JCHR (2025) 15(1), 221-227

Journal of Chemical Health Risks

sanad.iau.ir/journal/jchr

REVIEW ARTICLE

Characterization and Toxicity Mechanism of Environmental Risk Factors (Heavy Metals) and Reproductive Health: A Review Paper

Mohammad Reza Khaksar, Rahim Aali Dehchenari, Yadollah Ghafuri*

Research Center for Environmental Pollutants, Qom University of Medical Sciences, Qom, Iran

(Received: 1 July 2024 Accepted: 20 January 2025)

KEYWORDS

Toxicity;
Environmental;
Heavy metals,
Reproductive health

ABSTRACT: Environmental epidemiologic studies have identified many associations between human exposure to chemicals during pregnancy and maternal and child health outcomes. This study is a systematic review in which the impact of environmental hazards including kinetics and mechanisms of toxicity and ways of exposure to heavy metals on fetal health and fertility has been reviewed. Search in scientific sites and search engines including SID, Magiran, ScienceDirect, Google Scholar, PubMed, Springer and, Scopus have been done using the desired keywords along with the review of sources that have provided the impact of environmental factors on fetal health and fertility. Finding of this review study point to several evidences that prenatal maternal exposure to heavy metals is related to fetal epigenomic changes, direct effects on reproductive potential, retards of fetal growth and, other risks during pregnancy. Accordingly, to achieve preventative processes including assessment, diagnosis and, planning for health promotion during pregnancy, developing national preventive guidelines to reduce exposure to heavy metals during pregnancy is inevitable.

INTRODUCTION

With the industrialization of societies and changes in lifestyle, various types of environmental threats have emerged over time and have led to the occurrence of disorders in various organs of the human body [1, 2]. Infertility is one of the many medical problems in today's world, with its rate increasing by 50% since 1955, such that 10-15% of couples now suffer from this problem. According to the definition, infertility is the absence of pregnancy after one year of sexual intercourse without any contraceptive method. Environmental factors directly affect all body tissues, including reproductive tissues, and indirectly affect various receptors related to various systems. Environmental epidemiologic studies have identified many associations between human exposure to chemicals during pregnancy and maternal and child health outcomes; however, the underlying mechanisms remain largely unknown [3, 4]. Significant metabolic changes occur in pregnancy, including increased protein synthesis from amino acids to activate fetal growth and steroid hormone synthesis to support pregnancy [5]. Therefore, the understanding of metabolism has an increasing place in understanding both the normal physiological and pathological processes of pregnancy. Regardless of the mother's exposure routes, the fetus is exposed to several environmental pollutants during pregnancy. These pollutants can harm

---

*Corresponding author: yadollahghafuri@yahoo.com (Y. Ghafuri)
DOI: 10.60829/jchr.2025.1125630

implantation and the developmental path in a cumulative dose-additive manner [6-9].

The main known disorders and complications associated with such contact are fetal death, fetal loss, intrauterine growth restriction, premature birth, birth defects, childhood diseases, neuropsychological defects, early or delayed puberty, and some common cancers [3, 4]. Therefore, poisoning caused by various environmental pollutants during pregnancy has become a major health concern. In addition, one of the important mechanisms of the effect of environmental chemicals may involve oxidative stress caused by reactive oxygen species (ROS) [10]. An imbalance between ROS production and antioxidant ROS detoxification pathways is considered responsible for pregnancy-related disorders such as fetal death, early spontaneous abortion, intrauterine growth restriction, fetal death, preterm delivery, and low birth weight. To our knowledge, there is no comprehensive study that specifically states the impact of environmental factors with emphasis on heavy metals and the mechanism of effect and metabolic kinetics of these factors in the body and fetus and on fertility. Accordingly, this research aims to review studies related to the impact of environmental factors and hazards, including heavy metals, on fetal health and fertility.

