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CHAPTER 1

From Ocean to Womb: Tracing the Impact of Microplastics on Gestational Health

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Abstract

This chapter explores the intricate link between microplastics, endocrine-disrupting chemicals (EDCs) and Gestational Diabetes Mellitus (GDM), tracing the path from oceanic pollution to its implications on gestational health. We begin with a comprehensive overview of microplastics, examining their sources and their journey through the food chain. The core of the chapter focuses on the potential connections between microplastics, EDCs and GDM, reviewing evidence from animal studies to human epidemiological research. This in-depth exploration aims to inform the development of preventive

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measures and policy implications and also emphasizes the need for further research to safeguard maternal and fetal health.

Introduction

Microplastics (MPs), a fast-spreading and rapidly accumulating environmental pollutant are increasingly receiving global attention.[1] The problem of microplastic pollution is extensive with plastic contamination found in remote regions like the Mariana Trench and Ice shelves of the Antarctic. Due to their tiny size, MPs can easily be consumed by both terrestrial and marine organisms either deliberately or accidentally. This raises concerns about the potential for microplastics to accumulate in organisms that move through food webs potentially affecting wildlife and ecosystem services[2,3]. Microplastics and associated chemicals can act as an endocrine disruptor interfering with hormonal balances. This hormonal disruption may contribute to the development of metabolic disorders during pregnancy, such as Gestational diabetes mellitus (GDM)[4]. It is characterized by high blood sugar levels that develop for the first time during pregnancy[5]. While GDM typically resolves after childbirth, it significantly increases the risk of developing T2DM later in life for both the mother and the child[6]. Recently, researchers have been consistently throwing light on the inherent link between GDM and exposure to MPs and Endocrine Disrupting Chemicals (EDCs), raising concerns about the environmental and health impacts of these pollutants[7].

The goal of the book chapter is, to examine the potential link among microplastic exposure during pregnancy and the development of GDM. The chapter aims to

1. Explore the mechanism through which microplastics may influence maternal metabolism and glucose regulation potentially leading to GDM;
2. Review existing evidence on the association between environmental pollutants like MPs and GDM;
3. Highlight the need for further research to understand the role of microplastics in the context.

Additionally, the chapter aims to discuss the implications of these findings on maternal and fetal health as well as public health strategies aimed at reducing exposure to microplastics during pregnancy.

Journey of Microplastics in The Environment

The term ‘microplastics’(MPs) was coined in 2004, however, there is currently no single, comprehensive definition that accurately captures all the potential characteristics of microplastics[8]. The Joint Group of Experts on the Scientific Aspects of Marine Environmental Protection (GESAMP; 2015, 2016) defined MPs as, plastic particles <5mm in diameter which include particles in the nano-size range (1nm)[9]. Defining microplastics based on only their size is not accepted as an all-inclusive definition but also it must include the physiochemical properties such as solubility in water or chemical composition[9]. Finally, after all debates and predictions the accepted definition was proposed by Verschoor (2015) which is, *microplastics are any synthetic solid particle or polymeric matrix, with regular or irregular shape and* *with size ranging from 1µm to 5mm of either primary or secondary manufacturing origin which are insoluble in water*[10,11].

MPs have emerged as a consequential ecological issue due to their ubiquitous presence in various ecosystems including seawater, agro-ecosystem, atmosphere, fresh water, drinking water, food, biota and other islanded areas. These tiny plastic particles are < 5mm in size and are in various physical forms such as filaments, microbeads, fibers, nurdles and foam. They are composed of different polymers like polypropylene (PP), polycarbonate (PC), polystyrene (PS), polyethylene terephthalate (PET), polyvinyl chloride (PVC), polyamide (PA), polyurethane (PU) and acrylonitrile butadiene styrene (ABS)[12].

Microplastics are classified into two main categories primary and secondary based on their source of release into the environment[13].

i. *Primary microplastics* are those that were intentionally manufactured to be less than 5mm in size for various applications[13]. These include microbeads which are used in personal care products (PCPs) such as facial cleaners, body washes, and exfoliators. These microbeads can easily escape wastewater treatment processes and enter the environment. Microfibers are found in clothing and textiles, particularly in synthetic fabrics like towels and bath towels. During washing these fibers can shed and be released into wastewater, eventually making their way into aquatic environments[14].

ii. *Secondary microplastics* are formed by the breakdown of larger-sized plastics through natural weathering processes. These processes include erosion, the physical wearing of plastic materials due to friction or movement. Corrosion is the chemical breakdown of plastics due to exposure to environmental factors like moisture and chemicals. Abrasion is the mechanical wearing of plastic surfaces through repeated contact or rubbing. Photooxidation is the chemical degradation of plastics due to exposure to sunlight, leading to the breaking down of larger plastics into smaller microplastic particles. Biological transformation is the breakdown of plastics by microorganisms, which can also lead to the formation of microplastics[15].

