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Infection Susceptibility and Clinical Burden in Patients with Acquired Immune Dysfunction

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Abstract

Acquired immune dysfunction represents a critical clinical condition characterized by impaired immune response which leads to increased susceptibility to infections. Among the various causes, Human Immunodeficiency Virus (HIV) infection remains the most prominent and primarily targeting $CD4^+$ T helper cells on disrupting both innate and adaptive immunity. This review outlines the pathophysiological mechanisms underlying immune suppression including viral-mediated cellular destruction, cytokine dysregulation, oxidative stress, and immune checkpoint alterations. The role of exosomes in facilitating viral dissemination and chronic inflammation is also highlighted. Furthermore, the article discusses a broad spectrum of opportunistic infections of bacterial, viral, fungal, and parasitic that contribute to morbidity and mortality in immunocompromised individuals. Beyond HIV, other contributing factors such as malignancies, chemotherapy, corticosteroid use, biologic therapies, and chronic stress are explored in the context of secondary immune deficiency. The review also emphasizes the clinical burden associated with acquired immune dysfunction including recurrent infections, increased healthcare costs, and reduced quality of life. A multidisciplinary approach is essential for effective management and improved patient outcomes. This comprehensive overview provides insights into the mechanisms, complications, and broader implications of immune dysfunction in clinical practice.

1. Introduction

The immune system is essential for protecting the body against infectious agents such as bacteria, viruses, fungi, and parasites. When the immune system is weakened, it is considered acquired immune deficiency in individuals. The Human Immunodeficiency Virus (HIV) and acquired immunodeficiency syndrome (AIDS) represent one of the largest clinical risk factors for the human population. Globally, around 30 to 40 million people are living with HIV. In addition, about 75,000 to 80,000 new cases are reported each year. This also includes children in the age group of 0 to 14 years. Although antiretroviral therapy reduces risk factors, HIV treatment still requires a multidisciplinary approach in the healthcare sector (Pienaar and Botha, 2022). The immune system plays a vital role in the body's defense mechanism. It is a distributed network of cells and biomolecules. These components mainly originate from the bone marrow and circulate throughout the body. The immune system interacts with signaling molecules such as cytokines. It consists of two main types: innate immunity and adaptive immunity. Innate immunity provides a rapid response against antigens. It acts in a non-specific manner. This response involves immune cells such as natural killer cells, neutrophils, and macrophages. In contrast, adaptive immunity is responsible for immune memory. It is mainly mediated by T lymphocytes and B lymphocytes (Nicholson, 2016). The immune system varies from person to person. This variation is due to different environmental exposures. It plays an important role in determining human health and risk factors (Brodin and Davis, 2017). Acquired immune deficiency was first recognized in 1981. The main causative agents are HIV-1 and HIV-2. These viruses belong to the lentivirus family. They primarily attack human $CD4^+$ T cells (Sharp and Hahn, 2011). The most common causes

of acquired immune deficiency include transmission through infected partners. This includes intravenous drug users and homosexuality, particularly in men. AIDS was first recognized in hospitals in 1983. It became associated with infectious, neoplastic, and multiple diseases (Levine, 1993). HIV mainly causes suppression of cell-mediated immunity. It also leads to a reduction in the ratio of helper T cells to suppressor T cells (FAUCI et al., 1984). Acquired immune deficiency is increasingly observed in children. It is associated with high-risk backgrounds, haemophilia, and blood transfusion (Chang and Kim, 2001).

2. Pathophysiological Basis of Increased Infection Susceptibilty

The primary mechanism of immune compromise by HIV is the progressive dysfunction of $CD4^+$ T helper cells. These cells act as the central coordinators of the immune system. Structurally, the HIV virion consists of glycoprotein trimers gp120 and gp41 present in a lipoprotein envelope. Beneath this envelope lies the matrix protein p17. The capsid is formed by the nucleocapsid protein p24. Inside the capsid, there is single-stranded RNA (ssRNA) along with the reverse transcriptase enzyme. The HIV virus contains multiple genes that encode proteins responsible for its virulent activity. The tat gene supports early viral activity by forming Tat protein. The rev gene helps in the export of viral RNA from the nucleus to the cytoplasm of the host cell. The Vpr protein assists in the incorporation of RNA into non-dividing cells. The Vif gene increases infectivity by enhancing virus progeny formation. The nef gene causes downregulation of $CD4^+$ T helper cells and supports viral budding (Clark et al., 2017; van Heuvel et al., 2022). $CD4^+$ T helper cells act as co-receptors for approximately 17 different types of chemokine receptors. They also function as HIV receptors. Among these, CXCR4 and CCR5 are the major chemokine receptors present on $CD4^+$ T helper cells. The binding of gp120 and gp41 to $CD4^+$ cells leads to structural changes in the cell membrane (Figure 1 & 2). CCR5 is also expressed on macrophages, dendritic cells, and antigen-presenting cells (APCs). Therefore, the presence of these chemokine receptors facilitates the tropism of the HIV virus (Février et al., 2011; Juffermans et al., 2000).

