CHOINKA, Martyna, KONOPKA, Agata, WDOWIAK, Natalia, SZCZEPANIAK, Zuzanna, KALISIAK, Jakub, SZPERNALOWSKA, Anna, IVY MATSHABA, Vimbisoyashe and MRUGAŁA, Karolina. The Human Immunodeficiency Virus - a Review of the clinical aspects and detection of the infection. Quality in Sport. 2024;23:55368. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.23.55368
https://apcz.umk.pl/QS/article/view/55368

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 23.08.2024. Revised: 19.09.2024. Accepted: 28.09.2024. Published: 30.09.2024.

The Human Immunodeficiency Virus - a Review of the clinical aspects and detection of the infection

Martyna Choinka[1]; ORCID ID: 0009-0005-0951-3368;
m.choinka@op.pl

Agata Konopka[2]; ORCID ID: 0009-0000-1004-0629;
agatakonopka21@gmail.com

Natalia Wdowiak[3]; ORCID ID: 0009-0004-3894-9921;
natalia.wdowiak5@gmail.com

Zuzanna Szczepaniak[3]; ORCID ID: 0009-0004-8025-6037;
zuzanna.a.szczepaniak@gmail.com

Jakub Kalisiak[4]; ORCID ID: 0009-0000-2472-3148;
kubakalisiak@gmail.com

Anna Szpernalowska[5]; ORCID ID: 0009-0008-2016-5300;
aslowinska98@gmail.com

Vimbisoyashe Ivy Matshaba[6]; ORCID ID: 0009-0001-2219-2774;
vmatshaba3@gmail.com

Karolina Mrugała[6]; ORCID ID: 0009-0005-0153-595X;
karmru12@wp.pl

1. University Clinical Hospital in Poznan, Przybyszewskiego Str. 49, 60-355 Poznan, Poland
2. A. Falkiewicz Specialist Hospital in Wroclaw, Warszawska Str. 2, 52-114 Wrocław, Poland
3. Provincial Specialist Hospital in Wroclaw, H. Kamieńskiego Str. 73a, 51-124 Wrocław, Poland

4. Independent Public Complex of Health Care Facilities of the Ministry of Interior and Administration in Poznan, Dojazd Str. 34, 60-631 Poznan, Poland
5. Warsaw Southern Hospital, Rotmistrza Witolda Pileckiego Str. 99, 02-781 Warsaw, Poland
6. University Clinical Hospital in Poznan, Długa Str. 1/2, 61-848 Poznan, Poland;

* Correspondence: m.choinka@op.pl

Abstract:
Introduction: Currently, many people are infected with the human immunodeficiency virus (HIV). Transmission is primarily through sexual contact, with additional routes including mother-infant exposure to needles and needle sharing. Since the HIV/AIDS pandemic was first identified in 1981, more than 75 million people have been infected. Numerous new cases continue to be reported, and infection can become the starting point for the development of HIV. Clinical manifestations include acute retroviral syndrome, opportunistic infections, and dermatological, neuromuscular, and other complications. Despite advances in antiretroviral therapy (ART), challenges remain, including drug resistance, opportunistic infections, and persistent HIV reservoirs in some cell types. Early and accurate diagnosis is essential, and recommended testing protocols include fourth-generation serological tests and point-of-care (POC) testing. ART, which includes combinations of antiretroviral drugs, is the standard treatment, and ongoing research into gene therapy shows promise for the future.

Purpose of the work: The aim of this study is to review and characterize the clinical aspects and detection of human immunodeficiency virus infection.

Materials and methods: A comprehensive analysis of research papers available on PubMed, Google Scholar, Web of Science, Embase and Scopus was undertaken using the searchterms encompassing the following keywords: HIV, human immunodeficiency virus, ART, HIV manifestation, HIV detection, HIV diagnosis, HIV treatment.

Keywords: HIV, Human Immunodeficiency Virus, ART, HIV manifestation, HIV detection, HIV diagnosis, HIV treatment.

Introduction

Human immunodeficiency virus (HIV) is classified into two types: HIV-1 and HIV-2. The infection progresses through several stages: an acute phase with high viral replication, a chronic phase with ongoing immune activation and viral replication, and an advanced phase marked by a severe loss of CD4(+) T cells, leading to AIDS [1]. HIV is primarily transmitted through sexual contact, but also through maternal-infant exposure and needle sharing [2]. The virus mainly targets T helper cells, crucial for immune responses, causing a gradual weakening of the immune system. HIV also infects macrophages, dendritic cells, and resting T cells, which serve as reservoirs, allowing the virus to persist and evade the immune system and treatment [3]. Currently, a significant number of people are infected with the human immunodeficiency virus (HIV). Since the HIV/AIDS pandemic was first recognized in 1981,

