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Nanoplastics: A Growing Threat to Reproductive Health: "A Comprehensive Review"

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Abstract

Due to their widespread presence in the environment, nanoplastics (NPs) have given rise to serious worries over their possible hazardous to human health, particularly to the reproductive organs. A thorough evaluation and assessment of their toxicity to human organs

and tissues is necessary in light of the increasing concern and paucity of research on their health impacts. Over 15% of couples worldwide are affected by infertility, which is a rising global trend. Among the main causes of infertility are environmental factors, But nothing is known about how NPs affect the ovaries and testes. These particles interfere with the development of reproductive system in a size-dependent way. They can come into touch with the skin, swallow food, or breathe in. This review looking at how NPs negatively affect reproductive function, as well as the different phases of germ cell development and possible pathways. We also provide an overview of the combined reproductive toxicity of NPs and related pollutants. In light of the small scope of existing research, we support a move toward novel technologies and the use of multi-omics techniques to further relevant investigations. In order to create effective preventative This research looks at shape, type of polymer, and transferred toxins. This review will cover the consequences of natural pollutant exposure on human fertility, the deleterious effects of NPs on reproductive function, the different phases of germ cell development, and possible mechanisms. This paper thoroughly investigates the genesis, degrees of environmental toxicity, and possible effects of nanoplastics on human reproductive health. Understanding the risks posed by NPs and the toxicity processes that go along with them is made possible by this review. This review seeks to promote more study into the basic features of nanoplastics, biological reactions, and the harmful consequences they elicit owing to their specific qualities by drawing attention to the problem of NP pollution.

Keywords: Nanoplastics (NPs); Human exposure; Health effects; Hazards of NPs; Toxicity; Reproductive toxicity; Health effects.

Introduction

Human health is at serious danger due to the widespread presence of nanoplastics (NPs) in the environment, which includes soil, water, and the atmosphere. Ingestion and inhalation are the main ways that humans are exposed to nanoparticles (NPs), however skin contact is another possibility. Particles that are ingested, mainly those with sizes between 0.1 and 1 μm, spread throughout the body's tissues and organs, affecting all nine of the human biological systems, but especially the respiratory and digestive systems. The capacity of nanoparticles (NPs) to cause oxidative stress, trigger inflammatory reactions, modify lipid or energy metabolism, or change the expression of associated functional components is largely responsible for their detrimental consequences [1].

Concerns concerning the potential toxicity of nanoplastics (NPs) to human health have grown as a result of their widespread presence as environmental contaminants. This study explicitly looks at how NP exposure affects human fertility, with an emphasis on how NPs negatively affect reproductive function. It also examines the different phases of germ cell development and the underlying processes associated with these impacts [2]**.** Plastics are extensively employed in many items, such as food packaging, medical equipment, and polyvinyl chloride (PVC) products, to improve convenience and quality of life [3]**.**

Even while plastics are widely used for convenience and to enhance quality of life, improper management has resulted in massive plastic pollution, which has negative effects. Over the previous seven decades, Plastic production has expanded significantly [4,5]**.**To far, the oceans have accumulated more than 2000 tons of plastic waste, and this amount is still continuously growing [6]. Moreover, mpr than 12 million metric tons of plastic trash were thrown by coastal nations in 2010 alone [7]**.** The amount of pollution emitted from land is expected to rise tenfold by 2025 if ineffective waste management techniques are not put into place [8]**.**

Rise in pollutant led to an increase in pollution from both nanoplastics (NPs, diameter < 100 nm), polyethylene terephthalate (PET), polypropylene (PP), polyethylene and (PE), are some of the materials that MPs and NPs are made of. These plastic particles fit into either the major or secondary debris category, according to [9]. Secondary plastic debris develops when plastic fragments break apart in the environment or during usage, whereas primary plastic particles are made purposefully at particular sizes. As a result, secondary MPs/NPs have different sizes and shapes that affect how they are transported, distributed, and may even be harmful. Moreover, the aging process of secondary plastics may cause contaminants to accumulate, increasing MPs and NPs' detrimental effects [10] **.**

Both nanoplastics (NPs, diameter < 100 nm) and microplastics (MPs, 100 nm < diameter < 5 mm) are increasingly found in air, soil, water, and marine habitats globally, making plastic particles very persistent environmental contaminants [11]**.** After being thrown away, MPs age by a variety of processes, including as material deterioration, photo- and thermo-oxidation, and biodegradation [12]**.** MPs were identified in large quantities in soil [13]. Of these MPs, 59.81% had a size of smaller than 1 mm.