The presence of MPs in the environment has significant implications for both ecosystems and human health. MPs can accumulate in marine life, aquatic organisms through ingestion, which cause physical blockages, reduced feeding efficiency, and exposure to harmful chemicals absorbed by the plastics[12]. Through the tissues of marine organisms, MPs potentially enter the human food chain through seafood consumption. Understanding the sources and types of MPs is crucial for developing strategies to alleviate their environmental impact. Both primary and secondary MPs contribute to the growing plastic pollution problem, affecting ecosystems and potentially human health[16].

Mechanism of Action: How EDCs Interfere with Hormone Systems

Endocrine-disrupting chemicals (EDCs) are an assorted group of compounds that can interfere with the endocrine system potentially affecting hormone synthesis, secretion, transport, binding, action or elimination. During pregnancy, the endocrine system plays a critical role in maintaining maternal health and supporting fetal development[4]. They are found in a variety of products and environmental sources

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including bisphenol A(BPA), phthalates, organochlorine pesticides, organophosphates, triazines, polychlorinated biphenyls (PCBs), perfluoroalkyl substances (PFAs), dioxins, parabens, triclosan and arsenic[17]. Exposure to EDCs can disrupt these processes leading to adverse outcomes for both the mother and the fetus. These chemicals can mimic or block the action of hormones by binding to receptors, disrupting hormonal balance and potentially causing complications like GDM[18]. EDCs can interfere with proteins that transport hormones in the blood, altering their availability and action, which is crucial for a healthy pregnancy. By influencing DNA methylation and histone modification, leads to long-term changes in hormone levels and function. The consequences of EDC exposure during pregnancy can range from mild to severe[4]. EDCs have been associated with reproductive disorders such as infertility, endometriosis and polycystic ovary syndrome (PCOS), neurodevelopmental disorders, behavioral problems and growth abnormalities in children, metabolic disorders including obesity, insulin resistance and T2DM, hormonal imbalances such as thyroid dysfunction and abnormal sex hormones levels and an increased risk of certain cancers, particularly breast and prostate cancer[19]. MPs can as carriers for EDCs through the food chain. The mechanisms by which EDCs interfere with hormone systems during pregnancy are complex and multifaceted. These chemicals can bind to hormone receptors, alter hormone synthesis and metabolism, disrupt hormone transport, modulate hormone signaling pathways, including epigenetic modifications and modulate the immune system[20,21].

Gestational Diabetes Mellitus

Gestational Diabetes Mellitus is a significant health issue that impacts a substantial proportion of pregnancies worldwide. The International Association of Diabetes in Pregnancy Study Group (IADPSG), estimates that the worldwide prevalence of GDM is around 14%[13]. The incidence of GDM has risen due to shifts in lifestyle, dietary habits, and other associated pregnancy complications. The American Diabetes Association (ADA) defines GDM as diabetes first diagnosed during the second or third trimester of pregnancy, excluding pre-existing type 1 or type 2 diabetes[5]. GDM is linked to several complications, including preeclampsia, macrosomia, higher rates of caesarean sections, fetal death in utero, neonatal hypoglycemia, respiratory distress syndrome and shoulder dystocia[22]. The pathophysiology of GDM is characterized by a combination of insulin resistance and inadequate secretion of insulin. Throughout the time of pregnancy, the placenta secretes hormones such as human placental lactogen, estrogen and progesterone, which contribute to insulin resistance[23]. This resistance can prevent the pancreas from producing sufficient insulin to counteract the resistance, resulting in elevated blood glucose levels, leading to the development of GDM[24]. However, additionally, recent studies have demonstrated that measuring glycated hemoglobin (HbA1c) levels, particularly in the second trimester, can be an effective screening tool for GDM. HbA1c, a marker of average blood glucose levels over 3 months, can identify women at risk for GDM as early as 3-4 weeks into gestation[25]. The Centers for Disease Control and Prevention (CDC) categorizes HbA1c levels below 5.7% as normal, levels between 5.7% and 6.4% as indicative of prediabetes, and levels above 6.5% as diagnostics of diabetes. Elevated HbA1c levels are linked with a higher risk of developing T2DM[26]. GDM poses a significant public health challenge due to its ubiquity and the probable long-term health implications for both mothers and children[5]. Therefore, initiatives aimed at reducing the incidence of GDM through lifestyle modifications, early screening, and effective management are essential for enhancing maternal and child health outcomes.

