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Review Article

Human Immunodeficiency Virus (HIV) in the Old Adult and Geriatric Women Population: Review

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Abstract

With the improvement of Human Immunodeficiency Virus (HIV) treatment with Highly Active Antiretroviral Therapy (HAART),patients living with HIV have an increased life expectancy, and now many of these patients live to see geriatric age. In 2019, the American population age 65+ was 54.1 million, of which 30 million were geriatric women (55.4%). Data for HIV patients show that ~ 50% of patients living with HIV are geriatric. Particularly amongst the female population, certain age-related issues, such as vulvovaginal atrophy and the associated disruption of the vaginal mucosa, put geriatric women at higher risk for HIV acquisition. Additionally, aging Geriatric Women are less likely to use barrier contraception methods, which may also increase their risk of acquiring HIV. This review illustrates facts and data about HIV in the geriatric population, with an emphasis on women of geriatric age.

Keywords: HIV; Aging; Frailty; Geriatric Patients

Introduction

HIV-positive patients treated with antiretroviral therapy now have increased life expectancy and develop chronic illnesses that are often seen in older HIV-negative patients. Whether HIV accelerates or accentuates aging remains a source of ongoing debate [1]. HIV is commonly underdiagnosed in the elderly because many of the systemic consequences of HIV may look like normal aging. For example, HIV makes people more susceptible to cardiovascular disease, diabetes, renal disease, and cancer due to chronic inflammatory state. HIV can also lead to dementia, which may be mistaken for any of the other more common neurodegenerative processes. Due to the above reasons, it is commonly diagnosed at later, less manageable, stages than in younger people [2]. "However, most of the literature on human immunodeficiency virus (HIV) infection in older adults defines older as ≥50 years of age," which will also be the definition of "older" used in this literature review. The reason for this threshold is based on recent emerging evidence, which suggests that people with HIV experience geriatric and age-related conditions at relatively younger ages when compared to the general population [3].

Older adult geriatric patients are at increased risk of invasion by pathogenic organisms due to alterations in the barriers posed by the mucous membranes and skin. Gomez., *et al*. reported that "advanced age is associated with a breakdown of the epithelial barriers of the skin, lung and gastrointestinal tract, which enables invasion of delicate mucosal tissues by pathogenic organisms" [4].

Historically, HIV was prevalent predominantly in younger adults (in their 20s and 30s). Due to antiretroviral therapy, there has been an increasing percentage of older patients amongst all people with HIV [3]. Additionally, new HIV infections in older adults also contribute to the increasing numbers of older adults living

with HIV. For the aforementioned reasons, HIV in older patients was largely under-recognized until more recent years. Therefore, research is currently expanding without, to our knowledge, an encompassing review of the literature. The purpose of this review is to illustrate epidemiology, development, effects, and treatment of HIV in older populations.

Epidemiology of HIV in the geriatric population

According to the CDC, over 50% of people in the United States that were diagnosed with HIV were age 50 or older in 2018 [5]. For every individual with HIV aged 55 and older, about 95% of people knew their status [6].

Globally, the sum of people living with HIV in 2020 rose to 37.7 million, and according to the Joint United Nations Programme on HIV/AIDS, the incidence of HIV was estimated at about 1.5 million in 2021 (2022, August 10). It is important to acknowledge, however, that efforts to stop the spread of HIV have still been beneficial. The number of new cases of HIV has decreased by 48.3% from 2000 to 2020 (World Health Organization. (2022, May 19) [7]. Furthermore, the number of deaths from HIV related causes was 55% lower in 2020 compared to 2000. Despite this, the number of deaths due to HIV is still high at an estimate of 680,000 in 2020 [8]. Moreover, nearly one third of all patients with HIV had unsuppressed viral loads in 2019 with about one quarter (27%) of all people with HIV not receiving any treatment in 2020.

The proportion of individuals aged 50 years and older living with HIV continues to increase, becoming the age category with the most individuals infected with HIV [9]. In the United States, the number of people with diagnosed HIV increased from 945,560 to 1,025,744 and the rate increased from 293.4 to 309.8 from 2014-2018. The average rate of HIV diagnosis increased from 452.2 to 545.6 per year during this period. While the prevalence overall increased during this time, the proportion of those above 50 years of age who were living with HIV also increased from 421,792 to 518,568 persons (45% to 51%) [10]. The overall prevalence continued to increase, and by the end of 2019 the prevalence of HIV was 1,058,669, which further expanded to 1,070,604 by the end of 2020; the rate during this time also showed a slight increase from 319.0 to 321.9. Specifically, the prevalence of those living with HIV in persons aged 50 and older increased from 547,292 (52%) to 567355 (53%) during this time [11].

