ISSN 2348-0319 International Journal of Innovative and Applied Research [2023]
(Volume 11, Issue 12)
98-109

Journal home page: http://www.journalijiar.com

INTERNATIONAL JOURNAL
OF INNOVATIVE AND APPLIED RESEARCH

RESEARCH ARTICLE

Article DOI:10.58538/IJIAR/2066
DOI URL: *http://dx.doi.org/10.58538/IJIAR/2066*

Vascular Endothelial Growth Factor (VEGF) in Pregnancy: Exploring Its Multifaceted Roles and Clinical Implications

Emmanuel Ifeanyi Obeagu[1], Getrude Uzoma Obeagu[2,] Emmanuel Chinedu Onuoha[3]and Esther Namutosi[4]

[1]Department of Medical Laboratory Science, Kampala International University, Uganda.
[2]School of Nursing Science, Kampala International University, Uganda.
[3]Department of Haematology and Blood Transfusion, Faculty of Medical and Laboratory Science, Federal University Otuoke, Bayelsa State, Nigeria
[4]Department of Obstetrics and Gynecology, Kampala International University, Uganda.

Manuscript Info

Manuscript History
Received: 01 November 2023
Final Accepted: 16 December 2023
Published: December 2023

Keywords:
Vascular Endothelial Growth Factor (VEGF), Pregnancy Clinical Implications

Abstract

Vascular endothelial growth factor (VEGF) serves as a central mediator of vascular remodeling and neovascularization, essential components for successful pregnancy. This review aims to elucidate the diverse functions of VEGF in maternal vascular adaptations and placental development across the gestational timeline. Understanding the pivotal role of VEGF in maintaining vascular integrity, supporting placental function, and ensuring fetal nourishment is fundamental for comprehending the intricacies of pregnancy physiology and addressing pregnancy-associated disorders. Throughout pregnancy, the maternal circulatory system undergoes dynamic changes orchestrated by VEGF to accommodate the growing demands of the developing fetus. This section delineates VEGF's role in orchestrating vasodilation, angiogenesis, and increased vascular permeability, thereby optimizing blood flow to the placenta and sustaining adequate fetal oxygen and nutrient supply. Critical to fetal nourishment and development, the placenta relies significantly on VEGF-mediated processes for its formation and functionality. This segment explores VEGF's influence on trophoblast invasion, placental vascularization, and the establishment of an efficient maternal-fetal interface. It elucidates the impact of VEGF on

regulating fetal growth, nutrient exchange, and the prevention of pregnancy-related complications. Disruptions in VEGF signaling pathways have been associated with various pregnancy complications, including preeclampsia, intrauterine growth restriction (IUGR), and gestational diabetes. This section delves into the clinical implications of aberrant VEGF expression and function, highlighting their significance in early diagnosis, risk assessment, and potential therapeutic interventions targeting VEGF pathways. Emerging therapeutic strategies aimed at modulating VEGF signaling pathways present promising avenues for managing pregnancy-related complications. This section examines potential interventions, including VEGF supplementation, receptor modulation, and innovative gene therapies, offering insights into their potential for mitigating adverse pregnancy outcomes associated with VEGF dysregulation. VEGF emerges as a fundamental player in orchestrating maternal vascular adaptations, placental development, and fetal growth regulation throughout pregnancy. A deeper comprehension of VEGF's multifaceted roles not only enhances our understanding of reproductive physiology but also unveils potential avenues for targeted interventions to improve maternal and fetal health outcomes.

Corresponding Author: - Emmanuel Ifeanyi Obeagu, *Department of Medical Laboratory Science, Kampala International University, Uganda.*

Introduction: -

Pregnancy orchestrates a remarkable series of physiological adaptations, pivotal among which is the intricate regulation of vascular growth and remodeling essential for maternal-fetal health. At the crux of these adaptations lies the vascular endothelial growth factor (VEGF), a master regulator of angiogenesis and vasculogenesis crucial for the development and maintenance of the maternal-fetal vasculature. This review aims to comprehensively explore the multifaceted roles of VEGF throughout the stages of pregnancy, elucidating its profound contributions to maternal vascular changes, placental angiogenesis, and fetal development. Furthermore, it scrutinizes the clinical ramifications of VEGF dysregulation in pregnancy-related complications and evaluates potential therapeutic interventions targeting VEGF signaling pathways to ameliorate adverse maternal and fetal outcomes [1-10].

