



A Systematic Review on Factors Contributing to Infertility

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Abstract

Background: Infertility is a multifactorial reproductive health condition affecting approximately 10–15% of couples worldwide and continues to represent a major clinical and social challenge. Despite substantial advances in assisted reproductive technologies, diagnostic methods, and therapeutic interventions, many couples still face difficulties in achieving pregnancy. The impact of infertility extends beyond physical health, often leading to emotional distress, social pressure, and financial burdens, especially in societies where parenthood is highly valued. Consequently, understanding the broad spectrum of factors contributing to infertility remains essential for developing effective prevention and treatment strategies. **Aim:** The present review aims to systematically evaluate and synthesize current scientific literature concerning the diverse factors contributing to infertility. Particular attention is given to female and male reproductive factors, as well as lifestyle habits, environmental exposures, medical conditions, and age-related influences that may impair reproductive potential. **Methods:** A comprehensive literature search was conducted using major scientific databases, including PubMed, Scopus, and Web of Science, covering publications from 2000 through 2024. Studies examining causes and risk factors associated with infertility were included, encompassing both observational and interventional research designs. Eligible articles were screened, relevant data were extracted, and findings were summarized using a narrative synthesis approach to provide an integrated overview of current evidence. **Results:** The analysis demonstrated that infertility results from multiple interacting causes. Female-related factors account for approximately 40–50% of cases and commonly involve ovulatory disorders, fallopian tube damage, endometriosis, and uterine abnormalities. Male-related causes contribute to roughly 30–40% of infertility cases and include reduced sperm count, poor motility, abnormal morphology, and hormonal or genetic factors. Lifestyle influences such as obesity, smoking, alcohol consumption, substance abuse, and chronic stress were also repeatedly identified as significant contributors. Additionally, exposure to environmental pollutants and endocrine-disrupting chemicals has been increasingly recognized as detrimental to reproductive health. Advanced parental age further reduces fertility potential, particularly among women. Nevertheless, despite ongoing improvements in diagnostic evaluation, approximately 10–15% of infertility cases remain unexplained. **Conclusion:** Infertility arises from a complex interplay of biological, environmental, and lifestyle-related determinants. Preventive strategies, early clinical evaluation, lifestyle modifications, and advanced diagnostic tools are critical for improving reproductive outcomes. Future investigations should focus on unexplained infertility and underlying molecular and genetic mechanisms to enable more personalized and effective therapeutic approaches.

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Keywords: Environmental exposure, female factors, infertility, lifestyle influences, male infertility, systematic review

INTRODUCTION

Infertility is commonly defined as the inability to achieve a clinical pregnancy after at least twelve months of regular, unprotected sexual intercourse. It remains a significant global public health concern affecting individuals and couples across diverse socioeconomic and cultural settings [1]. According to estimates from the World Health Organization, nearly 48 million couples worldwide experience infertility, making it one of the most prevalent reproductive health challenges. Beyond the medical implications, infertility often carries profound psychological, emotional, financial, and social consequences. Couples may experience stress, anxiety, depression, relationship strain, and social stigma, particularly in communities where childbearing is closely linked to social identity and family expectations.

The underlying causes of infertility are multifactorial and can involve female factors, male factors, combined causes affecting both partners, or cases in which no clear reason can be identified. Female infertility commonly results from ovulatory disorders, including polycystic ovary syndrome and premature ovarian insufficiency, as well as structural abnormalities such as fallopian tube obstruction, pelvic inflammatory disease, and uterine abnormalities that interfere with implantation or pregnancy maintenance. Endometriosis and age-related decline in ovarian reserve also play significant roles in reducing female fertility potential [2].

Male infertility contributes substantially to overall infertility rates and is frequently associated with impaired sperm production, reduced sperm motility, abnormal sperm morphology, or obstruction within the reproductive tract. Conditions such as varicocele, hormonal imbalances, infections, genetic abnormalities, and exposure to environmental toxins may compromise male reproductive capacity. In addition, lifestyle factors including obesity, smoking, alcohol consumption, recreational drug use, chronic stress, and exposure to endocrine-disrupting chemicals have been recognized as modifiable contributors affecting fertility in both men and women.

