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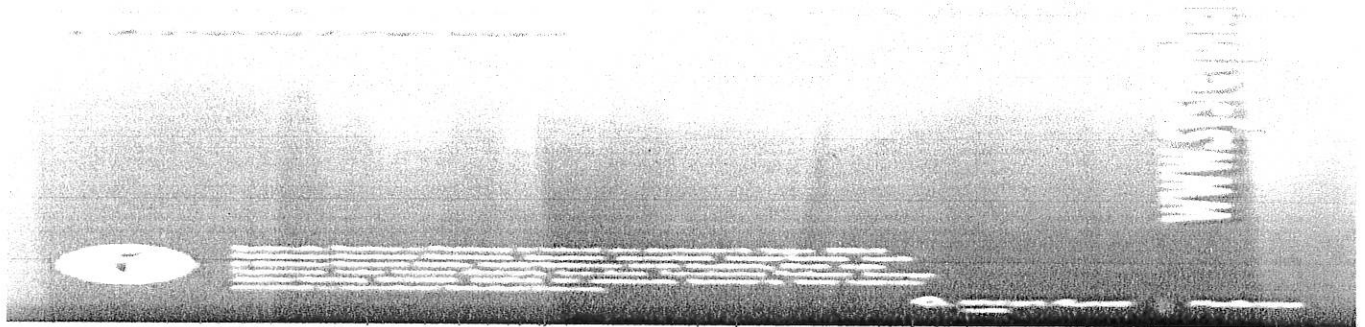


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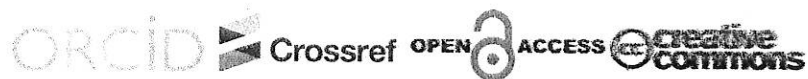
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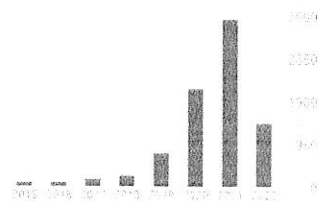
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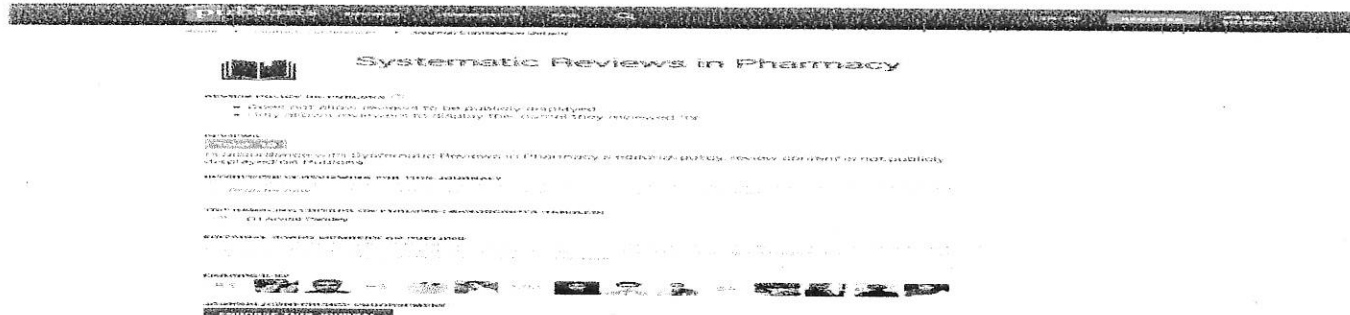
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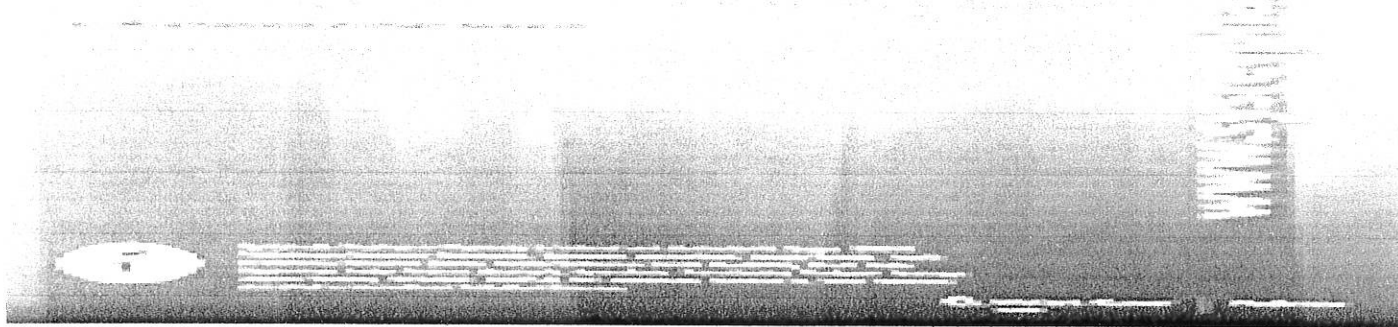
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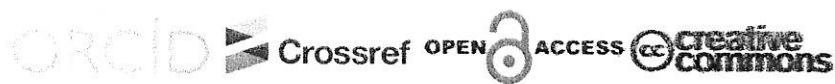