VEGF, a multifunctional cytokine, holds pivotal importance in mediating physiological responses, particularly in the context of pregnancy. Its role in promoting angiogenesis, endothelial cell proliferation, and vascular permeability has garnered attention due to its indispensable contribution to maternal adaptations and fetal well-being. Understanding the intricate mechanisms by which VEGF modulates vascular dynamics across gestation is not only

crucial for comprehending the complexities of maternal physiology but also offers avenues for therapeutic interventions in high-risk pregnancies [11-21].

Throughout pregnancy, maternal cardiovascular adaptations are paramount in meeting the escalating metabolic demands of the developing fetus. VEGF orchestrates a spectrum of changes, including vasodilation, remodeling of uteroplacental vessels, and augmentation of placental blood flow. Unraveling the role of VEGF in these adaptations illuminates its significance in ensuring optimal maternal-fetal circulation and nutrient exchange [22-31]. The placenta, an indispensable organ for fetal nourishment and oxygenation, heavily relies on VEGF-mediated processes for its development. VEGF governs trophoblast invasion, placental vascularization, and the establishment of an efficient maternal-fetal interface. Understanding VEGF's intricate involvement in placental angiogenesis sheds light on its role in modulating fetal growth and mitigating pregnancy-related complications [32-41]. Altered VEGF expression or function has been linked to various gestational pathologies such as preeclampsia, intrauterine growth restriction (IUGR), and gestational diabetes. This review examines the clinical ramifications of aberrant VEGF signaling, emphasizing its implications for early diagnosis, risk stratification, and potential therapeutic targets in pregnancy complications [42-50]. Emerging therapeutic avenues aimed at modulating VEGF signaling pathways present promising prospects for managing pregnancy-related complications. This section investigates potential interventions involving VEGF supplementation, receptor modulation, and innovative gene therapies, offering insights into their potential in mitigating adverse pregnancy outcomes associated with VEGF dysregulation.

VEGF in Maternal Vascular Adaptations

Maternal vascular adaptations during pregnancy are orchestrated to ensure adequate blood flow and nutrient supply to support the developing fetus. Vascular endothelial growth factor (VEGF) emerges as a central player in mediating these adaptations by regulating vasodilation, angiogenesis, and vascular permeability [51-64]. VEGF plays a crucial role in modulating vascular tone and diameter, thereby promoting vasodilation in maternal blood vessels. This vasodilatory effect is pivotal for adjusting blood flow to meet the heightened demands of the growing uterus and placenta. VEGF-mediated vasodilation facilitates increased uteroplacental blood flow, ensuring optimal oxygen and nutrient delivery to the developing fetus [65]. Throughout gestation, VEGF drives angiogenesis, stimulating the formation of new blood vessels and remodeling existing vasculature. This process is particularly prominent in the uterine arteries and spiral arteries, where VEGF promotes vessel enlargement and remodeling to accommodate increased blood flow. Proper remodeling facilitated by VEGF is essential for preventing maternal complications such as preeclampsia and ensuring efficient maternal-fetal nutrient exchange. VEGF is a key regulator of placental vascular development. It supports the growth and branching of fetal blood vessels within the placenta, enabling optimal exchange of gases and nutrients between maternal and fetal circulatory systems. Dysregulation of VEGF-mediated placental angiogenesis can lead to compromised placental function, potentially contributing to adverse pregnancy outcomes. VEGF also influences vascular permeability, regulating fluid dynamics within maternal tissues. Controlled vascular permeability facilitated by VEGF allows for appropriate transport of nutrients and fluid between maternal and fetal compartments. Disruption of this balance may lead to conditions like edema or impaired nutrient

transfer, impacting maternal and fetal health [66]. VEGF expression is intricately regulated in response to varying hormonal, metabolic, and mechanical cues during pregnancy. This adaptive response ensures appropriate maternal vascular adaptations in different stages of gestation, maintaining homeostasis and supporting the dynamic changes required for fetal growth and development.

