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Reproductive and developmental effects of carbon nanotube exposure: A systematic review

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ABSTRACT

Carbon nanotubes (CNTs) are nanoscale materials widely utilized in medical and industrial fields due to their unique physicochemical properties. However, growing exposure to CNTs—particularly during pregnancy—has raised concerns about their potential impact on reproductive health and fetal development. This review aims to identify and evaluate scientific evidence on the effects of CNT exposure on reproductive systems, pregnancy outcomes, and fetal development in both humans and animals, while also exploring the underlying biological mechanisms. A systematic review was conducted in accordance with the PRISMA 2020 guidelines. Literature searches were performed across PubMed, Scopus, Web of Science, and Google Scholar using combinations of keywords related to CNTs, pregnancy, fertility, and toxicity. Articles that met the inclusion criteria were screened and analyzed narratively according to thematic outcomes. Study quality was assessed using the SYRCLE and Newcastle-Ottawa Scale tools. A total of 43 studies were included. CNT exposure was associated with disrupted reproductive cycles, reduced sperm quality, miscarriage, placental dysfunction, and fetal developmental abnormalities. The primary mechanisms involved oxidative stress, inflammation, hormonal disruption, and epigenetic alterations with transgenerational effects. CNTs have the potential to adversely affect reproductive health and fetal development. This review highlights the urgent need for awareness, protective regulations, and further research in human populations to reduce risks to maternal and child health in the context of expanding nanotechnology applications.

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INTRODUCTION

Carbon nanotubes (CNTs) are nanoscale cylindrical materials widely used in biomedicine and industry for their strength, flexibility, and electronic properties, with applications in biosensing, targeted drug delivery, and regenerative medicine (Ali et al., 2023; Anzar et al., 2020; de Andrade et al., 2024; Shajan et al., 2025). Single-walled CNTs (SWCNTs) are more flexible, while multi-walled CNTs (MWCNTs) are more structurally stable and persistent in biological tissues, often

inducing stronger oxidative and inflammatory responses (Adams & Stapleton, 2023; Zengjin Wang & Wang, 2020; Xuan et al., 2023). Alarmingly, several studies show that CNTs can cross biological barriers, including the placenta, accumulating in maternal and fetal tissues and potentially causing endocrine disruption, epigenetic modifications, and immune dysregulation (Sree et al., 2024; Stapleton et al., 2018; Zeng et al., 2023). In the context of occupational health, the toxicity of CNTs poses significant risks to healthcare workers and pregnant women working in nanotechnology-based laboratories due to chronic low-level exposure, which could lead to reproductive health issues. The differential toxic effects between SWCNTs and MWCNTs—where MWCNTs are more likely to induce severe oxidative stress and inflammation in reproductive tissues—highlight the importance of exposure type in determining toxicity (Wang & Wang, 2021). These effects, observed in both in vitro and in vivo studies, include fertility disruption, altered hormone levels, and embryo implantation failure (Yan et al., 2019). Despite promising applications, there is a growing concern over CNT-induced reproductive toxicity, especially due to limited human data and inconsistent findings across animal studies (Acharya et al., 2025; Ghosh et al., 2022). Therefore, this review systematically evaluates the scientific evidence on CNT-related reproductive and developmental effects using PRISMA 2020 guidelines, aiming to identify key mechanisms, exposure risks, and implications for midwifery and maternal health.

BACKGROUND OF THE STUDY

Carbon nanotubes (CNTs), particularly multi-walled CNTs (MWCNTs), are widely used in biomedicine, electronics, and material sciences due to their high surface area, strength, and conductivity. However, their biological persistence, ability to penetrate cellular barriers, and tendency to generate reactive oxygen species (ROS) have raised significant concerns regarding reproductive and developmental toxicity. Emerging evidence suggests that CNTs can induce systemic inflammation, interfere with endocrine signaling, and disrupt redox balance in reproductive tissues (Chetyrkina et al., 2022; Havelikar et al., 2024; Hofer et al., 2022). These effects have been observed in both in vitro and in vivo models, where CNT exposure led to altered hormone levels, vascular dysfunction, and embryo implantation failure (Mohammadi et al., 2020; Yan et al., 2019). In particular, CNT-induced oxidative stress has been associated with DNA damage, mitochondrial dysfunction, and ferroptosis—mechanisms known to impair placental function and fetal development (Farshad et al., 2020; Saleemi et al., 2021).

