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Unveiling the Link: Investigating the Environmental Factors and Lifestyle Contributing to Infertility

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Abstract

Infertility is an emergent global public health issue in both the sexes. This comprehensive review delves into the intricate connections between environmental factors, lifestyle choices, and infertility. Research demonstrates that exposure to pollutants, toxins, and endocrine disruptors has profound effects on both male and female reproductive systems. Additionally, lifestyle factors such as elevated temperatures, smoking, obesity, and stress significantly contribute to the development of infertility. By analysing epidemiological studies, experimental research, and clinical observations, this review sheds light on the complex interplay between environmental factors, lifestyle choices, and infertility. It underscores the urgent need for further investigation to establish causal relationships and develop effective interventions. The findings of this review hold valuable insights for clinicians, researchers, and policymakers grappling with the challenges posed by infertility. A deeper understanding of the multifaceted factors influencing infertility will help inform targeted strategies for prevention, diagnosis, and treatment. By prioritizing research and implementing evidence-based interventions, we can hope to address the increasing prevalence of infertility and improve the overall reproductive health of individuals and populations worldwide.

Keywords: Environment, Lifestyle, Reproduction, Fertility, Environmental pollutants, Infertility

1. Emergence of Infertility

Infertility, a prevalent reproductive health concern, is defined as the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse, impacting a significant number of couples worldwide. The WHO, 2023 report estimates that 17.5% of the adult population - roughly 1 in 6 worldwide - experiences infertility. Infertility rates vary little between high-, middle-, and low-income countries, suggesting that this is a worldwide health issue (1). Lifetime prevalence was 17.8% in high-income countries and 16.5% in low- and middle-income countries. The global total fertility rate (TFR) has decreased from 5.09 children per woman to around 2.4 children per woman in 2023, while in India, the TFR has reduced from an estimated 5.9 children per woman in 1950 to approximately 2.1 children per woman in 2023 (2).

The decline in TFR is influenced by short-term socioeconomic and educational factors, addressable through policy changes and long-term environment, lifestyle, and genetics changes. Lifestyle factors play a significant role in the rising incidence of infertility (3). Sedentary lifestyles, obesity, smoking, excessive alcohol consumption, and poor nutrition have been identified as detrimental factors affecting both male and female fertility. Additionally, advanced maternal age is recognised as a significant contributor to infertility (4). The stress and psychological factors also significant in the context of infertility (5).

Environmental factors also come into play, with exposure to pollutants, chemicals, and endocrine disruptors potentially impacting reproductive health (6-8).

Hence, there is a need for enhanced research into the underlying causes of infertility, particularly in cases where the etiology remains unexplained. Despite advances in diagnostic techniques, a significant proportion of infertility cases are labelled as idiopathic, leaving couples without a clear understanding of the factors contributing to their reproductive challenges. Investigating the molecular, genetic, and epigenetic factors associated with infertility can provide valuable insights into its mechanisms and potentially lead to improved diagnostic and therapeutic approaches.

In summary, there are several unmet needs in the study of infertility, including understanding the underlying causes, investigating the impact of environmental and lifestyle factors, developing personalized treatment

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approaches, and addressing the psychosocial aspects of infertility. Therefore, this review focuses on the impact of environmental and lifestyle factors on reproductive health and infertility in both men and women, aiming to better understand the multifactorial nature of infertility and develop comprehensive strategies to support those experiencing challenges in achieving parenthood.

2. Overview of Male and Female infertility

2.1. Male infertility

It is estimated that worldwide 8-12% couples are suffering from infertility with 50% cases being attributed to male factors (9). Male infertility is influenced by sperm abnormalities (e.g., poor attributes, low count), hormonal imbalances impacting spermatogenesis and testosterone synthesis, genetic causes (e.g., chromosomal defects, translocations), oxidative stress, and lifestyle factors (e.g., tobacco, alcohol, drugs, obesity, diet). Declining sperm quality, resulting from birth defects, genetic disorders, lifestyle habits, and environmental exposures, contributes significantly to male infertility concerns. Evaluating sperm quality involves assessing parameters like motility, viability, morphology, developmental stage, and tail membrane integrity. Hormonal imbalances and genetic causes are directly linked to infertility. Oxidative stress from an imbalance between reactive oxygen species and antioxidants can damage sperm. Lifestyle factors and environmental exposures also negatively impact male fertility (10). Thus, recently researchers have considered various environmental factors like exposure to pollutants or toxicants, and lifestyle factors such as heat, smoking, obesity, and stress, when assessing human fertility (11). Understanding these factors is crucial for addressing male infertility and developing effective interventions.

