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REVIEW

Comparative Analysis of Virology and Pathogenesis of SARS-CoV-2 and HIV Infections: Implications for Public Health and Treatment Strategies

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Introduction: Coronavirus Disease 19 (COVID-19), caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV -2), and Human Immunodeficiency Virus (HIV) are significant 21st-century pandemics with distinct virological and clinical characteristics. COVID-19 primarily presents as an acute respiratory illness, while HIV leads to chronic immune suppression. Understanding their differences can enhance public health strategies and treatment approaches.

Purpose: This narrative review compares the virology, transmission, immune responses, and clinical outcomes of SARS-CoV-2 and HIV to inform treatment strategies and public health interventions.

Methods: A narrative review was conducted, synthesizing data from peer-reviewed literature and expert commentary from 2010 to 2024. Databases such as PubMed, Cochrane Library, and Google Scholar were searched for relevant studies.

Results: SARS-CoV-2 primarily spreads through airborne droplets and contaminated surfaces, while HIV transmits through direct contact with infected bodily fluids. The immune response to SARS-CoV-2 involves both innate and adaptive systems, potentially leading to a cytokine storm in severe cases. In contrast, HIV evades the immune system by integrating into host cells, resulting in chronic infection and progressive immune deterioration. Treatment for SARS-CoV-2 focuses on symptom management and prevention, with antiviral medications and vaccines playing crucial roles. Conversely, HIV treatment relies on antiretroviral therapy (ART) to suppress viral replication and maintain immune function.

Conclusion: The review highlights the acute nature of SARS-CoV-2 versus the chronic progression of HIV. Tailored prevention and treatment strategies are essential for effective disease management.

Recommendations: Public health strategies should address the unique transmission routes and progression of both viruses. Further research into vaccine development and therapeutic interventions is critical for improving disease management.

Keywords: COVID-19, HIV, viral transmission, immune response, disease progression

Introduction

COVID-19 is a contagious respiratory illness caused by the SARS-CoV-2 virus, first identified in late 2019,[1] SARS-CoV -2 infection can cause a wide range of symptoms, from mild ones like fever and cough to severe complications such as pneumonia, acute respiratory distress syndrome (ARDS), and even death, especially in older adults or those with underlying health conditions[2] and HIV (Human Immunodeficiency Virus) is a virus that attacks the immune system, specifically CD4+ T cells, weakening the body's ability to fight infections.[3] If untreated, it leads to AIDS (Acquired Immunodeficiency Syndrome), the final stage of HIV infection, where severe immune damage allows opportunistic infections and cancers to thrive.[4] The two are the most significant viral pandemics of the 21st century. Both viruses have drastically impacted global health, yet they differ significantly in their virology, transmission, immune responses, and disease progression.

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The long-term societal and economic impacts of both SARS-CoV-2 infection and HIV are profound and multi-faceted, affecting various aspects of life and public health systems. **Long-term Societal Impacts**: Both pandemics have highlighted weaknesses in public health systems. SARS-CoV-2 infection has led to increased investment in healthcare infrastructure, surveillance, and emergency preparedness.[5] Similarly, the HIV epidemic prompted the establishment of dedicated health programs and policies,[6] which continue to influence public health strategies today. **On Stigmatization and Mental Health**, HIV has historically been associated with stigma, affecting the mental health and social integration of those living with the virus.[7] SARS-CoV-2 infection has also led to stigmatization, particularly towards certain communities.[8] The long-term societal impact includes ongoing mental health challenges and the need for comprehensive support systems to address these issues. **Behavioral Changes** both pandemics have altered social behaviors. SARS-CoV-2 infection has led to increased awareness of hygiene practices and social distancing,[9] which may persist in some form. The HIV epidemic has influenced sexual health behaviors,[10] promoting safer sex practices and regular testing,[11] which continue to shape public health messaging. **On Education and Awareness** the response to both pandemics has increased public awareness about infectious diseases, prevention strategies, and the importance of vaccination.[12] This heightened awareness can lead to more informed communities and better health outcomes in the long run.[13]

In Long-term Economic Impacts, the economic burden of managing both pandemics is significant. SARS-CoV-2 infection has resulted in increased healthcare costs due to hospitalizations, long-term care for SARS-CoV-2 infection survivors, and vaccination programs.[14] HIV treatment, while effective, requires lifelong antiretroviral therapy, contributing to ongoing healthcare expenditures.[15] **Workforce Disruption**, SARS-CoV-2 infection has caused widespread job losses and economic instability, with long-term effects on employment rates and workforce participation.[16] The HIV epidemic has also impacted the workforce, particularly in regions heavily affected by the virus, leading to a loss of productivity and economic contributions from those living with HIV.[17] **In the context of Economic Inequality** both pandemics have exacerbated existing inequalities. SARS-CoV-2 infection disproportionately affected marginalized communities,[18] revealing gaps in access to healthcare and economic resources.[19] Similarly, the HIV epidemic has had a more severe impact on vulnerable populations, highlighting the need for targeted economic support and health interventions.[20] **Investment in Research and Development** there is urgency of both pandemics has spurred investment in medical research and development. SARS-CoV-2 infection has accelerated vaccine development and innovation in telehealth,[21] while the HIV epidemic has led to advancements in treatment and prevention strategies.[22] This investment can yield long-term benefits for public health and economic resilience. The long-term societal and economic impacts of SARS-CoV-2 infection and HIV are interconnected, influencing public health systems, social behaviors, mental health, and economic stability. Addressing these impacts requires comprehensive strategies that promote health equity, support mental health, and strengthen healthcare infrastructure.