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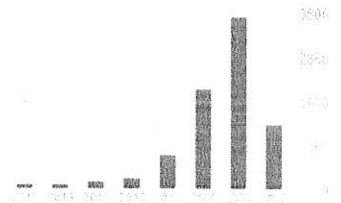
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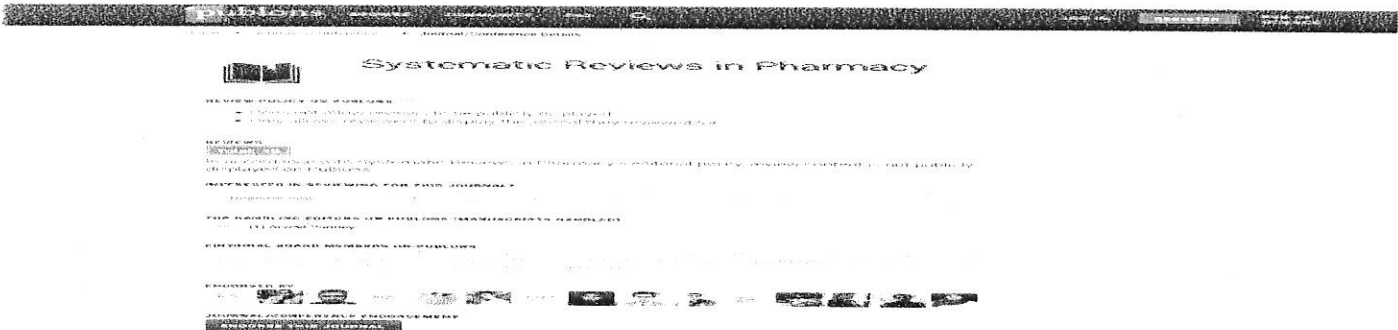
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# Correlation between Serum Cortisol Levels and Cd4 Counts in Treatment-Naïve Patients with HIV/AIDS Infection at Tertiary Hospital

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## ABSTRACT

The increased cortisol is significantly correlated with HIV mortality. The objective of this study was to analyze the correlation between serum cortisol levels and CD4 counts in treatment-naïve patients with HIV/AIDS infection. This was an analytical cross-sectional study. Total serum cortisol levels were measured by ADVIA Centaur® using chemiluminescence immunoassay and CD4 counts were measured by flow cytometry technique using BD FACS-Count CD4 reagents®. Among 58 samples of treatment-naïve patients with HIV/AIDS infection, the mean age was  $34.3 \pm 9$  years and they were predominantly male. Mean total cortisol levels was  $18.88 \pm 9.90$  µg/dL and 32.1% of samples had total cortisol levels of  $>22.4$  µg/dL. As much as 67.9% of the samples presented CD4 counts lower than 200 cells/mm<sup>3</sup>. There was a significant moderate negative

correlation between total cortisol levels and CD4 counts ( $r = -0.467$ ,  $p < 0.001$ ). Total cortisol levels were negatively correlated with CD4 counts. The higher the total cortisol levels of HIV/AIDS-positive patients, the lower the CD4 counts.

**Keywords:** cortisol, CD4, HIV/AIDS

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## INTRODUCTION

Human immunodeficiency virus (HIV) causes a serious health problem and has a big impact on Indonesian economics. Besides, HIV is rapidly growing, chronic, progressive and serious illness compared with other diseases.(1,2) HIV is a pandemic that has affected 36.7 million people worldwide in 2015. According to the Ministry of Health, in Indonesia between 1985 and 2016 there were 55,799 Indonesians who were infected with HIV and fell in AIDS conditions with high mortality rates and it became the number four cause of death in the world.(3,4) According to the Directorate General of Disease Prevention and Control, Ministry of Health, the mortality rate of HIV/AIDS patients in Indonesia as of March 2017 was reported as many as 14,754.(5) This created a complicated clinical problem so HIV prevention is very important and necessary.(6)

HIV infection is characterized by the suppression of cellular immunity that will affect many organ systems, including neuroendocrine.(7,8) CD4 cell count is also a major clue in asymptomatic patients.(9) Increased T cell activation is recognized as one of the main pathogenic characteristics of HIV infection and causes CD4 decline.(10) Factors affecting T cell activation have not been fully identified. Glucocorticoids, which are the final secretions of the HPA axis, are thought to affect T cell activation. Cortisol levels in patients with positive HIV infection are higher than cortisol levels in HIV negative patients.(11,11,12) The presence of hypercortisolism conditions will accelerate the progression of HIV disease and increase mortality.(13–16)

Several studies have shown that an increase in cortisol is associated with a faster progression of HIV infection to AIDS and a predictor of mortality. Increased cortisol is significantly correlated with HIV mortality.(16) The results of that study were supported by Leserman's research that an

increase in cortisol in HIV patients was associated with three markers of disease progression, i.e. AIDS, clinical conditions of AIDS and mortality. This study found that at each increase of 3 µg/dL in the cumulative mean of serum cortisol, there was an increased risk of AIDS by 40% and an increased risk of about 2.5 times of developing AIDS clinical symptoms or mortality.(13)