For NPs in humans, between five and seventeen3 MPs have been found in every food container manufactured by PS in China. The general population's average oral exposure to MPs [14]. Additionally, MPs and NPs have the ability to penetrate the human body by

breathing due to their extensive diffusion and environmental build-up [15,16] further state that people may be exposed to these particles through regular product interaction in their daily lives. As such, it is difficult to prevent exposure to plastic particles because they are present in both indoor and outdoor settings.

Approximately 50–70 million couples globally struggle with infertility; in the US, rates as high as 8.1% have been reported [17,18]. Half of instances of infertility are caused by variables that are equally related to men and women [19]. Environmental influences have a significant impact on the complicated process of human germ cell development [20].

According to recent study, male testicular toxicity and decreased sperm production might result from exposure to nanoplastics (NPs) [21]. Furthermore, NPs pollution has a deleterious effect on the viability of granulosa cells in females, which lowers mouse fertility [22]. The processes at play and the targeted germ cells.

The availability of well-characterized, homogeneous microplastic preparations in sufficient quantities for toxicity studies is limited, hindering our understanding of their potential hazards to reproduction [23]. Most published toxicity studies have focused on nanoplastics (NPs), However, the wide range of NP sizes, forms, and polymer matrices together with their corresponding chemical content in the environment implies that certain kinds could be more dangerous than others. Furthermore, heightened toxicity might be a result of the interaction between particles and chemicals. Research on rodents frequently employ tens exposure rates, which are probably far greater than actual exposures in humans or other animals [24]. This calls into question how applicable the research findings from these studies are to actual situations.

Microplastics Sources and Fate in the Environment

According to others finding [25]**,** fewer than 20% of microplastics come from marine sources, whereas more than 80% come from terrestrial sources. Microplastics have the ability to travel great distances all over the world because of their special lightweight, indestructibility, and buoyancy. According to [26]**,** the bulk of plastics that contaminate marine habitats come from land-based sources, fishing, aquaculture, and coastal tourism. It is estimated that more than 800 million tons of plastic in the ocean came from land-based sources. Micro- and nanoplastics are too small to be filtered out by conventional wastewater treatment methods, resulting in their introduction into rivers, oceans, and freshwater supplies [27]. Additionally, these particles can be found in soil and enter waterways through natural erosion. According to the United Nations Environment Program, 2010 saw the production of

275 million tons of plastic garbage, of which 4.8–12.7 million tons are thought to have leached into water systems [28].

Both primary and secondary sources are the source of both microplastics and nanoplastics. Primary sources include deliberate manufacturing of these particles for use in consumer and industrial products, including medicine delivery particles, cosmetic additives, cleanser exfoliants, and industrial air blasting. Secondary sources occur in both terrestrial and marine settings when larger plastic products break down into smaller, more microscopic particles [29].

Microplastics and nanoplastics originate from both primary and secondary sources within consumer and industrial sectors. Macroplastic products can degrade into micron-sized and subsequently nanoplastics through biological or non-biological processes. These particles are prevalent in both aquatic and terrestrial environments, ultimately entering the food chain and water supplies, leading to human uptake and bioaccumulation [30].

Plastics can degrade into micro- and nanoplastics through various processes, including both biodegradation and non-biodegradation. Non-biodegradation processes, such as thermal degradation, physical weathering, photodegradation, and thermo-oxidative degradation, involve the breakdown of plastic structures without biological intervention [31]. Thermal degradation, or heat degradation, is an artificial process, whereas bigger polymers break down into tiny pieces due to weathering, which causes physical deterioration. In contrast, the chemical bonds in plastics are broken down and transformed into monomeric forms by Water molecules are used in hydrolysis and UV light is used in photodegradation, two naturally occurring chemical reactions. Certain non-biodegradation processes alter the mechanical properties of polymeric structures, boosting their specific surface area and promoting physical-chemical interactions with microbes [32]. According to Lambert and [33], plastics can decompose more quickly when exposed to environmental bacteria and other microbes. These microorganisms generate extracellular enzymes capable of rupturing the chemical bonds found in polymer structures. The process's final result is smaller plastic particles with altered molecular configurations., which eventually forms nanoplastics. Billionths of nanoplastic particles may be produced from a single gram of macroplastic, greatly expanding its surface area. It is clear that nanoplastics are widely distributed in the marine environment given the enormous amounts of plastic that enter the oceans every day [34].