VEGF in Placental Angiogenesis and Development

The placenta, a dynamic and multifunctional organ, plays a central role in supporting fetal growth and development throughout pregnancy [67]. Vascular endothelial growth factor (VEGF) is a key orchestrator of placental angiogenesis and development, exerting profound effects on trophoblast invasion, vascularization, and the establishment of a functional maternal-fetal interface [68].

VEGF is instrumental in regulating trophoblast invasion, a critical process for establishing a robust maternal-fetal interface. VEGF facilitates the migration and invasion of trophoblast cells into the maternal decidua and myometrium, aiding in the remodeling of spiral arteries. Proper remodeling, mediated by VEGF, transforms these arteries into low-resistance vessels, ensuring adequate blood supply to the developing placenta [69].

VEGF plays a pivotal role in angiogenesis within the placenta, stimulating the formation and branching of fetal blood vessels. It promotes the proliferation and differentiation of endothelial cells, leading to the development of a complex vascular network essential for efficient gas and nutrient exchange between maternal and fetal circulatory systems. VEGF-mediated angiogenesis within the placenta is crucial for ensuring optimal fetal growth and development [70].

VEGF not only influences the structure of the placental vasculature but also regulates its functional capacity. It contributes to the permeability of placental blood vessels, facilitating the passage of oxygen, nutrients, and waste products between maternal and fetal circulations. Proper VEGF-mediated vascularization ensures the integrity of the maternal-fetal exchange interface, crucial for fetal nourishment and metabolic exchange [67].

VEGF expression within the placenta is dynamically regulated in response to varying physiological demands throughout gestation. This adaptive regulation ensures that placental angiogenesis and vascular development are finely tuned to meet the changing needs of the developing fetus. Any dysregulation in VEGF signaling may disrupt placental vascular development, potentially leading to adverse pregnancy outcomes such as intrauterine growth restriction (IUGR) or preeclampsia [71]. Understanding the central role of VEGF in placental angiogenesis opens avenues for potential therapeutic interventions aimed at optimizing placental function. Strategies targeting VEGF signaling pathways could potentially mitigate placental vascular dysfunction in high-risk pregnancies, offering prospects for improving fetal growth and mitigating pregnancy complications. VEGF emerges as a pivotal factor in orchestrating placental angiogenesis and vascular development, contributing significantly to the establishment of a functional maternal-fetal interface. Its multifaceted roles in trophoblast invasion, vascularization, and functional regulation underscore its critical importance in ensuring optimal placental function and fetal well-being throughout pregnancy.

Clinical Implications of VEGF Dysregulation in Pregnancy

Disruptions in the delicate balance of vascular endothelial growth factor (VEGF) signaling during pregnancy have profound clinical implications, potentially contributing to various pregnancy-related complications. Understanding the consequences of VEGF dysregulation is crucial for early identification, risk assessment, and management of these complications [72]. Dysregulated VEGF expression has been associated with the pathogenesis of preeclampsia, a hypertensive disorder characterized by new-onset hypertension and proteinuria after 20 weeks of gestation. Reduced VEGF levels or impaired VEGF signaling in the placenta may lead to inadequate placental perfusion, endothelial dysfunction, and the release of anti-angiogenic factors, contributing to the development of preeclampsia [73]. Aberrant VEGF expression can impact placental angiogenesis and vascular development, potentially leading to inadequate blood supply to the fetus. Insufficient VEGF-mediated vascularization within the placenta may result in reduced nutrient and oxygen exchange, contributing to intrauterine growth restriction (IUGR) and suboptimal fetal growth [71]. Altered VEGF levels have been observed in gestational diabetes mellitus, a condition characterized by glucose intolerance during pregnancy. VEGF dysregulation may affect placental angiogenesis and microvascular function, contributing to impaired glucose transport across the placenta and impacting fetal growth [74]. Disruptions in VEGF-mediated placental vascularization can lead to placental insufficiency, characterized by inadequate nutrient and oxygen supply to the fetus. This insufficiency may increase the risk of preterm birth, contributing to adverse neonatal outcomes associated with premature delivery [75]. VEGF levels or alterations in VEGF signaling pathways may hold diagnostic and prognostic value in identifying high-risk pregnancies prone to complications. VEGF assessment might assist clinicians in risk stratification and early intervention strategies aimed at mitigating adverse outcomes in affected pregnancies [76]. Understanding the role of VEGF dysregulation in pregnancy complications offers potential therapeutic avenues. Targeted interventions aimed at restoring VEGF balance or modulating VEGF signaling pathways could be explored as potential strategies to mitigate adverse pregnancy outcomes. The clinical implications of VEGF dysregulation in pregnancy span a spectrum of complications, ranging from hypertensive disorders to fetal growth abnormalities. Elucidating the role of VEGF in these complications not only aids in understanding their pathophysiology but also holds promise for potential interventions aimed at improving maternal and fetal outcomes in high-risk pregnancies.

