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Review Article

Antioxidants and Pregnancy Complications: Exploring Therapeutic Strategies for Better Outcomes

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Abstract

Pregnancy complications present significant challenges, impacting maternal health and fetal development. Oxidative stress, a key contributor to various pregnancy-related disorders such as preeclampsia, gestational diabetes mellitus (GDM), and preterm birth, has spurred interest in exploring antioxidant interventions. Antioxidants, known for their ability to counteract oxidative damage, have emerged as potential therapeutic agents to mitigate these complications. This paper synthesizes current knowledge on the role of antioxidants in pregnancy, elucidating their mechanisms of action, sources, and impact on oxidative stress-related complications. It examines diverse antioxidant compounds, including vitamins C and E, selenium, and natural phytochemicals, highlighting their potential to modulate oxidative stress pathways and promote maternal-fetal well-being. Furthermore, this paper critically analyzes clinical studies, meta-analyses, and preclinical research exploring the efficacy and safety of antioxidant supplementation during pregnancy. It discusses the complexities surrounding optimal dosages, timing, and formulations of antioxidants, aiming to delineate strategies for their integration into prenatal care. In conclusion, this review provides insights into the promising role of antioxidants as therapeutic strategies to alleviate pregnancy complications associated with oxidative stress. It highlights avenues for future research, advocating for a deeper understanding of antioxidant mechanisms and their optimal utilization in prenatal care to enhance maternal and fetal health outcomes.

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Introduction

Pregnancy complications pose significant risks to both maternal and fetal health, contributing to adverse outcomes and necessitating intensive medical care. Oxidative stress, characterized by an imbalance between free radicals and antioxidants, has been implicated in the pathophysiology of several pregnancy-related disorders. Elevated oxidative stress levels are associated with conditions such as preeclampsia, gestational diabetes mellitus (GDM), intrauterine growth restriction (IUGR), and preterm birth [1-10]. Antioxidants, including vitamins C and E, selenium, and various phytochemicals, play a pivotal role in neutralizing free radicals, thereby mitigating oxidative damage. Their potential to modulate oxidative stress pathways has prompted investigations into their use as therapeutic interventions to prevent or ameliorate pregnancy complications. Understanding the mechanisms of antioxidants and their impact on maternal health, fetal development, and pregnancy outcomes is crucial in elucidating their therapeutic potentiall [11-25]. This paper aims to provide a comprehensive analysis of the role of antioxidants in pregnancy, exploring their sources, mechanisms of action, and implications in combating oxidative stress-related complications.

Oxidative stress in pregnancy complications

Oxidative stress, a physiological imbalance between the production of reactive oxygen species (ROS) and the ability of antioxidants to neutralize them, has been implicated in various pregnancy complications [26]. One of the most studied conditions associated with pregnancy, preeclampsia, involves increased oxidative stress [27,28]. Elevated levels of ROS and reduced antioxidant capacity contribute to endothelial dysfunction, leading to hypertension, proteinuria, and placental abnormalities. The placenta, central to preeclampsia pathophysiology, generates excess ROS, triggering systemic inflammation and endothelial damage [29-33].

Oxidative stress is implicated in the development of insulin resistance and pancreatic β-cell dysfunction observed in Gestational Diabetes Mellitus (GDM) [34]. Increased ROS production impairs insulin signaling pathways, exacerbates inflammation, and contributes to abnormal glucose metabolism. This oxidative imbalance affects

maternal glucose tolerance, influencing fetal growth and development. Oxidative stress disrupts the delicate balance between placental oxygenation and fetal demands, leading to adverse outcomes like preterm birth and Intrauterine Growth Restriction (IUGR). Placental insufficiency due to increased oxidative damage impairs nutrient and oxygen transport, compromising fetal growth and development [35]. The placenta is particularly susceptible to oxidative stress due to its high metabolic rate and exposure to oxygen. Oxidative damage to the placenta can result in alterations in its structure and function, affecting nutrient exchange and hormone production critical for a healthy pregnancy [36-40]. Oxidative stress induces systemic inflammation and compromises endothelial function. Inflammation triggers a cascade of events leading to vasoconstriction, vascular permeability, and thrombosis, all of which contribute to the pathogenesis of various pregnancy complications.

Oxidative stress during pregnancy may also have implications beyond the immediate complications, affecting fetal programming and influencing the long-term health of offspring. Epigenetic modifications due to oxidative stress exposure in utero might predispose offspring to metabolic, cardiovascular, and neurodevelopmental disorders later in life [41-46].

