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Article *in* Annals of Immunology & Immunotherapy · March 2024

DOI: 10.23880/aii-16000184

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ISSN: 2691-5782

B Cell Dynamics in HIV Pathogenesis: Insights and Implications

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Review Article

Volume 6 Issue 1

Received Date: February 07 2024

Published Date: March 27, 2024

DOI: 10.23880/aii-16000184

Abstract

Human Immunodeficiency Virus (HIV) infection remains a global health challenge, with intricate interactions between the virus and the immune system, particularly B cells, significantly influencing disease progression. This review aims to provide a comprehensive examination of B cell dynamics during HIV pathogenesis, offering insights into the implications for therapeutic interventions, vaccine design, and the broader understanding of HIV-associated immune dysfunction. The review begins by outlining the epidemiology of HIV and emphasizing the critical impact of the virus on the immune system, with a specific focus on B cells. It explores the alterations in B cell subpopulations, including memory B cell depletion and dysregulation, highlighting their implications for immune function during HIV infection. This review consolidates current knowledge on B cell dynamics in HIV pathogenesis, providing a foundation for advancing our understanding of the intricate host-virus interactions. The insights gained from this exploration hold significant implications for the development of targeted therapeutic strategies and informed approaches to HIV prevention and treatment.

Keywords: Hypergammaglobulinemia; B Cell Exhaustion; HIV; Immune Dysfunction; Antiretroviral therapy; Vaccine development; Immune Checkpoint Inhibitors

Abbreviations: HIV: Human Immunodeficiency Virus; Tfh: T follicular Helper; ART: Antiretroviral therapy; SLE: Systemic Lupus Erythematosus.

Introduction

Human Immunodeficiency Virus (HIV) infection remains a formidable global health challenge, affecting millions of individuals and presenting complex dynamics that intricately involve the host immune system. Among the various components of the immune system, B cells play a pivotal role in orchestrating effective responses against pathogens. Understanding the nuanced interactions between HIV and B cells is crucial for unraveling the complexities of HIV pathogenesis, informing therapeutic strategies, and advancing vaccine development [1-10]. HIV, a retrovirus, selectively targets immune cells, primarily CD4+ T cells, leading to the progressive depletion of these critical components of the immune system. While the impact of HIV on T cells has been extensively studied, the intricate relationship between the virus and B cells has emerged as an area of growing importance. B cells, with their diverse functions ranging from antibody production to antigen presentation, contribute significantly to the host defense against pathogens [11-20].

This review seeks to provide a comprehensive examination of B cell dynamics during HIV infection, aiming to bridge current knowledge gaps and highlight the implications for both clinical practice and research endeavors. The exploration begins by setting the stage with an overview of the epidemiology and global impact of HIV,

underscoring the urgency of understanding the intricacies of the virus-host interplay.

B Cell Subpopulations in HIV

Human Immunodeficiency Virus (HIV) infection exerts a profound impact on B cell dynamics, influencing both the quantitative distribution and functional characteristics of distinct B cell subpopulations. One hallmark of HIV infection is the substantial depletion of memory B cells, which are crucial for mounting rapid and effective immune responses upon re-exposure to pathogens. The loss of memory B cells compromises the ability of the immune system to generate a robust and sustained response to HIV and other opportunistic infections, contributing to disease progression [21-30]. HIV infection disrupts the balance between B cell subsets, leading to an altered distribution of naïve and activated B cells. Persistent immune activation in HIV infection results in increased activation of B cells, contributing to Hypergammaglobulinemia and heightened susceptibility to exhaustion [31-35]. HIV interferes with the normal function of germinal centers, where B cells undergo affinity maturation and class switching. Impaired germinal center reactions contribute to the diminished quality of antibodies produced during HIV infection, impacting the effectiveness of humoral immune responses [36-40]. The crosstalk between B cells and T follicular helper (Tfh) cells within germinal centers is disrupted by HIV. Dysfunction in Tfh cells compromises their ability to provide optimal help to B cells, influencing the development of broadly neutralizing antibodies.

Despite ongoing antigenic stimulation, the generation of HIV-specific memory B cells is often inadequate. Understanding the evolution of HIV-specific B cell responses over the course of infection is critical for devising strategies to induce protective antibodies. Chronic HIV infection is associated with polyclonal B cell activation, leading to elevated levels of immunoglobulins. While Hypergammaglobulinemia may reflect a compensatory response, it can also contribute to immune dysfunction and exacerbate conditions such as autoimmune reactions [41-45]. Persistent antigenic stimulation in HIV infection leads to B cell exhaustion, characterized by increased expression of immune checkpoint molecules, such as PD-1. B cell exhaustion contributes to functional impairment, impacting antibody production and overall immune responses against the virus [46-50].