The disturbed HPA axis in HIV infection is the effect of inflammatory cytokines such as TNF-α, IL-1, and IL-6 which are secreted together in response to infection.(17,18) This cytokine activates the HPA axis through CRH stimulation which results in the release of the hormone ACTH with cortisol as a final result.(19) In patients with HIV/AIDS, the activation of the HPA axis causes an increase in cortisol levels which has different effects on Th1 and Th2, resulting in a change of Th1/Th2 balance.(20,21) Cortisol inhibits Th1 cytokines: IL-1, IL-2, TNF-α, and IFN-γ, which are the main proinflammatory cytokines.(22) and suppress apoptosis. At Th2, cortisol stimulates the production of IL-4, IL-10, IL-13 and induces apoptosis.(23) In addition to cytokine stimulation, increased cortisol in HIV infection is also caused by the release of HIV toxin products such as GP 120 and vpr. Vpr also acts as a coactivator of glucocorticoid receptors, thereby increasing viral replication.(24) Hypercortisol conditions can accelerate the development of HIV disease by stimulating viral replication, modifying programmed cell death, changing the secretion pattern of cytokines and T helper suppression.(25,26)

Some studies support the existence of a correlation between cortisol levels and CD4 counts. Several studies reported an increase in cortisol levels in HIV patients and showed a significant negative correlation with CD4 counts(11,27,28) Previous studies reported that cortisol levels at the start of a visit could predict a decrease in CD4 percentage on the



subsequent visits.(7) Other studies also report that an increase in initial serum cortisol can predict the length of stay and mortality.(14) Several other studies have shown inconsistent results.(16,29) This can be influenced by differences in the methods used in each study. Until now there have been no studies that identify the incidence of cortisol dysfunction in HIV/AIDS patients in Indonesia. The objective of this study was to analyze the correlation between serum cortisol levels and CD4 counts in treatment-naïve patients with HIV/AIDS infection.

## METHODOLOGY

This study was an observational analytic study with a cross-sectional analytic design. Fifty-six subjects were selected by consecutive sampling. Treatment naïve-patients with HIV/AIDS who were searching for treatment at HIV/AIDS Clinic at Dr. Soetomo Hospital, Surabaya, Indonesia were recruited by inclusion criteria, aged  $\geq 18$ -60 years, and willing to take part in the study by signing informed consent. Patients with a history of diabetes mellitus, chronic kidney disease, and liver cirrhosis, receiving corticosteroid therapy, had received antiretroviral therapy, had a history of alcohol use, pregnant, had fever and sepsis, were excluded from this study.

Research data were taken from the subjects by interview, physical examination, and blood sampling. Cortisol taken was morning cortisol between 7-9 am with a normal value of 4.3-22.4 ug/dL. CD4 count was determined by flow cytometry with BD FACSCount CD4 reagents. Blood specimens must be processed within 24 h after collection with a normal value of 500-1500 cells/mm<sup>3</sup>. HIV infection was proved using three methods of HIV testing, the HIV HIV SD, Intec, and Oncoprobe. Data were analyzed and presented in the form of frequency distribution tables and diagrams using SPSS version 22.0 software to determine the correlation of both variables. The interpretation of the results of the correlation test was based on the p-value, the strength of correlation and the correlation direction. A statistical test was regarded as significant if  $p < 0.05$ .

## RESULTS

The mean age of the subjects was 34.3 $\pm$ 9 years, with the age of the youngest 19 years and the oldest 57 years. Most of the subjects were male (78.6%). The highest risk factor for the incidence of HIV infection is risky anal sex. Based on the stage, clinical stages 2 and 3 were not significantly different, i.e. 39.3% and 32%, while clinical stages 1 and 4 were 10.7% and 17.9% respectively. The mean BMI of the patients was 21 kg/m<sup>2</sup> with the lowest BMI of 15.22 kg/m<sup>2</sup> and the highest was 32.74 kg/m<sup>2</sup>. As many as 50% of the subjects suffered from opportunistic infections with oral candidiasis as the most frequent, followed by chronic diarrhea (Table 1).

### Total serum cortisol levels in patients with HIV/AIDS

Mean total cortisol levels in 56 subjects were 18.88 $\pm$ 9.90  $\mu$ g/dL. Most subjects (62.50%) had normal total cortisol levels. Cortisol level as much as  $\geq 22.4$   $\mu$ g/dL was obtained in 18 patients (32.1%) and the levels of  $< 4$   $\mu$ g/dL were obtained in three patients. This study also assessed the mean total

cortisol levels at each stage of HIV (Table 2). Then, the post-hoc Bonferroni analysis was conducted to determine groups that had significant differences and a statistically significant difference in cortisol levels was obtained at stage 2 vs stage 3 and 4.

### CD4 count in HIV/AIDS patients

CD4 counts in the subjects varied between 1 cell/mm<sup>3</sup> to 710 cells/mm<sup>3</sup> with a median of 102.5 cells/mm<sup>3</sup> and an mean of 151.39 $\pm$ 165.66 cells/mm<sup>3</sup>. Thirty-eight patients (67.9%) had CD4 count of less than 200 cells/mm<sup>3</sup>, 11 patients (19.6%) with CD4 count of 200-349 cells/mm<sup>3</sup>, 4 patients (7.1%) had CD4 count of 350-499 cells/mm<sup>3</sup> and 3 patients (5.4%) had CD4 counts  $\geq 500$  cells/mm<sup>3</sup> (Figure 1).

