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Original Article

A Comprehensive Review Of COVID-19's Role In HIV Patients

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Abstract:
The impact of COVID-19 has substantially affected the lives of people. Individuals suffering from HIV have a risk of COVID-19 due to lowering their immune system leads to complications. Approximately 19 million people have been infected with COVID-19.Generally 39.9 million people were living with HIV at the end of 2023. HIV patients tend to have mental health issues such as depression, anxiety and post-traumatic stress. In some regions, healthcare resources and attention shifted towards managing COVID-19 cases. HIV acts primarily by destroying immune cells such as macrophages and $CD4^+$ cells called helper cells (normal range of $CD4^+$ is 500-1500). HIV infection leads to AIDS when T-cells are reduced below 200 cells per litter of blood. In this article, we systemically analyze the research work. This article includes all the information related to the diseases COVID-19 effects on HIV patients with advanced treatments.

KEYWORDS: HIV, COVID-19, $CD4^+$ cells, helper cell, AIDS

Introduction:

COVID-19 is a respiratory disease. It first appeared in late 2019 in Wuhan, China. It can cause mild to severe symptoms such as cough, fever, and difficulty breathing. Due to the sickness, there was a worldwide epidemic, which prompted extensive health precautions and immunization campaigns. [1] HIV is an autoimmune disease. The first case was observed in 1986 and was diagnosed by Dr Suniti Solomon and her student Dr.Sellappan Nirmala amongst six female sex workers in Chennai, Tamilnadu. Symptoms of HIV include fever, fatigue, weight loss, rash and sore throat. [2] Those living with HIV, especially those with low CD4 counts or un treated HIV, may be more susceptible to serious disease if they come into contact with COVID-19. This is a result of their already weakened immune systems. [3] As of right now, organ support is the only known treatment for COVID-19; severe instances necessitate hospital admission for supportive care, which includes artificial ventilation. [4] Estimated 37.6 million people globally are expected to be HIV positive by 2020; of these, 1.3 million adults and 160,000 new children were diagnosed with the virus in that year. It is estimated that around 19% of HIV-infected patients were not able to accept an antiretroviral medication refill during the epidemic. Approximately 16% of people living with HIV (PLWH) were unaware of their HIV status, 27% were unable to receive ART, and 34% of those who received ART did not have viral inhibition. [5] Due to the COVID-19 epidemic, some nations have recently experienced delays in the delivery of HIV services and care. Later than COVID-19 infections, PWLH may have high up morbidity and mortality rates as a result of this interference. On the other side, little is known about how COVID-19 has affected HIV services. [6] Hospitalized

with COVID-19 were twenty-three HIV individuals. Fifty-nine was the average age. [7]

Human Immuno Deficiency Virus can be classified into 2 groups:

1. Human immune deficiency virus type 1 (HIV-1)
2. Human immune deficiency virus type 2 (HIV-2)

The development of broadly effective vaccinations and antiretroviral treatments is greatly retard by the great genetic variety of the human immunodeficiency virus type 1 (HIV-1). One potential weakness of HIV-1 is the genetic barrier that occurs during transmission. Operate the genetically complicated viral inoculum to a homogenous founder population may be facilitated in part by the mucosal barrier. Sexual practice, concomitant STIs, anatomy, physiology, and other factors may all affect the mucosal barrier's effectiveness. However, intravenous drug users (IVDU) have also been found to exhibit a genetic obstruction, suggesting mechanisms not dependent on the mucosa. [8]

HIV-2 infection is common in West Africa and is becoming more widely identify outside of the continent. Contrary to HIV-1, the human immunodeficiency virus type 2 has limited neonatal transmission and is transmitted through intercourse and tainted blood. The simian immunodeficiency virus (SIV) and human immunodeficiency virus (HIV-2) are genetically greatly more similar than HIV-1. Based on biological and demographic evidence, it is possible that HIV-2 was originally spread from monkeys to humans. While HIV-1 infection results in the acquired immunodeficiency syndrome (AIDS), HIV-2 infection seem to have a significantly longer asymptomatic incubation period. These clinical findings are supported by the fact that HIV-2's genetic regulation is different from HIV-1's. There are not enough therapeutic research with HIV-2-positive individuals. [9]

