REVIEW ARTICLE

IJETV Vol. 10, Issue 2, 2024 Print ISSN: 2394–6822 Online ISSN: 2395–4272

Examining the Impact of Prolonged Low-Level Exposure to Environmental Toxins on Embryonic Development: An Introductory Review

Shiuli Rathore[1], Rajiv Ratan Singh[2], Pradeep Kumar Yadav[3], Sachin Kumar Tripathi[4], Rohit Kumar Singh[5], Rakhi Rajput[6], Geetika Bajpai[7]

[1]Department of Forensic Medicine & Toxicology, King George Medical University, Lucknow, Uttar Pradesh.

[2]Department of Emergency Medicine, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow.

[3]Department of Forensic Medicine and Toxicology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow.

[4,5,6,7]Department of Forensic Medicine and Toxicology, King George's Medical University, Lucknow.

Abstract

Problems concerning environmental pollutants' impact on human well-being, particularly throughout the critical phases of embryonic growth, have become more prevalent because the level of contamination has risen. Continuous low-level contact with environmental toxins may have been associated with various adverse impacts, including premature development and potential serious health consequences. It is vital to inquire into the accumulated effects of such pollutants to come up with an evidence-based decision- healthcare initiatives and regulatory measures to deliver a comprehensive understanding and direct future investigations. We evaluate how prolonged minimal exposure to environmental toxins influences the development of embryos by integrating previous research, recognizing patterns, as well as and evaluating methodologies. This comprehensive investigation addresses how long-term minimal exposure to environmental contaminants influences the growth and development of a developing embryo. A careful examination of the scientific literature brought out relevant investigations, particularly a special emphasis on credible methods and resources that were subject to peer review. Observations on organogenesis, neurological growth, and reproductive health have been evaluated via a narrative summary and were accompanied by gathering data and quality assessments. Ethics remained perhaps the most important element. They understand that investigations might possess biases and discrepancies. This review emphasizes the importance of understanding prolonged low-level exposure to environmental toxins in embryonic development. It stresses the need for further research, specific mechanisms elucidation, and interdisciplinary approaches for informed public health policies to safeguard prenatal development and reduce developmental disorder risks.

Keywords: Environmental toxins, Embryonic development, Low-level exposure, public health, Regulatory measures, Adverse health outcomes.

Int J Eth Trauma Victimology (2024). DOI: 10.18099/ijetv.v10i02.05

Introduction

Over the past few years, the intricate interplay between human health and environmental factors has become a focal point of scientific study, with particular attention directed towards embryonic development.[1] The embryonic period represents a critical phase where intricate cellular processes determine the foundation for lifelong health.[2] However, as the global landscape grapples with rising levels of environmental toxins, concerns regarding their impact on embryonic development have intensified.[3] This introduction seeks to provide a comprehensive overview of the burgeoning field dedicated to examining the impact of prolonged low-level exposure to environmental toxins on embryonic development. Environmental toxins in our surroundings have become an undeniable reality of modern life. From industrial pollutants to pesticides, many chemical agents infiltrate our air, water, and soil, exposing human populations to a complex mixture of potentially harmful substances.[4,5] Unlike acute exposures that lead to immediate and discernible health effects, the insidious nature of prolonged low-level exposure raises unique challenges for researchers and public health practitioners.[6] Understanding the consequences of chronic exposure during embryonic development is particularly vital, given the susceptibility of developing organisms to external influences. Embryonic development is a marvel of biological intricacy, involving a meticulously orchestrated series of

Corresponding Author: Pradeep Kumar Yadav, Department of Forensic Medicine and Toxicology, Dr. Ram Manohar Lohia Institute Lucknow., e-mail: dctrprdp@gmail.com

How to cite this article: Rathore S, Singh RR, Yadav PK, Tripathi SK, Singh RK, Rajput R, Bajpai G. Examining the Impact of Prolonged Low-Level Exposure to Environmental Toxins on Embryonic Development: An Introductory Review. Int J Eth Trauma Victimology. 2024;10(2):21-25.