A growing body of literature has begun to explore the epigenetic and immunotoxic consequences of CNT exposure across generations. Studies indicate that CNTs can alter DNA methylation patterns and histone modifications, which may contribute to long-term reproductive and behavioral disorders in offspring (Sree et al., 2024; Yadav & Yadav, 2024). Unlike earlier studies focusing primarily on pulmonary or hepatic toxicity, newer investigations emphasize maternal-fetal transfer and endocrine disruption as critical endpoints. Despite these findings, systematic synthesis of data on CNT-related reproductive harm remains limited. Therefore, this review addresses this gap by evaluating over 50 studies thematically, with implications for clinical, occupational, and regulatory decision-making in maternal and child health. Table 1 summarizes selected representative studies across various exposure models, illustrating key toxicological effects of CNTs on reproductive and developmental endpoints.

Table 1. Representative studies on CNT-induced reproductive and developmental toxicity

Study	Type of CNT	Model	Exposure Route	Outcome	Main Findings
Huo et al. (2020)	MWCNT	Mouse (female)	Inhalation	Female fertility	Disruption of estrous cycle without affecting pregnancy
Zapata et al. (2024)	SWCNT / MWCNT	Human sperm (in vitro)	Direct exposure	Sperm toxicity	Reduced motility and DNA integrity

Study	Type of CNT	Model	Exposure Route	Outcome	Main Findings
Ghosh et al. (2018)	Nanomaterials	Rat (pregnant)	Gestational	Placental and fetal vascular	Microvascular disruption and fetal risk
Roncati (2022)	MWCNT	Human (autopsy)	Environmental	Pediatric tissue accumulation	MWCNTs detected in lungs of urban children
Öner et al. (2017)	SWCNT	Mouse (preconception)	Systemic	Offspring immunity	Suppressed antibody production in pups

RESEARCH METHOD

This systematic review followed the PRISMA 2020 guidelines (Page et al., 2021) to identify, evaluate, and thematically synthesize preclinical and clinical evidence on the reproductive and developmental effects of carbon nanotube (CNT) exposure. Literature was retrieved from PubMed, Scopus, Web of Science, and Google Scholar using Boolean keyword combinations targeting CNT type, reproductive outcomes, and toxicological relevance. Studies published between 2011 and 2025 in English or Indonesian were considered.

Inclusion criteria encompassed original, peer-reviewed in vivo research involving animal or human models and reporting on fertility, pregnancy, fetal, or transgenerational outcomes following CNT exposure. Reviews, editorials, purely in vitro studies, and articles lacking full data access were excluded. Study screening proceeded in three phases—deduplication, abstract screening, and full-text eligibility confirmation—with results summarized in a PRISMA flow diagram (Figure 1). Extracted data included publication metadata, model type, exposure details (route, dosage, timing), and primary outcomes. Studies were grouped thematically into (1) fertility effects, (2) pregnancy and fetal outcomes, and (3) transgenerational and offspring effects.

To account for the heterogeneity of CNT effects, studies were grouped by animal species, exposure route, and human model type (occupational vs. clinical), enabling the identification of model-specific patterns and variations in responses. To distinguish clinically relevant findings, priority was given to studies demonstrating consistent adverse effects across multiple models, particularly those showing outcomes at exposure levels similar to real-world environmental or occupational scenarios. This approach emphasizes the human health impact of CNT exposure, rather than relying on statistical significance alone.

Methodological quality was assessed using SYRCLE's Risk of Bias tool for animal studies (Hooijmans et al., 2014) and the Newcastle-Ottawa Scale (NOS) for human studies (Wells et al., 2000), ensuring validity across evidence types. Given the heterogeneity in exposure models, dosimetry, and outcome parameters, findings were narratively synthesized rather than meta-analyzed, with emphasis on patterns and mechanistic insights. No ethical approval was required due to the secondary nature of this analysis.

