sciendo
10.2478/AMB-2025-00067

REVIEW

OXIDATIVE STRESS, DIETARY SUPPLEMENTATION AND HYPERTENSIVE DISORDERS IN PREGNANCY: A REVIEW

Z. Kirovakov

Department of Healthcare, Faculty for Public Health and Health care,
Prof. Dr. Assen Zlatarov University, Burgas – Bulgaria

Abstract. Objective. *To provide an understanding of the effects of oxidative stress and hypertensive disorders during pregnancy and the significance of dietary supplementation in addressing the related adverse outcomes and complications.* ***Methodology.*** *The review methodology was designed to provide a flexible but a comprehensive overview of pregnancy in terms of oxidative stress, hypertensive disorders and dietary supplementation through identification of applicable and relevant literature that was based on an inclusion and exclusion criteria that followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) framework for systematic reviews.* ***Findings.*** *Hypertensive disorders are a primary risk factor for adverse pregnancy outcomes, accounting for 14 percent of maternal mortality and occurring in up to 10 percent of all pregnancies. The mechanisms leading to oxidative stress during pregnancy can cause the excessive generation of highly reactive and unstable reactive oxygen species radicals, which can directly disrupt gestational processes such as oocyte maturation, luteolysis, and embryo implantation. Excessive production of reactive oxygen species can directly interfere with the placental membrane, which can disrupt the exchange of nutrients and oxygen between the mother and fetus, leading to poor embryo development and pregnancy complications. There is a direct association between imbalanced serum nutrient levels and adverse health outcomes during pregnancy, such as inflammation and dyslipidemia.* ***Conclusion.*** *The adverse pregnancy outcomes associated with genetic and biological risk factors, such as oxidative stress and hypertensive disorders, are preventable and manageable through proper hygienic conditions, appropriate lifestyle choices, and pharmacological and dietary interventions.*

Key words: *preeclampsia, intrauterine growth restriction, gestational diabetes mellitus, recurrent pregnancy loss, luteolysis*

Corresponding author: *Zlatko Kirovakov, Department of Midwifery care, Faculty of Health care, Medical University – Pleven 5800, Bulgaria, email: kirovakov@yahoo.com*

ORCID: *0009-0003-7643-5879*

Received: *03 December 2024;* ***Revised/Accepted:*** *21 May 2025*

INTRODUCTION

The fragility of pregnancy processes and related adverse outcomes that are attributed to biological and lifestyle etiological risk factors such as oxidative stress, poor dietary supplementation, and hypertensive disorders has become a significant area of interest in gestational scientific research. Specifically, there is an increased interest in research on the role of maternal genetics in the development of pregnancy-related complications with concerns on both maternal and fetal health concerning conditions which arise from the complex interactions between genetic factors, environmental influences and lifestyle choices [1]. Existing literature indicate that the largest proportion of maternal complications develop during the pregnancy with those that can lead to mortality being associated with biological processes that are caused by chronic conditions such as hypertensive disorders of pregnancy including gestational hypertension, preeclampsia and eclampsia, as well as other chronic diseases such as diabetes and vascular diseases [2, 3]. Hypertensive disorders have been cited as a primary risk factor for adverse pregnancy outcomes, accounting for 14 percent of maternal mortality and occurring in up to 10 percent of all pregnancies [4]. Also, apart from the adverse outcomes, gestational hypertensive disorders can be an underlying risk factor for future metabolic and cardiovascular adverse conditions for both the mother and the newborn, which can further cause other complications such as abdominal obesity, insulin resistance and impaired metabolic processes [5, 6]. An understanding of the direct gestational effects of hypertensive disorders and related biological risk factors, such as oxidative stress and dietary supplementation, can be important in the formulation of preventive strategies and treatment techniques for management of intergenerational pathological consequences of the related complications.

In pregnancy, oxidative stress has been implicated as a primary pathophysiological risk factor for adverse outcomes ranging from miscarriage, maternal vascular diseases, to pre-term labour. From a biological standpoint, oxidative stress is defined as the imbalance between free radicals, including the reactive oxygen species (ROS) and reactive nitrogen species (RNS), and the cellular antioxidant capacity, which leads to a compromised bodily anti-oxidation system that can cause cellular toxicity and macromolecular oxidative damage [7, 8]. The mechanisms leading to oxidative stress during pregnancy can cause the excessive generation of highly reactive and unstable reactive oxygen species (ROS) radicals, which can directly disrupt gestational processes such as oocyte maturation, luteolysis, and embryo implantation [9, 10].

