ISSN 2348-0319 International Journal of Innovative and Applied Research [2023]
(Volume 11, Issue 12)
86-97

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

INTERNATIONAL JOURNAL
OF INNOVATIVE AND APPLIED RESEARCH

RESEARCH ARTICLE

Article DOI:10.58538/IJIAR/2065
DOI URL:*http://dx.doi.org/10.58538/IJIAR/2065*

Exploring the Fascinating Intersection of Immunology and Tissue Regeneration in Pregnancy

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

[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.

Manuscript Info

Manuscript History
Received: 04 November 2023
Final Accepted: 08 December 2023
Published: December 2023

Keywords:
immunology, tissue regeneration, pregnancy, cytokines

Abstract

The immune system's intricate interplay with tissue regeneration during pregnancy stands as a captivating field of scientific inquiry, offering profound insights into both maternal physiology and regenerative medicine. This review synthesizes current knowledge on the multifaceted roles of the immune system in orchestrating tissue repair throughout gestation. From the establishment of pregnancy to fetal development, an array of immune cells, cytokines, and signaling pathways collaborates to create a conducive environment for tissue regeneration. Throughout pregnancy, the immune system demonstrates a delicate equilibrium, balancing tolerance towards the fetus while ensuring protection against pathogens. Key immune cell populations such as macrophages, natural killer cells, and regulatory T cells dynamically contribute to tissue repair by modulating inflammation and promoting angiogenesis. Furthermore, cytokines and growth factors, including interleukins and TGF-β, play pivotal roles in regulating cell behavior and extracellular matrix remodeling, thereby influencing tissue regeneration. Understanding these immune-mediated mechanisms in pregnancy has significant implications for regenerative medicine. Insights gleaned from the unique immune adaptations during gestation offer potential avenues for innovative therapeutic interventions in wound healing, organ regeneration, and various pathological conditions.

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

Introduction:-

Pregnancy is an extraordinary journey marked by intricate physiological adaptations and remarkable transformations within the maternal body. Beyond the miraculous development of a new life, it unveils a captivating interplay between the maternal immune system and the intricate processes of tissue repair and regeneration. This intersection of immunology and tissue biology during gestation constitutes a captivating frontier in both reproductive biology and regenerative medicine [1-6]. The immune system, conventionally recognized for its role in defending the body against pathogens, undergoes a series of finely orchestrated changes during pregnancy. These adaptations are not merely aimed at facilitating tolerance towards the semi-allogeneic fetus but also actively participate in nurturing a microenvironment that fosters tissue repair and regeneration [7-12]. Throughout the stages of pregnancy, from the initial implantation of the embryo to the establishment of the placenta and the subsequent fetal development, a symphony of immune cells, cytokines, and signaling molecules harmoniously collaborate to orchestrate a balance between immune tolerance and protection, while simultaneously promoting tissue healing [13-20].

Immunological cells, such as macrophages, natural killer cells, and regulatory T cells, assume pivotal roles in the modulation of inflammation, facilitation of angiogenesis, and the regulation of tissue microenvironments essential for efficient tissue regeneration. Moreover, the cytokine milieu, including the dynamic interplay of interleukins, growth factors, and TGF-β, intricately governs cellular behaviors, influencing tissue remodeling and repair mechanisms during pregnancy [21-30]. The comprehension of these intricate immune-mediated mechanisms not only unveils the marvels of maternal-fetal immunology but also holds immense promise for advancing our understanding of tissue regeneration. It offers a unique vantage point for exploring novel therapeutic strategies in regenerative medicine, opening doors to potential breakthroughs in treating various pathological conditions characterized by impaired tissue repair.

