https://doi.org/10.46344/JBINO.2026.v15i02.03

EXPLORING EOSINOPHIL BIOMARKERS IN STAGE III HIV/AIDS: IMPLICATIONS FOR DISEASE MONITORING AND TARGETED THERAPIES

***Emmanuel Ifeanyi Obeagu[1,2]**

[1]Division of Haematology, Department of Biomedical and Laboratory Science, Africa University, Zimbabwe.
[2]The Division of Molecular Medicine and Haematology, School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Email : emmanuelobeagu@yahoo.com

ABSTRACT

Eosinophils, traditionally known for their role in allergic responses and parasitic infections, have gained attention for their involvement in the pathogenesis of Stage III HIV/AIDS, a critical phase marked by severe immune dysfunction. In this review, we explore the diagnostic and prognostic implications of eosinophil biomarkers in HIV/AIDS. During Stage III, the immune system is severely compromised, leading to an increase in chronic inflammation and susceptibility to opportunistic infections. Eosinophils, by releasing inflammatory mediators, contribute to this immunopathology, with their presence and activation in tissues correlating with disease severity and progression. Biomarkers such as eosinophil cationic protein (ECP), eosinophil peroxidase (EPX), and major basic protein (MBP) offer promising diagnostic tools for monitoring HIV/AIDS progression. The role of eosinophils in Stage III HIV/AIDS is multifaceted. These cells are implicated in exacerbating immune activation and tissue damage, particularly in mucosal tissues, which are common sites of HIV replication. Elevated eosinophil activity can contribute to inflammation and accelerate disease progression, while their markers can serve as indicators of disease severity and therapeutic efficacy. Recent studies suggest that eosinophils may also interact with other immune cells, further influencing the inflammatory landscape. The use of eosinophil biomarkers could provide clinicians with valuable insights into the patient's immune status, complementing traditional diagnostic metrics such as CD4+ T cell count and viral load, and offering a more comprehensive approach to disease monitoring.

Keywords: *Eosinophils, HIV/AIDS, Stage III, Biomarkers, Targeted Therapies*

Introduction

HIV/AIDS remains one of the most significant global health challenges, with millions of individuals affected by the disease. The progression of HIV through various stages culminates in Stage III, or AIDS, which is characterized by severe immunosuppression and increased vulnerability to opportunistic infections and cancers. As the immune system deteriorates, patients experience a higher burden of inflammation, which plays a critical role in disease pathogenesis. In this context, eosinophils, a subset of white blood cells typically associated with allergic reactions and parasitic infections, have emerged as significant players in the immune dysregulation observed in HIV/AIDS, particularly in its advanced stages.[1-2] Eosinophils are typically recruited to sites of infection or inflammation, where they release a range of pro-inflammatory mediators, such as cytokines, growth factors, and cytotoxic proteins. In the setting of HIV, eosinophils are thought to contribute to chronic immune activation, which exacerbates the immune dysfunction that is a hallmark of Stage III HIV/AIDS. These cells can infiltrate various tissues, including the gastrointestinal tract and mucosal surfaces, which are key sites of viral replication in HIV infection. The role of eosinophils in these tissues is particularly important, as their activation can lead to tissue damage, promote inflammation, and further compromise immune function.[3-4] In Stage III HIV/AIDS, the body's ability to mount an effective immune response is severely compromised due to the depletion of CD4+ T cells, a critical subset of immune cells targeted by the HIV virus. As a result, the immune system enters a state of chronic inflammation, which contributes to both tissue damage and the development of opportunistic infections. Eosinophils, by releasing toxic molecules and engaging with other immune cells, contribute to this inflammatory cascade, potentially accelerating disease progression. The infiltration of eosinophils in tissues, particularly in areas with high viral load, raises the question of whether these cells are merely reactive to the infection or actively participate in promoting disease severity.[5-6]

Over the years, eosinophils have been implicated in a range of diseases, including asthma, allergic rhinitis, and eosinophilic esophagitis. More recently, researchers have begun to explore the role of eosinophils in chronic viral infections, particularly HIV. Studies have shown that elevated eosinophil numbers and the release of eosinophil-associated biomarkers, such as eosinophil cationic protein (ECP), eosinophil peroxidase (EPX), and major basic protein (MBP), are associated with HIV disease progression and immune dysfunction. These biomarkers, which are typically released during eosinophil activation, could serve as valuable tools for diagnosing and monitoring disease progression, particularly in Stage III HIV/AIDS.[7-8] The understanding of eosinophils in HIV/AIDS has expanded in recent years, particularly with the discovery of their role in immune modulation. Eosinophils are no longer viewed solely as participants in allergic responses but as complex immune cells involved in

regulating inflammation and tissue repair. In HIV/AIDS, the presence of eosinophils may reflect an ongoing inflammatory response that may not always be beneficial. In fact, eosinophil-driven inflammation could exacerbate the immunosuppressive state characteristic of Stage III, impairing the body's ability to control HIV replication and defend against opportunistic infections. Understanding the role of eosinophils in this context is crucial for identifying potential biomarkers for monitoring disease progression and assessing treatment efficacy.[9-10] In Stage III HIV/AIDS, the immune system is in a state of hyperactivation, with persistent viral replication and an increased burden of opportunistic infections. This state of chronic inflammation can lead to systemic tissue damage, particularly in the gastrointestinal tract, lungs, and other mucosal surfaces. Eosinophils play a dual role in this process, acting as both mediators of inflammation and agents of tissue repair. On the one hand, they release pro-inflammatory cytokines and cytotoxic granules that can damage surrounding tissues, while on the other hand, they produce growth factors that aid in tissue regeneration. This balance between destructive and reparative roles makes eosinophils an interesting target for therapeutic intervention.[11-12]

Despite the increasing recognition of eosinophils in HIV pathogenesis, much remains to be understood about their precise role in Stage III HIV/AIDS. While eosinophils are clearly involved in the immune response, it is not yet fully understood how they contribute to disease progression or how their activity can be modulated to improve patient outcomes. Recent studies have begun to investigate the relationship between eosinophil activity and the immune dysfunction seen in Stage III, suggesting that targeting eosinophil-related pathways could help reduce inflammation and tissue damage. This could, in turn, improve immune function and reduce the burden of opportunistic infections in Stage III HIV/AIDS patients.[13-14] The presence of eosinophil-associated biomarkers in blood and tissues could provide valuable insights into the progression of HIV/AIDS. For example, elevated levels of ECP, EPX, and MBP have been linked to increased inflammation and tissue damage, potentially serving as early indicators of disease progression. Moreover, these biomarkers could help assess the effectiveness of antiretroviral therapy (ART) by providing a complementary measure to the traditional viral load and CD4+ T cell count. As ART continues to evolve, incorporating eosinophil biomarkers into routine clinical practice could provide a more comprehensive understanding of a patient's immune status, allowing for better-tailored treatment regimens and more precise monitoring.[15-16] Eosinophils have also been identified as potential therapeutic targets in HIV/AIDS treatment. Research into the role of eosinophils in chronic inflammation suggests that therapies aimed at modulating eosinophil activity could help alleviate the inflammatory burden in Stage III HIV/AIDS. For instance, monoclonal antibodies targeting eosinophil-related cytokines, such as interleukin-5 (IL-5), could reduce eosinophil activation and infiltration into

tissues. Inhibiting IL-5 has already shown success in treating eosinophilic disorders, such as asthma, and could be applied to HIV/AIDS to mitigate chronic inflammation and improve patient outcomes. Additionally, therapies that promote the beneficial aspects of eosinophil activity, such as tissue repair and immune regulation, could complement traditional ART, potentially enhancing the immune reconstitution seen with treatment.[17]

Aim

The aim of this review is to explore the emerging role of eosinophils and their associated biomarkers in Stage III HIV/AIDS, with a focus on their potential utility in disease monitoring, identification of co-infections and complications, and development of targeted therapeutic strategies. Specifically, the study examines eosinophil biology, dysregulation patterns in advanced HIV, relevant biomarkers such as ECP and IL-5, and the clinical implications of modulating eosinophil activity in the context of immune reconstitution and systemic inflammation.