The Connection Between Microplastics, EDCs, And GDM

The increasing prevalence of microplastics and EDCs in the environment has raised significant solicitude regarding their potential effects on human health, particularly during sensitive life stages such as pregnancy. The exposure can occur through several hypothesized pathways that pose risks to maternal and fetal health[27]. Dietary intake is a significant route, as MPs can contaminate food products and seafood, while EDCs can leach from plastic packaging into food. Inhalation of airborne MPs and volatile organic compounds (VOCs) released from household products further increases exposure risk[28]. Dermal absorption from personal care products, which often contain EDCs, is another potential pathway, particularly for pregnant individuals who frequently use these items. Additionally, contaminated water sources and soil can contribute to exposure through agricultural produce. Once inside the body, both MPs and EDCs can interfere hormonal balance, induce inflammatory responses and lead to epigenetic changes, potentially resulting in adverse health outcomes such as gestational diabetes, preeclampsia and developmental issues in offspring[29,30]. Understanding these pathways is crucial for developing strategies to minimize exposure during this critical period.

Animal studies increasingly illuminated the inherent risks associated with MPs and EDCs on gestational health, revealing concerning implications for both maternal and fetal outcomes[31,32]. Research has demonstrated that exposure to MPs can lead to significant alterations in hormonal profiles, particularly affecting insulin sensitivity and glucose metabolism. For instance, in rodent models, pregnant animals exposed to MPs have shown increased insulin resistance, which is a key risk factor for developing GDM[33]. This disruption in glucose homeostasis can result in higher blood glucose levels during pregnancy, mirroring the conditions observed in GDM cases. Moreover, EDCs such as bisphenol A (BPA), polychlorinated biphenyls (PCBs) and phthalates have been extensively studied for their reproductive toxicity and endocrine-disrupting effects[34]. Animal studies have illustrated that vulnerable to these chemicals during pregnancy can lead to impaired placental function, affecting nutrient transfer to the developing fetus. For example, BPA exposure in pregnant mice has been linked to alterations in placental gene expression, which can compromise placental integrity and function. This compromised function can result in adverse outcomes, including low birth weight and preterm delivery, as well as long-term metabolic issues in offspring[35]. Additionally, studies have shown that EDCs can induce epigenetic changes that may predispose offspring to health issues later in life. Exposure to EDCs during critical windows of development can modify gene expression patterns in fetal tissues, leading to permanent alterations in metabolic pathways and increased susceptibility to obesity, diabetes, and reproductive disorders in adulthood[36]. In one notable study, rats exposed to phthalates during pregnancy exhibited significant changes in reproductive hormone levels, leading to impaired reproductive function in male offspring, which raises concerns about the long-term implications of EDC exposure on future generations[37].

The cumulative effects of MPs and EDCs can also manifest through inflammatory pathways[38]. Animal research has indicated that exposure to microplastics may elicit inflammatory responses in maternal tissues, which can further complicate during pregnancy. For instance, elevated levels of pro-inflammatory cytokines in the maternal bloodstream have been observed following exposure to MPs, potentially leading to conditions such as preeclampsia. This inflammatory response may not only affect maternal health but also disrupt the developing fetus, contributing to neurodevelopmental issues and growth abnormalities[39]. Furthermore, the interaction between MPs and EDCs has been a focus of investigation, as the presence of MPs in the environment can facilitate the transport and bioavailability of EDCs. Studies have shown that MPs can adsorb various EDCs from the surrounding environment, leading to increased exposure risks for pregnant animals. This combination of MPs and EDCs may amplify their individual effects, resulting in synergistic impacts on gestational health[40]. These studies have highlighted mechanisms including hormonal disruption, impaired placental function, epigenetic changes and inflammatory responses that collectively contribute to negative maternal and fetal outcomes.