over 75 million people have been infected [4]. New cases continue to emerge, and the infection can progress to HIV disease. Clinical manifestations of HIV include acute retroviral syndrome, opportunistic infections, and various complications affecting the skin, nervous system, and muscles. Although antiretroviral therapy (ART) has significantly improved outcomes, challenges such as drug resistance, opportunistic infections, and persistent HIV reservoirs in certain cell types remain. Early and accurate diagnosis is crucial, with fourth-generation serological tests and point-of-care (POC) testing being recommended [30]. ART, involving combinations of antiretroviral drugs, remains the standard treatment, and research into gene therapy offers hope for future advancements [5].

Epidemiology

The HIV/AIDS pandemic, first identified in 1981 with reports of Pneumocystis pneumonia, has led to over 75 million infections and 32 million deaths worldwide. The virus, HIV, was identified as the cause 2–3 years after the initial cases were reported, with its simian origins discovered later [4]. As of 2022, 39 million people were living with HIV, with the majority in sub-Saharan Africa. Despite progress in reducing new infections, 1.3 million new cases were reported in 2022, and the number of new infections is still rising in Eastern Europe, Central Asia, and the Middle East and North Africa. Alarmingly, there were 630,000 AIDS-related deaths in 2022, with women and girls, particularly in sub-Saharan Africa, disproportionately affected. Women are more likely to be on treatment than men, who tend to acquire HIV later and face higher mortality risks [5,6].

Clinical Manifestations

An estimated 40% to 70% of HIV-infected individuals experience "acute retroviral syndrome" or "primary HIV infection," typically presenting with symptoms such as fever, lymphadenopathy, pharyngitis, maculopapular rash, and myalgias. These symptoms usually appear 2 to 4 weeks after HIV transmission and resolve within 1 to 2 weeks. Laboratory findings include lymphopenia, CD4 cell depletion, and CD8 lymphocytosis. Other possible symptoms include odynophagia, hepatitis, myositis, and various neurological complications like encephalopathy and Guillain-Barré syndrome. In some cases, severe CD4 cell depletion can lead to opportunistic infections such as Pneumocystis carinii pneumonia (PCP) and Candida esophagitis, which should be treated as in late-stage HIV [7].

- **Dermatologic Manifestations**

In the symptomatic stage of HIV infection, several characteristic dermatoses may appear, including bacillary angiomatosis, which presents as red, wart-like lesions caused by *Bartonella henselae* infection. Hairy leukoplakia, which manifests as whitish, uneven lumps on the tongue, inner cheeks, and lips, is also highly indicative of HIV. Persistent or recurrent candidiasis, affecting the throat, vagina, or vulva, is common, as are cervical dysplasia and carcinoma in situ, both linked to chronic HPV infection. People living with HIV (PLWH) have a higher incidence of herpes zoster and post-herpetic neuralgia compared to the general population, even when they are on long-term antiretroviral therapy (ART) with undetectable viral loads and normal CD4 counts [8]. The advent of antiretroviral therapy (ART) has introduced immune reconstitution inflammatory syndrome (IRIS), which often manifests with skin involvement. HIV-infected individuals may also experience cutaneous manifestations due to other sexually transmitted diseases (STDs), complications from intravenous drug use (IVDU), and poor lifestyle choices. Common skin infections seen in immunocompetent

people, like tinea, verruca vulgaris, bacterial cellulitis, and staphylococcal scalded skin syndrome occur with equal or higher frequency in those with HIV [9,10]. Certain skin conditions, such as seborrheic dermatitis, psoriasis, urticaria, and vitiligo, are more prevalent among HIV patients. HIV-specific dermatoses include: papular pruritic eruptions, the most frequent dermatologic condition in HIV- positive patients, xeoderma or xerosis, eosinophilic folliculitis, prurigo nodularis, papular mucinosis, any type of acne, including vulgaris, rosacea, and conglobata. In advanced HIV stages, with lower CD4 counts, patients are prone to opportunistic infections like herpetic and mycobacterial infections, which may present differently in AIDS patients. While most skin disorders in HIV/AIDS can be managed in outpatient settings, some lead to significant morbidity and mortality [11,12].