Exosomes are extracellular vesicles measuring 30–150 nm in size. When gp120 binds to TSG101, it influences endosomal vesicular trafficking and cell survival. TSG101 is a key component of the ESCRT pathway. This interaction promotes the formation of exosomes. In HIV-infected cells, these exosomes contribute to viral release and spread to other host cells. As a result, infection susceptibility increases. Exosomes also play an important role in cell-to-cell communication. In addition, they contribute to latent HIV entry and chronic inflammation (Marca et al., 2025; Sampey et al., 2014). Acute HIV-1 infection (AHI) is a transient phase. During this period, there is massive apoptosis of $CD4^+$ T helper cells. A strong cytokine storm also occurs and drives the inflammatory response. This phase typically occurs within the first 12 weeks of infection. It is associated with increased transmission risk and higher detectability due to intense viral multiplication. During this stage, HIV ssRNA integrates with host DNA. It primarily targets $CD4^+$ cells in the lymphatic system. HIV also invades myeloid cells, where it can persist for long durations. There is also an initial eclipse phase lasting 7–21 days. During this phase, the virus remains undetectable (Ipp et al., 2014; McMichael et al., 2010). HIV affects both innate and adaptive immunity. It mainly targets $CD4^+$ T helper cells. Due to structural damage, these cells fail to activate B cells. This leads to the loss of humoral immune responses. Similarly, $CD4^+$ T helper cells fail to activate $CD8^+$ cytotoxic T cells. These cells are responsible for directly killing the virus. As a result, antiviral defense is weakened. HIV infection also leads to syncytium formation and cell rupture. $CD4^+$ T cells undergo activation-induced cell death. Caspase activation further triggers inflammatory cell death. Th1 and Th17 subsets attempt to restore $CD4^+$ cell populations. However, this recovery remains incomplete (Sevilya et al., 2018; Vidya Vijayan et al., 2017). There is also depletion of regulatory T cells (Tregs). This results in a loss of immune coordination. Pro-inflammatory cytokines such as TNF-α, IL-6, IL-17, and IL-1β are released in large amounts. This leads to a cytokine storm. Consequently, continuous immune destruction, cell death, and tissue damage occur. Increased levels of malondialdehyde (MDA) act as markers of oxidative stress. These further damages immune cells. A shift from Th1 to Th2 immune response is also observed. This shift increases IL-4, IL-5, and IL-10 production. At the same time, IL-2, IFN-γ, IL-12, and IL-17 are inhibited. This imbalance contributes to progressive immunodeficiency. Overproduction of TGF-β is another key feature. It suppresses both innate and adaptive immunity. It also promotes fibrosis of lymphoid tissue, continuous T-cell loss, and poor immune recovery. These changes ultimately contribute to the development of AIDS. Additionally, HIV reduces intracellular glutathione (GSH) levels. This results in oxidative stress and further cellular damage (Harrison-Gleason et al., 2026; Theron et al., 2017). HIV persistence is also linked to immune checkpoint dysregulation.

Immune inhibitory proteins include PD-1, CTLA-4, TIM-3, LAG-3, and TIGIT. HIV induces structural and transcriptional changes in $CD4^+$ T helper cells. It also causes cytosolic dysfunction and permanent DNA alterations. These changes increase PD-1 expression. As a result, $CD4^+$ T cell function is reduced. In addition, $CD8^+$ T cell activation is impaired, which weakens antiviral activity (Fromentin et al., 2016). HIV predominantly persists in macrophages and microglial cells. This persistence suppresses TLR3-mediated antiviral signaling pathways. Poly I:C-induced TLR3 activation is also impaired. This occurs through downregulation of the UNC93B1 protein. Consequently, interferon signaling (Type I and Type II) is affected. The JAK-STAT pathway is also compromised. These changes allow HIV to evade innate immune defense and establish persistent infection. $CD4^+$ T helper cells are highly abundant in the gut lamina propria. In this region, CCR5 expression is also high. This makes it a major target for HIV infection. As a result, mucosal damage is common in both acute and chronic phases. The extent of damage depends on $CD4^+$ T cell recovery and immune activation. Inflammation also plays a significant role, not just the virus alone. $CD8^+$ T cells possess Wnt ligand activity. This activates the canonical Wnt/β-catenin signaling pathway. This pathway has some antiviral effects against HIV. However, due to the severe depletion of $CD4^+$ T helper cells, $CD8^+$ T cell responses are not sufficient to control the infection. `HIV also impairs humoral immunity. It directly affects B cells and plasma cells. There is a rapid loss of interaction between $CD4^+$ T helper cells and B cells. Memory B cells ($CD27^+$) are significantly reduced. In addition, HIV causes immune overactivation, which leads to B cell dysfunction. This results in impaired immune memory and defective antibody responses (Arenas et al., 2023; Perdomo-Celis et al., 2019).