Plastic waste fragmentation is more rapid in coastal environments compared to the open ocean. Solar UV irradiation accelerates the oxidation of plastics, a primary degradation mechanism. Coastal areas, with their greater exposure to UV radiation and higher temperatures, facilitate this process. Furthermore, the presence of salt in these areas enhances plastic degradation [35]. Marine ecosystems, with their high saline content and diverse microbial populations, contribute to faster plastic breakdown than terrestrial environments [36].

Exposure Pathways and Bioaccumulation of Nanoplastics

Growing research indicates that nanoplastics (NPs) build up in the placenta, an essential organ in charge of the flow of nutrients between the mother and the fetus [37]. Research has repeatedly shown that nanoparticles (NPs) accumulate in the placental tissue of mice and rats, with consequential effects on both structure and function [38–40]. According to studies conducted by others [41-43]**,** exposure to NP has been associated with smaller placentas, fewer glycogen-containing cells in the placental endocrine-functioning junctional zone, and poorly established fetoplacental vasculature. Furthermore, abnormalities in uterine and placental immune cells, such as reduced uterine natural killer cells and changed macrophage ratios, may impair the remodeling of uterine spiral arteries [44].

Abnormalities in the metabolism of amino acids, carbohydrates, and lipids as well as in the complement and coagulation cascade pathways, are shown by transcriptomic and metabolic investigations of placentas exposed to nanoparticles [45]. These findings highlight the potential adverse effects of NP exposure on placental function and fetal development.

Recent studies have detected nanoparticle (NP) accumulation in human placental tissue from both vaginal and C-section deliveries in otherwise healthy pregnancies [46]. Patients' measured numbers of NPs ranged from 0.28 to 9.55 particles/g of tissue [47]. Ex vivo investigations in humans, animals, and in vitro that smaller size and greater concentration enhance the uptake of NPs by placental cells [48]. Exposure to NPs during gestation in maternal mice and rats has led to the accumulation of NPs in the heart, brain, placenta, and fetal compartment, generating worries about the possible negative effects on the short- and long-term health of progeny.

Impact of Microplastics on Human Health

NPs pose a concern to reproductive health because they can enter the human body through skin contact, ingestion, and inhalation. Exposure Routes: Plastics have a significant

influence on all facets of daily life, including home items, technology, and medical conditions and treatments. Consumers discard the majority of used plastics after only one use, which has become a major environmental issue since the plastics wind up in landfills, the ocean, and other bodies of water. Numerous quantities of these plastics are thrown away every day, and concerns about how hazardous these plastics are to the environment and to people have arisen as a result of the polymers' breakdown from micro to nano levels. Although the impacts of micro- and nanoplastics on the environment have been documented in a number of previous studies, nothing is known about how they affect the human body at the molecular or subcellular levels. In particular, there hasn't been enough research done on the possibility that systemic exposure may result from nanoplastics passing via the lungs, skin, and stomach [49].

This review looks at how male reproductive systems are harmed by nanoplastics (NPs), along with the underlying molecular processes.There has been a noticeable drop in the parameters used to analyze male semen. The process of spermatogenesis, This is the complex and continuous process of producing [50- 51]. Additionally, these components are necessary for spermatogenic processes including the development of spermatids and the control of spermatocyte meiosis [50]. Infertility in men may result from deviations from any one of these stages. A growing amount of studies suggests that MPs can build up in the testes and be harmful to reproduction [52-53].

Environmental contaminants, in particular endocrine-disrupting chemicals (EEDCs), have been linked to a deterioration in male reproductive health during the last eight decades [54] and (55) claim that exposure to EEDCs, such as heavy metals, certain organophosphorus pesticides, and di(2-ethylhexyl) phthalate (DEHP), can occur once or more and alter spermatogenesis. EEDCs have also been linked to cryptorchidism and other abnormalities of the male reproductive system[56].

