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Cardiac and respiratory complications among acquired immunodeficiency syndrome (AIDS) patients

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بسم الله الرحمن الرحيم

(هُوَ الَّذِي أَنزَلَ عَلَيْكَ الْكِتَابَ مِنْهُ آيَاتٌ مُّحْكَمَاتٌ هُنَّ أُمُّ الْكِتَابِ وَأُخَرُ مُتَشَابِهَاتٌ ۖ فَأَمَّا الَّذِينَ فِي قُلُوبِهِمْ زَيْغٌ فَيَتَّبِعُونَ مَا تَشَابَهَ مِنْهُ ابْتِغَاءَ الْفِتْنَةِ وَابْتِغَاءَ تَأْوِيلِهِ ۗ وَمَا يَعْلَمُ تَأْوِيلَهُ إِلَّا اللَّهُ ۗ وَالرَّاسِخُونَ فِي الْعِلْمِ يَقُولُونَ آمَنَّا بِهِ كُلٌّ مِّنْ عِندِ رَبِّنَا ۗ وَمَا يَذَّكَّرُ إِلَّا أُولُو الْأَلْبَابِ)

صدق الله العلي العظيم

من سورة ال عمران الاية ٧

الاهداء

الى الكادر التدريسي في جامعة ديالى عامة

ودكتور شكر محمود بشكل خاص

لدوره الفعال في التعليم والتوجيه نحو اهمية المعلومة والتعلم والتطور نحو الافضل

واهداء للاصدقاء والصديقات في كروب D للمرحلة السادسة لعام ٢٠٢١-٢٠٢٢ لدورهم في مشاركة المعلومة وايصالها للجميع

و لعائلة والاقارب

لدورهم في المساندة والدعم والاهتمام

اهدي لكم مشروعي البسيط ..

الشكر و التقدير

أحمد الله تعالى أولًا وآخرًا على الفضل العظيم الذي منحني إياه، ثم أتقدم بالشكر لمن فضلهما لا ينقطع عليَّ والدي الحبيبين على كل جهودهم منذ لحظة ولادتي إلى هذه اللحظات المباركة، أنتم يا أبي وأمي نجاحي وفرحتي وكل شيء جميل في حياتي، ويسرني أن

أوجه الشكر الجزيل لكل من نصحني أو أرشدني أو ساهم لو بشيء قليل أو وجهني في إعداد هذا البحث وإيصالي للمراجع والمصادر المطلوبة في أي مرحلة من المراحل التي مررت بها، وأشكر على وجه الخصوص الأستاذ الفاضل الدكتور: **"شكر محمود ياسين"**، على مساعدتي ومساندتي وإرشادي بالنصح والتعليم والتصحيح وعلى كل ما بذله معي، كما يسرني أن أشكر إدارة الكلية الموقرة: "كلية الطب- جامعة ديالى"، وأسأل الله أن يكون بحث التخرج هذا في صحيفة أعالمهم جميعًا، وأن يجزيهم تعالى خير الجزاء والحمد لله رب العالمين.

Abstract

The human immunodeficiency virus (HIV) is a retrovirus belonging to the family of lentiviruses. Retroviruses can use their RNA and host DNA to make viral DNA and are known for their long incubation periods. HIV causes severe damage to the immune system and eventually destroys it by using the DNA of CD4+ cells to replicate itself. In that process, the virus eventually destroys the CD4+ cells. The acquired immunodeficiency

syndrome (AIDS) was first identified in the early 1980s, it was believed to be constrained to a small number of risk groups. Cardiovascular and respiratory illnesses can strike at any stage of HIV infection, but cardiac morbidity and mortality are more common in the later stages. Almost any substance that can induce widespread infection in AIDS patients can affect the myocardium, but cardiac disease is frequently overshadowed by symptoms in other organs, primarily the brain and lungs. In this short review we tried to cover the most common cardiac and respiratory illnesses that exacerbate or caused by the HIV infection.