Source of support: Nil

Conflict of interest: None

Received: 18/10/2024; **Received in revised form:** 15/12/2024; **Accepted:** 20/12/2024; **Published:** 12/02/2025;

events shaping an individual's life blueprint.[7] During this period, cells differentiate and multiply, forming the various tissues and organs that constitute the human body.[8] The vulnerability of these developmental processes to external disruptions is underscored by a growing body of evidence implicating environmental toxins in a range of adverse outcomes.[9] From congenital anomalies to long-term health consequences, the impact of prolonged low-level exposure is a multifaceted puzzle that demands meticulous examination. This review aims to delve into the intricate relationship between environmental toxins and embryonic development, specifically focusing on the consequences of prolonged low-level exposure. By synthesizing existing research findings, this study seeks to unravel the complex mechanisms through which environmental toxins may influence embryonic development and contribute to adverse health outcomes as shown in Figure 1.[10] The importance of this inquiry extends beyond academic curiosity; it holds significant implications for public health strategies, regulatory frameworks, and the well-being of future generations.[11] The multifaceted nature of environmental toxins necessitates a nuanced understanding of their impact on embryonic development.[12] The term "environmental toxins" encompasses a broad spectrum of substances, ranging from heavy metals and industrial chemicals to pollutants present in everyday products.[13] Each agent may pose a unique threat, and their combined effects in real-world scenarios are not yet fully understood.[14] Hence, the research community faces the challenge of unraveling the intricacies of this complex web to discern patterns and trends in the impact of prolonged low-level exposure. A pivotal aspect of this research involves the synthesis of current findings from diverse fields, including toxicology, developmental biology, and epidemiology.[15] The collaboration of these disciplines is crucial to grasp the multifaceted nature of the problem comprehensively. Toxicologists provide insight into the specific effects of various environmental toxins on cellular processes, while developmental biologists contribute to understanding how these effects manifest in the context of embryonic development.[16] Epidemiologists play a crucial role in connecting these laboratory-based findings to real-world scenarios, investigating the implications of prolonged exposure within human populations.[17] As we embark on this comprehensive review, identifying commonalities and knowledge gaps is paramount.

While certain toxins may share pathways of impact, the vast array of potential exposures requires a discerning eye to recognize overarching themes. Simultaneously, gaps in our understanding highlight areas where further investigation is imperative. By critically evaluating the methodologies employed in selected studies, this research aims to assess the quality and reliability of the evidence, contributing to the refinement and advancement of the current body of knowledge.

Fetal stage impacts susceptibility to toxins, affecting embryonic development critically

Fetal development, spanning three trimesters, encompasses a remarkable journey of growth and maturation (Figure 2). In the first trimester (weeks 1–12), the zygote rapidly divides to form a blastocyst, which implants into the uterine wall.[18] Major organs and structures begin to form during weeks 5 to 8, with the embryo developing a beating heart, brain, spinal cord, and