Role of B Cells in HIV Transmission and Early Infection

The early stages of Human Immunodeficiency Virus (HIV) infection involve intricate interactions between the virus and various components of the immune system, including B cells. Understanding the role of B cells in HIV transmission and early infection is crucial for deciphering the dynamics that shape the course of the disease [51-55]. B cells contribute to mucosal immunity, forming an essential component of the first line of defense against pathogens at mucosal surfaces, including those involved in sexual transmission of HIV. Mucosal B cells play a key role in producing immunoglobulin A (IgA), which helps prevent the initial establishment of HIV infection by neutralizing the virus at mucosal entry points. B cells contribute to the early immune response through the production of antibodies that can mediate antibody-dependent cellular cytotoxicity (ADCC). ADCC involves the recognition of HIV-infected cells by antibodies, facilitating their destruction by immune cells, thereby restricting the initial spread of the virus [55-65]. Breast milk from HIV-positive mothers contains antibodies, including IgA, which can neutralize HIV. These antibodies contribute to passive immunity, offering protection to infants during breastfeeding [66-68].

However, vertical transmission remains a challenge, and understanding the dynamics of B cell-mediated immunity in breast milk is essential for developing interventions to prevent mother-to-child transmission.

Early HIV infection triggers germinal center reactions, where B cells undergo affinity maturation and class switching in response to viral antigens. The rapid initiation of germinal center reactions contributes to the early production of antibodies, although the quality and specificity of these antibodies may be insufficient to control the virus. Early HIV-specific B cell responses are often limited in scope and effectiveness, allowing the virus to establish a foothold in the host. The challenges in generating and maintaining memory B cells specific to HIV during the early stages contribute to the difficulty in achieving long-term protective immunity. B cells act as antigen-presenting cells, presenting viral antigens to CD4+ T cells, thus influencing the development of effective T cell responses against HIV. The interplay between B cells and T follicular helper (Tfh) cells within germinal centers is critical for shaping both B and T cell responses during early infection [69-73].

HIV-Induced Hypergammaglobulinemia

Hypergammaglobulinemia, characterized by elevated levels of immunoglobulins, is a notable immunological consequence of chronic HIV infection [74]. This phenomenon reflects a dysregulation of B cell function and immune homeostasis, with implications for both the course of HIV disease progression and associated complications. Persistent exposure to HIV antigens and continuous immune activation result in polyclonal B cell activation, leading to the production of a diverse array of antibodies [75]. The nonspecific

activation of B cells contributes to the elevated levels of immunoglobulins observed in the serum, encompassing various antibody specificities. Hypergammaglobulinemia in HIV infection primarily involves increased levels of immunoglobulin G (IgG) and immunoglobulin A (IgA) [76]. While IgM levels may not show a significant increase, the alterations in IgG and IgA play a crucial role in immune dysregulation. The excessive production of antibodies may compromise the specificity and effectiveness of antigen-specific immune responses, leading to impaired immune surveillance. Hypergammaglobulinemia is associated with an increased risk of autoimmune manifestations, as the nonspecific antibodies produced may target self-antigens, contributing to autoimmunity.

Elevated levels of immunoglobulins, particularly IgG, have been correlated with advanced HIV disease stages and a higher risk of developing opportunistic infections [77]. Hypergammaglobulinemia serves as a prognostic indicator, reflecting the degree of immune dysregulation and the potential for increased morbidity and mortality. HIV-induced Hypergammaglobulinemia is associated with dysfunctional germinal centers, where B cells undergo maturation and affinity maturation. The disruption of normal germinal center activity contributes to the diminished quality of antibodies produced, impacting the ability to mount effective humoral immune responses. Hypergammaglobulinemia in HIV infection is linked to the production of autoantibodies, contributing to autoimmune phenomena such as immune thrombocytopenia and systemic lupus erythematosus (SLE) [78]. Molecular mimicry, loss of immune tolerance, and chronic immune activation are proposed mechanisms for the development of autoantibodies. Antiretroviral therapy (ART) can partially normalize hypergammaglobulinemia by reducing viral replication and immune activation. However, complete restoration of B cell function and normalization of immunoglobulin levels may be challenging even with effective ART.