- **Neuromuscular manifestations and rheumatological symptoms:**

Peripheral neuropathy (PN) is the most common neurological complication of HIV infection, arising either from chronic HIV-associated distal sensory polyneuropathy (HIV-PN) or from treatment-related toxicity, known as antiretroviral toxic neuropathy (ATN) [13]. These conditions are significant due to their link with neuropathic pain and their negative impact on quality of life and function. Less common PN syndromes include autonomic neuropathy, inflammatory demyelinating polyneuropathies (AIDP and CIDP), PN associated with diffuse infiltrative lymphomatosis syndrome (DILS), other toxic PNs, and PNS vasculitis [14]. Autonomic neuropathy symptoms, such as resting tachycardia and orthostatic hypotension, often appear in advanced HIV stages, though its exact prevalence is unclear. AIDP and CIDP are rare and usually occur with mild to moderate immunosuppression. DILS affects about 3%–4% of HIV patients, while PNS vasculitis is rare but treatable [15]. Myalgia (muscle pain) and arthralgia (joint pain) are reported in about one-third of patients with PHI. Some cases of myalgia are associated with muscle weakness and elevated serum creatinine kinase levels [16]. Rhabdomyolysis, a severe muscle breakdown, has also been reported as part of PHI, sometimes leading to acute renal failure and nephrosis [17,18].

- **general symptoms**

Diarrhea is a significant issue for HIV-infected patients. Early studies suggested that around 50% of HIV-positive individuals experience diarrhea, but this might be an underestimate [19]. Those whose HIV risk factors include homosexuality or bisexuality are more prone to developing diarrhea and are more likely to have an identified enteric pathogen as the cause, compared to patients whose risk factors are heterosexuality or intravenous drug use [20]. Fever related to primary HIV infection (PHI) is generally mild, with an average temperature around 38.68°C, though about one-third of patients may experience a fever exceeding 39.8°C. Fever is one of the most common symptoms of PHI, affecting over 75% of patients. However, when fever is used along with other signs and symptoms as a diagnostic criterion, some studies report that 100% of patients experience it [21,22].

- **lymphatic symptoms**

Lymphadenopathy, though typically absent at the onset of primary HIV infection (PHI), appears in most cases during the second week of illness. It often affects the cervical, axillary, and inguinal regions. This clinical lymphadenopathy aligns with the initial widespread

dissemination of the virus, as HIV structural proteins have been detected early in lymph nodes. The occurrence of lymphadenopathy is usually accompanied by an increase in peripheral blood lymphocytes and generally resolves on its own [22,23].

- **symptoms of thrombocytopenia**

Chronic thrombocytopenia is a relatively common complication in about 10% of HIV-infected patients. HIV-related thrombocytopenia (HIV-TP) is clinically similar to immune thrombocytopenia (ITP) seen in HIV-negative individuals, but severe bleeding is rare even with very low platelet counts. Thrombocytopenia is often the first sign of HIV infection. Platelet counts typically remain above $20 \times 10^3/\mu L$ [24]. The low platelet counts in HIV-TP result from increased immune-mediated peripheral platelet destruction and impaired platelet production in the bone marrow. Additionally, thrombocytopenia in HIV-positive patients can be secondary to conditions like hypersplenism, bone marrow infiltration, or the myelosuppressive effects of medications [25]. This may manifest as easy bruising or petechiae, particularly on the palate, as well as tarry stools, rashes, fever, and bleeding [26].

- **gastrointestinal symptoms:**

Odynophagia (painful swallowing) is fairly common during primary HIV infection (PHI), affecting 29% to 75% of individuals. Ulcerative esophagitis may also be present. Esophageal candidiasis, which may be linked to significant immunosuppression during PHI, is also well-documented and might be exacerbated by esophageal ulceration. Anorexia and weight loss are common, often accompanied by vomiting and, in approximately one-third of patients, profuse watery diarrhea. Other gastrointestinal symptoms include acute hepatitis, gastrointestinal hemorrhage, and melena (dark, tarry stools) [22].

- **miscellaneous symptoms**

Other symptoms include conjunctivitis and acute pneumonitis. Cough is observed in about a quarter of PHI cases. There have also been reports of conditions such as aplastic anemia, vasculitis, pancreatic panniculitis, and pancreatitis [17].

- **opportunistic infections**

There have been case reports of opportunistic infections such as Pneumocystis carinii pneumonia occurring during primary HIV infection. Additionally, prolonged cryptosporidiosis associated with PHI has been documented. These infections suggest a temporary yet profound immunosuppression during this stage, but they do not meet the criteria for an AIDS diagnosis [22].

Listeriosis is an uncommon infection in patients with HIV. In those with AIDS or risk factors for HIV, listeriosis typically presents as bacteremia, meningitis, or endocarditis, similar to how it manifests in patients without HIV risk factors [27].

- **pelvic inflammatory disease.**

Pelvic inflammatory disease (PID) often occurs alongside HIV infection, and diagnosing PID can be more challenging in HIV-infected women compared to those who are uninfected. With HIV seroprevalence among women with PID ranging from 6.7% to 22%. HIV-infected

women may experience more frequent and severe episodes of PID. The decreased mucosal and systemic immune function due to HIV might contribute to the increased ascension of pathogenic organisms from the lower to the upper genital tract [28].

