The American Journal of Applied Sciences
ISSN 2689-0992 Volume 08 - 2026

Proceedings of Women in Academia, Research and Management for Work-life Initiatives for Sustainable Health & Empowering Safety (WARM-WISHES 2026)

Molecular Mechanisms of Air Pollution–Induced Reproductive Toxicity: Oxidative Stress, Endocrine Disruption and Epigenetic Alterations

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Received: 12 Apr 2026 | Received Revised Version: 22 Apr 2026 | Accepted: 17 May 2026 | Published: 23 May 2026

DOI: 10.37547/tajas/warm-13

Abstract

Widespread declines in fertility and the rising burden of reproductive disorders have increased the search for environmental determinants of reproductive health. Ambient air pollution is now recognized as a critical contributor to reproductive deterioration. Beyond its established respiratory effects, pollutants such as PM2.5, polycyclic aromatic hydrocarbons, nitrogen oxides, and heavy metals exert profound biological effects on reproductive systems.

This systematic review synthesizes mechanistic evidence published between 2015 and 2025 to elucidate how air pollution influences reproductive health through oxidative stress, endocrine disruption, and epigenetic reprogramming. Studies were systematically retrieved from PubMed and Scopus, focusing on experimental and epidemiological data.

Previous evidence has demonstrated that exposure to pollutants causes an overproduction of reactive oxygen species, leading to mitochondrial dysfunction, lipid peroxidation and genomic instability in germ cells. Air pollutants also induce endocrine disruption by disturbing the hypothalamic–pituitary–gonadal axis, leading to hormonal imbalances that impact gametogenesis and reproductive function. Importantly, emerging data suggest that epigenetic mechanisms, such as aberrant DNA methylation and changes in microRNA expression, are responsible for persistent and possibly transgenerational effects of exposure.

These pathways act not in isolation but as an integrated network driving reproductive toxicity. Despite significant advances, important gaps remain in long-term human studies, dose-response relationships, and sex-specific mechanisms. Addressing these challenges will be vital for designing targeted interventions and informing policies to reduce the reproductive health burden associated with air pollution.

Keywords: Air pollution; Reproductive toxicity; Oxidative stress; Endocrine disruption; Epigenetic changes.

Cite This Article: Shoeb, F., & Mukherjee, S. (2026). Molecular Mechanisms of Air Pollution–Induced Reproductive Toxicity: Oxidative Stress, Endocrine Disruption and Epigenetic Alterations. The American Journal of Applied Sciences, 113–124. https://doi.org/10.37547/tajas/warm-13

1.0 Introduction

Declining fertility and increasing reproductive disorders have become major issues in global health in the past few decades. While genetics, lifestyle and socioeconomic factors are responsible for these trends, there has been increasing focus on environmental exposures as important but modifiable determinants of reproductive health (Agarwal et al., 2018; Sharma et al., 2021). Among these, ambient air pollution has become a major concern due to its ubiquitous nature and well-established negative impacts on human health (World Health Organization, 2022; Carré et al., 2017).

Air pollution is a complex mixture of particulate matter (PM2.5 and PM10), gaseous pollutants such as nitrogen oxides (NO_2), sulfur dioxide (SO_2) and ozone (O_3) and toxic compounds including heavy metals and polycyclic aromatic hydrocarbons (PAHs) (Brook et al., 2010; Lelieveld et al., 2015). These pollutants are traditionally associated with respiratory and cardiovascular diseases but are more and more associated with reproductive function impairment in both males and females (La Merrill et al., 2020; Perin et al., 2010). Air pollution has been associated with reduced semen quality, hormonal disruption, ovarian problems and adverse pregnancy outcomes such as miscarriage, preterm delivery and low birth weight (Sharma et al., 2021; Liu et al., 2022; Slama et al., 2008).