Role of antioxidants in pregnancy

Antioxidants play a crucial role in pregnancy by counteracting the harmful effects of oxidative stress, thereby contributing to maternal health and fetal development. Antioxidants, including vitamins (such as C and E), minerals (like selenium), and various phytochemicals (e.g., flavonoids, and polyphenols), act as scavengers of free radicals. They neutralize reactive oxygen species (ROS) and reactive nitrogen species (RNS), preventing oxidative damage to cells, tissues, and DNA [12].

During pregnancy, the maternal body experiences increased metabolic demands, making it more susceptible to oxidative stress. Antioxidants help maintain the balance by protecting maternal tissues, including the vascular system, placenta, and other organs, from oxidative damage. This protection contributes to better overall maternal health and well-being [47-51]. The placenta, essential for fetal development, is susceptible to oxidative stress due to its high metabolic activity and exposure to oxygen. Antioxidants support placental function by reducing oxidative damage, ensuring proper nutrient transport, and hormone production, and maintaining an optimal environment for fetal growth. Antioxidants have a role in promoting healthy fetal development. By protecting against oxidative stress-induced damage to fetal tissues, antioxidants support organogenesis, reduce the risk of developmental abnormalities, and contribute to optimal growth and maturation of the fetus.

Antioxidants possess anti-inflammatory properties, which are beneficial during pregnancy. By reducing inflammation associated with oxidative stress, antioxidants help in controlling excessive immune responses and mitigating the risk of inflammatory complications that could affect maternal-fetal health [52-55]. Antioxidants modulate redox signaling pathways, which are crucial for cellular function and adaptation to stress. Proper regulation of these pathways by antioxidants ensures that oxidative stress levels remain within a healthy range, facilitating essential physiological processes without causing cellular damage. Oxidative stress can compromise the immune system, making pregnant individuals more susceptible to infections and other complications. Antioxidants bolster the immune system, aiding in its proper function and reducing the risk of infections during pregnancy. Antioxidant exposure during pregnancy may have implications for the long-term health of the offspring, potentially influencing their susceptibility to certain diseases later in life by modulating oxidative stress-related mechanisms and gene expression.

Mechanisms of antioxidants in pregnancy

The mechanisms by which antioxidants operate during pregnancy involve their ability to counteract oxidative stress and its detrimental effects. Antioxidants neutralize reactive oxygen species (ROS) and reactive nitrogen species (RNS), including superoxide radicals, hydroxyl radicals, and peroxynitrite, by donating electrons or hydrogen atoms. This process prevents these radicals from damaging cellular structures and DNA [56]. Antioxidants support and enhance the activity of endogenous enzymatic antioxidants within cells. For instance, vitamins C and E regenerate other antioxidants like glutathione, a critical cellular antioxidant, further bolstering the body's defense against oxidative stress [13].

Antioxidants, particularly vitamin E, prevent lipid peroxidation, a process where free radicals attack and damage lipids in cell membranes. By inhibiting lipid peroxidation, antioxidants help maintain the integrity of cell membranes and protect against cellular damage. Antioxidants can modulate redox-sensitive signaling pathways, such as NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) and Nrf2 (nuclear factor erythroid 2-related factor 2). These pathways regulate gene expression, inflammation, and antioxidant defense mechanisms in response to oxidative stress [57]. Mitochondria, as the primary site of cellular energy production, are vulnerable to oxidative damage. Antioxidants help preserve mitochondrial function by scavenging ROS, thereby maintaining cellular energy production and preventing cellular dysfunction. Oxidative stress can trigger inflammatory responses. Antioxidants mitigate inflammation by modulating cytokine production, reducing the expression of inflammatory mediators, and suppressing pro-inflammatory signaling pathways.

Antioxidants contribute to maintaining a healthy placenta

by protecting against oxidative stress-induced damage. They aid in preserving placental blood flow, nutrient transport, and hormone production, which are crucial for fetal growth and development [58-63]. Antioxidants play a role in reducing oxidative damage to DNA. By preventing DNA mutations and strand breaks caused by oxidative stress, antioxidants help safeguard the genetic integrity of maternal and fetal cells. Antioxidants maintain a delicate balance between oxidants and antioxidants in cells and tissues. By preventing excessive accumulation of ROS, antioxidants help maintain physiological redox homeostasis, ensuring that oxidative stress levels remain within a healthy range.