Role of the Immune System in Pregnancy

The role of the immune system in pregnancy is a complex and finely tuned orchestration aimed at supporting the physiological changes required for successful gestation while protecting both the mother and the developing fetus. Traditionally, the immune system's primary function involves defending the body against pathogens and foreign entities. However, during pregnancy, this system undergoes intricate adaptations to facilitate tolerance toward the fetus while maintaining the ability to respond to potential threats [31-40]. One of the most remarkable features of pregnancy is the immune system's ability to tolerate a semi-allogeneic fetus. The mother's immune system must modulate its responses to prevent rejection of the genetically different fetal tissues, which express paternal antigens. This tolerance involves a delicate balance between immune activation and suppression, orchestrated by various immune cells and regulatory molecules [41-50]. Throughout pregnancy, different subsets of immune cells, including macrophages, natural killer (NK) cells, dendritic cells, and regulatory T cells (Tregs),

play pivotal roles. Macrophages contribute to tissue repair, angiogenesis, and the maintenance of a tolerogenic environment. NK cells are involved in promoting placental development and function while regulating immune responses at the maternal-fetal interface. Tregs, crucial for immune tolerance, help prevent immune reactions against fetal antigens [51-52]. Cytokines, such as interleukins and TGF-β, exhibit intricate regulatory roles during pregnancy. They modulate immune cell functions, control inflammation, and influence tissue remodeling. Additionally, hormonal changes, especially those related to progesterone and estrogen, contribute to immune regulation and tolerance maintenance [53-66]. The placenta serves as the interface between maternal and fetal tissues and plays a crucial role in immune modulation. It secretes various molecules that establish an immunologically unique environment, preventing the mother's immune system from rejecting the fetus while safeguarding against infections [67. Dysregulation of immune responses during pregnancy can lead to complications such as miscarriage, preterm birth, preeclampsia, and fetal growth restriction. Understanding the immune mechanisms involved in these complications is crucial for developing preventive and therapeutic strategies. In essence, the immune system in pregnancy operates in a highly regulated manner to support fetal development while ensuring maternal health. Its ability to maintain tolerance toward the fetus while protecting against infections showcases the remarkable adaptability and complexity of the maternal immune response during gestation. Further research into these immunological mechanisms holds promise for improving pregnancy outcomes and advancing our understanding of immune-mediated tissue regeneration, offering potential avenues for therapeutic interventions in both maternal and fetal health.

Immune Cells and Tissue Repair

During pregnancy, the immune system's orchestration of various immune cell populations is crucial for tissue repair and regeneration. These immune cells actively participate in creating a microenvironment conducive to healing and supporting the physiological changes required for successful gestation [68]. These versatile immune cells are involved in virtually every stage of tissue repair. During pregnancy, macrophages exhibit phenotypic plasticity, shifting between pro-inflammatory (M1) and anti-inflammatory (M2) states as required. M2 macrophages are particularly important in promoting tissue healing by regulating inflammation, supporting angiogenesis (formation of new blood vessels), and clearing cellular debris, thus facilitating placental development and remodeling of maternal tissues [69]. NK cells play diverse roles in pregnancy, particularly at the maternal-fetal interface. These cells help in regulating blood flow to the placenta, supporting trophoblast invasion (a crucial step in placental development), and influencing the immune environment by secreting various cytokines and growth factors. Their balanced activity is essential for successful pregnancy outcomes. Tregs are a subset of T cells known for their immunosuppressive properties. During pregnancy, Tregs play a critical role in maintaining immune tolerance toward the fetus by suppressing excessive immune responses against fetal antigens. They help prevent immune-mediated damage to fetal tissues and contribute to establishing an immunotolerant environment at the maternal-fetal interface. These antigen-presenting cells are essential in immune surveillance and activation. In pregnancy, dendritic cells contribute to immune tolerance by presenting fetal antigens to maternal immune cells in a way that doesn't provoke an aggressive immune response against the fetus. They participate in the establishment of immune tolerance while balancing the need to protect against infections. These cells also contribute to the immune response during pregnancy, although their