The reproductive system is particularly prone to the effects of environmental insults due to its dependence on tightly regulated hormonal signaling pathways and the high susceptibility of germ cells to oxidative and chemical stress (Aitken & Roman, 2008; Agarwal et al., 2018). Emerging evidence indicates that the adverse effects of air pollutants are mediated by multiple interconnected molecular mechanisms. Among these, oxidative stress plays a pivotal role by causing excessive production of reactive oxygen species (ROS), which causes cellular damage, mitochondrial dysfunction and genomic instability (Valko et al., 2007; Agarwal et al., 2018). Many air pollutants are endocrine-disrupting agents, disrupting the hypothalamic-pituitary-gonadal (HPG) axis and affecting the synthesis, secretion and function of important reproductive hormones (Diamanti-Kandarakis et al., 2009; La Merrill et al., 2020).

Furthermore, recent advances in molecular biology have highlighted the role of epigenetic modifications—such as DNA methylation, histone alterations, and microRNA dysregulation—in mediating long-term and potentially transgenerational effects of pollutant exposure (Janssen et al., 2013; Breton et al., 2016).

There is growing evidence, but the exact molecular mechanisms of air pollution induced reproductive toxicity are not well understood, especially in terms of long-term human exposure and sex-specific responses (Carré et al., 2017; La Merrill et al., 2020). Therefore, an integrated synthesis of current knowledge is required to elucidate these mechanisms and recognize the key research gaps.

This review aims to systematically overview the molecular mechanisms of air pollution-induced reproductive toxicity, with special emphasis on oxidative stress, endocrine disruption and epigenetic changes. This work seeks to offer a mechanistic framework, by synthesizing findings from experimental and epidemiological studies, that can guide future research and support the development of targeted preventive strategies.

2.0 Types and Sources of Air Pollutants

Air pollution consists of a complex mixture of particulate and gaseous components originating from both anthropogenic and natural sources. These pollutants differ in their chemical composition, physical properties, and biological effects, yet many share the ability to induce reproductive toxicity through oxidative stress, endocrine disruption, and epigenetic mechanisms.

2.1 Particulate Matter (PM2.5 and PM10)

Particulate matter (PM) is one of the most studied air pollutants regarding reproductive health. Particulate matter (PM) is classified by aerodynamic diameter into coarse particles (PM10) and fine particles (PM2.5). Fine particulate matter is especially hazardous because its extremely small size enables it to travel deep into the respiratory tract and to enter systemic circulation. These particles are a mixture of organic compounds, metals, and secondary aerosols from combustion processes such as vehicular emissions, industrial activities, and biomass burning (Zhou et al., 2022).

PM is recognized as a vehicle for toxic compounds such as polycyclic aromatic hydrocarbons (PAHs), phthalates, and heavy metals, which enhance their bioavailability and toxicity. The exposure to PM2.5 is highly related to reduced fertility, disrupted gametogenesis and adverse pregnancy outcomes (Seli & Taylor, 2023; Liu et al., 2022).

2.2 Gaseous Pollutants

Gaseous air pollutants are nitrogen oxides (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO) and ozone (O_3) and are mainly produced from fossil fuel combustion, vehicular exhaust and industrial emissions. These pollutants contribute to oxidative stress and inflammation, which are the key mechanisms involved in reproductive toxicity.

Recent epidemiological studies have shown that exposure to NO_2 and O_3 is associated with decreased fecundability and reduced success rates in assisted reproductive technologies (Liu et al., 2022). These gases can also react with particulate matter to form secondary pollutants that further increase their biological effect.

2.3 Polycyclic Aromatic Hydrocarbons (PAHs)

Polycyclic aromatic hydrocarbons constitute a class of organic compounds produced through the incomplete combustion of organic substances such as coal, oil, wood, and tobacco. Sources of PAHs include automobile exhaust, industrial activities, and biomass combustion. The chemicals exist in the gaseous state as well as particulate forms, while high molecular weight PAHs are normally found in particulates.