Despite advances in reproductive medicine and diagnostic technologies, a notable proportion of infertility cases remain unexplained, suggesting that additional biological mechanisms may be involved. Emerging evidence points toward the importance of genetic susceptibility, epigenetic modifications, immune responses, and environmental influences in shaping reproductive outcomes. Continued research is, therefore, essential to clarify these mechanisms and improve preventive and therapeutic strategies.

This systematic review aims to provide an updated and comprehensive overview of the diverse factors contributing to infertility by integrating findings from epidemiological studies, clinical investigations, and experimental research. By synthesizing current evidence, the review seeks to support clinicians, researchers, and policymakers in developing improved diagnostic approaches and management strategies for affected individuals and couples [3].

METHODS

Search Approach

A thorough search was conducted in PubMed, Scopus, and Web of Science from January 2000 until March 2024. Search keywords consisted of “infertility,” “female infertility,” “male infertility,” “lifestyle factors,” “environmental exposure,” “age-related infertility,” and “unexplained infertility.”

Criteria for Inclusion and Exclusion

- *Inclusion*: Research exploring the causes or risk factors of infertility; observational studies (cohort, case-control, cross-sectional) and interventional research; reviews containing pertinent epidemiological information.
- *Exclusion*: Reports on individual cases, studies exclusively on animals (unless containing significantly relevant mechanistic information), and non-English studies.
- *Information Retrieval*: Two separate reviewers gathered information on study design, population, type of infertility factor, and significant results. Differences were settled through agreement.
- *Evaluation of Quality*: The Newcastle–Ottawa Scale (NOS) was utilized for observational studies, whereas the Cochrane Risk of Bias tool was employed for interventional trials.

Outcomes

Factors Related to Females

Female factors represented almost 40–50% of instances [4].

- *Ovulatory Issues:* Polycystic ovary syndrome (PCOS) is the most common, linked to hyperandrogenism and ongoing anovulation [5, 6]. Premature ovarian failure and hypothalamic amenorrhea also have significant roles [7].
- *Tubal Factors:* Leading causes of tubal damage include pelvic inflammatory disease, surgical adhesions, and genital tuberculosis [8].
- *Uterine Issues:* Fibroids, congenital defects, and intrauterine adhesions decrease the likelihood of successful implantation [9].
- *Endometriosis:* Disrupts pelvic structure and modifies immune response, impacting fertility [10].

Masculine Elements

Male factors were identified in 30–40% of infertility cases [11].

- *Semen Irregularities:* Decreased count, motility, and morphology are key indicators [12].
- *Varicocele:* Disrupts spermatogenesis via oxidative stress and elevated testicular temperature [13].
- *Genetic Influences:* Microdeletions of the Y chromosome and Klinefelter syndrome diminish reproductive capability [14].
- *Endocrine Conditions and Infections:* Hypogonadism, mumps orchitis, and sexually transmitted infections play a major role [15].

Lifestyle and Environmental Influences

- *Obesity:* Changes reproductive hormones, resulting in anovulation and decreased sperm quality [16].
- *Undernutrition:* Leads to hypothalamic suppression and irregularities in menstruation [17].
- *Substance Use:* Tobacco, alcohol consumption, and illicit drugs adversely affect reproductive health [18].
- *Stress:* Prolonged stress negatively affects the hypothalamic-pituitary-gonadal (HPG) axis [19].
- *Environmental Toxins:* Pesticides, heavy metals, and chemicals that disrupt the endocrine system negatively affect fertility [20].

Infertility Linked to Age

Women's fertility decreases after the age of 35, marked by a reduced ovarian reserve and a rise in chromosomal abnormalities [21]. Male fertility decreases more slowly, experiencing notable declines after the age of 40 [22, 23].