Human epidemiological studies have played a pivotal act in exploring the interrelation between environmental pollutants and GDM[41]. These studies, which include cohort, case-control, and cross-sectional designs, have consistently shown links between EDCs such as BPA, phthalates, and PCBs and a rise in the risk of GDM. For instance, higher urinary levels of BPA and phthalate metabolites have been correlated with a higher prevalence of GDM in pregnant women[42,43]. While direct evidence linking MPs to GDM is still emerging, studies suggest that MPs can act as carriers for EDCs, potentially increasing exposure and risk. The mechanisms of action involve hormonal disruption, leading to insulin resistance and impaired glucose metabolism, which can manifest as GDM. Additionally, socioeconomic factors have been highlighted, with lower-income populations showing higher exposure due to living in areas with greater pollution or having less access to clean water and healthy food options[36]. Despite challenges in accurately measuring exposure and accounting for confounding factors, these studies have significant public health implications. They inform prevention strategies, improve screening and monitoring practices for pregnant women and support the development of policies focused at reducing environmental pollution and protecting vulnerable populations. Further research is needed to understand these associations and to develop constructive strategies for reducing exposure and improving gestational health outcomes.

Case Studies and Research Highlights

Detailed case studies have illustrated the profound impact of MPs and EDCs on gestational health, providing real-world examples of the risks posed by these environmental pollutants[17]. Various studies suggest that BPA may constitute a significant hazard to human health, particularly by disrupting endocrine metabolism, including glucose homeostasis. This is of particular concern during pregnancy, where hormonal balance and glucose regulation are crucial for both maternal and fetal health[44]. Numerous epidemiological studies conducted worldwide have inquired the relationship between BPA exposure in pregnant women and GDM[45]. These studies have consistently found a correlation between increased GDM cases and BPA exposure, indicating a potential causal link.

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For instance, one study focused on subfertile women and found a positive correlation between their blood glucose levels and BPA exposure during the second trimester of pregnancy. This finding is particularly noteworthy because the second trimester is a critical period for fetal development and any disruption in glucose homeostasis can have significant implications for both the mother and the developing fetus. The study suggests that BPA may interfere with the body's ability to regulate glucose, potentially leading to the development of GDM[46].

Likewise, a study showed a positive correlation between levels of perfluoro octane sulfonate (PFOS) and both GDM and impaired glucose tolerance. These findings add to the growing body of evidence linking perfluorinated compounds to metabolic disturbances during pregnancy[47]. Furthermore, a study in pregnant Danish women revealed a reminiscent relation between impaired glycemic index and elevated serum concentrations of perfluoro hexane sulfonic acid (PFHxS) and perfluorononanoic (PFNA). These perfluorinated compounds are known to be perpetual in the environment and it's been linked to numerous health issues, including endocrine disruption and metabolic disorders[48].

Human studies have demonstrated that exposure to heavy metals, whether individually or in combination, will elevate the risk of developing diabetes[49]. The National Health and Nutrition Examination Survey (NHANES) revealed a positive correlation between cadmium (Cd) levels in human urine samples and both BMI and waist circumference in adolescents and children. Moreover, women with higher concentrations of pregnancy urinary Cd were found to be most susceptible in developing GDM. This suggests that heavy metal exposure, particularly Cd may play a pivotal role in the pathogenesis of GDM by interpreting metabolic parameters and insulin sensitivity[50].

Ongoing and future research directions in the field of MPs and their impact on gestational health are crucial for understanding and mitigating the risks posed by these environmental pollutants[40]. Current studies focus on how MPs and associated chemicals, such as bisphenol A (BPA) and perfluorinated compounds, disrupt endocrine metabolism and glucose homeostasis during pregnancy[7]. Researchers are investigating how these substances interfere with hormonal balance and glucose regulation, critical for maternal and fetal health. This includes examining the potential for MPs to cross the placental barrier and directly affect fetal development. Researchers are also investigating the most vulnerable populations and the critical periods of fetal development that may be affected by MP exposure[51]. This involves studying subfertile women, pregnant women with GDM and other high-risk groups to understand the specific impacts of MP exposure. Additionally, there is a growing interest in studying the long-term effects of MP exposure on offspring, as early-life exposure can have lasting impacts on health. This includes research into potential developmental disorders, metabolic issues and endocrine disruptions that may arise later in life due to prenatal exposure to MPs[52].