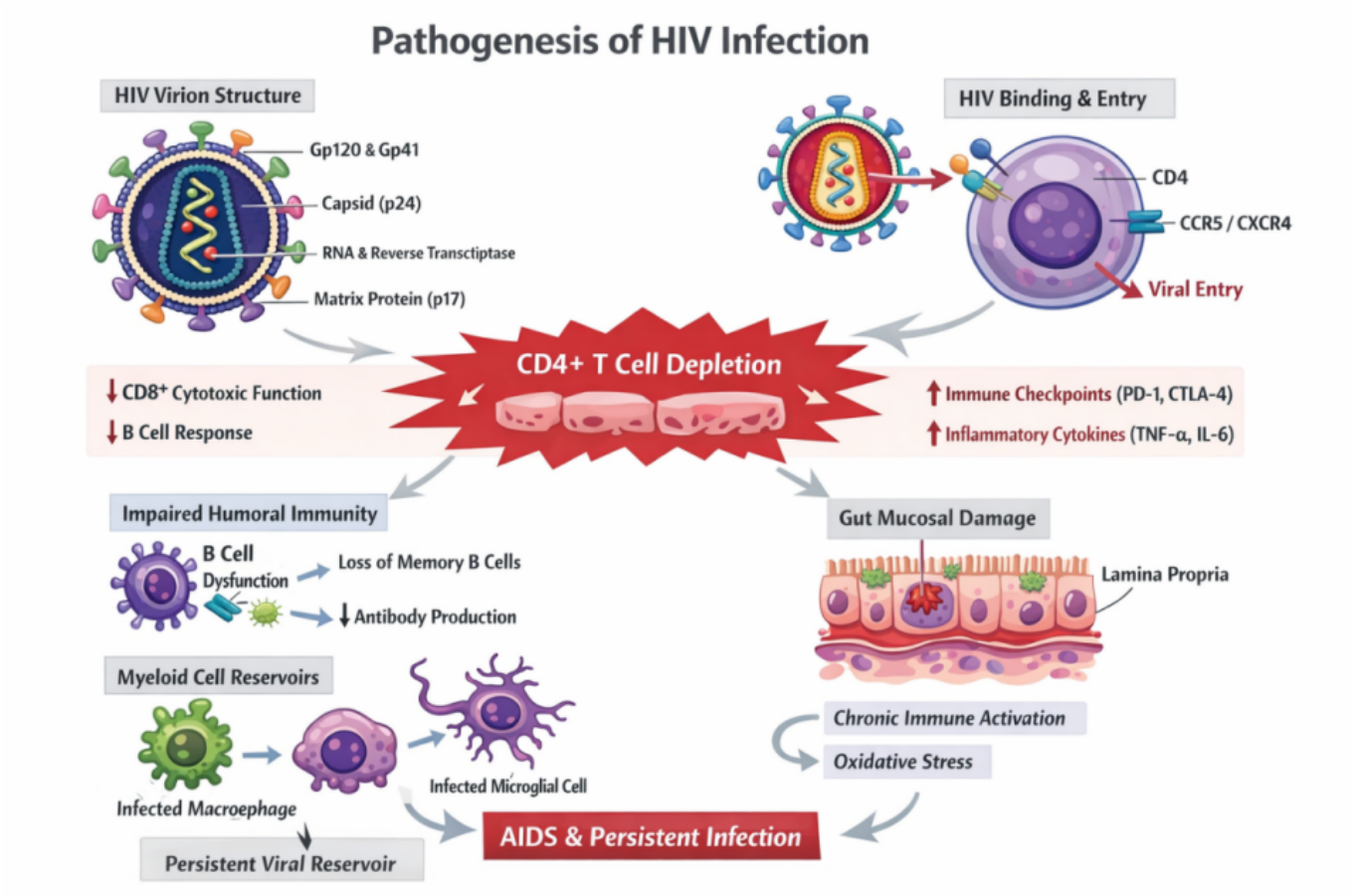

Figure 1: Schematic representation of HIV structure and mechanism of $CD4^+$ T cell infection. The figure illustrates the structural components of the HIV virion, including gp120 and gp41 envelope glycoproteins, matrix protein (p17), capsid protein (p24), and viral RNA with reverse transcriptase. It also depicts the interaction of HIV with $CD4^+$ T helper cells via CCR5 and CXCR4 co-receptors, leading to viral entry, replication, and progressive depletion of immune cells.