2.2. Female infertility

According to available data, it is estimated that approximately 15% of couples worldwide experience infertility issues (12). The prevalence of infertility among women in the United States is estimated to be around 10%, affecting approximately 6.1 million individuals aged 15-44 (13). However, it's important to note that the prevalence of female infertility can vary depending on factors such as age, geographic location, and underlying medical conditions. Infertility rates among women aged 15 to 34 years varied from 7.3% to 9.1%, rising to 25% for women aged 35 to 39 years, and reaching 30% for women aged 40 to 44 years, with higher rates observed in Eastern Europe, North Africa, and the Middle East globally (14).

Female factors include ovulation disorders, fallopian tube blockage, hormonal imbalances, and structural abnormalities of the reproductive organs, contribute to a substantial number of infertility cases. Female infertility can result from various causes such as polycystic ovary syndrome (PCOS), endometriosis, uterine fibroids, age-related decline in fertility, hormonal imbalance, and certain medical conditions or treatments that affect the reproductive system (11, 14).

3. Environmental Factors and Infertility

3.1. Effects of pollutants on male reproductive health

Environmental pollutants can have detrimental effects on male reproductive health. Exposure to certain pollutants, such as heavy metals, pesticides, industrial chemicals, and air pollutants, has been associated with reduced sperm quality and fertility issues. These pollutants can accumulate in the body over time and disrupt normal sperm production and function. They may induce oxidative stress, DNA damage, hormonal imbalances, and inflammation, all of which can negatively impact sperm health (11).

3.1.A Endocrine disrupting chemicals (EDCs)

Endocrine disrupting chemicals (EDCs) are chemical compounds that interfere with the normal functioning of the endocrine system, which regulates various bodily functions. Human exposure to EDCs occurs through packaged food products, contaminated food and water, plastics, medications, pesticides, and fertilizers. These chemicals can penetrate through the plasma membrane and bioaccumulate, leading to biomagnification in the food chain. Examples of EDCs include dioxins, such as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), released during natural processes like forest fires and industrial activities(15). Bisphenols, like bisphenol A, are commonly found in plastics and are released into the environment during production, use, and disposal of plastics (15). Phthalates, which are used in various industrial and consumer goods, can be absorbed by the body through skin contact, ingestion, and inhalation of contaminated air (17)Pesticides and herbicides, including dibromo chloropropane and ethylene dibromide, act as EDCs and are widely used in agriculture (18). These substances have the potential to disrupt the endocrine system and induce adverse health effects (19, 20).

A study involving 135 males exposed to dioxin at different ages found a strong correlation between prepubertal dioxin exposure and lower sperm concentration and motility (21) Another study in the USA. reported the widespread presence of bisphenols such as bisphenol A, bisphenol S, and bisphenol F in adults and children (22)Bisphenol A (BPA), a well-known endocrine disrupting chemical (EDC) used in plastic consumer products, negatively affects reproductive function by altering hormone production in Leydig cells, leading to abnormal sex hormone ratios, with the activation of CYP genes and c-Jun phosphorylation via the JNK/c-Jun signalling pathway playing a role (23). Pesticides like dibromo chloropropane and ethylene dibromide are related to altering Sertoli or Leydig cell function and causing damage to spermatozoa (24).

The causes of male infertility include automobile exhaust, factories, homes, fires, farms, and natural phenomena. Various pollutants, including particulate

matter, ozone, volatile organic compounds, sulphur dioxide, nitrogen oxides, polycyclic aromatic hydrocarbons (PAHs), carbon monoxide, and radiation, have detrimental effects on human health (25).

Studies have revealed that exposure to PM2.5 is associated with reduced sperm motility and progressive motility, with smoking exacerbating the negative impact (26). Air pollution has also been linked to a lower percentage of motile and morphologically normal sperm in men (27). Ozone exposure has been shown to reduce sperm concentration and count, while pollutants like PM10, SO2, and NO2 can affect sperm morphology and motility (28). Testosterone levels are negatively correlated with exposure to PM10, PM2.5, CO, and NOx, and increased exposure to PM2.5 and PM10 is associated with immature chromatin in sperm cells (29) .

The exact mechanisms by which air pollution affects male reproductive health and infertility are not fully understood. However, it is believed that the presence of heavy metals, such as zinc, lead, copper, and PAHs in automobile exhaust, disrupts hormonal balance, leading to abnormal steroidogenesis and gametogenesis, ultimately resulting in infertility (29). It has been associated with reduced sperm quality, including decreased motility, abnormal morphology, and DNA damage (11).