Review Methods

This review article was conducted through a comprehensive and systematic approach to explore the relevance of eosinophil biomarkers in Stage III HIV/AIDS. The methodology followed these key steps:

1. **Literature Search:** A detailed search of peer-reviewed literature was conducted across multiple electronic databases, including PubMed, Scopus, and Web of Science, covering publications up to January 2025. Keywords and search terms included combinations of "eosinophils," "HIV/AIDS," "Stage III HIV," "eosinophil biomarkers," "disease monitoring," and "targeted therapies." Reference lists from retrieved articles were also screened to identify additional relevant studies.
2. **Inclusion and Exclusion Criteria:** Studies were included if they (a) investigated eosinophil biomarkers in the context of HIV/AIDS, (b) discussed eosinophil functions or granule proteins, (c) focused on Stage III HIV/AIDS, or (d) explored the potential of eosinophil-targeted therapies. Exclusion criteria included studies unrelated to HIV/AIDS, reviews without new insights, and articles with insufficient methodological details or limited relevance to biomarkers.

Proposed Thesis and Conceptual Framework

Based on the synthesis of current evidence, we propose a guiding thesis that eosinophils in Stage III HIV/AIDS function as dual-role biomarkers, simultaneously reflecting the underlying immune dysregulation characteristic of advanced HIV infection and the burden of co-infections, particularly parasitic and opportunistic infections prevalent in this patient population.

In advanced HIV disease, profound CD4+ T-cell depletion disrupts immune homeostasis, resulting in chronic inflammation and aberrant immune activation. Eosinophils, through their cytotoxic granules and cytokine secretion (such as eosinophil cationic protein [ECP], interleukin-5 [IL-5], and eotaxins), mirror this immune dysregulation. Elevated eosinophil activation markers may thus serve as indicators of ongoing systemic inflammation or tissue damage.

Concurrently, eosinophilia and related biomarker elevations often arise from co-infections with helminths and other pathogens that induce type 2 immune responses. These infections complicate HIV management by amplifying immune activation and modifying treatment responses.

We therefore suggest a conceptual framework wherein monitoring eosinophil activity provides valuable clinical insights, especially in resource-limited settings where access to comprehensive diagnostic tools is limited. Serial measurement of eosinophil counts and associated biomarkers (e.g., ECP, IL-5, eotaxins) could serve as a practical adjunct for:

- Flagging subclinical inflammation: Identifying patients experiencing immune dysregulation or early IRIS manifestations before overt clinical symptoms.
- Detecting co-infection burden: Prompting targeted screening and treatment for parasitic or opportunistic infections that may otherwise be overlooked.
- Guiding immunomodulatory interventions: Informing decisions on the use of adjunctive therapies to mitigate harmful inflammation and improve immune reconstitution outcomes.

This dual-function role positions eosinophils as promising biomarkers that bridge immunological assessment and infectious disease management in Stage III HIV/AIDS, potentially improving patient outcomes through timely and tailored clinical interventions.

Eosinophils

Eosinophils are multifunctional granulocytic leukocytes that play an integral role in immune regulation, inflammation, and host defense. Traditionally associated with allergic responses and parasitic infections, eosinophils have now emerged as important modulators of immunity in a range of pathological conditions, including viral infections, malignancies, autoimmune disorders, and chronic inflammatory diseases. Their role in the context of HIV/AIDS, particularly in advanced stages of the disease, is of growing interest due to their potential contributions to immunopathology and immune reconstitution.[18-20]

Origin and Development

Eosinophils originate from hematopoietic stem cells in the bone marrow through a tightly regulated process of granulopoiesis. Under the influence of cytokines such as interleukin-3 (IL-3), granulocyte-macrophage colony-stimulating factor (GM-CSF), and most critically interleukin-5 (IL-5), eosinophil progenitors differentiate and mature within the bone marrow before entering the bloodstream. IL-5, in particular, is essential not only for eosinophil differentiation but also for their survival and activation in peripheral tissues. Once matured, eosinophils are released into the bloodstream, where they circulate briefly (approximately 8–12 hours) before migrating into various tissues, including the gastrointestinal tract, lungs, thymus, uterus, and spleen, where they may persist for days to weeks.[21-23]

Structure and Granule Composition

Morphologically, eosinophils are characterized by a bilobed nucleus and prominent cytoplasmic granules that stain

brightly with eosin, an acidic dye. These granules are loaded with a variety of cationic proteins including eosinophil cationic protein (ECP), eosinophil peroxidase (EPO), major basic protein (MBP), and eosinophil-derived neurotoxin (EDN). Each of these granule proteins exerts cytotoxic effects on pathogens and contributes to tissue inflammation and remodeling when released during activation or degranulation.[24-25]

Physiological Functions

The physiological role of eosinophils is far more diverse than once appreciated. While their classical function involves defense against helminthic parasites through degranulation and cytotoxicity, eosinophils also actively participate in modulating immune responses. They secrete a broad range of cytokines (e.g., IL-4, IL-5, IL-13, TNF-α), chemokines, growth factors, and lipid mediators that influence the behavior of T cells, B cells, dendritic cells, mast cells, and epithelial cells. In mucosal immunity, particularly in the gastrointestinal tract, eosinophils contribute to tissue homeostasis, immune surveillance, and microbial defense. They are also involved in tissue remodeling and repair, although this function may become pathological under chronic inflammatory conditions.[26-27]

Pathophysiology and Disease Associations

Eosinophils are central players in the pathophysiology of numerous diseases. In allergic disorders such as asthma, eosinophilic esophagitis, and atopic dermatitis, eosinophils contribute to inflammation and tissue damage through the release of toxic granule proteins and pro-inflammatory mediators. In parasitic infections, eosinophilia (elevated eosinophil count) is often a hallmark finding and reflects a type 2 immune response aimed at expelling helminths. In autoimmune and chronic inflammatory diseases, eosinophils have been implicated in tissue damage and fibrosis. They may exacerbate disease through persistent activation and recruitment to inflamed sites, where they can amplify local immune responses. Importantly, the presence of eosinophils in tumor microenvironments, though variable, suggests a dual role—potentially promoting tumor immunity or contributing to tumor progression depending on the context.[27-28]

Eosinophils in HIV/AIDS Pathogenesis

Eosinophils are a subset of white blood cells traditionally associated with allergic responses and parasitic infections, but emerging evidence has expanded their role to chronic viral diseases, including HIV/AIDS. These cells are involved in both the regulation of immune responses and tissue repair, yet their contribution to disease pathogenesis in HIV/AIDS, especially in advanced stages, remains an area of intense research. As HIV progresses to Stage III, or AIDS, the immune system is severely compromised, and chronic inflammation becomes a hallmark of disease progression. Eosinophils, through their release of toxic granules and pro-inflammatory mediators, contribute to the pathogenesis of HIV/AIDS, exacerbating immune dysfunction, tissue damage, and increasing susceptibility to opportunistic infections.[29]

Eosinophil Function in HIV/AIDS

Under normal circumstances, eosinophils participate in immune responses against parasitic infections and contribute to tissue repair and remodeling. However, in the context of HIV/AIDS, eosinophils have been shown to play a dual role. On one hand, they are involved in modulating immune responses, potentially supporting the immune system's fight against HIV infection and opportunistic pathogens. On the other hand, their activation in chronic inflammation leads to the release of toxic substances, such as eosinophil cationic protein (ECP), major basic protein (MBP), and eosinophil peroxidase (EPX), which can damage tissues and amplify the inflammatory environment. This imbalance between their protective and damaging roles is especially pronounced in Stage III HIV/AIDS, where the immune system is already weakened, and their presence in inflamed tissues further complicates disease progression.[30]

