RBMO

REVIEW

Plastic pollution in human reproduction: should we worry?

BIOGRAPHY

Claudio Fenizia, PhD, Associate Professor at the University of Milan, is a molecular immunologist with 15 years of academic research. As a NIH postdoctoral fellow, he studied antiviral responses and SARS-CoV-2. His current work investigates immune effects of micro-nanoplastics. He has authored over 60 papers, with over 1800 citations.

Martina Broggiato[a,1], Stefania Pezzana[a,1], Chiara Scaccabarozzi[b,c,e,1], Francesca Parisi[c,d], Claudia Vanetti[a], Chiara Katerina Guinea Montalvo[c,e], Valeria M Savasi[c,e,1,*], Claudio Fenizia[a,f,1,*]

KEY MESSAGE

Micro-nanoplastics (MNP) exposure may disrupt reproductive and pregnancy outcomes through oxidative stress, inflammation, endocrine effects and placental impairment. This review explores how MNP may affect biological systems, critically evaluates current sampling and detection methods, and recommends standardized methods and mechanistic human studies to improve future risk evaluation.

ABSTRACT

Micro- and nanoplastics (MNP) are pervasive pollutants, detected in every ecosystem. Human exposure is extensive, and their capacity to cross biological barriers and accumulate in tissues raises growing concerns about reproductive health and pregnancy outcomes. Research has shown the presence of MNP in human placenta, fetal meconium and amniotic fluid, confirming their ability to reach the fetal compartment, potentially increasing risks for fetal development. In women, MNP have also been detected in follicular fluid, although their specific effects remain to be determined. In-vitro studies have reported MNP-induced placental vascular damage, whereas murine models suggest impaired ovarian function, reduced oocyte quality and decreased pregnancy rates after MNP exposure. In men, MNP have been identified in testicular tissue and semen. Animal studies report decreased sperm count and quality, likely because of oxidative stress, hormonal disruption and inflammation. Various techniques are available for detecting MNP in biological tissues. Mass and Raman spectroscopy are among the most widely used, each offering specific advantages and limitations. Interpreting experimental data also requires caution, as many in-vitro and in-vivo models use unrealistically high doses of pristine polymers lacking environmental additives, potentially limiting the relevance of their findings to real-world exposures.

INTRODUCTION

The global production of plastic has dramatically increased, reaching nearly 413.8 million tons in 2023 (*Syberg et al., 2021*; *Nayanathara Thathsarani Pilapitiya and Ratnayake, 2024*; *Plastics Europe, 2024*). Because of improper management and disposal, the resulting plastic pollution has become one of the most significant environmental issues worldwide (*Huang et al., 2022*; *Kibria et al., 2023*; *Fayshal, 2024*). It is estimated that only 6–26% of plastic is recycled, indicating that most plastic waste enters the environment through various routes (*Huang et al., 2021*; *Ilechukwu et al., 2022*).

KEYWORDS

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[a] Department of Pathophysiology and Transplantation, University of Milan, via F Sforza 35, Milano, Italy
[b] Department of Obstetrics and Gynecology, 'Vittorio Emanuele III' Hospital, ASST Brianza, via G Leopardi 5, Carate Brianza, Monza e Brianza, Italy
[c] Department of Biomedical and Clinical Sciences, 'L Sacco' Hospital, University of Milan, via G B Grassi 74, Milan, Italy
[d] Department of Obstetrics and Gynecology L Mangiagalli' Hospital, University of Milan, via F Sforza 35, Milan, Italy
[e] Department of Woman, Mother and Neonate, 'V Buzzi' Children Hospital, ASST Fatebenefratelli Sacco, via L Castelvetro 32, Milan, Italy
[f] CRC Nano/microplastics on Environments, Medicine, Ecology, Systems Interaction Studies – NEMESIS, University of Milan, Italy
[1] Joint first authors.

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*Corresponding authors. E-mail addresses: valeria.savasi@unimi.it (V.M. Savasi), claudio.fenizia@unimi.it (C. Fenizia). https://doi.org/10.1016/j.rbmo.2025.105343 1472-6483/© 2025 The Author(s). Published by Elsevier Ltd on behalf of Reproductive Healthcare Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)
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Plastic is a non-biodegradable material, and its natural degradation is extremely slow. A variety of environmental factors contribute to degradation, including abrasion, thermo- and photo-oxidation and a range of biotic degradation pathways (*Wright et al., 2020*).

The natural degradation of plastics is extremely slow and it is initiated by a variety of environmental factors, including abrasion, thermo- and photo-oxidation, as well as a range of biotic degradation pathways (*Wright et al., 2020*), which generate sub-particles defined as microplastics when their diameters range between 1 μm to 5 mm, and nanoplastics when their diameters are within a range of 1 nm to 1 μm (*Zurub et al., 2024*).