Health and Treatment-Related Factors

Systemic conditions like diabetes and thyroid disorders are associated with infertility [24]. Cancer treatments – chemotherapy and radiotherapy – are damaging to the gonads [25]. Surgeries on the pelvis can result in adhesions and reduced fertility [26].

Unexplained Fertility Issues

Despite thorough assessments, 10–15% of couples still go undiagnosed [27]. Minor genetic, epigenetic, and immunological irregularities might be accountable [28].

DISCUSSION

This systematic review highlights the multifaceted and interconnected nature of factors contributing to infertility, underscoring that reproductive failure rarely results from a single cause. Instead, infertility typically arises from a combination of biological, medical, lifestyle, and environmental influences affecting one or both partners. Among female-related causes, disorders such as polycystic ovary syndrome (PCOS), endometriosis, and fallopian tube damage remain some of the most frequently identified contributors. PCOS often leads to irregular ovulation or anovulation, thereby reducing the chances of conception, while endometriosis can disrupt normal pelvic anatomy and impair fertilization and implantation. Similarly, tubal blockages or damage, often resulting from infections or previous surgeries, prevent the meeting of sperm and ovum, significantly decreasing fertility potential.

Male factors also play a substantial role in infertility, yet they are sometimes underrecognized or inadequately investigated. Conditions such as low sperm count, poor sperm motility, abnormal sperm morphology, and varicocele contribute considerably to impaired male reproductive function. Hormonal imbalances, infections, genetic abnormalities, and environmental exposures further influence semen quality and fertility outcomes. Increasing awareness of male infertility is, therefore, crucial for ensuring that both partners undergo appropriate evaluation and treatment.

Importantly, the review also emphasizes the growing recognition of lifestyle and environmental influences as modifiable risk factors. Obesity, poor dietary habits, smoking, alcohol consumption, chronic stress, and exposure to endocrine-disrupting chemicals negatively affect reproductive health in both men and women. Because these factors can often be modified through behavioral changes and public health interventions, they represent valuable opportunities for prevention and early intervention. Encouraging healthier lifestyles could substantially improve reproductive outcomes in many couples.

Age-related decline in fertility remains another critical concern, particularly as many individuals postpone parenthood for educational, professional, or personal reasons. This trend highlights the need for improved reproductive education and family planning strategies, enabling individuals to make informed decisions about the timing of childbearing. In addition, medical treatments such as chemotherapy, radiation therapy, and certain surgical procedures may compromise fertility, making fertility preservation strategies – such as gamete or embryo cryopreservation – especially important for patients undergoing such therapies.

Finally, the persistence of unexplained infertility in a significant proportion of couples reveals limitations in current diagnostic approaches. This gap underscores the need for continued research into molecular, genetic, epigenetic, and immunological mechanisms that may influence reproductive success. Advancing knowledge in these areas could lead to more accurate diagnostic tools and personalized treatment options, ultimately improving outcomes for couples facing infertility.

CONCLUSION

Infertility arises from a complex and dynamic interaction among biological, lifestyle, and environmental factors, making its management both challenging and highly individualized. Biological causes may involve hormonal disturbances, structural abnormalities, genetic influences, or impairments affecting either partner, while lifestyle habits such as poor nutrition, obesity, smoking, alcohol use, and chronic stress can further compromise reproductive potential. Environmental exposures, including pollutants and endocrine-disrupting chemicals, also play a growing role in reproductive dysfunction. Because these influences often coexist, effective management requires a comprehensive and multidisciplinary strategy rather than a single therapeutic solution.

Optimal care, therefore, combines appropriate medical or surgical treatments with lifestyle modification, psychological counseling, and the use of advanced assisted reproductive technologies when necessary. Emotional stress and social pressures related to infertility often impact mental well-being and relationships, so psychological support forms an important component of treatment. Preventive strategies, public awareness programs, and early fertility assessment can also improve reproductive outcomes. Looking ahead, future research must focus on identifying hidden genetic, molecular, and environmental contributors to infertility. Improved understanding of these mechanisms will help reduce the burden of unexplained infertility and enable more personalized and effective treatment approaches for affected couples.

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