PAHs are known endocrine disruptors that affect signaling of hormones through interference with hormone receptor functions. The chemicals may produce reactive oxygen species and DNA adducts, causing mutagenicity and infertility (Dai et al., 2023; Rafiee et al., 2023). There are also epidemiological studies showing an association between exposure to PAHs and adverse reproductive health effects, such as decreased fertility and poor fetal development (Zhang et al., 2025).

2.4 Heavy Metals

Heavy metals like Pb, Cd, Hg, and As are long-lasting contaminants in the environment that can be present in the atmosphere as part of particulate matter. Heavy metals result from emissions, mining, combustion of fossil fuels, and burning of wastes.

A wide variety of heavy metals act as endocrine disrupters, either by interfering with the physiological functions of hormones or acting as hormone antagonists, termed “metalloestrogens.” They affect estrogen signaling and reproductive health. Continuous exposure to heavy metals can cause spermatogenic problems, ovarian problems, and hormonal disorders (McClam et al., 2023; Zhang et al., 2024). Current research also demonstrates the involvement of oxidative stress and mitochondrial disruption in the mechanism of reproductive toxicity caused by heavy metals (Fan et al., 2024; Li et al., 2026).

2.5 Endocrine-Disrupting Chemicals (EDCs)

Apart from conventional pollutants, there are several chemicals found in air that are known as endocrine disrupting chemicals (EDCs), which include phthalates, bisphenol A, dioxins, and polychlorinated biphenyls (PCBs). These chemicals are emitted from different industrial operations, consumer goods, and burning operations.

The EDCs can be present in the gas form or adsorbed on particulate matter, making it easier for humans to breathe them in. It is widely accepted that EDCs affect hormone production, metabolism, and receptor signaling and hence disrupt reproductive development (Zhang et al., 2023; Gore et al., 2024). The latest research has highlighted the ability of these chemicals to cause epigenetic changes in the environment (Lin et al., 2025).

2.6 Combined and Mixed Pollutant Exposure

It should be noted that, in practice, people are subject to exposure to a combination of various substances. The effect of such combinations may be either additive or synergistic, leading to higher levels of toxicity. For example, particles carrying PAHs and heavy metals might trigger both oxidative stress and endocrine disruption at once, thus causing even more harmful reproductive results (Zhou et al., 2022; Dai et al., 2023).

Thus, knowledge about these relationships is crucial for the understanding of real-life situations. The major pollutants, their sources, and mechanisms are summarized in Table1.

Table 1: The major pollutants, their sources, and mechanisms summarized.

Pollutant	Primary Sources	Key Molecular Mechanisms	Reproductive Effects	Representative References
Particulate Matter (PM2.5, PM10)	Vehicular emissions, industrial processes, biomass burning, construction dust	ROS generation, oxidative stress, mitochondrial dysfunction, DNA damage, inflammation	Reduced sperm quality, impaired oocyte maturation, adverse pregnancy outcomes	(Liu et al., 2022; Zhou et al., 2022; Seli & Taylor, 2023)
Nitrogen Oxides (NO_2)	Traffic emissions, fossil fuel combustion, power plants	Oxidative stress, inflammatory signaling, endothelial dysfunction	Decreased fecundability, hormonal imbalance	(Liu et al., 2022; La Merrill et al., 2020)
Ozone (O_3)	Secondary pollutant formed by photochemical reactions	Lipid peroxidation, oxidative injury, cellular apoptosis	Impaired fertility, pregnancy complications	(Carré et al., 2017; Liu et al., 2022)
Sulfur Dioxide (SO_2)	Coal burning, industrial emissions	Oxidative stress, disruption of cellular metabolism	Reduced reproductive efficiency, fetal toxicity	(WHO, 2022; Sharma et al., 2021)
Polycyclic Aromatic Hydrocarbons (PAHs)	Incomplete combustion (vehicle exhaust, tobacco smoke, biomass burning)	DNA adduct formation, endocrine disruption (AhR activation), ROS generation	Sperm DNA damage, ovarian toxicity, infertility	(Perera et al., 2020; Seli & Taylor, 2023)
Heavy Metals (Pb, Cd, Hg, As)	Industrial emissions, mining, waste incineration, contaminated fuels	Endocrine disruption, oxidative stress, enzyme inhibition, epigenetic alterations	Hormonal imbalance, impaired spermatogenesis, ovarian dysfunction	(Tchounwou et al., 2021; La Merrill et al., 2020)
Endocrine-Disrupting Chemicals (EDCs) (e.g., phthalates, BPA, dioxins)	Plastics, industrial chemicals, combustion processes	Hormone receptor interference, altered gene expression, epigenetic modifications	Disrupted HPG axis, reduced fertility, developmental defects	(Diamanti-Kandarakis et al., 2009; La Merrill et al., 2020)
Mixed Pollutant Exposure	Combined environmental exposure (urban air pollution)	Synergistic ROS production, combined endocrine and epigenetic effects	Enhanced reproductive toxicity, transgenerational effects	(Zhou et al., 2022; Liu et al., 2022)