3.1. B. Radiations

The extensive use of electronic devices like mobile phones, televisions, and wireless devices exposes individuals to non-ionizing radiation. This long-term exposure can have genetic health effects on the male reproductive system, potentially increasing cancer risk(30-32). Radiofrequency radiation (RFR) emitted by various wireless products affects the central nervous, reproductive, and circulatory systems, causing sleep disturbances, fertility problems, increased heart rate, and elevated blood pressure. Testes are sensitive to RFR, leading to testicular tissue changes, decreased sperm count, disrupted DNA integrity, and increased blood-brain barrier permeability (33). RFR exposure generates reactive oxygen species, impacting the endocrine process and lowering testosterone levels, affecting spermatogenesis and sexual differentiation (34). Studies have shown that carrying cell phones in pockets damages sperm DNA (30).

3.1. C. Nanoparticles

Nanoparticles (NPs) <100 nm in size, with diverse shapes, are used in textiles, pharmaceuticals, sports equipment, and food, raising health concerns as they enter the body through inhalation, injection, ingestion, and skin penetration, particularly in cosmetics, dermatology, and food additives (35).

NPs' small size allows them to penetrate tissues, leading to cytotoxic effects, oxidative stress, and impaired spermatogenesis, contributing to male infertility (36).

Accumulation of NPs in reproductive cells disrupts fertility, impacts offspring development, and damages sperm morphology, motility, and DNA (37). Oxidative stress, induced by ROS, contributes to infertility, cell apoptosis, and impaired spermatogenesis in men. Various NPs, including Ag, TiO2, ZnO, Cu, and Ni, have been linked to oxidative stress in male reproductive organs (38). Exposure to Nickle NPs, including Ni leads to histopathological changes in seminiferous tubules, resulting in decreased sperm count (39).

Nanoparticles (NPs) interfere with the normal functioning of the Hypothalamic-pituitary-gonadal (HPG) axis, disrupting the hormonal balance. By inhibiting the secretion of FSH, LH, and testosterone from the pituitary and hypothalamus, NPs ultimately impact spermatogenesis, highlighting their adverse effects on male reproductive health (36).

B. Impact of excessive heat on sperm quality: Excessive heat adversely impacts sperm quality and male fertility. Prolonged exposure to high temperatures, from sources like tight clothing, saunas, hot tubs, laptops, and occupational heat, can impair sperm parameters. Increased scrotal temperature induces oxidative stress, damaging sperm DNA, reducing motility and count. It also disrupts hormonal regulation, further affecting reproductive function (40) . Awareness and precautions to minimize heat exposure are crucial for individuals and couples seeking to conceive.

3.1.D. Other environmental factors contributing to male infertility

Various environmental factors play a significant role in male infertility. Occupational hazards like heavy metals, radiation, and high temperature working environments can impair sperm production and function. Lifestyle factors, including smoking, excessive alcohol consumption, and obesity, further contribute to male infertility (41). Certain medications, such as anabolic steroids, chemotherapy drugs, and some antihypertensive medications, can have adverse effects on sperm production and quality (42). Additionally, some medical treatments like radiation therapy or surgeries in the pelvic area can also impact male fertility (43). Addressing these environmental factors and adopting healthier lifestyle choices can potentially improve male fertility outcomes.

3.2. Environmental Factors and Female Infertility

3.2. A Effects of pollutants on female reproductive health

3.2. A.a. Endocrine disruptor toxin:

Exposure to pollutants and environmental toxins can have adverse effects on female reproductive health. For example, exposure to EDCs found in plastics, pesticides, and industrial pollutants has been associated with various reproductive disorders in women. These chemicals can interfere with hormone regulation, menstrual function, and fertility (7) .

There is substantial evidence that chronic and

extended exposure to EDCs adversely affects fertility and fecundity in women, with long-term consequences and trans-generational effects (44). EDCs easily traverse the placenta and are abundant in breast milk, altering intrauterine health and fetal development (45).

Perfluoroalkyl compounds such as perfluorooctanoate (PFOA) and perfluoro octane sulfonate (PFOS), used in non-stick cookware and food packaging, have been associated with a reduction in fetal growth and birth weight (46). Bisphenol A (BPA) has been shown to have harmful effects on female reproduction, resulting in hormonal and behavioural consequences in children (47). Phthalates, commonly found in consumer goods and personal care products, have been linked to premature delivery, poor neurodevelopment, and adverse birth outcomes in females (48).

EDCs and certain pesticides, such as methoxychlor and DDT, have been found to exhibit estrogenic activity and disrupt the hormonal cycle by affecting the production of gonadotropin-releasing hormone (GnRH) and altering the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) (49). These compounds can interfere with the endocrine system, leading to hormonal imbalances that can impact female reproductive health.