Older patients with HIV are the most likely to die with the highest percentage of deaths and highest mortality rate compared to any other age group. In 2016, the average mortality rate for older patients was 11.3% and remained stable at 11.15% in 2019. When the COVID-19 pandemic hit, the mortality rate in older HIV patients increased to 12.3%. Although the mortality rate has been relatively stable, the proportion of older patients dying with HIV increased from 11325 (28.6%) in 2016 to 11821 (32.3%) in 2019, and with the COVID-19 pandemic, the proportion of older people dying with HIV increased to 30,403 (44.3%) [12].

The percentage of newly diagnosed cases of HIV in older patients are on the rise as well. According to the CDC, in 2018, about 6363 (17%) of the 37,968 new HIV diagnoses in the United States were made in older patients. [13]. By the end of 2019, of the 2,301,669 tested for HIV, there were 19,387 new diagnoses of HIV of which 3,536, or 18.2 percent, were over the age of 50 years. At the end of 2020, there were only 1,255,895 tests performed, which is about half as many as the year prior. While the total number of new HIV diagnoses decreased to 11,415, and to about 2,238 in the older population; the proportion actually increased to 19.6%. However, it is important to note that the above data may have been influenced by the COVID-19 pandemic [14]. More specifically, HIV prevention programs have been impacted by the COVID-19 pandemic-related demands on health services. Towards the end of 2021, globally, 1 in 6 (17%) of countries reported that they were unable to employ at least 25% of their HIV prevention services due to the pandemic [15]. From 2018 to 2019, commercial laboratory testing and National HIV Surveillance System reported a decrease in tests by 14.7% and HRSA UDS data from healthcare settings reported a 8.3% decrease in HIV screening tests. Additionally, in comparison to 2019, the total number of HIV tests funded by the CDC that were provided in health care settings decreased by 42.6% and non–health care settings decreased by 49.5% by 2020. The decreased distribution of tests explains why the number of overall new diagnoses decreased from 30,403 to 36,585 (-17%) from 2019 to 2020 [16].

Disease progression, treatment and treatment success continue to be challenges, especially in older populations. Based on data from 45 states and the District of Columbia in 2020, it was determined that older people tend to be diagnosed at late stages, while younger people tend to be diagnosed at earlier stages. Respectively, 26.7%

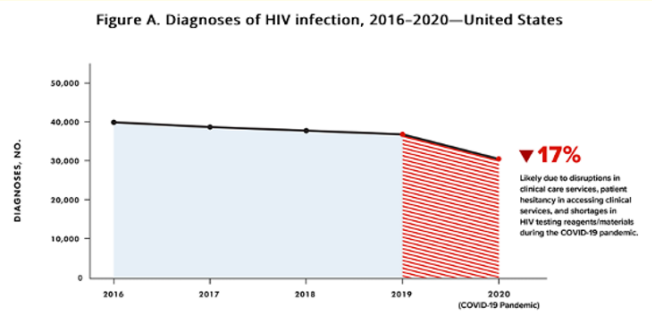

Figure 1: Diagnoses of HIV infection in 2016-2020. Source: CDC.gov.

"Diagnoses of HIV infection reported to CDC through December 2021. The annual number of HIV diagnoses in 2020 was 17% lower than 2019. The decline in 2020 was larger than the average yearly decline (2%–3%) observed during 2016–2019 [17].

to 37.8% of people aged 13 to 54 years were diagnosed at an earlier stage, while 9% to 34.8% in this age bracket were diagnosed at a later stage, defining their diagnosis as AIDS. Persons aged ≥55 years 23.6% vs 37.1% When evaluating the whole United States and Puerto Rico, Prep coverage for people at or above the age of 55 was 24.6%, while the highest coverage was in the 35-44 year olds at 30.2% Despite aging and poor Prep for those with HIV in all age categories, in recent literature from 2020 in 45 states and the District of Columbia, 66.3% of people with HIV that are 55 years or older, achieved viral suppression, which is the largest percentage of viral load suppression amongst all age categories. Following closely behind at 65.5% is the age group 45-54. The percentage achieving viral suppression in all other age categories is <63.5% [18].

Natural history of HIV infection in geriatric populations

Many HIV risk factors are the same for people of any age. These include men who have sex with other men, previous intercourse with someone with known positive HIV status, having multiple sexual partners, sharing needles and syringes, being diagnosed or treated for other sexually transmitted diseases, or having a sexual partner with any of the aforementioned risk factors, to name a few. It is important to consider modes of transmission to further educate on safety and reduce the spread in geriatric patients. Currently, the most common mode of HIV transmission for older adults is sexual exposure [19-21]. Additionally, injection drug use is an important but less common risk factor. In the United States, it accounted for 13 and 9 percent of new HIV infections in females and males respectively in 2017 [22]. It was also found that twenty-four percent of older intravenous drug users without a history of HIV use syringes after someone else [23].

