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RELATIONSHIP BETWEEN CD4 LEVELS AND MENSTRUAL DISORDERS IN WOMEN HIV PATIENTS AT DR SOETOMO HOSPITAL, SURABAYA

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Abstract

Background: HIV infection is an infection that attacks the immune system which has specific target cells that destroy CD4 T cells. Women who are infected with HIV will experience a decrease in CD4 levels which can have an impact on ovarian function where granulosa cells are the main source of ovarian reserves so this can cause menstrual cycles to be disrupted. Low CD4 levels can cause increased menstrual disorders. **The aim** of this study was to analyze the relationship between CD4 levels and the incidence of menstrual disorders in female HIV patients. **Method**:This study used a cross-sectional approach with an analytic observational method. The sample used was 50 HIV-positive women according to the inclusion and exclusion criteria, then interviewed and examined CD4 levels by flow cytometry. The r-Spearman statistical test was used to determine the significance level of the data obtained at the significance level of p≤0.05. **Result**:The results showed a significance value of p = 0.024, which means that there was a significant positive correlation between CD4 levels and the incidence of menstrual disorders in the study subjects. **The conclusion** of this study is that there are 92% of HIV-positive women experiencing menstrual disorders seen from CD4 levels

Keywords: CD4, Menstrual Disorders, HIV

INTRODUCTION

HIV is an infectious disease throughout the world with the trend of cases still showing a continuous increase and studies suggest that the number of reported cases is relatively less than the actual number of cases which are much higher[1]. According to UNAIDS (The Joint United Nations Program on HIV/AIDS), the number of people living with PLHIV (People Living with HIV/AIDS) until 2020 will reach 37.7 million people with 1.5 million new cases and 680 deaths[2]. New HIV cases at Dr. Soetomo Surabaya Hospital (2019) who underwent outpatient care were reported as many as 1,073 or 6% of the total other diseases[3].

The specific target cell for HIV infection is the CD4 lymphocyte cell which has a central function in the immune system[4]. This infection causes immune cells to become active, develop and differentiate into effector cells that secrete various cytokines[5]. More than half (56%) of women living with HIV experience abnormal menstruation with the prevalence of amenorrhea which can lead to decreased fertility[6]. Associated risk factors include decreased levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), and hyperprolactinemia[7]. HIV infection in women can also cause other health problems such as disorders of the reproductive system, cardiovascular, bone

metabolism, and psychological and sexual dissatisfaction[8].

CD4 T lymphocytes are the main receptors involved in fighting HIV infection so when an antigen is recognized, CD4 will regulate the body's specific immune response[4][9]. These specific functions can coordinate the production of antibodies and cytokines in the body[5]. HIV infection in women can affect the hypothalamus-pituitary system so that ovarian function is disrupted[10]. Several studies reported that as many as 48% of anovulatory cycles occurred in HIV women with low CD4 levels, causing an increase in abnormal menstruation[11]. Women infected with HIV will experience a decrease in CD4 levels which can impact on ovarian function targeting granulosa cells as the main source of ovarian reserves in humans so that this can cause menstrual cycles to be disrupted[12]. HIV infection has also been shown to have a direct effect on the ovaries which can lead to chronic anovulation, which is associated with irregular menstruation and pathological effects on reproductive function[13].

MATERIAL & METHODS

The study was conducted using a cross-sectional approach with an analytic observational method, namely measuring variables at the same time and the results of the measurements described the conditions at that time[14]. The sampling technique was carried out by consecutive sampling, namely patients who were under control or came to the UPIPI polyclinic at Dr Soetomo Hospital, Surabaya.

The study criteria were HIV-positive women aged 15-40 years, not currently pregnant or breastfeeding, had no history of gynecological disease, and had not used hormonal contraception in the last 3 months. Data collection was carried out by interviewing the researcher for 10-15 minutes with several prepared questions, then blood specimens were taken from the sampling room to measure CD4 levels using flocytometry. SPPS statistical test using Rank-Spearman with the aim of determining the significance level of the data obtained at the significance level of p≤0.05[15]. This research has received ethically proper information from the Ethics Committee of RSUD Dr. Soetomo Surabaya prepared by their choice and then save the equation as an image, either as a gif or jpeg file. These files should then be embedded within the text in an appropriate location.