3.0 Oxidative Stress as a Central Mechanism

Oxidative stress is one of the major pathways involved in reproductive toxicity due to imbalance between production and scavenging of reactive oxygen species (ROS), which cause damage to lipids, proteins, and DNA (Cohen et al., 2017; Aitken et al., 2022). Oxidative damage interferes with cellular homeostasis, thus causing dysfunction of reproductive processes in both sexes (Guerriero and D'Errico, 2022).

In terms of male reproduction, high amounts of ROS lead to poor sperm parameters, such as motility, morphology, and DNA integrity (Pedersen et al., 2013; Hussain et al., 2024). Sperm cells are especially sensitive to oxidative stress because of the presence of many polyunsaturated fatty acids in the membrane of the cells (Pedersen et al., 2013; Li et al., 2017). Moreover, oxidative stress affects sperm cell mitochondria, reducing their ability to generate energy for motility and fertilization of oocytes (Li et al., 2017; Hussain et al., 2024).

Oxidative stress negatively impacts female reproduction by disrupting follicular development, oocyte development, and steroidogenesis (D'Amico et al., 2023). This form of stress has been found to cause disorders like polycystic ovary syndrome, endometriosis, and early ovarian insufficiency through mechanisms involving ROS-induced cell death and modification of cellular signaling pathways (Dadvand et al., 2013; Klepac et al., 2018; Ammar et al., 2024). In addition, oxidative stress plays an important role in ovarian aging and diminished oocyte quality (Ammar et al., 2024).

Air toxins such as particulate matter and heavy metals, among others, are significant contributors to oxidative stress-induced reproductive toxicity due to their role in increasing production of ROS and inhibiting activities of antioxidants enzymes (Cohen et al., 2017; Breton et al., 2016; Bharadwaj et al., 2016; Hussain et al., 2024). These exposures have also been shown to be causally related to adverse reproductive health outcomes, including infertility, low birth weight, and developmental defects (Breton et al., 2016; Schultz et al., 2016; Ibrahim et al., 2024).

While intrinsic antioxidant systems help to defend against oxidative stress, prolonged exposure to environmental stress can surpass this ability, leading to oxidative damage and infertility (Bharadwaj et al., 2016; Guerriero & D'Errico, 2022). Thus, managing oxidative stress via antioxidants and decreasing environmental stresses constitutes an essential strategy for addressing reproductive toxicity (Schultz et al., 2016; Hehua et al., 2017; Rahman et al., 2026).

4.0 Endocrine Disruption

Endocrine disrupting chemicals (EDCs) represent environmental pollutants that disrupt the signaling process of hormones, resulting in disrupted reproduction and increased risk of reproductive diseases (Kahn et al., 2020; Bertram et al., 2022). Chemical compounds like BPA, phthalates, pesticides, and heavy metals have contributed significantly to low-level human exposure to endocrine-disrupting chemicals, posing major challenges in terms of reproductive health (Bertram et al., 2022).