MATERIALS AND METHODS

This study is a systematic review that examines the impact of environmental hazards, including kinetics and mechanisms of toxicity and ways of exposure to heavy metals. Search in scientific sites and search engines, including SID, Magiran, ScienceDirect, Google Scholar, PubMed, Springer, and Scopus, have been done using the desired keywords (Toxicity, Environmental, heavy metals, Reproductive health) along with the review of sources that have provided the impact of environmental factors on fetal health and fertility.

The types of studies included quantitative studies (including epidemiological models and quantitative risk assessment), qualitative, and mixed studies of any type of design. First, the abstracts of the articles were fully reviewed and, unrelated and repetitive articles were removed. Then, the full text of articles related to the subject was studied and evaluated. The reported articles, other groups except the medical treatment staff and the letter to the editor, were excluded from the current research. All stages of this study are carried out in the flow chart specific to PRISMA review studies [11].In all studies, the population and statistical sample, type of research, year of research, place of research, research tools, research findings, and results were examined. According to the components of the systematic review protocol (i.e., subject context, literature review, search strategy, study selection criteria, data extraction and analysis, and study quality assessment), all articles that have these criteria are included in the study. Articles that do not meet any of the criteria are excluded from the study . In this review study, the types of studies included the characteristics, mechanisms of toxicity and exposure to heavy metals during pregnancy and fetus have been discussed. Results were shown in the Table 1 about summary of studies on chemical hazards exposure (heavy metals) and reproductive health and in Table 2 studies on kinetics and toxicity mechanisms of heavy metals in reproduction health presented.

Table 1. Summary of studies on chemical hazards exposure (heavy metals) and reproductive health.

Pollutants	Type of Study	Location	Participants and sample size	Major conclusion	Reference
Cd, Cr,As, and Pb in the environment	Review Article	-	150 studies were reviewed	Exposure to environmental pollutants such as heavy metals during pregnancy leads to fetal epigenomic changes, including changes in global DNA methylation . The most important role of these metals as environmental hazards is through endocrine disruptor.	[12]
As	Review Article	-	145 studies were reviewed	Arsenic is considered to be an endocrine disruptor, which has a direct effect on reproductive potential.	[13]
As,Cd,Hg ,Pb, Mn, Cr	Five INMA project, cohorts	Childhood (INMA) Project in Spain	327 mother-infant pairs	The findings of this study show that the exposure of pregnant mothers to cadmium, mercury and, chromium by the penetration of these pollutants into the uterus affects the fetus and retards its growth. to investigate the relationship between the sex of the fetus, more data should be used.	[14]