Pyroptosis and EEDC-related spermatogenetic dysfunction have been explained by recent studies, excessive generation of reactive oxygen species (ROS), and autophagy [57-58]. Research has also indicated that exposure to nanoparticles (NPs) has detrimental effects on the function of the male reproductive system. A minimum human equivalent NP dosage of 0.016 mg/kg/day that can lower semen quality has been determined through animal tests [59]. According to others finding [60], NPs have been demonstrated to reduce ATP production, sperm viability, and DNA integrity during sperm swimming. This reduces the chance of gamete collision. Moreover, exposure to NP can alter the gut microbiota, which can induce

dysregulation of the IL-17A signaling pathway and spermatogenetic disease as well as the inhibition of the production of sex hormones [61]. Because organ systems are interdependent, damage caused by NP to the male reproductive system may result from harm to other essential organs [62].

One essential step in spermatogenesis is the exact regulation of germ cell maturation. Most seminiferous epithelia undergo as a result of exposure to nanoparticles (NPs) disrupting their germ cells at different times. Exposure to NPs has also been linked with the nuclear factor erythroid 2-related factor 2 (Nrf2)/heme oxygenase-1 (HO-1)/nuclear factor-kappa B (NF-kB) signaling pathway [63].According to findings of a research group (64), in vivo investigations on mouse sperm have demonstrated that NPs cause an increase in the ubiquitination of cell division cycle 42 (CDC42) and Ras-related C3 botulinum toxin substrate 1 (RAC1). Furthermore, it has been demonstrated that exposure to NP inhibits capacitation by reducing the polymerization of sperm F-actin [65]. According to others finding [66], an in vitro investigation utilizing human spermatozoa revealed that a 30-minute exposure to 50 and 100 nm nanoparticles might cause DNA breakage, mitochondrial malfunction, and an excess of reactive oxygen species (ROS). It's interesting to note that elevated heat shock protein 70 (HSP70) expression seems to guard against NP-induced sperm destruction. Taken together, these results emphasize how NPs may interfere with meiosis and maturation, among other phases of spermatogenesis, eventually influencing male fertility.

Nanoplastics and Reproductive Health in Different Populations

Through eating, cutaneous contact, and inhalation, humans are exposed to nanoplastics (NPs) [67]. Microplastics (MPs) are thought to be exposed to humans by ingestion and inhalation, with a yearly exposure predicted to be between 74,000 and 121,000 [68]. The overall NP particle exposure is probably substantially larger due to NPs' lower size. Numerous NPs are able to pass through the skin, stomach, and lungs' physiological barriers. Although they have been thoroughly addressed elsewhere, the intricate processes behind this translocation still need to be explored [69].

Future of Human Reproduction Threat with Nanoplastics

The impact of nanoparticle (NP) exposure during pregnancy on fetal growth profiles is not surprising, considering the critical role that placental health and function play in fetal development [70]. The study conducted by others [71] revealed that mouse models that were exposed to nanoparticles (NPs) with sizes varying from 90 nm to 5 μm during gestation

showed significant fetal growth restriction in the E15.5–E17 window of the second part of pregnancy. Compared to newborns who were not exposed, the average fetal weight was 12–15% lower. Others findings [72], include a shorter umbilical chord in fetuses exposed to NP and a poorer fetoplacental weight ratio, both of which are associated with fetal growth restriction due to inadequate energy transfer. These findings are compatible with Human instances of intrauterine growth restriction (IUGR) and fetal distress are combined with mouse models of hypoxia-mediated fetal growth restriction.

According to others finding [73], major developmental delays and embryonic abnormalities have been linked to the observed embryonic death and resorption in both mouse and chick embryo models. Most research, meanwhile, has not discovered a relationship between mother NP exposure and total litter size. The effects of NP exposure on fetal development and progeny birth weight in human cultures are little understood. Nonetheless, a recent study discovered an adverse relationship ($r = -0.82$, $p < 0.001$) between placental NP accumulation and birth weight in IUGR pregnancies. Similar associations were seen between newborn length, head circumference, and 1-minute APGAR ratings. NPs were identified in all 13 IUGR patients under investigation; up to 38 distinct NPs were evaluated in each sample. PE and PS were the most common polymers, with diameters ranging from 2.9 to 34.5 μm, according to [74].