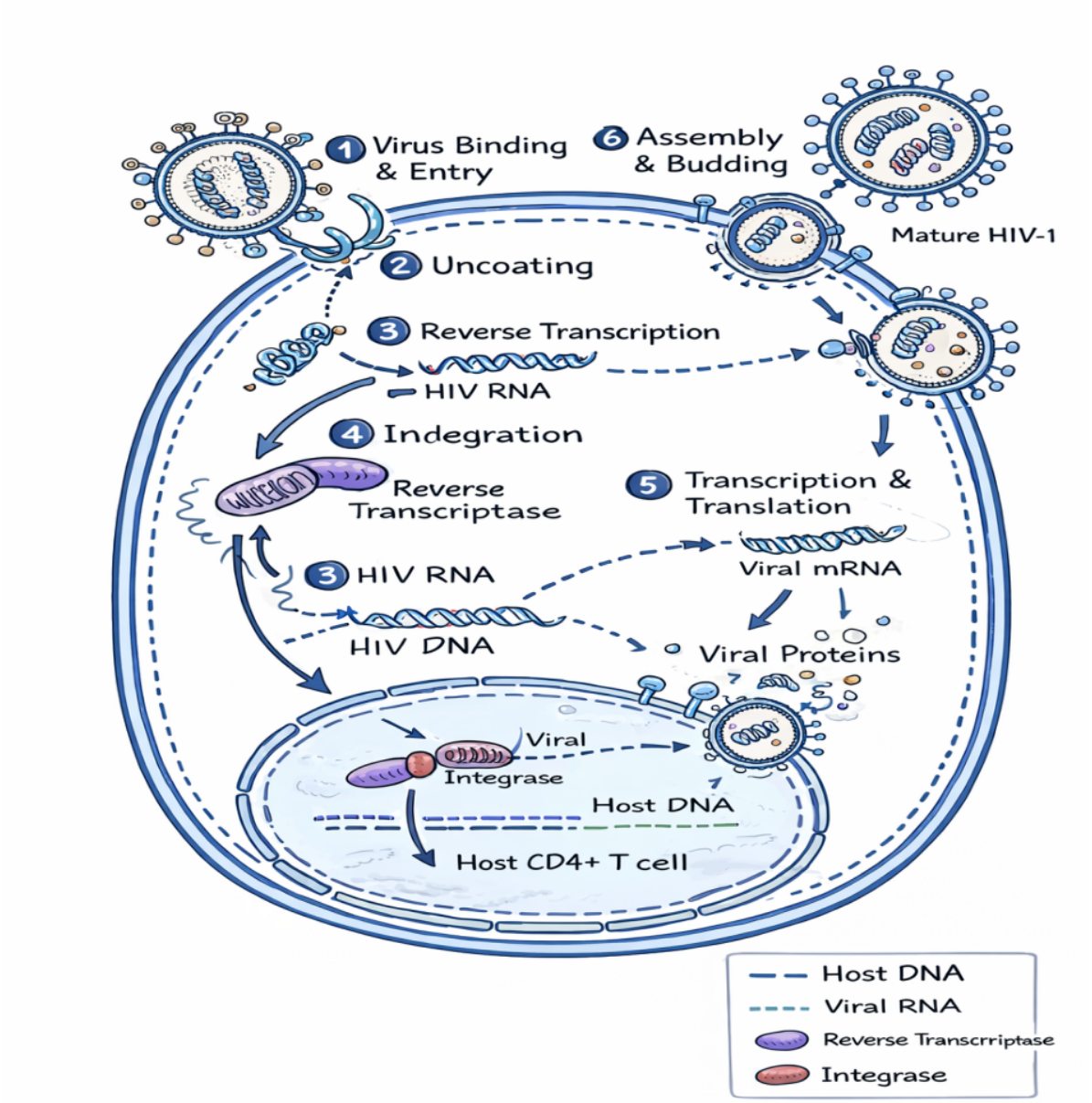

Figure 2: Pathophysiological mechanisms contributing to increased infection susceptibility in acquired immune dysfunction. The figure demonstrates key processes such as $CD4^+$ T cell depletion, cytokine storm, oxidative stress, immune checkpoint activation (PD-1, CTLA-4), exosome-mediated viral spread, and disruption of innate and adaptive immunity. These mechanisms collectively contribute to immune suppression and increased vulnerability to opportunistic infections.

3. Common Infectious Complications in Acquired Immune Dysfunction

Acquired immune dysfunction predisposes individuals to a wide spectrum of infectious complications. This occurs due to the progressive impairment of both cell-mediated and humoral immunity. As immune defenses weaken, patients become highly susceptible to opportunistic infections. These infections are caused by organisms that are normally controlled in immunocompetent hosts. Common infectious complications include recurrent bacterial infections such as tuberculosis, Pneumococcus pneumonia, and septicemia. Viral infections include Herpes simplex, Herpes zoster, cytomegalovirus, and Human papillomavirus. Fungal infections include oral and Esophageal candidiasis, Pneumocystis jirovecii pneumonia, and cryptococcosis. Parasitic infections include toxoplasmosis and cryptosporidiosis. These infections often present with severe, atypical, or recurrent clinical courses. Therefore, they are a major cause of morbidity and mortality in patients with acquired immune dysfunction (Sokulska et al., 2015).

Opportunistic fungal infections are predominantly found in HIV seropositive individuals. Among these, oral candidiasis is the most common complication of HIV infection. Patients with acquired immune deficiency may be infected with both albicans and non-albicans species

