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Placental Malaria: Implications for Intrauterine Growth Restriction

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Abstract

Placental malaria, characterized by Plasmodium parasites infecting the placenta, poses significant risks to maternal and fetal health, particularly in malaria-endemic regions. This review investigates the impact of placental malaria on intrauterine growth restriction (IUGR), a condition where the fetus does not grow adequately in the womb. The association between placental malaria and IUGR is well-documented, with evidence indicating that malaria-induced placental inflammation, vascular dysfunction, and oxidative stress can impair fetal growth and lead to adverse neonatal outcomes. Epidemiological studies have consistently shown a higher incidence of IUGR among infants born to mothers with placental malaria. The review examines biological mechanisms through which placental malaria contributes to IUGR, including compromised placental blood flow, nutrient deficiencies, and oxidative damage. These mechanisms disrupt the normal development and growth of the fetus, leading to low birth weight and increased risks of neonatal morbidity. Addressing placental malaria and its impact on IUGR requires effective public health strategies, including the implementation of intermittent preventive treatment during pregnancy, the use of insecticide-treated bed nets, and timely diagnosis and treatment of malaria. Additionally, improving maternal nutrition can help mitigate some of the adverse effects of placental malaria.

Keywords: *Placental Malaria, Intrauterine Growth Restriction, Malaria in Pregnancy, Placental Dysfunction, Fetal Growth*

Introduction

Malaria remains a critical global health issue, particularly in regions where the disease is endemic. Pregnant women are particularly vulnerable to malaria, which can lead to severe complications for both the mother and her fetus. One of the most concerning outcomes of malaria during pregnancy is placental malaria, a condition where Plasmodium parasites infect the placenta. This condition can have profound implications for fetal development, including a notable risk for intrauterine growth restriction (IUGR), where the fetus fails to grow adequately in the womb. Understanding

the relationship between placental malaria and IUGR is crucial for improving maternal and neonatal health outcomes. Placental malaria is defined by the presence of Plasmodium parasites within the placenta, which can lead to placental inflammation and dysfunction. The prevalence of placental malaria is closely linked to the incidence of malaria in pregnant women and varies by geographic region, with the highest rates observed in sub-Saharan Africa. Studies have shown that placental malaria affects a significant proportion of pregnant women in endemic areas, highlighting the urgent need for targeted interventions to address this issue. IUGR is a condition where the fetus does not achieve its expected growth potential, leading to reduced birth weight and increased risk of neonatal complications. IUGR can be caused by various factors, including maternal health conditions, nutritional deficiencies, and infections. Placental malaria is increasingly recognized as a significant contributor to IUGR. Infants born to mothers with placental malaria are at a higher risk of being born with IUGR, which can result in long-term health challenges and developmental delays.[1-10]

The biological mechanisms through which placental malaria leads to IUGR involve several interrelated factors. Placental malaria often causes inflammation and damage to the placental tissue, impairing its ability to effectively transport nutrients and oxygen to the fetus. Additionally, malaria-induced oxidative stress and vascular dysfunction in the placenta can further restrict fetal growth. Understanding these mechanisms is essential for developing effective strategies to mitigate the impact of placental malaria on fetal development. The consequences of IUGR are far-reaching and can affect both immediate and long-term neonatal health. Infants with IUGR are at increased risk for preterm birth, respiratory distress syndrome, and other neonatal complications. Furthermore, IUGR has been associated with an increased risk of chronic health conditions later in life, including cardiovascular disease and metabolic disorders. Addressing the underlying causes of IUGR, such as placental malaria, is crucial for improving neonatal health outcomes and reducing the burden of these long-term health issues. Addressing placental malaria and its impact on IUGR presents several public health challenges. In malaria-endemic regions, where healthcare resources may be limited, ensuring that pregnant women receive adequate preventive care and treatment for malaria is critical. Efforts to improve access to intermittent preventive treatment (IPT), insecticide-treated bed nets, and timely malaria diagnosis and treatment are essential for reducing the incidence of placental malaria and its associated complications. Current strategies for preventing and managing placental malaria include the use of IPT with antimalarial drugs during pregnancy, distribution of insecticide-treated bed nets, and prompt treatment of malaria infections. These interventions aim to reduce the prevalence of placental malaria and improve pregnancy outcomes. However, despite these efforts, challenges remain in ensuring widespread implementation and adherence to these preventive measures, particularly in resource-limited settings.[11-20]