RESULTS

Table 1: CD4 levels in female HIV patients

Indicator	Category (n=50)	
	Normal	Abnormal
CD4	23 (46%)	27 (54%)

Table 1 shows that the CD4 levels in 50 female HIV patients obtained normal values >500 cells/mm3 in 23 subjects (46%) and abnormal values <500 cells/mm3 in 27 subjects (54%). Based on the results of interviews with 50 subjects, it was found that 46 subjects (92%) had menstrual disorders in female HIV patients and 4 interviews with 50 subjects, it was found that 46 subjects (92%) had menstrual disorders in female HIV patients and 4 subjects (8%) did not experience menstrual disorders or were normal

Table 2: Menstrual Disorders in Female HIV Patients

Indicator	Types of Menstrual Disorders	Amount (n =50)
Normal (without menstrual disorders)		4 (8%)
Experiencing menstrual disorders		46 (92%)
	Heavy menstrual bleeding (HMB)	14 (28%)
	Prolonged menstrual bleeding (PMB)	9 (18%)
	Intermenstrual bleeding (IMB)	5 (10%)
	Polimenorea	9 (18%)
	Oligomenorrhea	2 (4%)
	Amenorrhea	12 (24%)

Table 3: Crosstab results of CD4 levels with normal menstruation and menstrual disorders

CD4 Level	Types of Menstrual Disorders													
	Menstrual Disorders		Amenorea		HMB		PMB		IMB		Polimenorea		Oligomenora	
	Yes	No (normal)	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Ab normal	27	0	12	15	5	22	5	22	3	24	5	22	0	27
(%)	100	0,0	44,4	55,6	18,5	81,5	18,5	81,5	11,1	88,9	18,5	81,5	0	100
Normal	19	4	0	23	9	14	4	19	2	21	4	19	2	21
(%)	82,6	17,4	0	100	39,1	60,9	17,4	82,6	8,7	91,3	17,4	82,6	8,7	91,3

Table 3 describes the results of the crosstab of CD4 levels with menstrual disorders, the result is that the proportion of HIV patients with abnormal CD4 levels and having menstrual disorders amenorrhoea is greater (44.4%) compared to HIV patients with normal CD4 levels (0%), the proportion in HIV patients with abnormal CD4 levels and having menstrual disorders HMB is smaller (18.5%) compared to HIV patients with normal CD4 levels (39.1%), the proportion of HIV patients with abnormal CD4 levels and having menstrual disorders PMB higher (18.5%) compared to HIV patients with normal CD4 levels (17.4%), the proportion of HIV patients with abnormal CD4 levels and having IMB menstrual disorders is greater (11.1%) than HIV patients with normal CD4 levels (8.74%), the proportion of HIV patients with abnormal CD4 levels and polymenorrheal menstrual disorder was greater (18.5%) compared to HIV patients with normal CD4 levels (17.4%), and the proportion of HIV patients with abnormal CD4 levels and having menstrual disorders oligomenorrhea is 0.0% compared to HIV patients with normal CD4 levels of 8.7%.

Hypothesis testing between the CD4 variable and menstrual disorders was carried out by analyzing the correlation test. In order to ascertain the type of correlation analysis employed, it is essential to assess the normality distribution through the utilization of the Shapiro-Wilk test due to the limited number of participants, which is 50 or fewer

Table 4: Results of the normality test for CD4 levels with menstrual disorders in female HIV patients

Variable	P-Value Shapiro Wilk	Interpretation
Menstrual Disorders	.000	Abnormal Distribution
CD4 values in HIV patients	.079	Normal Distribution

Table 4 shows that the Shapiro-Wilk test variable history of menstrual disorders has a significance value of p=0.000, namely p≤0.05 which means H0 is rejected so it can be concluded that the variable is not normally distributed and the CD4 level variable has a significance value of p=0.079 p>0 .05 which means H0 is accepted so it can be concluded that the variable is normally distributed. The data to be tested has a nominal and ordinal measurement scale.

Based on the distribution of data on a normal distribution of CD4 levels and menstrual disorders in female HIV patients with abnormal distribution, the Rank-Spearman non-parametric correlation test was used to analyze the correlation between CD4 levels and disorders in female HIV patients. The criteria applied involve a correlation that can be considered significant when the obtained p-value is less than the predetermined significance level of p≤0.05[16].

Table 5: Rank-Spearman results of CD4 levels with menstrual disorders in female HIV patients

Variable	Variable	r-Spearman	p-value	Decision
CD4 Level	Menstrual Disorders	0,024	0,05	H0 rejected

Table 5 shows a significance value of p = 0.024, which means p≤0.05 so it can be concluded that H0 is rejected, which means that there is a significant relationship between CD4 levels and menstrual disorders in female HIV/AIDS patients. The relationship between CD4 levels and menstrual disorders in female HIV patients is positive or unidirectional, which means that the lower the CD4 level, the more likely menstrual disorders will occur.

