals (EDC) may be associated with the development of endometriosis. Whether higher concentrations of persistent organochlorine pollutants (POP) in the body were associated with a greater incidence of endometriosis. The condition of endometriosis also seems to affect fertility in less direct ways such as damage to the sperm or egg.

**Polycystic ovarian syndrome (PCOS):**

PCOS is one of the common causes of female infertility. One of its primary features is high levels of androgens hormone. In women, high levels of hormone interfere with the growth, development and release of eggs during ovulation. This can cause the formation of fluid filled sacs, called as cysts in the ovaries. High androgen levels are associated with cysts in ovaries, it reduced or missing menstrual periods and cause infertility. women with PCOS are also at risk for diabetes and heart disease. Polycystic ovarian syndrome (PCOS) is a group of gynecological disorders related to the problems with the secretion of certain hormones, which can responsible to reproductive and other issue in women such as obesity, abnormal hair growth on the face or body and acne. Frequent complication of PCOS including irregular menstruation, development of ovarian cysts and insulin resistance. Natural killer cells play an important role in female sexual function. These cells are correlated with inductive failures. Natural killer cell cytotoxicity induced abortion or infertility and gene expression.

**Primary Ovarian Insufficiency (POI):**

Primary Ovarian Insufficiency (POI) is also known as premature ovarian failure. It happens when a woman's ovaries stop working normally before she reaches the age of 40.

This disorder mainly caused by an autoimmune response or by premature loss of eggs from ovary. The ovary is no longer produces eggs because it's lower production of estrogen in women under the age of 40. The symptoms of POI including infertility, higher risk of health conditions such as osteoporosis, thyroid problems and heart disease.

**Hormonal disorders:**

Hormonal disorders characterized with symptoms such as irregular menstrual cycles, excessive bleeding or very low bleeding, pelvic and abdominal cramps, absence of menstruation or long menstruation and excessive weight loss or weight gain. These can also call as ovulation disorder. The following factors cause hormonal disorders such as thyroid gland, pituitary gland and hypothalamus gland. These glands are responsible for production of sex hormones. Birth control pills, stress and hypothyroidism affect these glands.

**Fallopian tubes:**

Damaged or blocked fallopian tubes can cause infertility. It is also called as tubal infertility. They keep male sperm from getting to the egg or block the passage of the fertilized egg into the uterus. Causes of damaged or blocked fallopian tube include pelvic inflammatory disease, an infection of the uterus, fallopian tube due to chlamydia, gonorrhea or other sexually transmitted infections, previous surgery in the abdomen or pelvis including surgery for ectopic pregnancy where a fertilized egg implants and develops in a fallopian tube instead of the uterus and pelvic tuberculosis.

**Uterine and Cervical cause:**

Uterine and Cervical causes infertility by interfering with implantation or increasing the likelihood of a miscarriage. Benign polyps or tumors or fibroids or myomas are common in the uterus. A few can block fallopian tubes or interfere with implantation that affects fertility. Scarring of endometriosis or inflammation within uterus can disrupt implantation. However, many women become pregnant who have fibroids or polyps. Abnormal uterine from birth such as abnormally shaped uterus,

narrowing of the cervix can cause problems becoming pregnant. Cervical stenosis, it can be caused by an inherited malformation. Sometimes cervix cannot produce the best mucus to allow the sperm to travel through the cervix into the uterus.

**Sexually transmitted diseases (STD):**

Sexually transmitted diseases (STD) may also called as Sexually transmitted infection or venereal disease(VD). Infections such as chlamydia and gonorrhea can damage the fallopian tubes. STDs can cause valvodynia, vaginitis Painful intercourse, pelvic pain, and pelvic disorders. It usually occurs when sexually transmitted infections spread from the vagina to the womb(uterus), fallopian tubes or ovaries. The risk of sexually transmitted infection due to unprotected intercourse with multiple partners and that may cause fertility problems later. This does not mean that STDs are transmitted, infections are also be transmitted through sharing needles and breastfeeding.