Other pesticides, such as fenarimol and prochloraz, have been shown to inhibit the synthesis of estrogen by interfering with the conversion of androgens (24). These compounds disrupt the normal hormonal balance and can have detrimental effects on female reproductive function and fertility. Pesticide exposure in women has been associated with lower fertility rates, premature birth, low birth weight, spontaneous abortion, stillbirth, and developmental problems(50). It can also affect the time-to-pregnancy (TTP), with women exposed to pesticides having longer menstrual cycles (51). Pesticides disrupt hormone production, storage, release, and receptor activation, leading to estrogen deficiency, dysfunctional ovulation, premature ovarian failure (POF), and infertility (52). Furthermore, EDCs impact intrauterine health by interfering with fetal growth and development (5) . BPA, found in reusable plastic containers, can affect the morphology and function of the reproductive organs, and disrupt the hypothalamic-pituitary-ovarian axis (47).

Polycystic Ovary Syndrome (PCOS) is characterized by oligo anovulation, hyperandrogenism, and the presence of polycystic ovaries (53). EDCs, such as Bisphenol A (BPA), have been found to increase testosterone levels in porcine cells and show a positive correlation with androgen levels in women with PCOS (56). Phthalates have also been shown to induce steroidogenesis in mice (57). Additionally, exposure to cigarette smoke containing polycyclic aromatic hydrocarbons (PAH) during pregnancy has been associated with a higher risk of PCOS in offspring (20).

EDCs can impact various stages of follicular development and potentially produce epigenetic changes that influence future generations (58). Multi oocytic follicles (MOFs) formation is associated with anomalies in nest breakdown, and the quality and fertility capability of oocytes from MOFs are inferior to those from Uni oocyte follicles (58).

Environmental toxins like Bisphenol A (BPA) can induce meiotic defects and aneuploidies by causing double-stranded breaks and hindering repair mechanisms (59). Maternal age and lead toxicity also impact meiotic errors and germinal vesicle breakdown in oocytes (60). Diminished ovarian reserve (DOR) and primary ovarian insufficiency (POI) can be induced by environmental toxins acting on estrogen receptors (ER) and AhR, leading to a decrease in follicle count and fertility (58).

Exposure to endocrine-disrupting chemicals (EDCs) during pregnancy can have multigenerational effects on the mother, foetus, and subsequent generations, referred to as transgenerational effects (61).

3.2.A.b. Air pollutants

Air pollution caused by various human activities, including the use of fossil fuels, industrial emissions, vehicle exhaust, and chlorofluorocarbon aerosols, contributes to climate change, leading to adverse impacts on fertility. Climate change, characterized by increased global temperatures, is associated with risks of low birthweight, stillbirth, preterm birth, and in utero heat exposure linked to fetal congenital abnormalities (62, 63).

3.2.A.c Water and soil pollutants

Water and soil pollution caused by various man-made wastes, including household rubbish, agricultural and manufacturing waste, and oil spills, pose a significant threat to human health. These pollutants can lead to acute toxicity, mutagenesis, teratogenesis, and carcinogenesis(64). Endocrine disruptors have been found to interfere with germ cell nest disintegration, hinder follicle formation, and disrupt steroid hormone levels, leading to conditions such as endometriosis, polycystic ovarian syndrome (PCOS), and abnormal puberty (65).

3.2.B. Impact of environmental toxins on ovarian function

Environmental toxins can significantly impact ovarian function, leading to infertility in women. Dioxins, a group of persistent environmental pollutants, have been shown to disrupt normal ovarian function and contribute to reproductive disorders such as endometriosis (66). Endometriosis is a common health issue affecting women of reproductive age, characterized by the presence of endometrial tissue outside the uterus (67,68) .The toxic dioxin TCDD, which accumulates in the body and interacts with the aryl hydrocarbon receptor (AhR), is known to induce endometriosis (67)Improper activation of AhR by external substances can lead to endometriosis (68). Animal studies have demonstrated the potential of TCDD to induce endometriosis even with

acute exposure, and developmental exposure appears to have more harmful effects (60)Additionally, exposure to the EDC diethyl stilbestrol (DES) during pregnancy has been linked to endometriosis in daughters (69). Additionally, exposure to certain heavy metals like lead and cadmium has been linked to decreased ovarian reserve and impaired ovarian function (70).

3.2.C. Other environmental factors contributing to female infertility

Besides pollutants and toxins, other environmental factors can also contribute to female infertility. Lifestyle factors such as smoking, excessive alcohol consumption, and poor nutrition can negatively impact fertility and reproductive health in women. Smoking has been strongly associated with infertility, early menopause, and decreased ovarian function (3).

It is crucial to address these environmental factors and their impact on female infertility (Figure 2). By raising awareness, implementing preventive measures, and advocating for environmental policies that promote reproductive health, we can strive to protect women's fertility and improve their chances of successful conception.