Global health policies have also evolved significantly in response to the SARS-CoV-2 and HIV pandemics, emphasizing adaptive strategies for effective public health management.[23] Key developments include strengthening surveillance systems for early detection,[24] fostering international collaboration through initiatives like Covid-19 Vaccines Global Access (COVAX),[25] and prioritizing health equity to address disparities.[26] Investment in research and development has accelerated vaccine creation and improved HIV treatments.[27] Integration of health services has enhanced resilience, while a focus on preparedness ensures readiness for future health emergencies. These lessons aim to improve global health outcomes and create robust systems capable of addressing complex public health challenges.

Technological advances in diagnostics for SARS-CoV-2 infection have led to rapid developments in PCR and antigen tests, enabling quick and accurate detection of SARS-CoV-2.[28] Innovations like at-home testing kits and digital health applications have enhanced accessibility. For HIV, point-of-care testing and self-testing kits have improved early detection and increased testing rates, especially in underserved populations.[29] In treatment, antiviral options for SARS-CoV-2 infection, such as remdesivir and monoclonal antibodies, have proven effective, with ongoing research into long SARS-CoV-2 therapies.[30] For HIV, antiretroviral therapy (ART) has improved significantly with long-acting injectables and new drug classes that enhance adherence and reduce side effects.[31] In vaccine development, the rapid rollout of mRNA vaccines for SARS-CoV-2 has set a new standard for responding to infectious diseases.[32] Although an effective

HIV vaccine remains elusive, recent advances in vaccine research, including mRNA technology, are promising for future HIV prevention breakthroughs.[33]

The successful interventions for SARS-CoV-2 and HIV include New Zealand's response to the pandemic and Botswana's "Test and Treat" strategy for HIV. New Zealand implemented a strict lockdown in March 2020, along with comprehensive testing and contact tracing, resulting in one of the lowest SARS-CoV-2 infection rates globally.[34] The government's clear communication and public compliance were key to controlling the virus's spread, demonstrating the effectiveness of decisive action and community engagement. In Botswana, the "Test and Treat" strategy offers immediate antiretroviral therapy (ART) to all individuals diagnosed with HIV, regardless of CD4 count.[35] This approach has significantly reduced new infections and improved health outcomes, showcasing the effectiveness of early treatment in controlling the epidemic. Strong government commitment and international partnerships have supported this program, emphasizing the importance of integrated health services.[36]

Interdisciplinary approaches, they are essential in managing pandemics, with social sciences, economics, and behavioral sciences playing key roles. Social sciences help understand community behaviors, cultural norms, and health determinants, informing public health messaging during SARS-CoV-2 to enhance compliance with health guidelines.[37] Economic analysis assesses the cost-effectiveness of interventions and resource allocation, guiding governments in balancing public health measures with economic impacts during the pandemic, such as decisions on lockdowns and stimulus packages.[38] And final Behavioral sciences offer insights into human behavior and decision-making,[39] which are crucial for designing effective vaccination campaigns for both SARS-CoV-2 and HIV.[40] Understanding factors influencing vaccine uptake, like trust in healthcare systems and perceived risks, has been vital for improving vaccination efforts.

Limitation in the Current Studies

There are limited studies that provide a comprehensive comparison of HIV and SARS-CoV-2. For instance, a systematic review examining the epidemiology and outcomes of both viruses found that individuals with HIV face a significantly higher mortality risk from SARS-CoV-2, with a relative risk of 1.78 and a pooled mortality rate of 12.65%, varying regionally from 4% in Italy to 35% in the U.S..[41]

In another study, people living with HIV exhibited low SARS-CoV-2 seroprevalence, lower IgG concentrations, and lower neutralizing antibody titers compared to those without HIV.[42] Additionally, the study reviewed SARS-CoV-2 and HIV co-infection, highlighting high prevalence rates, clinical symptoms, and complications, which emphasizes the need for effective treatment and infection control in affected patients[43] and.[44]

Furthermore, another study compares HIV and SARS-CoV-2, focusing on their persistence in the body, challenges in vaccine development, and differing transmission mechanisms. This comparison underscores the necessity for ongoing research to enhance treatment and prevention strategies for both.[45]

Therefore, this narrative review compared and contrasted the etiology of SARS-CoV-2 and HIV infections, focusing on their viral characteristics, modes of transmission, pathogenesis, and clinical outcomes to bridge the existing limitation.

Aim

The aim of this study is to compare the virology and pathogenesis of SARS-CoV-2 infection and HIV, focusing on viral Characteristics, etiology, transmission, immune responses, Diagnosis, treatment and clinical outcomes. By contrasting the biological mechanisms of these pandemics, the study targets were to improve our understanding of disease progression and inform public health strategies and treatment approaches for managing viral infections.

