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# TRACE ELEMENTS AND FEMALE REPRODUCTIVE HEALTH: INSIGHTS INTO ESSENTIAL AND TOXIC METALS – A LITERATURE REVIEW

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## ABSTRACT

**Introduction and Purpose** This literature review explores the physiological and pathophysiological impact of selected trace elements—zinc, selenium, magnesium, cadmium, and lead—on women's reproductive health. These elements, while present in minute quantities, play critical roles in endocrine regulation, oocyte maturation, embryo development, and gestational outcomes. The aim of this paper is to consolidate and evaluate recent evidence from clinical trials, meta-analyses, and mechanistic studies to understand the significance of these elements in reproductive physiology and pathology.

**State of Knowledge** Zinc, selenium, and magnesium are essential micronutrients involved in enzymatic activity, mitochondrial stability, redox homeostasis, and hormonal balance, contributing positively to oocyte quality, fertilization, and pregnancy maintenance. Conversely, cadmium and lead are toxic heavy metals that bioaccumulate in reproductive tissues, exerting their detrimental effects via oxidative stress, endocrine disruption, and DNA damage. Emerging data highlight their contribution to infertility, miscarriage, preterm birth, and gynecological malignancies.

**Methods** This review synthesizes data from peer-reviewed journal articles retrieved from databases such as PubMed and Google Scholar. Selected literature includes randomized controlled trials, systematic reviews, cohort studies, and experimental models published primarily between 2015 and 2025. Keywords included such as "zinc fertility," "selenium pregnancy," "magnesium PMS," "cadmium infertility," and "lead miscarriage."

**Conclusions** Optimal reproductive health in women is dependent on the adequate intake and balanced metabolism of trace elements. Deficiency or excess—whether nutritional or environmental—can impair fertility and gestational success. Clinical awareness, public health strategies, and personalized supplementation protocols are essential to mitigate reproductive risks and enhance outcomes for women of reproductive age.

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## KEYWORDS

Zinc, Selenium, Magnesium, Cadmium, Lead, Fertility, Reproduction, Oocyte, Pregnancy, Oxidative Stress, Endocrine Disruption

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## Introduction

The interplay between micronutrients and female reproductive health has garnered increasing scientific attention due to rising infertility rates and the prevalence of gynecological disorders. Trace elements, though required in minimal concentrations, are indispensable for proper reproductive function. Essential elements such as zinc, selenium, and magnesium serve as cofactors in numerous enzymatic pathways and regulate key biological processes, including gametogenesis, hormone synthesis, fertilization, and implantation [1, 2]. On the other hand, toxic elements like cadmium and lead disrupt these physiological processes, exerting profound effects even at low exposure levels [19, 20, 22].

Modern environmental exposures, dietary shifts, and lifestyle factors have contributed to both micronutrient deficiencies and toxic metal accumulation in reproductive-age women. The consequences range from menstrual irregularities and polycystic ovary syndrome (PCOS) to recurrent pregnancy loss and infertility [2, 4, 6]. Understanding the dual role of essential and toxic trace elements in female reproduction is critical for developing preventive strategies, guiding supplementation, and formulating public health policies [6].

This review aims to integrate current knowledge regarding the biological functions, clinical implications, and therapeutic prospects of selected trace elements in the context of women's reproductive health. By focusing on five representative elements—zinc, selenium, magnesium, cadmium, and lead—we aim to delineate the spectrum of micronutrient influence from molecular pathways to clinical outcomes.

## The Role of Zinc in Women's Reproductive Health

Zinc (Zn) is an essential trace element that exerts fundamental biological functions within the female reproductive system. Despite its low concentration in the body, zinc participates in thousands of enzymatic and structural processes necessary for cellular integrity, hormone regulation, gametogenesis, fertilization, and embryonic development. Its deficiency can significantly impair fertility and pregnancy outcomes, particularly in women of reproductive age.