A Growing Concern: The Impact of Nanoplastics on Human Fertility

According to studies conducted by [56,75-77], and others, oral exposure to nanoplastics (NPs) in male mammals has been associated with a number of detrimental reproductive effects, including testicular accumulation, disrupted seminiferous epithelium, oxidative stress, mitochondrial dysfunction, and increased pro-inflammatory cytokines. Moreover, oxidative stress, endoplasmic reticulum stress, misfolding or degradation of tight junctional proteins in Sertoli cells, and disturbances in the blood-testis barrier have all been linked to these exposures [78]. In addition to decreased testicular androgen production and circulating levels of testosterone and luteinizing hormone (LH), functional effects of NP exposure include decreased sperm quantity and quality [79]. According to these results, male mammal NP exposure may have a major impact on testicular function, sperm quality, and the pituitary-gonadotropin endocrine signaling pathways [80].

Previous study [81] indicated that there is a proven decrease in human sperm production across the population at the same time as the exponential growth in plastic manufacturing worldwide. The possible effects of NP exposure on the health of male

reproduction are called into question by this association. Epigenetic programming activities during spermatogenesis affect male fertility, fetal health, and the long-term health of children [82]. Exposure to different testicular toxicants can alter these events. The control of gene expression and developmental processes, such as sperm production and germ cell differentiation, is largely dependent on epigenetic changes. Although there are few studies explicitly looking at how nanoplastics (NPs) affect the sperm epigenome in mammals, there is compelling evidence that common NP additions like phthalates and bisphenol A (BPA) can interfere with this crucial developmental process. It has been demonstrated that exposure to phthalates and BPA in rodent models causes changes in the germline's non-coding RNA expression, histone modifications, and DNA methylation patterns [83].

From Environment to Womb: The Journey of Nanoplastics and Reproductive Health

When it comes to their possible impacts on female reproductive toxicity, nanoplastics (NPs) are among the most researched plastic particles; yet, studies on the effects on male reproduction are still more common [84]. Oral exposure to nanoparticles has been shown to cause accumulation of these particles in developing follicles and uterine tissue in both rat and mouse models [85]. Reduced ovarian weight, cytoskeletal protein expression, and altered follicle dynamics—characterized by a rise in atretic and cystic follicles and a decrease in developing and mature follicles—are all seen by exposed animals.[86]. Concurrently, distinct changes in reproductive hormone signaling are observed, with decreased circulating concentrations of estradiol (E2) and anti-Müllerian hormone (AMH), and increased concentrations of luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

These NP exposures have functional and fecundity consequences, observable variations in the length of the estrous cycle, a decline in ovarian reserve, a reduction in the rate of embryo implantation, and reduced litter sizes [87]. These findings highlight the potential adverse effects of NP exposure on female reproductive health.

Nanoplastics NPs and Epigenetics

While existing research on the reproductive and developmental effects of nanoplastics (NPs) is primarily focused on single NP types, the available evidence suggests significant potential impacts. However, Determining if existing NP exposures cause significant human infertility or illness is difficult because to major information gaps[88].Notwithstanding the widespread exposure to a variety of NPs, precise exposure assessments are hampered by the inability to measure microplastics (MPs) in different matrices (food, dust, tissue, etc.), especially for particles smaller than 1 μm. Furthermore, the breadth of published research is

limited due to the scarcity of homogenous, well-characterized MP preparations in adequate amounts for toxicity investigations [25].

Additional research is necessary because of the wide range of nanoparticle sizes, shapes, polymer matrices, and related chemical content that may be found in the environment. Chemical additives included in NPs may circumvent physiological defense mechanisms and reach sensitive regions, therefore studies should take their potential toxicity into account. There is still uncertainty about how much these factors affect toxicity, and more investigation is required to assess the possible health impacts of various polymer kinds and additives [12].