Epidemiological Evidence

The epidemiological evidence linking placental malaria to intrauterine growth restriction (IUGR) provides valuable insights into the scope and impact of this association. Multiple studies have investigated how placental malaria affects fetal growth, revealing a consistent pattern of increased risk for IUGR among infants born to mothers with placental malaria. Several epidemiological

studies have documented the prevalence of placental malaria and its association with IUGR. For instance, research conducted in sub-Saharan Africa, a region with high malaria transmission rates, consistently finds a higher incidence of IUGR among infants born to mothers with placental malaria. The strength of the association between placental malaria and IUGR can vary depending on geographic region and study design. Research indicates that the prevalence and impact of placental malaria-related IUGR are influenced by factors such as local malaria transmission rates, the timing of malaria infections during pregnancy, and the presence of other co-infections or health conditions. For example, studies from West Africa, where malaria is highly endemic, often report higher rates of IUGR associated with placental malaria compared to regions with lower malaria transmission. The timing of malaria infection during pregnancy plays a crucial role in determining its impact on fetal growth. Studies have shown that malaria infections early in pregnancy may have different effects compared to infections later in gestation. Additionally, the severity of placental malaria, including the density of parasitic infection and the extent of placental damage, is associated with increased risk of IUGR. Severe placental malaria infections are more likely to lead to significant fetal growth restriction.[21-30]

Maternal factors such as age, nutritional status, and socio-economic conditions can also influence the relationship between placental malaria and IUGR. Research has shown that younger maternal age, poor nutritional status, and low socio-economic status are associated with higher risks of both placental malaria and IUGR. Longitudinal and cohort studies have provided robust evidence on the impact of placental malaria on fetal growth over time. For instance, the Malaria in Pregnancy Consortium conducted a large cohort study in several malaria-endemic countries and found a consistent association between placental malaria and IUGR across different settings. These studies have demonstrated that infants born to mothers with placental malaria have a higher likelihood of being born with restricted growth compared to their peers. The implementation of malaria prevention and control measures, such as intermittent preventive treatment (IPT) and insecticide-treated bed nets, has influenced the prevalence of placental malaria and its associated effects. Studies evaluating the impact of these interventions have shown that effective malaria control can reduce the incidence of placental malaria and, consequently, the risk of IUGR. Co-infections and comorbidities can complicate the relationship between placental malaria and IUGR. Studies have found that the presence of other infections, such as HIV or syphilis, can exacerbate the impact of placental malaria on fetal growth. The epidemiological evidence underscores the need for effective public health strategies to prevent and manage placental malaria and its impact on IUGR. Policymakers should prioritize malaria prevention programs, including IPT and bed net distribution, and ensure access to timely malaria treatment for pregnant women. Addressing the broader socio-economic factors that contribute to malaria and IUGR is also crucial for improving health outcomes.[31-40]

Biological Mechanisms

The biological mechanisms through which placental malaria contributes to intrauterine growth restriction (IUGR) involve a complex interplay of inflammation, vascular dysfunction, oxidative stress, and nutritional deficiencies. Understanding these mechanisms is crucial for developing effective strategies to mitigate the adverse effects of placental malaria on fetal development. One

of the primary mechanisms linking placental malaria to IUGR is placental inflammation. Plasmodium parasites infecting the placenta induce a strong inflammatory response, characterized by the recruitment of immune cells such as monocytes, macrophages, and T cells to the placental tissue. This inflammatory response can lead to the release of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which disrupt placental function. The inflammatory process can cause structural damage to the placenta, including the formation of syncytial knots and fibrin deposition, which can interfere with nutrient and oxygen transfer from the mother to the fetus. This placental dysfunction results in inadequate fetal growth, contributing to the development of IUGR. Malaria infection in the placenta can severely affect its vascular system. The placental vasculature is responsible for ensuring the efficient exchange of oxygen and nutrients between the mother and the fetus. Plasmodium-induced changes in the placental blood vessels, such as the formation of obstructive structures and the deposition of fibrin, can impair blood flow and reduce the delivery of essential nutrients to the fetus. Studies have shown that placental malaria is associated with increased levels of syncytial knots, which are abnormal accumulations of trophoblastic cells that can obstruct blood vessels and hinder placental perfusion. This impaired vascular function leads to reduced oxygen and nutrient supply to the fetus, resulting in IUGR.[41-50]