This study also calculated mean total cortisol levels in the CD4 groups (Table 3). The highest mean cortisol levels was 21.69 in  $< 200$  CD4 group with 38 samples. Then, we performed Bonferroni post-hoc analysis and obtained significant differences in cortisol levels in groups with CD4  $< 200$  and CD4 200-350.

### Correlation between total serum cortisol levels and CD4 count

To analyze the correlation between total cortisol levels and CD4 counts, we used Spearman's rank non-parametric correlation test and obtained a Spearman's r-value of -0.467 with a p-value  $< 0.001$ . This study also analyzed the correlation between serum cortisol levels and the CD4 group and obtained a Spearman's r value of -0,368 with  $p = 0.004$ . The results of this analysis indicated that there was a significant negative correlation between total cortisol levels and CD4 counts of the subjects. The correlation between total cortisol levels produced was negative or inverse as seen in Figure 2. This means that in HIV/AIDS patients, the higher the total cortisol level, the lower the CD4 count.

## DISCUSSION AND CONCLUSION

Among 56 subjects, this study showed a significant negative correlation between total cortisol level and CD4 count in the subjects. This means the higher the total cortisol level, the lower the CD4 count in HIV/AIDS patients. The predictive marker of mortality was increasing cortisol. This result was different from the previous studies. The difference was probably influenced by differences in research methods, some samples, inclusion and exclusion criteria and normal reference values used by each study. The subjects in those studies were HIV patients who had received antiretroviral drugs which affected the patient's CD4 count.(16) The number of patients was fewer and the examination method, as well as the cortisol normal reference value, were different.(29)

The examination of the total cortisol level in this study was carried out in the morning following the circadian rhythm. In normal individuals, the highest-circulating cortisol concentration is between 06.00 and 09.00 and lowest between 23.00 and 01.00.(30) Normal values of total serum cortisol level vary according to the method used. Immunoassays for cortisol can cross-react with other steroids, causing variability in measurable results.(31) In this study, most of the subjects having normal total cortisol

levels. This study was slightly different from other studies.(29) This was due to differences in the method of measuring total cortisol levels, ie radioimmunoassay using PC-RIA.MAS.STARTEC, and different cortisol cut-off values. This study used the chemiluminescence immunoassay method with the ADVIA. Centaur instrument with a normal value of 4.3-22.4 ug/dL and a smaller number of samples.

This study also assessed the mean total cortisol levels in each of the clinical stages of the patient. HIV in late-stage made more opportunistic infections, reflecting more inflammatory sources in the body.(32) Besides, the high percentage in clinical stages 3 and 4 was due to the lack of knowledge about HIV/AIDS and awareness of HIV testing so that the patients were diagnosed too late. The widespread stigma and discrimination also caused the patients to be embarrassed and afraid to take an HIV test or seek treatment.(33) Moreover, there were significant differences between stage 2 cortisol levels with stage 3 and 4 cortisol levels. Increased cortisol in several studies indicated an increase in cortisol levels in advanced HIV.(34) Other studies reported increased cortisol in 12.8% of asymptomatic HIV patients.(35) This increase in cortisol level is in response to an increase in the degree of disease due to HPA axis cytokine modulation, release of viral toxic products, the envelope protein gp120, and structural proteins Vpr and Tat, and changes in tissue sensitivity to glucocorticoids.(12,24,36,37) In this study, the cause of high total cortisol levels was the possibility of opportunistic infections and HIV infection itself. Half of the subjects suffered from opportunistic infections with the most common being oral candidiasis followed by chronic diarrhea. Globally, the most common opportunistic infections in HIV/AIDS patients are oral candidiasis, followed by unspecified tuberculosis, herpes zoster, pulmonary TB, and bacterial pneumonia.(38)

The most important biomarkers of disease stage and progression in patients with an HIV infection are the CD4 count.(39) The mean CD4 of this study is lower than that in other studies.(40,41) Difference in mean and median of CD4 in this study was because the majority of the subjects seeking treatment at an advanced stage and had CD4 count <200 cells/ $\mu$ L. There is a possibility that the subjects were late in knowing the diagnosis or seeking treatment. When there is a suspicion of HIV/AIDS or when an HIV/AIDS diagnosis has been established, the patients usually already have clinical manifestations, and there have already been opportunistic infections and advanced conditions. This is because a lack of knowledge about HIV/AIDS and/or infection or co-infection has been experienced, but asymptomatic (such as TB, hepatitis B, hepatitis C, toxoplasma, and cytomegalovirus),(42,43) which were not excluded from this study. Education regarding early screening of HIV for the public, especially groups at risk of HIV infection, is important to do because early HIV screening can improve quality of life and reduce morbidity and mortality. This study also compared the mean total cortisol in CD4 groups. Statistically significant differences in cortisol levels were found in the CD4 group <200 and 200-350. This result was different from that of other studies

which reported no significant difference between cortisol levels and CD4 groups.(27,28) This is because of the differences in reference values and selectivity of the subjects. Subjects in those studies did not distinguish patients who were hospitalized and outpatient either naïve or those who had received treatment.

This study had several limitations. Total cortisol levels in the subjects can still be influenced by other factors, such as blood albumin levels, which were not measured in this study. Examination of free cortisol levels may provide better results, but requires greater costs and special preparation. This study could not control the confounding factors, such as opportunistic infections, and did not measure cytokines that affected the HPA axis, which would affect the mechanism of cortisol increase, and did not have normal reference value that applied universally to measure cortisol levels.