Taken together, micro-and nanoplastics (MNP) are generally classified as primary or secondary based on their origin. Primary MNP are sub-particles intentionally produced for use in products, e.g. hand and facial cleaners, cosmetics and shower gels, or industrial applications (*Karbalaei et al., 2018*; *Prata et al., 2020*; *Yuan et al., 2022*). In contrast, secondary MNP originate from the loss of material integrity and fragmentation into polluting sub-particles (*Andrady, 2011*; *Yuan et al., 2022*; *Dube and Okuthe, 2023*). Micro- and nanoplastics are ubiquitously widespread in the environment.

Focusing on humans, the primary exposure routes through which MNP can reach organs and tissues are inhalation, ingestion and dermal contact (*Du et al., 2024*; *Zhao et al., 2024*; *Zurub et al., 2024*). It is estimated that an individual is exposed to about 74,000-121,000 microplastics per year, without considering exposure to nanoplastics, which is likely to make the estimate considerably higher (*Zurub et al., 2024*). Importantly, evidence shows that, after absorption, most MNP can cross the physiological barriers, access the circulatory system and systemically distribute throughout the body. This enables them to reach diverse organs, including the blood, lung, liver, colon, brain, placenta, and the male and female reproductive system, where they can stimulate an immune response, induce oxidative stress, and alter reproductive functions and offspring development (*D'Angelo and Meccariello, 2021*; *Deng et al., 2021*; *Yin et al., 2021*; *Dubey et al., 2022*; *Im et al., 2022*; *Du et al., 2024*; *Wang et al., 2024*; *Lamoree et al., 2025*; *Vanetti et al., 2025*). Additionally, MNP have been detected in body fluids such as feces, sputum, spermatozoa and breast milk (*Dissanayake et al., 2022*; *Marcelino et al., 2022*; *Wang et al., 2024*; *Yang et al., 2024*; *Zurub et al., 2024*). Their distribution depends on factors such as blood flow, tissue affinity and diffusion ability, and on the exposure pathway and particle characteristics (*Zhao et al., 2024*).

Despite growing evidence, the current understanding of the adverse effects of MNP on fertility and reproductive capacity is still limited. Although negative effects have been demonstrated in animal and human cell models *in vitro*, the in-vivo long-term effects of MNP exposure on reproductive capacity and potential transgenerational effects remain poorly understood and require further investigation.

For this reason, the main purpose of this narrative review is to explore and provide an overview of the effect of MNP on male and female reproductive systems, as well as their offspring.

MICROPLASTICS IN HUMAN REPRODUCTION

Microplastics in the male reproductive tract

After environmental exposure, MNP can cross the physiological barriers, access the circulatory system and systemically distribute throughout the body (*Montano et al., 2023*). Indeed, MNP have been detected through Raman microspectroscopy, pyrolysis-gas chromatography-mass spectrometry and deep learning in infrared spectroscopy (LD-IR)in human testicle and semen, with an average abundance of 11.60 $\pm$ 15.52 particles/g and 0.23 $\pm$ 0.45 particles/ml, respectively; the MNP size range measured was 20–100 μm for those detected in the testis and 2–6 μm for those detected in the semen. The most common polymer identified in testicles was polystyrene, whereas polyethylene and polyvinyl chloride (PVC) were predominant in the semen (*Montano et al., 2023*; *Zhao et al., 2023*). The detected plastic particles also differed in shape and dimensions: in testicles, fragments were the most common, whereas fibres and films were more prevalent in semen (*Zhao et al., 2023*; *Hu et al., 2024*).

Evidence indicates a gradual decline in the quality of human semen over the past decades, with sperm concentration dropping from 60 $\times$ 10^6/ml in 1980 to 16 $\times$ 10^6/ml in 2021 (*WHO, 1999*; *2010*). Although no scientific evidence establishes a direct causal link, the decline in fertility has occurred alongside increasing environmental pollution, including the widespread introduction and use of plastics, suggesting a potential association (*Zhang C et al., 2022*).

Furthermore, several types of MNP were detected by LD-IR imaging in prostate tissues in both para-tumoural and tumoural tissue samples. Preliminary evidence indicates that the total amount of MNP is higher in the tumoural tissue compared with the near-normal tissues, suggesting a potential association between MNP exposure and development or progression of prostate cancer (*de Souza et al., 2025*).

Unfortunately, limited data are available on the potential toxicity mechanisms of MNP exposure in the human male reproductive system. Therefore, further research is mandatory (*Deng et al., 2024*).