### 1. 1 Molecular and Cellular Functions of Zinc

Zinc is a cofactor for more than 300 enzymes and is involved in the structural stability of over 2000 transcription factors, including zinc-finger proteins. These proteins regulate gene expression critical for DNA replication, oxidative stress response, cell cycle control, and apoptosis. Zinc also modulates immune and endocrine functions, contributes to redox homeostasis, and influences intracellular signaling pathways essential for ovarian physiology and embryo development [1, 2].

The cellular distribution of zinc is tightly controlled by two transporter families: ZIP (SLC39) and ZnT (SLC30). The ZIP family mediates zinc influx into the cytoplasm, while ZnT regulates its efflux or storage in intracellular compartments. Proper functioning of these transporters is essential for follicular maturation, oocyte quality, and embryogenesis [1].

### 1. 2 Zinc in Ovarian Folliculogenesis and Oocyte Maturation

Zinc is indispensable in all stages of folliculogenesis. Adequate intracellular levels of zinc in the oocyte are required to maintain meiotic arrest at prophase I. A decline in zinc concentrations leads to premature meiotic resumption, abnormal spindle formation, chromosomal misalignment, and decreased developmental competence of the oocyte [1, 3].

Zinc deficiency adversely affects granulosa cell function, disrupts communication within the cumulus–oocyte complex (COC), and increases follicular atresia. In vivo studies have demonstrated that dietary zinc restriction results in reduced antral follicle count, altered anti-Müllerian hormone (AMH) levels, and increased oxidative stress in ovarian tissues [3, 4]. Moreover, zinc deficiency impairs mitochondrial dynamics and autophagy in granulosa cells, leading to increased apoptosis and impaired follicle development [3].

### 1.3 Zinc in Fertilization and Early Embryonic Development

Following sperm–egg fusion, oocytes release a surge of zinc ions, termed the zinc spark, which is crucial for zona pellucida hardening, cortical granule exocytosis, and the prevention of polyspermy. Zinc also mediates egg activation and regulates calcium oscillations, essential for the initiation of embryogenesis [1].

During preimplantation development, zinc is vital for symmetric cell division, epigenetic reprogramming, chromatin remodeling, and blastocyst formation. Zinc deficiency at this stage may result in early embryo arrest or implantation failure [1, 5].

### **1.4 Hormonal Regulation and Zinc's Endocrine Role**

Zinc influences the secretion and action of reproductive hormones, including FSH, LH, estrogen, and progesterone. It affects the hypothalamic-pituitary-gonadal axis and modulates the activity of key steroidogenic enzymes. Zinc also plays a role in insulin signaling, thus influencing ovarian function indirectly — particularly relevant in insulin-resistant conditions such as polycystic ovary syndrome (PCOS) [2, 4].

Zinc deficiency can lead to luteal phase dysfunction, anovulation, and menstrual irregularities. Supplementation may restore endocrine balance and improve fertility outcomes in zinc-deficient women [3].

## **2. Zinc and Female Reproductive Disorders**

### **2.1 Polycystic Ovary Syndrome (PCOS)**

Women with PCOS often present with low serum zinc levels, contributing to oxidative stress, insulin resistance, and endocrine dysfunction. Clinical trials have shown that zinc supplementation improves insulin sensitivity, reduces oxidative damage, and stabilizes lipid profiles in PCOS patients, potentially enhancing ovulatory cycles and pregnancy rates [2, 4, 6].

### **2.2 Dysmenorrhea and Endometriosis**

Zinc's anti-inflammatory and antioxidant properties contribute to the alleviation of menstrual pain in primary dysmenorrhea. It reduces the production of prostaglandins and inflammatory cytokines involved in uterine hypercontractility and ischemia. Although less studied, zinc may also be implicated in reducing oxidative and inflammatory damage in endometriotic lesions [2].

## **3. Zinc in Pregnancy and Fetal Development**

During pregnancy, zinc requirements increase due to rapid fetal cell proliferation, placental development, and maternal tissue expansion. Zinc deficiency is associated with miscarriage, intrauterine growth restriction (IUGR), congenital anomalies (especially neural tube defects), and impaired placentation [1, 6].