specific roles in tissue repair and regeneration are less understood compared to macrophages, NK cells, and Tregs. The collaborative efforts of these immune cell populations are crucial for successful tissue repair and remodeling in pregnancy. They create an environment that allows for maternal tissue adaptations necessary to accommodate the growing fetus and support placental development. Moreover, the immune cells at the maternal-fetal interface participate in the intricate dialogue between the maternal immune system and the semi-allogeneic fetus, ensuring immune tolerance while safeguarding against potential threats to maternal and fetal health. Understanding the dynamics of these immune cells and their contributions to tissue repair during pregnancy is essential not only for reproductive biology but also for advancing our knowledge of immune-mediated regenerative processes in various health contexts.

Cytokine Signaling and Tissue Remodeling

Cytokines, a diverse group of signaling molecules produced by various cells in the body, play pivotal roles in mediating tissue remodeling during pregnancy. These molecules are essential in regulating immune responses, inflammation, cell proliferation, differentiation, and tissue repair. Throughout gestation, cytokine signaling contributes significantly to the dynamic changes required for successful pregnancy and tissue regeneration [70]. Interleukins are a group of cytokines involved in modulating immune responses and cell communication. It helps in suppressing excessive immune responses that might harm the developing fetus. IL-6, on the other hand, has pleiotropic effects and plays a role in inflammation and tissue regeneration.[71] Transforming Growth Factor-Beta (TGF-β)is a multifunctional cytokine involved in various cellular processes, including cell growth, differentiation, and immune regulation. During pregnancy, TGF-β plays a critical role in promoting tissue repair and remodeling. It regulates immune cell function, supports the development of maternal-fetal tolerance, and contributes to maintaining tissue homeostasis in the placenta and other maternal tissues [72]. Tumor Necrosis Factor (TNF) is involved in inflammation and immune regulation. Although excessive TNF can be harmful during pregnancy and contribute to complications like preterm birth or preeclampsia, controlled levels of TNF are important for tissue repair processes. It contributes to the regulation of immune responses and tissue remodeling necessary for proper placental development and maternal adaptations to pregnancy. Various other cytokines and growth factors, such as vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF), also participate in tissue repair and angiogenesis during pregnancy. These molecules promote blood vessel formation, support tissue growth, and contribute to the structural changes required for successful gestation. The intricate balance and interactions among these cytokines and growth factors are crucial for regulating immune responses and tissue remodeling during pregnancy. They coordinate cellular behaviors, including cell proliferation, differentiation, and extracellular matrix remodeling, thereby influencing tissue repair and regeneration.

Impact on Regenerative Medicine

The profound insights gained from understanding the immune system's role in tissue regeneration during pregnancy have significant implications for the field of regenerative medicine. Pregnancy serves as a natural model where the immune system orchestrates controlled tissue repair and remodeling to support fetal development. These insights offer promising avenues for therapeutic interventions aimed at enhancing tissue regeneration beyond the context

of pregnancy. Studying the immune-mediated tissue repair mechanisms during pregnancy provides valuable insights into the intricate cellular and molecular processes involved in regeneration. This knowledge forms a foundational understanding of how immune cells, cytokines, and growth factors collaborate to create an environment conducive to tissue repair [73]. Insights gleaned from pregnancy-related tissue regeneration mechanisms offer potential therapeutic strategies for various pathological conditions characterized by impaired tissue repair. Applying the principles observed in pregnancy could inspire novel regenerative therapies for wound healing, tissue injuries, degenerative diseases, and conditions where tissue regeneration is compromised. Learning from the immune-driven tissue repair processes in pregnancy could inspire bioengineering approaches that mimic these mechanisms. Biomaterials and scaffolds designed to replicate the immune microenvironment observed during gestation may facilitate tissue regeneration in clinical settings. Manipulating immune responses, akin to the immunological adaptations in pregnancy, might be employed in regenerative medicine. Modulating immune cell behavior, cytokine signaling, or promoting immune tolerance could potentially enhance tissue regeneration and improve outcomes in regenerative therapies. Targeting specific immune cells, cytokines, or signaling pathways identified in pregnancy-related tissue repair may lead to the development of targeted therapies for regenerative purposes. Tailored interventions could facilitate tissue repair in a more precise and efficient manner. Translating findings from pregnancy-related immune-mediated tissue repair into clinical applications holds promise for addressing challenging clinical scenarios where tissue regeneration remains a significant hurdle, such as in chronic wounds, organ transplantation, and degenerative diseases. Overall, understanding the immune system's role in tissue regeneration during pregnancy offers a wealth of knowledge that could revolutionize regenerative medicine. Translating these findings into innovative therapies holds the potential to significantly improve clinical outcomes and address the unmet needs in tissue repair and regeneration across various medical disciplines.