Eosinophils and Immune Dysregulation

In Stage III HIV/AIDS, immune dysregulation is a key feature. The depletion of CD4+ T cells and chronic viral replication result in systemic immune activation and inflammation. Eosinophils, known for their involvement in inflammatory processes, become increasingly prominent in these environments. Their activation and recruitment to sites of chronic inflammation, particularly in mucosal tissues such as the gastrointestinal tract, where HIV replication is active, contribute to the pathogenesis. Infected tissues are further damaged by eosinophil-derived enzymes and inflammatory cytokines, leading to exacerbated tissue injury and enhanced viral replication. The persistent presence of eosinophils in these tissues may lead to a vicious cycle, where tissue damage and inflammation promote further immune dysfunction and disease progression.[31]

Eosinophils in HIV Reservoirs

The gastrointestinal tract is one of the primary reservoirs for HIV, and eosinophils have been found to accumulate in these mucosal tissues in HIV-infected individuals. The infiltration of eosinophils into these reservoirs can have a significant impact on both the local immune environment and the viral dynamics. Eosinophils are believed to play a role in maintaining mucosal inflammation and tissue remodeling, which may provide a favorable environment for continued viral replication. Moreover, the presence of eosinophils may inhibit the normal immune response against the virus, impeding the body's ability to clear infected cells and contribute to the persistence of HIV in these tissues (Figure 1). As a result, eosinophils may be involved in both the pathogenesis of HIV-associated gastrointestinal damage and in the maintenance of viral reservoirs.[32]

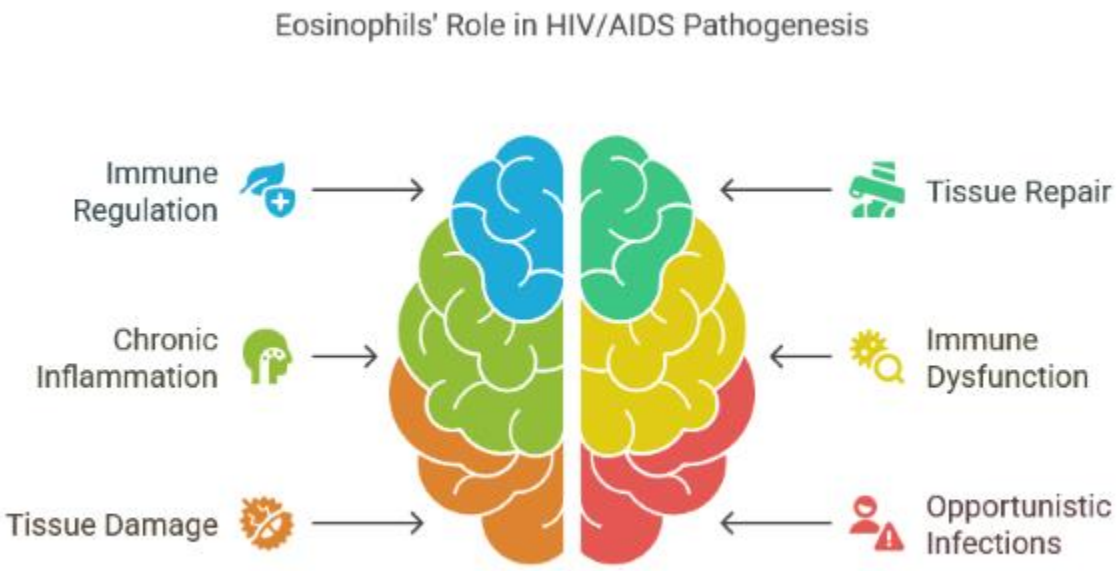

Figure 1: Eosinophils' Role in HIV/AIDS Pathogenesis

Eosinophil Biomarkers in HIV/AIDS Progression

Eosinophil-related biomarkers, including ECP, MBP, and EPX, have emerged as promising tools for monitoring HIV/AIDS progression. Elevated levels of these biomarkers in plasma and tissues can reflect increased eosinophil activation and tissue damage. Furthermore, their levels correlate with immune activation and the severity of inflammation, which are closely linked to disease progression in HIV/AIDS. Monitoring eosinophil biomarkers may provide valuable insights into the immune status of HIV-infected individuals, particularly during Stage III, where traditional markers such as CD4+ T cell count and viral load may not fully capture the extent of immune dysfunction. By using eosinophil biomarkers alongside other diagnostic tools, clinicians could better track disease progression and tailor treatment strategies.[33]

Eosinophils and Opportunistic Infections

Opportunistic infections are a major concern in Stage III HIV/AIDS, as the immune system is too weakened to fight off pathogens that would normally be harmless. Eosinophils, through their pro-inflammatory actions, are thought to contribute to the pathogenesis of these infections. For example, eosinophils have been implicated in the inflammation associated with respiratory infections, such as Pneumocystis jirovecii pneumonia, which is common in individuals with advanced HIV/AIDS. The presence of eosinophils in infected tissues may contribute to the recruitment of other immune cells, amplifying the inflammatory response and exacerbating tissue damage. This process can lead to a higher susceptibility to infections and worse

clinical outcomes. Therefore, understanding how eosinophils influence the immune response to opportunistic infections in HIV/AIDS may provide new therapeutic targets for managing these infections.[34]

Eosinophils in HIV-Related Inflammatory Diseases

HIV/AIDS is often accompanied by several inflammatory diseases, including HIV-associated neurocognitive disorders (HAND), HIV-related cardiovascular diseases, and inflammatory bowel disease. Eosinophils are known to contribute to inflammation in various organs, including the central nervous system, heart, and gastrointestinal tract. In the brain, for example, eosinophils may exacerbate neuroinflammation, contributing to the cognitive decline seen in HAND. In the cardiovascular system, eosinophil-mediated inflammation may play a role in HIV-related heart disease, contributing to atherosclerosis and other complications. Similarly, in the gut, eosinophils may drive inflammation in HIV-associated enteropathy, worsening the nutritional and immune challenges faced by individuals with advanced HIV. These conditions underscore the importance of eosinophils in the broader landscape of HIV-related inflammatory diseases.[35]

Therapeutic Targeting of Eosinophils in HIV/AIDS

Given the complex role of eosinophils in HIV/AIDS pathogenesis, they present a potential therapeutic target for modulating chronic inflammation and immune dysfunction. Several strategies have been proposed to modulate eosinophil activity, including the use of monoclonal antibodies targeting eosinophil-related cytokines such as interleukin-5 (IL-5). Inhibiting IL-5 has been shown to reduce eosinophil activation and infiltration in other diseases, such as asthma, and could have similar benefits in HIV/AIDS. Additionally, drugs that inhibit eosinophil degranulation or block the signaling pathways involved in their recruitment to inflamed tissues could be explored as adjunctive therapies to reduce inflammation and improve immune function in HIV/AIDS patients.[36]

Eosinophil-Mediated Tissue Repair in HIV/AIDS

While eosinophils are often viewed through the lens of their involvement in inflammation and tissue damage, they also play a role in tissue repair and remodeling. In HIV/AIDS, where chronic inflammation and tissue damage are prevalent, eosinophils may contribute to tissue regeneration in some contexts. Eosinophils release growth factors such as transforming growth factor-beta (TGF-β) and vascular endothelial growth factor (VEGF), which promote tissue healing and angiogenesis. However, this reparative function may be compromised in Stage III HIV/AIDS, where chronic inflammation and immune dysfunction dominate. Investigating the balance between eosinophil-driven tissue damage and repair in HIV/AIDS could reveal new insights into disease pathogenesis and potential therapeutic strategies.[37]

Eosinophil Biomarkers for Disease Monitoring in HIV/AIDS

Eosinophils, traditionally recognized for their role in allergic reactions and parasitic

infections, have increasingly been recognized as contributors to chronic inflammation in diseases like HIV/AIDS. In Stage III HIV/AIDS, characterized by immune system compromise and widespread inflammation, eosinophils have been shown to infiltrate various tissues, including the gastrointestinal tract, lungs, and lymphatic organs. Their presence and activity may be reflective of the immune status and disease progression, making eosinophil biomarkers valuable tools for disease monitoring in HIV-infected individuals. This article explores the potential of eosinophil-related biomarkers, such as eosinophil cationic protein (ECP), major basic protein (MBP), and eosinophil peroxidase (EPX), in the clinical management of HIV/AIDS.[38]