Experimental animal models confirm that maternal zinc deficiency leads to defective oocyte maturation, abnormal implantation, poor embryonic development, and placental insufficiency. Supplementation in zinc-deficient populations improves neonatal outcomes and may prevent gestational complications [1, 5].

## **4. Mitochondrial Function, Autophagy, and Oxidative Stress**

Zinc maintains mitochondrial integrity and regulates autophagy in ovarian cells. It activates mitophagy and prevents the accumulation of reactive oxygen species (ROS). Zinc deficiency impairs PI3K/AKT/mTOR and AMPK signaling pathways, leading to apoptosis of granulosa cells and oocyte deterioration [3, 4]. These mechanisms are particularly relevant in aging ovaries and metabolic diseases affecting fertility.

## **Selenium in Women's Health and Reproductive System**

Selenium (Se) is an essential trace element involved in numerous physiological processes crucial for female reproductive health. Its biological role is primarily mediated through selenoproteins, which exhibit antioxidant, anti-inflammatory, and endocrine-regulating properties. Selenium's relevance to female health spans from oocyte maturation to pregnancy maintenance, influencing fertility outcomes, hormonal regulation, and fetal development.

### **1. Biological Functions of Selenium and Selenoproteins**

Selenium's physiological impact arises from its incorporation into selenocysteine, the 21st amino acid, found in at least 25 human selenoproteins. Among them, glutathione peroxidases (GPx), thioredoxin reductases (TXNRD), and selenoprotein P (SELENOP) are critical to redox regulation, thyroid metabolism, and cellular signaling [7]. GPx enzymes protect reproductive tissues from oxidative stress, while SELENOP ensures effective Se transport and plays a key role in maternal-fetal Se transfer [6]. Disruption in selenoprotein expression can result in impaired folliculogenesis, defective implantation, and placental dysfunction [6, 7].

### **2. Selenium and Female Fertility**

Systematic reviews have demonstrated that selenium influences several determinants of fertility. Adequate selenium levels correlate with higher antioxidant activity in follicular fluid, improved oocyte quality, and increased follicular count [8]. Hyposemia is common in regions like Europe and Asia and has been

associated with reduced fertility [8]. Selenium supplementation has been shown to normalize anti-thyroid antibody levels, promote oocyte maturation, and support luteal function [8, 9]. Furthermore, selenoproteins such as GPX1, GPX3, and SELENOS have been localized in granulosa cells and theca interna of dominant follicles, underscoring their role in follicular selection and protection against reactive oxygen species [7].

### **3. Selenium in Pregnancy and Fetal Development**

During pregnancy, selenium demand increases, yet maternal plasma Se levels often decline, especially in the third trimester [4]. Selenium deficiency during gestation is linked to complications including miscarriage, intrauterine growth restriction, preeclampsia, and impaired immune and neurological development in the fetus [4, 5, 8]. Experimental studies on pregnant rats have shown that selenium supplementation ameliorates oxidative damage induced by toxicants (e.g., lead), restores sex hormone levels, and promotes fetal growth and reproductive organ development [9]. SELENOP and iodothyronine deiodinase 3 (DIO3) are expressed in uterine and placental tissues, suggesting roles in thyroid hormone regulation and trophoblast differentiation [6, 7].

### **4. Selenium Deficiency and Toxicity in Women**

Although selenium supplementation below 200 µg/day is generally safe and may improve fertility outcomes, both deficiency and excess are detrimental. Deficiency may impair antioxidant defense, reduce progesterone levels, and hinder implantation [8]. Toxic doses, however, can induce oxidative stress and disrupt endocrine homeostasis [6]. Dietary sources include seafood, cereals, meats, and dairy products, though soil selenium content significantly influences food Se levels [7].

### **5. Selenium and Gynecologic Disorders**

Beyond fertility and pregnancy, selenium may play a role in gynecologic pathology. Epidemiological studies have associated altered selenium levels with gynecologic cancers, especially cervical and endometrial cancer [5]. Increased selenium levels post-treatment suggest its protective or modulatory role [5]. Furthermore, selenium is under investigation for its role in modulating HPV-related oxidative stress and cellular transformation.