For older males, male-to-male sexual contact is the most common HIV transmission risk in the United States, Europe, and Australia [24]. In the United States among men who have sex with men (MSM) aged 55 or older, the number of new HIV diagnoses increased 5 percent from 2015-2019 (from 1635 to 1718), while in other age groups, infections in MSM decreased or stayed the same [25]. In a 2017 European study, however, older adults (age ≥50 years) were more likely to acquire HIV through heterosexual contact compared with younger adults [11]. In most of the rest of the world, HIV infection in males is most commonly acquired through heterosexual transmission. Conversely, for females aged 50 years or older, the primary exposure is through heterosexual contact. Certain age-related issues may cause older women to be at higher risk for HIV acquisition, such as vulvovaginal atrophy [20]. Vulvovaginal atrophy is a medical condition common amongst peri and post-menopausal females that is a result of declining estrogen levels. The hypoestrogenic state in turn causes a disruption of the vaginal mucosa and increases HIV acquisition in these patients [26]. Additionally, geriatric women are less likely to use barrier contraception methods to prevent pregnancy, which may put them at risk for HIV acquisition if they enter a new sexual partnership [20].

Delay in HIV diagnosis may lead to late HIV presentation. Underdiagnosis of HIV infection among older patients continues to be a significant problem. In 2016, the Centers for Disease Control reported that 35 percent of people aged 50 and older were diagnosed with AIDS at the time they were diagnosed with HIV, indicating that there is a shorter interval in contracting HIV to acquiring AIDS. This in turn reduces this population's chances of survival [27,28]. Older patients are less likely to get tested for the disease. In the United States, the Centers for Disease Control and Prevention (CDC) and US Preventive Services Task Force recommends everyone between ages 13-64 get tested for HIV at least once, but those with increased risk factors should undergo annual screening, including those aged 64 and older [29,30]. Older patients are less likely to be HIV tested for several reasons,

including not having enough information about the disease, not considering themselves at risk, potential embarrassment about asking for testing, or not receiving regular healthcare services. Additional causes include provider preconceptions of the patient or population's sexual activity and habits, which can result in failure to obtain a sexual history or to offer these patients testing. Older individuals are frequently not perceived by their clinicians as being at risk for HIV infection and, consequently, are less likely to be tested for HIV compared with younger adults [31]. Based on data from the CDC National Health Interview Survey data, only an estimated 25 percent of adults 50 years of age and older have been screened for HIV [32]. The COVID-19 pandemic also negatively impacted HIV screening (Figure 1) [33].

Despite many clinicians' perceptions, sexual activity remains common among older adults. In a survey of over 3000 older adults in the United States, sexual activity within the prior 12 months was reported by 73 percent of those aged 57 to 64 years, 53 percent of those aged 65 to 74 years, and 26 percent of those aged 75 to 85 years [34]. Failure to test older populations for HIV is a public health concern, therefore it is imperative to consider strategies to ensure patients know their status, can begin treatment, and prolong their lifespan. It was found that patients are actually more willing to be tested after being offered or encouraged by a provider and if they receive regular healthcare services [35,36]. Additionally, the American College of Physicians, the HIV Medicine Association, and other expert groups have recommended routine screening for the disease in older populations [37].

HIV's impact on various organ systems in geriatric patients

HIV itself can be a devastating disease if a patient is not adequately treated. Despite this, there is an increased likelihood that patients living with HIV will suffer other medical complications aside from HIV-related disease or AIDS-defining illnesses. Comorbidities in patients living with HIV include cardiovascular disease, diabetes, chronic kidney disease, dyslipidemia, malignancies, and hepatitis B and C [38]. It was also found that older patients living with HIV are twice as likely to have a medical comorbidity than those living with HIV below 50 [39]. In addition to this, these patients also are at increased risk of mental and behavioral health challenges, including depression, addiction, and isolation, in addition to dementia, cardiovascular disease, diabetes, respiratory distress, osteoporosis, frailty, and recurrent falls according to the National Institute on Aging [40-42].

