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Relationship of Sifilis Coinfection With CD4+ Count in PLHIV (People with Human Immunodeficiency Virus)

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ABSTRACT

Syphilis is a contagious infection transmitted through sexual contact (STI) and can affect various organs of the body caused by Treponema pallidum. Syphilis increases the chances of HIV transmission. Co-infection in which HIV and Treponema pallidum often occur together is caused by the same transmission pathways and risk factors. so it is quite common in HIV-infected people, Syphilis-HIV co-infection can reduce the number of CD4 + +, causing the condition of the immune system to become worse. The purpose of this study was to determine how the relationship between Syphilis co-infection and the number of CD4+ in ODHIV (People with Human Immunodeficiency). The type of research used was correlation research with a cross sectional design. 20 ODHIV with a history of / still suffering from syphilis were serologically examined for syphilis and CD4+ examination was carried out at the immunology laboratory of BBLabkesmas Surabaya. Data were analyzed by Fisher's exact test, from the results of Fisher's exact test can be seen the significance value = 0.05. The results of the study were 18 respondents out of 20 respondents showed reactive results in the RPR and Anti TP examinations, 2 respondents showed non-reactive results in the RPR examination and Reactive anti TP examination, so that 90% of respondents had syphilis co-infection. The average CD4+ count of the respondents was 713 cells/ul. where the normal value of adult healthy human CD4+ is 500 - 1500 cells/ul. The research data processed with Fisher's exact test resulted in a significant value of 0.521. which means the P value> 0.05. From this study it can be concluded that there is no relationship between syphilis co-infection and CD4+ count in ODHIV (people with Human Immunodeficiency Virus).

Keywords: HIV (Human Immunodeficiency Virus); Syphilis; Coinfection; CD4+

BACKGROUND

Syphilis is a sexually transmitted infection (STI) caused by Treponema pallidum, known as the "great imitator" for its ability to manifest in almost all organs. The initial symptoms include painless sores, which can infect the genitals, rectum, or mouth, and the disease is primarily spread through sexual contact (Fernandes and Ervianti 2020). Syphilis increases the risk of HIV (Human Immunodeficiency Virus) transmission by up to 300 times due to the presence of skin lesions or mucous membranes that allow the virus to enter the body (Kusuma et al. 2023).

HIV itself is a global concern, especially due to its rapid spread and the challenges in controlling it (Qurbaniah and Abrori 2017). In Indonesia, as of June 2022, the number of people living with HIV was estimated at 526,841, with East Java reporting 73,065 cases, making it the second highest in the country (Kementerian Kesehatan RI 2022).

Co-infection with HIV and syphilis is a significant public health issue, as both infections affect the immune system and can exacerbate each other's progression (Fernandes and Ervianti 2020; Nasrorudin

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2014). The shared transmission pathways and risk factors make co-infection common among certain populations, particularly men who have sex with men (MSM) (Setiarto and Br Karo T. T 2021). Syphilis has been shown to stimulate immune cell activation and accelerate HIV replication, further complicating the clinical outcomes for co-infected individuals (Alydrus et al. 2023).

A critical marker for monitoring the health of individuals with HIV is the CD4+ T lymphocyte count, which reflects the immune system's integrity. Studies have shown that syphilis-HIV co-infection can lead to a significant reduction in CD4+ counts, worsening the immune response and increasing vulnerability to other infections (Anggana Rafika Paramitasari et al. 2021; Pryono, Natalia, and RSA 2020; Samosir et al. 2022).

RESEARCH METHODS

This study adopts a correlational research design, appropriate for examining the relationship between syphilis co-infection and CD4+ cell counts in people living with HIV (PLHIV), without manipulating variables (Nursalam 2008; Wicaksono 2022). A cross-sectional approach was chosen to gather data at a single point in time, allowing for the assessment of correlations between these factors (Siyoto and Sodik 2015). The study population consists of PLHIV from the Surabaya community with a history of or current syphilis infection. Since the population size is unknown, the Cochran formula was used to estimate a sample size of 20 participants. Inclusion criteria include PLHIV aged 18 to 60 years, still infected or with a history of syphilis, and willing to participate. Exclusion criteria encompass those not meeting the inclusion criteria, unwilling participants, or pregnant individuals. A prospective sampling method was used, focusing on active recruitment and obtaining informed consent before blood sample collection (Agustianti et al. 2022). The research was conducted at the Immunology Laboratory of BBLabkesmas Surabaya between January and March 2024. The independent variable in this study is syphilis co-infection, determined through two serological tests: the Rapid Plasma Reagin (RPR) test, a non-treponemal test, and the Anti-Treponemal Pallidum (Anti-TP) test. A participant is classified as having syphilis co-infection if both tests yield reactive results; otherwise, the participant is considered not to have the co-infection. The RPR test, which uses the flocculation method for qualitative analysis, and the Anti-TP test, which employs chemiluminescent immunoassay (CLIA), both use EDTA plasma as the test material. The results of these tests are recorded on a nominal scale, with syphilis infection coded as 2 and no infection as 1. The dependent variable, CD4+ count, is measured using flow cytometry, specifically the BD FACSPresto device, with results expressed in cells per cubic millimeter (cells/mm^3) on a ratio scale. The study's tools and materials include the Flocculation Paper (Test Card), Rotator, Micropipette with Yellow Tip, Mindray CL-900i device, and K3EDTA plasma for the syphilis tests, as well as whole blood for the CD4+ cell count. Primary data, such as participants' names, genders, and ages, were collected via informed consent forms, while syphilis diagnostic results and CD4+ counts were obtained through laboratory testing. Data analysis was conducted using the chi-square test to assess the association between syphilis co-infection and CD4+ count, with a significance threshold set at 0.05 for rejecting the null hypothesis. In cases where the chi-square test was inapplicable, the Fisher Exact test was used, adhering to the same significance level. The confidentiality of all respondents was strictly maintained throughout the study and in any dissemination of the findings. Ethical clearance for this study was obtained from the appropriate ethics committee to ensure adherence to ethical

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standards in research involving human participants.