Oxidative stress, characterized by the excessive production of reactive oxygen species (ROS), is another key mechanism through which placental malaria affects fetal growth. Plasmodium infection induces oxidative stress in the placenta by generating ROS as a byproduct of the parasite's metabolic activities. These ROS can cause damage to placental cells and disrupt their normal function. Oxidative stress can impair the integrity of the placental barrier, leading to increased damage to fetal tissues and further compromising fetal growth. Additionally, oxidative stress is associated with increased levels of placental apoptosis (programmed cell death), which can exacerbate placental dysfunction and contribute to IUGR. Placental malaria can lead to maternal nutritional deficiencies and metabolic alterations that impact fetal growth. Malaria infection increases the metabolic demands on the mother, leading to reduced availability of essential nutrients such as iron, folate, and zinc. These nutrients are critical for fetal development and growth, and deficiencies can exacerbate the risk of IUGR. Iron deficiency, in particular, is commonly observed in pregnant women with malaria and can lead to anemia, which further reduces oxygen delivery to the fetus and impairs fetal growth. Additionally, malaria-induced changes in maternal metabolism can affect the availability of other nutrients necessary for normal fetal development. The placental immune response to malaria infection can affect fetal growth by disrupting the normal balance of immune regulation. Infected placentas often exhibit altered expression of immune-related genes and increased production of inflammatory mediators. This altered immune response can affect the placental microenvironment and impair its ability to support healthy fetal growth. For instance, increased levels of pro-inflammatory cytokines and chemokines can contribute to placental tissue damage and impaired nutrient transfer. Additionally, altered immune regulation may affect the ability of the placenta to adapt to malaria-induced stress, further compromising fetal growth.[51-60]

The integrity of the placental barrier, which separates maternal and fetal blood supplies, is essential for maintaining a healthy pregnancy. Plasmodium infection can disrupt the placental barrier by

causing structural changes in the trophoblast layer and increasing the permeability of the placenta. This disruption can lead to the leakage of harmful substances and further exacerbate fetal growth restriction. Disruption of the placental barrier also affects the transport of essential nutrients and oxygen to the fetus, contributing to the development of IUGR. The compromised barrier function may also allow for the entry of inflammatory mediators and parasites into the fetal circulation, further impacting fetal health. Genetic and epigenetic factors may play a role in the susceptibility of the placenta and fetus to malaria-induced growth restriction. Variations in genes related to immune response, inflammation, and oxidative stress can influence how the placenta responds to malaria infection and its impact on fetal growth. Epigenetic modifications, such as changes in DNA methylation and histone modification, may also affect placental gene expression and function in response to malaria infection. These modifications can have long-term effects on fetal development and contribute to the risk of IUGR. Co-infections and comorbid conditions can interact with placental malaria to exacerbate its effects on fetal growth. For example, the presence of other infections, such as HIV or syphilis, can compound the inflammatory and nutritional impacts of placental malaria. Additionally, pre-existing maternal health conditions, such as diabetes or hypertension, may influence the severity of placental malaria and its impact on IUGR. The effects of placental malaria and IUGR may extend beyond the immediate neonatal period. Infants born with IUGR due to placental malaria are at increased risk for long-term health issues, including developmental delays, cognitive impairments, and chronic diseases. Understanding the mechanisms through which placental malaria affects long-term fetal development is important for addressing the broader implications of IUGR.[61-70]

Implications for Maternal and Neonatal Health

Intrauterine growth restriction (IUGR) associated with placental malaria has significant implications for neonatal health. Infants born with IUGR are at a heightened risk of immediate complications, including preterm birth, respiratory distress syndrome, and difficulties with thermoregulation. These conditions arise due to the compromised growth and development of the fetus, which impacts its ability to adapt to the extrauterine environment. Additionally, IUGR infants are more likely to experience low birth weight, which is a critical determinant of neonatal morbidity and mortality. The effects of IUGR extend beyond the neonatal period and can have lasting consequences for long-term health. Research indicates that IUGR infants face an increased risk of developing chronic health conditions later in life. These include cardiovascular diseases, metabolic disorders such as obesity and type 2 diabetes, and neurodevelopmental delays. The early-life challenges associated with IUGR can contribute to a higher prevalence of these conditions in adulthood, a phenomenon known as the “developmental origins of health and disease” (DOHaD). Maternal health is also impacted by placental malaria and the resulting IUGR. Placental malaria can exacerbate existing maternal health issues and increase the likelihood of obstetric complications. For instance, malaria-induced anemia, a common issue in pregnant women with placental malaria, can lead to fatigue, increased risk of hemorrhage, and complications during delivery. Moreover, the presence of IUGR in the fetus often necessitates more intensive monitoring and management, which can add to the maternal healthcare burden.[71-75]