Microplastics in the female reproductive tract

In humans, the adverse effects of MNP on female fertility have garnered considerable attention in recent years (*Balali et al., 2024*). Existing evidence suggests a notable correlation between prolonged exposure to MNP and a decline in female fertility (*Weingrill et al., 2023*; *Balali et al., 2024*).

Recently, MNP have been detected in human follicular fluid, suggesting that plastic polymers can easily reach the ovarian tissue, raising concerns about a potential negative effect on female fertility (*Ni et al., 2025*). The most abundant polymers found in human follicular fluid are PVC, polyethylene, polystyrene, polypropylene, polyurethane, rubber and acrylonitrile butadiene styrene, with an average size of 11.5 $\pm$ 12.2 μm in length and 6.36 $\pm$ 5.1 μm in width, and a mean concentration of 122.3 plastic sub-particles/ml (*Grechi et al., 2023*; *Ni et al., 2025*).

The effects of MNP on human female reproductive tract are still unknown. In-vitro experiments on immortalized granulosa COV434 cells have demonstrated that exposure to nanoplastics reduce cell viability by

inducing oxidative stress, which, in turn, leads to an increased expression of apoptotic and oxidative stress markers and a subsequent cell cycle arrest (*Huang et al., 2023*). The short-term effects of MNP observed *in vitro* are, therefore, likely to be more pronounced *in vivo*, owing to the detrimental effects of MNP compounding over time. Further studies are needed to assess the effects of different plastic polymers on oocyte quality, and to determine how MNP influence female reproductive outcomes.

Microplastics in human pregnancy and offspring development

Generally, MNP contaminating water, soil and air have the potential to enter the food chain and disperse into the atmosphere (*Balali et al., 2024*). Once in the gastrointestinal, respiratory system, or both, MNP can easily translocate into the circulatory system and reach other organs, as well as cross biological barriers, i.e. the placenta, contaminating the amniotic fluid and the embryo. Similarly, as observed in ex-vivo placenta samples, smaller sub-particles may have a more significant energy-dependent transplacental movement and reach the fetus (*Grafmueller et al., 2015*; *Balali et al., 2024*). It has been demonstrated that MNP causes maternal damage during pregnancy and lactation, and can penetrate various fetal organs, including heart, liver, lungs and spleen, and affect the reproductive and nervous systems, causing transgenerational toxicity and disrupting embryonic development (*Braun et al., 2021*; *Ragusa et al., 2021*; *Zhu et al., 2023*; *Balali et al., 2024*; *Li J et al., 2024*; *Zurub et al., 2024*).

Raman microspectroscopy analysis and LD-IR imaging of human placentas collected from physiological pregnancies and caesarean sections confirmed the presence of MNP on the maternal and fetal sides, as well as in the chorioamniotic membranes (*Braun et al., 2021*; *Ragusa et al., 2021*; *Amereh et al., 2022*; *Halfar et al., 2023*; *Liu et al., 2023b*; *Weingrill et al., 2023*; *Zhu et al., 2023*). The identified fragments were mainly PVC and polypropylene, with a predominant size range between 5 and 10 μm (*Ragusa et al., 2021*; *Zhu et al., 2023*; *Zurub et al., 2024*).

Microplastics with sizes between 10 and 50 μm were found in amniotic fluid and placenta from women who had singleton physiological pregnancies complicated by preterm premature rupture of membranes (*Halfar et al., 2023*). Further data suggest that exposure of pregnant mothers to MNP correlates with pre-eclampsia, premature birth, stillbirth and spontaneous miscarriage (*Dusza et al., 2023*; *Paul et al., 2024*; *Xue et al., 2024*).

Although oxidative stress and immune dysregulation are recognized contributors to adverse pregnancy outcomes, additional research is needed to confirm the correlation between MNP exposure and these clinical conditions (*Amereh et al., 2022*). Moreover, plastic particles may also serve as vectors for harmful chemicals and additives, which can be released and interfere with fetal development, leading to long-term damage (*Amereh et al., 2022*; *Ragusa et al., 2022*; *Liu et al., 2023b*). Pilot research was conducted to determine the presence of MNP in mother–infant pairs using LD-IR. Here, MNP ranging between 2 and 50 μm in size were identified in human breast milk, fetal meconium, infant feces and baby formula, representing a great concern for infant health. The most frequently detected MNP across all samples were polyamide and polyurethane (*Ragusa et al., 2022*; *Liu et al., 2023a*; *Mišľanová et al., 2024*).