Eosinophil Cationic Protein (ECP)

Eosinophil cationic protein (ECP) is one of the most studied biomarkers for eosinophil activity. It is a highly charged, toxic protein released by eosinophils during activation and degranulation. Elevated levels of ECP are typically associated with allergic conditions and chronic inflammatory diseases. In HIV/AIDS, particularly during Stage III, elevated ECP levels are often indicative of ongoing inflammation and immune activation, which are characteristic of this stage of disease progression. ECP can be detected in both serum and mucosal secretions, and its levels correlate with markers of immune dysfunction such as CD4+ T-cell count and viral load. Therefore, ECP levels can be used as a surrogate marker for immune system activity and disease severity, offering a non-invasive method for tracking HIV progression and inflammatory status.[39-40]

Major Basic Protein (MBP)

Major basic protein (MBP) is another key eosinophil-derived protein that is implicated in inflammation and tissue damage. Like ECP, MBP is released during eosinophil activation and contributes to the toxic environment surrounding inflamed tissues. In HIV/AIDS, increased MBP levels have been linked to the severity of inflammation and the development of opportunistic infections. As MBP plays a role in tissue remodeling and fibrosis, its presence can also provide insights into the degree of tissue damage, particularly in mucosal and pulmonary tissues, which are commonly affected in advanced HIV. Monitoring MBP levels may help identify patients at risk for developing severe complications and offer a way to assess the effectiveness of therapeutic interventions aimed at reducing inflammation.[41]

Eosinophil Peroxidase (EPX)

Eosinophil peroxidase (EPX) is an enzyme released by eosinophils that plays a role in the generation of reactive oxygen species, which contribute to tissue damage and inflammation. EPX has been shown to be elevated in various conditions associated with chronic inflammation, including HIV/AIDS. In Stage III HIV/AIDS, where the immune system is heavily compromised, increased levels of EPX in the blood or tissues could reflect ongoing eosinophil activation and tissue damage. EPX levels may also correlate with the severity of mucosal damage in organs such as the gastrointestinal tract, where HIV replication is most active. Measuring EPX levels could,

therefore, be an important diagnostic tool for assessing the degree of tissue inflammation and damage in HIV-infected individuals.[42]

Eosinophil Count as a Diagnostic Marker

In addition to specific eosinophil-derived proteins, the total eosinophil count in peripheral blood can provide useful information regarding the degree of eosinophil activation. A high eosinophil count (eosinophilia) may signal an ongoing inflammatory response, which is commonly seen in individuals with HIV/AIDS, especially in those with advanced disease. Eosinophilia is often associated with opportunistic infections, allergic responses, or other inflammatory conditions. Regular monitoring of eosinophil counts may be particularly useful in detecting disease flare-ups, inflammatory episodes, or the emergence of new infections. Eosinophil counts, when used in conjunction with other markers such as CD4+ T-cell count and viral load, can provide a more comprehensive view of an individual's immune status and disease progression.[43]

Role of Eosinophil Biomarkers in Therapeutic Monitoring

Eosinophil biomarkers, including ECP, MBP, and EPX, could also play a role in assessing the effectiveness of therapeutic interventions. In HIV/AIDS management, antiretroviral therapy (ART) is the cornerstone of treatment. However, ART does not always fully resolve the chronic inflammation that characterizes the disease, particularly in Stage III. Eosinophil biomarkers may help monitor the inflammatory response to ART and other treatments aimed at reducing immune activation. For instance, a decrease in ECP or MBP levels following treatment initiation could indicate a reduction in eosinophil activation and inflammation, suggesting that the therapy is effectively controlling immune dysfunction. Conversely, persistent elevation of these markers may signal inadequate control of inflammation, necessitating adjustments to the treatment regimen.[44]

Eosinophils in HIV-Related Comorbidities

In Stage III HIV/AIDS, patients often experience comorbidities such as cardiovascular disease, respiratory infections, and gastrointestinal complications. Eosinophils have been implicated in the pathogenesis of several HIV-related comorbidities, making their biomarkers potentially valuable for monitoring these conditions. For example, elevated ECP levels have been associated with HIV-related cardiovascular diseases, such as atherosclerosis and myocardial infarction, where eosinophil-mediated inflammation contributes to vascular damage. Similarly, eosinophils play a role in respiratory diseases such as Pneumocystis jirovecii pneumonia, a common opportunistic infection in HIV-infected individuals. Monitoring eosinophil biomarkers could help identify those at risk for these comorbidities, facilitating early intervention and management.[45]

Eosinophil Biomarkers in Immune Dysregulation

One of the key challenges in managing HIV/AIDS, especially in Stage III, is the complex immune dysregulation that occurs as a result of chronic viral replication and immune activation. Eosinophils, through their release of inflammatory mediators, contribute to the

ongoing immune activation seen in HIV/AIDS. By measuring eosinophil biomarkers, clinicians can gain insights into the extent of immune dysregulation and identify individuals at higher risk for complications such as opportunistic infections, autoimmune disorders, and cardiovascular disease. Eosinophil-related biomarkers could therefore serve as a useful adjunct to traditional immune monitoring markers, offering a more comprehensive view of the immune landscape in HIV-infected individuals.[46]

Eosinophil Biomarkers and Personalized Medicine

As HIV/AIDS care moves toward more personalized approaches, the inclusion of eosinophil biomarkers in disease monitoring could help tailor treatment plans to individual patients. By incorporating eosinophil biomarkers into routine clinical practice, healthcare providers could more effectively stratify patients based on their inflammatory burden and immune status. This personalized approach could inform decisions regarding ART initiation, the use of adjunctive therapies aimed at reducing inflammation, and the management of comorbid conditions. Additionally, understanding the role of eosinophils in HIV pathogenesis may lead to the development of new therapeutic targets, providing further opportunities for precision medicine in HIV care.[47-48] Figure 2: Eosinophil Biomarker in HIV/AIDS (provided by the author).