Placental malaria and associated IUGR are linked to an increased risk of preterm birth. Preterm infants, defined as those born before 37 weeks of gestation, face a higher incidence of complications such as respiratory distress syndrome, intraventricular hemorrhage, and infections. The need for preterm delivery in cases of severe IUGR can complicate the neonatal course and increase the likelihood of adverse outcomes. IUGR resulting from placental malaria can impair neonatal growth and developmental milestones. IUGR infants often experience delays in physical and cognitive development compared to their peers. Early interventions and follow-up care are essential to address developmental delays and support optimal growth. However, the challenges associated with IUGR can place additional strain on healthcare resources and support systems. The healthcare system faces a significant burden due to the complications arising from placental malaria and IUGR. Managing the additional needs of IUGR infants, including specialized neonatal care and early developmental interventions, requires resources and expertise. Additionally, the increased risk of maternal complications can place additional demands on healthcare providers, necessitating comprehensive care approaches to manage both maternal and neonatal health effectively. The public health implications of placental malaria and IUGR highlight the need for effective malaria control strategies and maternal health interventions. Public health initiatives should focus on reducing malaria transmission, improving access to intermittent preventive treatment (IPT) and insecticide-treated bed nets, and ensuring timely diagnosis and treatment of malaria in pregnant women. Addressing these factors can help reduce the incidence of placental malaria and its associated complications, including IUGR. Nutritional support and socio-economic factors play a crucial role in mitigating the impact of placental malaria and IUGR. Ensuring adequate maternal nutrition and addressing socio-economic disparities can help reduce the risk of IUGR and improve overall health outcomes. Programs aimed at improving maternal nutrition, especially in malaria-endemic regions, are essential for supporting fetal growth and development. Integrated care approaches that address both malaria prevention and management, as well as maternal and neonatal health, are essential for improving outcomes. Collaboration between public health authorities, healthcare providers, and community organizations can enhance the effectiveness of malaria control programs and ensure comprehensive care for pregnant women and their infants.[76-80]

Prevention and Treatment Strategies

Intermittent preventive treatment (IPT) is a cornerstone of malaria prevention in pregnant women. IPT involves administering antimalarial medication at scheduled intervals during pregnancy, regardless of whether the woman shows symptoms of malaria. The World Health Organization (WHO) recommends IPT with sulfadoxine-pyrimethamine (SP) in areas where malaria transmission is moderate to high. IPT helps reduce the incidence of placental malaria and its associated complications, including IUGR. Regular implementation of IPT can significantly decrease the prevalence of placental malaria and improve maternal and fetal health outcomes. Insecticide-treated bed nets (ITNs) are a crucial preventive measure against malaria transmission. ITNs provide a barrier between the pregnant woman and malaria-carrying mosquitoes, reducing the risk of infection. The widespread distribution and use of ITNs have been shown to lower the incidence of malaria and placental malaria in pregnant women. Public health campaigns promoting the use of ITNs and ensuring their availability in malaria-endemic regions are essential for

preventing malaria during pregnancy and reducing the risk of IUGR. Early diagnosis and prompt treatment of malaria are vital for managing placental malaria and preventing its complications. Pregnant women with suspected malaria should undergo rapid diagnostic tests (RDTs) or microscopy to confirm the presence of Plasmodium parasites. Once diagnosed, appropriate antimalarial treatment should be administered based on the local guidelines and drug resistance patterns. Effective treatment not only addresses the immediate infection but also helps prevent the progression to placental malaria and its impact on fetal growth. Improving maternal health and nutrition is critical for reducing the impact of placental malaria and IUGR. Nutritional supplementation, including iron, folate, and other essential vitamins and minerals, can help mitigate the effects of malaria-related anemia and support fetal growth. Programs aimed at enhancing maternal nutrition, particularly in malaria-endemic regions, can help reduce the risk of IUGR and improve overall pregnancy outcomes. Health education on balanced diets and access to nutritional supplements should be integrated into antenatal care services.[81-83]