Hg,Pb,As,Cd ,Cr, Sn	Cross-sectional study	In five regions of Greenland: North America	509 pregnant Inuit women ≥18 years of age	The detection of heavy metals such as lead, cadmium and chromium in the mother's blood indicates their presence in the blood of the fetus, which can affect the development of the fetus based on the gender-dependent dose-response relationship.	[15]
Cd ,Hg,Pb,As, Zn	Prospective case-control study	Barcelona Center of Maternal-Fetal and Neonatal Medicine	178 mother-infant pairs	The findings of this study show that with the increase of cadmium levels in the serum of the mother and fetus, the negative effects of heavy metals on birth weight appear, and this is a very important point in confirming the role of exposure to heavy metals such as cadmium in reducing the weight of the fetus.	[16]
Cd, As, Hg, Pb	Prospective study (Birth Cohort Study)	New Hampshire in the UN	1159 women's	The investigation focused on concentrations of As, Cd, Hg and, Pb were measured in the placenta. Measured placental outcomes were weight, efficiency, area ,and eccentricity. The Placental weight is a mediator between Cd in the placenta and infant birth weight.	[17]
Thallium (Tl)	Prospective case-control study	China	3080 pregnant women	The results of this study state that exposure to thallium metal (Tl) before the birth of the fetus can cause a sex-specific effect on anthropometric measurements, so that a tendency to reduce the child's height and weight, especially in growing girls, in the future.	[18]
Cd	Systematic review	-	A total of eight original research articles were reviewed	The results obtained from this research state that cadmium changes the DNA epigenetic positions of the placenta and newborns and specific gender differences are seen for DNA methylation changes related to exposure to cadmium, which justifies the interference with DNA methyl transferases.	[19]
Pb, Hg, Cd, As through breast milk intake, in addition to in utero exposure	Research article	Regions in Ghana	114 mother- by pairs babies were 3 months old	A significant population of infants in the surveyed areas have been exposed to mercury, arsenic, and lead through breast milk, which causes very negative consequences for them, and it is necessary to intervene in this regard to maintain their health level.	[20]
As,Cd,Ni, and Ur	Original Research Article	From the rural New Hampshire	462 participants Birth Cohort Study	Exposure to arsenic in household water is increasing regardless of the quality of nutrition, which indicates the high concentration of arsenic in drinking water in the studied population.	[21]
As,Cd, Pb, Methyl Mercury,Hg	Review article	-	124 studies were reviewed	Toxic substances include drugs, pesticides, heavy metals, and food additives that may accumulate in the placenta and be transferred to developing fetuses, and will have a significant impact on vulnerable infants and children worldwide. Symptoms and physiological outcomes are directly associated with the different heavy metals, the location of the accumulation, the amount of accumulation ,and the chronicity of the accumulation.	[22]
As compounds,Ba compounds, Br compounds,Cd compounds ,Cr compounds,Pb compounds ,Hg compounds ,Ag compounds	Subject in review	-	98 studies were reviewed	Harmful effects on health caused by exposure to these types of metals and intermediary compounds determined that cardiovascular diseases, neurological and neurobehavioral disorders, hematological and immunological disorders, and hearing disorders can be mentioned. Of course, the carcinogenic nature of these compounds should not be ignored. Therefore, the type of heavy metal and its chemical form, time and amount of dose and intensity of effect should be considered in determining the toxic effect of these compounds.	[23]
Hg,Cd,Cr,Pb	Review	-	36 studies were reviewed	Autism spectrum disorder (ASD) in parental age is linked to toxic heavy metals including Pb, Hg, Cd, and As	[24]
Hg,Pb,Cd,Al,As,Ni,Mn,Cr	Review	Federation of India	114 studies were reviewed	These compounds inhibit spermatogenesis by disrupting the hormonal regulation of the hypothalamus-pituitary pathway, and along with the induction of oxidative stress, they inhibit reproductive performance, especially in men.	[25]
Hg,Pb,Cd	Review	-	123 studies were reviewed	Heavy and toxic metals such as cadmium, mercury,and lead have known teratogenic effects in various animal models such as fish, frogs, mice, rats, hamsters, chickens, and monkeys.	[26]
Pb,Cd,As	Original research	Turkey	30 women as a patient group with missed abortion.60 healthy pregnant women as control group	Placenta tissue due to exposure to toxic heavy metals such as lead, cadmium and arsenic has a significant role in abortions in the second trimester of pregnancy.	[27]
Cd	Original research	China	A total of 107 pairs of healthy pregnant women	By weakening the function of the blood-placental barrier in the fetus, the risk of exposure to cadmium in the fetus increases greatly.	[28]
Hg, As,Pb	Review	-	54 studies were reviewed	Potential adverse effects of heavy metals on fetal growth or gestational age according to the strength of evidence, moderate was reported.	[29]

Table 2. Summary studies on kinetics and toxicity mechanisms of heavy metals in reproduction health