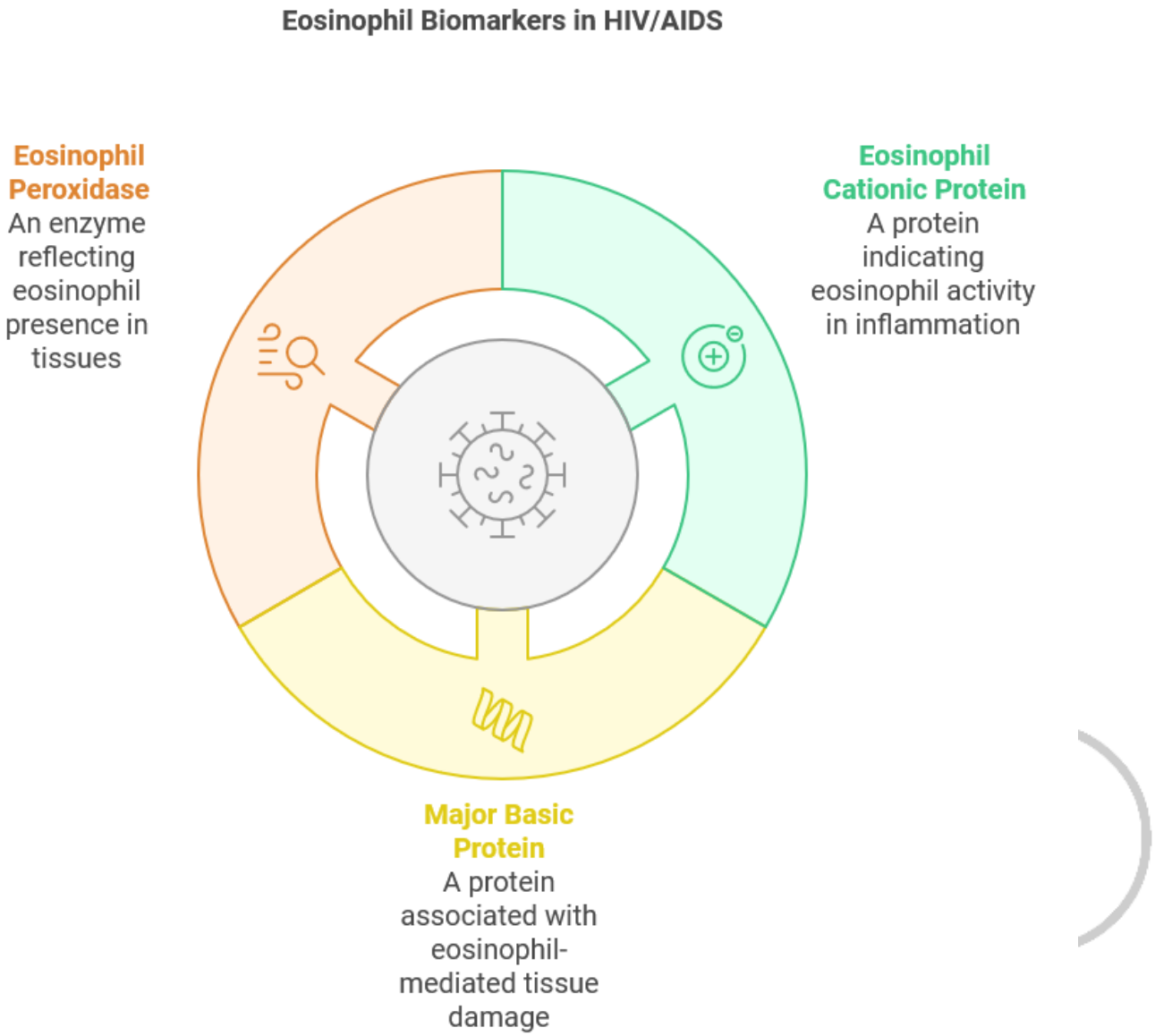

Figure 2: Eosinophil Biomarker in HIV/AIDS

Targeted Therapies Modulating Eosinophil Function in HIV/AIDS

The immune response in HIV/AIDS is characterized by chronic inflammation and dysregulation, contributing to the progression of the disease, especially in later stages like Stage III. Eosinophils, traditionally associated with allergic responses, have emerged as critical players in the inflammatory milieu of HIV/AIDS. They contribute to tissue damage, immune activation, and persistent inflammation, exacerbating the clinical manifestations of the disease. Targeting eosinophil function, including their recruitment, activation, and degranulation, offers a novel therapeutic strategy to reduce inflammation and improve outcomes in HIV-infected individuals. This section delves into various

targeted therapies aimed at modulating eosinophil function, emphasizing their potential for improving disease management in HIV/AIDS.[49]

1. Inhibition of Eosinophil Recruitment

Eosinophil recruitment to inflammatory sites is a key step in the pathogenesis of inflammation in HIV/AIDS. The chemokine eotaxin (CCL11) and its receptor CCR3 are central to the recruitment and accumulation of eosinophils in tissues. Targeting this axis presents a promising strategy to reduce eosinophilic inflammation in HIV-infected tissues. Monoclonal antibodies or small molecules that block eotaxin or CCR3 could potentially inhibit eosinophil migration to the site of infection, thereby reducing inflammatory damage. By limiting eosinophil infiltration, these therapies may alleviate the chronic inflammation observed in organs such as the lungs, gastrointestinal tract, and lymphoid tissues in HIV/AIDS, potentially reducing opportunistic infections and improving patient outcomes.[48-49]

2. Modulation of Eosinophil Activation

Eosinophil activation is a critical step in the release of pro-inflammatory cytokines and cytotoxic proteins that contribute to tissue injury in HIV/AIDS. The activation of eosinophils can be modulated by targeting the IL-5 signaling pathway, which is involved in eosinophil differentiation, activation, and survival. Monoclonal antibodies such as mepolizumab, which target IL-5 or its receptor, have shown promise in treating eosinophilic inflammation in conditions such as asthma. Similar strategies could be applied to HIV/AIDS to reduce eosinophil activation. By inhibiting IL-5 signaling, these therapies could reduce eosinophil activation and the subsequent release of damaging mediators, helping to manage inflammation and improve immune function in HIV-infected individuals.[41-42]

3. Inhibition of Eosinophil Degranulation

Eosinophil degranulation leads to the release of cytotoxic proteins like eosinophil cationic protein (ECP) and major basic protein (MBP), which contribute to inflammation and tissue damage in HIV/AIDS. Inhibiting eosinophil degranulation could be a valuable therapeutic strategy to reduce the harmful effects of these activated cells. Research into small molecules or inhibitors that target the signaling pathways involved in degranulation, such as calcium influx or RhoA GTPase, could provide novel treatments for modulating eosinophil function. By preventing degranulation, these therapies may limit tissue damage, improve immune regulation, and reduce the risk of opportunistic infections in HIV-infected individuals.[43]

4. Targeting Eosinophil Extracellular Trap (EET) Formation

Eosinophils have been shown to form extracellular traps (EETs), which are composed of DNA and antimicrobial proteins that help neutralize pathogens but can also contribute to tissue damage and inflammation. In HIV/AIDS, EETs may exacerbate the inflammatory response, particularly in tissues vulnerable to infection and injury. Targeting the formation of EETs could present a novel approach to reducing tissue damage and inflammation in HIV-infected individuals. Inhibitors that block the enzymes involved in EET

formation, such as NADPH oxidase or PAD4, could be explored as potential therapies to mitigate the harmful effects of EETs in HIV/AIDS. By limiting EET formation, these therapies could help alleviate chronic inflammation and improve overall disease management.[44]

5. Combination Therapies Targeting Eosinophils and Immune Activation

Given the complex nature of immune dysregulation in HIV/AIDS, combination therapies targeting both eosinophils and broader immune activation may offer enhanced therapeutic benefits. Antiretroviral therapy (ART) remains the cornerstone of HIV treatment, but combining ART with immunomodulatory agents targeting eosinophils could help address the inflammatory component of the disease. For instance, combining IL-5 inhibition with ART could suppress eosinophil-driven inflammation while controlling viral replication. Additionally, therapies targeting other aspects of immune activation, such as co-stimulatory molecules or pro-inflammatory cytokines, may complement eosinophil-targeted approaches. This combined approach could lead to more effective management of chronic inflammation, improve immune function, and reduce the risk of opportunistic infections.[45]

6. Addressing Eosinophil-Induced Tissue Remodeling

Eosinophils contribute to tissue remodeling and fibrosis through the secretion of matrix metalloproteinases (MMPs), which degrade the extracellular matrix and promote tissue damage. In HIV/AIDS, chronic inflammation and immune activation can lead to the development of fibrosis in various organs, such as the lungs and gastrointestinal tract, which exacerbates disease progression. Therapies that target eosinophil-driven tissue remodeling could help prevent fibrosis and preserve organ function. Inhibitors of MMPs or TGF-β, a key growth factor involved in fibrosis, could be explored to reduce the fibrotic process. By modulating eosinophil activity and limiting fibrosis, these therapies could improve long-term outcomes in HIV-infected individuals.[46]

7. Personalized Approaches to Targeting Eosinophil Function

HIV/AIDS is a heterogeneous disease with variable immune responses among individuals. Personalized treatment approaches are crucial to optimize therapeutic outcomes. By identifying biomarkers associated with eosinophil activation or inflammation, clinicians could tailor therapies to individual patients based on their specific immune profiles. Genetic markers or immune signatures that predict eosinophil function could guide the selection of targeted therapies, ensuring that patients receive the most effective treatments for their condition. Personalized approaches could also help mitigate the risk of adverse effects, such as increased susceptibility to opportunistic infections or immune suppression, by selecting the appropriate combination of therapies based on the patient's immune status.[47]