Therapeutic Potential of Targeting VEGF Signaling

Understanding the pivotal role of vascular endothelial growth factor (VEGF) in pregnancy-related complications has prompted investigations into potential therapeutic interventions targeting VEGF signaling pathways. Strategies aimed at modulating VEGF signaling hold promise for managing and potentially mitigating adverse pregnancy outcomes associated with VEGF dysregulation. Augmenting VEGF levels through supplementation or enhancing VEGF receptor activation presents a potential therapeutic approach. This strategy aims to restore VEGF balance, particularly in conditions characterized by reduced VEGF expression or impaired receptor function, such as preeclampsia or intrauterine growth restriction (IUGR). Clinical trials assessing the safety and efficacy of VEGF supplementation or receptor agonists are warranted. [77] Beyond VEGF, therapies targeting related angiogenic factors involved in placental angiogenesis, such as placental growth factor (PlGF), could hold therapeutic potential. Combined

therapies targeting multiple angiogenic factors might offer synergistic effects, potentially addressing the multifactorial nature of pregnancy-related complications [78]. Innovative approaches involving gene therapies or molecular interventions aimed at modulating VEGF expression or downstream signaling pathways are under exploration. Precise manipulation of VEGF-related genes or pathways holds potential for tailored therapeutic interventions, although their clinical applicability in pregnancy requires further investigation. Repurposing or developing drugs targeting angiogenesis pathways, including VEGF inhibitors or angiogenesis inhibitors, may offer therapeutic avenues in managing specific pregnancy complications. However, cautious consideration of potential off-target effects and fetal safety profiles is crucial before their clinical implementation. Stratifying high-risk pregnancies based on VEGF-related biomarkers or genetic predispositions might enable personalized therapeutic approaches. Tailored interventions targeting specific VEGF-related abnormalities could improve efficacy and minimize potential adverse effects. Implementing preventive measures or early interventions aimed at preserving VEGF-mediated vascular adaptations may hold promise in mitigating the onset or severity of pregnancy complications. Lifestyle modifications, nutritional interventions, or pharmacological agents could potentially modulate VEGF pathways to support healthy pregnancy outcomes. Robust clinical trials evaluating the safety and efficacy of interventions targeting VEGF signaling pathways in pregnancy are essential. Translational research efforts bridging basic science discoveries with clinical applications are vital for realizing the therapeutic potential of targeting VEGF signaling in pregnancy-related complications. While the therapeutic modulation of VEGF signaling pathways presents promising avenues for managing pregnancy-related complications, rigorous research, and clinical validation are imperative. Advancing our understanding of VEGF-related mechanisms and conducting well-designed trials will pave the way for innovative therapeutic interventions, potentially improving maternal and fetal outcomes in high-risk pregnancies.

Conclusion

Vascular endothelial growth factor (VEGF) stands as a fundamental regulator in the orchestration of intricate processes vital for a successful pregnancy. Its multifaceted roles in maternal vascular adaptations, placental angiogenesis, and fetal development underscore its significance in ensuring optimal maternal-fetal health throughout gestation. However, dysregulation of VEGF signaling pathways can contribute to a spectrum of pregnancy-related complications, including hypertensive disorders, intrauterine growth restriction, and impaired placental function. The elucidation of VEGF's pivotal involvement in pregnancy complications not only deepens our understanding of their underlying pathophysiology but also unveils potential avenues for therapeutic interventions. Strategies targeting VEGF signaling pathways hold promise for mitigating adverse outcomes associated with VEGF dysregulation. Augmenting VEGF levels, modulating VEGF receptors, exploring gene therapies, or employing angiogenesis-targeted drugs are among the innovative approaches under investigation.