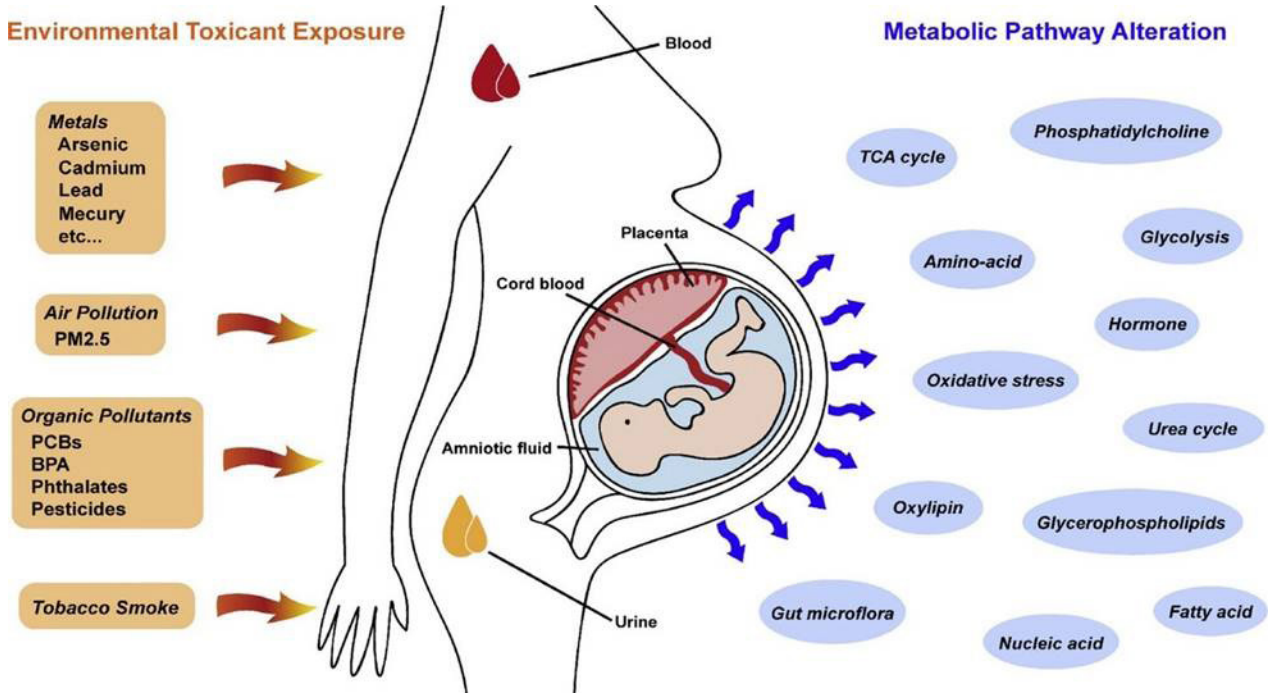

Figure 1: Environmental toxicant exposure and its metabolic pathway alteration

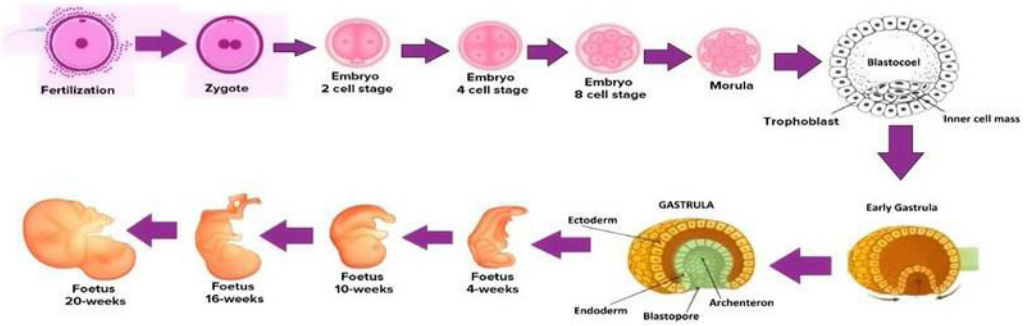

Figure 2: Stages of embryonic development

limb buds. By weeks 9 to 12, the embryo transitions into a fetus, with defined facial features, developing fingers and toes, and initial movements.[19] The second trimester (weeks 13–26) witnesses rapid growth and maturation as bones harden, sex organs differentiate, and the fetus gains coordination. Lanugo hair covers the skin, and quickening the mother's perception of fetal movements may occur.[20] In the third trimester (weeks 27-birth), the fetus continues to mature, with further brain development, lung maturation, and weight gain. As the due date approaches, the fetus may descend into the pelvis in preparation for birth.[21]