(Table 1). Due to low CD4+ cell counts, the genotypes and phenotypes of fungal species vary clinically and biologically. This variation makes diagnosis and treatment difficult and also affects outcome prediction. HIV destroys both innate and adaptive immunity. In addition, it reduces the number of Th17 cells (neutrophils). This reduction promotes the growth of Candida species. Even commensal organisms present in the oral and pharyngeal regions can transform into virulent forms. These organisms secrete aspartyl proteinases. This further reduces host defense and enhances HIV viral protein interaction (Martinez-Martinez et al., 2026). A low CD4+ cell count (less than 200 cells/μL) increases the risk of oropharyngeal candidiasis. Over time, these infections may become resistant to azole antifungal drugs. Another important fungal disease is Pneumocystis jirovecii infection. This organism causes life-threatening pneumonia and is commonly seen in HIV-infected individuals due to severe immunocompromisation (Table 2). The growth of Pneumocystis jirovecii is usually observed when CD4+ cell counts fall below 200 cells/μL. The first-line treatment is sulfamethoxazole combined with trimethoprim. However, mutations in the dihydropteroate synthetase gene can lead to drug resistance. This reduces the effectiveness of treatment, especially due to frequent drug use in HIV patients (Ambe et al., 2020). Cryptococcus neoformans is another opportunistic fungal infection. It commonly causes meningitis in HIV-infected individuals. It is also known as Torula histolytica. This infection is typically seen when CD4+ cell counts fall below 50 cells/μL. It is frequently observed in patients with HIV, along with conditions such as diabetes mellitus, respiratory illness, and hematological malignancies. Cryptococcus neoformans can cause isolated pulmonary infections. It is also associated with neurological complications. This organism is one of the most common co-infections in HIV patients, accounting for approximately 60–70% of cases. Hepatitis co-infection is also common in HIV-infected individuals. It contributes significantly to liver-related morbidity. The major viruses involved include HBV, HCV, and HDV. Another virus, human pegivirus, is also commonly observed in patients with hepatitis C who are co-infected with HIV. In addition, co-infection with HSV virus is frequently seen. These infections show multiple reactivation episodes in HIV-infected individuals. This is mainly due to severe mucosal damage in patients with acquired immune dysfunction (Kassaza et al., 2022; Yoon et al., 2020).

Table 1: Common Opportunistic Infections in Acquired Immune Dysfunction and Their Clinical Characteristics

INFECTION	PATHOGEN	COMMOM SITES AFFECTED	TYPICAL SYMPTOMS	CD4+ T HELPER CELLS
Pneumocystis pneumonia (PCP)	Fungal	Lungs	Shortness of breath, dry cough, fever	<200 μl
Oral/Esophageal candidiasis	Fungal	Mouth, throat, esophagus	White patches, painful swallowing	<200 μl
Tuberculosis (pulmonary/ extra pulmonary)	Bacterial	Lungs, lymph nodes, disseminated	Cough, weight loss, night sweats	Variable, often <500 μl
Toxoplasmosis	Parasitic	Brain	Headache, confusion, seizures	<100 μl
Cryptococcal meningitis	Fungal	Brain, meninges	Headache, fever, altered mental status	<100 μl
Cytomegalovirus (CMV) retinitis	Viral	Eyes, gut, lungs	Vision loss, diarrhea	<50 μl
Mycobacterium avium complex (MAC)	Bacterial	Blood, intestines	Fever, diarrhea, anemia	<50 μl
Cryptosporidiosis	Parasitic	Intestines	Chronic watery diarrhea	<100 μl

4. Disease Specific Context of Aquired Immune Dysfunction

Acquired immune dysfunction is not limited to patients with HIV. It can also occur in various non-HIV-related conditions. These include malignancies, steroid therapy, biologics, chronic stress, and environmental conditions. Chemotherapy is widely used for the treatment of malignancies. However, it causes immune disruption in an aggressive manner. It affects both cell-mediated immunity and humoral responses. As a result, patients become susceptible to multiple opportunistic infections. Corticosteroids are widely used as pharmacological agents to suppress immune responses. They are commonly used in autoimmune diseases. They are also

used to prevent graft-versus-host reactions in solid organ transplantation. Corticosteroids such as dexamethasone are frequently used as first-line treatment in conditions like melanoma and lung cancer. They are also used to reduce edema. However, prolonged use of dexamethasone leads to destruction of naïve T cells. It also upregulates CTLA-4 (Cytotoxic T-Lymphocyte–Associated Protein 4) signaling. This ultimately weakens the immune response (Srivastava et al., 2023; Swildens et al., 2022).

Biologics are widely used in the treatment of neoplastic and autoimmune conditions. These agents can cause immune suppression. Therefore, they are responsible for secondary immune deficiency in patients. This increases the risk of opportunistic infections. Biologic treatments can alter immune responses. As a result, they increase the risk of upper respiratory infections. Malignancies are also associated with immune suppression. In patients with HIV/AIDS, the most common malignancy reported is Kaposi sarcoma. This occurs when CD4+ T helper cells are severely depleted due to systemic HIV infection. Herpes infections are also commonly observed in these individuals. Kaposi herpes virus (KSHV), also known as HSV-8, is responsible for this malignancy (Thakker and Verma, 2016). Kaposi sarcoma is a low-grade vascular tumor. It has multiple histological variants. It can also occur in patients receiving corticosteroids and rituximab therapy. In autoimmune diseases, immune suppression is often done intentionally as part of treatment. This helps to control disease progression. However, it also increases the risk of secondary infections due to reduced immunity (Oprita et al., 2023). Chronic stress and environmental disorders also contribute to immune dysfunction. They alter neuroendocrine function. As a result, both innate and adaptive immunity are reduced. This leads to immune suppression. Consequently, susceptibility to infections increases and contributes to clinical burden.