Despite considerable progress, the current understanding on the potential short- and long-term adverse effects of plastic particle exposure on human pregnancy and fetal development remains limited. Hence, further research is needed to better understand the potential harmful mechanisms of MNP on infants and to reduce exposure to these contaminants during pregnancy and lactation (*Mišľanová et al., 2024*).

Interestingly, the plastic materials accumulated in humans have changed over time. A retrospective study conducted in Hawaii, which analysed human placenta samples between 2006 and 2021, revealed significant shifts in polymer composition, particle size and shape, with a marked increase in unidentified MNP, often associated with newer additives (*Halfar et al., 2023*; *Weingrill et al., 2023*). Along with these qualitative changes, a quantitative rise in MNP has occurred in human placentas, both in number of affected placentas and the particle abundance per cotyledon, reflecting the global increase in plastic production and pollution (*Weingrill et al., 2023*). The abundance of MNP, however, seems to decrease with increasing particle size, indicating that smaller plastic particles represent the predominant components (*Zhu et al., 2023*).

Transmission electron microscopy analysis of human placenta samples revealed the presence of particles consistent with MNP on the surface of placental villi, within various placental cell layers, and in the surrounding extracellular space (*Ragusa et al., 2022*). Additionally, structural changes in intracellular organelles, such as dilated rough endoplasmic reticulum and swollen mitochondria, have been observed in syncytiotrophoblast cells, suggesting a possible link between the presence of MNP and cellular damage (*Ragusa et al., 2022*). The observed morphological alterations may reflect a sustained cellular response aimed at degrading and eliminating plastic particles, which are recognized as foreign bodies within placental tissue. Prolonged enzymatic degradation processes can lead to the accumulation of reactive oxygen species (ROS), potentially resulting in DNA damage, cell cycle arrest, inflammation and apoptosis, thereby contributing to placental dysfunction.

The effects of microplastics on in vitro human-derived cellular models

The in-vitro effects of MNP were investigated in different placental cell types, revealing size-dependent transport behaviour. The choriocarcinoma cell lines, ACH-3P and JEG-3, showed better permeability to 50 nm MNP than BeWo b30 and JAR cells. In contrast, larger MNP (490 nm) were less able to cross the BeWo and ACH-3P barriers (*Rothbauer et al., 2017*).

Subsequent experiments on JEG-3 cells exposed to MNP revealed increased oxidative stress, DNA damage, cell cycle arrest in G1 or G2 phases, and signs of inflammation and apoptosis. Interestingly, it was observed that smaller sizes corresponded to a stronger inhibition of protein Kinase A activity (*Shen et al., 2022*). A comparable phenomenon was observed in in-vitro experiments on immortalized COV434 granulosa cells, wherein exposure to MNP resulted in reduced cell viability, which in turn led to augmented expression of apoptotic biomarkers and cell cycle arrest (*Huang et al., 2023*).

Additionally, MNP have been found to exert a deleterious effect on human umbilical vein endothelial cells (HUVEC), resulting in a dose- and size-dependent

reduction of cell viability and capillary formation capacity (*Lee et al., 2021*; *Zhang M et al., 2022*). These effects are associated with the suppression of angiogenic signalling pathways and the inhibition of wound healing and cell migration. The induction of apoptosis, demonstrated by an increase in ROS production, has been associated with cell death via autophagy and necrosis. Furthermore, RNA-sequencing analysis revealed significant changes in the gene expression profiles of HUVEC exposed to MNP (*Lee et al., 2021*; *Zhang M et al., 2022*).

Moreover, depending on their size, MNP were observed to cause cell membrane damage, promote the formation and accumulation of autophagosomes, and inhibit autophagic flux, resulting in lysosomal damage in HUVEC (*Lu et al., 2022*).

THE EFFECTS OF MICROPLASTICS ON IN VIVO MURINE MODELS

Effect of micro- and nanoplastics on the male reproductive tract in murine models

The detrimental effects of MNP on fertility have been the subject of many animal studies. Specifically, research involving the administration of MNP orally shed a light on their effect on spermatogenesis in male mice (*Xie et al., 2020*; *Hou et al., 2021*; *Jin et al., 2025*).

These studies demonstrated that MNP administration impair male fertility by increasing inflammation and NF-κB activity, thus leading to increased apoptosis in testicular tissue, oxidative stress, decreased testosterone levels, increased sperm abnormalities and a significant decrease in sperm quantity and motility (*Xie et al., 2020*; *Hou et al., 2021*; *Jin et al., 2025*). Further research showed that MNP induce testicular damage and sperm apoptosis through the p53 signalling pathway (*Lu et al., 2023*).