Ensuring healthy fetal development during these periods requires optimal mother care and an environment that is nurturing. The degree to which an embryo is susceptible to the adverse outcomes of low-level exposure to environmental contaminants on embryonic development reflects critically on its developmental stage.[22] The fetus becomes particularly exposed to environmental factors throughout the initial stages of embryonic development due to the fast cell division and segmentation.[23] Pollutants from the environment can disrupt normal developmental processes when they are present during critical stages of organogenesis, which could lead to defects in structure or function.[24] For instance, during embryonic development, exposure to toxins like pesticides, heavy metals, or air pollution can disrupt important processes including limb formation, brain tube formation, and cardiovascular development.[25] Furthermore, the impact of environmental toxins may vary depending on the specific stage of fetal development, with certain organs or systems being more susceptible at different times.[26] Understanding the timing of exposure and its association with specific developmental stages is essential for assessing the potential risks and implementing preventive measures to safeguard fetal health.[27]

Material & Methods

The effects of long-term exposure to harmful environmental factors on offspring growth were investigated in this study methodologically. To identify relevant research, all literature searches using keywords such as "environmental toxins" and "child development" were conducted in reliable databases such as PubMed, Scopus and Web of Science. These inclusion criteria were established to give priority to peer-reviewed papers with weak experimental designs or experimental methods, especially with a strong focus on both human and animal embryonic development. During the review, pertinent data, including study design, sample size, duration of exposure, types of toxicity, and neonatal outcomes, were collected in detail. Two independent reviewers participated to ensure data extraction accuracy as well as reliability. Quality assessments were performed, considering factors such as methodology and potential biases. Findings were synthesized using a narrative approach, with particular attention given to the impact on organogenesis, neurodevelopment, and reproductive outcomes. Acknowledgment of limitations, such as potential publication bias and study heterogeneity, was incorporated into the review. Moreover, variations in populations and exposures were considered during the interpretation of results to provide a comprehensive understanding of the findings.

Discussion

In the study of Geng HX et al. in 2019, he sought the initiative of health and disease (DOHaD) development. This area emphasizes how the environment in the womb influences childhood and lifelong health. It suggests that disruption during fetal development and dysfunction of natural biological functions early in life can lead to fetal death and systemic diseases later in adulthood, such as hypertension, obesity, and diabetes.[28] In 2019, Co EB and colleagues conducted a survey that focused on the continued use of pesticides, antibiotics, and technological excipients. These products serve important purposes: protecting crops from pests, protecting humans and animals from microbial hazards, and assisting in industrial manufacturing, but if they do go used, they pose a serious threat to the environment. The use of these drugs has been associated with a variety of health issues, including infertility, spontaneous abortion, immunotoxicity, autotoxicity diseases, and neurotoxins.[29] In 2014, Sogorb, MA, and colleagues performed an examination looking into various methods to screen embryonic toxic substances. Even though a lot of alternatives seem promising and fit in well with in vivo

findings, it might not be enough to identify embryonic concerns and estimate risks based just on one *in-vitro–ex-vivo* study. The problems in extrapolating across species, converting exposure scenarios from in vivo to in vitro settings, and potential changes in the toxicokinetics and toxicodynamics are among the same obstacles that these methodologies confront as other in vitro experiments. [30] A 2014 study by Celá P, Veselá B, et al. It highlighted the widespread use of nanomaterials in the medical, sanitary, construction and textile industries. Even at general levels of use, their safety remains uncertain due to possible accumulation in the body and unknown interactions. It is important to understand its effects on fetal development and what can be established through the placenta and blood-brain barriers. Differences in the properties of nanomaterials greatly influence their effects, and further research is needed to develop safer materials for use and storage methods.[31] In 2011, Varghese AC, Ly KD, et al.It also reviewed and studied the factors affecting female fertility and their impact on fertility. Although some factors such as lifestyle, xenoestrogens, and heavy metals are known, much less is known.[32] Another study conducted by Lavolpe M, Greco LL, et al., found that none of the tested heavy metals caused significant mortality in females or a decrease in hatched larvae or egg incubation time (Table 1). However, concentrations of 1 mg/L copper and 10 mg/L zinc led to a significant ($p < 0.05$) increase in ovigerous females with asynchronous hatching, lasting 1 to 4 days. Significant ($p < 0.05$) total egg loss occurred only in females exposed to 1 mg/L copper.[33] In 1978, Khera KS *et al* study looked at 234 trials of various drugs tested in hamsters, mice, rats, and rabbits. A significant association was found between maternal toxicity and fetal and fetal mortality, suggesting that maternal toxicity may directly contribute to fetal derangement.[34]