Table 2: Disease Conditions Associated with Acquired Immune Dysfunction: Mechanisms and Clinical Outcomes

Disease / Clinical Context	**Cause of Immune Dysfunction**	**Primary Immune Components Affected**	**Mechanism of Immune Suppression**	**Associated / Opportunistic Infections or Outcomes**
HIV/AIDS	Direct viral infection of immune cells	$CD4^+$ T helper cells	Progressive depletion of $CD4^+$ T cells leading to impaired cell-mediated immunity	Kaposi sarcoma, herpesvirus infections, Pneumocystis jirovecii, CMV
Malignancies (general)	Tumor-induced immune dysregulation	Cellular and humoral immunity	Tumor microenvironment–mediated immune evasion and immune exhaustion	Increased susceptibility to opportunistic infections
Chemotherapy-treated malignancies	Cytotoxic effects of chemotherapeutic agents	T cells, B cells, neutrophills	Bone marrow suppression and lymphocyte depletion affecting both cell-mediated and humoral immunity	Multiple opportunistic bacterial, viral, and fungal infections
Corticosteroid therapy	Pharmacological immune suppression	Naïve T cells, antigen-presenting cells	Destruction of naïve T cells and upregulation of CTLA-4 signaling, resulting in reduced immune activation	Reactivation of latent infections, fungal and viral infections
Dexamethasone therapy	Long-term or high-dose steroid exposure	T-cell–mediated immunity	Enhanced inhibitory immune checkpoint signaling (CTLA-4), suppression of cytokine production	Increased infection risk, impaired anti-tumor immunity
Biologic therapies (e.g., rituximab)	Targeted immune cell depletion	B cells and adaptive immunity	Selective immune pathway inhibition leading to secondary immune deficiency	Upper respiratory tract infections, opportunistic infections
Autoimmune diseases (on	Therapeutic immune modulation	Adaptive immune responses	Intentional suppression of immune pathways to control autoimmunity	Secondary infections due to immune suppression
Organ transplantation	Immunosuppressive drugs to prevent graft rejection	T-cell–mediated immunity	Suppression of T-cell activation to prevent graft-versus-host reaction	Opportunistic viral, bacterial, and fungal infections

Kaposi Sarcoma	KSHV/HHV-8 infection with immune suppression	$CD4^+$ T cells, endothelial immune	Viral oncogenesis facilitated by immune deficiency	Vascular tumor development, herpesvirus co-
Chronic stress & environmental exposure	Neuroendocrine-immune interaction	Innate and adaptive immunity	Sustained cortisol elevation causing immune dysregulation	Increased susceptibility to infections

5. Clinical Burden and Health Outcomes

Acquired immune dysfunction has a major impact on psychosocial and economic burden in patients. Immune system deregulation leads to recurrent infections, malignancies, and chronic systemic diseases. Some immune-related disorders also arise from genetic conditions. These factors increase morbidity and mortality. They also lead to long-term complications and chronic illness. Patients with chronic diseases such as diabetes mellitus and chronic obstructive pulmonary disease experience increased complications and severity. These patient groups also have a higher risk of cancers, especially lymphoma. As a result, treatment becomes highly expensive. It also leads to productivity loss due to long-term medical care. Therefore, multidisciplinary management is required to address this clinical burden. Pulmonary infections are common in immunodeficient individuals. This is especially seen in patients with long-term illness and associated comorbidities. Common variable immunodeficiency (CVID) is a rare innate-specific antibody deficiency. This group of patients shows a high clinical burden. They present with multiple complications such as bronchiectasis, autoimmune disorders, gastrointestinal disorders, solid cancers, and lymphoma. These conditions increase the mortality rate. Delay in the diagnosis of CVID further increases the health burden. Viral infections pose a high risk in acquired immune dysfunction. They significantly increase patient morbidity. These infections are commonly associated with respiratory complications in both adults and children. This is mainly due to sinopulmonary infections. In addition, viral diseases can affect multiple systems. These include systemic, cutaneous, central nervous system (CNS), respiratory, and gastrointestinal (GIT) systems.

6. Conclusion

Acquired immune dysfunction is a multifaceted condition. It has profound implications on human health. It is mainly driven by the progressive deterioration of immune competence. HIV-induced depletion of $CD4^+$ T helper cells remains the cornerstone of immune impairment. However, non-HIV-related factors also play significant roles. These include malignancies, immunosuppressive therapies, and environmental stressors. The resulting immune imbalance leads to increased vulnerability to opportunistic infections. These infections are major contributors to morbidity and mortality. Advances in understanding molecular and cellular mechanisms have improved knowledge of disease progression. These mechanisms include cytokine dysregulation, oxidative stress, immune checkpoint alterations, and exosome-mediated viral propagation. Despite improvements in therapeutic strategies such as antiretroviral therapy, the clinical burden still persists. This highlights the need for early diagnosis, preventive strategies, and comprehensive care. Future research should focus on targeted immunomodulatory therapies. It should also emphasize personalized treatment approaches to restore immune function and reduce disease complications. Overall, addressing acquired immune dysfunction requires an integrated and multidisciplinary framework. This approach is essential to improve long-term clinical outcomes and enhance patient quality of life.

