Association between red blood cell indices and CD4 count in HIV-positive reproductive women

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Abstract. Red blood cell indices, hemoglobin, and hematocrit reflect rapidity of HIV disease progression. This study aims to determine red blood cell indices and CD4 count in HIV-positive reproductive women. This study was a cross sectional study conducted at AIDS outpatient clinic at Haji Adam Malik General Hospital, Medan Indonesia. All seropositive reproductive women within antiretroviral therapy consented for blood count and CD4 examination. Data were collected and analyzed with SPSS 19. In subjects with CD4≤350 mm\(^3\), mean hemoglobin was 10.95 ± 2.01, hematocrit was 31.83 ± 5.04%, MCV was 84.17 ± 11.41, MCH was 25.98 ± 2.65, and MCHC was 32.18 ± 2.17. Mean hemoglobin, hematocrit, and MCH value was significantly lower in subjects with CD4 ≤350 mm\(^3\) (p=0.014; p=0.001; p=0.01; respectively). Lower Hb, Ht, and MCH associated with the lower CD4 count.

1. Introduction
Hemoglobin levels reflect rapidity of disease progression rates and independently predict prognosis across demographically diverse cohorts.\textsuperscript{1} Decrease rates of hemoglobin also correlated with falling CD4 counts.\textsuperscript{2} In ART treatment, monitoring of hemoglobin is important. Patients who developed severe anemia before the initiation of ART were at an increased risk of death.\textsuperscript{3} There have been suggestions that increases in hemoglobin are predictive of both disease progression and treatment success.\textsuperscript{1}

Nowadays, women represent 47% of HIV-positive cases globally. Of these less than 50% of them are aware of their infection, and 84% are in the reproductive age group.\textsuperscript{4} HIV-infected women were at high risk of transmitting this disease into the future newborn. Therefore, this study will be conducted to determine if blood hemoglobin measurement could be as an indicator for the progression of HIV/AIDS in reproductive women living in the underserved area.

2. Methods
This study was a cross sectional study conducted at AIDS outpatient clinic at Haji Adam Malik General Hospital, Medan Indonesia. All seropositive reproductive women within antiretroviral therapy were in this study. This study has an agreement with the Local Ethical Committee of the University of Sumatera Utara.

Blood was for complete blood count and CD4 count. The complete blood count was by determining automated blood analyzer. The normal reference range for blood hemoglobin was 12.0-
18.0 g/dl, and that of blood hematocrit was 37.55%. The definition of anemia chosen for this study was, therefore, blood hemoglobin less than 12 g/dl and blood hematocrit less than 37%. The T lymphocytes of CD4 was by counting flow cytometer. As CD4 is used to stage HIV/AIDS, guide treatment decisions for HIV-infected persons, and evaluate the effectiveness of therapy, we classified CD4 to $\leq$200 mm$^3$ or $>200$ mm$^3$.

All data was collected and presented in the results section. Associations were by evaluating the Pearson's correlation test. For all statistical comparisons, SPSS 19 was with the level of significance of $p<0.05$.

3. Results
A total of 37 HIV-positive reproductive women were enrolled in this study. Mean hemoglobin was 12.28 ± 1.45 g/dL, hematocrit was 35.53 ± 3.87%, MCV was 91.54 ± 11.51 fl, MCH was 30.84 ± 5.15 fl, and MCHC was 33.34 ± 1.70 fl (Table 1).

Table 1. Distribution of red blood cell indices.

| Red blood cell | Mean ± SD  |
|----------------|------------|
| Hb             | 12.28 ± 1.45 |
| Ht             | 35.53 ± 3.87 |
| MCV            | 91.54 ± 11.51 |
| MCH            | 30.84 ± 5.15 |
| MCHC           | 33.34 ± 1.70 |

In subjects with CD4≤350 mm$^3$, mean hemoglobin was 10.95 ± 2.01, hematocrit was 31.83 ± 5.04%, MCV was 84.17 ± 11.41, MCH was 25.98 ± 2.65, and MCHC was 32.18 ± 2.17. In subjects with CD4>350 mm$^3$, mean hemoglobin was 12.53 ± 5.04, hematocrit was 37.5 ± 2.91, MCV was 92.97 ± 11.15, MCH was 31.78 ± 5.00, and MCHC was 33.56 ± 1.53. From all red blood cell indices, hemoglobin, hematocrit, and MCH showed significant association with the CD4 count. Mean hemoglobin, hematocrit, and MCH value was significantly lower in subjects with CD4≤350 mm$^3$ ($p=0.014$; $p=0.001$; $p=0.01$; respectively) (Table 2).