Pollutants	Type of Study	Location	Participants and sample size	Major conclusion	Reference
Pb,Cd,As, Hg,Cr,Fe, Al	Review			Metal toxicity depends upon the route of exposure, absorbed dose ,and duration of exposure. Oxidative stress induced by free radical formation, acts as a pseudo element of the body and interferes with metabolic processes are toxicity mechanisms of heavy metals in reproduction health.	[30]
Pb,Cd,As,Hg	Review	-	41 studies were reviewed	Inhibition of heme biosynthesis about Lead toxicity, kidney-proximal tubular injury (proteinuria) lung - local irritation and inhibition of alpha1antitrypsin associated with Cd, dissociation of salts precipitates proteins and destroy smucosal membranes, necrosis of proximal tubular epithelium and inhibition of sulfhydryl (-SH) group containing enzymes are Hg toxicity.	[31]
Toxicity of metal compounds	Review	Moscow	120 studies were reviewed	The toxicity of a metal compound is related to factors such as oxidation state, ligands, solubility, particle morphology, environmental properties, and other factors. Therefore, with accurate measurement, it is possible to find the chemical effectiveness of metal compounds on the system based on sensitivity.	[32]
Cd, Pb,Hg, As	Systematic Review	-	108 studies were reviewed	The results of this research confirmed the quantitative relationship between heavy metals and hormonal and metabolic changes regarding polycystic ovary syndrome (PCOS).	[33]
Cd	Review	-	144 studies were reviewed	Cadmium as a environmental contaminants can lead to liver, lung, and kidney damage, as well as cause the occurrence of other metabolic and molecular diseases at the cell level, such as the effect on the complex process of inflammation and oxidative stress.	[34]
Cd, Pb, As	Review Article	-	93 studies were reviewed	DNA methylation, Epigenetic modification, expression of aberrant microRNA (miRNA), and histone modification, are mechanisms by which the effects of their toxicity are applied as endocrine disruptors	[35]

In the process of assessing the risk of exposure to environmental factors, several factors, including timing and amount of exposure, genetics, and sexuality, should be determined [2]. In this review study, only the characteristics, mechanisms of toxicity, and exposure to heavy metals during pregnancy and fetus are discussed. A study by Bommarito PA et al. about exposure to environmental contaminants during pregnancy showed that Cd, Cr, and Pb altered global DNA methylation, gene-specific CpG methylation, and microRNA expression [12]. Arsenic exposure as a heavy metal and endocrine disruptor during pregnancy and early childhood has been considered in many studies. Shama V et al. showed that arsenic exposure affects the reproductive potential of the organism. These harmful effects of arsenic could be directly caused by classical hormones secreted from endocrine cells into the interstitial fluid. These hormones diffuse into the bloodstream to be distributed to all parts of the body [13]. Results of a cross-sectional and birth cohort study of Pregnant Women's Exposure to Metals and fetal growth outcomes revealed that concentrations of chromium, cadmium, and nickel were higher than normal ranges. Copper and cadmium were significantly associated with adverse outcomes for the birth of the fetus. In this study, toxic metals in maternal blood can adversely influence fetal growth and development. Food, daily intake, and lifestyle factors are important sources of heavy metals [14]. Studying heavy metals exposure and correlation with fetal growth restriction by Sabra S et al. shows that fetal birth weight was negatively correlated with the fetal serum level of Cd ($p < 0.001$). This result suggests the impact of heavy metal risk on fetal growth [15]. Punshon T et al. examined the relationships between placental concentrations of Cd, As, Hg, and Pb and measures of placental growth and functioning, including placental weight and placental efficiency. The results revealed that the Cd concentration of the placenta was also associated with reductions in placental efficiency, and no appreciable differences were observed with other elements (As, Hg, or Pb) [17]. Juan Qi et al. investigated prenatal thallium exposure and poor growth in early childhood.