Keywords: Human immune deficiency virus (HIV), acquired immunodeficiency syndrome (AIDS). Cardiac illnesses, respiratory illnesses.

Introduction

The immune system protects the body by recognizing antigens on invading bacteria and viruses and reacting to them. An antigen is any substance that induces a state of sensitivity and immune responsiveness. These antigens interact with antibodies and immune cells, initiating an immune response. This process destroys the antigen, allowing the body to be free of infections. Types of antigens include bacteria, viruses, fungi, and parasites. When the immune system is weakened or destroyed by a virus such as HIV, the body is left vulnerable to infections (1). The human immunodeficiency virus (HIV) is a retrovirus belonging to the family of lentiviruses. Retroviruses can use their RNA and host DNA to make viral DNA and are known for their long incubation periods. Like other retroviruses, HIV infects the body, has a long incubation period (clinical latency), and ultimately causes the signs and symptoms of disease, here AIDS. HIV causes severe damage to the immune system and eventually destroys it by using the DNA of CD4+ cells to replicate itself. In that process, the virus

eventually destroys the CD4+ cells (1). The acquired immunodeficiency syndrome (AIDS) was first identified in the early 1980s, it was believed to be constrained to a small number of risk groups. As more information became known about the epidemiologic picture of HIV transmission, it became clear that the infection was transmitted primarily through sexual contact and blood (including through injection-drug use), as well as perinatally (2). In the United States, HIV type 1 (HIV-1) is the predominant virus, whereas HIV type 2 (HIV-2) is endemic in other areas of the world (e.g., West Africa). In 2018, approximately 38,000 new cases of HIV infection were diagnosed in the United States and its territories (3). Although perinatal transmission in the United States has decreased to very low levels owing to routine screening for HIV and initiation of antiretroviral therapy (ART) in HIV-infected women during pregnancy, cases in adolescents and adults decreased by just 7% between 2014 and 2018 (4). Since 1998 the US Public Health Service has recommended the use of combination antiretroviral therapy (ARV) to prevent mother-to-child HIV transmission. Because zidovudine and other nucleoside analogues can affect nuclear and mitochondrial DNA replication, the safety of in utero exposure to these drugs is of concern . In addition, there is inadequate fetal and neonatal safety data for non-nucleoside analogues and protease inhibitors. Efavirenz, a non-nucleoside analogue, is considered a potential teratogen on the basis of animal data and case reports (5).

Aim of study

To demonstrate the most common cardiac and respiratory complications and diseases of HIV patients.

Review of literature

Cardiovascular illness can strike at any stage of HIV infection, but cardiac morbidity and mortality are more common in the later stages. Almost any substance that can induce widespread infection in AIDS patients can affect the myocardium, but cardiac disease is frequently overshadowed by symptoms in other organs, primarily the brain and lungs. As a result, the number of AIDS patients having cardiac involvement at autopsy much outnumbers the number of individuals with serious cardiac illness throughout their lifetime (6). In two-thirds of AIDS patients, cardiac abnormalities are discovered at autopsy, and more than 150 reports of cardiac problems have been published. Clinical and autopsy studies have found that the prevalence of cardiac anomalies in HIV-positive patients ranges from 25% to 75% (7).

When HIV infects a person, it causes platelet activation and endothelial dysfunction, both of which can contribute to atherosclerosis. HIV can directly enter myocytes in rat models and cause cardiac damage, which can lead to myocardial dysfunction (8).

A long-term cohort study discovered a link between HIV infection and CVD. HIV-positive patients had a higher risk of incident coronary artery disease, percutaneous coronary intervention, coronary artery bypass surgery, sudden cardiac mortality, heart failure, and chronic renal disease than the general population, but a reduced risk of atrial fibrillation (9). In coronary arteries, unstable plaque is more likely to rupture and cause cardiovascular events than stable plaque. In one study, 41 HIV-positive and 101 HIV-negative people with a median age of 45 to 48 years were matched for significant CVD risk factors and had multidetector spiral coronary computed tomography angiography. HIV-positive people were more likely to develop high-risk plaques, such as low-attenuation plaque

(P=.02), which was more likely to be associated with the macrophage activation marker soluble (s) CD163 (10).