It is worth noting that pregnant women are highly susceptible to oxidative stress as a result of the systematic inflammatory bodily responses attributed to pregnancy-related biological process and the amplification of the condition can directly contribute reproductive failure and adverse pregnancy outcomes and complications such as recurrent pregnancy loss, intrauterine growth restriction, and even maternal mortality [11]. Indeed, the adverse pregnancy outcomes associated with genetic and biological risk factors such as oxidative stress and hypertensive disorders are preventable and manageable through proper hygienic conditions, appropriate lifestyle choices, and pharmacological and dietary interventions [12, 13]. In the recent past, there has been increased interest in the significance of dietary supplementation in pregnancy and its influences on the mother's health and the developmental processes of the fetus. The present review provides a scientific analysis of existing literature on dietary supplementation, oxidative stress and hypertensive disorders in pregnancy to inform on effective preventive strategies and treatment techniques for the related adverse outcomes.

METHODOLOGY

The present review aims to provide an understanding of the effects of oxidative stress and hypertensive disorders during pregnancy and the significance of dietary supplementation in addressing the related adverse outcomes and complications. Considering the broader scientific scope of the topic, the review methodology is designed to provide a flexible but a comprehensive overview of pregnancy in terms of oxidative stress, hypertensive disorders and dietary supplementation through identification of applicable and relevant literature that was based on an inclusion criteria and explored using the Boolean operator "OR" and "AND". A flexible but structured search strategy was based on the inclusion and exclusion criteria, which was guided by specific keywords including "oxidative stress", "hypertensive disorders", "dietary supplementation", "preeclampsia", "intrauterine growth restriction", "gestational diabetes", and "recurrent pregnancy loss". It is important to note that there were other related keywords that were used during the search process, considering the wider scope of the topic of the research and also, two or more of the keywords were combined to narrow down to the specific articles of interest.

The primary focus of the inclusion criteria was scientific articles and research papers that focused on

the research topic and were published within the past five years, between 2019 and 2024, and written in English. The included articles and research papers were required to focus on the research topic, as well as its implications for practice and future research directions. Any additional articles that met the inclusion criterion and could not be identified through database searches were identified through cross-referencing and hand searches of the reference lists of the included articles. The screening of the selected articles started with the removal of duplicate articles that might have been present in more than one database. The suitability of the remaining articles was confirmed through a second application of the inclusion and exclusion criteria. An independent review was then performed to create the final list of studies that met the review objectives. After selecting the appropriate and relevant studies, specific facets of information associated with the variables of interest in the review were extracted.

DISCUSSION

The review findings highlight a wide range of adverse pregnancy outcomes that are directly attributed to the biological mechanisms of oxidative stress and hypertensive disorders, and their disruptive effects on gestational and reproductive processes. First, an included review article highlights the biological effect of reactive oxygen species (ROS) on reproductive processes including maturation of oocytes, development of the embryo, luteolysis, and fertility, as well as disruption of the reproductive functions of different female systems such as ovaries, fallopian tubes, and embryos [14]. Different studies further report an association between oxidative stress and gestational problems that are directly related to placental pathology. It is reported that excessive production of ROS can directly interfere with the placental membrane, disrupting the exchange of nutrients and oxygen between the mother and the fetus, which can lead to poor embryo development and pregnancy complications [15, 16]. The findings further indicate a correlation between the quantity of free radicals and the occurrence of gestational diabetes mellitus (GDM), where women with the condition produce more free radicals compared to those without [17]. On the same note, women with GDM have been found to release 8-isoprostane at a higher rate compared to those without the condition, which highlights a positive correlation with plasma glucose and suggests a link between glycemic control and lipid peroxidation [18, 19]. Surprisingly, the findings indicate reduced placental sensitivity to oxidative stress among women with GDM, attributed to the accumulation of antioxidants in the placenta emanating from the effects of oxidative stress experienced by the developing fetus, which offers cellular protection against lipid peroxidation.