Pathophysiology of SARS-CoV-2 and HIV infections

A review of the immunological response and pathogenesis of COVID-19 infections has been done. [6, 10] To put it briefly, the four structural proteins of SARS-CoV-2—spike (S), membrane (M), envelop (E), and nucleocapsid (N)—define this beta coronavirus.[11] Attachment, penetration, biosynthesis, maturity, and release are the five stages of the SARS-CoV-2 life cycle. [6] The SARS-CoV-2 receptor is angiotensin converting enzyme 2 (ACE2). [12, 13] The lung, heart, ileum, kidney, and bladder all have important levels of ACE2 expression, according to single-cell RNA sequencing data. [14] Moreover, individuals with COVID-19 have been reported to experience anosmia, or an abrupt loss of smell. [15] However, neither olfactory sensory neurons nor olfactory bulb neurons showed evidence of ACE2. [16]

The virus cause by infected cells moves to the lower airway after SARS-CoV-2 infects the epithelial cells of the upper respiratory tract, where it infects alveolar macrophages and bronchial and alveolar epithelial cells. [17] Viral-infected epithelial cells die as a effect of innate immunity, and antigen-presenting cells (APC) such macrophages and dendritic cells (DCs) phagocytosis them. To give T cells viral antigens, the APC move to draining lymph nodes. [6, 10]

The immune system's defense against the coronavirus depends heavily on both CD4+ and CD8+ T cells [21]. While CD8+ T cells have the ability to directly destroy virally infected cells, CD4+ T cells stimulate B cells to encourage the development of virus-specific antibodies. [10] Lung biopsy results in interstitial mononuclear inflammatory infiltrates that are mostly lymphocyte-dominated in cases of severe COVID-19. [18] In addition, reports of pulmonary edema and desquamation of pneumocystis with the formation of hyaline membranes, indicative of acute respiratory distress syndrome (ARDS), have been made. [19]