Justification or Significance of the Study

Comparing and contrasting the etiology of **SARS-CoV-2 infection** and **HIV infection** is highly significant given that both viruses represent two of the most devastating pandemics of the 21st century. Understanding their differences in **viral structure, transmission mechanisms, immune responses, and disease progression** is crucial for several reasons:

1. **Improved Public Health Strategies**: By analyzing the distinct transmission pathways and disease mechanisms of SARS-CoV-2 and HIV, this study can inform more effective public health strategies, particularly in prevention, diagnosis, and treatment. Such insights are critical for addressing both current and future viral pandemics.
2. **Tailored Treatment Approaches**: The comparative study will help health professionals recognize the unique therapeutic needs for managing SARS-CoV-2 infection, an acute viral infection, and HIV, a chronic retroviral infection. This knowledge could also guide the development of targeted treatments and vaccines by emphasizing the differing immune system responses elicited by each virus.
3. **Resource Allocation and Health System Preparedness**: The differences in disease progression and management demands between SARS-CoV-2 and HIV can help policymakers better allocate healthcare resources, ensuring that health systems are adequately prepared to address the acute, high-transmission nature of SARS-CoV-2 infection alongside the long-term management of HIV.
4. **Global Health Impact**: Both SARS-CoV-2 infection and HIV disproportionately affect vulnerable populations. By understanding how the etiology of each virus interacts with demographic factors, such as age, immune status, and comorbidities, this study contributes to the ongoing effort to reduce health inequities worldwide.
5. **Scientific Knowledge Advancement**: This study will contribute to the growing body of knowledge on viral pathogenesis and immune responses, facilitating ongoing research into viral infections and potential future pandemics.

This comparison offers vital insights that can improve treatment protocols, shape public health policies, and enhance global pandemic preparedness.

Methods

This study follows a narrative review methodology, synthesizing information from peer-reviewed journals, scientific reports, and expert commentary. The review focused on identifying key differences between SARS-CoV-2 infection and HIV in terms of their etiology, transmission mechanisms, immune responses, and clinical outcomes. The search strategy included the use of search terms like; SARS-CoV-2, COVID-19, HIV, HIV/AIDs, Transmission, Treatment, Management, Etiology, Disease progression, immune response, Immune Evasion, Target cells and clinical outcomes combining the terms with Boolean operators (AND, OR) to create comprehensive search strings. Literature was selected based on relevance to the comparison of these two pandemics, with a focus on publications from 2010 to 2024. Key databases used for sourcing literature included PubMed, Scopus, Cochrane Library, and Google Scholar. Studies were excluded if they did not provide comparative data or focused on unrelated aspects of either virus and if they were not in English. Data were analyzed qualitatively, comparing both viruses' virology, clinical features, and management strategies. The Overall, rationale for these criteria was to ensure that the literature included in the study is relevant, high-quality, and directly aligned with the research objectives, ultimately enhancing the validity and reliability of the review's findings.

Narrative Review Findings

Viral Classification and Structure

SARS-CoV-2 belongs to the Coronaviridae family and is an enveloped, positive-sense, single-stranded RNA virus.[46] Its structure includes the spike (S) glycoprotein, which facilitates entry into host cells via the angiotensin-converting enzyme 2 (ACE2) receptor.[47] On the other hand, HIV is a member of the Retroviridae family, specifically the Lentivirus genus.[48] HIV is also an enveloped RNA virus, but its genetic material is diploid, meaning it contains two copies of single-stranded RNA.[49] Unlike SARS-CoV-2, HIV uses reverse transcriptase to convert its RNA into DNA, which integrates into the host genome. Understanding the viral classification and structure of SARS-CoV-2 and HIV has significant implications for public health and treatment strategies. For public health, insights into the spike glycoprotein of SARS-CoV-2 aid in effective vaccine development, while the complexity of HIV's envelope proteins presents challenges. Knowledge of SARS-CoV-2's entry via the ACE2 receptor informs infection control measures like mask-wearing and handwashing, whereas HIV's transmission highlights the need for safe practices. Ongoing surveillance of coronaviruses is essential to

prevent outbreaks, and continuous monitoring of HIV mutations is crucial for effective treatment. In terms of treatment, the structure of SARS-CoV-2 guides the development of antiviral drugs, while understanding HIV's reverse transcription process aids in creating effective therapies. Combination therapies for both viruses can enhance treatment efficacy and reduce resistance, with personalized strategies based on viral profiles being vital for optimal outcomes.

Mechanism of Host Cell Entry

SARS-CoV-2 infects host cells primarily through binding of the spike protein to the ACE2 receptor, which is highly expressed in the respiratory tract and other tissues.[47] This binding facilitates fusion of the viral envelope with the host cell membrane, allowing entry of the viral genome into the host cell cytoplasm for replication.[50] In contrast, HIV targets the CD4+ T lymphocytes by binding its envelope glycoproteins (gp120 and gp41) to the CD4 receptor and a co-receptor, usually CCR5 or CXCR4. This fusion allows HIV to enter the host immune cells, leading to immune system compromise. The mechanisms of host cell entry for SARS-CoV-2 and HIV have significant public health and treatment strategy implications. SARS-CoV-2 primarily infects host cells by binding its spike protein to the ACE2 receptor, which is abundant in the respiratory tract, facilitating viral entry and replication. This knowledge informs public health measures, such as the importance of mask-wearing and social distancing to limit transmission. In contrast, HIV targets CD4+ T lymphocytes by binding its envelope glycoproteins to the CD4 receptor and a co-receptor (CCR5 or CXCR4), leading to immune system compromise. Understanding these entry mechanisms is crucial for developing targeted antiviral therapies and vaccines, as it allows for the design of interventions that can block viral entry and mitigate the impact of these viruses on public health.