Diagnostics

HIV is primarily transmitted sexually in most parts of Europe. As a result, it is recommended to offer HIV testing to all sexually active individuals who present for medical care under specific circumstances: those displaying symptoms consistent with acute retroviral illness, such as fever, fatigue, rash, headache, lymph node enlargement, pharyngitis, myalgia, nausea, vomiting, and diarrhea. Individuals with AIDS-defining conditions or other indicator conditions often associated with HIV infection. People with a past or current history of STIs. Sexual contacts of individuals known to be infected with HIV. Sexually active men who have sex with men (MSM), heterosexual men and women, transgender women with casual partners, and transgender men. Individuals who inject drugs and share needles. Those who report sexual contact with a partner from a country with high HIV prevalence. Individuals who received blood products before routine HIV screening. Pregnant women, regardless of risk factors. People using pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis for sexual exposure (PEPSE). Individuals who have been sexually assaulted. Those voluntarily seeking testing, especially if they have never been tested before. People involved in chemsex (drug use during sexual activity). Individuals with new sexual partners or those who exchange sex for money or goods. Children of mothers with HIV who have no documented previous negative test [29].

Recommended Tests for HIV Diagnosis

1. Laboratory Tests:

Fourth-Generation Serological Tests detect both the HIV p24 antigen (typically around 2 weeks after infection) and anti-HIV antibodies (detectable 4-12 weeks after infection). The serological tests used should differentiate between HIV-1 and HIV-2 infections. For verification of reactive serological test results, it is recommended to use molecular tests (NAAT – nucleic acid amplification test) [30]. Nucleic acid amplification tests (NATs) play a crucial role in shortening the time between HIV infection and diagnosis, which is vital for reducing transmission during the acute phase of HIV. NATs are particularly beneficial for diagnosing HIV in children under 18 months and for distinguishing between HIV-1 and HIV-2 [31]. A negative fourth-generation screening test result at 6 weeks post-exposure is sufficient to conclude the diagnostic process. However, if PEP (Post-Exposure Prophylaxis) or PrEP (Pre-Exposure Prophylaxis) has been used, the diagnostic process should be concluded 6-8 weeks after the completion of medication. In cases where there is suspicion of acute retroviral syndrome or very early HIV infection, urgent referral to a specialized clinic is recommended for verification of the diagnosis and potential immediate initiation of treatment, regardless of the screening test result [30]. Advanced diagnostic techniques have rapidly become essential for the laboratory diagnosis and monitoring of HIV-1 infections. The primary diagnostic tool remains the fourth-generation “combo” immunoassay, which detects both HIV antibodies and antigens. However, the misuse of nucleic acid amplification tests

(NAAT) can lead to false positives, particularly in patients undergoing immunotherapy. While HIV rapid antibody tests are convenient for use in primary health care settings and mobile clinics, they are generally less sensitive and specific than antibody-antigen combo immunoassays [32].

2. Point-of-Care (POC) Tests:

It is recommended to widely use rapid HIV diagnostic tests (also known as Rapid Tests), which should be available at consultation and diagnostic centers, clubs, checkpoints, and even in medical offices. These tests may not always be a substitute for laboratory tests, so their characteristics should be compared. When using tests outside of medical facilities, it is crucial to adhere to the manufacturer's recommendations regarding storage, medical waste disposal, and safety protocols, particularly when tissue integrity is compromised. A negative result from a third-generation POC test can be used to rule out infection if conducted 12 weeks after the last exposure (it is essential to check the specific characteristics of the test used). If a reactive result is obtained in non-medical settings, it is important to explain the result to the patient (noting the possibility of a false-positive result) and provide the result with a note advising immediate verification at a specialized clinic. A referral should not be required for access to the clinic [30].

3. Home Testing

It is recommended to promote the widespread use of self-testing kits. These tests should be readily available in pharmacies, drugstores, and for online purchase. Products introduced to the market must have CE certification and come with a leaflet explaining when and how to perform the test and how to interpret the results, including the possibility of false-negative and false-positive results. The leaflet must also include clear instructions advising individuals that in the case of a reactive (positive) result, they should visit a specialized clinic for further testing. It should also provide information on where to seek psychological support if needed [30].

Following a positive HIV diagnosis, it is essential to promptly refer the newly diagnosed individual to an appropriate specialist HIV treatment center for further management and care [33]. This ensures timely access to comprehensive care, including antiretroviral therapy (ART), regular monitoring, and support services necessary to manage the condition effectively and improve long-term health outcomes [29].