There has been a recent paradigm shift from receptor-mediated toxicity to the role of epigenetics in endocrine disruption (Tapia-Orozco et al., 2017; Acharjee et al., 2023). The importance of epigenetics lies in their role in modulating gene expression in the processes of gametogenesis, steroidogenesis, folliculogenesis, and embryo implantation (Bure et al., 2022; Acharjee et al., 2023). These processes are disrupted by EDCs, leading to permanent changes in reproductive genes (Bure et al., 2022; Acharjee et al., 2023).

Physiologically, endocrine-disrupting chemicals interfere with the functioning of the hypothalamic–pituitary–gonadal axis and impair cell functions, such as that of granulosa, Sertoli, and Leydig cells, causing hormone synthesis and gamete maturation to be disrupted (Kahn et al., 2020). At a molecular level, these chemicals have been shown to affect the functioning of DNA methylation-related enzymes, which results in abnormal gene expression of key reproductive processes.

The mechanism of action of bisphenol A, one of the most widely studied endocrine-disrupting chemicals, has been identified as interfering with DNA methylation of estrogen receptor genes, such as ESR1 and CYP19A1, thus causing ovarian failure and steroid synthesis issues (Bhandari et al., 2019; Palak et al., 2023). Furthermore, bisphenol A impacts the epigenetic processes of histone modification, thus causing transcriptional repression of reproductive genes (D'Cruz et al., 2022). Similarly, endocrine-disrupting chemicals belonging to phthalate groups, like di(2-ethylhexyl) phthalate (DEHP), have been associated with the disruption of DNA methylation and histone acetylation processes, thereby impairing testosterone synthesis and spermatogenesis (Yang et al., 2025; Tian et al., 2024).

The chemicals found in pesticides, including DDT, have also been found to cause transgenerational epigenetic changes, such as DNA methylation of germ cells, and have been shown to negatively impact reproductive function in subsequent generations (Ben Maamar et al., 2019; Wu et al., 2020). Similarly, organophosphate pesticides have been reported to result in abnormal microRNAs and developmental signaling disruptions (Tran et al., 2021).

Heavy metals, such as cadmium and lead, have been identified to cause endocrine disruption through oxidative stress and epigenetics. Heavy metals have been known to cause global hypomethylation and gene-specific hypermethylation, as well as modifications of histones, leading to defects in steroidogenesis and infertility (Zhang et al., 2024; Li et al., 2023).

Importantly, exposure to EDCs during critical developmental windows can lead to persistent and transgenerational epigenetic changes, increasing the risk of reproductive disorders such as polycystic ovary syndrome, endometriosis, and infertility (Hiam *et al.*, 2019).

Overall, endocrine disruption in reproductive toxicity is mediated by a complex interaction between hormonal imbalance and epigenetic reprogramming as illustrated in Figure 1. Understanding these mechanisms is crucial for identifying early biomarkers of exposure and developing targeted strategies to mitigate the long-term reproductive effects of environmental contaminants.