Viral Replication and Lifecycle

SARS-CoV-2 has a relatively short replication cycle, leading to rapid viral replication in infected tissues.[51] The virus uses host ribosomes to translate its RNA genome into viral proteins, which are assembled into new virions and released to infect more cells. HIV's replication cycle is more complex. After entering the host cell, HIV reverse transcribes its RNA into DNA, which integrates into the host genome.[52] This proviral DNA can remain latent for years, establishing a chronic infection that may not immediately produce symptoms but allows long-term persistence. Understanding the viral replication and lifecycle of SARS-CoV-2 and HIV has important implications for public health and treatment strategies. SARS-CoV-2's relatively short replication cycle enables rapid viral proliferation in infected tissues, highlighting the need for swift public health interventions to contain outbreaks and reduce transmission. This knowledge informs the development of antiviral therapies that target specific stages of the viral lifecycle, aiming to inhibit replication and prevent the spread of the virus. In contrast, HIV's more complex replication cycle involves reverse transcription of its RNA into DNA, which integrates into the host genome and can remain latent for years, leading to chronic infection. This understanding underscores the importance of long-term monitoring and treatment strategies, such as antiretroviral therapy, to manage HIV effectively and prevent disease progression. Overall, insights into the replication mechanisms of both viruses are crucial for designing effective public health responses and therapeutic interventions.

Immune Evasion Strategies

Both SARS-CoV-2 and HIV have evolved mechanisms to evade the host immune system, but in different ways.[53] SARS-CoV-2 employs multiple strategies, including delaying interferon responses and inducing a hyperinflammatory state (eg, cytokine storms), which contributes to severe SARS-CoV-2 infection in some patients. HIV, by contrast, targets and depletes CD4+ T cells, which are central to the immune response.[54] Over time, this depletion leads to immunosuppression, rendering the host vulnerable to opportunistic infections and diseases characteristic of acquired immunodeficiency syndrome (AIDS). The immune evasion strategies employed by both SARS-CoV-2 and HIV have significant implications for public health and treatment strategies. SARS-CoV-2 utilizes mechanisms such as delaying interferon responses and triggering hyperinflammatory states, which can lead to severe infections and complicate treatment approaches. In contrast, HIV specifically targets and depletes CD4+ T cells, crucial for orchestrating the immune response, resulting in long-term immunosuppression and increased susceptibility to opportunistic infections and AIDS-related conditions. Understanding these distinct immune evasion tactics is essential for developing effective public health interventions

and treatment protocols. Strategies must focus on enhancing immune responses, improving early detection and management of infections, and tailoring therapies that address the unique challenges posed by each virus, ultimately aiming to mitigate their impact on individual and community health.

SARS-CoV-2 generally causes an acute infection, though in some cases, viral RNA may persist for extended periods, especially in individuals with long SARS-CoV-2 infection.[55] However, the virus does not typically establish true latency. HIV, on the other hand, establishes latency by integrating its DNA into the host genome,[56] allowing the virus to persist for the lifetime of the individual even with antiretroviral therapy. The persistence and latency of SARS-CoV-2 and HIV present distinct challenges for public health and treatment strategies. While SARS-CoV-2 primarily causes acute infections, there are instances where viral RNA can persist in individuals, particularly those with prolonged infections, raising concerns about long-term health effects and the potential for ongoing transmission. In contrast, HIV establishes true latency by integrating its DNA into the host genome, enabling the virus to remain dormant and evade the immune system despite the use of antiretroviral therapy. This fundamental difference necessitates tailored public health approaches; for SARS-CoV-2, strategies should focus on early detection and management of prolonged infections to prevent complications, while for HIV, efforts must continue to address the challenges of viral latency and the need for lifelong treatment. Understanding these dynamics is crucial for developing effective interventions that can mitigate the impact of both viruses on individual and community health.

Etiology of SARS-CoV-2 Infection

Pathogen

COVID-19 is caused by the SARS-CoV-2 virus, a novel coronavirus first identified in late 2019.[1] This virus belongs to the Coronaviridae family, a group of enveloped, single-stranded RNA viruses known for causing respiratory infections in both humans and animals.[57] SARS-CoV-2 shares genetic similarities with other coronaviruses, particularly SARS-CoV, which was responsible for the 2003 outbreak of Severe Acute Respiratory Syndrome (SARS), and MERS-CoV, which caused the Middle East Respiratory Syndrome (MERS) outbreak in 2012.[58] These related viruses highlight the pattern of emerging zoonotic infections that have the potential to cause global pandemics. The pathogenesis of SARS-CoV-2 highlights important public health implications, emphasizing the need for effective interventions like vaccination and surveillance. Understanding its infection mechanisms is crucial for developing targeted treatments and response strategies, ultimately enhancing preparedness against future zoonotic pandemics and improving management of severe COVID-19 cases.