The underlying mechanisms for these effects involve the production of ROS, which activate mitogen-activated protein kinases, including p38 and c-Jun N-terminal kinase. These molecular alterations contribute to the disruption of spermatogenesis, with MNP-induced apoptosis occurring in the seminiferous tubules. This is demonstrated by the upregulation of pro-inflammatory markers and the pro-apoptotic protein Bax in testicular tissue (*Xie et al., 2020*; *D'Angelo and Meccariello, 2021*; *Hou et al., 2021*; *Jin et al., 2021a*).

In addition, the expression of proteins related to the blood–testis barrier (BTB) was examined. These include focal adhesion kinase, a tight junction regulator, mTOR (mammalian target of rapamycin) complexes (mTOR1 and mTOR2), the basal ectoplasm specialization proteins N-cadherin and beta-catenin and tight junction proteins, such as ZO-1 and occludin. The altered regulation of these proteins indicates a disruption in the integrity of the BTB. A compromised BTB can further exacerbate the detrimental effects on spermatogenesis by allowing harmful substances to reach the germ cells, thereby impairing male fertility (*Wei et al., 2021*; *Jin et al., 2025*). Taken together, these findings show how MNP-induced inflammation, oxidative stress and BTB disruption converge to compromise spermatogenesis and male fertility.

Another significant mechanism contributing to MNP-induced reproductive toxicity is mitochondrial dysfunction. Micro- and nanoplastics exposure has been demonstrated to reduce mitochondrial membrane potential and adenosine triphosphate production, primarily through the process of oxidative stress. Mitochondrial damage, however, seems to be reversible upon interruption of MNP exposure, suggesting the potential for cellular turnover to restore mitochondrial health. The degree of toxicity and recovery is influenced by the physicochemical properties of the MNP particles, such as their size, shape and surface characteristics. This highlights the importance of these factors in determining the extent of damage (*Liu T et al., 2022*; *Liu et al., 2024*; *Jin et al., 2025*).

Specifically, certain MNP, such as palmitic acid-modified microplastics, interfere with androgen receptor activity, thereby impairing testosterone regulation. In contrast, other types of MNP, such as PMMA-MPs, have milder effects. These findings underscore the critical role that both type of plastic and their capacity to adsorb essential molecules, such as testosterone, play in determine their effect on male reproductive health. This highlights the necessity of distinguishing between various plastic types when assessing their effects on male hormonal pathways and reproductive function (P *Zhang et al., 2024*).

The last point to be considered is the size of MNP. It has been demonstrated that larger microplastics induce more severe testicular toxic effects compared with nanoparticles (*Lv et al., 2025*). This suggests the existence of distinct mechanisms by which particles of different sizes affect cellular metabolism and physiological functions.

Furthermore, MNP induce alterations in the BTB and modify gene expression involved in the production of steroid hormones (*Gao et al., 2023*). In addition to direct effects on hormone regulation, exposure to MNP combined with inflammatory agents, such as lipopolysaccharides, led to reduced sperm counts, decreased testosterone levels and lower steroidogenic protein expression, all while increasing inflammation in testicular tissues. Interestingly, the combined exposure did not amplify oxidative stress, highlighting the complex interactions between these stressors (*Li Y et al., 2024*).

Moreover, it has been observed that MNP modify the composition of the gut microbiome, resulting in a decrease in beneficial bacteria and an increase in pro-inflammatory bacteria. Importantly, these changes were found to be reversible with probiotic intervention, suggesting that dietary and environmental strategies may mitigate male reproductive harm (*Xu R et al., 2024*).

Effect of micro- and nanoplastics on the female reproductive tract in murine models

Recent studies in animal models documented a negative effect of MNP on fertility by damaging the uterus, ovaries, endocrine glands and hypothalamic–pituitary axis, causing alterations in ovarian function, follicular development and hormonal balance, ultimately impairing fertility (*Balali et al., 2024*; *Zhang Z et al., 2024*; *Xia et al., 2025*).

Exposure to MNP in female mice showed induce reproductive impairments, including ovarian enlargement, reduced follicle counts, and decreased pregnancy rates and embryo production. These outcomes are closely linked to oxidative stress, with granulosa cell death occurring via apoptosis and pyroptosis. Moreover,

MNP induce uterine fibrosis, leading to endometrial thinning, which collectively undermines ovarian capacity, oocyte maturation and overall quality (*Afreen et al., 2023*).