Unraveling the Complexities: Nanoplastics and Reproductive Dysfunction

Numerous investigations have suggested a link between female reproductive harm and nanoparticle (NP) exposure. It has been demonstrated to be disrupted when Oryziasmelastigma was exposed to polystyrene microplastics (PS-MPs) for 60 days. This reduction in plasma concentrations of testosterone (T) and 17β-estradiol (E2) has been shown [Wang et al."Kunming mice were administered oral damages to germ cells have resulted in decreased rates of oocyte maturation, fertilization, and embryonic development. A link has been observed, according to others [53], between the first polar body extrusion rate and the survival rate [14].Experimental studies conducted later on have demonstrated that exposure to PS-MP might cause ovarian inflammation and reduced oocyte quality. Even though the results of these studies show that exposure to MP is harmful to female reproduction, more research is necessary to fully understand the underlying processes.

Nanoplastics and Female Reproductive Health

The use of nanoplastics in a wide range of consumer goods has increased convenience and quality of life [46]. Nonetheless, extensive plastic pollution has been caused by improper management, with unfavorable effects [57-62]. The poisonous and dangerous materials, such as plastic additives, that linger in the environment are carried by nanoplastics themselves. Crucially, these particles show improved bioavailability throughout the food chain. Research has shown that nanoplastics negatively impact aquatic species' ability to reproduce, and evidence of both micro- and nanoplastics has been discovered in human reproductive organs, including the placenta. Nonetheless, a substantial amount of information is still unknown about the possible effects of nanoplastics on animals' reproductive systems, including human reproductive systems [22].

Moreover, according to estimates by others [44], coastal nations disposed of between 4.7 and 12.7 million metric tons of plastic debris in 2010. According to [28], in the absence of efficient waste management, it is anticipated that the amount of plastic trash released from land would grow tenfold by 2025.Nanoplastics (NPs, diameter < 100 nm) pollution has been made worse by the growth of plastic trash NPs can be derived from a number of materials, including as polystyrene (PS), polyethylene (PE), polyvinyl chloride (PVC), polyethylene terephthalate (PET), and polypropylene (PP)[33-67]. It is possible to classify these plastic particles as main or secondary trash. Secondary plastic debris is created when plastic fragments break apart in the environment or during usage, whereas primary plastic particles are made purposefully at particular sizes. As a result, secondary NPs have a range of sizes and shapes that affect their dispersion, transport, and possible toxicity. Moreover, pollutants may accumulate as secondary plastics age, worsening the negative impacts of NPs [43-75].
According to others findings [3, 81], nanoplastics (NPs) are persistent environmental contaminants that have been found in air, soil, rivers, lakes, and marine ecosystems globally in rising amounts. after being thrown away, MPs age by a variety of processes, including as material deterioration, photo- and thermo-oxidation, and biodegradation [58]. A 78.00 ± 12.91 items/kg in shallow soil and 62.50 ± 12.97 items/kg in deep soil were discovered to have an abundance of nanoparticles (NPs) in soil, with 59.81% of these NPs measuring smaller than 1 mm in size [52].

Tire wear particles make up around 1 to 10% of atmospheric particulate matter with a diameter of 2.5 μm or less (PM2.5) and 0.8 to 8.5% of particulate matter with a diameter of 10 μm or less (PM10) [56]. Global estimates place annual tire wear emissions per capita at 0.81 kg [47]. The main way that humans are exposed to NPs is by ingestion. Every food container manufactured by PS in China has been shown to contain NPs, with an abundance varying from 5 to 173 portions for every container [85]. The estimated mean oral exposure to nanoparticles (NPs) in the general population is 0.24–1.4 items/kg bodyweight (bw)/day; however, it is expected that this figure will rise in the future [85]. It's possible for NPs to infiltrate the human body by breath due to their extensive dispersion and environmental buildup [60]. Moreover, people may be exposed to these particles through regular product interaction in their everyday lives [50]. As a result, plastic particles are difficult to prevent exposure to since they are present in both indoor and outdoor contexts.

Worldwide, 50–70 million couples struggle with infertility; in the US, rates as high as 8.1% have been reported [29, 63, 64]. 50% of instances of infertility are due to a combination

of male and female variables [59]. The production of human germ cells is a complicated process that is very sensitive to external conditions [27].