Transmission

Airborne transmission is the primary mode by which SARS-CoV-2 spreads, as the virus is carried through respiratory droplets expelled when an infected person coughs, sneezes, talks, or breathes.[59] These droplets can travel short distances and potentially infect nearby individuals. In addition to airborne transmission, the virus can spread via fomite transmission, which occurs when individuals touch contaminated surfaces and then inadvertently transfer the virus to their mouth, nose, or eyes[60] Furthermore, aerosol transmission, involving smaller particles that can remain suspended in the air for longer periods, also plays a significant role, particularly in enclosed or poorly ventilated spaces.[59] Importantly, the virus can be transmitted by asymptomatic individuals who show no visible symptoms, which complicates efforts to control its spread and has significantly contributed to the rapid global transmission of SARS-CoV-2 infection.[61] This combination of multiple transmission routes underscores the challenges of containing the virus in both community and healthcare settings. The public health implications of SARS-CoV-2 are profound, primarily due to its airborne transmission through respiratory droplets and aerosols, which can infect individuals in close proximity or in poorly ventilated spaces. Additionally, fomite transmission complicates control efforts, as the virus can linger on surfaces. The ability of asymptomatic individuals to spread the virus further exacerbates the challenge of containment, making it essential for public health strategies to focus on comprehensive measures such as widespread vaccination, improved ventilation in indoor spaces, and rigorous hygiene practices. These multifaceted transmission routes necessitate a coordinated response to effectively mitigate the spread of COVID-19 in both community and healthcare settings.

Target Cells

SARS-CoV-2 gains entry into human cells by binding to the angiotensin-converting enzyme 2 (ACE2) receptor, which is abundantly expressed in several key organs, including the lungs, heart, kidneys, and intestine.[62] The high expression of ACE2 in these tissues explains why the virus can affect multiple organ systems. Once the virus binds to the ACE2 receptor, it penetrates the host cell and hijacks its cellular machinery to facilitate viral replication. This process predominantly occurs in the respiratory epithelium, where the virus rapidly multiplies, causing inflammation and damage to lung tissue. As viral replication increases, it can lead to the development of COVID-19 pneumonia, a condition characterized by inflammation of the lung tissue and impaired oxygen exchange.[63] This respiratory involvement is one of the hallmarks of severe SARS-CoV-2 infection cases, particularly in vulnerable individuals such as the elderly or those with pre-existing conditions. The implications of SARS-CoV-2 targeting cells highlight critical public health and treatment strategies. The virus's entry through the angiotensin-converting enzyme 2 (ACE2) receptor, prevalent in vital organs like the lungs, heart, and kidneys, underscores the potential for multi-organ impact. This mechanism facilitates viral replication primarily in the respiratory epithelium, leading to inflammation and damage, which can result in severe conditions such as COVID-19 pneumonia. Understanding these pathways emphasizes the need for targeted therapeutic approaches, including antiviral treatments and strategies to protect vulnerable populations, particularly the elderly and those with pre-existing health conditions, to mitigate the severe outcomes associated with the virus.

Immune Response

The body responds to SARS-CoV-2 infection by activating both the innate and adaptive immune systems, which work together to combat the virus.[64] The innate immune response is the body's first line of defense, providing a rapid, nonspecific response to the virus. This includes the activation of immune cells such as macrophages and natural killer cells, which aim to contain the infection. Following this, the adaptive immune response kicks in, providing a more targeted defense. This response involves the production of specific antibodies that recognize and neutralize SARS-CoV-2, typically developing within 1–2 weeks after infection.[65] Additionally, T-cell responses are crucial for clearing the virus from the body, as cytotoxic T cells directly attack infected cells, while helper T cells assist in coordinating the immune response.[66] However, in some individuals, especially those with severe SARS-CoV-2 infection, the immune response becomes dysregulated, leading to a hyperinflammatory state known as a cytokine storm. This excessive release of inflammatory cytokines can cause widespread tissue damage, particularly in the lungs, and contribute to complications such as acute respiratory distress syndrome (ARDS) and multi-organ failure.[67] While many individuals successfully clear the virus with the help of an effective immune response, those who experience a cytokine storm are at a higher risk of severe illness and death. Thus, while immune responses are essential for controlling the infection, an overactive response can lead to life-threatening complications. The immune response to SARS-CoV-2 infection has significant public health and treatment strategy implications. The body activates both innate and adaptive immune systems to combat the virus, with the innate response providing immediate, nonspecific defense through immune cells like macrophages and natural killer cells. The subsequent adaptive response, characterized by the production of specific antibodies and T-cell activation, is crucial for effectively clearing the virus. However, in some individuals, particularly those with severe infections, the immune response can become dysregulated, resulting in a cytokine storm that leads to severe complications such as acute respiratory distress syndrome (ARDS) and multi-organ failure. This highlights the importance of monitoring immune responses in patients and developing treatment strategies that not only enhance effective immune function but also mitigate the risks of hyperinflammation. Targeted therapies, such as corticosteroids and other anti-inflammatory agents, may be essential in managing severe cases to prevent life-threatening outcomes while supporting the immune system's ability to control the infection.