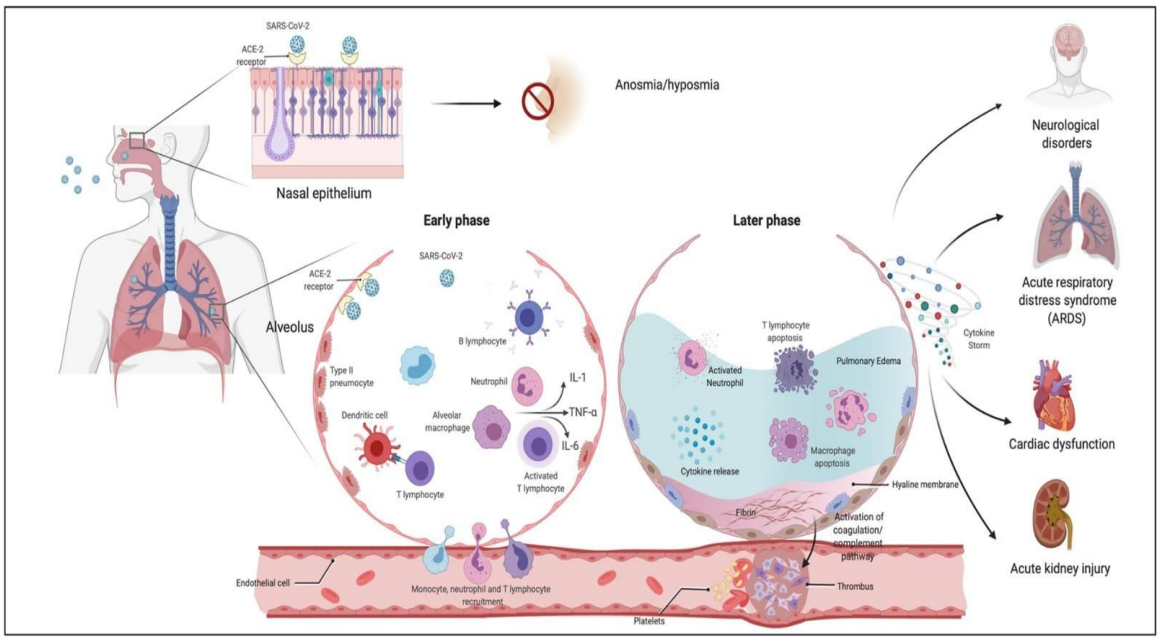

Fig.1: Pathophysiology and clinical manifestations of COVID-19.

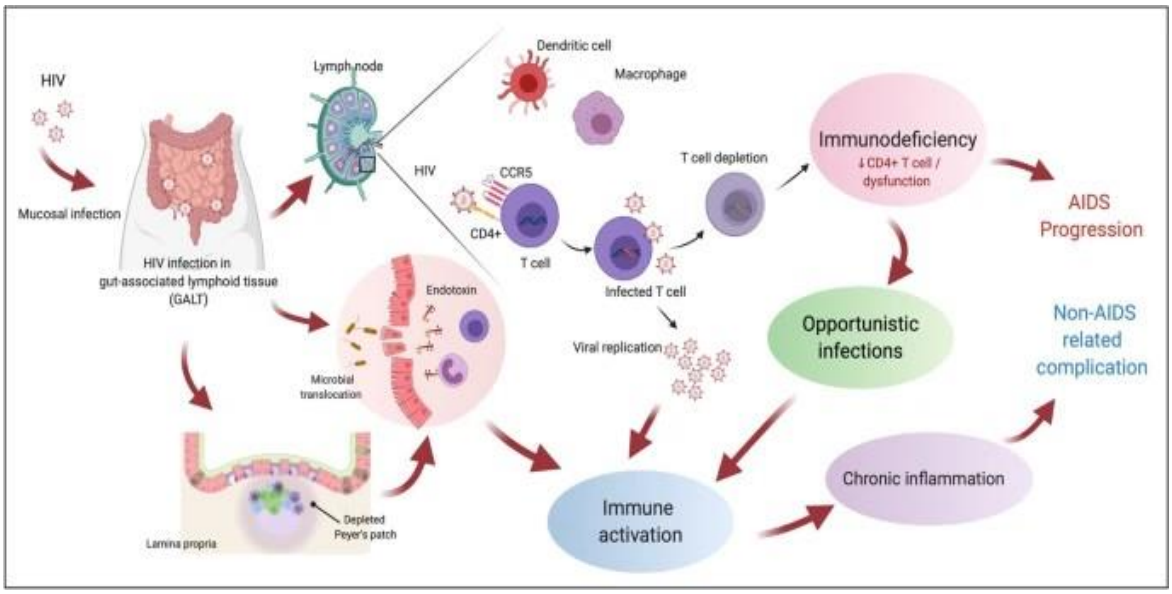

Fig.2: Reaction of the host immune system after HIV exposure.

Lifestyle of patients

Participants Investigated reported any changes in body weight during SD (Social Distancing) and disclosed how they regarded their own health. [20] The number of weekly days they consumed various foods before and during SD was examined in diet-related questionnaires. There were three sets of questions that we arranged. [1] Beans, raw and cooked vegetables, whole fruits, and fish were included in the first group of foods that were thought to be preventive against chronic diseases. [2] The foods deemed by various studies as neutral or controversial regarding the risk of chronic diseases (fruit juices, milk, red meat, chicken, or other poultry) made up the third set. The second set included unhealthy eating markers (sodas and soft drinks, sweets and candies, and snacks replacing meals). [20, 21, 22] Details regarding the kind and location of the activity, as well as the number of weekly days and daily length of each activity, were included in the questions regarding physical activity. We developed a variable based on the responses about whether or not to practice physical activity. During SD, participants were questioned regarding any changes in the amount of time they spent sitting in front of the TV, computer, smartphone, or other devices. The questions about