Impact on Antibody Responses

Hypergammaglobulinemia, a hallmark of chronic HIV infection, significantly influences the quality and efficacy of antibody responses. Chronic stimulation of B cells in Hypergammaglobulinemia leads to the production of a multitude of antibodies, including nonspecific and low-affinity antibodies [79]. The abundance of nonspecific antibodies diminishes the overall specificity of the antibody pool, reducing the efficiency of recognizing and neutralizing HIV-specific antigens. Hypergammaglobulinemia is often accompanied by dysfunctional germinal centers, where B cells undergo affinity maturation. The impaired germinal center reactions result in antibodies with reduced affinity for HIV antigens, compromising their ability to effectively neutralize the virus. Hypergammaglobulinemia is associated with the production of autoantibodies and polyreactive antibodies that recognize multiple antigens [80]. Polyreactive antibodies may have a higher propensity for nonspecific binding, potentially interfering with the recognition of HIV-specific epitopes. The predominance of IgG and IgA in hypergammaglobulinemia alters the immunoglobulin isotype distribution. While IgG and IgA are essential for immune defense, their dysregulated production may skew immune responses and contribute to ineffective antibody-mediated control of HIV. The presence of nonspecific antibodies and altered immunoglobulin profiles may compromise the efficiency of antibody-dependent cellular cytotoxicity (ADCC). Impaired ADCC may contribute to the persistence of HIV-infected cells, hindering the immune system's ability to clear the virus. Hypergammaglobulinemia is linked to the production of autoantibodies, potentially leading to autoimmune manifestations. Autoimmune antibodies may interfere with the immune system's ability to focus on HIV-specific targets, contributing to immune dysfunction.

B Cell Exhaustion and Immune Dysfunction

B cell exhaustion is a phenomenon characterized by functional impairment and decreased responsiveness, and it plays a significant role in the immune dysfunction observed during chronic HIV infection [81]. Chronic exposure to HIV antigens leads to persistent stimulation of B cells over an extended period. Prolonged antigenic stimulation contributes to the induction of B cell exhaustion, characterized by altered functionality and reduced responsiveness. B cells undergoing exhaustion exhibit an increased expression of immune checkpoint molecules, such as programmed cell death protein 1 (PD-1) and programmed death-ligand 1 (PD-L1) [82]. Interaction between PD-1 on B cells and PD-L1 on other immune cells results in inhibitory signaling, dampening B cell responses and contributing to immune dysfunction. B cell exhaustion hinders the processes of class switching and affinity maturation, crucial for the production of high-affinity antibodies. The impaired functionality of exhausted B cells leads to the production of antibodies with reduced efficacy in neutralizing HIV and other pathogens.

B cell exhaustion interferes with the formation of long-lived memory B cells, impairing the establishment of immunological memory [83]. The compromised generation of memory B cells limits the ability of the immune system to mount effective recall responses upon re-exposure to the virus. B cells rely on interactions with Tfh cells within germinal centers for proper maturation. B cell exhaustion disrupts this collaboration, further hindering effective immune responses. The impaired crosstalk between exhausted B cells and Tfh cells contributes to the overall dysfunction of humoral immunity. The degree of B cell

exhaustion has been correlated with the progression of HIV infection to advanced stages [84]. Higher levels of exhausted B cells may serve as a predictive marker for poor clinical outcomes and increased susceptibility to opportunistic infections. Therapeutic approaches involving checkpoint inhibitors, which block the inhibitory signaling pathways, are being explored to alleviate B cell exhaustion. Effective ART can partially reverse B cell exhaustion by reducing viral replication and immune activation, contributing to immune restoration. B cell exhaustion poses challenges for the development of effective HIV vaccines, as exhausted B cells may exhibit suboptimal responses to vaccination. Designing vaccines that specifically target exhausted B cells or incorporating strategies to mitigate B cell exhaustion is crucial for enhancing vaccine efficacy.

Implications for HIV Treatment and Vaccine Development

The profound impact of B cell dynamics, including hypergammaglobulinemia and B cell exhaustion, in HIV infection has critical implications for both treatment strategies and the development of effective vaccines [85]. Hypergammaglobulinemia and B cell exhaustion can be partially addressed by effective ART, which reduces viral replication and immune activation. Successful ART contributes to the restoration of immune function, including improvements in B cell responses and the reduction of hypergammaglobulinemia. Investigating the use of checkpoint inhibitors to alleviate B cell exhaustion holds promise as a therapeutic strategy. Tailoring interventions based on individual B cell dynamics may be crucial for optimizing treatment outcomes. Managing autoimmune manifestations associated with hypergammaglobulinemia may require targeted therapies addressing B cell dysregulation.