Nevertheless, while these therapeutic avenues offer potential, translating these strategies into clinical practice necessitates comprehensive research, robust clinical trials, and a thorough understanding of the delicate balance between therapeutic efficacy and fetal safety. Personalized approaches based on biomarkers or genetic profiling may further enhance the precision and efficacy of VEGF-targeted interventions in high-risk pregnancies. The evolving landscape of

research in VEGF signaling pathways in pregnancy underscores the need for interdisciplinary collaboration, rigorous translational studies, and ethical considerations in therapeutic development. By advancing our understanding of VEGF-mediated mechanisms and leveraging innovative interventions, there exists a prospect to mitigate adverse pregnancy outcomes and improve maternal and fetal health.

References

1. Ochei KC, Obeagu EI, Ugwu GU, George CN (2014). Prevalence Of Trichomonas Vaginalis Among Pregnant Women Attending Hospital in Irrua Specialist Teaching Hospital in Edo State, Nigeria. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), 2014; 13(9 Ver. II):79-82*
2. Obeagu EI, Obeagu GU, Ogunnaya FU. Deep vein thrombosis in pregnancy: A review of prevalence and risk factors. Int. J. Curr. Res. Chem. Pharm. Sci. 2023;10(8):14-21.
3. Obeagu EI, Obeagu GU. Molar Pregnancy: Update of prevalence and risk factors. Int. J. Curr. Res. Med. Sci. 2023;9(7):25-8.
4. Obeagu EI, Obeagu GU, Adepoju OJ. Evaluation of haematological parameters of pregnant women based on age groups in Olorunsogo road area of Ido, Ondo state. J. Bio. Innov11 (3). 2022:936-41.
5. 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.
6. 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.
7. Cornish EF, Filipovic I, Åsenius F, Williams DJ, McDonnell T. Innate immune responses to acute viral infection during pregnancy. Frontiers in Immunology. 2020:2404.
8. Obeagu EI, Obeagu GU, Igwe MC, Alum EU, Ugwu OP. Neutrophil-Derived Inflammation and Pregnancy Outcomes.Newport International Journal Of Scientific And Experimental Sciences 4(2):10- 19.https://doi.org/10.59298/NIJSES/2023/10.2.1111
9. 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.
10. 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.
11. Boldeanu L, Dijmărescu AL, Radu M, Siloşi CA, Popescu-Drigă MV, Poenariu IS, Siloşi I, Boldeanu MV, Novac MB, Novac LV. The role of mediating factors involved in angiogenesis during implantation. Romanian Journal of Morphology and Embryology. 2020;61(3):665.
12. 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.

13. 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.
14. 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.
15. 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.
16. Obeagu EI, Ikpenwa JN, Chukwueze CM, Obeagu GU. Evaluation of protein C, protein S and fibrinogen of pregnant women in Owerri Metropolis. Madonna University Journal of Medicine and Health Sciences ISSN: 2814-3035. 2022;2(1):292-8.https://madonnauniversity.edu.ng/journals/index.php/medicine/article/view/57.
17. Obeagu EI, Obeagu GU, Adepoju OJ. Evaluation of haematological parameters of pregnant women based on age groups in Olorunsogo road area of Ido, Ondo state. J. Bio. Innov11 (3). 2022:936-41.
18. Obeagu EI. An update on utilization of antenatal care among pregnant Women in Nigeria. Int. J. Curr. Res. Chem. Pharm. Sci. 2022;9(9): 21-6.DOI: 10.22192/ijcrcps.2022.09.09.003
19. Okoroiwu IL, Obeagu EI, Obeagu GU. Determination of clot retraction in preganant women attending antenatal clinic in federal medical centre Owerri, Nigeria. Madonna University Journal of Medicine and Health Sciences ISSN: 2814-3035. 2022;2(2):91-7.
20. Obeagu EI, Hassan AO, Adepoju OJ, Obeagu GU, Okafor CJ. Evaluation of Changes in Haematological Parameters of Pregnant Women Based on Gestational Age at Olorunsogo Road Area of Ido, Ondo State. Nigeria. Journal of Research in Medical and Dental Science. 2021;9(12):462-.links/61b1e32f0c4bfb675178bfa7/Evaluation-of-Changes-in-Haematological-Parameters-of-Pregnant-Women-Based-on-Gestational-Age-at-Olorunsogo-Road-Area-of-Ido-Ondo-State-Nigeria.pdf.
21. 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.
22. Owen MD, Baker BC, Scott EM, Forbes K. Interaction between metformin, folate and vitamin B12 and the potential impact on fetal growth and long-term metabolic health in diabetic pregnancies. International journal of molecular sciences. 2021;22(11):5759.
23. Obeagu EI. Gestational Thrombocytopaenia. J Gynecol Women's Health. 2023;25(3):556163.links/64b01aa88de7ed28ba95fccb/Gestational-Thrombocytopaenia.pdf.
24. Jakheng SP, Obeagu EI, Abdullahi IO, Jakheng EW, Chukwueze CM, Eze GC, Essien UC, Madekwe CC, Madekwe CC, Vidya S, Kumar S. Distribution Rate of Chlamydial Infection According to Demographic Factors among Pregnant Women Attending Clinics