8. Risks and Challenges of Eosinophil-Targeted Therapies

While targeting eosinophil function presents promising therapeutic opportunities, several challenges remain. Eosinophils play complex roles in immune responses, and their modulation may have

unintended consequences, such as increasing susceptibility to infections or altering the balance of immune responses. Moreover, the dynamic nature of HIV infection, with its constantly evolving immune environment, complicates the development of therapies that specifically target eosinophils. Careful monitoring and risk assessment will be essential in the clinical implementation of these therapies. Additionally, the potential for eosinophil-targeted therapies to interact with other immune cells and cytokine pathways necessitates further research to ensure their safety and efficacy in the context of HIV/AIDS.[48]

9. Long-Term Effects and Safety Considerations

As with any emerging therapy, the long-term effects of modulating eosinophil function in HIV/AIDS must be carefully considered. Chronic suppression of eosinophil function could lead to unforeseen consequences, including an impaired response to infections or a shift in immune balance. Longitudinal studies are needed to evaluate the safety and effectiveness of eosinophil-targeted therapies over extended periods. Additionally, the potential for drug resistance or immune escape mechanisms must be monitored to ensure that these therapies remain effective in the face of evolving HIV strains. Ensuring the durability and safety of eosinophil-targeted therapies will be key to their successful integration into HIV/AIDS treatment regimens.[49]

Future Directions in Eosinophil-Based Research in HIV/AIDS

As eosinophils continue to be recognized for their diverse roles in immune regulation and inflammatory responses, their contribution to HIV/AIDS pathogenesis and disease progression is becoming a focal point for innovative research. Understanding the precise mechanisms by which eosinophils influence the immune landscape in HIV, particularly in advanced stages like Stage III, presents new avenues for therapeutic interventions. Future research should focus on exploring several critical areas to optimize eosinophil-based approaches for disease management and therapeutic development.

1. Eosinophil Signaling Pathways in HIV Pathogenesis

Future studies should aim to elucidate the signaling pathways that regulate eosinophil activation, recruitment, and survival in the context of HIV infection. Identifying key molecular players involved in eosinophil trafficking, such as eotaxin-CCR3 signaling, could lead to the development of targeted therapies to control eosinophil-mediated inflammation. Additionally, understanding how HIV-specific factors, such as viral proteins or cytokines, influence eosinophil behavior will provide insights into their role in both acute and chronic phases of the infection. These findings could uncover potential targets for novel anti-inflammatory interventions tailored to modulate eosinophil responses in HIV-infected individuals.[49]

2. The Role of Eosinophils in Immune Activation and Co-infections

Eosinophils may influence immune activation in HIV/AIDS by interacting with other immune cells such as T cells,

macrophages, and dendritic cells. Investigating how eosinophils contribute to chronic immune activation, which is a hallmark of HIV progression, could provide new perspectives on managing immune dysregulation. Additionally, exploring the role of eosinophils in co-infections commonly seen in HIV, such as tuberculosis or fungal infections, could improve our understanding of their impact on disease severity and therapeutic outcomes. Research focused on eosinophil interactions in the context of co-infections could potentially lead to improved therapeutic strategies that address multiple facets of HIV-related complications.[39]

3. Biomarkers for Disease Monitoring and Prognosis

The identification of eosinophil-associated biomarkers that correlate with disease progression, immune activation, or response to therapy represents a promising research avenue. Profiling eosinophil-related molecules, such as eosinophil cationic protein (ECP) or IL-5, in HIV-infected individuals could offer insights into the inflammatory burden and help predict disease outcomes. Longitudinal studies assessing the dynamics of eosinophil biomarkers in response to antiretroviral therapy (ART) or other immune modulators could provide valuable prognostic indicators, aiding in personalized treatment approaches. Additionally, the development of non-invasive diagnostic tools that monitor eosinophilic inflammation could facilitate early detection of complications and improve patient care.

4. Eosinophils and the Microbiome in HIV/AIDS

Recent research highlights the interplay between the immune system and the gut microbiome in HIV infection. Since eosinophils are involved in mucosal immunity, particularly in the gastrointestinal tract, further investigation into their role in gut-associated lymphoid tissue (GALT) in HIV/AIDS could yield important findings. Understanding how eosinophils interact with the microbiome could provide insights into the dysbiosis (microbial imbalance) observed in HIV-infected individuals and its implications for disease progression. Future studies could explore whether modulating eosinophil function could restore microbial balance or prevent microbial translocation, thereby improving immune homeostasis in the gut and reducing systemic inflammation.

5. Eosinophil-Based Therapies: Challenges and Innovations

As eosinophil-targeted therapies show promise in other inflammatory diseases, research into their application in HIV/AIDS is still in its infancy. Future studies should investigate the safety, efficacy, and long-term effects of therapies that modulate eosinophil function, particularly in the context of chronic HIV infection. Exploring combination therapies that target both eosinophil-mediated inflammation and viral replication will be crucial for optimizing patient outcomes. Additionally, understanding the potential risks, such as immune suppression or increased susceptibility to opportunistic infections, is vital for the development of eosinophil-based treatments. Innovative strategies to enhance the selectivity and specificity of

eosinophil-targeted therapies, while minimizing off-target effects, should be a priority for future research.

6. Eosinophil-HIV Interaction in Tissue-Specific Inflammation

Tissue-specific eosinophilic infiltration is a key feature of chronic inflammation in HIV/AIDS. Further research is needed to explore the role of eosinophils in specific organs affected by HIV, such as the lungs, brain, and gastrointestinal tract. Investigating how eosinophils contribute to organ-specific damage and dysfunction could provide insights into the pathophysiology of HIV-associated comorbidities, such as cardiovascular disease, pulmonary complications, and neurocognitive impairment. Identifying eosinophil-mediated pathways involved in tissue remodeling and fibrosis in these organs may uncover therapeutic targets to mitigate long-term damage and improve the quality of life for people living with HIV.

7. Eosinophils and Immunotherapy for HIV

Eosinophils play a central role in immune modulation, and their involvement in HIV pathogenesis suggests that they could be targeted to enhance immune responses through immunotherapy. Future research could explore the potential of eosinophil-based immunotherapies to boost immune function in HIV-infected individuals. For example, enhancing eosinophil activity could promote anti-viral immunity, improve the control of opportunistic infections, or boost responses to vaccines. Investigating the synergistic effects of eosinophil-targeted therapies in combination with other immunotherapies, such as checkpoint inhibitors or immune adjuvants, could open up new therapeutic possibilities for HIV.

8. Eosinophil Interactions with Antiretroviral Therapy (ART)

The relationship between eosinophils and ART remains poorly understood, but it is crucial for determining how these therapies influence eosinophil function in HIV-infected individuals. Some ART drugs, particularly those with immunomodulatory properties, may influence eosinophil recruitment or activation. Understanding how eosinophils interact with ART could help identify potential drug interactions or side effects that exacerbate inflammation or immune dysfunction. Additionally, research into the effects of ART on eosinophil subsets or specific eosinophil functions (e.g., cytokine release, degranulation) may reveal ways to enhance ART efficacy while managing eosinophilic inflammation.

9. Eosinophil Targeting in HIV-Induced Autoimmunity

HIV-induced autoimmunity is another area that warrants further investigation in the context of eosinophils. Eosinophils may contribute to autoimmune responses by influencing the activation of autoreactive T cells or the production of autoantibodies. Studying the role of eosinophils in HIV-associated autoimmune diseases, such as systemic lupus erythematosus (SLE) or rheumatoid arthritis, could reveal new therapeutic targets. Targeting eosinophils in these conditions may help prevent or mitigate autoimmune flare-ups in HIV-infected individuals and reduce the overall burden of immune-mediated diseases.

10. Gene Editing and Eosinophil Function Modulation

As gene editing technologies such as CRISPR-Cas9 continue to evolve, future research may explore the possibility of modifying eosinophil function at the genetic level. Gene editing could be used to selectively modulate eosinophil activation or recruitment, providing a precision medicine approach to treating eosinophil-related inflammation in HIV/AIDS. Moreover, genetic studies may identify specific eosinophil-related genes or mutations that contribute to the disease progression or treatment resistance in HIV-infected populations. Such advancements could pave the way for personalized therapies that target eosinophils based on an individual's genetic profile.