The most prevalent cardiovascular consequence of HIV infection is pericardial effusion. Prior to the advent of highly active antiretroviral therapy (HAART), the occurrence of this consequence was believed to be between 5% and 46%, with an annual incidence of 11%–17%. (11). The causes of pericardial effusion in HIV and/or AIDS patients vary, although despite thorough testing, no etiologic agent has been discovered in the majority of instances. Ascites has been linked to pericardial effusion, pleural effusion, and pericardial effusion. The pattern could indicate the existence of polyserositis, a broad serous-effusive condition that affects the pleural, peritoneal, and pericardial surfaces. People with AIDS who have pericardial effusion have a total T-cell count that is equivalent to patients who do not have pericardial effusion, but they have a much lower serum albumin level and a lower CD4 count than patients who do not have pericardial effusion (12). Infective endocarditis or nonbacterial thrombotic (marantic) endocarditis can develop in AIDS patients. Marantic endocarditis is becoming more common in HIV-positive patients who are in the advanced or terminal stages of the disease, and it's often linked to malignancy, inanition, or HIV wasting syndrome (13). In the general population, the prevalence of heart failure ranges from 0.4 percent to 2%. Ventricular dysfunction that is asymptomatic is more common. 10 In the general population, however, the prevalence of asymptomatic left ventricular systolic dysfunction in the age period 35 to 44 years is 1%. In an HIV-infected patient treated with nucleoside reverse transcriptase drugs, a recent study found a link between cardiomyopathy and significant mitochondrial damage. Following the termination of the medicines and the commencement of heart failure treatment, cardiac condition improved

(14). At autopsy, about one-third of AIDS patients had histopathologic evidence of myocarditis, but in more than 80% of the cases, no particular etiology could be determined.Common pathogens found in patients with AIDS-related myocarditis include *Toxoplasma gondii*, *Mycobacterium tuberculosis*, and *Cryptococcus neoformans*. Other infective agents that have been reported are *Mycobacterium avium-intracellulare* complex, *Aspergillus fumigatus*, *Candida albicans*, *Coccidioides immitis*, cytomegalovirus, and herpesvirus types 1 and 2. HIV itself has been implicated as a cause of myocarditis. Since cardiac myocytes do not possess CD4 receptors that would allow a virus to attach itself and enter the cell by the usual mechanism, it is not clear how a virus enters the myocytes (15).

With an estimated frequency of 8%–30%, HIV-related illness is now recognized as a major cause of dilated cardiomyopathy. Prior to the advent of HAART, the annual incidence of dilated cardiomyopathy in HIV patients was estimated to be 15.9 per 1000. Dilated cardiomyopathy is related with a low CD4 level and is usually found in the late stages of AIDS (fewer than 400 cells per milliliter). In 83 percent of patients with dilated cardiomyopathy diagnosed on the basis of histopathologic features, myocarditis caused by HIV or another viral agent, such as group B coxsackievirus (17%), cytomegalovirus (6%), or Epstein-Barr virus (3%), was discovered (16).

Primary pulmonary hypertension, which was originally documented in hemophilic HIV-infected patients, affects about 0.5 percent of patients with HIV infection, compared to a yearly incidence of about 1 to 2 per 1 million people in the general population. There is no correlation between CD4 levels and illness stage. Although opportunistic lung infections can cause right ventricular dysfunction, or cor pulmonale, there is no link

between pulmonary hypertension and these infections. The prognosis is terrible, and patients who are HIV-negative have a similar prognosis. 19 Right cardiac catheterization remains the gold standard for diagnosing pulmonary hypertension and ruling out secondary manifestations; nonetheless, echocardiography is very effective in this regard (17).Cerebral artery aneurysms are frequent in children vertically infected with HIV. In adults, a number of case reports describe aneurysms of the aorta and peripheral and cerebrovascular arteries sometimes necessitating surgical repair (18).