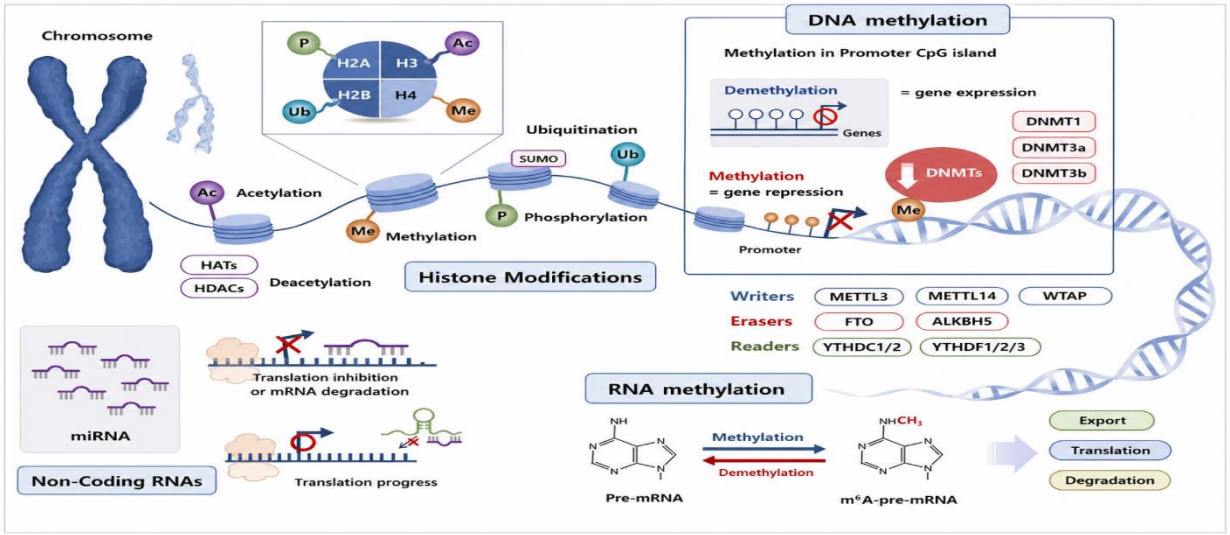

Figure 1: Overview of the primary epigenetic mechanisms – including histone modifications, DNA methylation, RNA methylation, and non-coding RNAs (miRNAs) – which serve as key targets for endocrine disruption by altering gene expression pathways.

5.0 Epigenetic Alterations

Epigenetic modifications serve as major players in reproductive toxicity since they can affect gene expression without changing the DNA sequence (Yu et al., 2024; Saftić Martinović et al., 2024). They involve DNA methylation, histone modification, and non-coding RNAs, all of which affect the regulation of chromatin structure, transcriptional processes, and reproduction (Yu et al., 2024; Liang et al., 2025). Such epigenetic mechanisms also help stabilize the genome and maintain its memory to ensure future reproductive effects (Saftić Martinović et al., 2024).

Environmental exposure is one of the most important factors involved in epigenetic deregulation. Particulates, heavy metals, pesticides, and endocrine-disrupting chemicals (EDCs) have already been proven to affect epigenetic modifications and thus contribute to endocrine disruption, poor ovarian function, and adverse pregnancy results (Yu et al., 2024; Wang et al., 2024). Current research confirms that environmental toxins cause comprehensive disturbances associated with DNA methylation, histone modifications, and RNA involvement, resulting in infertility and reproductive problems (Wu, 2024; Liang et al., 2025).

One of the mechanisms that have been extensively studied in the area of reproductive toxicity is DNA methylation. This mechanism controls gene expression through inhibition of transcription factor binding and chromatin condensation (Yu et al., 2024; Shacfe et al., 2023). Environmental pollutants, for instance, cadmium, BPA, interfere with DNA methylation via changes in DNA methyltransferase function leading to either global hypomethylation or gene hypermethylation (Yu et al., 2024; Liang et al., 2025). This results in poor oocyte maturation, decreased fertility, and is commonly associated with conditions like polycystic ovary syndrome (PCOS), endometriosis, and premature ovarian insufficiency (POI) (Yu et al., 2024; Saftić Martinović et al., 2024).

Epigenetic alterations such as histone post-translational modifications, including histone acetylation and histone methylation, control the opening up of the chromatin structure and hence gene transcription (Yu et al., 2024). Histone post-translational modifications can either up- or

down-regulate gene transcription depending on the target histone modification site (Yu et al., 2024). Exposure to environmental factors impairs the function of histone modifiers, resulting in the abnormal activation or repression of genes (Liang et al., 2025; Wu, 2024). Histone modifications have been associated with decreased endometrial receptivity and embryo implantation (Yu et al., 2024; Wang et al., 2024).