**Female Cancers:**

Female cancers such as Breast cancer, Endometrial cancer, Ovarian cancer, Cervical cancer, Vulva cancer and Vaginal cancer may affect fertility. Cancer treatment as chemotherapy, radiation therapy and surgery that harms the reproductive organs can cause infertility. High doses of this therapy can destroy some or all of the eggs in the ovaries that can cause fertility problems and early menopause.

**Obesity:**

Research shows that obesity is associated with increased production of androgens in adult women and during late female pubescence or adolescence. Androgens are often called “male hormones” because male’s bodies produce more than do women’s bodies but both male and female requires certain levels of androgens for normal health. Changes in hormonal level including increases in androgen level can disrupt female reproductive cycles and lead to infertility. Obesity increases the risk in women of asthma as well as pregnancy loss. Asthma is associated with the increased risks of

becoming pregnant and failing to maintain a viable pregnancy.

**Psychological factors:**

Although a few studies have found that an association between stress and the probability of conception. An enzyme alpha amylase in saliva has been linked with increased or high levels of stress. Study shows that probability of pregnancy is lower for women with higher levels of alpha amylase. Some research studies reported that anxiety and depression are both significant factor in infertility. The medications used to treat infertility including leuprolide, clomiphene and gonadotropins are associated with psychological symptoms such as anxiety, depression, stress and irritability.

**Diet:**

High Dietary fiber intake reduces fertility in women. Research findings showed that dietary fiber consumption is related with breast cancer and reproduction. The effect of lower fiber consumption increases the estrogen hormonal level which is an important factor for reproduction and breast cancer. Hence, researchers suggest that diet could be a factor that contributes to infertility in some women.

**Environmental and lifestyle factors:**

Environmental factors such as fertilizers, pesticides, plastics, radiation and other chemicals are contributing to declining fertility. This sharp decline in fertility is being attributed to lifestyle factors including obesity, nutrition, mobile phone use, food habits, cigarette smoking, alcohol consumption, and marijuana. Anabolic steroids and taking medications to treat bacterial infections also affect fertility.

**Impact of Cigarette Smoking:**

Research has implicated that cigarette smoking is positively associated with lower fertility in women. It affects the women’s reproductive hormones including estradiol, progesterone, follicle stimulating hormone (FSH) and luteinizing hormone (LH) across the menstrual cycle, specifically in delayed conception. Level of FSH and LH hormone increases abnormally on cigarette smoking women, and high levels of these hormone causes infertility.

**Weight:**

Being overweight and underweight significantly may affect normal ovulation. Being a healthy body mass index (BMI) may increase the chances of getting pregnant and frequent ovulation.

**Societal factors:**

Researchers found that caste, residence, education status, occupation, family size and socio economic status were significantly associated with infertility. Women who live in urban area are more vulnerable than rural area in case of fertility. Because of chemicals such as polluted air from factories, vehicles and electric generators, rampant use of plastics. In addition, frequent use of detergents, cosmetic and pesticides.

**Health related factors:**

Higher fertility is significantly associated with ectopic pregnancy, miscarriage and still birth. Women who have asthma with and without hay fever have significant with higher pregnancy losses than women have without asthma.

**Unexplained Infertility:**

Sometimes the exact cause of infertility is never found. A various minor factors in both male and female could cause unexplained infertility. Although it's frustrating to get no distinct answer and these problems may correct itself with time. But people should not delay the treatment for pregnancy.

**CONCLUSION**

From the reviewed studies, it is concluded that having a healthy lifestyle, doing regular tests and checkups under medical supervision and maintaining normal body weight, quit smoking, avoid alcohol, reduce stress, limit caffeine, controlling and identifying of chronic diseases can prevent from infertility issue. Prevention and encourage for taking treatment of sexually transmitted disease and delaying pregnancy are amongst the purported good preventive measures to tackle infertility amongst infertile couple. Infertility in women will be treated by medicine, minor surgery, laparoscopic, hormonal therapy and avoiding early pregnancy failure. This article is useful

and beneficial for all medical and scientific researchers who want to uproot infertility.

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