Now, we will discuss the concomitant respiratory diseases and complication associated with HIV infection.

The lungs are a frequent site of opportunistic infection in immunocompromised patients, and noninfectious pulmonary disorders associated with HIV infection and antiretroviral treatments are increasingly common. HIV infection decreases humoral immunity by affecting the generation of particular antibodies through quantitative and functional abnormalities in CD4+ cells. This raises the risk of bacterial infections, such as sinusitis and pneumonia, and the risk of pneumonia develops as the CD4+ lymphocyte count drops. Users of intravenous injecting drugs are at a higher risk than the general population, and neutropenia is a separate risk factor. Trimethoprim (TMP)-sulfamethoxazole (SMX) prophylaxis appears to minimize the incidence of bacterial pneumonia, but it should not be administered only for that purpose because it increases the chance of bacterial resistance. Because bacterial pneumonia is an independent

predictor of progression to AIDS and mortality, it may hasten the advancement of HIV illness (19).

The most common bacterial pathogens are *Streptococcus pneumoniae* and *Haemophilus influenzae*. Pneumonia caused by *Mycoplasma, Legionella,* and *Chlamydia* can occur, but it's rare, especially in people with severe immunosuppression. In individuals with advanced HIV disease, *Rhodococcus equi*, an aerobic Gram-positive acid-fast bacillus, can induce localized consolidation, endobronchial disease, and cavitation. Even in the absence of risk factors such as neutropenia, corticosteroid usage, or hospital-acquired infection, *Pseudomonas aeruginosa* pneumonia can develop in patients with very low CD4+ lymphocyte counts (usually 50 cells/mL). *Nocardia asteroides* is a species of Nocardia. In HIV-positive people, it can produce nodules, consolidation, cavitation, pleural effusions, empyema, and intrathoracic lymphadenopathy (20-21*).* When the tuberculosis and HIV epidemics collided, it resulted in a global public health disaster. Millions of people worldwide, particularly in developing nations, are infected with HIV and *Mycobacterium tuberculosis.* Tuberculosis is the most prevalent pulmonary consequence of HIV infection in Africa, with at least one-third of all tuberculosis infections occurring in HIV patients. In the United States, HIV-associated TB is also frequent, particularly among injection drug users (22). Although active tuberculosis in AIDS patients appears to be treatable in the vast majority of cases, HIV-infected patients with multidrug-resistant tuberculosis continue to have a poor prognosis. Tuberculosis appears to hasten the progression of HIV infection, as tuberculosis predicts the onset of subsequent opportunistic diseases. The development of tuberculosis increases overall mortality by around one-third, according to a major study of over 5,000 HIV-infected people in Europe (23).

Patients with HIV infection develop pulmonary histoplasmosis, blastomycosis, and coccidioidomycosis as a result of either progressive primary infection or reactivation of latent disease once immunosuppressed. Because there were no surveillance mechanisms in place, the frequency of these illnesses in endemic areas was never completely explored. As a result, it's unclear whether the incidence is decreasing in the era of HAART. Despite established standards, diagnosing fungal infections in HIV-positive people remains difficult. For HIV-positive people living in endemic areas, there is no effective prophylaxis, therefore limiting exposure appears to be the best method to avoid infection. Surveillance in endemic areas will be required to assess the efficacy of prophylaxis. Furthermore, given the toxicity of amphotericin B, stronger medications are required to treat these infections (24). Pneumonia caused by *Pneumocystis jiroveci* (previously known as *Pneumocystis carinii*) was the first opportunistic infection to be identified in AIDS patients, and it has always been a significant source of disease and mortality. Rather than modifying our terminology to 'PJP' to suit the new nomenclature, it has been agreed that PCP be used to refer to the word *'Pneumocystispneumonia.' P. jiroveci* was once assumed to be a parasite, but genetic study revealed that it is actually a fungus that only infects humans, while P. carinii is only pathogenic in immunocompromised rats. The organism cannot be cultured reliably outside the lung, and its source is still not identified, so the precise route of transmission is unknown, but may be from human to human (25).