In conclusion, the total cortisol level was negatively correlated with CD4 counts in HIV/AIDS patients. The higher the total cortisol level, the lower the CD4 count.

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#### REFERENCES

1. Ardianto A, Khairunisa SQ, Kotaki T, Witaningrum AM, Qushray M, Juniasuti J, et al. The Prevalence Of Human Immunodeficiency Virus-1 (Hiv-1) Subtypes And Transmission Method Among Hiv/Aids Infection Patient In Tulungagung, East Java Indonesia. *Indones J Trop Infect Dis*. 2015;5(5):124-8.
2. Latif AI, Irwan AM. Models and benefits of palliative care for the quality of life of people with hiv: A systematic review. *HIV Nurs* [Internet]. 2019;19(4):80-5. Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-85078775535&partnerID=40&md5=d5951b0c3a15fb78c3e7d9418ca285a8>
3. Organization WH. 2008 Report on the Global AIDS Epidemic. World Health Organization; 2008.
4. Indonesia Ministry of Health. *Infodatin AIDS*. Jakarta: Ministry of Health; 2017.
5. Directorate General for Disease Prevention and Control Ministry of Health. *Report on Progress of HIV-AIDS & Sexually Transmitted Infectious Diseases (PIMS) for I Quarter 2017*. 2017.
6. Toetik Koesbardiati, Kinasih SE, Mas'adah S. Integrating The Roles Of Stakeholders In Preventing The Hiv/Aids Transmission In East Java, Indonesia.

- Indones J Trop Infect Dis. 2017;6(5):124–30.
7. Chittiprol S, Kumar AM, Shetty KT, Kumar HR, Saishchandra P, Rao RSB, et al. HIV-1 clade C infection and progressive disruption in the relationship between cortisol, DHEAS and CD4 cell numbers: a two-year follow-up study. *Clin Chim Acta* [Internet]. 2009/07/01. 2009 Nov;409(1–2):4–10. Available from: <https://pubmed.ncbi.nlm.nih.gov/19676196>
  8. Medhanie EK, Lukman M, Massi MN, Manggau MA. Effectiveness of Tenofovir (TDF) / Emtricitabine (FTC) Versus Zidovudine (AZT)/ Lamivudine (3TC) in combination with Efavirenz (EFV) in Antiretroviral-Naïve HIV-infected patients (N Eritrea. *Int J Pharm Clin Res* [Internet]. 2015;7(5):364–7. Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-84965148870&partnerID=40&md5=08e702d77d33428416bf75557e9483cc>
  9. Lubis R, Bulgiba AM. Anti-retroviral therapy of HIV infected patients. *J Heal Transl Med* [Internet]. 2014;17(1):18–22. Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-84920691942&partnerID=40&md5=2e7e5f9a7508ce0e24e84959a14756c5>
  10. Douek DC, Picker LJ, Koup RA. T cell dynamics in HIV-1 infection. *Annu Rev Immunol* [Internet]. 2001/12/19. 2003;21:265–304. Available from: <https://pubmed.ncbi.nlm.nih.gov/12524385>
  11. Lortholary O, Christeff N, Casassus P, Thobie N, Veyssier P, Trogoff B, et al. Hypothalamo-pituitary-adrenal function in human immunodeficiency virus-infected men. *J Clin Endocrinol Metab* [Internet]. 1996 Feb;81(2):791–6. Available from: <https://pubmed.ncbi.nlm.nih.gov/8636305>
  12. Norbiato G, Bevilacqua M, Vago T, Taddei A, Clerici C. Glucocorticoids and the immune function in the human immunodeficiency virus infection: a study in hypercortisolemic and cortisol-resistant patients. *J Clin Endocrinol Metab* [Internet]. 1997 Oct;82(10):3260–3. Available from: <https://pubmed.ncbi.nlm.nih.gov/9329349>
  13. Leserman J, Pettito JM, Gu H, Gaynes BN, Barroso J, Golden RN, et al. Progression to AIDS, a clinical AIDS condition and mortality: psychosocial and physiological predictors. *Psychol Med* [Internet]. 2002 Aug;32(6):1059–73. Available from: <https://pubmed.ncbi.nlm.nih.gov/12214787>
  14. Rotman-Pikoleiny P, Rouach V, Chen O, Gur HG, Limor R, Stern N. Serum cortisol levels in patients admitted to the department of medicine: Prognostic correlations and effects of age, infection, and comorbidity. *Am J Med Sci* [Internet]. 2006 Aug;332(2):81–7. Available from: <https://pubmed.ncbi.nlm.nih.gov/16909051>
  15. Peterson S, Moran P, Epel E, Sinclair E, Kemeny ME, Deeks SG, et al. Cortisol patterns are associated with T cell activation in HIV. *PLoS One* [Internet]. 2013 Jul 26;8(7):e63429–e63429. Available from: <https://pubmed.ncbi.nlm.nih.gov/23922644>
  16. Wen Y, Ding HB, Chen W, Zhou Y, Wang W, Wang Y, et al. Correlation of baseline hormonal disorders with immunological failure and mortality in male HIV patients during follow-up. *Medicine (Baltimore)* [Internet]. 2016;95(52):e5732. Available from: <http://europepmc.org/abstract/MED/28033281>
  17. Uotani T, Miftahussurur M, Yamaoka Y. Effect of bacterial and host factors on Helicobacter pylori eradication therapy. *Expert Opin Ther Targets*. 2015;19(12):1637–50.
  18. Miftahussurur M, Yamaoka Y. Helicobacter pylori virulence genes and hsp66 genetic polymorphisms as risk factors for peptic ulcer disease. *Expert Rev Gastroenterol Hepatol*. 2015;9(12):1535.
  19. Kino T, Gragerov A, Slobodskaya O, Tsopanomichelou M, Chrousos GP, Pavlakis GN. Human immunodeficiency virus type 1 (HIV-1) accessory protein Vpr induces transcription of the HIV-1 and glucocorticoid-responsive promoters by binding directly to p300/CBP coactivators. *J Virol* [Internet]. 2002 Oct;76(19):9724–34. Available from: <https://pubmed.ncbi.nlm.nih.gov/12208951>
  20. Klein SA, Dobmeyer JM, Dobmeyer TS, Pape M, Ottmann OG, Helm EB, et al. Demonstration of the Th1 to Th2 cytokine shift during the course of HIV-1 infection using cytoplasmic cytokine detection on single cell level by flow cytometry. *AIDS* [Internet]. 1997 Jul 15;11(9):1111–8. Available from: <https://pubmed.ncbi.nlm.nih.gov/9233457>
  21. DeKruyff RH, Fang Y, Umetsu DT. Corticosteroids enhance the capacity of macrophages to induce Th2 cytokine synthesis in CD4+ lymphocytes by inhibiting IL-12 production. *J Immunol* [Internet]. 1998 Mar 1;160(5):2231–7. Available from: <https://pubmed.ncbi.nlm.nih.gov/9498762>
  22. Putra A, Ridwan FB, Putriwati AI, Kustiyah AR, Wirastuti K, Sadyah NAC, et al. The role of trf-α induced mscs on suppressive inflammation by increasing tgf-β and il-10. *Open Access Maced J Med Sci* [Internet]. 2018;6(10):1779–83. Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-85058173547&doi=10.3889%2Foaamjms.2018.404&partnerID=40&md5=6908e25e563688a397dd5a7c3d77a036>
  23. Elenkov IJ. Glucocorticoids and the Th1/Th2 balance. *Ann N Y Acad Sci* [Internet]. 2004 Jun;1024:136–46. Available from: <https://pubmed.ncbi.nlm.nih.gov/15265778>
  24. Silverman MN, Pearce BD, Biron CA, Miller AH. Immune modulation of the hypothalamic-pituitary-adrenal (HPA) axis during viral infection. *Viral Immunol* [Internet]. 2005;18(1):41–76. Available from: <https://pubmed.ncbi.nlm.nih.gov/15802953>
  25. Haddad JJ, Saadé NE, Safieh-Garabedian B. Cytokines and neuro-immune-endocrine interactions: a role for the hypothalamic-pituitary-adrenal revolving axis. *J Neuroimmunol* [Internet]. 2002 Dec;133(1–2):1–19.