Non-coding RNA (ncRNA), which includes microRNA and long non-coding RNAs, functions as an important regulator of post-transcriptional regulation and is highly sensitive to changes in the environment (Yu et al., 2024; Saftić Martinović et al., 2024). NcRNAs have been implicated in various reproductive disorders, including defective folliculogenesis, hormone imbalances, and infertility (Yu et al., 2024; Agarwal et al., 2024).

Importantly, epigenetic alterations induced by environmental toxicants can be transmitted across generations. Exposure to EDCs such as BPA and phthalates modifies germ cell epigenetic programming, resulting in transgenerational effects on fertility, embryonic development, and disease susceptibility (Yu *et al.*, 2024; Liang *et al.*, 2025). These findings highlight the long-term and heritable impact of environmental exposures on reproductive health (Saftić Martinović *et al.*, 2024).

Overall, epigenetic mechanisms act as a crucial interface between environmental exposures and reproductive toxicity. Disruption of these processes contributes to infertility, pregnancy complications, endocrine dysfunction, and reproductive tract diseases (Yu *et al.*, 2024; Wang *et al.*, 2024). Advances in epigenetic research, including biomarker discovery and targeted therapeutic strategies, offer promising opportunities for improving diagnosis, prevention, and treatment of environmentally induced reproductive disorders (Agarwal *et al.*, 2024; Saftić Martinović *et al.*, 2024).

6.0 Effects on Male Reproductive System

Male reproductive health has been found to be negatively affected by exposure to air pollution through mechanisms such as oxidative stress and endocrine disruption. Airborne pollutants like particulate matter, heavy metals, and polycyclic aromatic hydrocarbons may find their way into the bloodstream and affect testicular physiology, which is very prone to stress since it requires a lot of energy for optimal functioning (Agarwal et al., 2018; Sharma et al., 2021; Seli and Taylor, 2023).

One such mechanism that has been established involves increased ROS production, which causes sperm membrane lipid peroxidation, fragmentation of DNA in the sperm nuclei, and apoptosis of the germ cells (Valko et al., 2007; Seli and Taylor, 2023; Wang et al., 2024). Such changes ultimately result in low sperm concentration, poor motility, and an unusual shape. Furthermore, airborne pollutants have been found to interfere with the HPG axis, affecting spermatogenesis by decreasing testosterone synthesis (La Merrill *et al.*, 2020; Zhou *et al.*, 2022).

Recent studies have further identified mitochondrial dysfunction and ferroptosis as emerging contributors to pollutant-induced germ cell damage, highlighting novel molecular targets (Wang *et al.*, 2024; Zhang *et al.*, 2023).

7.0 Effects on Female Reproductive System

Air pollution adversely impacts female reproductive health by affecting ovulation, hormonal imbalance, and pregnancies. Several epidemiological investigations have found significant correlations between exposure to air pollution and low ovarian reserve, menstrual cycle disorders, and poor assisted reproduction results (Liu et al., 2022; Seli and Taylor, 2023; Zhang et al., 2023).

On a molecular level, oxidative stress is a fundamental factor that leads to the destruction of follicles and compromised quality of the egg cells. Increased ROS levels inhibit the proper functioning of mitochondria and meiosis, resulting in decreased chances of fertilization (Agarwal et al., 2018; Wang et al., 2024).

Moreover, air pollution acts as an endocrine disruptor, inhibiting the production of sex hormones and their pathways, specifically estrogen and progesterone (Diamanti-Kandarakis *et al.*, 2009; La Merrill *et al.*, 2020).

Recent studies further report that exposure to fine particulate matter is associated with increased risks of miscarriage, preterm birth, and placental dysfunction, mediated through oxidative stress and inflammation (Zhang *et al.*, 2023; Wang *et al.*, 2024).