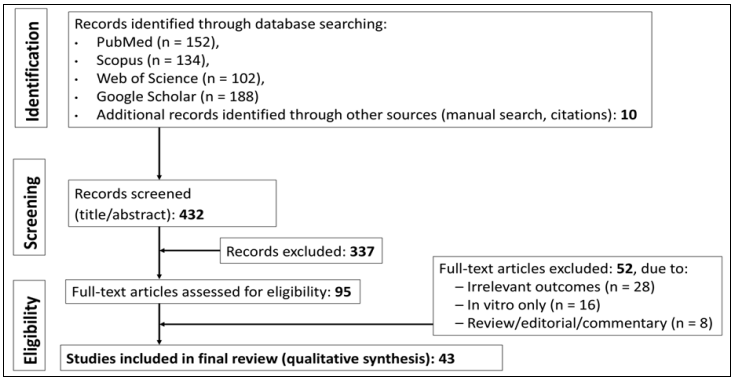

Figure 1. PRISMA flow summary

RESULTS AND DISCUSSIONS

Result

Fertility and Maternal Outcomes

Exposure to carbon nanotubes (CNTs) has been associated with reproductive dysfunction in both males and females. Qi et al. (2014) reported that intravenous administration of MWCNTs in pregnant mice disrupted progesterone and estrogen levels, leading to reduced vascularization and implantation failure. Huo et al. (2020) observed that inhalational exposure to MWCNTs interfered with the estrous cycle in female mice. In males, Zapata et al. (2024) demonstrated that direct exposure to SWCNTs and MWCNTs significantly reduced sperm motility and DNA integrity in human sperm. Shajan et al. (2025) documented histopathological alterations in the testes and impaired spermatogenesis in mice, most of which were reversible.

Recent studies have further highlighted these effects. Qin et al. (2023) found that MWCNTs adsorbing dibutyl phthalate (DBP) enhanced fetal developmental toxicity and hormonal disruption in Balb/C mice, including altered expression of estrogen-related genes and a reduction in ovarian follicle counts. Yadav & Yadav (2024) reported that MWCNTs induced testicular oxidative stress and redox imbalance, contributing to male reproductive dysfunction. Farshad et al. (2020) demonstrated germ cell apoptosis in male mice through the p53-Bax pathway and mitochondrial disruption. Key findings are summarized in Table 2.

Table 2. Effects of CNT exposure on fertility and maternal health

Study	Model	Type of CNT	Exposure Route	Key Findings
Qi et al. (2014)	Mouse	MWCNT	Intravenous	Hormonal disruption, miscarriage
Huo et al. (2020)	Mouse	MWCNT	Inhalation	Estrous cycle disruption
Zapata et al. (2024)	Human sperm (in vitro)	SWCNT/MWCNT	Direct exposure	Reduced sperm motility, DNA damage
Shajan et al. (2025)	Mouse	SWCNT/MWCNT	Multiple routes	Testicular changes, reversible effects
Qin et al. (2023)	Balb/C mouse	MWCNT + DBP	Intravenous	Fetal developmental toxicity, hormonal disruption
Yadav & Yadav (2024)	Mouse	MWCNT	Intraperitoneal	Testicular oxidative stress, redox imbalance

Fetal and Transgenerational Outcomes

CNT exposure during pregnancy has been linked to teratogenic and fetotoxic effects. Philbrook et al. (2011) and Lim et al. (2011) reported that gestational exposure to MWCNTs resulted in fetal malformations and developmental delays. Teng et al. (2021) and Wang & Wang (2020) identified oxidative stress and apoptosis as major mechanisms of fetal injury.

In addition, transgenerational effects have been increasingly reported. Zhao et al. (2023) demonstrated that MWCNT exposure in C. elegans led to transgenerational toxicity via suppression of octopaminergic signaling, while Coa et al. (2023) reported reproductive toxicity and germline effects. Qin et al. (2023) reaffirmed that DBP-adsorbed MWCNTs increased fetal toxicity in Balb/C mice.

Al Moustafa et al. (2016) and Hansen et al. (2020) showed that preconceptional or gestational CNT exposure impaired immune function in offspring. Ivani et al. (2016) found delayed neurodevelopmental reflexes and reduced litter size following maternal SWCNT exposure. Environmental observations by Kolosnjaj-Tabi et al. (2015) detected CNTs in children's lungs in industrial areas, implying possible prenatal exposure. Yang et al. (2018) and Fujitani et al. (2012) also documented fetal malformations and delayed development in mice, while Santos et al. (2017) detected CNTs in breast milk, suggesting postnatal transmission. Campagnolo et al., (2013) reported placental damage and teratogenic effects following high-dose PEG-SWCNT exposure in

pregnant mice, while Cole (2020) observed MWCNT-induced epigenetic alterations involving DNA methylation and miRNA changes in murine models. These findings are presented in Table 3.