4. Lifestyle factors and Infertility (Figure 1)

4.1 Lifestyle Factors and Male Infertility

4.1.A. Tobacco use and its detrimental effects on male fertility

The global prevalence of tobacco smoking remains high, with an estimated 19% of the adult population using tobacco products: 33% among males and 6% among females (71). There are studies on adverse impact of tobacco smoke on male fertility (72,73). Nicotine, a psychoactive substance found in high concentrations within the seminal plasma of tobacco smokers, can cross the blood-testis barrier and cause harm to germ cells (74). Tobacco smoke contains various toxic and mutagenic substances, including nicotine and its metabolite cotinine, which have been associated with detrimental effects on sperm parameters and genetic/epigenetic aberrations in spermatozoa (75). There is conflicting evidence on how tobacco smoke affects male fertility , but the reported adverse effects on germlines and mature spermatozoa cannot be ignored (75). A systematic review and meta-analysis of 16 studies, including 10,823 infertile male participants (5,257 smokers and 5,566 non-smokers), demonstrated that smokers had a 26% higher likelihood of having oligo zoospermia compared to non-smokers. Smokers also had significantly higher morphological defects in spermatozoa, particularly in the head, neck, and tail regions, when compared to non-smokers) (76). Furthermore, the available evidence supports the concept that nicotine and other chemicals present in tobacco can permeate the blood-testis barrier and act as mutagens on human germ cells (77). Also, Tobacco smoke has the potential to induce changes in sperm microRNA expression and DNA methylation patterns in other cells, which can persist even after smoking cessation. Therefore, the negative impact of tobacco smoke on male fertility and highlight the importance of avoiding smoking for individuals and couples planning

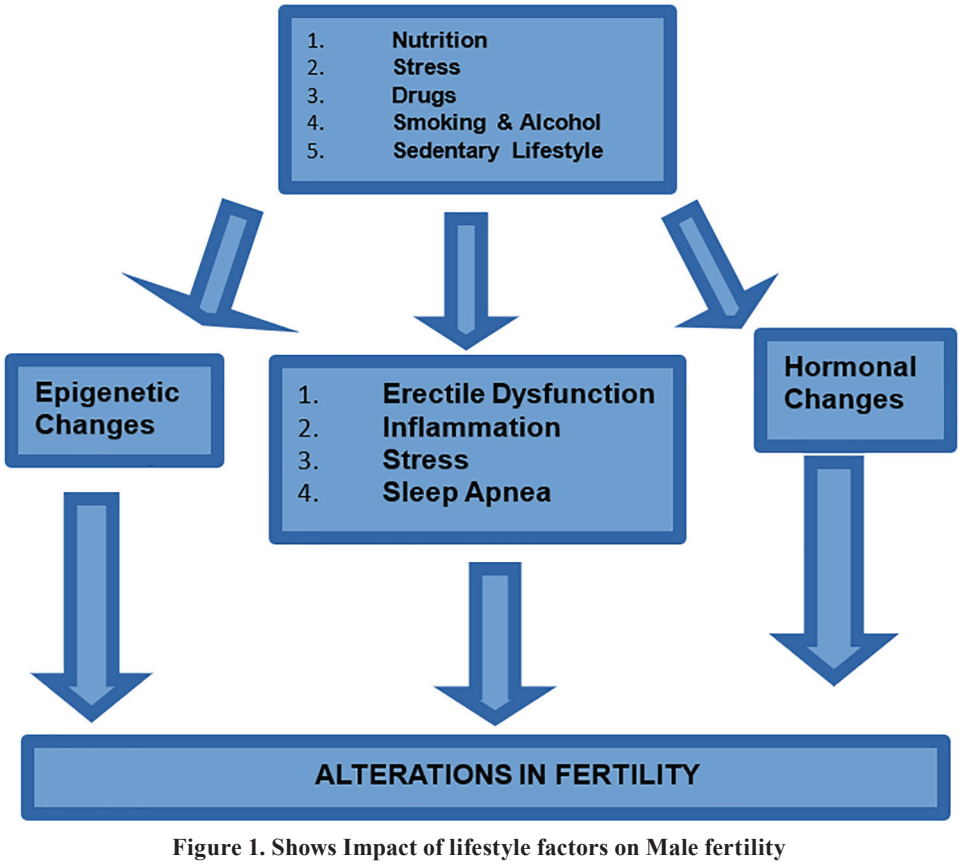

Figure 1. Shows Impact of lifestyle factors on Male fertility

to conceive.