The combination of exposure to MNP and environmental toxins has been demonstrated to exacerbate reproductive dysfunction. This combination results in substantial ovarian impairment in female rats, manifesting as the presence of follicular cysts, haemorrhage in the ovarian medulla, increase in secondary and atrophic follicles, and fibrosis. Furthermore, hormonal imbalances, oxidative stress and alterations in metabolic pathways have been observed. The activation of the TGF-β1/Smad3 signalling pathway has been identified as a pivotal factor in these processes, suggesting that its inhibition may offer a therapeutic approach to mitigate the observed toxic effects (*Xu K et al., 2024*).

Similarly, MNP have been shown to reduce the number of follicles and decrease anti-Müllerian hormone levels, a critical marker of ovarian reserve, through the induction of ovarian fibrosis via Wnt/β-Catenin signalling. This process is further exacerbated by oxidative stress, which triggers granulosa cell apoptosis and leads to disrupted ovarian function. Additionally, MNP have been associated with an imbalance in key cellular pathways, such as those regulating fibrosis and cell survival, amplifying the detrimental effects on reproductive health. These findings highlight the potential long-term effect of MNP on female fertility and underline the importance of addressing environmental pollutants as contributors to reproductive disorders (*An et al., 2021*).

Interestingly, MNP exposure can cause notable sexual dimorphism. Research reported reductions in FSH, LH and testosterone levels in male mice after MNP exposure. On the other hand, female mice showed opposite hormonal trends (*Wei et al., 2022*). Female mice also experience a decrease in ovarian reserve, with fewer follicles and smaller ovaries, whereas male mice have testicular damage and impaired sperm quality. These findings suggest that female reproductive health may be more susceptible to the toxicity of MNP, possibly owing to hormonal fluctuations, such as those occurring during the menstrual cycle, which increase susceptibility to environmental toxins (*Jin et al., 2021b*; *Liu Z et al., 2022*; *Zhang et al., 2023a*; *Balali et al., 2024*; *Fang et al., 2024*).

Effect of micro- and nanoplastics on pregnancy and offspring development in murine models

After maternal exposure, MNP have been detected in murine fetal tissues, including the liver, brain, lung, kidney and heart, potentially causing complications in immune function, metabolism and offspring reproduction (*Budhwar et al., 2025*). Indeed, existing evidence suggests maternal exposure to MNP can result in miscarriage and impair the function of trophoblast cells in pregnant mice, which is essential for placental development (*Balali et al., 2024*).

Exposure to MNP leads to an increased rate of embryonic resorption, alterations in the size of uterine arterioles and modifications in the composition of immune cells within the placenta. Notably, a decline in decidual natural killer cells, which are crucial for early pregnancy and may influence fetal development, has been observed; furthermore, exposure to MNP has been shown to disrupt the balance between type 1 and type 2 (M1 and M2) macrophages and to alter the levels of cytokines, which may potentially affect embryo implantation (*Hu et al., 2021*).

Micro- and nanoplastics have been detected in the placenta, but only those of nanometer size that have crossed the blood–placental barrier to reach the fetal brain, in particular the thalamus, where they alter its development. This is mediated by the induction of oxidative stress and reduced production of γ-aminobutyric acid. Anxiety-like behaviours, indicating a risk of neurobiological disorders, were observed in offspring exposed to MNP (*Yang et al., 2022*).

Moreover, evidence shows that the effect of maternal exposure to MNP in mice and the consequent intergenerational effects on offspring, in which size and concentration play a critical role in male offspring, changes biochemical parameters. This has been observed in the metabolism of glycolipids (triglycerides and cholesterol), amino acids and carnitine, as well as in energy metabolism (*Luo et al., 2019*).

In addition, during development of mice offspring, exposure to high doses (≥500 μg/day) of MNP causes brain dysfunction and cognitive deficits, whereas lower doses have negligible effects. This suggests that high doses significantly increase the risk of neurodevelopmental problems. In addition, maternal exposure to MNP was transferred to the offspring through breast milk, but not through the placenta. Consistent with previous research on sex-differentiated brain development, this study showed that MNP exposure altered brain sexual dimorphism by interfering with oestrogen signalling, resulting in cognitive deficits in women. In conclusion, MNP exposure during development causes neurodevelopmental disorders, including cognitive deficits, and may contribute to brain dysfunction (*Jeong et al., 2022*).

In offspring, exposure to MNP during critical prenatal and early life stages has been shown to delay puberty, alter oestrous cycles and significantly reduce fertility. Specifically, male offspring had severe reproductive disorders, including reduced sperm counts and viability. Furthermore, behavioural effects in offspring have also been reported (*Dou et al., 2024*).

The collective evidence points to a direct damage of the maternal reproductive system by MNP and transgenerational effects on offspring (*Zhang et al., 2023b*; *Inam, 2025*).