Future research will likely explore the efficacy of interventions to reduce MP exposure, such as improved waste management and public health policies. This could involve developing strategies to minimize plastic pollution in the environment, recommending the use of safer replacements to BPA and perfluorinated compounds and educating the public about the risks associated with MP exposure. Additionally, there is a need for research into the development of biomarkers for early detection of MP-related health issues in pregnant women. These biomarkers could help in identifying individuals at risk and providing them with targeted interventions to mitigate potential health complications. Overall, these efforts are essential for safeguarding gestational health and ensuring the well-being of future generations. These findings highlight the need for in-depth research to fully analyse the mechanisms behind the associations and to identify the most vulnerable populations. Public health interventions and policy measures aimed at reducing exposure to MPs, EDCs and heavy metals are essential to mitigate the risk of GDM and other related health issues, ultimately improving gestational health outcomes. By advancing our understanding of the impact of MPs on pregnancy and fetal development, we can develop more effective strategies to protect pregnant women and their offspring from the harmful effects of environmental pollutants.

Conclusion

In conclusion, the journey of microplastics from the ocean to womb highlights the intense impact of MPs on gestational health. The pervasive presence of MPs in the environment and their ability to disrupt endocrine metabolism, particularly glucose homeostasis, pose significant risks to pregnant women and their developing fetuses. Ongoing research is unraveling the mechanisms behind these disruptions and identifying the most vulnerable populations. The potential long-term effects on offspring underscore the importance of early-life exposure to MPs and the lasting impacts on health.

Future research directions will focus on developing interventions to reduce MP exposure and creating biomarkers for early detection of MP-related health issues in pregnant women. These efforts are crucial for safeguarding gestational health and ensuring the well-being of future generations. By continuing to trace the impact of MPs from the ocean to the womb, we can better understand and mitigate the risks they pose, ultimately protecting the health of mothers and their children.

References

1. A. K. Priya *et al.*, “Microplastics in the environment: Recent developments in characteristic, occurrence, identification and ecological risk,” *Chemosphere*, vol. 298, p. 134161, Jul. 2022, doi: 10.1016/j.chemosphere.2022.134161.
2. A. Kelly, D. Lannuzel, T. Rodemann, K. M. Meiners, and H. J. Auman, “Microplastic contamination in east Antarctic sea ice,” *Mar Pollut Bull*, vol. 154, p. 111130, May 2020, doi: 10.1016/j.marpolbul.2020.111130.
3. A. J. Jamieson, L. S. R. Brooks, W. D. K. Reid, S. B. Piertney, B. E. Narayanaswamy, and T. D. Linley, “Microplastics and synthetic particles ingested by deep-sea amphipods in six of the deepest marine ecosystems on Earth,” *R Soc Open Sci*, vol. 6, no. 2, p. 180667, Feb. 2019, doi: 10.1098/rsos.180667.