- Available from: <https://pubmed.ncbi.nlm.nih.gov/12446003>
26. Tsoli M, Katsas G. Immune System Effects on the Endocrine System. In: Endotext [Internet]. MDText.com, Inc.; 2018.
  27. Meena LP, Rai M, Singh SK, Chakravarty J, Singh A, Goel R, et al. Endocrine changes in male HIV patients. *J Assoc Physicians India* [Internet]. 2011 Jun;59:365–71. Available from: <https://pubmed.ncbi.nlm.nih.gov/21751580>
  28. Christeff N, Nunez EA, Gougeon ML. Changes in cortisol/DHEA ratio in HIV-infected men are related to immunological and metabolic perturbations leading to malnutrition and lipodystrophy. *Ann N Y Acad Sci* [Internet]. 2000;917:962–70. Available from: <https://pubmed.ncbi.nlm.nih.gov/11268428>
  29. Tripathy SK, Agrawala RK, Baliarsingha AK. Endocrine alterations in HIV-infected patients. *Indian J Endocrinol Metab* [Internet]. 2015;19(1):143–7. Available from: <https://pubmed.ncbi.nlm.nih.gov/25593642>
  30. Raff H, Sharma ST, Nieman LK. Physiological basis for the etiology, diagnosis, and treatment of adrenal disorders: Cushing's syndrome, adrenal insufficiency, and congenital adrenal hyperplasia. *Compr Physiol* [Internet]. 2014 Apr;4(2):739–69. Available from: <https://pubmed.ncbi.nlm.nih.gov/24715566>
  31. Levine A, Zagoory-Sharon O, Feldman R, Lewis JG, Weller A. Measuring cortisol in human psychobiological studies. *Physiol Behav* [Internet]. 2006/10/19. 2007 Jan 30;90(1):43–53. Available from: <https://pubmed.ncbi.nlm.nih.gov/17055006>
  32. Saragih RH, Mardiah AI, Purba GCF, Syahrini H. Association of serum ferritin levels with immunological status and clinical staging of HIV patients: A retrospective study. In: IOP Conference Series Earth and Environmental Science. Institute of Physics Publishing; 2018.
  33. Singh, A. Percutaneous coronary intervention vs coronary artery bypass grafting in the management of chronic stable angina: A critical appraisal (2010) *Journal of Cardiovascular Disease Research*, 1 (2), pp. 54–58. DOI: 10.1016/S0975-3583(10)12003-8
  34. Pohan HT. Opportunistic infection of HIV-infected/AIDS patients in Indonesia: problems and challenge. *Acta Med Indones* [Internet]. 2006;38(3):169–73. Available from: <https://pubmed.ncbi.nlm.nih.gov/17175600>
  35. Hoshino Y, Yamashita N, Nakamura T, Iwamoto A. Prospective examination of adrenocortical function in advanced AIDS patients. *Endocr J* [Internet]. 2002 Dec;49(6):641–7. Available from: <https://pubmed.ncbi.nlm.nih.gov/12625414>
  36. Collazos J, Mayo J, Martínez E, Ibarra S. Serum cortisol in HIV-infected patients with and without highly active antiretroviral therapy. *AIDS* [Internet]. 2003 Jan 3;17(1):123–6. Available from: <https://pubmed.ncbi.nlm.nih.gov/12478079>
  37. Bons J, Moreau L, Lefebvre H. Adrenal disorders in human immunodeficiency virus (HIV) infected patients. *Ann Endocrinol (Paris)* [Internet]. 2013/11/19. 2013 Dec;74(5–6):508–14. Available from: <https://pubmed.ncbi.nlm.nih.gov/24262982>
  38. Chrousos GP, Zapanti ED. Hypothalamic-pituitary-adrenal axis in HIV infection and disease. *Endocrinol Metab Clin North Am* [Internet]. 2014 Sep;43(3):791–806. Available from: <https://pubmed.ncbi.nlm.nih.gov/25169568>
  39. Low A, Gavrilidis G, Larke N, B-Lajoie M-R, Drouin O, Stover J, et al. Incidence of Opportunistic Infections and the Impact of Antiretroviral Therapy Among HIV-Infected Adults in Low- and Middle-Income Countries: A Systematic Review and Meta-analysis. *Clin Infect Dis* [Internet]. 2016/03/06. 2016 Jun 15;62(12):1595–603. Available from: <https://pubmed.ncbi.nlm.nih.gov/26951573>
  40. Lumbanraja SN, Siregar DS. Association between red blood cell indices and CD4 count in HIV-positive reproductive women. In: IOP Conf Series: Earth and Environmental Science [Internet]. Institute of Physics Publishing; 2018. Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-85045672326&doi=10.1088%2F1755-1315%2F125%2F1%2F012027&partnerID=40&md5=f3d9f7b9374edf2337a3c29866b0e23d>
  41. Ajayi AO, Ajayi EA, Fasakin KA. CD4+ T-lymphocytes cell counts in adults with human immunodeficiency virus infection at the medical department of a tertiary health institution in Nigeria. *Ann Afr Med* [Internet]. 2009;8(4):257–60. Available from: <https://pubmed.ncbi.nlm.nih.gov/20133549>
  42. Kilanu KR, Kumar A, Sippy N. CD4 cell counts in adults with newly diagnosed HIV infection in Barbados. *Rev Panam Salud Publica* [Internet]. 2004 Nov;16(5):302–7. Available from: <https://pubmed.ncbi.nlm.nih.gov/15729978>
  43. Ainun N, Yuniastuti E, Roosheroe AG. HIV pada Geriatri. *J Penyakit Dalam Indones*. 2016;3(2):106–14.
  44. Ray K, Gupta SM, Bala M, Muralidhar S, Kumar J. CD4/CD8 lymphocyte counts in healthy, HIV-positive individuals & AIDS patients. *Indian J Med Res* [Internet]. 2006 Sep;124(3):319–30. Available from: <https://pubmed.ncbi.nlm.nih.gov/17085836>