Enhanced antenatal care is essential for monitoring and managing the health of pregnant women at risk of malaria. Regular antenatal visits allow for early detection of malaria and its complications, including signs of IUGR. Healthcare providers should assess maternal and fetal health through routine screenings, including ultrasound examinations to monitor fetal growth. Close monitoring and timely interventions can help address any issues related to placental malaria and IUGR, ensuring better health outcomes for both mother and baby. Research into malaria vaccination offers promising potential for preventing malaria during pregnancy. The RTS,S/AS01 vaccine, while primarily targeted at young children, is an example of ongoing efforts to develop effective malaria vaccines. Future research and development of vaccines specifically for pregnant women could provide an additional tool for preventing placental malaria and reducing the risk of IUGR. Continued investment in vaccine research is crucial for advancing malaria control strategies. Drug resistance is a growing concern in malaria treatment, which can impact the effectiveness of prevention and treatment strategies. Monitoring and addressing drug resistance is essential for maintaining the efficacy of antimalarial medications. Strategies to combat drug resistance include the development of new antimalarial drugs, ensuring proper treatment adherence, and using combination therapies. Public health efforts should focus on maintaining drug efficacy and adapting treatment guidelines based on resistance patterns. Community-based interventions play a vital role in malaria prevention and management. Community health workers can facilitate the distribution of ITNs, provide education on malaria prevention, and offer screening and treatment services. Engaging communities in malaria control efforts and promoting health-seeking behaviors can enhance the effectiveness of prevention and treatment strategies. Community involvement is essential for addressing barriers to access and ensuring that interventions reach the populations most at risk.[84-87]

Integrating malaria prevention and treatment with broader maternal and child health programs can improve the effectiveness of interventions. Combining malaria control measures with antenatal care, maternal nutrition programs, and child health services can provide a comprehensive approach to addressing the health needs of pregnant women and their infants. This integrated approach helps ensure that malaria prevention is part of a holistic strategy for improving maternal and neonatal health. Effective policy and advocacy are crucial for supporting malaria prevention and treatment

efforts. Governments, international organizations, and non-governmental organizations (NGOs) should advocate for increased funding, resources, and support for malaria control programs. Policy initiatives should focus on improving access to IPT, ITNs, and prompt treatment, as well as addressing the socio-economic factors that contribute to malaria risk. Collaborative efforts and sustained commitment are essential for reducing the burden of placental malaria and its impact on IUGR.[88-89]

Conclusion

Placental malaria remains a significant global health challenge, particularly in malaria-endemic regions where it profoundly impacts maternal and neonatal health. The association between placental malaria and intrauterine growth restriction (IUGR) underscores the urgent need for effective prevention and management strategies to mitigate the adverse effects of this condition. The review highlights the complex interplay of biological mechanisms, including placental inflammation, vascular dysfunction, oxidative stress, and nutritional deficiencies, which contribute to impaired fetal growth and increased risk of IUGR.

Effective prevention strategies such as intermittent preventive treatment (IPT) with antimalarial drugs, the use of insecticide-treated bed nets (ITNs), and prompt diagnosis and treatment of malaria are essential for reducing the prevalence of placental malaria and its associated complications. These measures, coupled with enhanced antenatal care and maternal nutritional support, play a crucial role in improving pregnancy outcomes and reducing the incidence of IUGR. The implications of placental malaria and IUGR extend beyond immediate neonatal health, impacting long-term growth and development, as well as posing challenges to healthcare systems and public health policies. Addressing these challenges requires a multi-faceted approach that integrates malaria control efforts with broader maternal and child health programs. Public health initiatives should prioritize the implementation of effective malaria prevention and treatment strategies while also addressing socio-economic factors that contribute to the risk of malaria and IUGR.

References

1. Uneke CJ. Impact of placental Plasmodium falciparum malaria on pregnancy and perinatal outcome in sub-Saharan Africa: part III: placental malaria, maternal health, and public health. The Yale journal of biology and medicine. 2008;81(1):1.
2. Gontie GB, Wolde HF, Baraki AG. Prevalence and associated factors of malaria among pregnant women in Sherkole district, Benishangul Gumuz regional state, West Ethiopia. BMC Infectious Diseases. 2020; 20:1-8.
3. 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.
4. 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.

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. links/608a6728a6fdccaebdf52d94/Assessment-of-Haematological-Changes-in-Pregnant-Women-of-Ido-Ondo.pdf.
6. 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.
7. 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.
8. 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. 2022;2(2):1-9.
9. Bonilla FA, Oettgen HC. Adaptive immunity. Journal of Allergy and Clinical Immunology. 2010;125(2): S33-40.
10. 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.
11. Obeagu EI, Ibeh NC, Nwobodo HA, Ochei KC, Iwegbulam CP. Haematological indices of malaria patients coinfected with HIV in Umuahia. Int. J. Curr. Res. Med. Sci. 2017;3(5):100-104.
12. Feeney ME. The immune response to malaria in utero. Immunological reviews. 2020 ;293(1):216-229.
13. Opeyemi AA, Obeagu EI. Regulations of malaria in children with human immunodeficiency virus infection: A review. Medicine. 2023;102(46): e36166.
14. Obeagu EI, Chijioke UO, Ekelozie IS. Malaria rapid diagnostic test (RDTs). Ann Clin Lab Res. 2018;6(4):275.
15. Ogomaka IA, Obeagu EI. Methods of Breast Feeding as Determinants of Malaria Infections among Babies in IMO State, Nigeria. International Journal of Medical Science and Dental Research. 2019;2(01):17-24.
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. 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). 2022:936-941.