Disease Progression

SARS-CoV-2 infection presents with a broad spectrum of clinical manifestations, ranging from cases where individuals show no symptoms at all to severe instances of respiratory failure.[68] In many cases, the infection can remain mild or asymptomatic, making it difficult to detect and control, especially in community settings. For those who do develop

symptoms, the disease typically progresses quickly, with signs such as fever, cough, and fatigue emerging within 2 to 14 days after exposure to the virus.[69] This rapid onset of symptoms is characteristic of the acute phase of the infection, where the body's immune system is actively responding to the viral invasion. In severe cases, particularly among the elderly and individuals with pre-existing health conditions such as heart disease, diabetes, or chronic respiratory diseases, SARS-CoV-2 infection can escalate to life-threatening complications. One of the most severe outcomes is acute respiratory distress syndrome (ARDS), a condition where fluid builds up in the lungs, severely impairing the ability to breathe and oxygenate the blood. If ARDS progresses, it can lead to multi-organ failure as vital organs like the heart, kidneys, and liver are deprived of oxygen, ultimately resulting in death in the most critical cases.[70] These severe complications underscore the critical need for early intervention and targeted care, especially for high-risk populations. The progression of SARS-CoV-2 disease has profound implications for public health and treatment strategies. The wide range of clinical manifestations, from asymptomatic cases to severe respiratory failure, complicates detection and control efforts, particularly in community settings where mild or asymptomatic infections may go unnoticed. For symptomatic individuals, the rapid onset of symptoms within 2 to 14 days post-exposure necessitates prompt medical attention to prevent escalation to severe complications, such as acute respiratory distress syndrome (ARDS) and multi-organ failure, especially in vulnerable populations like the elderly and those with pre-existing health conditions. This highlights the importance of early intervention strategies, including timely testing, contact tracing, and targeted care for high-risk groups, to mitigate severe outcomes and reduce mortality rates. Public health initiatives must focus on educating communities about the potential severity of the disease and the importance of seeking medical care at the first sign of symptoms to improve overall health outcomes.

Etiology of HIV Infection

Pathogen

HIV, a retrovirus from the Lentivirus genus, is known for its ability to cause long-term infection.[71] As a single-stranded RNA virus, it integrates its genetic material into the DNA of the host cell, establishing a persistent and chronic infection.[72] There are two distinct types of HIV: HIV-1, which is the most prevalent worldwide, and HIV-2, which is less common and primarily confined to West Africa.[73] Both types share similar modes of transmission but differ in virulence and geographical distribution. The pathogenesis of HIV has critical implications for public health and treatment strategies. As a retrovirus that integrates its genetic material into the host's DNA, HIV establishes a chronic infection that can lead to long-term health complications, including acquired immunodeficiency syndrome (AIDS). The existence of two distinct types, HIV-1 and HIV-2, necessitates tailored public health approaches, as HIV-1 is more prevalent globally while HIV-2 is primarily found in West Africa. Effective treatment strategies, including antiretroviral therapy (ART), are essential for managing the infection and preventing transmission. Public health initiatives must focus on increasing access to testing, education about transmission modes, and promoting adherence to treatment to reduce the incidence of new infections and improve the quality of life for those living with HIV. Additionally, addressing stigma and ensuring equitable healthcare access are vital components of a comprehensive response to the HIV epidemic.

Transmission

HIV is primarily transmitted through direct contact with infected bodily fluids, including blood, semen, vaginal fluids, and breast milk.[74] Transmission can occur via the genitourinary tract[75] or through oral sex[76] with key routes being sexual contact, needle sharing, blood transfusions, and mother-to-child transmission during childbirth or breastfeeding.[77] Unlike COVID-19, which spreads through respiratory droplets, HIV requires direct fluid exchange and is not transmitted through casual contact or airborne means.[78] The transmission dynamics of HIV have significant implications for public health and treatment strategies. As HIV is primarily spread through direct contact with infected bodily fluids—such as blood, semen, vaginal fluids, and breast milk—public health initiatives must prioritize education on safe practices to reduce transmission risk. Key routes of transmission, including sexual contact, needle sharing, blood transfusions, and mother-to-child transmission, highlight the need for targeted interventions. Strategies such as promoting safe sex practices, providing access to clean needles, and implementing routine screening for pregnant women can effectively reduce new infections.

Additionally, increasing awareness and access to pre-exposure prophylaxis (PrEP) and antiretroviral therapy (ART) can empower individuals to protect themselves and their partners. Comprehensive public health campaigns that address stigma and promote testing and treatment adherence are essential to curbing the spread of HIV and improving health outcomes for affected populations.

Target Cells

HIV targets macrophages,[79] **CD4+ T cells** and dendritic cells, which are key components of the **immune system**.[80] The virus gains entry into these cells by binding to the CD4 receptor on the cell surface, and this interaction is facilitated by co-receptors CCR5 or CXCR4, depending on the viral strain. Once inside the host cell, HIV undergoes reverse transcription, converting its RNA genome into DNA. This newly formed viral DNA is then integrated into the host cell's genome, a process that establishes a latent reservoir of the virus, enabling it to persist in the body and evade immune detection and antiretroviral therapy.[81] This ability to form latent reservoirs makes HIV particularly challenging to eliminate, as the virus can remain dormant and reactivate under favorable conditions. The targeting of key immune cells by HIV has profound implications for public health and treatment strategies. By primarily infecting macrophages, CD4+ T cells, and dendritic cells, HIV undermines the body's immune response, leading to increased vulnerability to opportunistic infections and other diseases. The virus's mechanism of entry, which involves binding to the CD4 receptor and utilizing co-receptors like CCR5 or CXCR4, necessitates the development of targeted therapies that can block these interactions. Furthermore, the ability of HIV to integrate its genetic material into the host's genome and establish latent reservoirs complicates treatment efforts, as these dormant cells can evade both immune detection and antiretroviral therapy. Public health strategies must therefore focus on not only improving access to ART to manage active infections but also on research into therapies that can target and eliminate these latent reservoirs. Additionally, ongoing education about the importance of adherence to treatment and regular monitoring is essential to maintain viral suppression and prevent transmission, ultimately aiming for a functional cure for those living with HIV.