DISCUSSION

In this study, the evaluation of immune status, correlation of disease progression, and severity of HIV infection were assessed by measuring CD4 levels, which typically fall within the normal range of 500-1200 cells/mm^3. In accordance with WHO provisions a CD4 value of less than 500 cells/mm3 indicates low immunodeficiency [17][2][18]. In this study, 27 subjects (54%) had low or abnormal CD4 levels and 23 subjects (46%) had normal CD4 values. At the beginning of infection, the HIV virus does not immediately cause the death of the cells it infects, but first undergoes replication so that there is an opportunity to develop in the patient's body and will gradually destroy CD4 T lymphocytes up to a certain number[19]. The CD4 molecule is the main receptor involved in fighting HIV infection where when the antigen is recognized, TCD4 lymphocytes will regulate the body's specific immune response[4]. The specific function of CD4 T lymphocytes is to coordinate the production of B lymphocyte antibodies to antigens[20], produce cytokines, and induce cytotoxic lymphocytes. This crucial function makes CD4 T lymphocytes an important element of the body's immune system so CD4 dysfunction and destruction will impair the ability to respond to HIV infection[21]. The immune system can control HIV infection, but over time HIV will cause a decrease in the number of CD4 lymphocyte cells, disruption of homeostasis, and the function of other cells in the immune system[22].

Based on the crosstab results of CD4 levels with menstrual disorders, the results obtained were that the proportion of HIV patients with abnormal CD4 levels and had

menstrual disorders amenorrhoea was greater (44.4%) compared to HIV patients with normal CD4 levels (0%), the proportion in HIV patients with abnormal CD4 levels and having menstrual disorders HMB are smaller (18.5%) than HIV patients with normal CD4 levels (39.1%), the proportion of HIV patients with abnormal CD4 levels and having menstrual disorders PMB is higher (18.5%) compared to HIV patients with normal CD4 levels (17.4%), the proportion of HIV patients with abnormal CD4 levels and having IMB menstrual disorders is greater (11.1%) compared to HIV patients with low levels CD4 normal (8.74%), the proportion of HIV patients with abnormal CD4 levels and polymenorrhea is greater (18.5%) compared to HIV patients with normal CD4 levels (17.4%), the proportion of HIV patients with abnormal CD4 levels and having menstrual disorders oligomenorrhea is 0.0% compared to HIV patients with normal CD4 levels of 8.7%. Consistent with various prior studies, this finding aligns with the observation that menstrual irregularities are notably more prevalent in women who have HIV, with a 29.1% occurrence rate encompassing amenorrhea, oligomenorrhea, irregular menstruation, and secondary dysmenorrhea [23]. Additionally, it was noted that women living with HIV/AIDS and lower CD4 counts are more likely to experience this menstrual disorder, especially those with values <200 cells/mm^3. In this study, the rate of amenorrhoea was higher by 44.4% whereas oligomenorrhea did not occur in female HIV patients with low CD4. Low CD4 levels can increase the risk of opportunistic infections, accelerate the progression of other diseases, and the risk of cardiovascular disease [24]. Research by Ohihoin, et al. (2021) stated that menstrual disorders were found more frequently in patients with CD4 counts below 200 cells/mm3 than in patients with CD4 counts above 200 cells/mm3. The mean CD4 cell count was 725 cells/mm3 across the study's HIV-positive population [25]. Helen (2008) in her study comparing women with CD4 counts between 200-500 cells/mm3 with women whose CD4 counts were below 100 cells/mm^3 showed a prevalence of amenorrhoea of 9% and 19%, respectively. This shows that the lower the CD4 level, the greater the occurrence of menstrual disorders in female HIV patients[26]. Research findings indicate that women who have progressed to advanced stages of HIV infection (characterized by CD4 levels falling below 200 cells/mm3) are at a higher risk of encountering irregular menstrual cycles[27]. Moreover, women exhibiting advanced HIV symptoms such as wasting, loss of body fat, anemia, and nutritional issues are also prone to experiencing alterations in their menstrual patterns, as these conditions can disrupt the hormonal regulation of the menstrual cycle[28][29].

Observations of ovarian function among HIV-infected women found that about 23% of them had abnormal levels of Anti-Mullerian Hormone (AMH), 57% had abnormal Follicle Stimulating Hormone (FSH) and 63% had abnormal numbers of antral follicles. This suggests that being HIV positive is associated with premature ovarian insufficiency leading to decreased CD4 cell counts and possibly further disease progression [30]. Overall 55.9% had abnormal menstruation in female HIV patients and there was no independent correlation between abnormal menstruation and CD4 cell count or years since HIV diagnosis affected by Anti-Retroviral (ART)[6].

High or above normal CD4 levels are associated with fewer problems with menstruation than those with CD4 values below 500 cells/mm3 or not normal[31]. The same study also showed that higher CD4 cell counts in HIV-infected women correlated with fewer menstrual abnormalities[32]. Based on the research results and discussion, it can be shown that there is a significant correlation between low CD4 levels and menstrual disorders that occur in female HIV patients

CONCLUSION

In this study, there was a significant positive correlation between low CD4 levels and menstrual disorders that occur in female HIV patients.

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Ethical issues:

Name the ethics committee that has approved the study?

Komite Etik Penelitian Kesehatan RSUD Dr Soetomo Surabaya

Competing interests:

Reproductive Health Sciences

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