A large proportion of research studies identified hypertensive disorders as being a primary factor that hinders normal cardiovascular functioning during pregnancy. It is reported that hypertensive disorders are directly associated with maternal hemodynamic alterations, which are a consequence of pre-existing maternal cardiovascular adverse conditions or as a result of significant changes in gestational cardiovascular load [20]. The changes of the gestational cardiovascular load dictate the severity of the adverse pregnancy outcomes, which often show from the first trimester but can be detected before the appearance of the clinical symptoms [21, 22]. Further, the findings highlight the persistence of the hemodynamic alterations, which can predispose the woman to long-term cardiovascular conditions and adverse pregnancy outcomes [23]. In comparison with normotensive pregnancy, it is reported that hypertensive-related pregnancies are characterized by adverse outcomes such as a high ventricular mass, increased systemic vascular resistance (SVR) and concentric hypertrophy [24-26]. The findings further show reduced intravascular volume expansion for mothers with hypertensive disorders, even though there was conflicting evidence on cardiovascular changes associated with gestational hypertension [27, 28]. On the same note, hypertensive disorders were directly linked with preeclampsia, which was characterized by reduced stroke volume, myocardial performance index, and cardiac dysfunction, which was reported in almost half of mothers with preeclampsia [29]. The findings further demonstrate increased cardiovascular dysfunction in pregnant women with preeclampsia as compared to those with gestational hypertension, with changes being more pronounced at the early stages of both conditions [30]. The findings highlight the need for early identification of women with underlying and clinically inactive cardiovascular risk factors for the development of preventive and therapeutic interventions to reduce the effects of adverse pregnancy outcomes.

Dietary supplementation is one of the effective preventive strategies and therapeutic interventions that can be used to address adverse pregnancy effects caused by the genetic, biological, environmental and lifestyle factors. The review findings note that adequate nutrition is a crucial component of healthcare for maternal and fetal health during pregnancy, considering that pregnant women are susceptible to nutritional deficiencies caused by increased nutrient needs for fetal growth and development, as well as maternal metabolic changes attributed to the devel-

opment of tissues [31, 32]. It is reported that dietary supplementation during pregnancy has a significant influence on the health outcomes of both the mother and the fetus, considering that the growth and development of the latter are dependent on the mother [33]. According to the research findings, an unbalanced diet is a primary risk factor for the development of cardiovascular conditions such as GDM and, therefore, plays a pathophysiological role in the development of gestational hypertensive disorders [34, 35]. Also, the findings show a direct association between imbalanced nutrient serum levels and adverse health outcomes during pregnancy, such as inflammation and dyslipidemia [36]. Further, the findings indicate a correlation between poor nutrient status of a pregnant mother in terms of low levels of magnesium, zinc, and vitamins with increased risk for preeclampsia [37, 38]. On the same note, high serum triglycerides and fatty acids and reduced calcium intake, which are signs of poor nutritional status, have also been associated with increased risk for preeclampsia and other related adverse pregnancy outcomes [39]. The review findings recommend ideal nutrient and dietary supplementation as effective preventive strategies for pregnancy-related complications, as well as improvements in fetal growth and development.

The findings identify different dietary supplements and highlight their role in improving pregnancy outcomes for pregnant mothers who might face complications during the gestational period. According to the findings, L-arginine can be an important dietary supplement that can act as a substrate for the production of nitric oxide (NO) and is a potent endothelium-derived vasodilator that plays a crucial role in maintaining the endothelial adaptive regulatory mechanisms for vasodilatation in healthy pregnancy. As a gestational supplement, L-arginine reduces the risk of preeclampsia by improving the levels of plasma nitric oxide, which enhances vascular function and increases fetal birth weight while also reducing adverse birth outcomes and enhancing epigenetic reprogramming effects of the fetus [40]. L-citrulline, a metabolite of L-arginine, was identified as another dietary supplement that is responsible for increased nitric oxide production and improved vascular function while reducing hypertensive disorder risk factors such as blood pressure and placental fibrosis, and the risk of preeclampsia [41]. The findings indicate that L-citrulline is more biologically available as compared to L-arginine, which highlights its ease of access and applicability in gestational processes [42]. Also, L-citrulline was found to promote fetal growth and protein synthesis while also reducing the risk of fetal renal dysfunction and improving long-term anti-hypertensive and epigenetic effects [2]. The review further identifies other gestational dietary supplements, such as calcium, vitamins D, C, and E, all of which play crucial roles in promoting healthy pregnancy outcomes by reducing the incidence of preeclampsia, reducing placental inflammation, improving calcium metabolism, and enhancing uterine artery blood flow. The dietary supplements are also cited as playing a crucial role in offspring reprogramming effects, such as blood pressure modulation, controlling changes in DNA methylation, and reducing the risk of renal dysfunction.