Immune Response

The body's immune response to HIV involves both humoral and cell-mediated immunity, which initially mount a defense against the virus. However, HIV is able to evade immune detection by mutating rapidly and hiding within immune cells, making it difficult for the immune system to target and eliminate the virus effectively.[82] This persistent evasion leads to the gradual depletion of CD4+ T cells, a critical component of the immune system, progressively weakening the body's defenses. Without treatment, this decline in immune function eventually results in the onset of AIDS (Acquired Immunodeficiency Syndrome).[83] Although antibodies are produced in response to the infection, they are insufficient to clear the virus, and over time, the immune system becomes increasingly compromised, further enabling the virus to spread unchecked.[82] The immune response to HIV presents significant challenges for public health and treatment strategies. While the body initially activates both humoral and cell-mediated immunity to combat the virus, HIV's ability to rapidly mutate and hide within immune cells allows it to evade detection and effectively undermine the immune system. This evasion leads to the progressive depletion of CD4+ T cells, which are essential for a robust immune response, ultimately resulting in the onset of AIDS if left untreated. The production of antibodies in response to HIV infection is insufficient for viral clearance, and as the immune system becomes increasingly compromised, the risk of opportunistic infections and further transmission escalates. Public health initiatives must therefore emphasize the importance of early diagnosis and immediate initiation of antiretroviral therapy (ART) to preserve immune function and prevent disease progression. Additionally, ongoing research into vaccines and immune-based therapies is crucial to enhance the immune response against HIV and improve long-term health outcomes for those living with the virus.

Disease Progression

HIV infection progresses over years,[84] in contrast to the rapid progression observed in SARS-CoV-2 infection, which can advance within days or weeks. After the initial acute phase, where flu-like symptoms might appear,[69] HIV enters a chronic asymptomatic phase that can persist for years.[72] If left untreated, HIV ultimately progresses to AIDS, a condition marked by severe immune dysfunction, opportunistic infections, and cancers.[85] However, with antiretroviral

therapy (ART), HIV can be effectively managed as a chronic disease, thereby preventing its progression to AIDS.[52] The progression of HIV infection has significant implications for public health and treatment strategies, particularly when compared to the rapid progression of other viral infections like SARS-CoV-2. After the initial acute phase, which may present with flu-like symptoms, HIV can enter a chronic asymptomatic phase that can last for years, allowing the virus to persist undetected. If untreated, this chronic infection eventually leads to AIDS, characterized by severe immune dysfunction and increased susceptibility to opportunistic infections and cancers. However, the advent of antiretroviral therapy (ART) has transformed HIV into a manageable chronic disease, enabling individuals to maintain their health and prevent progression to AIDS. Public health initiatives must focus on increasing access to testing and ART, promoting early diagnosis, and ensuring adherence to treatment. Additionally, education about the importance of regular medical care and monitoring is essential to sustain viral suppression and improve the quality of life for those living with HIV, ultimately reducing the burden of AIDS-related complications in the population.

Comparison of Etiology

Viral Structure

Both SARS-CoV-2 and HIV are RNA viruses, but they differ significantly in their genetic material and replication mechanisms. SARS-CoV-2 is classified as a positive-sense single-stranded RNA virus, meaning its RNA can be directly translated into proteins by the host cell's machinery.[50] In contrast, HIV is a retrovirus that reverse transcribes its RNA into DNA before integrating it into the host's genome.[86] Additionally, SARS-CoV-2 is an enveloped virus characterized by spike proteins that specifically bind to the ACE2 receptor on host cells, facilitating viral entry.[87] HIV, on the other hand, also has an envelope but features different glycoproteins that bind to CD4 receptors on T-cells, which is crucial for its infection process.[88]

Transmission Mechanisms

SARS-CoV-2 is primarily transmitted through the respiratory route, via droplets or aerosols, which makes it highly contagious, particularly in close-contact settings where the virus can spread easily through the air.[89] In contrast, HIV transmission occurs through direct contact with infected bodily fluids, such as blood, semen, vaginal fluids, or breast milk, making it less transmissible compared to SARS-CoV-2. HIV transmission is typically associated with intimate contact, such as sexual activity, or exposure to contaminated blood.[78] The difference in transmission routes reflects the varying modes of spread and infection control measures required for each virus.

Immune Response

SARS-CoV-2 can induce an acute, hyperinflammatory response known as a cytokine storm, particularly in severe cases of SARS-CoV-2 infection, which can lead to significant tissue damage and complications. Despite this, most individuals with a functioning immune system are able to recover from the acute phase of the illness.[90] In contrast, HIV targets and progressively destroys key components of the immune system, specifically CD4+ T-cells, leading to a gradual and sustained immune deficiency if left untreated.[81] This continuous destruction of immune cells results in a long-term vulnerability to opportunistic infections and other complications, distinguishing HIV's impact on immune function from the more acute and often recoverable effects of SARS-CoV-2.