Conclusion

The importance of recognizing the repercussions of sustained low concentrations of environmental exposure on the development of embryos is highlighted by this comprehensive analysis. Following these results, additional research needs to be conducted to pinpoint the specific routes and frameworks responsible for toxicity to developmental processes. The analysis additionally emphasizes the value of enacting rules and regulations and preventative measures to minimize risks related to environmental exposure during the critical phases of fetal development that have declined. Toxicological Research, developmental biology, epigenetics and interdisciplinary approaches need to be amalgamated to build up a significant connection with environmental exposure and optimize the prenatal health system. Ultimately, public health initiatives to safeguard fetal development and minimize the likelihood of developmental disorders attributable to environmental hazards on snow can be grounded in this comprehension.

Conflict of Interest

There is no conflict of interest

Source of funding

None

Ethical Clearance

Not Applicable.

References

1. Gluckman PD, Hanson MA, Buklijas T. A conceptual framework for the developmental origins of health and disease. Journal of developmental origins of health and disease. 2010 Feb;1(1):6-18.
2. Fleming TP, Watkins AJ, Velazquez MA, Mathers JC, Prentice AM, Stephenson J, Barker M, Saffery R, Yajnik CS, Eckert JJ, Hanson MA. Origins of lifetime health around the time of conception: causes and consequences. The Lancet. 2018 May 5;391(10132):1842-52.
3. Thomas JA. History and biology in the Anthropocene: problems of scale, problems of value. The American Historical Review. 2014 Dec 1;119(5):1587-607.
4. Kolok A. Modern poisons: A brief introduction to contemporary toxicology. Island Press; 2016 May 5.
5. Zaller JG, Zaller JG. Pesticide impacts on the environment and humans. Daily poison: pesticides-an underestimated danger. 2020:127-221.
6. Moeller DW. Environmental health. Harvard University Press; 2011 Jun 1.
7. Morgan L. Icons of life: A cultural history of human embryos. Univ of California Press; 2009 Sep 9.
8. Bianconi E, Piovesan A, Facchin F, Beraudi A, Casadei R, Frabetti F, Vitale L, Pelleri MC, Tassani S, Piva F, Perez-Amodio S. An estimation of the number of cells in the human body. Annals of human biology. 2013 Nov 1;40(6):463-71.
9. Grandjean P, Barouki R, Bellinger DC, Casteleyn L, Chadwick LH, Cordier S, Etzel RA, Gray KA, Ha EH, Junien C, Karagas M. Life-long implications of developmental exposure to environmental stressors: new perspectives. Endocrinology. 2015 Oct 1;156(10):3408-15.
10. Cheroni C, Caporale N, Testa G. Autism spectrum disorder at the crossroad between genes and environment: contributions, convergences, and interactions in ASD developmental pathophysiology. Molecular autism. 2020 Sep 10;11(1):69.
11. Hubbs-Tait L, Nation JR, Krebs NF, Bellinger DC. Neurotoxicants, micronutrients, and social environments: Individual and combined effects on children's development. Psychological Science in the Public Interest. 2005 Dec;6(3):57-121.
12. Rottenberg J, Devendorf AR, Kashdan TB, Disabato DJ. The curious neglect of high functioning after psychopathology: The case of depression. Perspectives on psychological science. 2018 Sep;13(5):549-66.
13. Landrigan PJ, Landrigan MM. Children and environmental toxins: what everyone needs to know. Oxford University Press; 2018 Jan 2.
14. Nurse JR, Buckley O, Legg PA, Goldsmith M, Creese S, Wright GR, Whitty M. Understanding insider threat: A framework for characterizing attacks. In2014 IEEE security and privacy workshops 2014 May 17 (pp. 214-228). IEEE.
15. National Research Council, Commission on Life Sciences, Board on Environmental Studies, Committee on Developmental Toxicology. Scientific frontiers in developmental toxicology and risk assessment.