DISCUSSION

Plastic pollution represents a global emergency, with growing evidence revealing the presence of MNP in various human tissues, including male and female reproductive systems. The extent to which the exposure to MNP affects fertility, fetal development and offspring health, however, as well as the toxicological mechanisms involved, remains unclear. It has been reported that, given their ubiquity, particularly in urban settings, MNP may disrupt endocrine function, leading to hormonal imbalances that could affect fertility and reproductive health (*Amereh et al., 2020*). The precise mechanisms behind the harmful effects on endocrine and reproductive systems, however, have not yet been fully elucidated.

Recent evidence also suggests that MNP may access the bloodstream from the maternal respiratory system and the gastrointestinal tract, eventually

reaching the placenta (*Arumugasaamy et al., 2019*). Furthermore, MNP could potentially reach the testes or ovaries through other pathways, such as the lymphatic system (*Hong et al., 2023*). It is plausible that MNP could alter multiple cellular regulatory pathways in the placenta, such as immune mechanisms, growth-factor signalling and maternal–fetal communication. These alterations may result in adverse pregnancy outcomes, including preeclampsia and fetal growth restriction (*Ilekis et al., 2016*). The presence of MNP in the placenta (*Ragusa et al., 2021*) demonstrates potential translocation of MNP into the fetal environment, potentially affecting fetal development. For instance, MNP have been detected in the amniotic fluid and in the meconium**,** leading to stillbirth, preterm birth and spontaneous miscarriage. In murine models, MNP exposure during pregnancy reduces fetal development by 12%**,** and induce structural changes in fetal brain regions essential for motor and cognitive function, contributing to the onset of postnatal brain abnormalities (*Braun et al., 2021*; *Halfar et al., 2023*; *Harvey et al., 2023*; *Liu et al., 2023a*; *Yang et al., 2024*). The absence of consistent experimental methodologies, however, creates significant gaps in understanding the aetiological mechanisms behind these observations and the potential transgenerational implications of MNP in humans.

The challenge in studying toxicological effects of MNP on the reproductive system lies in the limited availability of suitable techniques and models. Lack of standardized methodologies for measuring MNP exposure and assessing their physiological effects complicates the interpretation of data across studies. For instance, a major issue is the difficulty of simulating the long-term, low-level exposure that humans experience in real-world environments. Most animal models are exposed to high, acute doses of MNP, which do not accurately reflect the chronic exposure humans experience through food, air, water and consumer products, limiting the relevance of the findings (*Vanetti et al., 2025*). As a result, many studies fail to capture the cumulative effects of chronic exposure over time, which are likely more representative of real-world risks (*Hong et al., 2023*). The diverse nature of plastic particles, which vary in size, composition and chemical additives, further complicates the understanding of their toxicological effects. Different types of plastics may have different toxicity levels, depending on their chemical composition and additives. For instance, polystyrene is commonly used in research studies, but humans are exposed to various MNP, such as polyethylene and PVC (*Salthammer, 2022*). Therefore, studies based on polystyrene MNP only do not fully reflect real-life exposure. Moreover, although the real-life versions of MNP have an irregular shape, most MNP used in many studies are spherical (*Hong et al., 2023*). Investigating the reproductive toxic effects upon exposures to polyethylene, PVC and other MNP in different size and shape, as well as their ability to cross biological barriers, i.e. placenta and blood–brain barrier, is crucial for a more accurate evaluation of the MNP-associated detrimental mechanisms.

Additionally, common techniques of MNP detection in samples should also be standardized. Currently, no gold standard method has been established for detecting MNP in biological samples (*Schwabl et al., 2019*). Commonly used techniques of detection rely on mass spectrometry and Raman spectroscopy (*Matavos-Aramyan, 2024*). Both have distinct advantages and limitations. Techniques based on mass spectroscopy, e.g. pyrolysis-gas chromatography-mass spectroscopy, thermoextraction and desorption, coupled with gas chromatography-mass spectroscopy and liquid chromatography-mass spectroscopy) are highly sensitive to detecting smaller particle sizes (even