## **Magnesium in Women's Reproductive Health**

Magnesium (Mg) is a vital trace element essential for over 600 enzymatic reactions and fundamental cellular processes including ATP metabolism, DNA and RNA synthesis, and oxidative phosphorylation. It plays a critical role in maintaining neuromuscular, cardiovascular, and metabolic functions. Women, due to the hormonal fluctuations across the lifespan, experience unique magnesium requirements that influence reproductive physiology, fertility, pregnancy outcomes, and menopausal health [10, 11].

### **2. Magnesium Metabolism and Homeostasis**

Approximately 99% of total body magnesium is intracellular, primarily stored in bones (60%) and soft tissues, with only 1% present in extracellular fluids. Its absorption primarily occurs in the ileum and colon, and is tightly regulated by renal excretion and gastrointestinal absorption in response to dietary intake and physiological needs [10, 12]. Subclinical magnesium deficiency is prevalent among women, particularly due to dietary insufficiency, hormonal factors, and medication use [13].

### **3. Magnesium in Women's Health Across the Lifespan**

#### **3.1 Premenstrual Syndrome (PMS)**

Magnesium deficiency has been implicated in the pathogenesis of PMS, characterized by mood swings, irritability, fatigue, and abdominal discomfort. Studies show that women with PMS often present with lower intracellular magnesium levels compared to healthy controls. Supplementation with magnesium, particularly in combination with vitamin B6, has shown to reduce PMS symptoms more effectively than magnesium alone [10, 14]. Magnesium's anti-inflammatory properties and its role in prostaglandin E1 synthesis may explain its clinical benefits [10, 15].

### **3.2 Polycystic Ovary Syndrome (PCOS)**

PCOS is associated with insulin resistance, systemic inflammation, and oxidative stress — all conditions in which magnesium plays a regulatory role. While magnesium monotherapy shows limited benefit on glycemic and oxidative stress markers in PCOS, its co-supplementation with other agents (e.g. vitamin E, zinc-calcium-vitamin D) significantly improves serum insulin, HOMA-IR, triglycerides, and hs-CRP levels [16]. These synergistic effects support magnesium's potential as adjunct therapy in PCOS management [16].

### **3.3 Pregnancy, Pre-eclampsia and Eclampsia**

Magnesium sulfate remains a cornerstone in the management of pre-eclampsia and eclampsia due to its anticonvulsant, vasodilatory, and anti-inflammatory properties [11, 12]. Mg supplementation has shown to reduce uterine hypercontractility, promote placental perfusion, and decrease the risk of preterm labor [11]. Its action involves modulation of prostacyclin (PGI<sub>2</sub>), endothelin, thromboxane (TXA<sub>2</sub>), and enhancement of nitric oxide availability [11].

In assisted reproduction, particularly IVF cycles, rising estrogen levels have been linked to alterations in serum magnesium levels. Although total serum magnesium does not significantly change, its ionized fraction may be suppressed by increasing estradiol, potentially affecting vascular and metabolic homeostasis [13].

### **3.4 Menopause and Bone Health**

Estrogen enhances magnesium uptake in soft tissue and bone. Postmenopausal magnesium deficiency has been associated with increased risk of osteoporosis and cardiovascular disease [11]. Magnesium is required for parathyroid hormone (PTH) secretion and vitamin D activation, both essential for calcium homeostasis and bone metabolism [12]. Estrogen-Mg interactions may partly explain why premenopausal women are relatively protected from ischemic heart disease and osteoporosis, a protection that diminishes with menopause [11].

## **4. Magnesium and Fertility Preservation**

Chemotherapeutic agents such as cyclophosphamide induce ovarian follicular apoptosis, leading to early ovarian insufficiency. Animal studies have demonstrated that magnesium sulfate administration reduces follicular atresia, limits granulosa cell apoptosis (via reduced TUNEL and cleaved caspase-3 expression), and preserves the primordial follicle pool [15]. These findings suggest magnesium's potential role in fertility preservation strategies for women undergoing cytotoxic therapies.