in Zaria Metropolis, Kaduna State, Nigeria. South Asian Journal of Research in Microbiology. 2022;13(2):26-31.
25. 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.
26. Obeagu EI, Abdirahman BF, Bunu UO, Obeagu GU. Obsterics characteristics that effect the newborn outcomes. Int. J. Adv. Res. Biol. Sci. 2023;10(3): 134-43.DOI: 10.22192/ijarbs.2023.10.03.016
27. Obeagu EI, Ogunnaya FU. PREGNANCYINDUCED HAEMATOLOGICAL CHANGES: A KEY TO MARTERNAL AND CHILD HEALTH. European Journal of Biomedical. 2023;10(8):42-3.links/64c890bddb38b20d6dad2c5c/PREGNANCY-INDUCED-HAEMATOLOGICAL-CHANGES-A-KEY-TO-MARTERNAL-AND-CHILD-HEALTH.pdf.
28. Ezeoru VC, Enweani IB, Ochiabuto O, Nwachukwu AC, Ogbonna US, Obeagu EI. 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.
29. 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.
30. 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.
31. Obeagu EI, Ofodile AC, Okwuanaso CB. A review of urinary tract infections in pregnant women: Risks factors. J Pub Health Nutri. 2023; 6 (1). 2023; 137:26-35.links/63c3a9116fe15d6a571e8bba/A-review-of-urinary-tract-infections-in-pregnant-women-Risks-factors.pdf.
32. Huang Z, Huang S, Song T, Yin Y, Tan C. Placental angiogenesis in mammals: a review of the regulatory effects of signaling pathways and functional nutrients. Advances in Nutrition. 2021;12(6):2415-34.
33. Obeagu EI, Obeagu GU, Musiimenta E. Post partum 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
34. Obeagu EI, Obeagu GU, Ogunnaya FU. Deep vein thrombosis in pregnancy: A review of prevalence and risk factors. Int. J. Curr. Res. Chem. Pharm. Sci. 2023;10(8): 14-21.DOI: 10.22192/ijcrcps.2023.10.08.002
35. 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.
36. 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