CONCLUSION

The present review focused on providing a scientific understanding of the effects of oxidative stress and hypertensive disorders on pregnancy outcomes and the significance of dietary supplementation in addressing the nutritional deficiencies that might further exacerbate the pre-existing adverse conditions and outcomes. The review shows that the largest proportion of maternal complications develop during pregnancy, with those that can lead to mortality being associated with biological processes that are caused by chronic conditions, including hypertensive disorders of pregnancy and oxidative stress. The mechanisms leading to oxidative stress during pregnancy can cause the excessive generation of highly reactive and unstable reactive oxygen species (ROS) radicals, which can directly disrupt gestational processes such as oocyte maturation, luteolysis, and embryo implantation. Pregnant women are highly susceptible to oxidative stress as a result of the systemic inflammatory bodily responses attributed to pregnancy-related biological processes, and the amplification of the condition can directly contribute to reproductive failure and adverse pregnancy outcomes. However, the adverse pregnancy outcomes associated with genetic and biological risk factors such as oxidative stress and hypertensive disorders are preventable and manageable through proper hygienic conditions, appropriate lifestyle choices, and pharmacological and dietary interventions.

Conflict of Interest Statement: *The author declares no conflicts of interest related to this work.*

Funding: *The author did not receive any financial support from any organization for this research work.*

Ethical statement: *This study has been performed in accordance with the ethical standards as laid down in the Declaration of Helsinki.*