Challenges and Future Direction

While remarkable progress has been made in understanding the immune system's role in tissue regeneration during pregnancy, several challenges persist, and future directions in research aim to address these complexities. Despite advances, the precise molecular mechanisms underlying immune-mediated tissue repair in pregnancy remain incompletely understood. Further research is needed to unravel the intricate signaling pathways, gene regulatory networks, and interactions among immune cells and cytokines involved in facilitating tissue regeneration. Understanding the temporal and spatial dynamics of immune cell responses and cytokine signaling during different stages of pregnancy-related tissue repair is crucial. Investigating how these dynamics vary across gestational periods and in different tissue microenvironments will provide a more comprehensive understanding. Harnessing the immune system for therapeutic interventions in regenerative medicine requires a deeper understanding of how to precisely manipulate immune responses without triggering adverse effects. Research focusing on targeted immunomodulation strategies tailored for specific tissue regeneration contexts is warranted. Bridging the gap between basic research findings and clinical applications is a key challenge. Translating the knowledge gained from pregnancy-related immune-mediated tissue repair into practical regenerative therapies requires extensive preclinical studies and validation in human clinical trials. Ensuring the safety and efficacy of immune-based regenerative therapies is paramount.

Comprehensive studies addressing the potential risks, long-term effects, and immunological responses associated with these interventions are essential before their widespread clinical implementation. Considering the diversity among individuals and the variability in immune responses during pregnancy is crucial. Future studies should encompass diverse populations to better understand how different genetic, environmental, and health factors influence immune-mediated tissue repair processes. Collaboration among immunologists, obstetricians, tissue engineers, and clinicians is imperative to combine expertise from various disciplines. This collaborative approach will foster a more comprehensive understanding and facilitate the development of innovative strategies in regenerative medicine. Leveraging advanced technologies, such as single-cell sequencing, imaging modalities, and organoid models, can provide deeper insights into immune cell behaviors and tissue regeneration processes in pregnancy. Developing more sophisticated model systems that mimic the complexity of pregnancy-related tissue repair will be invaluable.

Conclusion

The intricate interplay between the immune system and tissue regeneration during pregnancy stands as a captivating frontier, offering profound insights into both maternal physiology and regenerative medicine. Throughout gestation, the immune system orchestrates a delicate balance between immune tolerance towards the semi-allogeneic fetus and the imperative need for tissue repair and regeneration. This finely tuned immunological response involves a diverse array of immune cells, cytokines, and signaling pathways collaborating to create a conducive environment for successful pregnancy and maternal tissue remodeling.

The collaborative efforts of interdisciplinary research, leveraging advanced technologies, and fostering diverse perspectives are integral in unlocking the full potential of immune-based strategies in regenerative medicine. By addressing these challenges and pursuing these future directions, we can aspire to revolutionize therapeutic interventions, offering novel avenues for enhancing tissue repair, improving patient outcomes, and transforming the landscape of regenerative medicine across a spectrum of health conditions. Ultimately, the elucidation of the immune system's role in tissue regeneration during pregnancy not only deepens our understanding of the complexities of human biology but also holds the promise of translating this knowledge into transformative therapies that benefit patients worldwide.