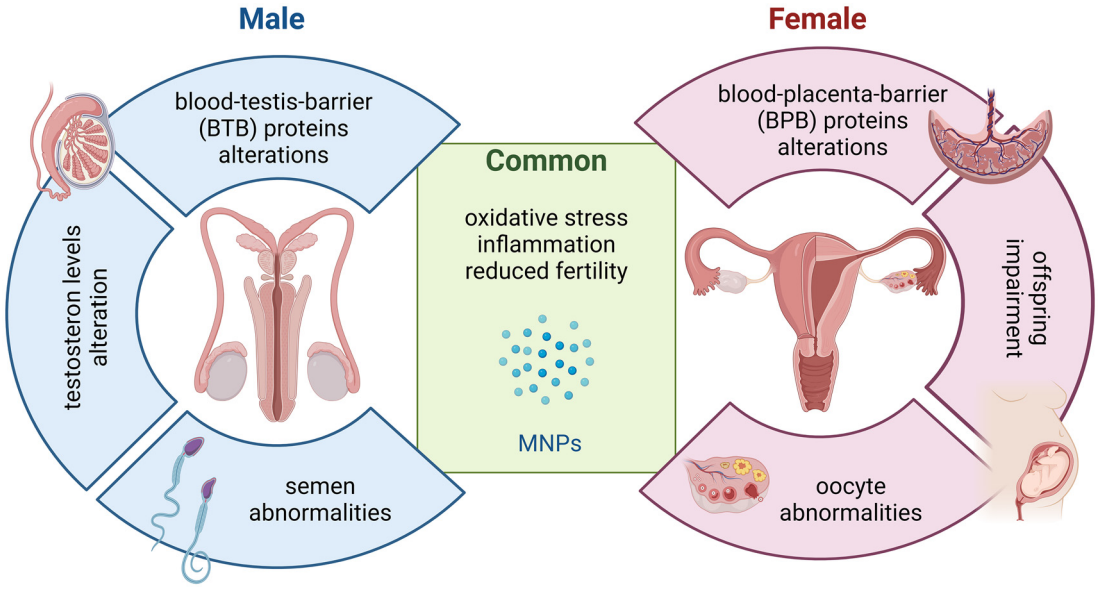

FIGURE 1 Possible micro- and nanoplastics (MNP)-related pathogenic mechanisms involved in the male and female reproductive tract. Micro- and nano-plastics seem to interfere with fertility through increased levels of oxidative stress and inflammation in both the male and female reproductive tracts. Alterations in the blood–testis barrier (BTB), testosterone levels and semen quality may represent the pathways that lead to impaired reproductive function in men. In the same way, alterations in blood–placenta barrier (BPB) and oocyte abnormalities may be linked to alterations of the reproductive functions in female and offspring impairment.

nanoplastics). Thet can quantify chemical additives, plasticizers and degradation products present in microplastics, offering detailed chemical profiles (*Dümichen et al., 2017*; *Picó and Barceló, 2020*; *Matavos-Aramyan, 2024*). It is limited, however, by the need to manually handle the particles and may lack the ability to directly visualize the distribution of microplastics in tissues (*Matavos-Aramyan, 2024*). Raman spectroscopy, on the other hand, is a non-destructive technique that provides high spatial resolution, making it ideal for visualizing the distribution of microplastics in biological samples (*Araujo et al., 2018*). It allows for direct observation of plastic particles within tissues without damaging the sample. Its sensitivity, however, is generally lower compared with mass spectroscopy, and it may be limited in the detection of trace quantities of MNP or the chemical additives associated with them. Overall, the polymer identification by Raman spectroscopy is more reliable than the mass spectrometry, although more time consuming and with a higher limit of detection.

Lastly, another crucial point of concern is the difficulty in establishing reliable control groups. Microplastics are ubiquitous in the environment, making it nearly impossible to find individuals who have not been exposed to them. This widespread exposure complicates the identification of a truly 'unexposed' control group. Furthermore, distinguishing whether MNP are directly causing health pathologies or are merely a correlated factor or a consequence needs to be clarified.

Given these complexities, more sophisticated models and standardized methods need to be developed so that human exposure scenarios can be better replicated, comparisons can be made across studies and a clearer understanding of MNP toxicological effects can be fostered.

The growing evidence of the harmful effects of MNP on human health and their effect on the environment have led to the introduction of legislative and regulatory measures. These include the following: the European Union Marine Strategy Framework Directive; California's Safe Drinking Water Act; the European Union-wide ban on microbeads expanded under REACH in 2023; and the draft global plastics agreement. The success of a global treaty, however, will rely on the establishment of clear baselines, a reduction in plastics targets and the establishment of an independent science-policy interface free from conflicts of interest (*Thompson et al., 2024*).

In conclusion, the growing body of evidence suggests that MNP pose significant risks to human reproductive health, potentially affecting fertility, hormonal regulation and fetal development. Considerable gaps, however, remain in understanding the mechanisms of these effects and their long-term implications. The limitations of current experimental models, methodologies and detection techniques hinder progress in this context. Further research is crucial to unravel the potential effect of MNP on current and future generations. Addressing the challenge of plastic pollution and protecting reproductive health must remain a global priority. **FIG. 1**

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