Current Gaps in the Literature

Despite emerging interest in the role of eosinophils as immunological biomarkers in Stage III HIV/AIDS, several critical gaps remain that limit the full clinical integration of eosinophil monitoring:

1. **Paucity of Longitudinal Data on Eosinophil Trajectories during ART**
Most existing studies provide cross-sectional snapshots of eosinophil counts or activity at a single time point, often at diagnosis or during opportunistic infections. However, the dynamic changes in eosinophil populations throughout the course of antiretroviral therapy (ART) are poorly characterized. Longitudinal studies tracking eosinophil levels in conjunction with viral load suppression and CD4+ recovery is essential to understand their potential as markers of immune reconstitution or ongoing inflammation.
2. **Limited Research on Eosinophil-Derived Cytokines as Predictive Tools for IRIS**
Immune Reconstitution Inflammatory Syndrome (IRIS) represents a significant challenge in managing advanced HIV. While eosinophil-derived cytokines such as IL-5 and eotaxins are implicated in inflammatory processes, their predictive value and mechanistic roles in IRIS onset remain underexplored. Rigorous clinical studies investigating cytokine profiles before and after ART initiation could clarify whether these markers may identify patients at high risk of IRIS and guide preemptive interventions.
3. **Need for Population-Specific Reference Ranges in HIV-Endemic Regions**
Eosinophil counts and activation markers can vary widely based on genetic background, environmental exposures, and endemic infections, particularly parasitic diseases that are prevalent in many HIV-endemic areas. There is a critical need to establish population-specific reference ranges and adjust interpretations accordingly to avoid misclassification of eosinophilia or eosinopenia. This is especially important to differentiate between HIV-related immune changes and comorbid conditions.
4. **Scarcity of High-Quality Interventional Studies**
Currently, few randomized controlled trials or intervention studies have evaluated how targeting eosinophil activity might influence HIV disease progression or treatment outcomes. Understanding whether modulating eosinophil function (e.g., with anti-IL-5 therapies) could ameliorate inflammation or prevent

complications like IRIS would represent a major advancement.

5. **Integration with Other Biomarkers for Comprehensive Immune Profiling** Eosinophil biomarkers have rarely been studied alongside other immune and inflammatory markers in HIV, such as monocyte activation markers, T-cell exhaustion phenotypes, or cytokine networks. Multimodal biomarker panels may provide better predictive power and should be a focus of future research.

Conclusion

Eosinophils are emerging as significant players in the pathogenesis and progression of HIV/AIDS, particularly in its advanced stages, such as Stage III. As our understanding of their multifaceted roles in immune modulation, inflammation, and tissue responses deepens, eosinophils present promising diagnostic and prognostic biomarkers for monitoring disease progression and therapeutic efficacy. Despite the challenges in fully elucidating their functions, recent research underscores their potential in both exacerbating and mitigating HIV-related immune dysfunction. The exploration of eosinophil-targeted therapies holds promise for modulating the inflammatory environment associated with HIV infection, particularly in managing complications arising from chronic immune activation, co-infections, and organ-specific inflammation. By identifying eosinophil-related biomarkers and exploring their signaling pathways, future research may provide invaluable insights into how eosinophils contribute to immune system dysregulation and how their modulation could lead to improved treatment outcomes.

References

1. Macchia I, La Sorsa V, Urbani F, Moretti S, Antonucci C, Afferni C, Schiavoni G. Eosinophils as potential biomarkers in respiratory viral infections. Frontiers in Immunology. 2023; 14:1170035.
2. Ramana KV, Sabitha V, Rao R. A study of alternate biomarkers in HIV disease and evaluating their efficacy in predicting T CD4+ cell counts and disease progression in resource poor settings in highly active antiretroviral therapy (HAART) era. Journal of Clinical and Diagnostic Research: JCDR. 2013; 7(7):1332.
3. Gama WM, Frank CH, Almeida TV, Dos Santos DS, Chaves YO, da Silva DF, Orlandi PP, Pereira FR, Magalhães GF, Baptista BJ, de Oliveira Silva VL. Immunologic biomarkers, morbidity and mortality among HIV patients hospitalised in a Tertiary Care Hospital in the Brazilian Amazon. BMC Infectious Diseases. 2021; 21:1-9.
4. Venkataramana K. A study of biological markers in HIV disease progression and management in the highly active antiretroviral therapy (HAART) era. American Journal of Bioscience and bioengineering. 2013; 1(2):24-37.
5. Obeagu EI, Obeagu GU. Maternal Eosinophilic Responses in HIV-Positive Pregnant Women: Unraveling Immunological Dynamics for Improved Maternal-Fetal Health. Elite Journal of Immunology. 2024; 2(1):47-64.
6. Muema DM, Akilimali NA, Ndumnego OC, Rasehlo SS, Durgiah R, Ojwach DB, Ismail N, Dong M, Moodley A, Dong KL, Ndhlovu ZM. Association between the cytokine storm, immune cell dynamics, and viral

replicative capacity in hyperacute HIV infection. BMC medicine. 2020; 18:1-7.
7. Attia EF, Bhatraju PK, Triplette M, Kosamo S, Maleche-Obimbo E, West TE, Richardson BA, Zifodya JS, Eskander S, Njiru CD, Warui D. Endothelial activation, innate immune activation, and inflammation are associated with postbronchodilator airflow limitation and obstruction among adolescents living with HIV. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2020; 83(3):267-277.
8. Chimbetete T, Choshi P, Pedretti S, Porter M, Roberts R, Lehloenya R, Peter J. Skin infiltrating T-cell profile of drug reaction with eosinophilia and systemic symptoms (DRESS) reactions among HIV-infected patients. Frontiers in Medicine. 2023; 10:1118527.
9. Cobre AF, Morais AA, Selege F, Stremel DP, Wiens A, Ferreira LM, Tonine FS, Pontarolo R. Use of Biochemical Tests and Machine Learning in the Search for Potential Diagnostic Biomarkers of COVID-19, HIV/AIDS, and Pulmonary Tuberculosis. Journal of the Brazilian Chemical Society. 2024; 35(7):e-20240020.
10. Hoffman M, Ipp H, Phatlhane DV, Erasmus RT, Zemlin AE. E-Selectin and markers of HIV disease severity, inflammation and coagulation in HIV-infected treatment-naïve individuals. African Health Sciences. 2018; 18(4):1066-1075.
11. Boulware DR, Meya DB, Bergemann TL, Wiesner DL, Rhein J, Musubire A, Lee SJ, Kambugu A, Janoff EN, Bohjanen PR. Clinical features and serum biomarkers in HIV immune reconstitution inflammatory syndrome after cryptococcal meningitis: a prospective cohort study. PLoS medicine. 2010; 7(12):e1000384.
12. Landis S, Suruki R, Maskell J, Bonar K, Hilton E, Compton C. Demographic and clinical characteristics of COPD patients at different blood eosinophil levels in the UK clinical practice research datalink. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2018; 15(2):177-184.
13. Obeagu EI, Obeagu GU. Preventive measures against HIV among Uganda's youth: Strategies, implementation, and effectiveness. Medicine (Baltimore). 2024; 103(44):e40317.
14. Obeagu EI, Obeagu GU. Protecting maternal health: Strategies against HIV and malaria in pregnancy. Medicine (Baltimore). 2024; 103(36):e39565.
15. Obeagu EI, Obeagu GU, Ukibe NR, Oyebadejo SA. Anemia, iron, and HIV: decoding the interconnected pathways: A review. Medicine (Baltimore). 2024; 103(2):e36937.
16. Obeagu EI, Obeagu GU. Platelet index ratios in HIV: Emerging biomarkers for immune health and disease management. Medicine (Baltimore). 2024; 103(12):e37576.
17. Obeagu EI, Obeagu GU, Ede MO, Odo EO, Buhari HA. Translation of HIV/AIDS knowledge into behavior change among secondary school adolescents in Uganda: A review. Medicine (Baltimore). 2023; 102(49):e36599..
18. Sanchez Santos A, Socorro Avila I, Galvan Fernandez H, Cazorla Rivero S, Lemes Castellano A, Cabrera López C. Eosinophils: old cells, new directions. Frontiers in Medicine. 2025; 11:1470381.
19. Gatti DM, Reynolds LA. Thymic Eosinophils: What Are You Doing Here?. Journal of Leukocyte Biology. 2025:qiaf001.
20. Sahli W, Vitte J, Desnues B. Eosinophils and COVID-19: Insights into immune complexity