REFERENCES

1. Kirovakov Z, Konova E, Hinkova N, Markova S. Algorithm for Prevention of Recurrent Pregnancy Loss and Adverse Pregnancy Outcomes in Patient with Inherited Thrombophilia. International Journal of Medical Science and Clinical Invention [Internet]. 2024 Aug 21;11(08):7226–35. Available from: https://doi.org/10.18535/ijmsci/v11i8.02
2. Man AWC, Zhou Y, Xia N, Li H. Dietary supplements and vascular function in hypertensive disorders of pregnancy. Pflugers Arch. 2023 Jul;475(7):889-905. doi: 10.1007/s00424-023-02810-2
3. Gliozheni O, Gliozheni E. Some solutions to reduce maternal mortality. Donald School Journal of Ultrasound in Obstetrics & Gynecology [Internet]. 2018 Dec 1;14(1):56–60. Available from: https://doi.org/10.5005/jp-journals-10009-1615.
4. Khedagi AM, Bello NA. Hypertensive Disorders of Pregnancy. Cardiol Clin. 2021 Feb;39(1):77-90. doi: 10.1016/j.ccl.2020.09.005.
5. Wang Z, Chen J, Zhu L, Jiao S, Chen Y, Sun Y. Metabolic disorders and risk of cardiovascular diseases: a two-sample mendelian randomization study. BMC Cardiovasc Disord. 2023 Oct 31;23(1):529. doi: 10.1186/s12872-023-03567-3.
6. Poon LC, Nguyen-Hoang L, Smith GN, et al. Hypertensive disorders of pregnancy and long-term cardiovascular health: FIGO Best Practice Advice. International Journal of Gynecology & Obstetrics. 2023 Jan 1;160(S1):22–34. doi.org/10.1002/ijgo.14540
7. T. Hussain et al., "The Role of Oxidative Stress and Antioxidant Balance in Pregnancy," Mediators of Inflammation, vol. 2021, pp. 1–11, Sep. 2021, doi: 10.1155/2021/9962860.
8. Chiarello DI, Abad C, Rojas D, Toledo F, Vázquez CM, Mate A, Sobrevia L, Marín R. Oxidative stress: Normal pregnancy versus preeclampsia. Biochim Biophys Acta Mol Basis Dis. 2020 Feb 1;1866(2):165354. doi: 10.1016/j.bbadis.2018.12.005.
9. Duhig K, Chappell LC, Shennan AH. Oxidative stress in pregnancy and reproduction. Obstet Med. 2016 Sep;9(3):113-6. doi: 10.1177/1753495X16648495.
10. Pham C, Thomson S, Chin ST, et al; Barwon Infant Study Investigator Group. Maternal oxidative stress during pregnancy associated with emotional and behavioural problems in early childhood: implications for foetal programming. Mol Psychiatry. 2023 Sep;28(9):3760-3768. doi: 10.1038/s41380-023-02284-9.
11. Grzeszczak K, Łanocha-Arendarczyk N, Malinowski W, et al. Oxidative Stress in Pregnancy. Biomolecules. 2023 Dec 9;13(12):1768. doi: 10.3390/biom13121768.
12. Parikh NI, Gonzalez JM, Anderson CAM, et al; Council on Cardiovascular and Stroke Nursing; and the Stroke Council. Adverse Pregnancy Outcomes and Cardiovascular Disease Risk: Unique Opportunities for Cardiovascular Disease Prevention in Women: A Scientific Statement From the American Heart Association. Circulation. 2021 May 4;143(18):e902-e916. doi: 10.1161/CIR.0000000000000961.
13. Phoswa WN, Khaliq OP. The Role of Oxidative Stress in Hypertensive Disorders of Pregnancy (Preeclampsia, Gestational Hypertension) and Metabolic Disorder of Pregnancy (Gestational Diabetes Mellitus). Oxid Med Cell Longev. 2021 May 31;2021:5581570. doi: 10.1155/2021/5581570.
14. Kaltsas A. et al., The Silent Threat to Women's Fertility: Uncovering the Devastating Effects of Oxidative Stress. Antioxidants, 2023;12(8),1490. doi: 10.3390/antiox12081490.
15. Guerby P, Tasta O, Swiader A, et al. Role of oxidative stress in the dysfunction of the placental endothelial nitric oxide synthase in preeclampsia. Redox Biol. 2021 Apr;40:101861. doi: 10.1016/j.redox.2021.101861.
16. Garcia V, Sessa WC. Endothelial NOS: perspective and recent developments. Br J Pharmacol. 2019 Jan;176(2):189-196. doi: 10.1111/bph.14522.
17. Lyu Y, Wang G, Sun Z, et al. The association of maternal fat-soluble antioxidants in early pregnancy with gestational diabetes mellitus: a prospective cohort study. Nutr Diabetes. 2022 Dec 9;12(1):49. doi: 10.1038/s41387-022-00227-x.
18. Saucedo R, Ortega-Camarillo C, Ferreira-Hermosillo A, et al. Role of Oxidative Stress and Inflammation in Gestational Diabetes Mellitus. Antioxidants (Basel). 2023 Sep 29;12(10):1812. doi: 10.3390/antiox12101812.
19. Daneshzad E, Tehrani H, Bellissimo N, Azadbakht L. Dietary Total Antioxidant Capacity and Gestational Diabetes Mellitus: A Case-Control Study. Oxid Med Cell Longev. 2020 Oct 8;2020:5471316. doi: 10.1155/2020/5471316.
20. Giorgione V, O'Driscoll J, Coutinho CM, et al. Peripartum echocardiographic changes in women with hypertensive disorders of pregnancy. Ultrasound Obstet Gynecol. 2022 Mar;59(3):365-370. doi: 10.1002/uog.23745.
21. Mulder EG, de Haas S, Mohseni Z, et al. Cardiac output and peripheral vascular resistance during normotensive and hypertensive pregnancy – a systematic review and meta-analysis. BJOG. 2022 Apr;129(5):696-707. doi: 10.1111/1471-0528.16678
22. Ling HZ, Guy GP, Bisquera A, et al. Maternal hemodynamics in screen-positive and screen-negative women of the ASPRE trial. Ultrasound Obstet Gynecol. 2019 Jul;54(1):51-57. doi: 10.1002/uog.20125.
23. Reddy M, Wright L, Rolnik DL, et al. Evaluation of Cardiac Function in Women With a History of Preeclampsia: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2019 Nov 19;8(22):e013545. doi: 10.1161/JAHA.119.013545.
24. Countouris ME, Villanueva FS, Berlacher KL, et al. M. Association of Hypertensive Disorders of Pregnancy With Left Ventricular Remodeling Later in Life. J Am Coll Cardiol. 2021 Mar 2;77(8):1057-1068. doi: 10.1016/j.jacc.2020.12.051.
25. Eghan P, Folson AA, Donkor A, et al. Relationship between hypertensive disorders of pregnancy (HDP) and cardiac remodeling during pregnancy: Systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2024 Jul;298:108-115. doi: 10.1016/j.ejogrb.2024.05.003.
26. Garcia-Gonzalez C, Nunez E, Zhang H, et al. Maternal and Offspring Cardiovascular Function following Pregnancy with Hypertensive Disorder. Diagnostics (Basel). 2023 Jun 8;13(12):2007. doi: 10.3390/diagnostics13122007.
27. Giorgione V, Ridder A, Kalafat E, et al. Incidence of postpartum hypertension within 2 years of a pregnancy complicated by pre-eclampsia: a systematic review and meta-analysis. BJOG. 2021 Feb;128(3):495-503. doi: 10.1111/1471-0528.16545. Epub 2020 Oct 21.
28. Malek AM, Wilson DA, Turan TN, et al. Maternal Coronary Heart Disease, Stroke, and Mortality Within 1, 3, and 5 Years of Delivery Among Women With Hypertensive Disorders of Pregnancy and Pre-Pregnancy Hypertension. J Am Heart Assoc. 2021 Feb;10(5):e018155. doi: 10.1161/JAHA.120.018155.
29. Dall'Asta A, D'Antonio F, Saccone G, et al. Cardiovascular events following pregnancy complicated by pre-eclampsia with emphasis on comparison between early- and late-onset forms: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2021 May;57(5):698-709. doi: 10.1002/uog.22107.