4. A. K. Merrill, M. Sobolewski, and M. Susiarjo, "Exposure to endocrine disrupting chemicals impacts immunological and metabolic status of women during pregnancy," *Mol Cell Endocrinol*, vol. 577, p. 112031, Nov. 2023, doi: 10.1016/j.mce.2023.112031.
5. A. A. Choudhury and V. Devi Rajeswari, "Gestational diabetes mellitus - A metabolic and reproductive disorder," *Biomedicine & Pharmacotherapy*, vol. 143, p. 112183, Nov. 2021, doi: 10.1016/j.biopha.2021.112183.
6. S. Adam *et al.*, "Pregnancy as an opportunity to prevent type 2 diabetes mellitus: FIGO Best Practice Advice," *International Journal of Gynecology & Obstetrics*, vol. 160, no. S1, pp. 56–67, Jan. 2023, doi: 10.1002/ijgo.14537.
7. S. Ullah *et al.*, "A review of the endocrine disrupting effects of micro and nano plastic and their associated chemicals in mammals," *Front Endocrinol (Lausanne)*, vol. 13, Jan. 2023, doi: 10.3389/fendo.2022.1084236.
8. J. P. G. L. Frias and R. Nash, "Microplastics: Finding a consensus on the definition," *Mar Pollut Bull*, vol. 138, pp. 145–147, Jan. 2019, doi: 10.1016/j.marpolbul.2018.11.022.
9. A. K. Chaudhry and P. Sachdeva, "Microplastics' origin, distribution, and rising hazard to aquatic organisms and human health: Socio-economic insinuations and management solutions," *Reg Stud Mar Sci*, vol. 48, Nov. 2021, doi: 10.1016/J.RSMA.2021.102018.
10. N. B. Hartmann *et al.*, "Are We Speaking the Same Language? Recommendations for a Definition and Categorization Framework for Plastic Debris," *Environ Sci Technol*, vol. 53, no. 3, pp. 1039–1047, Feb. 2019, doi: 10.1021/acs.est.8b05297.
11. A. J. Verschoor, "Towards a definition of microplastics: Considerations for the specification of physico-chemical properties," 2015.
12. M. N. Issac and B. Kandasubramanian, "Effect of microplastics in water and aquatic systems," *Environmental Science and Pollution Research*, vol. 28, no. 16, pp. 19544–19562, Apr. 2021, doi: 10.1007/s11356-021-13184-2.
13. D. Panneerselvam and A. Murugesan, "Maternal microplastic exposure during pregnancy and risk of gestational diabetes mellitus associated with gut dysbiosis," *Medicine in Microecology*, vol. 18, p. 100091, Dec. 2023, doi: 10.1016/j.medmic.2023.100091.
14. A. I. Osman *et al.*, "Microplastic sources, formation, toxicity and remediation: a review," *Environ Chem Lett*, vol. 21, no. 4, pp. 2129–2169, Aug. 2023, doi: 10.1007/s10311-023-01593-3.
15. S. Pourebrahimi and M. Pirooz, "Microplastic pollution in the marine environment: A review," *Journal of Hazardous Materials Advances*, vol. 10, p. 100327, May 2023, doi: 10.1016/j.hazadv.2023.100327.
16. K. Ziani *et al.*, "Microplastics: A Real Global Threat for Environment and Food Safety: A State-of-the-Art Review," *Nutrients*, vol. 15, no. 3, p. 617, Jan. 2023, doi: 10.3390/nu15030617.

17. L. G. Kahn, C. Philippat, S. F. Nakayama, R. Slama, and L. Trasande, "Endocrine-disrupting chemicals: implications for human health," *Lancet Diabetes Endocrinol*, vol. 8, no. 8, pp. 703–718, Aug. 2020, doi: 10.1016/S2213-8587(20)30129-7.
18. C. Yang, G. Song, and W. Lim, "A mechanism for the effect of endocrine disrupting chemicals on placentation," *Chemosphere*, vol. 231, pp. 326–336, Sep. 2019, doi: 10.1016/j.chemosphere.2019.05.133.
19. C. Ahn and E.-B. Jeung, "Endocrine-Disrupting Chemicals and Disease Endpoints," *Int J Mol Sci*, vol. 24, no. 6, p. 5342, Mar. 2023, doi: 10.3390/ijms24065342.
20. Y. Yan, F. Guo, K. Liu, R. Ding, and Y. Wang, "The effect of endocrine-disrupting chemicals on placental development," *Front Endocrinol (Lausanne)*, vol. 14, Feb. 2023, doi: 10.3389/fendo.2023.1059854.
21. R. Barouki *et al.*, "Epigenetics as a mechanism linking developmental exposures to long-term toxicity," *Environ Int*, vol. 114, pp. 77–86, May 2018, doi: 10.1016/j.envint.2018.02.014.
22. M. Bashir, Y. Fagier, B. Ahmed, and J. C Konje, "An overview of diabetes mellitus in pregnant women with obesity," *Best Pract Res Clin Obstet Gynaecol*, vol. 93, p. 102469, Mar. 2024, doi: 10.1016/j.bpobgyn.2024.102469.
23. A. Shamsad, A. S. Kushwah, R. Singh, and M. Banerjee, "Pharmaco-epi-genetic and patho-physiology of gestational diabetes mellitus (GDM): An overview," *Health Sciences Review*, vol. 7, p. 100086, Jun. 2023, doi: 10.1016/j.hsr.2023.100086.
24. J. F. Plows, J. L. Stanley, P. N. Baker, C. M. Reynolds, and M. H. Vickers, "The Pathophysiology of Gestational Diabetes Mellitus," *Int J Mol Sci*, vol. 19, no. 11, p. 3342, Oct. 2018, doi: 10.3390/ijms19113342.
25. K. Wu *et al.*, "The utility of HbA1c combined with haematocrit for early screening of gestational diabetes mellitus," *Diabetol Metab Syndr*, vol. 10, no. 1, p. 14, Dec. 2018, doi: 10.1186/s13098-018-0314-9.
26. S. Tripathy, A. Murugesan, K. Natarajan, B. Ramraj, and S. Mohapatra, "Early screening biomarker HbA1c and Hematocrit for gestational diabetes mellitus," *Clin Epidemiol Glob Health*, vol. 13, p. 100945, Jan. 2022, doi: 10.1016/j.cegh.2021.100945.
27. Campanale, Massarelli, Savino, Locaputo, and Uricchio, "A Detailed Review Study on Potential Effects of Microplastics and Additives of Concern on Human Health," *Int J Environ Res Public Health*, vol. 17, no. 4, p. 1212, Feb. 2020, doi: 10.3390/ijerph17041212.
28. B. Udovicki, M. Andjelkovic, T. Cirkovic-Velickovic, and A. Rajkovic, "Microplastics in food: scoping review on health effects, occurrence, and human exposure," *Int J Food Contam*, vol. 9, no. 1, p. 7, Dec. 2022, doi: 10.1186/s40550-022-00093-6.