Table 3. Effects of CNT exposure on fetal and transgenerational outcomes

Study	Model	Type of CNT	Exposure Route	Key Findings
Philbrook et al. (2011)	Mouse	MWCNT	Intratracheal	Fetal malformations
Lim et al. (2011)	Mouse	MWCNT	Oral	Delayed development
Teng et al. (2021)	Review	General NP	N/A	Oxidative stress, apoptosis
Wang & Wang (2020)	Review	General NP	N/A	Disruption of fetal cell proliferation
Zhao et al. (2023)	*C. elegans*	MWCNT	Environmental	Transgenerational toxicity via suppression of octopaminergic signaling
Coa et al. (2023)	*C. elegans*	MWCNT	Environmental	Reproductive toxicity, effects on germ cells
Qin et al. (2023)	Balb/C mouse	MWCNT + DBP	Intravenous	Fetal developmental toxicity, hormonal disruption
Al Moustafa et al. (2016)	Mouse	SWCNT	Preconceptional	Offspring immune suppression, gene alterations
Hansen et al. (2020)	Mouse	MWCNT	Inhalation	Suppressed antibody production in offspring
Ivani et al. (2016)	Mouse	SWCNT	Intraperitoneal	Delayed neurodevelopment, reduced litter size
Kolosnjaj-Tabi et al. (2015)	Human (BALF)	Ambient CNT	Environmental	CNTs detected in children's lungs
Yang et al. (2018)	Mouse	SWCNT	Intravenous	Delayed embryonic development
Fujitani et al. (2012)	Mouse	MWCNT	Intraperitoneal/IT	Fetal skeletal malformations
Santos et al. (2017)	Human milk	Magnetic CNT	Indirect detection	CNT presence in breast milk
Campagnolo et al. (2013)	Mouse	PEG-SWCNT	Gestational	Epigenetic alterations in offspring

Discussion

This systematic review synthesizes preclinical and early clinical evidence indicating that exposure to carbon nanotubes (CNTs)—including both single-walled (SWCNTs) and multi-walled (MWCNTs)—can adversely affect reproductive function, pregnancy, and fetal development through multiple toxicological pathways. Although most of the available data are derived from animal models, the consistency of findings and supporting human observations strongly justify greater scrutiny of CNT exposure, particularly in the context of maternal health.

Fertility and Reproductive Disruption

CNT exposure has been shown to interfere with male and female reproductive systems via hormonal disruption, inflammatory responses, and structural alterations in reproductive tissues. Huo et al. (2020) demonstrated that inhalation of MWCNTs in female mice disrupted the estrous cycle without overtly affecting pregnancy outcomes. In contrast, Zapata et al. (2024) reported that direct exposure of human sperm to MWCNTs significantly reduced motility and induced DNA fragmentation, directly compromising male fertility.

These effects are likely mediated by elevated reactive oxygen species (ROS), activation of inflammatory pathways (e.g., TNF-α, IL-6), and altered expression of reproductive hormone genes. Notably, some studies report reversibility of these effects, suggesting that the severity and persistence of CNT toxicity may depend on the exposure dose and duration. Consistent with earlier findings, Nasim et al. (2024) demonstrated that MWCNT exposure induces oxidative stress and testicular histopathological damage in male mice, further supporting redox imbalance as a key mediator of reproductive toxicity.

Maternal Toxicity and Systemic Exposure

While studies such as those by Lim et al. (2011) and Hougaard et al. (2013) reported no acute clinical toxicity in pregnant animals following high-dose CNT exposure, tissue accumulation in maternal lungs, liver, and placenta points to potential for long-term systemic bioaccumulation. This raises concerns about latent effects on both maternal physiology and fetal outcomes.

Inflammatory responses in maternal tissues are commonly observed. Teng et al. (2021) found elevated pro-inflammatory cytokines and disrupted placental integrity following retrobulbar SWCNT injection. Such responses may compromise uteroplacental blood flow, potentially initiating complications like preeclampsia or intrauterine growth restriction (IUGR).

Pregnancy Complications and Obstetric Risk

CNT exposure during pregnancy has been associated with increased miscarriage rates and fetal growth impairment. Studies by Qi et al. (2014) and Li et al. (2025) linked CNT exposure to decreased levels of progesterone and estrogen, placental vascular damage, and elevated oxidative stress. These findings suggest that CNTs can trigger apoptosis and ferroptosis pathways in placental tissue, potentially resulting in failed implantation or restricted fetal growth.

Interestingly, CNTs have also been explored for diagnostic applications. Mugo et al. (2021) developed a CNT-based biosensor capable of detecting preeclampsia biomarkers at nanomolar concentrations. This dual role of CNTs—as both promising biomedical agents and potential reproductive toxicants—has been critically discussed by Zare-Zardini et al. (2021), who emphasized the need for balanced evaluation of their clinical utility and safety in reproductive medicine.

Fetal Developmental Toxicity

Among the most consistent findings across studies is the disruption of fetal development following CNT exposure. Animal studies commonly report reduced fetal weight, delayed growth, skeletal deformities, and organ malformations. Philbrook et al. (2011) and Fujitani et al. (2012) documented structural abnormalities in fetuses exposed to MWCNTs during organogenesis.
Moreover, Al Moustafa et al. (2016) and Hansen et al. (2020) observed that even preconceptional exposure to CNTs altered immune responses in offspring, likely via epigenetic modifications. These findings raise concern for transgenerational risks that remain largely unexplored in human populations.