18. Obeagu EI, Obeagu GU, Egba SI, Emeka-Obi OR. Combatting Anemia in Pediatric Malaria: Effective Management Strategies. Int. J. Curr. Res. Med. Sci. 2023;9(11):1-7.
19. Hassan AO, Oso OV, Obeagu EI, Adeyemo AT. Malaria Vaccine: Prospects and Challenges. Madonna University journal of Medicine and Health Sciences ISSN: 2814-3035. 2022;2(2):22-40.
20. 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.
21. Moya-Alvarez V, Abellana R, Cot M. Pregnancy-associated malaria and malaria in infants: an old problem with present consequences. Malaria journal. 2014; 13:1-10.
22. 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
23. 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. 2022;2(2):91-97. https://madonnauniversity.edu.ng/journals/index.php/medicine/article/view/67.
24. 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.
25. 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 Jun 21;5(2):113-121.
26. Obeagu EI. Gestational Thrombocytopaenia. J Gynecol Women's Health. 2023;25(3):556163. links/64b01aa88de7ed28ba95fccb/Gestational-Thrombocytopaenia.pdf.
27. 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):10-19.
28. Dobaño C, Berthoud T, Manaca MN, Nhabomba A, Guinovart C, Aguilar R, Barbosa A, Groves P, Rodríguez MH, Jimenez A, Quimice LM. High production of pro-inflammatory cytokines by maternal blood mononuclear cells is associated with reduced maternal malaria but increased cord blood infection. Malaria Journal. 2018; 17:1-3.
29. Obeagu EI, Busari AI, Uduchi IO, Ogomaka IA, Ibekwe AM, Vincent CC, Chijioke UO, Okafor CJ, Okoroiwu HU, Adike CN. Age-Related Haematological Variations in Patients with Asymptomatic Malaria in Akure, Ondo State, Nigeria. Journal of Pharmaceutical Research International. 2021;33(42B):218-24.
30. 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):380-386.

31. Ogbonna CO, Obeagu EI, Ufelle SA, Ogbonna LN. Evaluation of haematological alterations in children infected by Plasmodium falciparum Species in Enugu, Enugu State, Nigeria. Journal of Pharmaceutical Research International. 2021;33(1):38-45.
32. Appay V. The physiological role of cytotoxic CD4+ T-cells: the holy grail? Clinical & Experimental Immunology. 2004;138(1):10-13.
33. Okorie HM, Obeagu EI, Obarezi HC, Anyiam AF. Assessment of some inflammatory cytokines in malaria infected pregnant women in Imo State Nigeria. International Journal of Medical Science and Dental Research. 2019;2(1):25-36.
34. 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.
35. Nwosu DC, Obeagu EI, Ezenwuba C, Agu GC, Amah H, Ozims SJ, Nwanjo HU, Edward A, Izuchukwu IF, Amadike JN, Nwagwu AJ. Antioxidant status of children with Plasmodium falciparum malaria in Owerri municipal council of Imo state. Int. J. Curr. Res. Chem. Pharm. Sci. 2016;3(8):40-46.
36. Harrington WE, Kakuru A, Jagannathan P. Malaria in pregnancy shapes the development of foetal and infant immunity. Parasite immunology. 2019;41(3): e12573.
37. 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.
38. Anyiam AF, Arinze-Anyiam OC, Omosigho PO, Ibrahim M, Irondi EA, Obeagu EI, Obi E. Blood Group, Genotype, Malaria, Blood Pressure and Blood Glucose Screening Among Selected Adults of a Community in Kwara State: Implications to Public Health. Asian Hematology Research Journal. 2022;6(3):9-17.
39. Madekwe CC, Madekwe CC, Obeagu EI. Inequality of monitoring in Human Immunodeficiency Virus, Tuberculosis and Malaria: A Review. Madonna University journal of Medicine and Health Sciences. 2022;2(3):6-15.
40. Offie DC, Ibekwe AM, Agu CC, Esimai BN, Okpala PU, Obeagu EI, Ufelle SA, Ogbonna LN. Fibrinogen and C-Reactive Protein Significance in Children Infected by Plasmodium falciparum Species in Enugu, Enugu State, Nigeria. Journal of Pharmaceutical Research International. 2021;33(15):1-8.
41. Obeagu EI, Ogunnaya FU. PREGNANCYINDUCED HAEMATOLOGICAL CHANGES: A KEY TO MARTERNAL AND CHILD HEALTH. European Journal of Biomedical. 2023;10(8):42-43. links/64c890bddb38b20d6dad2c5c/PREGNANCY-INDUCED-HAEMATOLOGICAL-CHANGES-A-KEY-TO-MARTERNAL-AND-CHILD-HEALTH.pdf
42. 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.
43. 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): 14-17.DOI: 10.22192/ijcrms.2023.09.02.003