37. Onyenweaku FC, Amah HC, Obeagu EI, Nwandikor UU, Onwuasoanya UF. Prevalence of asymptomatic bacteriuria and its antibiotic susceptibility pattern in pregnant women attending private ante natal clinics in Umuahia Metropolitan. Int J Curr Res Biol Med. 2017;2(2): 13-23.DOI: 10.22192/ijcrbm.2017.02.02.003
38. Okoroiwu IL, Chinedu-Madu JU, Obeagu EI, Vincent CC, Ochiabuto OM, Ibekwe AM, Amaechi CO, Agu CC, Anoh NV, Amadi NM. Evaluation of Iron Status, Haemoglobin and Protein Levels of Pregnant Women in Owerri Metropolis. Journal of Pharmaceutical Research International. 2021;33(27A):36-43.
39. Obeagu EI, Njar VE, Obeagu GU. Infertility: Prevalence and Consequences. Int. J. Curr. Res. Chem. Pharm. Sci. 2023;10(7):43-50.
40. 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 Aug 25;33(42A):53-65.
41. 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
42. 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
43. 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.
44. 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
45. 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.
46. 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 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
47. Emannuel G, Martin O, Peter OS, Obeagu EI, Daniel K. Factors Influencing Early Neonatal Adverse Outcomes among Women with HIV with Post Dated Pregnancies Delivering at Kampala International University Teaching Hospital, Uganda. Asian Journal of Pregnancy and Childbirth. 2023;6(1):203-11.http://research.sdpublishers.net/id/eprint/2819/.
48. 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
49. Obeagu EI, Obeagu GU. Postpartum haemorrhage among women delivering through spontaneous vaginal delivery: Prevalence and risk factors. Int. J. Curr. Res. Chem. Pharm. Sci. 2023;10(8): 22-6.DOI: 10.22192/ijcrcps.2023.10.08.003
50. 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.
51. Ibebuike JE, Ojie CA, Nwokike GI, Obeagu EI, Nwosu DC, Nwanjo HU, Agu GC, Ezenwuba CO, Nwagu SA, Akujuobi AU. Factors that influence women's utilization of

primary health care services in Calabar Cros river state, Nigeria. Int. J. Curr. Res. Chem. Pharm. Sci. 2017;4(7):28-33.
52. Obeagu EI, Muhimbura E, Kagenderezo BP, Nakyeyune S, Obeagu GU. An Insight of Interleukin-6 and Fibrinogen: In Regulating the Immune System. J Biomed Sci. 2022;11(10):83.
53. Obeagu EI, Muhimbura E, Kagenderezo BP, Uwakwe OS, Nakyeyune S, Obeagu GU. An Update on Interferon Gamma and C Reactive Proteins in Sickle Cell Anaemia Crisis. J Biomed Sci. 2022;11(10):84.
54. Obeagu EI, Okoroiwu IL, Obeagu GU. Relationship between Thrombopoietin and Interleukin 3: A Review. Int J Curr Res Chem Pharm. Sci. 2022;9(1):7-13.
55. Obeagu EI, Okoroiwu IL, Nwanjo HU, Nwosu DC. Evaluation of interferon-gamma, interleukin 6 and interleukin 10 in tuberculosis patients in Umuahia. Ann Clin Lab Res. 2019;7(2):307.
56. Obeagu EI, Hamisi S, Bunu UO. An update on cytokine storm in covid-19 infection: Pivotal to the survival of the patients. Int. J. Adv. Res. Biol. Sci. 2023;10(3):171-80.
57. Obeagu E, Felix CE, MTB O, Chikodili UM, Nchekwubedi CS, Chinedum OK. Studies on some cytokines, CD4, iron status, hepcidin and some haematological parameters in pulmonary tuberculosis patients based on duration of treatment in Southeast, Nigeria. African Journal of Biological Sciences. 2021;3(1):146-56.
58. Obeagu EI, Amedu GO, Okoroiwu IL, Okafor CJ, Okun O, Ochiabuto OM, Ukeekwe CO. Evaluation of plasma levels of interleukin 6 and iron status of football players in a Nigerian university. Journal of Pharmaceutical Research International. 2021;33(59B):383-8.
59. Obeagu EI, Anierobi CC, Eze GC, Chukwueze CM, Makonyonga RD, Amadi NM, Hassan R. Evaluation of Plasma Levels of Interleukin 6 and Iron Status of Volleyball Players in a Nigerian University. Journal of Advances in Medical and Pharmaceutical Sciences. 2022;24(6):18-23.
60. Obeagu EI, Esimai BN, Ugwu LN, Ramos GF, Adetoye SD, Edupute EC. Neutrophil to Lymphocyte Ratio and Some Cytokines in Pateints with Schizophrenia after Antipsychotic Therapy in Southeast, Nigeria. Asian Journal of Medical Principles and Clinical Practice. 2022;5(4):47-52.
61. Obeagu EI, Johnson AD, Arinze-Anyiam OC, Anyiam AF, Ramos GF, Esimai BN. Neutrophils to Lymphocytes Ratio and Some Cytokines in Patients with Schizophrenia in Southeast, Nigeria. International Journal of Research and Reports in Hematology. 20220;5(2):107-12.
62. Obeagu EI. Gender-based assessment of tumour necrosis factor–alpha and interleukin–6 of patients with Schizophrenia in Nigeria. Int. J. Adv. Res. Biol. Sci. 2022;9(9):29-35.
63. Ifeanyi OE, Vincent CC, Ugochi CM. Studies on some cytokines of apparently healthy Nigerian women aged 10-40 years. Int. J. Curr. Res. Med. Sci. 2019;5(12):24-30.
64. Obeagu EI, Obeagu GU, Guevara ME, Okafor CJ, Bot YS, Eze GC, Amadi NM, Jakheng EW, Uwakwe OS. Evaluation of Plasma Levels of Interleukin 6 and Iron of Volleyball Players Based on Heights and Weight of a Nigerian University Students. Asian Journal of Medicine and Health. 2022;20(10):147-52.
65. Osol G, Ko NL, Mandalà M. Plasticity of the maternal vasculature during pregnancy. Annual review of physiology. 2019; 81:89-111.