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. 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.
12. 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.
13. 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.
14. 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.
15. 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.
16. 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.

17. 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
18. 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.
19. 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.
20. 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.
21. Shanley LC, Mahon OR, Kelly DJ, Dunne A. Harnessing the innate and adaptive immune system for tissue repair and regeneration: Considering more than macrophages. Acta Biomaterialia. 2021; 133:208-21.
22. Obeagu EI. Gestational Thrombocytopaenia. J Gynecol Women's Health. 2023;25(3):556163.links/64b01aa88de7ed28ba95fccb/Gestational-Thrombocytopaenia.pdf.
23. 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.
24. 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 Feb 23;33(4):10-9.
25. 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
26. 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.
27. 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.
28. 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.
29. 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.
30. Obeagu EI, Ofodile AC, Okwuanaso CB. A review of urinary tract infections in pregnant women: Risks factors. J Pub Health Nutri. 2023; 6 (1):26-35.links/63c3a9116fe15d6a571e8bba/A-review-of-urinary-tract-infections-in-pregnant-women-Risks-factors.pdf.
31. Maxwell AJ, You Y, Aldo PB, Zhang Y, Ding J, Mor G. The role of the immune system during pregnancy: General concepts. InReproductive Immunology 2021: 1-21. Academic Press.
32. 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
33. 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
34. 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.
35. 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
36. 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
37. 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.
38. Obeagu EI, Njar VE, Obeagu GU. Infertility: Prevalence and Consequences. Int. J. Curr. Res. Chem. Pharm. Sci. 2023;10(7):43-50.
39. 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.
40. 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
41. Robertson SA, Petroff MG, Hunt JS. Immunology of pregnancy. Australia USA. 2015; 2:1835-74.
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. Yang F, Zheng Q, Jin L. Dynamic function and composition changes of immune cells during normal and pathological pregnancy at the maternal-fetal interface. Frontiers in immunology. 2019; 10:2317.
52. 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.
53. Yang D, Dai F, Yuan M, Zheng Y, Liu S, Deng Z, Tan W, Chen L, Zhang Q, Zhao X, Cheng Y. Role of transforming growth factor-β1 in regulating fetal-maternal immune tolerance in normal and pathological pregnancy. Frontiers in Immunology. 2021; 12:689181.
54. 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.
55. 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.
56. 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.

57. 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.
58. 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.
59. 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.
60. 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.
61. 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.
62. 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.
63. 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. 2022;5(2):107-12.
64. 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.
65. 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.
66. 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.
67. Schumacher A, Sharkey DJ, Robertson SA, Zenclussen AC. Immune cells at the fetomaternal interface: how the microenvironment modulates immune cells to foster fetal development. The Journal of Immunology. 2018;201(2):325-34.
68. Tsai SL. The molecular interplay between progenitors and immune cells in tissue regeneration and homeostasis. Journal of Immunology and Regenerative Medicine. 2020; 7:100024.
69. Parasar P, Guru N, Nayak NR. Contribution of macrophages to fetomaternal immunological tolerance. Human immunology. 2021;82(5):325-31.
70. Yockey LJ, Iwasaki A. Interferons and proinflammatory cytokines in pregnancy and fetal development. Immunity. 2018;49(3):397-412.
71. Cheng SB, Sharma S. Interleukin-10: a pleiotropic regulator in pregnancy. American Journal of Reproductive Immunology. 2015;73(6):487-500.

72. Latifi Z, Nejabati HR, Abroon S, Mihanfar A, Farzadi L, Hakimi P, Hajipour H, Nouri M, Fattahi A. Dual role of TGF-β in early pregnancy: clues from tumor progression. Biology of reproduction. 2019;100(6):1417-30.
73. Godwin JW, Rosenthal N. Scar-free wound healing and regeneration in amphibians: immunological influences on regenerative success. Differentiation. 2014;87(1-2):66-75.