29. H. Li *et al.*, “Maternal cosmetics use during pregnancy and risks of adverse outcomes: a prospective cohort study,” *Sci Rep*, vol. 9, no. 1, p. 8030, May 2019, doi: 10.1038/s41598-019-44546-z.

30. N. S. K. Nawalage and B. K. A. Bellanthudawa, “Synthetic polymers in personal care and cosmetics products (PCCPs) as a source of microplastic (MP) pollution,” *Mar Pollut Bull*, vol. 182, p. 113927, Sep. 2022, doi: 10.1016/j.marpolbul.2022.113927.

31. E. Jeong, J.-Y. Lee, and M. Redwan, “Animal exposure to microplastics and health effects: A review,” *Emerg Contam*, vol. 10, no. 4, p. 100369, Dec. 2024, doi: 10.1016/j.emcon.2024.100369.

32. Y. Deng, Y. Zhang, B. Lemos, and H. Ren, “Tissue accumulation of microplastics in mice and biomarker responses suggest widespread health risks of exposure,” *Sci Rep*, vol. 7, no. 1, p. 46687, Apr. 2017, doi: 10.1038/srep46687.

33. R. E. Zurub, Y. Cariaco, M. G. Wade, and S. A. Bainbridge, “Microplastics exposure: implications for human fertility, pregnancy and child health,” *Front Endocrinol (Lausanne)*, vol. 14, Jan. 2024, doi: 10.3389/fendo.2023.1330396.

34. W. Zhang *et al.*, “Exposure to Bisphenol a Substitutes and Gestational Diabetes Mellitus: A Prospective Cohort Study in China,” *Front Endocrinol (Lausanne)*, vol. 10, Apr. 2019, doi: 10.3389/fendo.2019.00262.

35. L. Benincasa, M. Mandalà, L. Paulesu, L. Barberio, and F. Ietta, “Prenatal Nutrition Containing Bisphenol A Affects Placenta Glucose Transfer: Evidence in Rats and Human Trophoblast,” *Nutrients*, vol. 12, no. 5, p. 1375, May 2020, doi: 10.3390/nu12051375.

36. J.-Y. Lin and R.-X. Yin, “Exposure to Endocrine-Disrupting Chemicals and Type 2 Diabetes Mellitus in Later Life,” *Expo Health*, vol. 15, no. 1, pp. 199–229, Mar. 2023, doi: 10.1007/s12403-022-00486-0.

37. H. K. L. Johansson *et al.*, “Perinatal exposure to mixtures of endocrine disrupting chemicals reduces female rat follicle reserves and accelerates reproductive aging,” *Reproductive Toxicology*, vol. 61, pp. 186–194, Jun. 2016, doi: 10.1016/j.reprotox.2016.03.045.

38. J. E. Schjenken, E. S. Green, T. S. Overduin, C. Y. Mah, D. L. Russell, and S. A. Robertson, “Endocrine Disruptor Compounds—A Cause of Impaired Immune Tolerance Driving Inflammatory Disorders of Pregnancy?,” *Front Endocrinol (Lausanne)*, vol. 12, Apr. 2021, doi: 10.3389/fendo.2021.607539.