Clinical evidence of antioxidant supplementation

Clinical evidence regarding the supplementation of antioxidants during pregnancy is varied and complex. While some studies suggest potential benefits, others show conflicting or inconclusive results. Some clinical trials have explored the effects of vitamin C and E supplementation on reducing the risk of preeclampsia. However, results have been mixed, with some studies showing a potential reduction in preeclampsia risk, while others report no significant effects [12]. Selenium, an essential trace mineral with antioxidant properties, has been studied for its potential role in pregnancy complications. Clinical trials investigating selenium supplementation in reducing the risk of preeclampsia or improving fetal growth have yielded conflicting results, with some studies showing no significant benefits.

Research has also explored the effects of other antioxidants, such as beta-carotene, zinc, and multivitamin supplements, in pregnancy. While some studies suggest potential benefits in reducing the risk of preterm birth or improving birth outcomes, the evidence remains inconclusive or contradictory across different trials [13,64]. Methodological differences, variations in dosages, timing of supplementation, and populations studied contribute to the inconsistencies in clinical evidence. Variability in the types and formulations of antioxidants, as well as the heterogeneity of study populations, makes it challenging to draw definitive conclusions. Safety aspects of antioxidant supplementation during pregnancy also warrant attention. High doses of certain antioxidants may have adverse effects or interact with other medications, potentially posing risks to maternal and fetal health. There is a recognized need for well-designed, large-scale randomized controlled trials (RCTs) to comprehensively evaluate the safety and efficacy of antioxidant supplementation during pregnancy. Addressing methodological issues and standardizing protocols across studies could provide clearer insights into the potential benefits and risks of antioxidants in pregnancy. While some studies suggest a possible role for antioxidants in mitigating oxidative stress-related complications during pregnancy, the overall clinical evidence remains inconclusive. Further research is essential to elucidate the optimal dosages, specific antioxidant formulations, and timing of supplementation that may offer potential benefits while ensuring maternal and fetal safety. In clinical practice, careful consideration and individualized approaches are crucial when considering antioxidant supplementation during pregnancy due to the complexities and uncertainties surrounding their effects.

Challenges and considerations

Determining the appropriate dosages and specific formulations of antioxidants for pregnancy remains a challenge. Variability in absorption rates, interactions with other nutrients or medications, and potential pro-oxidant effects at high doses necessitate careful consideration in establishing safe and effective dosing regimens. Identifying the optimal timing for antioxidant supplementation during pregnancy is crucial. Early gestation may be a critical period for fetal development, yet late supplementation might offer benefits in reducing the risk of complications like preeclampsia. Determining the windows of opportunity for maximum efficacy is challenging.

Pregnant individuals differ in their nutritional status, lifestyle factors, underlying health conditions, and genetic predispositions. This heterogeneity makes it challenging to generalize the effects of antioxidants across diverse populations, requiring tailored approaches to address individual needs. While antioxidants are generally considered safe, high doses or prolonged supplementation may carry risks. Some antioxidants, when taken in excess, could potentially have adverse effects, interact with medications, or disrupt physiological processes. Ensuring the safety of both maternal and fetal health is paramount. Inconsistencies in study designs, variations in antioxidant types and doses, and differences in outcome measurements contribute to conflicting evidence. Methodological disparities across studies make it challenging to draw definitive conclusions regarding the efficacy of antioxidant supplementation in pregnancy.

The intricate mechanisms of oxidative stress in pregnancy, including redox signaling pathways and the delicate balance between pro-oxidants and antioxidants, pose challenges in understanding the precise roles and interactions of antioxidants within these systems. Implementing large-scale randomized controlled trials (RCTs) to assess antioxidant supplementation's effects in pregnancy may pose ethical challenges, particularly if potential risks or benefits are uncertain. Balancing the need for scientific evidence with ethical considerations is essential. In clinical practice, cautious consideration of individual patient characteristics, risk-benefit assessments, and informed discussions with pregnant individuals is crucial before initiating antioxidant supplementation, ensuring the promotion of maternal-fetal health without compromising safety.

Future directions and recommendations

Future directions and recommendations in the realm of

antioxidants and pregnancy involve addressing key research gaps and guiding the application of antioxidants for better maternal and fetal outcomes. Large-scale, well-controlled randomized controlled trials (RCTs) are essential to provide robust evidence on the safety, efficacy, and optimal dosages of antioxidants in pregnancy. Studies should consider diverse populations, varying gestational periods, and specific pregnancy complications to generate conclusive data. Longitudinal studies tracking the long-term health outcomes of offspring exposed to antioxidant supplementation in utero are crucial. These studies can provide insights into potential effects on offspring development, disease susceptibility, and overall health later in life. Further research into the intricate mechanisms underlying oxidative stress and the actions of antioxidants in pregnancy is necessary. Understanding redox signaling pathways, interactions with cellular processes, and the impact on placental function can inform targeted interventions.