and vaccine safety. Clinical and Translational Allergy. 2025; 15(3):e70050.
21. Hillson K, Fontanella S, Almeida H, Pavlou B, Lajunen K, Irving S, Testa I, Bingham Y, Oritz KM, Lacbay S, Hay S. Point-of-Care Blood Eosinophils to Predict Preschool Wheeze Attacks. Allergy. 2025; 80(4):1038-1046.
22. Ito E, Hayashizaki R, Hosaka T, Yamane T, Miyata J, Isobe Y, Arita M. Eosinophils and pleural macrophages counter regulate IL-33-elicited airway inflammation via the 12/15-lipoxygenase pathway. Frontiers in Immunology. 2025; 16:1565670.
23. Obeagu EI, Obeagu GU. Impact of Maternal Eosinophils on Neonatal Immunity in HIV-Exposed Infants: A Review. Elite Journal of Immunology. 2024; 2(3):1-8.
24. Obeagu EI, Obeagu GU. Eosinophilic Changes in Placental Tissues of HIV-Positive Pregnant Women: A Review. Elite Journal of Laboratory Medicine. 2024;2(1):14-32.
25. Obeagu EI. Comprehensive insights into eosinophil interactions in sickle cell anemia severity. Haematol Int J. 2024; 8(1):00223.
26. Obeagu EI, Obeagu GU. Exploring Eosinophil-Driven Immune Responses in the Uterine Microenvironment of HIV-Positive Pregnant Women: Implications for Maternal-Fetal Health. Elite Journal of Nursing and Health Science. 2024; 2(3):100-117.
27. Obeagu EI, Obeagu GU. Leukocyte dynamics in female reproductive health: roles and mechanisms. Annals of Medicine and Surgery. 2025:10-97.
28. Obeagu EI, Obeagu GU. Eosinophil Dynamics in Pregnancy among Women Living with HIV: A Comprehensive Review. Int. J. Curr. Res. Med. Sci. 2024; 10(1):11-24.
29. Masenga SK, Elijovich F, Hamooya BM, Nzala S, Kwenda G, Heimburger DC, Mutale W, Munsaka SM, Zhao S, Koethe JR, Kirabo A. Elevated eosinophils as a feature of inflammation associated with hypertension in virally suppressed people living with HIV. Journal of the American Heart Association. 2020; 9(4):e011450.
30. Skiest DJ, Keiser P. Clinical significance of eosinophilia in HIV-infected individuals. The American journal of medicine. 1997; 102(5):449-453.
31. Macchia I, La Sorsa V, Urbani F, Moretti S, Antonucci C, Afferni C, Schiavoni G. Eosinophils as potential biomarkers in respiratory viral infections. Frontiers in Immunology. 2023; 14:1170035.
32. Chorba TL, Nkengasong J, Roels TH, Monga B, Maurice C, Maran M, Djomand G. Assessing Eosinophil Count as a Marker of Immune Activation among Human Immunodeficiency Virus—Infected Persons in Sub-Saharan Africa. Clinical infectious diseases. 2002; 34(9):1264-1266.
33. Chou A, Serpa JA. Eosinophilia in patients infected with human immunodeficiency virus. Current HIV/AIDS Reports. 2015; 12:313-316.
34. Ramdial PK, Morar N, Dlova NC, Aboobaker J. HIV-associated eosinophilic folliculitis in an infant. The American journal of dermatopathology. 1999; 21(3):241-246.
35. Obeagu EI, Bluth MH. Eosinophils and Cognitive Impairment in Schizophrenia: A New Perspective. Journal of Blood Medicine. 2024:227-237.
36. Jiang AP, Jiang JF, Guo MG, Jin YM, Li YY, Wang JH. Human blood-circulating basophils capture HIV-1 and mediate viral trans-infection of CD4+ T cells. Journal of virology. 2015; 89(15):8050-8062.
37. Gama WM, Frank CH, Almeida TV, Dos Santos DS, Chaves YO, da Silva DF, Orlandi

PP, Pereira FR, Magalhães GF, Baptista BJ, de Oliveira Silva VL. Immunologic biomarkers, morbidity and mortality among HIV patients hospitalised in a Tertiary Care Hospital in the Brazilian Amazon. BMC Infectious Diseases. 2021; 21:1-9.

38. Paganelli R, Fanales-Belasio E, Scala E, Carmini D, Mezzaroma I, Pinter E, Aiuti F. Serum eosinophil cationic protein (ECP) in human immunodeficiency virus (HIV) infection. Journal of allergy and clinical immunology. 1991; 88(3):416-418.
39. Fang SL, Fan TC, Fu HW, Chen CJ, Hwang CS, Hung TJ, Lin LY, Chang MD. A novel cell-penetrating peptide derived from human eosinophil cationic protein. PloS one. 2013; 8(3):e57318.
40. Baranova SV, Dmitrienok PS, Buneva VN, Nevinsky GA. HIV-infected patients: Cross site-specific hydrolysis of H2a and H2b histones and myelin basic protein with antibodies against these three proteins. Biomolecules. 2020; 10(11):1501.
41. Afonso JP, Tomimori J, Michalany NS, Nonogaki S, Porro AM. Pruritic papular eruption and eosinophilic folliculitis associated with human immunodeficiency virus (HIV) infection: a histopathological and immunohistochemical comparative study. Journal of the American Academy of Dermatology. 2012; 67(2):269-275.
42. Perelló R, Miró O, M Miró J, Moreno A. Role of the eosinophil count in discriminating the severity of community-acquired pneumonia in HIV-infected patients. Critical Care. 2008; 12:1-2.
43. Obeagu EI, Obeagu GU. Maternal Eosinophilic Responses in HIV-Positive Pregnant Women: Unraveling Immunological Dynamics for Improved Maternal-Fetal Health. Elite Journal of Immunology. 2024;2(1):47-64.
44. Chimbetete T, Choshi P, Pedretti S, Porter M, Roberts R, Lehloenya R, Peter J. Skin infiltrating T-cell profile of drug reaction with eosinophilia and systemic symptoms (DRESS) reactions among HIV-infected patients. Frontiers in Medicine. 2023; 10:1118527.
45. Stokes SC, Tankersley MS. HIV: Practical implications for the practicing allergist–immunologist. Annals of Allergy, Asthma & Immunology. 2011; 107(1):1-9.
46. Jiang AP, Jiang JF, Guo MG, Jin YM, Li YY, Wang JH. Human blood-circulating basophils capture HIV-1 and mediate viral trans-infection of CD4+ T cells. Journal of virology. 2015; 89(15):8050-8062.
47. Kuang FL. Approach to patients with eosinophilia. Medical Clinics. 2020; 104(1):1-4.
48. Chen CB, Hung WK, Wang CW, Lee CC, Hung SI, Chung WH. Advances in understanding of the pathogenesis and therapeutic implications of drug reaction with eosinophilia and systemic symptoms: an updated review. Frontiers in Medicine. 2023; 10:1187937.
49. Mkhize-Kwitshana ZL, Taylor M, Jooste P, Mabaso ML, Walzl G. The influence of different helminth infection phenotypes on immune responses against HIV in co-infected adults in South Africa. BMC Infectious Diseases. 2011; 11:1-1.