Fig. 1 False positive and negative test results for HIV[30]

Serological Tests		Molecular Tests	
False Negative Results	**False Positive Results**	**Negative Results in an Infected Patient**	**Positive Results in an Uninfected Patient**
Low concentration of anti-HIV antibodies in the sample, which can be seen in the early phase of infection, AIDS, or other immunodeficiencies.	Presence of autoantibodies	Testing during the very early phase of infection (less than 10 days).	Preanalytical or analytical errors, such as mixing up blood samples.
LEVI syndrome (long-acting early viral inhibition syndrome).	Acute infections such as EBV, HSV, or Treponema pallidum.	Preanalytical or analytical errors, such as mixing up blood samples.	Sample contamination.
Infection with HIV variants not detectable by the test, such as some HIV-1 groups and HIV-2.	Recent vaccinations within one month of testing.	Presence of HIV replication control without antiretroviral therapy (elite controllers) or those effectively treated with cART.	
High doses of biotin supplementation.	Pregnancy.	Extremely rare virus mutations.	
Conditions like hypo- and agammaglobulinemia.	Post-transplant status.	LEVI syndrome (long-acting early viral inhibition syndrome).	
Errors in performing the test according to the manufacturer's instructions.	Rare cases of blood and immunoglobulin transfusions.		
Mislabeling or mixing up blood samples.	Administration of experimental HIV vaccines.		
	Improper handling of blood samples, such as repeated thawing.		
	Mislabeling or mixing up blood samples.		

Treatment

Treatment for Primary HIV Infection (PHI) is recommended for all cases based on several important factors. Firstly, initiating therapy can improve clinical symptoms, including severe general symptoms and neurological issues that may arise during PHI. Early therapy offers significant benefits both virologically and immunologically. Virologically, it reduces the HIV viral load set-point, the size of the viral reservoir, and limits viral genetic evolution. Immunologically, early treatment decreases immune activation and inflammation, helps

preserve immune function and the integrity of lymphoid tissue, and may provide protection to the neurological system and gut. Furthermore, it might enhance post-treatment control and the response to future eradication strategies [29; 34-36].

Main groups of drugs used in the treatment of HIV-infected patients [30]:

- NRTI (Nucleos(t)ide reverse transcriptase inhibitors)
- NNRTI (Non-nucleoside reverse transcriptase inhibitors)
- PI (Protease inhibitors)
- FI (Fusion inhibitors)
- InSTI (Integrase inhibitors)
- CCR-5 (CCR-5 inhibitors)
- AI (Attachment inhibitors)
- CAI (Capsid protein inhibitors)
- MAB (Monoclonal antibodies).

To improve the pharmacokinetic properties of certain protease inhibitors and integrase inhibitors used in HIV treatment, enhancing agents like ritonavir (r) and cobicistat (COBI) are used [30].

Starting antiretroviral therapy (ART) is recommended for all individuals diagnosed with HIV, regardless of their CD4 count. This recommendation is based on evidence from studies such as the START and TEMPRANO trials, HPTN 052, and the PARTNER Study. These studies have demonstrated that early initiation of ART significantly reduces the morbidity and mortality associated with HIV infection [34]. Current HIV treatment typically involves a combination of three antiretroviral drugs, two NRTIs in combination with: an integrase inhibitor (InSTI), an NNRTI, or a ritonavir(r)/cobicistat-boosted PI (COBI) [30], while pre-exposure prophylaxis (PrEP) for HIV prevention generally consists of a two-drug regimen. Both regimens usually require consistent, once-daily dosing to maintain their efficacy and reduce the risk of treatment failure or the development of drug resistance [37].

First-line therapy regimen for people who have not previously used antiretroviral therapy:

Although antiretroviral therapy (ART) does not eradicate the infection, it effectively suppresses viral replication and reduces viral load, thereby preventing the progression to AIDS. This shifts HIV from being a once-fatal condition to a manageable chronic illness. However, the need for prolonged treatment can result in the emergence of drug-resistant strains and is often accompanied by side effects like anorexia, nausea, vomiting, and diarrhea, which can lead some patients to discontinue therapy [2].

There are also studies being conducted on the use of gene therapy, using therapeutic delivery of nucleic acids to the patient's cells. This method requires further research, but seems promising [38].