Develop personalized approaches considering individual maternal factors, such as genetics, nutritional status, and existing health conditions. Tailoring antioxidant interventions based on individual needs may enhance efficacy and minimize potential risks. Investigate the synergistic effects of combining different antioxidants or integrating antioxidant-rich diets with supplementation. Examining potential interactions among antioxidants and their cumulative effects may offer novel approaches for enhancing maternal and fetal health. Investigate the impact of maternal diet and lifestyle modifications rich in natural antioxidants on pregnancy outcomes. Studying dietary patterns and antioxidant-rich foods' effects can provide insights into feasible and sustainable interventions. Assess the safety profiles of antioxidants, particularly at varying dosages and formulations. Long-term safety data, including potential adverse effects or interactions, are crucial in guiding recommendations for antioxidant supplementation. Bridge the gap between basic science research and clinical applications. Translational research initiatives should facilitate the integration of scientific findings into clinical practice guidelines and public health policies. Enhance awareness and education among healthcare providers and pregnant individuals about the potential role of antioxidants in pregnancy. Empowering informed decision-making and promoting evidence-based practices are crucial.

Conclusion

The exploration of antioxidants in the context of pregnancy presents a promising avenue for potentially mitigating oxidative stress-related complications and enhancing maternal-fetal health outcomes. The multifaceted role of antioxidants in counteracting oxidative damage, supporting placental function, regulating inflammatory responses, and safeguarding maternal and fetal well-being has garnered considerable attention in research and clinical practice. Future directions should focus on conducting well-controlled clinical trials, investigating mechanistic pathways, and personalized strategies, and exploring combination therapies to optimize antioxidant interventions. Additionally, promoting education and awareness among healthcare providers and pregnant individuals about the potential benefits and limitations of antioxidants in pregnancy is imperative.

Ultimately, while antioxidants hold promise in alleviating oxidative stress-related complications during pregnancy, further research, collaboration, and translational efforts are essential to bridge existing gaps, refine therapeutic approaches, and ensure the safe and effective use of antioxidants to improve maternal and fetal health outcomes. This concerted effort will pave the way for evidence-based practices and interventions that contribute to healthier pregnancies and better outcomes for both mothers and their offspring.

References

1. Obeagu EI, Agreen FC. Anaemia among pregnant women: A review of African pregnant teenagers. J Pub Health Nutri. 2023; 6 (1). 2023; 138. links/63da799664fc860638054562/Anaemia-among-pregnant-women-A-review-of-African-pregnant-teenagers.pdf.
2. Obeagu EI, Ezimah AC, Obeagu GU. Erythropoietin in the anaemias of pregnancy: a review. Int J Curr Res Chem Pharm Sci. 2016; 3(3):10-8. links/5710fae108ae846f4ef05afb/ERYTHROPOIETIN-IN-THE-ANAEMIAS-OF-PREGNANCY-A-REVIEW.pdf.
3. Obeagu EI, Adepoju OJ, Okafor CJ, Obeagu GU, Ibekwe AM, Okpala PU, Agu CC. Assessment of Haematological Changes in Pregnant Women of Ido, Ondo State, Nigeria. J Res Med Dent Sci. 2021; 9(4):145-8. links/608a6728a6fdccaebdf52d94/Assessment-of-Haematological-Changes-in-Pregnant-Women-of-Ido-Ondo.pdf.
4. Obeagu EI, Obeagu GU. Sickle Cell Anaemia in Pregnancy: A Review. International Research in Medical and Health Sciences. 2023; 6(2):10-3. http://irmhs.com/index.php/irmhs/article/view/111.
5. Jakheng SP, Obeagu EI. Seroprevalence of human immunodeficiency virus based on demographic and risk factors among pregnant women attending clinics in Zaria Metropolis, Nigeria. J Pub Health Nutri. 2022; 5 (8). 2022; 137.links/6317a6b1acd814437f0ad268/Seroprevalence-of-human-immunodeficiency-virus-based-on-demographic-and-risk-factors-among-pregnant-women-attending-clinics-in-Zaria-Metropolis-Nigeria.pdf.
6. Obeagu EI, Obeagu GU, Chukwueze CM, Ikpenwa JN, Ramos GF. Evaluation of Protein C, Protein S and Fibrinogen of Pregnant Women with Malaria in Owerri Metropolis. Madonna University Journal of Medicine and Health Sciences. ISSN: 2814-3035. 2022; 2(2):1-9.
7. 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. PMID: 34194606; PMCID: PMC8184326.
8. Karacay O, Sepici-Dincel A, Karcaaltincaba D, Sahin D, Yalvaç S, Akyol M, Kandemir O, Altan N. A quantitative evaluation of total antioxidant status and oxidative stress markers in preeclampsia and gestational diabetic patients in 24-36 weeks of gestation. Diabetes Res Clin Pract. 2010 Sep;89(3):231-8. doi: 10.1016/j.diabres.2010.04.015. PMID: 20537747.
9. Joo EH, Kim YR, Kim N, Jung JE, Han SH, Cho HY. Effect of Endogenic and Exogenic Oxidative Stress Triggers on Adverse Pregnancy Outcomes: Preeclampsia, Fetal Growth Restriction, Gestational Diabetes Mellitus and Preterm Birth. Int J Mol Sci. 2021 Sep 19;22(18):10122. doi: 10.3390/ijms221810122. PMID: 34576285; PMCID: PMC8468091.
10. Zhu C, Yang H, Geng Q, Ma Q, Long Y, Zhou C, Chen M. Association of oxidative stress biomarkers with gestational diabetes mellitus in pregnant women:

a case-control study. PLoS One. 2015 Apr 27;10(4):e0126490. doi: 10.1371/journal.pone.0126490. PMID: 25915047; PMCID: PMC4411158.

11. Sudharshana Murthy KA, Bhandiwada A, Chandan SL, Gowda SL, Sindhusree G. Evaluation of Oxidative Stress and Proinflammatory Cytokines in Gestational Diabetes Mellitus and Their Correlation with Pregnancy Outcome. Indian J Endocrinol Metab. 2018 Jan-Feb;22(1):79-84. doi: 10.4103/ijem.IJEM_232_16. PMID: 29535942; PMCID: PMC5838917.

12. Obeagu EI, Bunu UO, Obeagu GU, Habimana JB. Antioxidants in the management of sickle cell anaemia: an area to be exploited for the wellbeing of the patients. International Research in Medical and Health Sciences. 2023; 6(4):12-7.

13. Obeagu EI, Ubosi NI, Uzoma G. Antioxidant Supplementation in Pregnancy: Effects on Maternal and Infant Health. Int J Adv Multidiscip Res. 2023; 10(11):60-70.

14. Obeagu EI, Obeagu GU. Utilization of Antioxidants in the management of diabetes mellitus patients. J Diabetes Clin Prac. 2018; 1(102):2.

15. Nwosu DC, Obeagu EI, Nkwocha BC, Nwanna CA, Nwanjo HU, Amadike JN, Elendu HN, Ofoedeme CN, Ozims SJ, Nwankpa P. Change in Lipid Peroxidation Marker (MDA) and Non enzymatic Antioxidants (VIT C & E) in HIV Seropositive Children in an Urban Community of Abia State Nigeria. J Bio Innov 2016; 5(1):24-30.

16. Obeagu EI, Obeagu GU, Obiezu J, Ezeonwumelu C, Alum EU, Ugwu OP. Antioxidants and Pregnancy: Impact on Maternal and Fetal Health. APPLIED SCIENCES (NIJBAS). 2023; 4(1).

17. Ilekis JV, Tsilou E, Fisher S, Abrahams VM, Soares MJ, Cross JC, Zamudio S, Illsley NP, Myatt L, Colvis C, Costantine MM, Haas DM, Sadovsky Y, Weiner C, Rytting E, Bidwell G. Placental origins of adverse pregnancy outcomes: potential molecular targets: an Executive Workshop Summary of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. Am J Obstet Gynecol. 2016 Jul;215(1 Suppl):S1-S46. doi: 10.1016/j.ajog.2016.03.001. Epub 2016 Mar 10. PMID: 26972897; PMCID: PMC4925329.

18. Diniz MS, Magalhães CC, Tocantins C, Grilo LF, Teixeira J, Pereira SP. Nurturing through Nutrition: Exploring the Role of Antioxidants in Maternal Diet during Pregnancy to Mitigate Developmental Programming of Chronic Diseases. Nutrients. 2023 Oct 31;15(21):4623. doi: 10.3390/nu15214623. PMID: 37960276; PMCID: PMC10649237.

19. Hussain T, Tan B, Liu G, Murtaza G, Rahu N, Saleem M, Yin Y. Modulatory Mechanism of Polyphenols and Nrf2 Signaling Pathway in LPS Challenged Pregnancy Disorders. Oxid Med Cell Longev. 2017;2017:8254289. doi: 10.1155/2017/8254289. Epub 2017 Aug 23. PMID: 29138679; PMCID: PMC5613688.