The results showed that prenatal thallium exposures might have a sex-specific effect on child anthropometric measurements in the first 2 years of life [18]. Recent research on epigenetic effects in humans from prenatal exposure to cadmium has determined that cadmium alters epigenetic signatures in placental and neonatal DNA. In addition, some studies show sex-specific differences in cadmium-associated DNA methylation changes [19]. Results of a review study about heavy metals during pregnancy and the health of breastfed children showed that these toxic compounds, including heavy metals and food additives, may accumulate in breast milk and be transferred to breastfeeding infants or transferred across the placenta to developing fetuses [22]. Rosalia Pascal showed that lactating women and pregnant must be aware of harmful heavy metals that act as Endocrine Disruptor Compounds (EDCs) and are exposed by food intake and on pregnancy and development. This study mentioned the effect of these dangerous compounds through changing body hormones and their performance. Major evidence of heavy metal effects on prenatal exposure has been found for intrauterine growth disorder and preeclampsia. Impaired fetal growth due to the accumulation of metals in the placenta has also been reported [35].

Pregnancy rate reduction and increased miscarriage occurrence in contaminated areas by heavy metals, including Cadmium, Chromium-Nickel, Arsenic, Copper, Lead, and Mercury, in the southeast of São Paulo State, Brazil, pregnancy occurrence was noticed compared to the control area [36]. In the review study for fetal growth in environmental epidemiology, heavy metals as part of endocrine-disrupting compounds (EDCs) will be able to interfere with hormones. One of the important consequences of exposure to heavy metals during pregnancy is the accumulation of toxic metals such as lead in the maternal body in females before pregnancy that may be transferred to the fetus through the placenta and later via lactation [37].

CONCLUSIONS

This review study aimed to classify and summarize the existing literature study about environmental exposure to heavy metals, pregnancy, and fetal growth. We highlighted characteristics of outcome and mechanisms of heavy metals toxicity. The present review study revealed that prenatal maternal exposure to heavy metals is related to fetal epigenomic changes, direct effects on reproductive potential, retards of fetal growth, and other risks during pregnancy. Accordingly, developing national preventive guidelines to reduce exposure to heavy metals during pregnancy is inevitable to achieve preventative processes, including assessment, diagnosis, and planning for health promotion during pregnancy.

ETHICAL CONSIDERATION

This project has been supported by the Qom University of Medical Sciences Health and ethic code number IR.MUQ.REC.1403.147

REFERENCES

1. Abdollahi M., Khaksar M.R., 2023. Sodium Dimethyldithiocarbamate. Encyclopedia of Toxicology, 4nd ed. Elsevier. pp. 601-606.

2. Ghafuri Y., Nabizadeh R., 2017. Composition and quantity of cytotoxic waste from oncology wards: A survey of environmental characterization and source management of medical cytotoxic waste. Biosci Biotechnol Res Commun. 10(3),438-4.

3. Pajewska-Szmyt M., Sinkiewicz-Darol E., Gadzała-Kopciuch R., 2019. The impact of environmental pollution on the quality of mother's milk. Environmental Science and Pollution Research. 26,7405-27.

4. Pikounis T.D., Amann K.L., Jackson B.P., Punshon T., Gilbert-Diamond D., Korrick S., Karagas M.R., Cottingham K.L.,2024. Urinary biomarkers of exposure to toxic and essential elements: A comparison of infants fed with human milk or formula. Environmental Epidemiology. 8(1), e286.

5. Triche E.W., Hossain N., 2007. Environmental factors implicated in the causation of adverse pregnancy outcome. InSeminars in perinatology . 31(4), 240-242.

6]. Yurdakök K., 2015. Lead, mercury, and cadmium in breast milk. Journal of Pediatric and Neonatal Individualized Medicine (JPNIM).4(2),e040223

7. Jafarzadeh S, Fard RF, Ghorbani E, Saghafipour A, Moradi-Asl E, Ghafuri Y., 2020. Potential risk assessment of heavy metals in the Aharchai River in northwestern Iran. Physics and Chemistry of the Earth. Parts A/B/C.1;115,102812.

8. Mostafaii G., Bakhtyari Z., Atoof F., Baziar M., Fouladi-Fard R., Rezaali M., Mirzaei N., 2021. Health risk assessment and source apportionment of heavy metals in atmospheric dustfall in a city of Khuzestan Province, Iran. Journal of Environmental Health Science and Engineering. 19,585-601.