physical activity, self-perceived status, and diet were taken from Brazilian epidemiological research. A self-evaluation of sleep as well as other sleep indices were examined using items modified from the Pittsburg Sleep Quality Questionnaire. [23] Healthy lifestyle factors have been found to be protective against inflammation. These factors include a healthy body mass index (BMI, which is calculated as weight in kilograms divided by height in meters squared), abstinence from cigarette smoking, [25] a healthy diet, [26] moderate alcohol consumption, [27] regular exercise, [28] and adequate sleep. [29] A dose-dependent relationship has been found between adherence to several healthy lifestyle factors and reduced mortality from infectious diseases, including COVID-19, as well as less severe COVID-19 disease. [30, 31]

Diagnosis

There are three primary test types for COVID-19 diagnosis that can be used to meet all of these clinical and epidemiological needs: i) Rapid antigen or antibody tests; ii) serological tests; iii) molecular RT-PCR swab tests. [32] Rapid antigen or antibody testing, immunoenzymatic serological testing, and RT-PCR-based molecular testing are the most widely used and approved procedures. These three different kinds of diagnostic testing can all be used at the exact time of infection. Importantly, kits, reagents, and molecular probes can only be used for diagnostics if they have been validated by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), and if they have been approved by the FDA and the EMA for use in the United States and Europe. [33] In addition to these traditional approaches, additional diagnostic techniques are being developed, tested, or are being used in research settings right now. The wide range of techniques to accurately diagnose COVID-19 infection and assess the epidemiological spread of the pandemic includes digital PCR, isothermal amplification techniques, biosensors, diagnostic methods based on CRISPR/CA's (clusters of regularly interspaced short palindromic repeats/Cas), and electron microscopy. [34, 35] HIV type 1 (HIV-1) immunoglobulin G (IgG) antibodies were discovered by first-generation immunoassays employing viral lysate as the antigen; however, antibody responses to distinct HIV-1 clades were not observed. [36, 37] After the infection, they tested positive about 7-8 weeks later. [38] Current, commonly used diagnostics have higher sensitivity and specificity than first-generation assays. With the help of a substrate, fixed HIV proteins can produce a pattern that can be interpreted as positive, negative, or indeterminate. This is what the Western blot assay looks for in antibodies. A less used method is the immunofluorescence assay (IFA), which analyzes for the presence of antibodies by combining serum or plasma samples with T cells that express HIV antigens. A fluorescent molecule coupled to an antihuman antibody is then used to identify bound antibodies. [39] Although Alere DetermineHIV1/2Ag/Ab combo, a combination antigen (Ag)/antibody (Ab) fast HIV assay, has been developed, it is not yet authorized for use in the United States. Unfortunately, the information that is now available shows that this assay is not as sensitive to HIV infection as the laboratory assays are, nor does it detect HIV p24 antigen at the same concentrations as laboratory-based fourth-generation assays. [40, 41] The experimental pipeline includes other fast tests that detect p24 antigen in addition to this commercial assay. [42, 43]

