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INTERNATIONAL JOURNAL
OF INNOVATIVE AND APPLIED RESEARCH

RESEARCH ARTICLE

Article DOI: 10.58538/IJAR/2061

DOI URL: <http://dx.doi.org/10.58538/IJAR/2061>

Neutrophil Dynamics and Host Defense Mechanisms in Pregnant Women Infected with *Trichomonas vaginalis*

Emmanuel Ifeanyi Obeagu¹, Emmanuel Chinedu Onuoha² and Getrude Uzoma Obeagu³

1 Department of Medical Laboratory Science, Kampala International University, Uganda.

2 Department of Haematology and Blood Transfusion, Faculty of Medical and Laboratory Science, Federal University Otuoke, Bayelsa State, Nigeria

3 School of Nursing Science, Kampala International University, Uganda.

Manuscript Info

Manuscript History

Received: 03 November 2023

Final Accepted: 12 December 2023

Published: December 2023

Keywords:

Trichomonas Vaginalis, Neutrophils, Pregnancy, Host Defense Mechanisms, Immune Response, Parasite Evasion, Therapeutic Interventions

Abstract

Trichomonas vaginalis, a prevalent sexually transmitted parasite, poses substantial risks to maternal health during pregnancy, eliciting a multifaceted immune response crucial for host defense. Neutrophils, as primary innate immune effectors, play a pivotal role in combatting this infection within the intricate immunological landscape of pregnancy. This comprehensive review aims to elucidate the complex interplay between *Trichomonas vaginalis* infection and the dynamic responses of neutrophils in pregnant women, exploring mechanisms of neutrophil recruitment, activation, effector functions, and the parasite's evasion strategies. Insights into neutrophil dynamics and activation mechanisms reveal their essential functions in combating *T. vaginalis*, encompassing chemotaxis, phagocytosis, release of reactive oxygen species, and formation of neutrophil extracellular traps. Furthermore, the review discusses how pregnancy-associated immunomodulation influences neutrophil function in response to this parasitic infection. Concurrently, the elucidation of *T. vaginalis* evasion tactics—surface antigen variation, adhesion strategies, and immune subversion—underscores the complexity of host-parasite interactions and the challenges faced by neutrophils in eradicating the parasite. Considering the clinical implications, particularly adverse pregnancy outcomes and maternal morbidity associated with *T. vaginalis* infection, the review addresses current treatment modalities, management challenges during pregnancy, and potential therapeutic strategies targeting neutrophil responses and immune modulation. In conclusion, understanding the intricate interplay between *T. vaginalis* infection and neutrophil dynamics within pregnancy's immunological context provides valuable insights into potential therapeutic targets. This review advocates for further research aiming to enhance our understanding of neutrophil-parasite interactions and develop targeted interventions to ameliorate adverse outcomes associated with *T. vaginalis* infection in pregnant women.

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

Trichomonas vaginalis, a flagellated protozoan parasite, stands as one of the most prevalent sexually transmitted infections globally, exerting significant implications for maternal health during pregnancy [1]. Among the myriad of complications that afflict expectant mothers, the interplay between this parasitic infection and the intricate immunological landscape of pregnancy unveils a captivating yet complex relationship. Neutrophils, as primary innate immune cells, emerge as key orchestrators in combating Trichomonas vaginalis, shaping the host defense mechanisms within this unique physiological state [2-3]. The epidemiology of Trichomonas vaginalis during pregnancy portrays an alarming prevalence, underscoring its potential impact on maternal health and pregnancy outcomes. Heightened susceptibility to this parasite during gestation, attributed to hormonal, anatomical, and immunological changes, demands a thorough exploration of the immune responses elicited, with a particular focus on the role of neutrophils within this specialized immunological milieu [4]. Neutrophils, traditionally regarded as the first line of defense against invading pathogens, manifest a multifaceted response upon encountering Trichomonas vaginalis. Their dynamic interplay includes chemotaxis to the site of infection, phagocytosis, degranulation, and the formation of neutrophil extracellular traps (NETs), aiming to eliminate the parasite and mitigate its pathological consequences. However, the parasite's evasion strategies, including surface antigen variation and immune modulation, present formidable challenges to neutrophil-mediated eradication, emphasizing the complexity of host-pathogen interactions [5-6]. Moreover, the immunomodulatory effects inherent to pregnancy impart significant alterations in neutrophil function and immune responses, potentially influencing the host defense mechanisms against Trichomonas vaginalis. Understanding these modifications within the pregnant immunological milieu is pivotal in delineating the nuances of neutrophil dynamics and their efficacies in combating this parasitic infection.