Table 1. General characteristics of patients with HIV/AIDS at at Infectious Disease Intermediate Care Clinic of Dr. Soetomo General Hospital, Surabaya, Indonesia

Characteristics	Results (n=56)
Age (years)	
Mean ± SD	34.3 ± (9)
Range (min. – max)	(19-57)
Age groups (years)	
<20 years, n (%)	1 (1.8)
20–29 years, n (%)	18 (32.1)
30–39 years, n (%)	22 (39.3)
40–49 years, n (%)	10 (17.9)
≥50 years, n (%)	5 (8.95)
Sex	
Male, n (%)	44 (78.6)
Female, n (%)	12 (21.4)
Risk factors	
Risky anal sex, n (%)	29 (53.6)
Risky vaginal sex, n (%)	22 (39.3)
Injectable drugs, n (%)	5 (7.1)
Clinical stage	
Stage 1, n (%)	6 (10.7)
Stage 2, n (%)	22 (39.3)
Stage 3, n (%)	18 (32.1)
Stage 4, n (%)	10 (17.90)
Body Mass Index (kg/m <sup>2</sup> )	
Mean ± SD	21.0 ± 4
Range (min – max)	(15.22–32.74)
Opportunistic infection	28 (50)
Oral candidiasis, n (%)	13 (46.4)
Chronic diarrhea, n (%)	7 (25)
Pulmonary TB, n (%)	4 (14.3)
Extrapulmonary TB, n (%)	2 (7.1)
CMV, n (%)	1 (3.6)
PCP, n (%)	1 (3.6)
Without opportunistic infection	28 (50)