HIV's impacts on mental, behavioral, and cognitive health in geriatric patients

Increasing age is a risk factor for HIV-associated neurocognitive disorders [43,44]. The most severe form of HIV-associated neurocognitive disorders is HIV-associated dementia, which classically manifests as a subacute onset of impairments in subcortical function, such as decreased attention/concentration and psychomotor slowing. Although the overall prevalence of HIV-associated neurocognitive disorders has not changed since the early days of the HIV/AIDS epidemic, milder forms, including asymptomatic neurocognitive impairment and mild neurocognitive disease, have become more frequent manifestations.

Social isolation and loneliness

In the general population, social isolation (an objective measure of social networks) and loneliness (a subjective measure) are associated with increased mortality. In HIV patients older than 60 years, loneliness was a predictor of functional decline and death [45].

HIV's impacts on the circulatory system in geriatric patients

Increased survival among individuals with HIV has given way to increased prevalence of metabolic disorders such as glucose intolerance and diabetes mellitus, lipodystrophy, and dyslipidemia, which all increase the risk of cardiovascular disease in Geriatric patients with HIV. Kaplan., *et al*. concluded that "Among HIV-infected adults, in addition to antiretroviral drug exposures, being overweight and having a low-income level were associated with increased predicted CHD risk. This suggests a need to target HIV-infected men and women with these characteristics for vascular risk factor screening" [46].

HIV's impacts on the respiratory system in geriatric patients

Respiratory diseases represent a substantial burden in geriatric patients. In the Veterans Aging Cohort Study (VACS), consisting of 33,420 veterans with HIV and 66,840 veterans without HIV matched by age, sex, race, and ethnicity, the incidence of chronic obstructive pulmonary disease, lung cancer, pulmonary hypertension, pulmonary fibrosis, and pulmonary infections was significantly more common among veterans with HIV [47]. On the other hand, old age increases the risk of Pneumocystis pneumonia (PCP). Clusters of PCP have been reported in older individuals who did not have predisposing illnesses like HIV [48]. HIV increases

the risk of respiratory compromise and PCP in geriatric patients. Observational studies have also suggested that some cancers (ie, lung, liver, anal) are occurring at relatively younger ages of diagnosis among patients with HIV compared with the general population. In a study of 15 HIV and cancer registry databases in the United States, including 212,055 persons with AIDS (restricted to non-White Hispanic persons and Black persons), the age at cancer diagnosis did not differ between AIDS patients and individuals without HIV after adjustments for different age compositions of the populations at risk, with the exception of lung and anal cancer (occurring at age 50 and 42 years versus 54 and 45 years in the controls without HIV) and Hodgkin lymphoma (occurring at age 42 versus 40 years) [49].

HIV impacts on the gastrointestinal system of geriatric patients

The gastrointestinal mucosal lining gets weaker with age. Gomez., *et al*. reported that "advanced age is associated with a breakdown of the epithelial barriers of the gastrointestinal tract, which enables invasion of delicate mucosal tissues by pathogenic organisms" [4].

HIV's impacts on the renal system in geriatric patients

HIV infection affects the kidneys in different ways. Aging also has its effect on kidney function. GFR declines with age [50]. The combination of HIV and aging imposes a duple risk on the kidneys. The side effects of medications triple fold the risk. The risks of CKD and AKI are higher in HIV-infected adults than in the general population [51,52].

HIV's impacts on the locomotive system in geriatric patients

The locomotive system gets weaker as we age, increasing the risk of falls. Falls were reported with increased frequency in HIV geriatric patients. Twenty-four per cent of 303 HIV-infected participants reported at least one fall compared with 18% of 233 HIV-uninfected participants (P = 0.27). However their data included relatively young patients with male average age of 54.9 (48,62) and female average age of 49.7 (43,55). Observational cohorts have not clearly demonstrated increased risk of falls in older adults living with HIV; although in one study of males, balance problems were more prevalent [53].

Peripheral nerve damage also plays a significant role in increasing falls risk in HIV geriatric patients. Increased age is a risk factor for peripheral neuropathy. Evans., *et al*. concluded that aging was associated with peripheral neuropathy despite virologic and immunologic control of HIV [54].

Frailty

Frailty is often defined as a state of decline and vulnerability in older adults, characterized by weakness and decreased physiologic reserve, which results in increased risk for multiple adverse outcomes. With the accumulation of multiple health problems, it is likely that many people aging with treated HIV infection may be identified as frail [55].

Sarcopenia

Sarcopenia defined as the loss of muscle mass and function associated with aging, is of relevance in aging. muscle mass declines by approximately 1–2% per year after age 50 [56].

Geriatric patients are prone to sarcopenia due to poor oral intake and the prevalence of gastrointestinal tract problems [57]. HIV infection increases the risk of sarcopenia. Early in the HIV epidemic, prior to the initiation of ART, a myopathy associated with HIV was noted as a rare complication of HIV infection [58].