9. Soleimani A., Toolabi A., Mansour S.N., Abdolahnejad A, Akther T, Fouladi-Fard R., Miri M., Mohammadi A. 2024. Health risk assessment and spatial trend of metals in settled dust of surrounding areas of Lake Urmia, NW Iran. International Journal of Environmental Analytical Chemistry. 104(5),1172-85.

10. Khaksar M.R., Navaei-Nigjeh M., Daniali M., Rahimifard M., 2020. Multi-organ Toxicity Attenuation by Cerium Oxide and Yttrium Oxide Nanoparticles: Comparing the Beneficial Effects on Tissues Oxidative Damage Induced by Sub-Acute Exposure to Diazinon. Pharmaceutical Nanotechnology. 8, 1-14.

11. Pati D., Lorusso L.N., How to write a systematic review of the literature. HERD. 2018. Health Environments Research & Design Journal. 11(1),15-30.

12. Bommarito P.A., Martin E., Fry R.C., 2017. Effects of prenatal exposure to endocrine disruptors and toxic metals on the fetal epigenome. Epigenomics. 9(3), 333-50.

13. Gangopadhyay S., Sharma V., Chauhan A., Srivastava V., 2019. Potential facet for prenatal arsenic exposure paradigm: linking endocrine disruption and epigenetics. Nucleus. 62, 127–142 . https://doi.org/10.1007/s13237-019-00274-3

14. Freire C., Amaya E., Gil F., Murcia M., LLop S., Casas M., Vrijheid M., Lertxundi A., Irizar A., Fernández-Tardón G., Castro-Delgado R.V., 2019. Placental metal concentrations and birth outcomes: The Environment and Childhood (INMA) project. International Journal of Hygiene and Environmental Health. 222(3),468-78.

15. Bank-Nielsen P.I., Long M., Bonefeld-Jørgensen E.C., 2019. Pregnant inuit women's exposure to metals and association with fetal growth outcomes. Int J Environ Res Public Health. 16(7). http://www.ncbi.nlm.nih.gov/pubmed/30939809

16. Sabra S., Malmqvist E., Saborit A., Gratacós E., Gomez Roig M.D., 2017. Heavy metals exposure levels and their correlation with different clinical forms of fetal growth restriction. PLoSOne. 12(10),e0185645. http://www.ncbi.nlm.nih.gov/pubmed/28985223

17. Punshon T., Li Z., Jackson B.P., Parks W.T., Romano M., Conway D., 2020. Placental metal concentrations in relation to placental growth, efficiency and birth weight. Environ Int .126,533–42. http://www.ncbi.nlm.nih.gov/pubmed/30851484

18. Qia J., Laia Y., Lianga C., Yanc S., Huanga K., Panc W., Fenga L., Jianga L., Zhua P., Haoa J., Tonga S., 2019. Prenatal thallium exposure and poor growth in early childhood: A prospective birth cohort study. Environment International. 123, 224–230.

19. Vilahur N., Vahter M., Broberg K., 2015. The Epigenetic Effects of Prenatal Cadmium Exposure. Curr Envir Health Rpt. 2,195–203.

20. Bansa1 D.K., Awua A.K., Boatin R., Adom T., Brown-Appiah1 E.C., Amewosina K.K., Diaba A., Datoghe D., Okwabi W., 2017. Cross-sectional assessment of infants' exposure to toxic metals through breast milk in a prospective cohort study of mining communities in Ghana. BMC Public Health. 17, 505,1-12.