Declarations

Ethics approval statement

Not applicable

Consent to participate

Not applicable

Consent to publish

Not applicable

Data Availability Statement

The data are available from the corresponding author upon reasonable request

Competing Interests

The authors declare that they have no conflict of interest

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Author contribution

Conceptualization, Data curation, Investigation, Formal analysis, Writing, review, and editing: K.M & D.M.

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References

1. Ambe, N.F., Longdoh, N.A., Tebid, P., Bobga, T.P., Nkfusai, C.N., Ngwa, S.B., Nsai, F.S., Cumber, S.N., 2020. The prevalence, risk factors and antifungal sensitivity pattern of oral candidiasis in HIV/AIDS patients in Kumba District Hospital, South West Region, Cameroon. Pan African Medical Journal 36. https://doi.org/10.11604/pamj.2020.36.23.18202
2. Arenas, V.R., Rugeles, M.T., Perdomo-Celis, F., Taborda, N., 2023. Recent advances in CD8+ T cell-based immune therapies for HIV cure. Heliyon 9, e17481. https://doi.org/10.1016/j.heliyon.2023.e17481
3. Brodin, P., Davis, M.M., 2017. Human immune system variation. Nat. Rev. Immunol. 17, 21–29. https://doi.org/10.1038/nri.2016.125
4. Chang, K.H., Kim, J.M., 2001. Review : Characteristics of HIV Infection / AIDS in Korea. Korean J. Intern. Med. 16, 1–7. https://doi.org/10.3904/kjim.2001.16.1.1
5. Clark, E., Nava, B., Caputi, M., 2017. Tat is a multifunctional viral protein that modulates cellular gene expression and functions. Oncotarget 8, 27569–27581. https://doi.org/10.18632/oncotarget.15174
6. FAUCI, A.S., MACHER, A.M., LONGO, D.L., LANE, H.C., ROOK, A.H., MASUR, H., GELMANN, E.P., 1984. Acquired Immunodeficiency Syndrome: Epidemiologic, Clinical, Immunologic, and Therapeutic Considerations. Ann. Intern. Med. 100, 92–106. https://doi.org/10.7326/0003-4819-100-1-92
7. Février, M., Dorgham, K., Rebollo, A., 2011. CD4+ T Cell Depletion in Human Immunodeficiency Virus (HIV) Infection: Role of Apoptosis. Viruses 3, 586–612. https://doi.org/10.3390/v3050586
8. Fromentin, R., Bakeman, W., Lawani, M.B., Khoury, G., Hartogensis, W., DaFonseca, S., Killian, M., Epling, L., Hoh, R., Sinclair, E., Hecht, F.M., Bacchetti, P., Deeks, S.G., Lewin, S.R., Sékaly, R.-P., Chomont, N., 2016. CD4+ T Cells Expressing PD-1, TIGIT and LAG-3 Contribute to HIV Persistence during ART. PLoS Pathog. 12, e1005761. https://doi.org/10.1371/journal.ppat.1005761
9. Harrison-Gleason, J., Yerlioglu, K.L., Halle, A.W., Hultquist, J.F., Martinelli, E., 2026. Double, double toil and trouble: transforming growth factor beta (TGF-β) in HIV infection. Front. Immunol. 16. https://doi.org/10.3389/fimmu.2025.1738092
10. Ipp, H., Zemlin, A.E., Erasmus, R.T., Glashoff, R.H., 2014. Role of inflammation in HIV-1 disease progression and prognosis. Crit. Rev. Clin. Lab. Sci. 51, 98–111. https://doi.org/10.3109/10408363.2013.865702
11. Juffermans, N.P., Paxton, W.A., Dekkers, P.E.P., Verbon, A., de Jonge, E., Speelman, P., van Deventer, S.J.H., van der Poll, T., 2000. Up-regulation of HIV coreceptors CXCR4 and CCR5 on CD4+ T cells during human endotoxemia and after stimulation with (myco)bacterial antigens: the role of cytokines. Blood 96, 2649–2654. https://doi.org/10.1182/blood.V96.8.2649
12. Kassaza, K., Wasswa, F., Nielsen, K., Bazira, J., 2022. Cryptococcus neoformans Genotypic Diversity and Disease Outcome among HIV Patients in Africa. Journal of Fungi 8, 734. https://doi.org/10.3390/jof8070734
13. Levine, A.M., 1993. AIDS-Related Malignancies: the Emerging Epidemic. JNCI Journal of the National Cancer Institute 85, 1382–1397. https://doi.org/10.1093/jnci/85.17.1382
14. Marca, R. Della, Giugliano, R., Zannella, C., Acunzo, M., Parimal, P., Mali, A., Chianese, A., Iovane, V., Galdiero, M., De Filippis, A., 2025. Role of exosomes in viral infections: a narrative review. Virus Res. 361, 199644. https://doi.org/10.1016/j.virusres.2025.199644
15. Martinez-Martinez, Y.B., Huante, M.B., Naqvi, K.F., Shah, M.N., Lisinicchia, J.G., Files, M.A., Perez, J., Gelman, B.B., Endsley, M.A., Endsley, J.J., 2026. HIV impairs and exploits pulmonary Th17 and Th22 cell-mediated immune responses to Mycobacterium tuberculosis. PLoS Pathog. 22, e1013897. https://doi.org/10.1371/journal.ppat.1013897
16. McMichael, A.J., Borrow, P., Tomaras, G.D., Goonetilleke, N., Haynes, B.F., 2010. The immune response during acute HIV-1 infection: clues for vaccine development. Nat. Rev. Immunol. 10, 11–23. https://doi.org/10.1038/nri2674
17. Nicholson, L.B., 2016. The immune system. Essays Biochem. 60, 275–301. https://doi.org/10.1042/EBC20160017
18. Oprita, A., Cotan, H., Celmare, D., Emilescu, R., 2023. Rituximab-Induced Kaposi Sarcoma in HIV-Negative Patients: A Narrative Review. Cureus. https://doi.org/10.7759/cureus.45365
19. Perdomo-Celis, F., Taborda, N.A., Rugeles, M.T., 2019. CD8+ T-Cell Response to HIV Infection in the Era of Antiretroviral Therapy. Front. Immunol. 10. https://doi.org/10.3389/fimmu.2019.01896
20. Pienaar, A.E., Botha, J.-A.E., 2022. The Value of a Motor Intervention for 3 to 6-Year-Old Children Infected with and Affected by HIV. Int. J. Environ. Res. Public Health 19, 2967. https://doi.org/10.3390/ijerph19052967
21. Sampey, G.C., Meyering, S.S., Asad Zadeh, M., Saifuddin, M., Hakami, R.M., Kashanchi, F., 2014. Exosomes and their role