Table 2. Distribution of red blood cell indices in CD4 ≤350 mm$^3$ and >350 mm$^3$.

| CD4      | Hb            | Ht            | MCV           | MCH           | MCHC          |
|----------|---------------|---------------|---------------|---------------|---------------|
| $\leq$350 mm$^3$ | 10.95 ± 2.01  | 31.83 ± 5.04  | 84.17 ± 11.41 | 25.98 ± 2.65  | 32.18 ± 2.17  |
| >350 mm$^3$     | 12.53 ± 5.04  | 37.5 ± 2.91   | 92.97 ± 11.15 | 31.78 ± 5.00  | 33.56 ± 1.53  |

$a$Significant

4. Discussion
The most important biomarkers of disease stage and progression in patients with an HIV infection are the CD4 count and HIV RNA concentration. Hematological abnormalities can influence or predict the prognosis of peoples with HIV infection. Hematological abnormalities were affected in all seropositive patients regardless of age, sex and ART. This may result from the effects of HIV infection direct or indirectly to bone marrow, adverse reactions to medications, opportunistic infections, or nutritional disorder. Other study showed that soluble factors like HIV proteins and cytokines may inhibit the growth of hematopoietic cells in the bone marrow.

In this study, mean hemoglobin was 12.28 ± 1.45 g/dL, hematocrit was 35.53 ± 3.87%, MCV was 91.54 ± 11.51 fl, MCH was 30.84 ± 5.15 fl, and MCHC was 33.34 ± 1.70 fl. Red blood cell indices were also abnormal in HIV-positive patients. Red blood cell (RBC) indices, such as the mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH), RBC count, and hemoglobin
level are indicators of redox homeostasis and normal biosynthesis of RBC membrane lipids, may also reflect mitochondrial dysfunction.\(^3\)

From all red blood cell indices, lower hemoglobin, hematocrit, and MCH showed significant association with the lower CD4 count. Another study showed varies results regarding of red blood cell indices. In Obirikorang et al. study, the significant difference of Hb, Ht, MCV between CD4 count <200, CD4 count 200-499, and CD4 count >500 were shown. However no significant difference between the MCH of the control group and the various groups of the test subjects.\(^9\) In Ositadinma study, Ht, MCH, and MCHC were showed significantly lower in HIV-positive subjects compared to control (p<0.05).\(^10\) In Kallianpur study, HIV-positive patients were shown to have lower MCV, lower MCH, lower RBC count (p<0.01). MCH was significantly higher in HIV-positive subjects on ART than those not on ART this serves to confirm the effectiveness of ART in improving the quality of life of HIV patients.\(^11\) Further research is needed to gain more knowledge on this marker.

5. Conclusion
Lower Hb, Ht, and MCH were associated with the lower CD4 count.

References
[1] Paton N I, Sangeetha S, Earnest A and Bellamy R 2006 The impact of malnutrition on survival and the CD4 count response in HIV infected patients starting antiretroviral therapy HIV Med. 7(5) 323–30
[2] Anastos K, Shi Q, French A L, Levine A, Greenblatt R M, Williams C, et al. 2004 Total lymphocyte count, hemoglobin, and delayed-type hypersensitivity as predictors of death and AIDS illness in HIV-1-infected women receiving highly active antiretroviral therapy JAIDS 35(4) 383-92
[3] Ledru E, Diagbouga S, Meda N, Sanou P T, Dahourou H, Ledru S, Dembele A, Zoubga A and Durand G 1998 A proposal for basic management of HIV disease in west Africa: use of clinical staging and haemogram data Int. J. STD AIDS 9(8) 463-70
[4] Marfatia Y S, Archana S and Divyesh M 2004 A clinicoepidemiological study of HIV in females Indian J. Sex Transm. Dis. 25(2) 74-7
[5] Sabin C A, Griffioen A, Yee T T, Emery V C, Martinez E M, Phillips A N, et al. 2002 Markers of HIV-1 disease progression in individuals with haemophilia coinfected with hepatitis C virus: a longitudinal study Lancet 360 1546-51
[6] Akinbami A, Oshinaike O, Adeyemo T, Adediran A, Dosunmu O, Dada M, et al. 2010 Haematologic abnormalities in treatment-naive HIV Patients Infect. Dis.: Res. Treatment 3 45-9
[7] Tripathi A K, Misra R, Kalra P, Gupta N and Ahmad R 2005 Bone marrow abnormalities in HIV disease J. Assoc. Physic. India 53 705-11
[8] Alem M, Kena T, Baye N, Ahmed R and Tilahun S 2013 Prevalence of anaemia and associated risk factors among adult HIV patients at the anti-retroviral therapy clinic at the University of Gondar Hospital, Gondar, Northwest Ethiopia Open Access Sci. Rep. 2 6-11
[9] Obirikorang C and Yeboah F A 2009 Blood hemoglobin measurement as a predictive indicator for the progression of HIV/AIDS in resource-limited setting J. Biomed. Sci. 16(1) 102
[10] Ositadinma, et al. Haemorheology and red cell indices in HIV positive individuals on antiretroviral therapy in delta state, Nigeria
[11] Kallianpur A R, Wang Q, Jia P, Hulgan T, Zhao Z, Branholtz-Sloan J, et al. Anemia and red blood cell indices predict HIV associated neurocognitive impairment in the highly active antiretroviral therapy era Cleveland Clinic