Disease Course

SARS-CoV-2 infection generally presents as an acute illness, with symptoms emerging shortly after infection and typically resolving or progressing to severe outcomes within a matter of weeks.[91] This acute phase is characterized by a rapid onset of symptoms such as fever, cough, and difficulty breathing, and while many recover within a few weeks, some may experience severe complications or prolonged symptoms. In contrast, HIV has a chronic progression that begins with an initial acute phase, which can be asymptomatic or present with flu-like symptoms shortly after infection. Following this, HIV enters a latent phase that can last for several years, during which the virus persists in the body with a gradual decline in immune function.[48] Without treatment, this chronic infection eventually leads to AIDS, a condition

marked by severe immunosuppression and increased susceptibility to opportunistic infections and cancers. Thus, while SARS-CoV-2 infection often resolves relatively quickly, HIV represents a long-term, progressive disease requiring ongoing management to prevent progression to AIDS.

Treatment and Management

SARS-CoV-2 infection is managed through a combination of vaccines and antiviral treatments. Vaccines are designed to elicit protective immunity against the virus, significantly reducing the risk of severe illness and transmission.[92] In addition to vaccines, antiviral treatments such as remdesivir and monoclonal antibodies are used to mitigate the severity of the illness and support recovery in infected individuals.[92] These treatments work by inhibiting viral replication or neutralizing the virus directly. In contrast, HIV management relies on lifelong antiretroviral therapy (ART), which effectively suppresses viral replication and helps maintain immune function. While ART does not eliminate the virus from the body, it reduces the viral load to undetectable levels, preventing disease progression and transmission.[93] The treatment and management strategies for HIV and SARS-CoV-2 highlight distinct yet critical approaches in public health. For SARS-CoV-2, management primarily involves vaccination to elicit protective immunity, significantly reducing the risk of severe illness and transmission, alongside antiviral treatments like remdesivir and monoclonal antibodies that inhibit viral replication and support recovery. In contrast, HIV management necessitates lifelong antiretroviral therapy (ART), which effectively suppresses viral replication and maintains immune function, although it does not eliminate the virus from the body. ART reduces the viral load to undetectable levels, thereby preventing disease progression to AIDS and minimizing the risk of transmission. Public health strategies must therefore prioritize vaccination campaigns and access to antiviral treatments for SARS-CoV-2 while ensuring that individuals living with HIV have consistent access to ART and related healthcare services. This dual focus is essential for managing both infections effectively and improving overall public health outcomes.

Conclusion

The comparative analysis of SARS-CoV-2 and HIV reveals critical insights into their viral characteristics, mechanisms of host cell entry, and replication cycles. These differences emphasize the importance of targeted public health strategies and treatment approaches tailored to the unique challenges posed by each virus. By leveraging this knowledge, healthcare systems can better manage viral infections, improve patient outcomes, and enhance overall public health resilience against future pandemics.

Recommendations

For Public Health Strategies; Governments and health organizations should develop distinct prevention and control strategies for SARS-CoV-2 and HIV, taking into account their unique transmission routes and disease progression.

Need for Tailored Treatment Approaches; Healthcare providers should differentiate between managing the acute viral infection of SARS-CoV-2 and the chronic retroviral nature of HIV, ensuring appropriate treatments and interventions are applied.

For Research and Development; Ongoing research into vaccines, therapeutic options, and immune system responses for both SARS-CoV-2 and HIV should continue, with attention to their unique characteristics.

Healthcare System Preparedness; Policies should focus on strengthening health system capacities to address both short-term viral outbreaks like SARS-CoV-2 infection and long-term conditions like HIV, ensuring adequate resources and care for each.

Global Health Equity, more attention should be given to vulnerable populations disproportionately affected by both pandemics, ensuring equitable access to healthcare, vaccines, and treatments.

Limitations of the Study

Narrative reviews, while valuable for summarizing and synthesizing existing literature, have their own limitations, such as the potential for incomplete coverage, difficulty in assessing quality, lack of systematic methodology, and subjectivity. These limitations were addressed using the following strategies:

To tackle the potential for incomplete coverage, we conducted a comprehensive literature search using multiple databases (eg, PubMed, Scopus, Cochrane Library, and Google Scholar) and relevant keywords to ensure a wide range of studies were considered. Regarding the difficulty in assessing quality, we implemented transparent reporting by clearly documenting the criteria used for including or excluding studies, as referenced in the methods section, along with the rationale for their selection to enhance transparency. To overcome the lack of systematic methodology, we adopted a structured framework for organizing the review, which included defining specific research questions, objectives, and themes to guide the narrative synthesis. Additionally, we established clear inclusion and exclusion criteria for selecting studies, which helped maintain consistency and reduce bias in the selection process. Finally, to address subjectivity in narrative reviews, we employed a collaborative approach by involving three researchers in the review process to provide diverse perspectives and minimize individual biases.

Abbreviations

ARDS, Acute Respiratory Distress Syndrome; ACE2, Angiotensin-Converting Enzyme 2; CCR5, C-C Chemokine Receptor Type 5; CXCR4, C-X-C Chemokine Receptor Type 4; COVID-19, Coronavirus Disease 2019; DNA, Deoxyribonucleic Acid; RNA, Ribonucleic Acid; HIV, Human Immunodeficiency Virus; AIDs, Acquired Immunodeficiency Syndrome; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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