Osteoporosis

Osteoporosis is a geriatric syndrome. Disordered bone metabolism is prevalent in adults with HIV. Multiple factors include physical inactivity, decreased intake of calcium and vitamin D, cigarette smoking, alcohol use, depression, opiate use, and low testosterone levels contribute to the increased prevalence and amplify the age-related risk of decreased bone density and fragility fractures [59]. Antiretroviral toxicities, especially from tenofovir disoproxil fumarate (TDF) also contribute to increased osteoporosis prevalence [60].

HIV management in geriatric patients

Highly active antiretroviral therapy (HAART) is a treatment regimen typically composed of a combination of three or more antiretroviral drugs. HAART may also be called antiretroviral therapy (ART) or combination antiretroviral therapy (cART). A key cornerstone of HAART is the co-administration of different drugs that inhibit viral replication by several mechanisms so that the propagation of a virus with resistance to a single agent becomes inhibited by the action of the other two agents. Management

of a HAART regimen is a multifaceted process that should be administered by, or in consultation with, a provider with specific training as defined by the Infectious Diseases Society of America. This approach is central to optimizing patient care, as studies have demonstrated provider experience positively correlates with improved patient outcomes [61-64]. This combination therapy is primarily indicated to treat human immunodeficiency virus type 1 (HIV-1) infected patients. For the treatment of HIV, there are more than 25 different medications in six different classes. The standard of care for most treatment-naïve patients is a combination of two nucleoside reverse transcriptase inhibitors (typically tenofovir-emtricitabine) plus one non-nucleoside reverse transcriptase inhibitor or integrase strand transfer inhibitor. Alternative classes or different drugs within each class may be recommended when patients have concurrent conditions, medication interactions, or have developed resistance to an agent [65-67].

Immunologic recovery with ART

Most studies have demonstrated that despite successful ART and viral suppression, immune recovery is less robust with increasing age, highlighting the importance of diagnosis and treatment of HIV earlier [68].

Older HIV patients tend to be more adherent with antiretroviral medications than younger individuals with a higher rates of viral suppression [69,70]. However, there is a concern about the safety and tolerability of ART in these patients given the decrease of renal and hepatic function with age. There are few studies that have examined the tolerability and safety of ART in older patients with HIV [71]. In one retrospective study in Germany involving patients with age >60 years it showed that there was an increased rate of dolutegravir discontinuation due to neuropsychiatric effects [72]; however, a subsequent Spanish study did not find similar association between older age and dolutegravir discontinuation [73]. Drug toxicity in the older age group may be related to age-associated physiological changes that alter pharmacokinetics, such as increased adiposity (which affects distribution of fat-soluble drugs), increased gastric pH, decreased albumin levels, and changes in the cytochrome p450 enzyme system [74].

Polypharmacy is a known geriatric syndrome. ART increases the risk of polypharmacy. The American Geriatrics Society Beers Criteria and the screening tool of older people's prescriptions/ screening tool to alert to right treatment (STOPP/START) criteria includes examples of potentially inappropriate medications [75]. A thorough review of all medications and supplements is an important component of care for older patients with HIV. The European AIDS Clinical Society guidelines include an algorithm for approaching prescribing in older people with HIV and include selected examples of drug classes to avoid in older adults with HIV [76].

Conclusion

- About 50% of prevalent HIV patients are geriatric patients. HIV in geriatric patients increases the risk and progression of geriatric syndromes.
- Geriatric patients have similar risk factors for contracting HIV as younger patients.
- Geriatric patients are less likely to be tested and screened for HIV due to provider misconceptions and patient miseducation. This can ultimately result in late diagnosis and delays in treatment, a short HIV-AIDS interval period, and increased morbidity and mortality in this population.
- Certain age-related issues put geriatric women at higher risk for HIV acquisition such as vulvovaginal atrophy and the associated disruption of the vaginal mucosa which increases HIV acquisition in geriatric women. Additionally, aging geriatric women are less likely to use contraception barrier.
- Geriatric patients with HIV are more likely to have medical comorbidities than younger patients with HIV. These include cardiovascular disease, diabetes, chronic kidney disease, dyslipidemia, malignancies, and hepatitis B and C.
- HIV affects multiple organ processes and bodily systems in geriatric patients.
- HIV-positive patients treated with antiretroviral therapy now have increased life expectancy, increasing the prevalence of the disease.
- Geriatric patients with HIV develop chronic illnesses that are also often seen in older HIV-negative patients.
- Given this information, there is an increased need for education regarding HIV modes of transmission, stigma about the disease, and how HIV impacts the body of geriatric patients.

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