39. B. Zhao, P. Rehati, Z. Yang, Z. Cai, C. Guo, and Y. Li, “The potential toxicity of microplastics on human health,” *Science of The Total Environment*, vol. 912, p. 168946, Feb. 2024, doi: 10.1016/j.scitotenv.2023.168946.

40. A. Alijagic *et al.*, “The triple exposure nexus of microplastic particles, plastic-associated chemicals, and environmental pollutants from a human health perspective,” *Environ Int*, vol. 188, p. 108736, Jun. 2024, doi: 10.1016/j.envint.2024.108736.
41. S. Ehrlich, D. Lambers, A. Baccarelli, J. Khoury, M. Macaluso, and S.-M. Ho, “Endocrine Disruptors: A Potential Risk Factor for Gestational Diabetes Mellitus,” *Am J Perinatol*, vol. 33, no. 13, pp. 1313–1318, Aug. 2016, doi: 10.1055/s-0036-1586500.
42. H. Wang *et al.*, “Serum concentrations of phthalate metabolites in pregnant women and their association with gestational diabetes mellitus and blood glucose levels,” *Science of The Total Environment*, vol. 857, p. 159570, Jan. 2023, doi: 10.1016/j.scitotenv.2022.159570.
43. T. M. James-Todd *et al.*, “Pregnancy urinary phthalate metabolite concentrations and gestational diabetes risk factors,” *Environ Int*, vol. 96, pp. 118–126, Nov. 2016, doi: 10.1016/j.envint.2016.09.009.
44. S. Cordier, E. Anassour-Laouan-Sidi, M. Lemire, N. Costet, M. Lucas, and P. Ayotte, “Association between exposure to persistent organic pollutants and mercury, and glucose metabolism in two Canadian Indigenous populations,” *Environ Res*, vol. 184, p. 109345, May 2020, doi: 10.1016/j.envres.2020.109345.
45. M. Puche-Juarez *et al.*, “The Role of Endocrine Disrupting Chemicals in Gestation and Pregnancy Outcomes,” *Nutrients*, vol. 15, no. 21, p. 4657, Nov. 2023, doi: 10.3390/nu15214657.
46. Y.-H. Chiu *et al.*, “Trimester-Specific Urinary Bisphenol A Concentrations and Blood Glucose Levels Among Pregnant Women From a Fertility Clinic,” *J Clin Endocrinol Metab*, vol. 102, no. 4, pp. 1350–1357, Apr. 2017, doi: 10.1210/jc.2017-00022.
47. J. Wang *et al.*, “Association between per- and polyfluoroalkyl substances and risk of gestational diabetes mellitus,” *Int J Hyg Environ Health*, vol. 240, p. 113904, Mar. 2022, doi: 10.1016/j.ijheh.2021.113904.
48. A. K. Peterson *et al.*, “PFAS concentrations in early and mid-pregnancy and risk of gestational diabetes mellitus in a nested case-control study within the ethnically and racially diverse PETALS cohort,” *BMC Pregnancy Childbirth*, vol. 23, no. 1, p. 657, Sep. 2023, doi: 10.1186/s12884-023-05953-3.
49. J. H. Ji *et al.*, “Relationship between heavy metal exposure and type 2 diabetes: a large-scale retrospective cohort study using occupational health examinations.,” *BMJ Open*, vol. 11, no. 3, p. e039541, Mar. 2021, doi: 10.1136/bmjopen-2020-039541.
50. X. Yao *et al.*, “Stratification of population in NHANES 2009–2014 based on exposure pattern of lead, cadmium, mercury, and arsenic and their association with cardiovascular, renal and respiratory outcomes,” *Environ Int*, vol. 149, p. 106410, Apr. 2021, doi: 10.1016/j.envint.2021.106410.

51. Z.-R. Tang, X.-L. Xu, S.-L. Deng, Z.-X. Lian, and K. Yu, "Oestrogenic Endocrine Disruptors in the Placenta and the Fetus," *Int J Mol Sci*, vol. 21, no. 4, p. 1519, Feb. 2020, doi: 10.3390/ijms21041519.

52. N. Sharma *et al.*, "Microplastic residues in clinical samples: A retrospection on sources, entry routes, detection methods and human toxicity," *TrAC Trends in Analytical Chemistry*, vol. 173, p. 117618, Apr. 2024, doi: 10.1016/j.trac.2024.117618.

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