in CNS viral infections. J. Neurovirol. 20, 199–208. https://doi.org/10.1007/s13365-014-0238-6

22. Sevilya, Z., Chorin, E., Gal-Garber, O., Zelinger, E., Turner, D., Avidor, B., Berke, G., Hassin, D., 2018. Killing of Latently HIV-Infected CD4 T Cells by Autologous CD8 T Cells Is Modulated by Nef. Front. Immunol. 9. https://doi.org/10.3389/fimmu.2018.02068
23. Sharp, P.M., Hahn, B.H., 2011. Origins of HIV and the AIDS Pandemic. Cold Spring Harb. Perspect. Med. 1, a006841–a006841. https://doi.org/10.1101/cshperspect.a006841
24. Sokulska, M., Kicia, M., Wesołowska, M., Hendrich, A.B., 2015. Pneumocystis jirovecii—from a commensal to pathogen: clinical and diagnostic review. Parasitol. Res. 114, 3577–3585. https://doi.org/10.1007/s00436-015-4678-6
25. Srivastava, S., Siddiqui, S., Singh, S., Chowdhury, S., Upadhyay, V., Sethi, A., Kumar Trivedi, A., 2023. Dexamethasone induces cancer mitigation and irreversible senescence in lung cancer cells via damaging cortical actin and sustained hyperphosphorylation of pRb. Steroids 198, 109269. https://doi.org/10.1016/j.steroids.2023.109269
26. Swildens, K.X., Sillevis Smitt, P.A.E., van den Bent, M.J., French, P.J., Geurts, M., 2022. The effect of dexamethasone on the microenvironment and efficacy of checkpoint inhibitors in glioblastoma: a systematic review. Neurooncol. Adv. 4. https://doi.org/10.1093/noajnl/vdac087
27. Thakker, S., Verma, S.C., 2016. Co-infections and Pathogenesis of KSHV-Associated Malignancies. Front. Microbiol. 7. https://doi.org/10.3389/fmicb.2016.00151
28. Theron, A.J., Anderson, R., Rossouw, T.M., Steel, H.C., 2017. The Role of Transforming Growth Factor Beta-1 in the Progression of HIV/AIDS and Development of Non-AIDS-Defining Fibrotic Disorders. Front. Immunol. 8. https://doi.org/10.3389/fimmu.2017.01461
29. van Heuvel, Y., Schatz, S., Rosengarten, J.F., Stitz, J., 2022. Infectious RNA: Human Immunodeficiency Virus (HIV) Biology, Therapeutic Intervention, and the Quest for a Vaccine. Toxins (Basel). 14, 138. https://doi.org/10.3390/toxins14020138
30. Vidya Vijayan, K.K., Karthigeyan, K.P., Tripathi, S.P., Hanna, L.E., 2017. Pathophysiology of CD4+ T-Cell Depletion in HIV-1 and HIV-2 Infections. Front. Immunol. 8. https://doi.org/10.3389/fimmu.2017.00580
31. Yoon, H.A., Felsen, U., Wang, T., Pirofski, L., 2020. Cryptococcus neoformans infection in Human Immunodeficiency Virus (HIV)-infected and HIV-uninfected patients at an inner-city tertiary care hospital in the Bronx. Med. Mycol. 58, 434–443. https://doi.org/10.1093/mmy/myz082