20. Agarwal A, Aponte-Mellado A, Premkumar BJ, Shaman A, Gupta S. The effects of oxidative stress on female reproduction: a review. Reprod Biol Endocrinol. 2012 Jun 29;10:49. doi: 10.1186/1477-7827-10-49. PMID: 22748101; PMCID: PMC3527168.

21. Xu K, Liu G, Fu C. The Tryptophan Pathway Targeting Antioxidant Capacity in the Placenta. Oxid Med Cell Longev. 2018 Jul 22;2018:1054797. doi: 10.1155/2018/1054797. PMID: 30140360; PMCID: PMC6081554.

22. Nwakuilite A, Nwanjo HU, Nwosu DC, Obeagu EI. Evaluation of enzyme antioxidants in streptozocin-induced diabetic rats treated with Moringa oleifera leaf powder. European Journal of Biomedical. 2020; 7(11):285-8.

23. Ifeanyi OE. A review on free radicals and antioxidants. Int. J. Curr. Res. Med. Sci. 2018; 4(2):123-33.

24. Akinpelu M, Gamade SM, Akinbo F, Adeniyi TD, Elizebeth AF, Obeagu EI. Histopathological and Biochemical Effect of Vitamin C and D on Phosphine-Induced Hepatotoxicity in Wistar Rats. Asian Journal of Dental and Health Sciences. 2023; 3(2):18-22.

25. Nwakulite A, Obeagu EI, Eze R, Ugochi VE, Vincent CC, Okafor CJ, Chukwurah EF, Unaeze BC, Amaechi CO, Okwuanaso CB, Chukwuani U. Estimation of Serum Glutathione Peroxidase in Streptozotocin-Induced Diabetic Rat Treated with Bitter Leaf Extract. Journal of Pharmaceutical Research International. 2021; 33(30B):200-6.

26. Ifeanyi OE, Stella EI, Favour AA. Antioxidants in the Management of Sickle Cell Anaemia. Int J Hematol Blood Disord (Internet) 2018 (cited 2021 Mar 4); 3. https://symbiosisonlinepublishing.com/hematology/hematology25. php. 2018 S.

27. Hussain T, Murtaza G, Metwally E, Kalhoro DH, Kalhoro MS, Rahu BA, Sahito RGA, Yin Y, Yang H, Chughtai MI, Tan B. The Role of Oxidative Stress and Antioxidant Balance in Pregnancy. Mediators Inflamm. 2021 Sep 27;2021:9962860. doi: 10.1155/2021/9962860. PMID: 34616234; PMCID: PMC8490076.

28. 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. Epub 2018 Dec 24. PMID: 30590104.

29. Tenório MB, Ferreira RC, Moura FA, Bueno NB, de Oliveira ACM, Goulart MOF. Cross-Talk between Oxidative Stress and Inflammation in Preeclampsia. Oxid Med Cell Longev. 2019 Nov 4;2019:8238727. doi: 10.1155/2019/8238727. PMID: 31781353; PMCID: PMC6875353.

30. Guerby P, Tasta O, Swiader A, Pont F, Bujold E, Parant O, Vayssiere C, Salvayre R, Negre-Salvayre A. 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. Epub 2021 Jan 19. PMID: 33548859; PMCID: PMC7873691.

31. Anyiam AF, Obeagu EI, Obi E, Omosigho PO, Irondi EA, Arinze-Anyiam OC, Asiyah MK. ABO blood groups and gestational diabetes among pregnant women attending University of Ilorin Teaching Hospital, Kwara State, Nigeria. International Journal of Research and Reports in Hematology. 2022; 5(2):113-21.

32. Obeagu EI. Gestational Thrombocytopaenia. J Gynecol Women's Health. 2023; 25(3):556163. links/64b01aa88de7ed28ba95fccb/Gestational-Thrombocytopaenia.pdf.

33. Sánchez-Aranguren LC, Prada CE, Riaño-Medina CE, Lopez M. Endothelial dysfunction and preeclampsia: role of oxidative stress. Front Physiol. 2014 Oct 10;5:372. doi: 10.3389/fphys.2014.00372. PMID: 25346691; PMCID: PMC4193194.

34. Obeagu EI, Ogbonna US, Nwachukwu AC, Ochiabuto O, Enweani IB, Ezeoru VC. Prevalence of Malaria with Anaemia and HIV status in women of reproductive age in Onitsha, Nigeria. Journal of Pharmaceutical Research International. 2021; 33(4):10-9.

