Factors Associated with HIV and Syphilis Co-Infection

Subjects: Public, Environmental & Occupational Health

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Human immunodeficiency virus (HIV)–syphilis co-infection poses a threat to certain populations, and patients may have considerably poorer health outcomes due to these infections. Males—particularly men who have sex with men—compose the overwhelming majority of co-infected cases. Additional risk factors include a low CD4 cell count, current or past sexually transmitted infections, and a high number of sexual partners.

co-infection HIV syphilis

1. Introduction

Human immunodeficiency virus (HIV) is a bloodborne retrovirus transmitted through direct contact between blood, broken skin, or mucosal tissue; the virus can be transmitted sexually [1]. The virus targets CD4+ T cells, resulting in gradual immunological loss and abnormalities. This occurs until significant immunodeficiency develops and patients present with oncological or infectious complications, such as Kaposi's sarcoma and toxoplasmosis, associated with a characteristic progression of disease known as acquired immunodeficiency syndrome (AIDS) [2]. In 2020, there were 37,700,000 people living with HIV (PLWH), with 680,000 people dying due to HIV-related causes [3]. While the availability of antiretroviral (ARV) drugs has been valuable for increasing the life expectancy for PLWH across the world, this population nonetheless faces health issues, even if they are on treatment. For example, PLWH tend to be at increased risk for malignancies and cardiovascular disease, and have been shown to report lower health-related quality of life when compared to those who do not have HIV [4][5][6].

Another important sexually transmitted infection (STI) that has an impact on the health of certain populations is syphilis, which is caused by the spirochetes bacteria *Treponema Pallidum*. It is estimated that, every year, there are approximately 6 million cases of syphilis across the globe amongst individuals aged 15–49 [7]. More than 300,000 annual fetal and neonatal deaths are attributed to syphilis infection [8]. Syphilis spreads through direct contact, with patients developing characteristic syphilitic sores. It follows a typical progression that can last for years, with symptoms mimicking other diseases [9]. The primary stage of syphilis is characterized by a singular chancre, which is a firm, round, painless lesion, which can progress to a secondary stage characterized by skin rashes and mucous membrane lesions; if left untreated, this may further progress to tertiary syphilis, which can have severe multi-organ consequences; a notable complication is the development of neurosyphilis, which can cause dementia, paralysis, and eventual death [9][10]. While syphilis is curable and preventable, structural barriers such as legal difficulties, policies, criminalization, violence, and discrimination limit its management [11].

While HIV and syphilis pose health concerns for those infected with one of these pathogens, the threat becomes even larger in cases of co-infection. For this reason, the co-infection of the two pathogens is increasingly being understood as a major public health concern. HIV–syphilis co-infection has numerous consequences on health, impacting treatment outcomes, transmission, and the physiological response to infection [12][13]. The downregulation of innate and acquired immune responses in HIV contribute to the increased susceptibility to syphilis co-infection [14]; reciprocally, syphilis has also been shown to increase HIV transmission through increased viral loads and decreased CD4+ T-cells in PLWH receiving ARV treatment [14]. Along with the lower CD4 cell count being an important immunological marker of HIV progression, the CD4/CD8 ratio has been shown to be an important marker associated with non-AIDS diseases, such as diabetes, pulmonary emphysema, and coronary artery disease; notably, a low CD4/CD8 ratio has been associated with higher morbidity and mortality [15][16][17]. Critically, HIV–syphilis co-infection has been shown to worsen immune recovery, decrease ARV effectiveness, and increase the risk of neurocognitive and ophthalmic issues [12][18].

In consideration of the major health risks posed by HIV and syphilis co-infection, there is a clear need to determine the factors relating to co-infection, and to understand what populations are at the highest risk. Having a clear understanding of such risks will assist in public health programs that can maximize prevention and ensure the best possible health outcomes for vulnerable populations.

2. Factors Associated with HIV and Syphilis Co-Infection

Those who are most vulnerable to HIV–syphilis co-infection are male and MSM. These are findings that are consistent and hold in contexts across the globe. Among this demographic, those with a high number of sexual partners, those who are aged 25–34, and those who inconsistently use condoms are at the most vulnerable. Despite the widespread availability of ARVs across the globe, a high proportion of individuals were shown to have high viral loads and low CD4 cell counts, which is likely to have contributed to the contraction of syphilis. Considering that the COVID-19 pandemic has negatively impacted ARV adherence across different settings [19][20][21], there is an urgent need for the enactment of policy that can remove barriers to accessing HIV care, and to lower the financial costs of treatment. This can happen at the national level for countries by increasing the funding of public health budgets towards the provision of resources for HIV care, providing patient-centered delivery schedules of ARV prescription refills, and utilizing electronic dispensing tools for medications and adherence monitoring [22][23][24].

MSM are the most vulnerable group to HIV–syphilis co-infection. Therefore, public health programs need to be developed and focused on supporting MSM who are currently living with these infections. Interventions focusing on prevention should hence also be directed towards MSM with mono-infection of HIV or syphilis, while such interventions concurrently raise awareness of the dangers of co-infection. One such program is currently being developed, where an app equips MSM with the tools to better understand their risk of contracting an STI, thus helping them become more aware of the level of their risk when having sex with new partners [25]. Having MSM sexual health influencers encourage peers to test for HIV and/or syphilis has shown potential in encouraging MSM to self-test, and may also offer utility in a public health context [26]. Policy considerations to further support MSM

can revolve around destigmatizing efforts, both for co-infection and for MSM as a whole. Considering that HIV stigma, particularly towards MSM, in the healthcare setting has been described as a deterrent to seeking care [27] [28], policy considerations should be made for the removal of such barriers for these vulnerable individuals.

Among MSM, having receptive anal sex has also been shown to be an important vulnerability for co-infection. This is a pattern that has also been shown to hold for STI transmission in general, with a proposed explanation being that an insufficient amount of lubrication of the rectum area can lead to mucosal trauma, and therefore higher vulnerability to STI transmission [29].

Amongst MSM, the highest rates of co-infection were amongst Asian populations. It is important to note that, in a number of nations, Asian and Black/African populations make up only a small proportion of the population. Possible reasons for the disproportionately high rates in Asian and Black/African groups may include a lack of culturally competent care, and racial prejudice/discrimination in healthcare settings. This further emphasizes a need for care that offers more cultural sensitivity, and to remove unjust barriers in healthcare settings.

Concomitant or prior history of STIs was shown to be a risk factor for infection, particularly hepatitis B/C, HPV, and previous syphilis infections.

The important factors that increase the vulnerability of HIV–syphilis co-infection include being male, being MSM, having a low CD4 cell count, having a high number of sexual partners, being single, and having prior or current STIs. These findings can be applied to improve the overall health outcomes for vulnerable and marginalized groups by informing programs and policies.

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