21. Pikounis T.D., Amann K.L., Jackson B.P., Punshon T., Gilbert-Diamond D., Korrick S., Karagas M.R., Cottingham K.L., 2024. Urinary biomarkers of exposure to toxic and essential elements: A comparison of infants fed with human milk or formula. Environmental Epidemiology. 8(1), e286

22. Palmieri J.R., Meacham S. Brunette J., Miluski T., Dhanju S., Stein S., 2019. Effects heavy metal and organic contaminants during pregnancy and lactation on child health. J Clin Case Rep Trials. 2, 26-34.

23. Mulware S.J., 2020. Toxicity of Heavy Metals, A. Subject in Review. International Journal of Recent Research in Physics and Chemical Sciences. 6(2), 30-43.

24. Al O., Ex F., R P., I B.M., I S., 2023. Heavy Metal Toxicity: A Potential Risk Factor for Autism. Journal of Experimental and Basic Medical Sciences.4(3),192-6.

25. Manfol F.P., Nantia E.A., Wang K., Moundipa P.F., Mathu P.P., 2014. Heavy Metal Induced Toxicity on Male Reproductive Function. Contemporary Topics in Life Sciences. 19,1-26.

26. Mobarak Y., 2008. Review of the developmental toxicity and teratogenicity of three environmental contaminants (cadmium, lead and mercury). Catrina: The International Journal of Environmental Sciences. 3(1),31-43.

27. Baser E., kırmızı D.A., Turksoy V.A., Onat T., Çaltekin M.D., Kara M., Yalvac E.S.,2020. Environmental Exposures in the Etiology of Abortion:

Placental Toxic and Trace Element Levels. Zeitschrift für Geburtshilfe und Neonatologie. 224(06), 339-347.

28. Dong X., Ding A., Hu H., Xu F., Liu L., Wu M., 2023. Placental barrier on cadmium transfer from mother to fetus in related to pregnancy complications. International Journal of Women's Health. 179-190.

29. Windham G., Fenster L., 2008. Environmental contaminants and pregnancy outcomes. Fertility and sterility. 89(2),e111-6.

30. Jaishankar M., Tseten T., Anbalagan N., Mathew B.B., Beeregowda K.N., 2014. Toxicity, mechanism and health effects of some heavy metals. Interdiscip Toxicol. 7(2), 60–72.

31. Magelsir H.M., 2016. Heavy metal toxicity-metabolism, absorption, distribution, excretion and mechanism of toxicity for each of the metals. World News of Natural Sciences. (4),20-32.

32. Egorova K.S., Ananikov V.P., 2017. Toxicity of metal compounds: knowledge and myths. Organometallics. 36(21),4071-90.

33. Srnovršnik T., Virant-Klun I., Pinter B., 2023. Heavy Metals and Essential Elements in Association with Oxidative Stress in Women with Polycystic Ovary Syndrome, A Systematic Review. Antioxidants. 12, 1398. https://doi.org/10.3390/antiox12071398

34. A. Antar S., Halouani A., Gad C., Al-Karmalawy A., 2024. An Overview of the Mechanisms of Cadmium-Induced Toxicity in the Male Reproductive System. Pharmaceutical Sciences. 30(1), 36-53.

35. Gómez-Roig M.D., Pascal R., Cahuana M.J., García-Algar O., Sebastiani G., Andreu-Fernández V., Martínez L., Rodríguez G., Iglesia I., Ortiz-Arrabal O., Mesa M.D., 2021. Environmental exposure during pregnancy: influence on prenatal development and early life: a comprehensive review. Fetal diagnosis and therapy. 48(4),245-57.

36. Guimarães M.T., Cunha M.G., Carvalho D.P., Ribeiro T.S., Martins L.C., Braga A.L., Pereira L.A., 2015. Influence of environmental contamination on pregnancy outcomes. Environmental Science and Pollution Research. 22, 14950-9.

37. Kamai E.M., McElrath T.F., Ferguson K.K., 2019. Fetal growth in environmental epidemiology: mechanisms, limitations, and a review of associations with biomarkers of non-persistent chemical exposures during pregnancy. Environmental Health. 18,1-30.