4.1.B. Influence of alcohol consumption and drug abuse on reproductive health

Understanding the impact of heavy alcohol consumption on male infertility is crucial, considering the significant number of reproductive-age male alcoholics. Recent studies from different regions have consistently shown a negative effect of heavy drinking on semen quality. For instance, studies in China, Italy, Brazil, and Denmark have reported reduced sperm concentrations, motility, and increased DNA fragmentation in heavy drinkers compared to moderate drinkers or abstainers. These findings highlight the detrimental effects of alcohol on male reproductive health (78).

A meta-analysis of 40 studies found that alcohol intake decreased semen volume and antioxidant enzymes in male reproductive health. No significant effects were observed on other semen parameters or sperm DNA fragmentation. Alcohol consumption lowered testosterone, follicle-stimulating hormone, and luteinizing hormone levels but had no significant impact on other sex hormones (79).

4.1.C. Link between obesity and male infertility :

In 2018, El Salam referred to obesity as the "enemy of male fertility", affecting a significant global population of 400 million adults (80). Obesity has been linked to changes in semen parameters, including reduced testicular volume, decline in semen quality, and impaired spermatogenesis and can serves as a biomarker for infertility (81). Abnormal sex hormone levels are commonly observed in obese males, as obesity disrupts intracellular endocrine communication and influences body temperature, leading to heat stress and decreased testosterone formation (82) .

Obesity induces physiological changes in the male reproductive system mainly through hypothalamic-pituitary-gonadal (HPG) axis. It stimulates alterations in sperm function plausibly through DNA fragmentation of sperm DNA. Obesity leads to erectile dysfunction by decreasing testosterone levels and eliciting a systemic inflammatory response due to release of inflammatory cytokines (8,83).

4.1.D. Dietary choices and their impact on male reproductive system

Lifestyle factors, including diet, have been implicated in male infertility, along with genetic and idiopathic factors. Dairy products, such as milk and particularly cheese, are also known to contain significant quantities of natural oestrogens and the intake of phytoestrogens via the diet has been shown to lower serum testosterone levels in some, but not all, studies (84). A healthy dietary pattern was associated with a lower risk of infertility (85). Lifestyle factors, including diet, have been implicated in male infertility, along with genetic and idiopathic factors. They emphasise that adhering to a healthy diet can significantly reduce the risk of infertility by 48%. Understanding the causes of male infertility has improved in recent years, but there is still a need for further advancements in awareness and treatment options.

4.2 Lifestyle Factors and Female Infertility (Figure 2)

4.2.A. Influence of smoking on female fertility

Excessive smoking is a significant risk factor for ovulatory disorders in young women and has negative effects on pregnancy outcomes, including early pregnancy loss, preterm delivery, low birth weight,

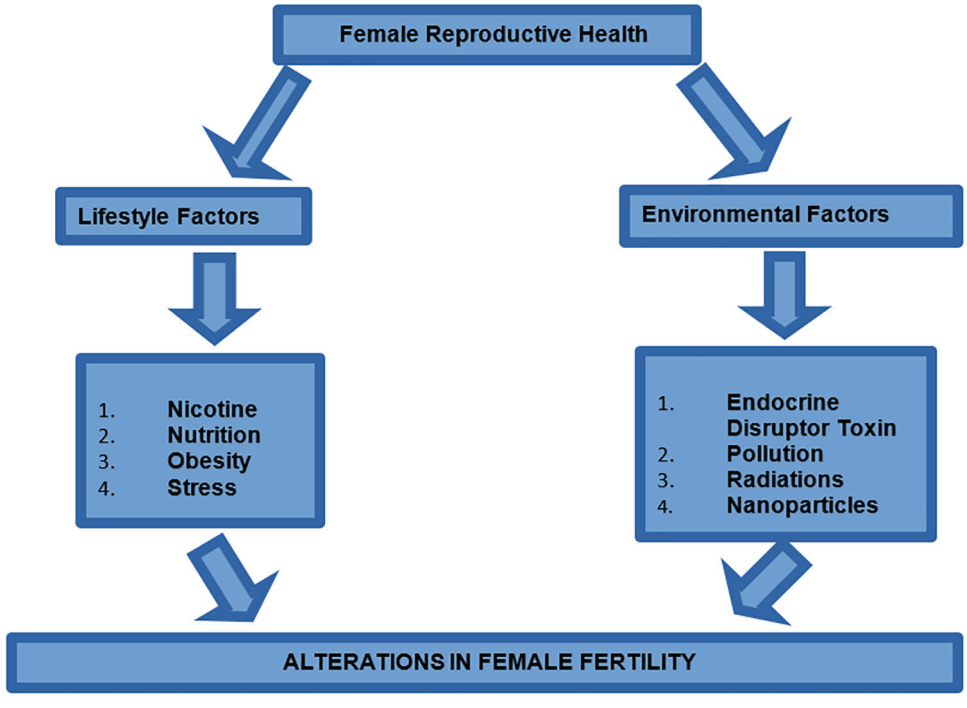

Figure 2. Impact of Lifestyle and environmental factors on female infertility

and increased risk of depression in the child (86). Nicotine in tobacco easily enters breast milk and impacts fetal neurodevelopment via multiple mechanisms.