## **5. Supplementation Considerations and Public Health Relevance**

Despite the availability of magnesium-rich foods (e.g., green leafy vegetables, legumes, nuts, whole grains), dietary intake in many populations remains below recommended levels, particularly among women. Factors contributing to magnesium deficiency include processed diets, gastrointestinal disorders, use of diuretics, PPIs, and high calcium intake which may antagonize magnesium absorption [10, 12, 13]. Routine assessment of magnesium status is seldom performed but may be crucial in reproductive-age women, especially those with PMS, PCOS, or undergoing ART.

## **The Impact of Cadmium on Women's Reproductive Health**

Cadmium (Cd) is a highly toxic, non-essential heavy metal widely recognized for its detrimental impact on human health. Due to its capacity to bioaccumulate in various tissues and disrupt endocrine, cellular, and epigenetic pathways, cadmium poses a significant threat to women's reproductive health. This chapter provides a comprehensive review of the effects of cadmium on female fertility, pregnancy outcomes, hormonal regulation, and gynecologic malignancies, based on recent research and meta-analytical data.

### **1. Sources, Bioaccumulation, and Toxicokinetics**

Cadmium exposure in women arises primarily from dietary intake, cigarette smoke, and environmental pollution. Industrial activities such as smelting, electroplating, and battery manufacturing are major contributors to atmospheric cadmium release. Once absorbed, cadmium is stored in soft tissues—particularly kidneys, liver, and reproductive organs—due to its long biological half-life of 10–30 years [19, 21].

Notably, women in cadmium-contaminated regions have shown elevated blood and endometrial levels of this metal [17, 25]. Because cadmium is poorly excreted, chronic low-dose exposure results in progressive tissue accumulation, making it a long-term hazard to reproductive function [19, 21].

## 2. Disruption of Reproductive Endocrinology

Cadmium is a potent endocrine disruptor. It interferes with the hypothalamic-pituitary-gonadal axis and inhibits steroidogenic enzymes responsible for estrogen and progesterone synthesis [19, 20]. Evidence from both human and animal studies shows that cadmium exposure alters serum sex hormone levels, disrupts menstrual cyclicality, and contributes to conditions such as premature ovarian insufficiency (POI) and anovulation [20, 22].

Additionally, cadmium acts as a metalloestrogen by mimicking the effects of estradiol through activation of estrogen receptor  $\alpha$  (ER $\alpha$ ), thereby influencing gene expression in hormone-sensitive tissues [26].

## 3. Fertility Impairment and Infertility

The relationship between cadmium exposure and female infertility is well-documented. In a large NHANES-based cross-sectional analysis of American women aged 20–44 years, urinary cadmium levels were significantly associated with infertility, especially in the second and third exposure quartiles (OR up to 4.11) [18].

Furthermore, elevated cadmium concentrations in endometrial tissue have been reported in over 90% of women with unexplained infertility, compared to only 34% of fertile controls. These findings suggest that cadmium may impair endometrial receptivity or embryo implantation without disrupting ovulation or oocyte quality.

## 4. Pregnancy Outcomes and Perinatal Risk

Chronic exposure to cadmium is associated with a range of adverse pregnancy outcomes. A systematic review and meta-analysis revealed significantly higher blood cadmium levels in women with spontaneous abortions compared to controls (SMD = 3.39; 95% CI 2.17–4.61) [23]. These findings have been echoed in earlier observational studies from cadmium-contaminated areas in Poland, which showed increased rates of miscarriage, preterm birth, and low birth weight in exposed populations [24].

Cadmium may exert teratogenic effects by disrupting placental development, impairing angiogenesis, and increasing oxidative stress in utero [20, 22, 23].

## 5. Oxidative Stress and Cellular Damage

Cadmium induces the generation of reactive oxygen species (ROS) while simultaneously depleting cellular antioxidants such as glutathione. This results in lipid peroxidation, mitochondrial dysfunction, and DNA damage in ovarian and endometrial tissues [22].