Hypergammaglobulinemia, characterized by nonspecific antibody production, poses challenges for the design of HIV vaccines [86]. The presence of diverse and nonspecific antibodies may interfere with the induction of potent and targeted immune responses by vaccines. B cell exhaustion negatively influences vaccine responses, limiting the generation of robust and durable immune memory. Designing vaccines that consider the altered B cell dynamics in HIV-infected individuals is critical. Strategies to induce Broadly Neutralizing Antibodies (bNAbs), even in the context of B cell exhaustion, are essential for developing vaccines capable of preventing diverse HIV strains. Recognizing the heterogeneity in B cell responses and tailoring treatment strategies on an individual basis may optimize outcomes. Considering individual variations in B cell dynamics when developing vaccines may improve vaccine responses across diverse patient populations. Incorporating B cell monitoring into long-term care plans for individuals living with HIV can provide insights into the effectiveness of treatment and vaccine interventions. Vigilant monitoring for complications associated with hypergammaglobulinemia and B cell exhaustion, such as autoimmune manifestations, is crucial for timely intervention.

Conclusion

The intricate interplay between HIV and B cell dynamics underscores the complexity of immune responses in the context of chronic infection. Hypergammaglobulinemia, B cell exhaustion, and altered B cell subpopulations collectively contribute to immune dysfunction, influencing disease progression and posing challenges for therapeutic interventions and vaccine development. Hypergammaglobulinemia, characterized by elevated levels of immunoglobulins, reflects a dysregulation of B cell function and has implications for immune homeostasis. The resulting nonspecific antibody responses, while indicative of ongoing immune activation, may compromise the specificity and efficacy of antibody-mediated control of HIV. Addressing hypergammaglobulinemia requires a nuanced understanding of its underlying mechanisms and the development of targeted therapeutic strategies.

B cell exhaustion represents a state of functional impairment, with consequences for antibody production, immune memory, and collaboration with other immune cells. The upregulation of immune checkpoint molecules, such as PD-1/PD-L1, contributes to the inhibitory signaling that hinders effective B cell responses. Therapeutic avenues involving checkpoint inhibitors and precision medicine approaches offer hope for mitigating B cell exhaustion and restoring immune function in HIV-infected individuals. The implications for vaccine development are profound, as hypergammaglobulinemia and B cell exhaustion pose challenges to the induction of robust and specific immune responses. Designing vaccines that consider the altered B cell landscape, exploring checkpoint inhibitors in conjunction with vaccination, and striving for individualized vaccine approaches are critical for overcoming these challenges.

References

1. Obeagu EI, Okwuanaso CB, Edoho SH, Obeagu GU (2022) Under-nutrition among HIV-exposed Uninfected Children: A Review of African Perspective. Madonna University journal of Medicine and Health Sciences 2(3): 120-127.

2. Obeagu EI, Alum EU, Obeagu GU (2023) Factors associated with prevalence of HIV among youths: A review of Africa perspective. Madonna University journal of Medicine and Health Sciences 3(1): 13-18.

3. Obeagu EI (2023) A Review of Challenges and Coping Strategies Faced by HIV/AIDS Discordant Couples. Madonna University journal of Medicine and Health Sciences 3(1): 7-12.

4. Obeagu EI, Obeagu GU (2023) An update on premalignant cervical lesions and cervical cancer screening services among HIV positive women. J Pub Health Nutri 6(2): 141.

5. Ezeoru VC, Enweani IB, Ochiabuto O, Nwachukwu AC, Ogbonna US, et al. (2021) Prevalence of Malaria with Anaemia and HIV status in women of reproductive age in Onitsha, Nigeria. Journal of Pharmaceutical Research International 33(4): 10-19.

6. Emmanuel UK, Chinedum OK, Obeagu EI (2017) Evaluation of laboratory logistics management information system in HIV/AIDS comprehensive health facilities in Bayelsa State, Nigeria. Int J Curr Res Med Sci 3(1): 21-38.

7. Obeagu EI, Obeagu GU, Musiimenta E, Bot YS, Hassan AO (2023) Factors contributing to low utilization of HIV counseling and testing services. Int J Curr Res Med Sci 9(2): 1-5.

8. Obeagu EI, Obeagu GU (2022) An update on survival of people living with HIV in Nigeria. J Pub Health Nutri 5(6): 129.

9. Offie DC, Obeagu EI, Akueshi C, Njab JE, Ekanem EE, et al (2021) Facilitators and barriers to retention in HIV care among HIV infected MSM attending Community Health Center Yaba, Lagos Nigeria. Journal of Pharmaceutical Research International 33(52B): 10-19.

10. Obeagu EI, Ogbonna US, Nwachukwu AC, Ochiabuto O, Enweani IB, et al. (2021) Prevalence of Malaria with Anaemia and HIV status in women of reproductive age in Onitsha, Nigeria. Journal of Pharmaceutical Research International 33(4): 10-19.

11. Odo M, Ochei KC, Obeagu EI, Barinaadaa A, Eteng UE, et al. (2020) TB Infection Control in TB/HIV Settings in Cross River State, Nigeria: Policy Vs Practice. Journal of Pharmaceutical Research International 32(22): 101-119.