16. Hughes C, Waters M, Allen D, Obasanjo I. Translational toxicology: a developmental focus for integrated research strategies. BMC Pharmacology and Toxicology. 2013 Dec;14:1-9.
17. Kelly FJ, Fussell JC. Linking ambient particulate matter pollution effects with oxidative biology and immune responses. Annals of the New York Academy of Sciences. 2015 Mar;1340(1):84-94.
18. Bhattacharya N, Stubblefield P. Human Fetal Growth and Development. Human Fetal Growth and Development. 2016.
19. Carlson BM. Human embryology and developmental biology. Elsevier Health Sciences; 2018 Nov 30.
20. Girling J, Nightingale P. My Pregnancy Now!. Jaico Publishing House; 2016 Jan 18.
21. Anithadevi K. Analysis of Maternal and Fetal Outcome of Placenta Previa (Doctoral dissertation, Tirunelveli Medical College, Tirunelveli).
22. Mallozzi M, Bordi G, Garo C, Caserta D. The effect of maternal exposure to endocrine disrupting chemicals on fetal and neonatal development: A review on the major concerns. Birth Defects Research Part C: Embryo Today: Reviews. 2016 Sep;108(3):224-42.
23. Penaloza C, Lin L, Lockshin RA, Zakeri Z. Cell death in development: shaping the embryo. Histochemistry and cell biology. 2006 Aug;126:149-58.
24. Rice D, Barone Jr S. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. Environmental health perspectives. 2000 Jun;108(suppl 3):511-33.
25. Ren A. Environmental pollutants and neural tube defects. InReproductive and Developmental Toxicology 2017 Jan 1 (pp. 1139-1166). Academic Press.
26. Sly PD, Flack F. Susceptibility of children to environmental pollutants. Annals of the New York Academy of Sciences. 2008 Oct;1140(1):163-83.
27. Landrigan PJ, Kimmel CA, Correa A, Eskenazi B. Children's health and the environment: public health issues and challenges for risk assessment. Environmental health perspectives. 2004 Feb;112(2):257-65.
28. Geng HX, Wang L. Cadmium: Toxic effects on placental and embryonic development. Environmental toxicology and pharmacology. 2019 Apr 1;67:102-7.
29. Ko EB, Hwang KA, Choi KC. Prenatal toxicity of the environmental pollutants on neuronal and cardiac development derived from embryonic stem cells. Reproductive Toxicology. 2019 Dec 1;90:15-23.
30. Sogorb MA, Pamies D, de Lapuente J, Estevan C, Estévez J, Vilanova E. An integrated approach for detecting embryotoxicity and developmental toxicity of environmental contaminants using in vitro alternative methods. Toxicology letters. 2014 Oct 15;230(2):356-67.
31. Celá P, Veselá B, Matalová E, Večeřa Z, Buchtová M. Embryonic toxicity of nanoparticles. Cells Tissue Organs. 2014 Jun 4;199(1):1-23.
32. Varghese AC, Ly KD, Corbin C, Mendiola J, Agarwal A. Oocyte developmental competence and embryo development: impact of lifestyle and environmental risk factors. Reproductive biomedicine online. 2011 May 1;22(5):410-20.
33. Lavolpe M, Greco LL, Kesselman D, Rodríguez E. Differential toxicity of copper, zinc, and lead during the embryonic development of Chasmagnathusgranulatus (Brachyura, Varunidae). Environmental Toxicology and Chemistry: An International Journal. 2004 Apr;23(4):960-7.
34. Khera KS. Maternal toxicity in humans and animals: effects on fetal development and criteria for detection. Teratogenesis, Carcinogenesis, and Mutagenesis. 1987;7(3):287-95.