The findings from two Phase III clinical trials, ATLAS-2M and FLAIR, presented at the CROI 2020, the two-drug injectable formulation of cabotegravir (CAB) and rilpivirine (RPV) is effective, safe, and well-tolerated in patients with HIV [39]. The recent approval of Cabenuva (CAB + RPV) by Health Canada marks a significant advancement in long-term HIV treatment options. Additionally, broadly neutralizing antibodies (bNAbs), which exhibit wide-ranging effectiveness against HIV, are being explored as potential long-acting antiviral therapies. Sang et al. from the Fener Chen laboratory at the Harbin Institute of Technology in

China have summarized these advancements, along with other long-acting treatment modalities like implants, vaginal rings, and nanotherapies. These innovations show great potential in reducing the risk of virologic failure by providing sustained drug release [40].

Obstacles to curing the infection

Early HIV infection severely damages gut mucosal immunity, leading to compromised gut barrier integrity and systemic immune activation. This persistent activation contributes to ongoing inflammation and disease progression, even under antiretroviral therapy (ART). HIV's retention in lymphoid tissues causes local immune responses and scarring, which disrupts tissue architecture and limits immune cell access to critical factors, reducing ART's effectiveness in boosting CD4(+) T-cell counts [39]. HIV establishes latent reservoirs in various tissues early in infection, presenting a major challenge for eradication. Despite ART's success in managing HIV, the persistence of the virus in tissue reservoirs remains a significant barrier to a cure [41,42]. Studies show that HIV can persist in the central nervous system (CNS) even with undetectable blood levels, and about 50% of people on ART experience HIV-associated neurocognitive disorders. Fletcher et al.'s review highlights the need for antiretrovirals with better organ penetration and strategies to improve ART's effectiveness, especially in the brain [43]. Additionally, adherence issues leading to drug resistance underscore the importance of developing long-acting antiretroviral formulations to enhance treatment outcomes [40].

Conclusions:

The HIV/AIDS pandemic has had a devastating global impact. Despite advancements in treatment, the disease continues to cause significant morbidity and mortality, highlighting the need for ongoing public health efforts [4]. HIV infection is marked by a complex progression from acute to chronic phases, ultimately leading to AIDS due to the significant loss of CD4(+) T cells [1]. This underscores the importance of early detection and intervention. Early diagnosis through targeted testing and immediate initiation of antiretroviral therapy (ART) is crucial in managing HIV effectively [34]. ART has transformed HIV from a fatal disease to a manageable chronic condition [2]. HIV presents with a wide range of clinical symptoms, including dermatologic, neuromuscular, and gastrointestinal manifestations [13-28]. While current ART regimens are effective, they do not eliminate the virus completely [2]. Persistent viral reservoirs pose a significant challenge, and there is a need for continued research into new treatments, including gene therapy, which may offer future breakthroughs in curing or more effectively managing HIV [38].

Disclosure:

Authors' contribution:

Conceptualization: Martyna Choinka
Methodology: Natalia Wdowiak, Zuzanna Szczepaniak
Software: Jakub Kalisiak
Check: Karolina Mrugała
Formal Analysis: Agata Konopka, Martyna Choinka
Investigation: Natalia Wdowiak, Jakub Kalisiak
Resources: Vimbisoyashe Ivy Matshaba

Data Curation: Anna Szpernalowska
Writing-Rough Preparation: Martyna Choinka, Natalia Wdowiak, Agata Konopka
Writing-Review and Editing: Karolina Mrugała, Zuzanna Szczepaniak
Visualization: Vimbisoyashe Ivy Matshaba
Supervision: Martyna Choinka, Agata Konopka
Project Administration: Anna Szpernalowska, Vimbisoyashe Ivy Matshaba

All authors have read and agreed with the published version of the manuscript.

Funding statement:
The study did not receive special funding.
Institutional review board statement:
Not applicable.
Informed consent statement:
Not applicable.
Data availability statement:
Not applicable.
Conflict of interest:
The authors declare no conflict of interest

References:

1. Moir S, Chun TW, Fauci AS. Pathogenic mechanisms of HIV disease. *Annu Rev Pathol*. 2011;6:223-248. doi:10.1146/annurev-pathol-011110-130254
2. van Heuvel Y, Schatz S, Rosengarten JF, Stitz J. Infectious RNA: Human Immunodeficiency Virus (HIV) Biology, Therapeutic Intervention, and the Quest for a Vaccine. *Toxins (Basel)*. 2022;14(2):138. Published 2022 Feb 14. doi:10.3390/toxins14020138
3. Fanales-Belasio E, Raimondo M, Suligoi B, Buttò S. HIV virology and pathogenetic mechanisms of infection: a brief overview. *Ann Ist Super Sanita*. 2010;46(1):5-14. doi:10.4415/ANN_10_01_02
4. De Cock KM, Jaffe HW, Curran JW. Reflections on 40 Years of AIDS. Emerg Infect Dis. 2021;27(6):1553-1560. doi:10.3201/eid2706.210284
5. The Urgency of Now: AIDS at a Crossroads: 2024 UNAIDS Global AIDS Update. Joint United Nations Programme on HIV/AIDS 2024. https://crossroads.unaids.org.
6. van Schalkwyk C, Mahy M, Johnson LF, Imai-Eaton JW. Updated Data and Methods for the 2023 UNAIDS HIV Estimates. *J Acquir Immune Defic Syndr*. 2024;95(1S):e1-e4. doi:10.1097/QAI.0000000000003344
7. Lobo Antuña M, Suárez EU, Calpena Martínez S, Lage Estebañez F, Fortes Alén J, de Górgolas Hernández-Mora M. Fever, Myalgias, and Weakness in a Patient with HIV. *Am J Med*. 2022;135(7):848-850. doi:10.1016/j.amjmed.2022.01.052
8. Hentzien M, Bonnet F, Bernasconi E, et al. Immune response to the recombinant herpes zoster vaccine in people living with HIV over 50 years of age compared to non-HIV age-/gender-matched controls (SHINGR'HIV): a multicenter, international, non-randomized clinical trial study protocol. *BMC Infect Dis*. 2024;24(1):329. Published 2024 Mar 19. doi:10.1186/s12879-024-09192-5

9. Mohseni Afshar Z, Goodarzi A, Emadi SN, et al. A Comprehensive Review on HIV-Associated Dermatologic Manifestations: From Epidemiology to Clinical Management. *Int J Microbiol*. 2023;2023:6203193. Published 2023 Jul 18. doi:10.1155/2023/6203193
10. Khondker L. Dermatological manifestations of HIV/AIDS patients. *Journal of Enam Medical College.* 2019;9(3):185–188. doi: 10.3329/jemc.v9i3.43249
11. Hira SK, Wadhawan D, Kamanga J, et al. Cutaneous manifestations of human immunodeficiency virus in Lusaka, Zambia. *J Am Acad Dermatol*. 1988;19(3):451-457. doi:10.1016/s0190-9622(88)70197-8
12. Emlet CA, Shippy RA. HIV/AIDS treatments. J Gerontol Soc Work. 2008;50 Suppl 1:131-49. doi: 10.1080/01634370802137850. PMID: 18924390.
13. Schifitto G, McDermott MP, McArthur JC, et al. Markers of immune activation and viral load in HIV-associated sensory neuropathy. Neurology. 2005; 64:842–848.5.546–55
14. Morgello S, Estanislao L, Simpson D, et al. HIV-associated distal sensory polyneuropathy in the era of highly active antiretroviral therapy: the Manhattan HIV Brain Bank. Arch Neurol. 2004;61:
15. Harrison TB, Smith B. Neuromuscular manifestations of HIV/AIDS. *J Clin Neuromuscul Dis*. 2011;13(2):68-84. doi:10.1097/CND.0b013e318221256f
16. Kaku M, Simpson DM. Neuromuscular complications of HIV infection. *Handb Clin Neurol*. 2018;152:201-212. doi:10.1016/B978-0-444-63849-6.00016-5
17. Pedersen C, Lindhardt BO, Jensen BL, et al. Clinical course of primary HIV infection: consequences for subsequent course of infection. *BMJ*. 1989;299(6692):154-157. doi:10.1136/bmj.299.6692.154
18. Kinloch-de Loës S, de Saussure P, Saurat JH, Stalder H, Hirschel B, Perrin LH. Symptomatic primary infection due to human immunodeficiency virus type 1: review of 31 cases. *Clin Infect Dis*. 1993;17(1):59-65. doi:10.1093/clinids/17.1.59
19. Simon D. Evaluation of diarrhea in HIV-infected patients. *Gastrointest Endosc Clin N Am*. 1998;8(4):857-867. doi:10.1016/S1052-5157(18)30236-8
20. Olmos M, Molina C, Piskorz E, et al. Diarrea y SIDA: técnicas diagnósticas más complejas; mejores resultados terapéuticos [Diarrhea and AIDS: more complex diagnostic techniques; better therapeutic results]. *Acta Gastroenterol Latinoam*. 1996;26(2):91-100.
21. De Munter P, Peetermans WE, Derdelinckx I, Vanderschueren S, Van Wijngaerden E. Fever in HIV-infected patients: less frequent but still complex. *Acta Clin Belg*. 2012;67(4):276-281. doi:10.2143/ACB.67.4.2062672
22. Tindall B, Barker S, Donovan B, et al. Characterization of the acute clinical illness associated with human immunodeficiency virus infection. *Arch Intern Med*. 1988;148(4):945-949.
23. Apoola A, Ahmad S, Radcliffe K. Primary HIV infection. *Int J STD AIDS*. 2002;13(2):71-78. doi:10.1258/0956462021924613
24. Scaradavou A. HIV-related thrombocytopenia. *Blood Rev*. 2002;16(1):73-76. doi:10.1054/blre.2001.0188
25. Ballem PJ, Belzberg A, Devine DV et al. Kinetic studies of the mechanism of thrombocytopenia in patients with human immunodeficiency virus infection. N Engl J Med 1992; 327: 1779–1784.
26. Gauer RL, Braun MM. Thrombocytopenia. *Am Fam Physician*. 2012;85(6):612-622.