Neutrophil Dynamics and Activation

Neutrophils, as pivotal innate immune effectors, orchestrate a multifaceted response against Trichomonas vaginalis, the causative agent of one of the most prevalent sexually transmitted infections globally. Within the distinctive immunological milieu of pregnancy, neutrophils undergo dynamic changes in their activation, recruitment, and effector functions in response to Trichomonas vaginalis, contributing significantly to the host defense mechanisms [7-10]. Upon encountering Trichomonas vaginalis, a cascade of signaling events triggers the recruitment of neutrophils to the site of infection. Chemotactic signals, including cytokines, chemokines, and damage-associated molecular patterns (DAMPs), guide the migration of neutrophils from the circulation to the infected tissues, aiming to contain and eliminate the parasite [11]. Neutrophils employ phagocytosis as a primary mechanism to engulf and internalize Trichomonas vaginalis, initiating intracellular killing processes. This process involves the formation of phagosomes followed by fusion with lysosomes, releasing antimicrobial peptides, proteases, and reactive oxygen species (ROS) to eliminate the parasite. [12] Activation of neutrophils in response to Trichomonas vaginalis triggers the release of **Neutrophil Extracellular Traps (NETs)**—a web-like structure comprising DNA, histones, and antimicrobial proteins—to ensnare and neutralize the parasite. However, the parasite's mechanisms to evade NET-mediated killing pose challenges to the efficacy of this neutrophil effector mechanism [13]. Neutrophils generate **Reactive Oxygen Species (ROS)**, such as superoxide anions and hydrogen peroxide, as part of their antimicrobial arsenal against Trichomonas vaginalis. These reactive molecules exert cytotoxic effects, aiding in the eradication of the parasite. However, the delicate balance between ROS-mediated killing and potential tissue damage underscores the complexity of neutrophil responses [14-16]. The unique immunological milieu of pregnancy exerts modulatory effects on neutrophil function and responses. Hormonal fluctuations, altered cytokine profiles, and changes in immune cell populations during gestation influence neutrophil activation and their ability to mount an effective response against Trichomonas vaginalis [17-18]. The intricate dynamics of neutrophil activation and effector functions in response to Trichomonas vaginalis underscore the complexities of host-pathogen interactions within the pregnant immunological landscape. Understanding these mechanisms is critical in devising targeted interventions to enhance neutrophil-mediated immunity and mitigate adverse outcomes associated with T. vaginalis infection during pregnancy.

Parasite Evasion Mechanisms and Immune Subversion

Trichomonas vaginalis, a prevalent sexually transmitted parasite, employs an array of sophisticated evasion strategies to subvert host immune responses, presenting formidable challenges to effective immune clearance, particularly within the distinctive immunological milieu of pregnancy. Understanding the parasite's evasion mechanisms is pivotal in elucidating the complexities of host-parasite interactions and devising strategies to counteract immune subversion [19-20]. *Trichomonas vaginalis* exhibits remarkable phenotypic plasticity through the expression of variable surface proteins (VSPs), enabling rapid antigenic variation. This antigenic switching mechanism allows the parasite to evade host immune recognition, facilitating persistence and chronic infection, particularly within the vaginal mucosa during pregnancy [21-24]. The parasite's adherence to host cells, mediated by surface adhesins and lectins, not only facilitates colonization but also serves as a mechanism to evade immune detection. *Trichomonas vaginalis* modulates host immune responses by inducing an immunosuppressive microenvironment, hindering effective neutrophil responses and impairing the activation of other immune effectors [25]. *Trichomonas vaginalis* exerts immunomodulatory effects by influencing cytokine profiles, altering immune cell activation, and dampening inflammatory responses. By disrupting the balance between pro-inflammatory and anti-inflammatory mediators, the parasite manipulates immune signaling pathways, thereby evading immune recognition and clearance mechanisms [26]. *Trichomonas vaginalis* possesses robust antioxidant defense mechanisms, including enzymes such as superoxide dismutase and peroxiredoxins, enabling the parasite to counteract host-derived oxidative stress. This contributes to the parasite's resilience against neutrophil-mediated killing and aids in immune evasion strategies [27]. *Trichomonas vaginalis* deploys mechanisms to evade neutrophil-mediated killing, including resistance to **Neutrophil Extracellular Trap (NET)**-induced toxicity or degradation by nucleases released by the parasite. This evasion strategy diminishes the efficacy of neutrophil defense mechanisms and contributes to the parasite's persistence [28]. *Trichomonas vaginalis* demonstrates adaptability to the specific immunological changes associated with pregnancy. The altered hormonal milieu and immunomodulatory effects during gestation potentially influence the parasite's survival strategies, complicating the host immune responses and perpetuating the infection [29]. The elucidation of *Trichomonas vaginalis* evasion tactics and immune subversion strategies provides critical insights into the challenges faced by the host immune system, particularly during pregnancy. Understanding these mechanisms is crucial in developing targeted therapeutic interventions to counteract parasite evasion, mitigate adverse outcomes, and enhance immune clearance of *T. vaginalis* in pregnant women.