Smokers have reduced fertility, ovulatory disorders, and negative pregnancy outcomes. Excessive smoking indicates psychological stress, impacting fertility in young women. During pregnancy, it affects the child, especially with low/high birth weights, increasing depression risk in later life (87,88) .

Smoking affects neuroendocrine function. It alters hormones in the hypothalamic-pituitary-adrenal (HPA) axis, lowers estrogen availability, and raises FSH levels. Excessive smoking increases catecholamine biosynthesis. Women smoking 10-20 cigarettes per day have altered FSH and progesterone levels. These hormonal disruptions, along with a compromised uterine environment, contribute to menstrual irregularities, ovulatory disorders, and reduced pregnancy rates (86)

4.2.B. Effects of alcohol consumption on female infertility

In 2020, 9% of women overall and 17% of women aged 18 to 25 years had an alcohol use disorder (89). Despite awareness of the negative effects, alcohol consumption remains prevalent among women(78). Prenatal exposure to alcohol through placenta has teratogenic effects and is associated with infertility. Mechanisms of teratogenicity include oxidative stress, increased apoptosis, and impaired antioxidant capacity. High-dose alcohol consumption leads to menstrual irregularities, low birth weight, spontaneous abortion, fetal hypoxia, intrauterine growth restriction (IUGR), fetal alcohol syndrome (FAS), birth defects, and developmental disabilities. Alcohol use affects endocrine functioning, disrupting the hypothalamic-pituitary-gonadal (HPG) axis and hormone secretion (90,91)

4.2.C. Relationship between obesity and female infertility

The incidence of infertility is significantly higher in overweight women compared to those with normal weight, with a threefold increased risk (26). Adolescent-onset obesity in females is often associated with menstrual abnormalities, insulin resistance, polycystic ovary syndrome (PCOS), anovulation, and infertility. Obesity is a metabolic disease characterized by elevated insulin levels, which subsequently increase ovarian androgen secretion (92). Excessive adipose tissue converts androgens into estrogen, leading to negative feedback on the hypothalamic-pituitary axis and a decrease in gonadotropin production (93) . Reduced gonadotropin levels inhibit ovarian activity, resulting in menstrual abnormalities and infertility. Additionally, women with a body mass index (BMI) over 30 kg/m2 have a higher risk of fetal malformations, including spina bifida, anencephaly, neural tube defects, and orofacial clefts during pregnancy (83). Addressing weight management and its associated health risks is essential for improving fertility outcomes in overweight women.

4.2.D. Dietary choices and their impact on female reproductive system

Diet plays a crucial role in female fertility. A healthy and balanced diet is associated with improved reproductive function, while an unhealthy diet can have negative effects on fertility. Several factors contribute to this relationship. Inadequate intake of essential nutrients, such as vitamins, minerals, and antioxidants, can disrupt normal hormonal function and impair reproductive processes. For example, deficiencies in folic acid, iron, and vitamin D have been linked to increased infertility risk (94). Also, excessive consumption of unhealthy foods, such as highly processed foods, refined carbohydrates, and sugary beverages, can lead to weight gain, insulin resistance, and hormonal imbalances. These conditions are associated with conditions like polycystic ovary syndrome (PCOS) and ovulatory disorders, leading to infertility (95).

Furthermore, a high intake of trans fats has been linked to ovulatory infertility, while a diet rich in omega-3 fatty acids, found in fish and nuts, has been associated with improved fertility. It is important for women trying to conceive to adopt a healthy and well-balanced diet, including a variety of fruits, vegetables, whole grains, lean proteins, and healthy fats. This can help optimize hormonal balance, support reproductive health, and increase the chances of successful conception. The Western-model nutrition negatively affects ovulation and semen quality due to high-glycemic-index carbohydrates, processed meat, saturated fatty acids, and low intake of fruits, vegetables, fibre, and vitamins (96).

4.2.E. Socio-economic and demographic factors

Socio-economic and demographic factors play a significant role in infertility. Age, poor socioeconomic status, high parity, unsafe childbirth, and postpartum mismanagement have been identified as factors that can affect fertility (86). Studies have shown that the literacy rate, empowerment, job opportunities, access to contraception, and family planning methods influence fertility rates (97). Rural women tend to have higher fertility rates compared to urban women, and fertility statuses can vary based on religious membership (86). Additionally, women's social position, early marriage, and the prevalence of sexually transmitted infections (STIs) can also impact fertility. HIV-positive women generally have lower fertility rates than HIV-negative women, regardless of ART usage (98).