12. Obeagu EI, Eze VU, Alaeboh EA, Ochei KC (2016) Determination of haematocrit level and iron profile study among persons living with HIV in Umuahia, Abia State, Nigeria. J BioInnovation 5(4): 464-471.

13. Ifeanyi OE, Obeagu GU (2015) The values of prothrombin time among HIV positive patients in FMC owerri. International Journal of Current Microbiology and Applied Sciences 4(4): 911-916.

14. Izuchukwu IF, Ozims SJ, Agu GC, Obeagu EI, Onu I, et al. (2016) Knowledge of preventive measures and management of HIV/AIDS victims among parents in Umuna Orlu community of Imo state Nigeria. Int J Adv Res Biol Sci 3(10): 55-65.

15. Chinedu K, Takim AE, Obeagu EI, Chinazor UD, Eloghosa O, et al. (2017) HIV and TB co-infection among patients who used Directly Observed Treatment Short-course centres in Yenagoa, Nigeria. IOSR J Pharm Biol Sci 12(4): 70-75.

16. Oloro OH, Oke TO, Obeagu EI (2022) Evaluation of Coagulation Profile Patients with Pulmonary Tuberculosis and Human Immunodeficiency Virus in Owo, Ondo State, Nigeria. Madonna University journal of Medicine and Health Sciences 2(3): 110-119.

17. Nwosu DC, Obeagu EI, Nkwocha BC, Nwanna CA, Nwanjo HU, et al. (2016) Change in Lipid Peroxidation Marker (MDA) and Non enzymatic Antioxidants (VIT C & E) in HIV Seropositive Children in an Urban Community of Abia State. Nigeria. J Bio Innov 5(1): 24-30.

18. Igwe CM, Obeagu IE, Ogbuabor OA (2022) Clinical characteristics of people living with HIV/AIDS on ART in 2014 at tertiary health institutions in Enugu, Nigeria. J Pub Health Nutri 5(6): 130.

19. Ifeanyi OE, Obeagu GU, Ijeoma FO, Chioma UI (2015) The values of activated partial thromboplastin time (APTT) among HIV positive patients in FMC Owerri. Int J Curr Res Aca Rev 3(4): 139-144.

20. Obiomah CF, Obeagu EI, Ochei KC, Swem CA, Amachukwu BO (2018) Hematological indices o HIV seropositive subjects in Nnamdi Azikiwe University teaching hospital (NAUTH), Nnewi. Ann Clin Lab Res 6(1): 1-4.

21. Emmanuel OUK, Ochei KC, Osuala EO, Obeagu EI, Onwuasoanya UF (2017) Impact of prevention of mother to child transmission (PMTCT) of HIV on positivity rate in Kafanchan, Nigeria. Int J Curr Res Med Sci 3(2): 28-34.

22. Aizaz M, Abbas FA, Abbas A, Tabassum S, Obeagu EI (2023) Alarming rise in HIV cases in Pakistan: Challenges and future recommendations at hand. Health Science Reports 6(8): e1450.

23. Obeagu EI, Amekpor F, Scott GY (2023) An update of human immunodeficiency virus infection: Bleeding disorders. J Pub Health Nutri 6(1): 139.

24. Obeagu EI, Scott GY, Amekpor F, Ofodile AC, Edoho SH, et al. (2022) Prevention of New Cases of Human

Immunodeficiency Virus: Pragmatic Approaches of Saving Life in Developing Countries. Madonna University journal of Medicine and Health Sciences 2(3): 128-134.

25. Walter O, Anaebo QB, Obeagu EI, Okoroiwu IL (2022) Evaluation of Activated Partial Thromboplastin Time and Prothrombin Time in HIV and TB Patients in Owerri Metropolis. Journal of Pharmaceutical Research International 34(3A): 29-34.

26. Odo M, Ochei KC, Obeagu EI, Barinaadaa A, Eteng EU, et al. (2020) Cascade variabilities in TB case finding among people living with HIV and the use of IPT: assessment in three levels of care in cross River State, Nigeria. Journal of Pharmaceutical Research International 32(24): 9-18.

27. Jakheng SP, Obeagu EI (2022) Seroprevalence of human immunodeficiency virus based on demographic and risk factors among pregnant women attending clinics in Zaria Metropolis, Nigeria. J Pub Health Nutri 5(8): 137.

28. Obeagu EI, Obeagu GU (2023) A Review of knowledge, attitudes and socio-demographic factors associated with non-adherence to antiretroviral therapy among people living with HIV/AIDS. Int J Adv Res Biol Sci 10(9): 135-142.