In granulosa cells, cadmium-induced oxidative stress triggers apoptosis and follicular atresia, reducing ovarian reserve and steroidogenic capacity [22]. Prolonged oxidative imbalance may also accelerate ovarian aging and contribute to POI [22].

## 6. Cadmium and Gynecological Cancers

Cadmium's role in gynecological malignancies has gained increasing attention. It has been implicated in the pathogenesis of endometrial, ovarian, and cervical cancers due to its genotoxic and epigenetic effects [26]. These include DNA methylation changes, histone modifications, and interference with tumor suppressor gene expression.

A study evaluating cadmium levels in women with various uterine pathologies revealed significantly higher median blood cadmium concentrations among patients with endometrial cancer compared to those with benign conditions. Women with above-median cadmium levels had a 5.25-fold increased risk of endometrial cancer (OR = 5.25; 95% CI 1.56–17.72) [17].

## 7. Endometrial Concentration and Implantation Failure

Direct measurement of cadmium in endometrial biopsies has shown a striking difference between fertile and infertile women. The median cadmium level among infertile women reached 19.58  $\mu\text{g/L}$ , while it remained nearly undetectable in fertile controls [25]. This accumulation may impair endometrial receptivity by affecting stromal cell differentiation, decidualization, and angiogenesis [25].

Animal studies suggest that intrauterine cadmium disrupts embryo implantation without impairing ovulation, further supporting its selective action on the endometrial environment [25].

## 8. Public Health Implications and Recommendations

Given the ubiquity of cadmium exposure and its long biological half-life, mitigating strategies are critical. These include:

- Smoking cessation programs, as tobacco is a major non-occupational source of cadmium.
- Regulation of cadmium levels in food and drinking water.
- Routine monitoring in women with unexplained infertility or recurrent pregnancy loss.
- Incorporation of cadmium screening in environmental health assessments for reproductive-age women.

Cadmium's classification as a Group 1 human carcinogen by IARC further underscores its public health importance [21, 26].

## Lead and Its Impact on Women's Reproductive Health

Lead (Pb) is a ubiquitous environmental and industrial pollutant with no known physiological role in the human body. It is classified as a Group 2A carcinogen by the International Agency for Research on Cancer (IARC), indicating its probable carcinogenicity to humans. Chronic exposure to lead poses significant risks to female reproductive health, affecting endocrine function, menstrual regularity, pregnancy outcomes, and potentially contributing to gynecological malignancies. The toxic effects of lead are primarily mediated through oxidative stress, endocrine disruption, DNA damage, and epigenetic modifications [17, 22, 26].

### 1. Sources and Mechanisms of Exposure

Women may be exposed to lead through various environmental and occupational sources, including contaminated air, soil, water, food, tobacco smoke, and industrial byproducts. Lead accumulates in the bones, from where it can be mobilized during pregnancy and lactation, leading to fetal exposure [17]. The primary mechanisms of lead toxicity include generation of reactive oxygen species (ROS), inhibition of antioxidant enzymes, interference with calcium signaling, disruption of hormonal pathways, and impairment of DNA repair processes [22].

### 2. Impact on Female Fertility and Menstrual Function

Chronic lead exposure has been associated with alterations in the hypothalamic–pituitary–ovarian axis, resulting in menstrual irregularities, delayed menarche, anovulation, and reduced fecundity [26]. Women living in lead-contaminated areas demonstrate a higher prevalence of infertility, prolonged time-to-pregnancy, and increased rates of menstrual disorders [24]. Lead has been shown to interfere with gonadotropin-releasing hormone (GnRH) secretion and pituitary sensitivity, thereby impairing luteinizing hormone (LH) and follicle-stimulating hormone (FSH) regulation [22].

### 3. Pregnancy Complications and Fetal Development

Maternal exposure to lead has been conclusively linked to adverse pregnancy outcomes, including spontaneous abortion, preterm delivery, intrauterine growth restriction (IUGR), and low birth weight (LBW) [20]. A systematic review and meta-analysis confirmed that elevated maternal blood lead levels significantly increase the risk of spontaneous miscarriage and fetal loss [23]. Lead crosses the placental barrier and accumulates in fetal tissues, contributing to impaired neurodevelopment, reduced head circumference, and shorter crown-heel length in neonates [20].