66. Bates DO, Hillman NJ, Pocock TM, Neal CR. Regulation of microvascular permeability by vascular endothelial growth factors. Journal of anatomy. 2002;200(5):523-34.
67. Burton GJ, Fowden AL, Thornburg KL. Placental origins of chronic disease. Physiological reviews. 2016;96(4):1509-65.
68. Albrecht ED, Pepe GJ. Estrogen regulation of placental angiogenesis and fetal ovarian development during primate pregnancy. The International journal of developmental biology. 2010;54(2-3):397.
69. Wheeler KC, Jena MK, Pradhan BS, Nayak N, Das S, Hsu CD, Wheeler DS, Chen K, Nayak NR. VEGF may contribute to macrophage recruitment and M2 polarization in the decidua. PloS one. 2018;13(1): e0191040.
70. Chen DB, Zheng J. Regulation of placental angiogenesis. Microcirculation. 2014;21(1):15-25.
71. Ortega MA, Fraile-Martínez O, García-Montero C, Sáez MA, Álvarez-Mon MA, Torres-Carranza D, Álvarez-Mon M, Bujan J, García-Honduvilla N, Bravo C, Guijarro LG. The pivotal role of the placenta in normal and pathological pregnancies: a focus on preeclampsia, fetal growth restriction, and maternal chronic venous disease. Cells. 2022;11(3):568.
72. Kornacki J, Gutaj P, Kalantarova A, Sibiak R, Jankowski M, Wender-Ozegowska E. Endothelial dysfunction in pregnancy complications. Biomedicines. 2021;9(12):1756.
73. Qu H, Khalil RA. Vascular mechanisms and molecular targets in hypertensive pregnancy and preeclampsia. American Journal of Physiology-Heart and Circulatory Physiology. 2020;319(3):H661-81.
74. Pietro L, Daher S, Rudge MV, Calderon ID, Damasceno DC, Sinzato YK, Bandeira CL, Bevilacqua E. Vascular endothelial growth factor (VEGF) and VEGF-receptor expression in placenta of hyperglycemic pregnant women. Placenta. 2010;31(9):770-80.
75. Huang Z, Huang S, Song T, Yin Y, Tan C. Placental angiogenesis in mammals: a review of the regulatory effects of signaling pathways and functional nutrients. Advances in Nutrition. 2021;12(6):2415-34.
76. Laviv Y, Wang JL, Anderson MP, Kasper EM. Accelerated growth of hemangioblastoma in pregnancy: the role of proangiogenic factors and upregulation of hypoxia-inducible factor (HIF) in a non-oxygen-dependent pathway. Neurosurgical Review. 2019; 42:209-26.
77. Xin X, Yang S, Ingle G, Zlot C, Rangell L, Kowalski J, Schwall R, Ferrara N, Gerritsen ME. Hepatocyte growth factor enhances vascular endothelial growth factor-induced angiogenesis in vitro and in vivo. The American journal of pathology. 2001;158(3):1111-20.
78. Jena MK, Sharma NR, Petitt M, Maulik D, Nayak NR. Pathogenesis of preeclampsia and therapeutic approaches targeting the placenta. Biomolecules. 2020;10(6):953.