Recent advances and treatment

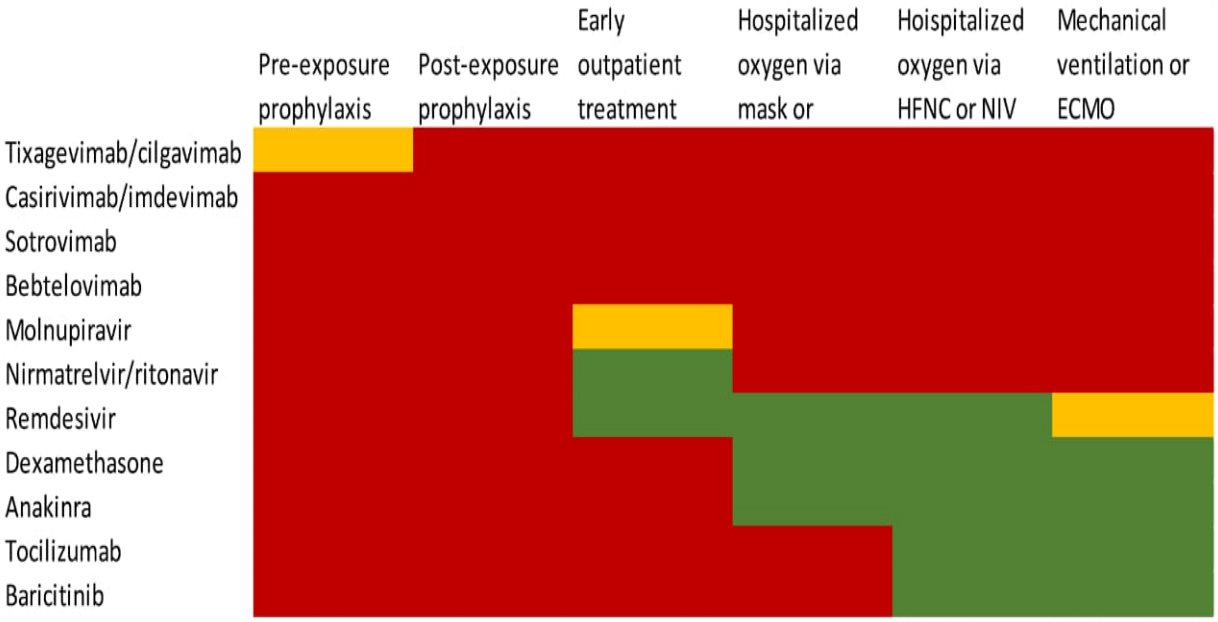

Fig.3 Present guidance for COVID-19 treatment.

Red: This is no longer suggested to use this treatment.
Orange: In a lack of other options or for specific groups and locations, this treatment is recommended.
Green: It is highly recommended that all patients undergo this treatment.
This evaluation does not address immunization, although it should be noted that all guidelines suggest PWH to receive booster doses and the entire SARS-CoV-2 vaccine. Multiple research studies have shown that PWH and healthy controls have similar levels of immunogenicity with current vaccinations, especially when CD4 counts are well preserved, for both the primary and booster shots. [44-48] Immunogenicity has been linked to CD4 counts <250 cells/mL, and it seems that PWH lose humoral immunity from vaccinations more quickly, indicating the need for booster shots. In the end, a meta-analysis revealed that PWH performed equally to various immunizations. [49] As CYP3A4 is responsible for utilizing nirmatrelvir, introducing ritonavir to this regimen enhances nirmatrelvir's pharmacokinetics and increases its bioavailability. [50] Remdesivir is an approved aimed antiviral regimen for COVID-19 that acts as a direct-acting nucleotide prodrug inhibitor of the SARS-CoV-2 RNA-dependent RNA polymerase. Originally, remdesivir was examined and approved for the treatment of patients demanding hospitalization and additional oxygen. [51] A highly conserved epitope that would be functionally maintained while SARS-CoV-2 evolves has been proposed to be the target of a monoclonal antibody that neutralizes all sarbecoviruses. [52] There are certain mRNA vaccines currently being researched that target HIV antigens for both therapeutic and preventative uses. mRNA vaccines encoding HIV antigens might be able to lower populations during future studies. [53, 54]

Conclusion:
A detailed examination of COVID-19's impacts on HIV patients shows both direct and indirect effects, indicating to a complex description of the disease's effects. HIV-positive people have a greater exposed to severe COVID-19 outcomes, such as higher hospitalization and mortality rates, particularly when they have weakened immune systems. The review highlights that although antiretroviral medication (ART) has helped to improve HIV management, there is still a critical need to evaluate how it reacts with COVID-19 medicines. Further complicating management, the epidemic has made it more difficult to obtain regular HIV care and drugs. These results emphasize

the necessity of integrated healthcare strategies to address the particular vulnerabilities that HIV patients face during pandemics, ensuring that COVID-19 prevention and treatment, as well as appropriate HIV management, are achieved.

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