8.0 Transgenerational and Developmental Effects

Emerging research indicates that air may cause lasting epigenetic changes that affect future generations. Air pollutants may modify gene expression through DNA methylation, histone modification, and changes in microRNAs (Janssen et al., 2013; Breton et al., 2016; Zhou et al., 2022).

Recent research has shown that prenatal exposure to air pollution leads to lasting epigenetic changes in the placenta and germ cells, which could have consequences for reproductive health in future generations (Zhang *et al.*, 2023; Wang *et al.*, 2024).

However, the extent to which these epigenetic changes are stable and heritable remains uncertain, particularly in human populations (La Merrill *et al.*, 2020).

9.0 Interaction of Multiple Mechanisms

The mechanism behind air pollution-induced reproductive toxicity involves intricate interplay among oxidative stress, endocrine disruption, and epigenetic modifications. Oxidative stress serves as the crucial intermediary factor that mediates the effect of pollutants on subsequent molecular-level events, such as DNA methylation and gene expression (Valko et al., 2007; Breton et al., 2016).

There is emerging research indicating that simultaneous exposure to several pollutants leads to synergistic outcomes, causing higher levels of ROS generation and endocrine disruption (Zhou et al., 2022; Wang et al., 2024). Additionally, endocrine disruptors increase oxidative stress mechanisms, establishing a positive feedback cycle that worsens reproductive health issues (Diamanti-Kandarakis *et al.*, 2009).

10.0 Research Gaps

There are still some limitations in studying air pollution-caused reproductive toxicity. One key issue is the absence of long-term human studies which can prove the existence of a causal relationship between air pollution and reproductive toxicity (Carré et al., 2017; Wang et al., 2024).

Most researches concentrate on one pollutant but not multiple ones which makes the calculation of cumulative effect of air pollution complicated (Lelieveld et al., 2015; Zhou et al., 2022). Moreover, sex-based studies in relation to female reproductive system are scarce (La Merrill *et al.*, 2020).

Recent literature also highlights the need for validated biomarkers and standardized exposure assessment methods (Zhang *et al.*, 2023).

11.0 Future Perspectives

In future research, there should be a use of multi-omics to further investigate the changes that arise from pollutants. With developments in genomics, proteomics, and metabolomics, new possibilities have arisen regarding finding new biomarkers and new therapies (Breton et al., 2016; Wang et al., 2024).

Also, it is worth noting that recent studies have highlighted the need for precision environmental health approaches when assessing susceptibility and risk exposure (Zhang et al., 2023). Improving environmental regulation and public health interventions will help mitigate reproductive risks posed by air pollution (World Health Organization, 2022).

12.0 Conclusion

Air pollution represents a significant threat to reproductive health through interconnected mechanisms involving oxidative stress, endocrine disruption, and epigenetic alterations (Sharma *et al.*, 2021; Liu *et al.*, 2022; Wang *et al.*, 2024).

While substantial progress has been made, further research incorporating recent advances and longitudinal data is required to fully elucidate these mechanisms and translate findings into effective prevention strategies.

Declarations

The authors hereby declare that the manuscript submitted for consideration is an original work and has not been published or submitted elsewhere for publication. The authors take full responsibility for the integrity, accuracy, and ethical compliance of the work presented in the manuscript, including all revisions made in response to reviewer comments.

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Conflict of Interest and Ethical Compliance: All authors confirm that:

- **i.)** Any potential conflicts of interest, whether financial or non-financial, have been fully disclosed. – NA
- **ii.)** All sources of funding and financial support received for the conduct of the study have been appropriately acknowledged, including any updates made during revision. – NA
- **iii.)** Necessary ethical approvals have been obtained from the relevant institutional or regulatory bodies for studies involving human participants, animals, or sensitive data, wherever applicable, and are clearly stated in the manuscript. - NA

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