30. Zhao G, Bhatia D, Jung F, Lipscombe L. Risk of type 2 diabetes mellitus in women with prior hypertensive disorders of pregnancy: a systematic review and meta-analysis. Diabetologia. 2021 Mar;64(3):491-503. doi: 10.1007/s00125-020-05343-w.
31. Marshall NE, Abrams B, Barbour LA, et al. The importance of nutrition in pregnancy and lactation: lifelong consequences. Am J Obstet Gynecol. 2022 May;226(5):607-632. doi: 10.1016/j.ajog.2021.12.035.
32. Parrettini S, Caroli A, Torlone E. Nutrition and Metabolic Adaptations in Physiological and Complicated Pregnancy: Focus on Obesity and Gestational Diabetes. Front Endocrinol (Lausanne). 2020 Nov 30;11:611929. doi: 10.3389/fendo.2020.611929.
33. Qin Y, Xie L. Nutrition and Supplements during Pregnancy: A Vital Component in Building the Health and Well-Being of Both the Mother and the Developing Baby. Nutrients. 2023 Jul 31;15(15):3395. doi: 10.3390/nu15153395.
34. Ciulei MA, Smith ER, Perumal N, et al. Nutritious Supplemental Foods for Pregnant Women from Food Insecure Settings: Types, Nutritional Composition, and Relationships to Health Outcomes. Curr Dev Nutr. 2023 Apr 28;7(6):100094. doi: 10.1016/j.cdnut.2023.100094.
35. Koivuniemi E, Hart K, Mazanowska N, et al. Food Supplement Use Differs from the Recommendations in Pregnant Women: A Multinational Survey. Nutrients. 2022 Jul 15;14(14):2909. doi: 10.3390/nu14142909.
36. Dingena CF, Arofikina D, Campbell MD, et al. Nutritional and Exercise-Focused Lifestyle Interventions and Glycemic Control in Women with Diabetes in Pregnancy: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. Nutrients. 2023 Jan 9;15(2):323. doi: 10.3390/nu15020323.
37. Broś-Konopielko M, Białek A, Johne M, Czajkowski K. Increased LC PUFA Levels in the Serum of Pregnant Women and Their Children as a Result of Dietary Supplementation with 'Omega' Fatty Acids. Nutrients. 2023 Jan 2;15(1):231. doi: 10.3390/nu15010231.
38. Peng H, Xu H, Wu J, et al. Maternal high-fat diet disrupted one-carbon metabolism in offspring, contributing to nonalcoholic fatty liver disease. Liver Int. 2021 Jun;41(6):1305-1319. doi: 10.1111/liv.14811.
39. Lassi ZS, Padhani ZA, Rabbani A, et al. Effects of nutritional interventions during pregnancy on birth, child health and development outcomes: A systematic review of evidence from low- and middle-income countries. Campbell Syst Rev. 2021 Jun 21;17(2):e1150. doi: 10.1002/cl2.1150.
40. Weckman AM, McDonald CR, Baxter JB, et al. Perspective: L-arginine and L-citrulline Supplementation in Pregnancy: A Potential Strategy to Improve Birth Outcomes in Low-Resource Settings. Adv Nutr. 2019 Sep 1;10(5):765-777. doi: 10.1093/advances/nmz015.
41. Ortiz-Cerda T, Mosso C, Alcudia A, et al. Pathophysiology of Preeclampsia and L-Arginine/L-Citrulline Supplementation as a Potential Strategy to Improve Birth Outcomes. Adv Exp Med Biol. 2023;1428:127-148. doi: 10.1007/978-3-031-32554-0_6.
42. Man AWC, Zhou Y, Lam UDP, et al. l-Citrulline ameliorates pathophysiology in a rat model of superimposed preeclampsia. Br J Pharmacol. 2022 Jun;179(12):3007-3023. doi: 10.1111/bph.15783.