5. SSCombined Environmental and Lifestyle Factors

5.1. Interplay between environmental and lifestyle factors in infertility

The interplay between environmental and lifestyle factors plays a crucial role in the development of infertility. Various environmental factors, such as exposure to pollutants, chemicals, radiation, and certain

medications, can have detrimental effects on reproductive health. Additionally, unhealthy lifestyle choices, including smoking, excessive alcohol consumption, and drug abuse, have been shown to significantly impact fertility. Poor nutrition, obesity, and sedentary behaviour are also lifestyle factors that can contribute to infertility. Furthermore, stress and psychological factors can disrupt the delicate hormonal balance necessary for successful reproduction. Recognizing and addressing these environmental and lifestyle factors is essential for improving fertility outcomes and promoting overall reproductive health (3). By making positive changes in our environment and adopting healthy lifestyle practices, we can enhance our chances of achieving successful conception and healthy pregnancies.

5.2. Cumulative effects of multiple factors on reproductive health

The reproductive health of both males and females can be influenced by a combination of multiple factors. These factors include genetic predisposition, lifestyle choices, environmental exposures, and socio-economic conditions. For males, factors such as smoking, excessive alcohol consumption, obesity, exposure to environmental pollutants, and certain medical conditions can impact sperm quality and fertility. In females, age, hormonal imbalances, obesity, smoking, alcohol consumption, exposure to environmental toxins, stress, and certain medical conditions can affect menstrual regularity, ovulation, and overall fertility (99). It is important to consider the cumulative effects of these various factors as they can have a synergistic impact on reproductive health in both men and women.

6. Prospects

Future research directions on environmental factors and lifestyle contributions to infertility involve several key areas. Longitudinal studies are needed to track individuals over time, providing evidence on the impact of environmental exposures and lifestyle factors on fertility. Mechanistic studies can explore molecular pathways underlying reproductive health for targeted interventions. Biomonitoring programs can assess environmental toxin levels in individuals. Intervention trials are crucial to evaluate the effectiveness of lifestyle modifications and environmental interventions. Understanding reproductive epigenetics and socioeconomic-cultural influences is important. Male factor infertility research should be prioritized. Advanced technologies like omics approaches can provide comprehensive insights. Evidence-based guidelines are needed for minimizing environmental hazards and promoting healthy lifestyles for better reproductive health.

7. Conclusion

A wide range of environmental and lifestyle factors, such as diet, smoking, excessive alcohol consumption, exposure to industrial pollutants, electromagnetic radiation, stress, and sedentary behavior, have been identified as potential contributors to impaired fertility in both men and women. These factors induce oxidative stress within the reproductive tract, which can negatively impact reproductive health. Infertility in turn, associated with an increased risk of breast, endometrial, and ovarian cancers, metabolic syndrome, cardiovascular disease, diabetes, and endocrine disorders. The understanding of environmental and lifestyle factors can reduce the development of infertility. It is crucial to understand these factors and implement appropriate regulatory measures and protective behaviours to control exposure levels and mitigate the risk of infertility. By recognizing the influence of these factors and making necessary changes, individuals and couples can improve their chances of conceiving and maintaining a healthy pregnancy. Taking proactive steps to create a supportive reproductive environment through lifestyle modifications and minimizing exposure to harmful substances is essential for promoting fertility and overall reproductive well-being.

FIGO (The International Federation of Gynaecology and Obstetrics) has established guidelines to address infertility and provide a comprehensive approach to its management. These guidelines emphasize the assessment and management of underlying causes of infertility, including ovulatory dysfunction, tubal factors, uterine abnormalities, and male factor infertility. They also highlight the importance of preconception counselling, education, and the provision of appropriate treatment options such as assisted reproductive technologies (ART). Additionally, the guidelines advocate for promoting legislation to reduce environmental chemical exposure, ensuring a healthy food system, integrating environmental health into healthcare, and championing environmental justice. By actively engaging with governments, healthcare professionals can help prevent exposure to hazardous chemicals, promote healthy lifestyles, educate patients about avoiding toxic environmental chemicals, and advocate for global environmental justice.

In conclusion, by recognizing and addressing these factors, we can take proactive steps to mitigate their effects and promote reproductive health. Further research is needed to delve deeper into the mechanisms through which these factors influence infertility and to explore novel interventions and preventive strategies. Ultimately, there is paucity of data on combined impact of lifestyle and environmental factors on infertility. By unravelling the intricate connections among environmental factors, lifestyle choices, and infertility, we can diligently strive towards forging a robust, health-conscious environment, while empowering individuals and couples in their profound voyage towards parenthood.

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