29. Obeagu EI, Onuoha EC (2023) Tuberculosis among HIV Patients: A review of Prevalence and Associated Factors. Int J Adv Res Biol Sci 10(9): 128-134.

30. Obeagu EI, Ibeh NC, Nwobodo HA, Ochei KC, Iwegbulam CP (2017) Haematological indices of malaria patients coinfected with HIV in Umuahia. Int J Curr Res Med Sci 3(5): 100-114.

31. Jakheng SP, Obeagu EI, Abdullahi IO, Jakheng EW, Chukwueze CM, et al. (2022) 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 13(2): 26-31.

32. Viola N, Kimono E, Nuruh N, Obeagu EI (2023) Factors Hindering Elimination of Mother to Child Transmission of HIV Service Uptake among HIV Positive Women at Comboni Hospital Kyamuhunga Bushenyi District. Asian Journal of Dental and Health Sciences 3(2): 7-14.

33. Okorie HM, Obeagu EI, Okpoli HCH, Chukwu SN (2020) Comparative study of enzyme linked immunosorbent assay (Elisa) and rapid test screening methods on HIV, Hbsag, Hcv and Syphilis among voluntary donors in. Owerri, Nigeria. J Clin Commun Med 2(3): 180-183.

34. Ezugwu UM, Onyenekwe CC, Ukibe NR, Ahaneku JE, Onah CE, et al. (2021) Use of ATP, GTP, ADP and AMP as an Index of Energy Utilization and Storage in HIV Infected Individuals at NAUTH, Nigeria: A Longitudinal, Prospective, Case-Controlled Study. Journal of Pharmaceutical Research International 33(47A): 78-84.

35. Emannuel G, Martin O, Peter OS, Obeagu EI, Daniel K (2023) 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 6(1): 203-211.

36. Igwe MC, Obeagu EI, Ogbuabor AO, Eze GC, Ikpenwa JN, et al. (2022) Socio-Demographic Variables of People Living with HIV/AIDS Initiated on ART in 2014 at Tertiary Health Institution in Enugu State. Asian Journal of Research in Infectious Diseases 10(4): 1-7.

37. Vincent CC, Obeagu EI, Agu IS, Ukeagu NC, Onyekachi-Chigbu AC (2021) Adherence to Antiretroviral Therapy among HIV/AIDS in Federal Medical Centre, Owerri. Journal of Pharmaceutical Research International 33(57A): 360-368.

38. Igwe MC, Obeagu EI, Ogbuabor AO (2022) Analysis of the Factors and Predictors of Adherence to Healthcare of People Living with Hiv/Aids in Tertiary Health Institutions in Enugu State. Madonna University journal of Medicine and Health Sciences 2(3): 42-57.

39. Madekwe CC, Madekwe CC, Obeagu EI (2022) Inequality of monitoring in Human Immunodeficiency Virus, Tuberculosis and Malaria: A Review. Madonna University journal of Medicine and Health Sciences 2(3): 6-15.

40. Echendu GE, Vincent CC, Ibebuike J, Asodike M, Naze N, et al. (2023) Weights of Infants Born to Hiv Infected Mothers: A Prospective Cohort Study in Federal Medical Centre, Owerri, Imo State. European Journal of Pharmaceutical and Medical Research 10(8): 564-568.

41. Nwosu DC, Nwanjo HU, Okolie NJ, Ikeh K, Obeagu EI, et al. (2015) Biochemical Alterations in Adult HIV Patients on Antiretrqviral Therapy. World Journal of Pharmacy and Pharmaceutical Sciences 4(3): 153-160.

42. Obeagu EI, Obeagu GU (2015) Effect of CD4 Counts on Coagulation Parameters among HIV Positive Patients in Federal Medical Centre, Owerri, Nigeria. Int J Curr Res Biosci Plant Biol 2(4): 45-49.

43. Obeagu EI, Nwosu DC (2019) Adverse drug reactions in HIV/AIDS patients on highly active antiretro viral therapy: a review of prevalence. Int J Curr Res Chem Pharm Sci 6(12): 45-48.

44. Obeagu EI, Scott GY, Amekpor F, Obeagu GU (2023) Implications of CD4/CD8 ratios in Human Immunodeficiency Virus infections. Int J Curr Res Med Sci 9(2): 6-13.

45. Obeagu EI, Ochei KC, Okeke EI (2016) Assessment of the level of erythropoietin in persons living with HIV in Umuahia. Int J Curr Res Med Sci 2(4): 28-30.

46. Ifeanyi OE, Obeagu GU (2015) The Values of CD4 Count, among HIV Positive Patients in FMC Owerri. Int J Curr Microbiol App Sci 4(4): 906-910.