44. 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
45. Arama C, Quin JE, Kouriba B, Östlund Farrants AK, Troye-Blomberg M, Doumbo OK. Epigenetics and malaria susceptibility/protection: A missing piece of the puzzle. Frontiers in Immunology. 2018; 9:1733.
46. 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
47. 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
48. 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.
49. Obeagu EI, Njar VE, Obeagu GU. Infertility: Prevalence and Consequences. Int. J. Curr. Res. Chem. Pharm. Sci. 2023;10(7):43-50.
50. 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.
51. Broen K, Brustoski K, Engelmann I, Luty AJ. Placental Plasmodium falciparum infection: causes and consequences of in utero sensitization to parasite antigens. Molecular and biochemical parasitology. 2007;151(1):1-8.
52. 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):41-49.
53. Ogbonna LN, Ezeoru VC, Ofodile AC, Ochiabuto OM, Obi-Ezeani CN, Okpala PU, Okafor CJ, Obeagu GU, Busari AI, Obeagu EI. Gender Based Variations of Haematological Parameters of Patients with Asymptomatic Malaria in Akure, Ondo State, Nigeria. Journal of Pharmaceutical Research International. 2021;33(8):75-80.
54. Eberendu IF, Ozims SJ, Agu GC, Amah HC, Obasi CC, Obioma-Elemba JE, Ihekaire DE, Ibanga IE, Amah CC, Obeagu EI, Nwosu DC. Impact of human activities on the breeding of mosquitoes of human disease in Owerri metropolis, Imo state. Int J Adv Res Biol Sci IJARBS. 2017;4(12):98-106.
55. Obeagu EI, Ofodile AC, Okwuanaso CB. A review on socio economic and behavioral aspects of malaria and its control among children under 5 years of age in Africa. J Pub Health Nutri. 2023; 6 (1): 136.
56. Djontu JC, Siewe Siewe S, Mpeke Edene YD, Nana BC, Chomga Foko EV, Bigoga JD, Leke RF, Megnekou R. Impact of placental Plasmodium falciparum malaria infection on the Cameroonian maternal and neonate's plasma levels of some cytokines known to regulate T cells differentiation and function. Malaria journal. 2016; 15:1-1.

57. 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
58. Obeagu EI, Gamade SM, Obeagu GU. The roles of Neutrophils in pregnancy. Int. J. Curr. Res. Med. Sci. 2023;9(5): 31-35.DOI: 10.22192/ijcrms.2023.09.05.005
59. Obeagu EI, Obeagu GU. Molar Pregnancy: Update of prevalence and risk factors. Int. J. Curr. Res. Med. Sci. 2023;9(7): 25-28.DOI: 10.22192/ijcrms.2023.09.07.005
60. Kabyemela E, Gonçalves BP, Prevots DR, Morrison R, Harrington W, Gwamaka M, Kurtis JD, Fried M, Duffy PE. Cytokine profiles at birth predict malaria severity during infancy. PloS one. 2013;8(10):e77214.
61. 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
62. 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):203-211. http://research.sdpublishers.net/id/eprint/2819/.
63. 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
64. 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
65. 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.
66. 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):380-386.
67. Obeagu EI, Ogunnaya FU, Obeagu GU, Ndidi AC. SICKLE CELL ANAEMIA: A GESTATIONAL ENIGMA. migration. 2023; 17:18.
68. Harrington WE, Kakuru A, Jagannathan P. Malaria in pregnancy shapes the development of foetal and infant immunity. Parasite immunology. 2019;41(3):e12573.
69. Ifeanyi OE, Uzoma OG. A review on erythropietin in pregnancy. J. Gynecol. Womens Health. 2018;8(3):1-4. https://www.academia.edu/download/56538560/A_Review_on_Erythropietin_in_Pregnancy.pdf.
70. Ifeanyi OE. A review on pregnancy and haematology. Int. J. Curr. Res. Biol. Med. 2018;3(5): 26-8.DOI: 10.22192/ijcrbm.2018.03.05.006