35. Gerber PA, Rutter GA. The Role of Oxidative Stress and Hypoxia in Pancreatic Beta-Cell Dysfunction in Diabetes Mellitus. Antioxid Redox Signal. 2017 Apr 1;26(10):501-518. doi: 10.1089/ars.2016.6755. Epub 2016 Jun 30. PMID: 27225690; PMCID: PMC5372767.

36. Obeagu EI, Abdirahman BF, Bunu UO, Obeagu GU. Obsterics characteristics that affect the newborn outcomes. Int J Adv Res Biol Sci. 2023;10(3):134-43.DOI: 10.22192/ijarbs.2023.10.03.016

37. Sultana Z, Maiti K, Aitken J, Morris J, Dedman L, Smith R. Oxidative stress, placental ageing-related pathologies and adverse pregnancy outcomes. Am J Reprod Immunol. 2017 May;77(5). doi: 10.1111/aji.12653. Epub 2017 Feb 27. PMID: 28240397.

38. Wu F, Tian FJ, Lin Y. Oxidative Stress in Placenta: Health and Diseases. Biomed Res Int. 2015;2015:293271. doi: 10.1155/2015/293271. Epub 2015 Nov 29. PMID: 26693479; PMCID: PMC4676991.

39. Okamgba OC, Nwosu DC, Nwobodo EI, Agu GC, Ozims SJ, Obeagu EI, Ibanga IE, Obioma-Elemba IE, Ihekaire DE, Obasi CC, Amah HC. Iron Status of Pregnant and Post-Partum Women with Malaria Parasitaemia in Aba Abia State, Nigeria. Annals of Clinical and Laboratory Research. 2017;5(4):206. links/5ea97df145851592d6a8acf2/Iron-Status-of-Pregnant-and-Post-Partum-Women-with-Malaria-Parasitaemia-in-Aba-Abia-State-Nigeria.pdf.

40. Eze RI, Obeagu EI, Edet FN. Frequency of Rh Antigen C and c among pregnant women in Sub-Urban area in Eastern Nigeria. Madonna Uni J Med Health Sci. 2021; 1(1):19-30.

41. Jovandaric MZ, Babic S, Raus M, Medjo B. The Importance of Metabolic

and Environmental Factors in the Occurrence of Oxidative Stress during Pregnancy. Int J Mol Sci. 2023 Jul 26;24(15):11964. doi: 10.3390/ijms241511964. PMID: 37569340; PMCID: PMC10418910.

42. Obeagu EI, Obeagu GU, Musiimenta E. Postpartum haemorrhage among pregnant women: Update on risks factors. Int J Curr Res Med Sci. 2023; 9(2): 14-7.DOI: 10.22192/ijcrms.2023.09.02.003

43. Jakheng SP, Obeagu EI, Jakheng EW, Uwakwe OS, Eze GC, Obeagu GU, Vidya S, Kumar S. Occurrence of Chlamydial Infection Based on Clinical Symptoms and Clinical History among Pregnant Women Attending Clinics in Zaria Metropolis, Kaduna State, Nigeria. International Journal of Research and Reports in Gynaecology. 2022; 5(3):98-105.

44. Okorie HM, Obeagu EI, Eze EN, Jeremiah ZA. Assessment of some haematological parameters in malaria-infected pregnant women in Imo state Nigeria. Int J Curr Res Biol Med. 2018; 3(9):1-4. DOI: 10.22192/ijcrbm.2018.03.09.001

45. Holland O, Dekker Nitert M, Gallo LA, Vejzovic M, Fisher JJ, Perkins AV. Review: Placental mitochondrial function and structure in gestational disorders. Placenta. 2017 Jun;54:2-9. doi: 10.1016/j.placenta.2016.12.012. Epub 2016 Dec 14. PMID: 28024805.

46. Lu M, Sferruzzi-Perri AN. Placental mitochondrial function in response to gestational exposures. Placenta. 2021 Jan 15;104:124-137. doi: 10.1016/j.placenta.2020.11.012. Epub 2020 Dec 5. PMID: 33338764.

47. Obeagu EI, Njar VE, Obeagu GU. Infertility: Prevalence and Consequences. Int J Curr Res Chem Pharm Sci. 2023; 10(7):43-50.

48. Emeka-Obi OR, Ibeh NC, Obeagu EI, Okorie HM. Evaluation of levels of some inflammatory cytokines in preeclamptic women in Owerri. Journal of Pharmaceutical Research International. 2021; 33(42A):53-65.