Clinical Implications and Therapeutic Perspectives

Trichomonas vaginalis infection during pregnancy poses significant clinical implications, necessitating tailored therapeutic approaches to mitigate adverse outcomes and ensure optimal maternal and fetal health. Understanding the challenges in managing this prevalent parasitic infection within the context of pregnancy is pivotal for developing effective therapeutic strategies and improving clinical outcomes [30-40]. *Trichomonas vaginalis* infection during pregnancy is associated with various adverse outcomes, including preterm birth, low birth weight, premature rupture of membranes, and increased susceptibility to other sexually transmitted infections. These complications underscore the importance of timely diagnosis and management strategies to minimize risks to maternal and neonatal health [41-52]. The management of *Trichomonas vaginalis* infection during pregnancy poses unique challenges, primarily due to safety concerns associated with the use of antiparasitic medications in expectant mothers. Limited therapeutic options approved for use during pregnancy necessitate careful consideration of risks and benefits in choosing appropriate treatment regimens [53-62]. Routine screening for *Trichomonas vaginalis* infection during prenatal care remains crucial for early detection and timely intervention. Incorporating accurate diagnostic methods, such as nucleic acid amplification tests or point-of-care testing, into antenatal care protocols can facilitate prompt identification and treatment of infected individuals [63-74]. Tailoring treatment strategies involves considering safety profiles and efficacy of available medications during pregnancy. Nitroimidazoles, such as metronidazole and tinidazole, are commonly used, but their use in the first trimester requires cautious evaluation due to potential teratogenic effects [75-83]. Exploring combination therapies or alternative treatment approaches, including topical agents or adjunctive therapies, warrants consideration to enhance therapeutic efficacy and minimize potential risks associated with single-agent regimens [84-90]. Implementing preventive measures, such as promoting safe sexual practices and partner treatment, along with patient education, is pivotal in preventing recurrent infections and reducing the risk of transmission [91-96]. Continued research endeavors focusing on the safety and efficacy of antiparasitic agents, the development of novel therapeutics targeting parasite virulence factors, and the assessment of vaccine candidates against *Trichomonas vaginalis* infection are essential for advancing treatment options for pregnant women. Strategizing comprehensive care approaches that encompass screening, safe and effective treatment options, preventive measures, and patient education are critical in mitigating the clinical implications of *Trichomonas vaginalis* infection in pregnant women. Advancing research efforts and developing

targeted therapeutic interventions hold promise for improving maternal and neonatal outcomes in the context of this prevalent parasitic infection during pregnancy [97-100].

Conclusion:-

Trichomonas vaginalis infection poses a significant health concern for pregnant women, presenting challenges in diagnosis, treatment, and potential adverse outcomes. Within the unique immunological context of pregnancy, the intricate interplay between the parasite's evasion mechanisms and the host immune responses underscores the complexities of managing this infection during gestation. Neutrophils, as primary innate immune effectors, play a pivotal role in combating *Trichomonas vaginalis*; however, the parasite's ability to evade immune clearance through surface antigen variation, adhesion strategies, and immune subversion presents formidable challenges to effective clearance mechanisms, especially in pregnant women. The clinical implications of *T. vaginalis* infection during pregnancy, including adverse birth outcomes and challenges in treatment, emphasize the necessity for tailored therapeutic approaches. The limited safety data regarding antiparasitic medications in pregnancy necessitates a cautious approach in selecting treatment regimens, while continual research efforts are crucial to expand therapeutic options and enhance efficacy while minimizing risks. Early screening, accurate diagnosis, preventive measures, and patient education play critical roles in mitigating the impact of *Trichomonas vaginalis* infection in pregnant women. Advances in diagnostic techniques, exploration of alternative treatment modalities, and the development of preventive strategies are pivotal for improving clinical outcomes and reducing the burden of this infection on maternal and neonatal health. A multifaceted approach encompassing early detection, safe and effective treatment options, preventive measures, and ongoing research initiatives is essential in addressing the clinical implications of *Trichomonas vaginalis* infection during pregnancy. Enhancing our understanding of host-parasite interactions and advancing therapeutic strategies tailored to the unique immunological environment of pregnancy holds promise for improving maternal and neonatal outcomes in the context of this prevalent parasitic infection.

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