RESULTS AND DISCUSSION

This study examined the association between syphilis co-infection and CD4+ counts among 20 HIV-positive individuals (ODHIV) from a community in Surabaya. The respondents, all male and aged between 18 and 45 years, were in the early stages of HIV infection (Stages I and II) and were undergoing antiretroviral therapy (ART), which necessitated regular monitoring of their CD4+ counts. Notably, 70.4% of respondents were within the most productive age range, as reported in prior studies (Rohmatullailah and Fikriyah 2021). HIV Stage I is characterized by the absence of clinical symptoms or only persistent generalized lymphadenopathy, while Stage II involves more visible symptoms such as sores around the lips and itchy skin rashes (Sherman and Marylee 2018).

Table 1. Results of syphilis co-infection status and CD4+ levels

Syphilis co-infection status	Normal CD4+ Counts	Below normal range CD4+ Count
Co-infections	14	4
Non-Co-infection	2	0

Laboratory analysis of syphilis co-infection involved the RPR and Anti-TP tests. Results indicated that 18 out of 20 respondents had syphilis co-infection, while the remaining 2 showed a history of syphilis without current infection, as evidenced by non-reactive RPR but reactive Anti-TP tests. CD4+ counts were measured for all respondents, with an average count of 713 cells/µL, falling within the normal range of 500-1500 cells/µL as defined by WHO. Of the 18 respondents with syphilis co-infection, 14 had normal CD4+ counts, while 4 had counts below the normal range. The 2 respondents without syphilis co-infection both had normal CD4+ counts.

Data Analysis

The Fisher Exact test was used to analyze the data, resulting in a p-value of 0.521, indicating no significant correlation between syphilis co-infection and CD4+ counts in this population.

DISCUSSION

The findings suggest that syphilis co-infection does not have a significant impact on CD4+ counts among HIV-positive individuals. This result aligns with prior research indicating that during the early stages of syphilis infection, CD4+ counts might temporarily increase due to immune responses against Treponema pallidum. These responses include mononuclear cell proliferation and lymphocyte activation, which help in controlling the infection. Previous studies have shown that CD4+ counts often remain stable or return to normal after the acute phase of syphilis, with no lasting impact on overall immune function (Pryono et al. 2020).

Furthermore, the temporary decreases in CD4+ counts observed in some respondents during early syphilis may result from increased HIV replication and immune responses to syphilis, with Fas-mediated apoptosis also playing a role. The presence of syphilis as a co-infection can complicate the clinical management of ODHIV due to its potential to accelerate HIV transmission (Alfarisy, Djajakusumah, and Damailia 2022). Some researchers have noted a significant increase in memory T cells in response to T. pallidum antigens, which may lead to temporary fluctuations in CD4+ levels during the systemic phase of syphilis (Jarzebowski 2012). This study's findings are consistent with other research that reports transient reductions in CD4+ counts during acute infections, with subsequent recovery following appropriate

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syphilis treatment (Ajeng Puspa Dewi and Retno Pudjiati 2019).

The lack of a significant correlation between syphilis co-infection and CD4+ counts highlights the need for further research to explore other factors that may influence CD4+ levels in PLHIV. Additionally, the study's limitations, including the small sample size and the focus on a specific population, should be acknowledged, and future studies should aim to address these limitations by including a larger and more diverse sample.

CONCLUSION

This study aimed to investigate the association between syphilis co-infection and CD4+ count in PLHIV (People with Human Immunodeficiency Virus). The results indicated no significant association between syphilis co-infection and CD4+ count (P = 0.521), suggesting that syphilis co-infection does not notably impact CD4+ levels in this population. The study identified syphilis co-infection in 18 out of 20 respondents (90%), highlighting the prevalence of this co-infection in PLHIV. Additionally, the average CD4+ count among respondents was found to be 713 cells/µL, which is within the normal range for healthy adults. These findings suggest that while syphilis co-infection is common among PLHIV, it does not significantly alter CD4+ counts. However, further research is needed to explore the dynamics of syphilis and HIV co-infection, particularly before and after syphilis treatment, to better understand the potential implications on immune function.

Further research is needed to investigate the impact of syphilis infection on CD4+ counts in PLHIV, particularly before and after syphilis treatment, and to examine factors such as medication adherence and sexual behavior. Strengthening the role of the Health Office in providing support and monitoring PLHIV undergoing treatment is crucial. Additionally, ongoing efforts should be made to educate PLHIV about maintaining a healthy lifestyle, using contraceptives, practicing safe sex, and adhering to medication regimens to reduce the risk of co-infections

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