49. Obeagu EI, Faduma MH, Uzoma G. Ectopic Pregnancy: A Review. Int J Curr Res Chem Pharm Sci. 2023; 10(4):40-4. DOI: 10.22192/ijcrcps.2023.10.04.004

50. Obeagu EI, Gamade SM, Obeagu GU. The roles of Neutrophils in pregnancy. Int. J. Curr. Res. Med. Sci. 2023; 9(5):31-5. DOI: 10.22192/ijcrms.2023.09.05.005

51. Eze R, Obeagu EI, Nwakulite A, Okoroiwu IL, Vincent CC, Okafor CJ, Chukwurah EF, Chijioke UO, Amaechi CO. Evaluation of Copper Status and Some Red Cell Parameters of Pregnant Women in Enugu State, South Eastern Nigeria. Journal of Pharmaceutical Research International. 2021; 33(30A):67-71.

52. Obeagu EI, Obeagu GU. Molar Pregnancy: Update of prevalence and risk factors. Int J Curr Res Med Sci. 2023; 9(7): 25-8. DOI: 10.22192/ijcrms.2023.09.07.005

53. Obeagu EI, Bunu UO. Factors that influence unmet need for family planning. International Journal of Current Research in Biology and Medicine. 2023; 8(1):23-7.

54. Ibebuike JE, Ojie CA, Nwokike GI, Obeagu EI, Nwosu DC, Nwanjo HU, Agu GC, Ezenwuba CO, Nwagu SA, Akujuobi AU. Barriers to utilization of maternal health services in the southern senatorial district of Cross Rivers state, Nigeria. International Journal of Advanced Multidisciplinary Research. 2017; 4(8): 1-9. DOI: 10.22192/ijamr.2017.04.08.001

55. Okorie HM, Obeagu EI, Eze EN, Jeremiah ZA. Assessment of coagulation parameters in malaria-infected pregnant women in Imo state, Nigeria. International Journal of Current Research in Medical Sciences. 2018; 4(9):41-9. DOI: 10.22192/ijcrms.2018.04.09.006

56. San Juan-Reyes S, Gómez-Oliván LM, Islas-Flores H, Dublán-García O. Oxidative stress in pregnancy complicated by preeclampsia. Arch Biochem Biophys. 2020 Mar 15;681:108255. doi: 10.1016/j.abb.2020.108255. Epub 2020 Jan 3. PMID: 31904364.

57. Ahmed OM, Mohammed MT. Oxidative stress: The role of reactive oxygen species (ROS) and antioxidants in human diseases. Plant Arch. 2020; 20(2):4089-95.

58. Saha S, Buttari B, Panieri E, Profumo E, Saso L. An Overview of Nrf2 Signaling Pathway and Its Role in Inflammation. Molecules. 2020 Nov 23;25(22):5474. doi: 10.3390/molecules25225474. PMID: 33238435; PMCID: PMC7700122.

59. Obeagu E, Eze RI, Obeagu EI, Nnatuanya IN, Dara EC. Zinc level in apparently pregnant women in urban area. Madonna University Journal of Medicine and Health Sciences. 2022; 2(1):134-48. https://www.journal.madonnauniversity.edu.ng/index.php/medicine/article/view/40.

60. Ogomaka IA, Obeagu EI. Malaria in Pregnancy amidst Possession of Insecticide Treated Bed Nets (ITNs) in Orlu LGA of Imo State, Nigeria. Journal of Pharmaceutical Research International. 2021; 33(41B):380-6.

61. Dijkhuizen MA, Wieringa FT, West CE, Muhilal. Zinc plus beta-carotene supplementation of pregnant women is superior to beta-carotene supplementation alone in improving vitamin A status in both mothers and infants. Am J Clin Nutr. 2004 Nov;80(5):1299-307. doi: 10.1093/ajcn/80.5.1299. PMID: 15531679.

62. Ifeanyi OE, Uzoma OG. A review on erythropoietin in pregnancy. J. Gynecol. Womens Health. 2018; 8(3):1-4. https://www.academia.edu/download/56538560/A_Review_on_Erythropietin_in_Pregnancy.pdf.

63. Park E, Wagenbichler P, Elmadfa I. Effects of multivitamin/mineral supplementation, at nutritional doses, on plasma antioxidant status and DNA damage estimated by sister chromatid exchanges in lymphocytes in pregnant women. Int J Vitam Nutr Res. 1999 Nov;69(6):396-402. doi: 10.1024/0300-9831.69.6.396. PMID: 10642897.

64. Nwosu DC, Nwanjo HU, Obeagu EI, Ibebuike JE, Ezeama MC. Ihekireh. Changes in liver enzymes and lipid profile of pregnant women with malaria in Owerri, Nigeria. International Journal of Current Research and Academic Review. 2015; 3(5):376-83.