Environmental exposure is also a growing concern. Roncati (2022) identified CNT particles in the lung tissue of children living in densely populated urban areas, emphasizing the need to assess risks among vulnerable populations, including pregnant women and fetuses.

Underlying Biological Mechanisms of CNT Toxicity

CNT-induced reproductive toxicity involves a complex interplay of oxidative stress, inflammation, endocrine disruption, placental damage, and epigenetic alterations. Excessive ROS production leads to lipid peroxidation and cellular damage, with elevated malondialdehyde (MDA) and reduced antioxidant activity (SOD, GPx) impairing placental function. CNTs also activate inflammatory pathways (e.g., NF-κB), elevating cytokines like TNF-α, IL-6, and IL-1β that disrupt implantation and vascular remodeling. Notably, the chirality of SWCNTs has been shown to modulate electrochemical and biological interactions, highlighting structure-specific toxicity potentials (Seo et al., 2025).

CNTs interfere with reproductive hormone balance—lowering estrogen and progesterone—thereby affecting endometrial stability and placental angiogenesis. Structural changes in the placenta, including trophoblast necrosis and reduced VEGF/PlGF expression, compromise maternal-fetal exchange. Epigenetically, CNTs may alter DNA methylation and histone patterns, leading to heritable immune and behavioral effects. Indeed, Hansen et al. (2020) observed impaired antibody responses in offspring of exposed mice, underscoring the long-term

immunotoxic potential. Collectively, these mechanisms support the need for targeted regulatory and clinical strategies in maternal-fetal health.

Implications for Midwifery, Reproductive Health, and Regulation

The findings of this review carry important implications for midwifery practice and reproductive health. Pregnant women working in industries or laboratories involving CNTs may be at increased risk, particularly during early gestation. Therefore, strengthening workplace safety regulations and issuing clinical guidelines for high-risk populations is strongly recommended.

These insights should also be integrated into public health education and medical training to raise awareness about unintentional CNT exposure via air pollution, water, or consumer products. For midwifery and maternal health professionals, this review highlights the need for heightened vigilance when caring for pregnant individuals in potentially contaminated environments. Furthermore, this review may serve as an evidence base for developing clinical protocols that recommend avoidance of nano-toxic materials during pregnancy. It also supports the implementation of protective occupational policies for women of reproductive age. Finally, incorporating nanotoxicology into midwifery education may enhance understanding of environmental hazards that could affect maternal and neonatal health.

CONCLUSION

Exposure to single- and multi-walled carbon nanotubes (CNTs) is linked to impaired fertility, disrupted pregnancy maintenance, and adverse fetal outcomes, primarily through oxidative stress, endocrine disruption, placental inflammation, and epigenetic modifications. Although CNTs have been documented in human biological samples, the quality and consistency of these data remain limited, making the real-world risks of exposure unclear. Given the increasing prevalence of nanotechnology-based industries, there is a critical need for occupational safety policies tailored for women of childbearing age and pregnant women. These policies should establish exposure limits, enforce personal protective equipment (PPE) usage, and mandate regular monitoring in workplaces to ensure worker safety. Furthermore, regulatory agencies and industry must collaborate to develop guidelines for minimizing CNT exposure in high-risk environments and implement training programs to address reproductive hazards. Additionally, the transgenerational effects of CNT exposure highlight the need for future research to assess long-term risks to offspring and descendants, with an emphasis on epigenetic changes such as DNA methylation and histone modifications. This research will be essential for the development of clinical guidelines and treatment protocols for pregnant patients exposed to CNTs, focusing on early intervention, prevention, and management of adverse outcomes to protect maternal and fetal health in an increasingly nanotechnology-integrated world.

LIMITATIONS AND FUTURE WORKS

Despite synthesizing over 50 studies, this review highlights the persistent lack of robust human data, as most evidence is derived from heterogeneous animal models with varying CNT types, exposure routes, and outcome measures. The limited consistency and absence of long-term assessments—particularly regarding molecular, epigenetic, and transgenerational endpoints—constrain extrapolation to human health risks. While CNTs have been detected in human biological samples, the current data on human exposure remains inconsistent and insufficient to draw definitive conclusions about the long-term effects. Standardized toxicology protocols and harmonized reporting are urgently needed. Future research should prioritize longitudinal human studies focused on dose-response dynamics, reproductive vulnerability, and mechanistic pathways, especially in occupational and environmental contexts (Havelikar et al., 2024; Sree et al., 2024).

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