47. Obeagu EI, Okeke EI, Andrew AC (2016) Evaluation of haemoglobin and iron profile study among persons living with HIV in Umuahia, Abia state, Nigeria. Int J Curr Res Biol Med 1(2):1-5.

48. Alum EU, Ugwu OP, Obeagu EI, Okon MB (2023) Curtailing HIV/AIDS Spread: Impact of Religious Leaders. Newport International Journal of Research in Medical Sciences (NIJRMS) 3(2): 28-31.

49. Obeagu EI, Obeagu GU, Paul-Chima UO (2023) Stigma Associated With HIV. AIDS: A Review. Newport International Journal of Public Health and Pharmacy (NIJPP) 3(2): 64-67.

50. Alum EU, Obeagu EI, Ugwu OP, Aja PM, Okon MB (2023) HIV Infection and Cardiovascular diseases: The obnoxious Duos. Newport International Journal of Research in Medical Sciences (NIJRMS) 3(2): 95-99.

51. Ibebuike JE, Nwokike GI, Nwosu DC, Obeagu EI (2018) A Retrospective Study on Human Immune Deficiency Virus among Pregnant Women Attending Antenatal Clinic in Imo State University Teaching Hospital. International Journal of Medical Science and Dental Research 1 (2): 19-24.

52. Obeagu EI, Obarezi TN, Omeh YN, Okoro NK, Eze OB (2014) Assessment of some haematological and biochemical parametrs in HIV patients before receiving treatment in Aba, Abia State, Nigeria. Res J Pharma Biol Chem Sci 5(2): 825-830.

53. Obeagu EI, Obarezi TN, Ogbuabor BN, Anaebo QB, Eze GC (2014) Pattern of total white blood cell and differential count values in HIV positive patients receiving treatment in Federal Teaching Hospital Abakaliki, Ebonyi State, Nigeria. International Journal of Life Science, Biotechnology and Pharama Research 3(1): 186-189.

54. Obeagu EI (2023) A Review of Challenges and Coping Strategies Faced by HIV/AIDS Discordant Couples. Madonna University journal of Medicine and Health Sciences 3 (1): 7-12.

55. Oloro OH, Obeagu EI (2022) A Systematic Review on Some Coagulation Profile in HIV Infection. International Journal of Innovative and Applied Research 10(5): 1-11.

56. Nwosu DC, Obeagu EI, Nkwuocha BC, Nwanna CA, Nwanjo HU, et al. (2015) Alterations in superoxide dismutiase, vitamins C and E in HIV infected children in Umuahia, Abia state. International Journal of Advanced Research in Biological Sciences 2(11): 268-271.

57. Obeagu EI, Malot S, Obeagu GU, Ugwu OP (2023) HIV resistance in patients with Sickle Cell Anaemia. Newport International Journal of Scientific and Experimental Sciences (NIJSES) 3(2): 56-59.

58. Ifeanyi OE, Uzoma OG, Stella EI, Chinedum OK, Abum SC (2018) Vitamin D and insulin resistance in HIV sero positive individuals in Umudike. Int J Curr Res Med Sci 4(2): 104-108.

59. Ifeanyi OE, Leticia OI, Nwosu D, Chinedum OK (2018) A Review on blood borne viral infections: universal precautions. Int J Adv Res Biol Sci 5(6): 60-66.

60. Nwovu AI, Ifeanyi OE, Uzoma OG, Nwebonyi NS (2018) Occurrence of Some Blood Borne Viral Infection and Adherence to Universal Precautions among Laboratory Staff in Federal Teaching Hospital Abakaliki Ebonyi State. Arch Blood Transfus Disord 1(2): 1-3.

61. Chinedu K, Takim AE, Obeagu EI, Chinazor UD, Eloghosa O, et al. (2017) HIV and TB co-infection among patients who used Directly Observed Treatment Short-course centres in Yenagoa, Nigeria. IOSR J Pharm Biol Sci 12(4): 70-75.

62. Offie DC, Obeagu EI, Akueshi C, Njab JE, Ekanem EE, et al. (2021) Facilitators and barriers to retention in HIV care among HIV infected MSM attending Community Health Center Yaba, Lagos Nigeria. Journal of Pharmaceutical Research International 33(52B): 10-19.

63. Obeagu EI, Obeagu GU, Ede MO, Odo EO, Buhari HA (2023) Translation of HIV/AIDS knowledge into behavior change among secondary school adolescents in Uganda: A review. Medicine (Baltimore) 102(49): e36599.

64. Anyiam AF, Arinze AOC, Irondi EA, Obeagu EI (2023) Distribution of ABO and rhesus blood grouping with HIV infection among blood donors in Ekiti State Nigeria. Medicine (Baltimore) 102(47): e36342.