71. 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):376-383.
72. 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.
73. Elemchukwu Q, Obeagu EI, Ochei KC. Prevalence of Anaemia among Pregnant Women in Braithwaite Memorial Specialist Hospital (BMSH) Port Harcourt. IOSR Journal of Pharmacy and Biological Sciences. 2014;9(5):59-64.
74. Natama HM, Moncunill G, Rovira-Vallbona E, Sanz H, Sorgho H, Aguilar R, Coulibaly-Traoré M, Somé MA, Scott S, Valéa I, Mens PF. Modulation of innate immune responses at birth by prenatal malaria exposure and association with malaria risk during the first year of life. BMC medicine. 2018; 16:1-5.
75. Akandinda M, Obeagu EI, Katonera MT. Non Governmental Organizations and Women's Health Empowerment in Uganda: A Review. Asian Research Journal of Gynaecology and Obstetrics. 2022;8(3):12-26.
76. Gamde MS, Obeagu EI. IRON DEFICIENCY ANAEMIA: ENEMICAL TO PREGNANCY. European Journal of Biomedical. 2023;10(9):272-275. links/64f63358827074313ffaae7b/IRON-DEFICIENCY-ANAEMIA-ENEMICAL-TO-PREGNANCY.pdf.
77. 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.
78. Emeka-Obi OR, Ibeh NC, Obeagu EI, Okorie HM. Studies of Some Haemostatic Variables in Preeclamptic Women in Owerri, Imo State, Nigeria. Journal of Pharmaceutical Research International. 2021;33(42B):39-48.
79. 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):22-26.
80. Obeagu EI, Obeagu GU. Sickle Cell Anaemia in Pregnancy: A Review. International Research in Medical and Health Sciences. 2023;6(2):10-13.
81. Mutabingwa TK, Bolla MC, Li JL, Domingo GJ, Li X, Fried M, Duffy PE. Maternal malaria and gravidity interact to modify infant susceptibility to malaria. PLoS medicine. 2005;2(12):e407.
82. Gamble C, Ekwaru PJ, Garner P, Ter Kuile FO. Insecticide-treated nets for the prevention of malaria in pregnancy: a systematic review of randomised controlled trials. PLoS medicine. 2007;4(3):e107.
83. Okoko BJ, Enwere G, Ota MO. The epidemiology and consequences of maternal malaria: a review of immunological basis. Acta tropica. 2003;87(2):193-205.
84. Dobaño C, Berthoud T, Manaca MN, Nhabomba A, Guinovart C, Aguilar R, Barbosa A, Groves P, Rodríguez MH, Jimenez A, Quimice LM. High production of pro-inflammatory cytokines by maternal blood mononuclear cells is associated with reduced maternal malaria but increased cord blood infection. Malaria Journal. 2018; 17:1-3.

85. Umbers AJ, Stanisic DI, Ome M, Wangnapi R, Hanieh S, Unger HW, Robinson LJ, Lufele E, Baiwog F, Siba PM, King CL. Does malaria affect placental development? Evidence from in vitro models. PLoS One. 2013;8(1):e55269.
86. Arama C, Quin JE, Kouriba B, Östlund Farrants AK, Troye-Blomberg M, Doumbo OK. Epigenetics and malaria susceptibility/protection: A missing piece of the puzzle. Frontiers in Immunology. 2018; 9:1733.
87. Gbedande K, Carpio VH, Stephens R. Using two phases of the CD 4 T cell response to blood-stage murine malaria to understand regulation of systemic immunity and placental pathology in Plasmodium falciparum infection. Immunological reviews. 2020;293(1):88-114.
88. Lindsay SW, Thomas MB, Kleinschmidt I. Threats to the effectiveness of insecticide-treated bednets for malaria control: thinking beyond insecticide resistance. The Lancet Global Health. 2021;9(9):e1325-1331.
89. Akinleye SO, Falade CO, Ajayi IO. Knowledge and utilization of intermittent preventive treatment for malaria among pregnant women attending antenatal clinics in primary health care centers in rural southwest, Nigeria: a cross-sectional study. BMC pregnancy and childbirth. 2009; 9:1-9.