Pregnancy Outcomes and Nanoplastics

Previous studies [37, 71] indicated that overuse of nanoplastics (NPs) has led to a throwaway culture and an increase in the amount of persistent plastic pollution in the environment. Recent research has looked at the possible negative effects of NPs on the results of pregnancies in animal models and at the cellular level. Human placenta and meconium have been found to contain nanoplastics, suggesting prenatal exposure [4]. According to (1), chronic ingestion of microplastics (MPs) in mice has been associated with dysbiosis of the gut microbiota, intestinal barrier failure, and metabolic abnormalities. These results underscore the need for more study to fully understand the effects of NPs on human health and the environment, as well as the possible health hazards associated with exposure to them. The biological effects of nanoparticles (NPs) on the health of expecting mothers and their offspring are a major issue, as evidenced by findings of NP deposition in the human placenta [2]. NPs may infiltrate the mother's body by inhalation, skin contact, or ingestion, eventually reaching the placenta via the circulatory system. These particles, along with associated additives, can then cross the placenta and enter the fetal body and amniotic fluid. Animal and *in vitro* studies have provided growing evidence of the harmful effects of plastic particles on fetuses and the placenta. Research suggests that maternal exposure to NPs during pregnancy and breastfeeding can lead to permanent alterations in the neural cell composition and brain histology of offspring [5].

Mechanisms of nanoplasticstoxicity in reproduction

When combined with other poisons, nanoplastics (NPs) may increase their toxicity to reproduction. In these co-exposure situations, synergistic effects are frequently seen, but further study is required to completely comprehend their consequences [15-66]. NPs enhance polyethylene microplastics' (PE-MPs) reproductive toxicity in mice testes, according to an RNA-seq analysis from a recent research [14]. This co-exposure changed the physiology and spermatogenesis of the sperm. The enhanced repercussions that have been found might perhaps be attributed to the sensitizing effect of oxidative stress induced by nanoparticles, even if NP exposure alone might still contribute to reproductive damage [14].

NPs have also been demonstrated to worsen the harm that polystyrene microplastics (PS-MPs) cause to whiteleg shrimp (Litopenaeusvannamei) during gonadal development,

upsetting hormone balance and proper metabolism [32]. This effect is not limited to mammals[74].

Phenanthrene (Phe) exposure in the mother can transfer Phe to the children, which causes an increase in accumulation in developing embryos [59]. Zebrafish have also shown the combined impacts of triphenylphosphate (TPhP) and polystyrene microplastic/nanoplastic (PS-MP/NP) exposure, with comparable results in terms of ovarian dysfunction [34]. It is noteworthy that the effects of these exposures vary depending on a person's sex; this is covered in more detail in the section that follows.

Protecting Future Generations: Addressing the nanoplastics Challenge

In the study of nanoplastics (NPs) in animal models (mice and rats), Drosophila melanogaster, and other invertebrate species are the most common experimental models used. Every model has pros and cons of its own [59]. Fruit flies are an excellent model to study the long-term consequences of NP exposure across generations because of their quick reproductive cycle. They are economical for these kinds of investigations because of their short lifetime and high offspring production [72].

Nonetheless, the direct application of results to human situations is restricted by the physiological and anatomical distinctions between invertebrate and mammalian models. Although rodent models are better at simulating exposure to human NP, they still have limitations, including high breeding costs and prolonged development periods that lead to fewer offspring per birth. According to others finding [26], these characteristics have made it more difficult to undertake transgenerational investigations using mouse models. Although there is a great need for epidemiological studies on human NP exposure, particularly concerning , variations in NP sources, animal models have been researched for a long time [87]. Calculated equivalent were found using extrapolation techniques in humans using current technologies [88].

Conclusions

While there is mounting evidence that nanoplastics (NPs) can accumulate in several human organs, the fundamental mechanisms responsible for this toxicity still be ambiguous. This analysis examines the harm that NPs do to the reproductive systems of both men and women. Future research, considering the limitations of existing studies should focus on the effects of NPs that are related to size and dose. To enhance the application of the findings, study designs should closely mirror real-world exposure scenarios, accounting for plastics' origins and potential co-exposure with other toxins. Furthermore, larger sample sizes and a broader

geographic scope are needed for studies to have a deeper understanding of NP exposure and its health impacts.

Conflicts of Interest

The authors declare no conflict of interest.

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