65. Echefu SN, Udosen JE, Akwiwu EC, Akpotuzor JO, Obeagu EI (2023) Effect of Dolutegravir regimen against other regimens on some hematological parameters, CD4 count

and viral load of people living with HIV infection in South Eastern Nigeria. Medicine (Baltimore) 102(47): e35910.

66. Opeyemi AA, Obeagu EI (2023) Regulations of malaria in children with human immunodeficiency virus infection: A review. Medicine (Baltimore) 102(46): e36166.

67. Alum EU, Obeagu EI, Ugwu OPC, Samson AO, Adepoju AO, et al. (2023) Inclusion of nutritional counseling and mental health services in HIV/AIDS management: A paradigm shift. Medicine (Baltimore) 102(41): e35673.

68. Aizaz M, Abbas FA, Abbas A, Tabassum S, Obeagu EI (2023) Alarming rise in HIV cases in Pakistan: Challenges and future recommendations at hand. Health Sci Rep 6(8): e1450.

69. Ugwu OP (2023) Hematologic Support in HIV Patients: Blood Transfusion Strategies and Immunological Considerations. Applied Sciences (NIJBAS) 3(3): 9-15.

70. Obeagu EI, Ubosi NI, Uzoma G (2023) Storms and Struggles: Managing HIV Amid Natural Disasters. Int J Curr Res Chem Pharm Sci 10(11):14-25.

71. Obeagu EI, Obeagu GU (2023) Human Immunodeficiency Virus and tuberculosis infection: A review of prevalence of associated factors. Int J Adv Multidiscip Res 10(10): 56-62.

72. Obeagu EI, Malot S, Obeagu GU, Ugwu OP (2023) HIV resistance in patients with Sickle Cell Anaemia. Newport International Journal of Scientific and Experimental Sciences (NIJSES) 3(2): 56-59.

73. Alum EU, Ugwu OP, Obeagu EI, Aja PM, Okon MB, et al. (2023) Reducing HIV Infection Rate in Women: A Catalyst to reducing HIV Infection pervasiveness in Africa. International Journal of Innovative and Applied Research 11(10): 1-6.

74. Upton J (2014) Immunodeficiencies with hypergammaglobulinemia: a review. Lympho Sign Journal 2(2): 57-73.

75. Moir S, Fauci AS (2017) B-cell responses to HIV infection. Immunological reviews 275(1): 33-48.

76. Nagase H, Agematsu K, Kitano K, Takamoto M, Okubo Y, et al. (2001) Mechanism of hypergammaglobulinemia by HIV infection: circulating memory B-cell reduction with plasmacytosis. Clinical immunology 100(2): 250-259.

77. Patel EU, Gianella S, Newell K, Tobian AA, Kirkpatrick AR, et al. (2017) Elevated cytomegalovirus IgG antibody levels are associated with HIV-1 disease progression and immune activation. Aids 31(6): 807-813.

78. Abdurakhmanov A, Zandman G (2015) HIV Spectrum and autoimmune diseases. InInfection and Autoimmunity pp: 371-392.

79. Cooper L, Good JKL (2020) Dysregulation of humoral immunity in chronic infection. Immunology and cell biology 98(6): 456-466.

80. Taubert R, Engel B, Diestelhorst J, Hupa-Breier KL, Behrendt P, et al. (2022) Quantification of polyreactive immunoglobulin G facilitates the diagnosis of autoimmune hepatitis. Hepatology 75(1): 13-27.

81. Haas A, Zimmermann K, Oxenius A (2011) Antigen-dependent and-independent mechanisms of T and B cell hyperactivation during chronic HIV-1 infection. Journal of virology 85(23): 12102-12113.

82. Abaza A, Idris FS, Shaikh HA, Vahora I, Moparthi KP, et al. (2023) Programmed cell death protein 1 (PD-1) and programmed cell death ligand 1 (PD-L1) immunotherapy: a promising breakthrough in cancer therapeutics. Cureus 15(9): e44582.

83. Tarlinton D, Good-Jacobson K (2013) Diversity among memory B cells: origin, consequences, and utility. Science 341(6151): 1205-1211.

84. Fenwick C, Joo V, Jacquier P, Noto A, Banga R, et al. (2019) T-cell exhaustion in HIV infection. Immunological reviews 292(1): 149-163.

85. Sacco KA, Abraham RS (2018) Consequences of B-cell-depleting therapy: hypogammaglobulinemia and impaired B-cell reconstitution. Immunotherapy 10(8): 713-728.

86. Klasse PJ, Sanders RW, Cerutti A, Moore JP (2012) How can HIV-type-1-Env immunogenicity be improved to facilitate antibody-based vaccine development? AIDS Research and Human Retroviruses 28(1): 1-15.