The skin is the most common location of involvement in Kaposi sarcoma (KS), the most common cancer in people living with HIV. Human herpesvirus (HHV)-8 causes KS. In severe KS, visceral involvement is prevalent, and it can affect the airways, lung tissue, mediastinal lymph

nodes, and pleura. Although mucocutaneous lesions are common in patients with thoracic KS, the lung may be the only site of disease in up to 15% of cases (26). The effusions are frequently exudative and sanguineous when KS affects the pleura, although the cytological test is non-diagnostic. Due to the focal character of the pleural lesions and the primary involvement of the visceral pleura rather than the parietal pleura, closed pleural biopsy specimens are rarely positive for KS. Because establishing a diagnosis usually needs a thoracoscopic or open pleural biopsy, the presence of pleural involvement with KS in a patient with cutaneous disease and a serosanguineous effusion without a reasonable other explanation is frequently inferred (19).

Lung cancer is more common in those living with HIV, especially in the years when combination antiretroviral therapy became the standard of care. Despite the fact that most HIV-positive people are current or past smokers, their risk of lung cancer appears to be higher, even when incidence ratios are adjusted for smoking. Microsatellite changes reflecting genomic instability are far more common in HIV-associated lung malignancies, suggesting that they may play a role in their development (27).

Conclusion

HIV infection is a world scale problem with significant morbidity, mortality and psychological burden on the patients. The disease infect the immune system primarily but can involve and affect the other systems. In this review we focused on cardiovascular and respiratory complications and comorbidities that associated with HIV infection and how to prevent them if possible. There are a lot of complication and mainly due to the immunosuppresd condition of the patient. The nature of the problems need more research and investigations to discover the exact pathology and to find solutions for them.

الملخص

فيروس نقص المناعة البشرية (HIV) هو فيروس ارتجاعي ينتمي إلى عائلة الفيروسات البطيئة. يمكن للفيروسات القهقرية استخدام الحمض النووي الريبي والحمض النووي المضيف لصنع الحمض النووي الفيروسي وهي معروفة بفترات حضانة طويلة. يسبب فيروس نقص المناعة البشرية ضررًا شديدًا لجهاز المناعة ويدمره في النهاية باستخدام الحمض النووي لخلايا + CD4 لتكرار نفسها. في هذه العملية، يدمر الفيروس في النهاية خلايا + CD4. تم التعرف على متلازمة نقص المناعة المكتسبة (الإيدز) لأول مرة في أوائل الثمانينيات ، وكان يُعتقد أنها مقيدة بعدد صغير من الفئات المعرضة للخطر. يمكن أن تصيب أمراض القلب والأوعية الدموية والجهاز التنفسي في أي مرحلة من مراحل الإصابة بفيروس نقص المناعة البشرية ، ولكن الامراضية والوفيات القلبية أكثر شيوعًا في المراحل المتأخرة. تقريبا أي جرثومة يمكن أن تسبب عدوى منتشرة في مرضى الإيدز يمكن أن تؤثر على عضلة القلب، ولكن أمراض القلب كثيرا ما تطغى عليها الأعراض في الأعضاء الأخرى ، وخاصة الدماغ والرئتين. حاولنا في هذا الاستعراض القصير تغطية أمراض القلب والجهاز التنفسي الأكثر شيوعًا والتي تتفاقم أو تسببها عدوى فيروس العوز المناعي البشري.

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