Furthermore, elevated cord blood lead levels correlate negatively with birth length and weight. Blood lead concentrations  $\geq 10$   $\mu\text{g/dL}$  have been associated with a threefold increase in the risk of preterm birth and a fourfold increase in the incidence of small-for-gestational-age infants [20].

### 4. Endometrial Toxicity and Implantation

Recent studies have highlighted the presence of lead in the endometrial tissue of women with unexplained infertility, suggesting its potential role in impairing endometrial receptivity [25]. Lead accumulation in the endometrium may disrupt the window of implantation and hinder embryo–endometrium communication, contributing to implantation failure. Additionally, lead-induced oxidative stress and inflammation may compromise the integrity of endometrial tissue and affect decidualization [26].

## 5. Lead as a Metalloestrogen and Carcinogen

Lead exhibits estrogen-mimicking properties, acting as a metalloestrogen by binding to estrogen receptors, particularly ER $\alpha$ . This mechanism contributes to the pathogenesis of hormone-dependent gynecological malignancies such as endometrial, cervical, and ovarian cancers [17, 26, 21]. Lead induces carcinogenesis through both genotoxic and epigenetic pathways, including inhibition of DNA repair, global DNA hypomethylation, and activation of oncogenes. Moreover, it potentiates the production of ROS, which causes DNA strand breaks and lipid peroxidation, further contributing to malignant transformation [21].

## 6. Epidemiological Evidence

In regions with high environmental lead contamination, women exhibit increased rates of spontaneous abortions, pregnancy-induced hypertension, and reduced parity [24]. A Polish study demonstrated that women residing in villages with high soil lead content had significantly fewer full-term pregnancies and lower birth weights compared to women in uncontaminated areas [24]. Other epidemiological studies corroborate these findings, emphasizing the reproductive toxicity of lead even at low exposure levels [23].

## Discussion

This review highlights the complex and dual role of trace elements in female reproductive health, emphasizing the importance of maintaining a balance between essential micronutrients and toxic metal exposure. Zinc, selenium, and magnesium appear to support reproductive function through their involvement in antioxidant defense, hormonal regulation, and cellular homeostasis, whereas cadmium and lead consistently demonstrate harmful effects mediated by oxidative stress, endocrine disruption, and epigenetic alterations.

Oxidative stress emerges as a key mechanism linking both micronutrient deficiency and toxic metal exposure to impaired fertility and adverse pregnancy outcomes. Essential elements contribute to redox balance and mitochondrial function, while toxic metals promote reactive oxygen species generation and cellular damage. Additionally, interactions with the endocrine system are evident, as beneficial elements support hormonal pathways, whereas cadmium and lead may act as metalloestrogens, disrupting normal reproductive signaling.

Although the detrimental effects of cadmium and lead are relatively consistent across studies, evidence regarding the benefits of micronutrient supplementation remains heterogeneous. This variability may result from differences in study design, baseline nutritional status, and exposure levels. Moreover, much of the available evidence is derived from observational studies and experimental models, limiting causal inference.

Several limitations of the current literature should be acknowledged, including heterogeneity of study populations, inconsistent exposure assessment, and insufficient control for confounding factors. The lack of large, well-designed clinical trials further restricts the ability to establish clear clinical recommendations.

## Conclusions

Trace elements, whether essential or toxic, exert profound influences on women's reproductive health. Zinc, selenium, and magnesium play a critical role in oocyte quality, hormonal regulation, and pregnancy maintenance, offering promising avenues for nutritional interventions. Conversely, cadmium and lead represent significant environmental threats, associated with infertility, miscarriage, and gynecological diseases through mechanisms involving oxidative stress, endocrine disruption, and epigenetic alterations. The findings of this review emphasize the importance of maintaining appropriate levels of essential trace elements while minimizing exposure to toxic metals for female reproductive health. Further well-designed studies are needed to clarify causal relationships and to inform evidence-based clinical and public health strategies.

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