27. Kales CP, Holzman RS. Listeriosis in patients with HIV infection: clinical manifestations and response to therapy. *J Acquir Immune Defic Syndr (1988)*. 1990;3(2):139-143.
28. Korn AP. Pelvic inflammatory disease in women infected with HIV. *AIDS Patient Care STDS*. 1998;12(6):431-434. doi:10.1089/apc.1998.12.431
29. Gökengin D, Wilson-Davies E, Nazlı Zeka A, et al. 2021 European guideline on HIV testing in genito-urinary medicine settings. *J Eur Acad Dermatol Venereol*. 2021;35(5):1043-1057. doi:10.1111/jdv.17139
30. Parczewski M, Witak-Jędra M, Aksak-Wąs B, red. *Zasady opieki nad osobami zakażonymi HIV : zalecenia PTN AIDS 2023*. Polskie Towarzystwo Naukowe AIDS; 2023.
31. Hans L, Allmen NV, Edelmann A, et al. Early Diagnosis of HIV-1 and HIV-2 Using Cobas HIV-1/HIV-2 Qualitative Test: A Novel Qualitative Nucleic Acid Amplification Test for Plasma, Serum, and Dried Blood Spot Specimens. *J Acquir Immune Defic Syndr*. 2021;87(5):1187-1195. doi:10.1097/QAI.0000000000002713
32. Lu H, Tang YW. Myths in the laboratory diagnosis of HIV infection. *Emerg Microbes Infect*. 2019;8(1):1240-1242. doi:10.1080/22221751.2019.1656550
33. Pittaway H, Barnard S, Wilson E et al. SH:24-user perspectives on an online sexual health service. Sex Transm Infect 2016; 92: A19–A20
34. https://www.eacsociety.org/guidelines/eacs-guidelines/
35. Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. *MMWR Recomm Rep*. 2021;70(4):1-187. Published 2021 Jul 23. doi:10.15585/mmwr.rr7004a1
36. Bekker LG, Beyrer C, Mgodi N, et al. HIV infection [published correction appears in Nat Rev Dis Primers. 2023 Sep 11;9(1):48. doi: 10.1038/s41572-023-00464-z]. *Nat Rev Dis Primers*. 2023;9(1):42. Published 2023 Aug 17. doi:10.1038/s41572-023-00452-3
37. Gulick RM, Flexner C. Long-Acting HIV Drugs for Treatment and Prevention. *Annu Rev Med*. 2019;70:137-150. doi:10.1146/annurev-med-041217-013717
38. Margolis DM, Koup RA, Ferrari G. HIV antibodies for treatment of HIV infection. *Immunol Rev*. 2017;275(1):313-323. doi:10.1111/imr.12506
39. Sang Y, Ding L, Zhuang C, Chen F. Design strategies for long-acting anti-HIV pharmaceuticals. *Curr Opin Pharmacol*. 2020;54:158-165. doi:10.1016/j.coph.2020.10.005
40. Huerta L. Editorial: Anti-infective 2020: HIV-From pathogenesis to treatment. *Curr Opin Pharmacol*. 2020;54:x-xii. doi:10.1016/j.coph.2020.12.001
41. Yang X, Su B, Zhang X, Liu Y, Wu H, Zhang T. Incomplete immune reconstitution in HIV/AIDS patients on antiretroviral therapy: Challenges of immunological non-responders. J Leukoc Biol. 2020 Apr;107(4):597-612. doi: 10.1002/JLB.4MR1019-189R. Epub 2020 Jan 22. PMID: 31965635; PMCID: PMC7187275.
42. Pitman MC, Lau JSY, McMahon JH, Lewin SR. Barriers and strategies to achieve a cure for HIV. *Lancet HIV*. 2018;5(6):e317-e328. doi:10.1016/S2352-3018(18)30039-0
43. Avedissian SN, Dyavar SR, Fox HS, Fletcher CV. Pharmacologic approaches to HIV-associated neurocognitive disorders. *Curr Opin Pharmacol*. 2020;54:102-108. doi:10.1016/j.coph.2020.09.003