Table 2. Serum cortisol levels in each stage

Stage	Mean	SD	n (sample)
Stage 1	16.85	6.71	6
Stage 2	13.51	6.58	22
Stage 3	21.16	10.46	18
Stage 4	27.83	9.62	10
Total of Patients			56

Table 3. Serum cortisol levels in the CD4 groups

CD4	Mean Cortisol	SD	n
>500	15.59	4.1	3
>350-499	14.98	5.7	4
200-350	14.98	5.7	11
<200	21.69	10.21	38
Total			56

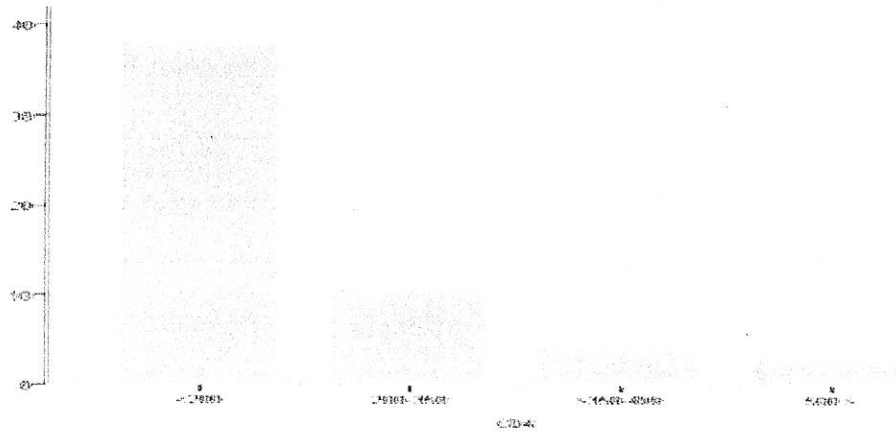


Figure 1. Distribution of CD4 counts

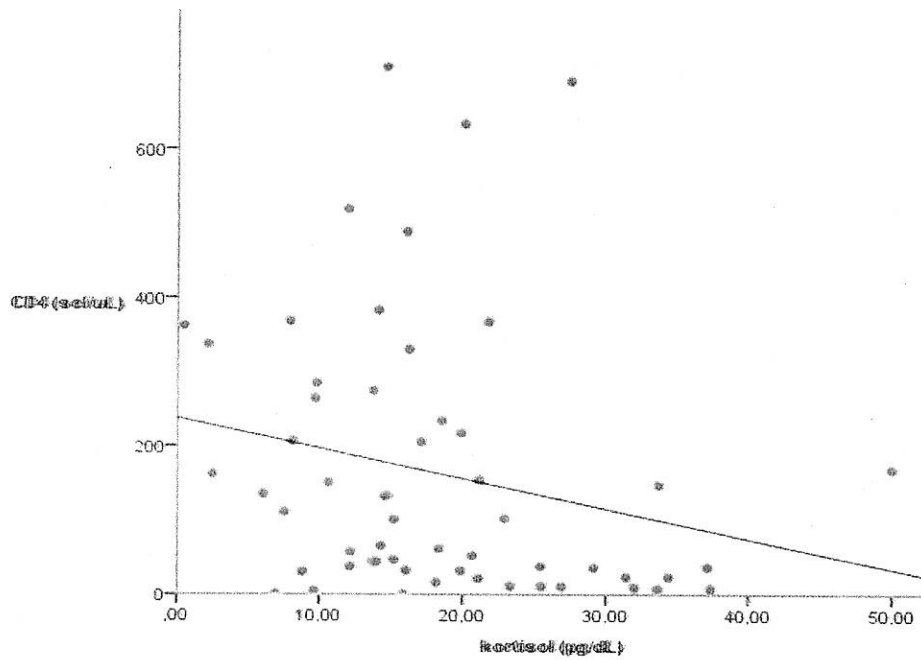


Figure 2. Correlation between total serum cortisol levels and CD4 count

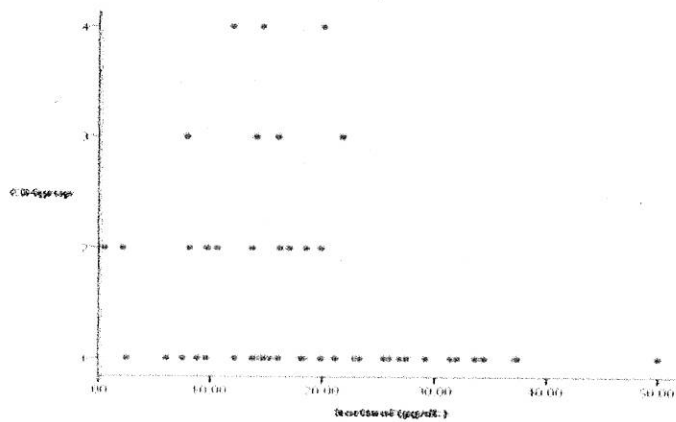


Figure 3. Correlation of total serum cortisol levels and CD4 group

Note: 1. CD4 <math>< 200</math>; 2. CD4 200-350; 3. CD4 >350-499; 4. CD4 > 500