

Relationship between Red blood cell parameters and immune status in HIV infected females

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Abstract

Background & Objectives: The Hematologic changes in Human immunodeficiency virus (HIV) infection are well established as the most important complication of the disease. These abnormalities are clinically important in many patients. Hemoglobin levels reveal rapidity of disease development rates and independently predict prognosis. Significance of Red cell distribution width lies in establishing the differential diagnosis of anemia. The intention of this study was to explore red blood cell parameters and immune status and to estimate the relationship between RBC indices and immune status.

Methods: The purpose of this study was to understand the relationship between RBC parameters and immune status in HIV patients. Subjects for the study were the reports of hundred HIV patients who are not on anti retroviral therapy, registered in the ART centre. RBC parameters and CD4 cell counts were studied.

Results: Among the 52 HIV infected female patients, the CD4 count was significant and positively correlated with MCV, MCH, MCHC, Hemoglobin (HB) and hematocrit (PCV) values. However, insignificant but negative association could be seen between RDW and RBC. Sample median CD4 was 495cells/cmm. However, minimum was 20cells/cmm and maximum was 1300cells/cmm. These two extreme points had an influence on the median. Majority, i.e. 35 females had less than the median CD4 count. The range was 1280cells/cmm indicated that the variability was too high.

Conclusion: It is well known that HIV infection is frequently associated with hematologic manifestations, thus affecting the RBC parameters. Anemia influences the natural history of HIV by increasing the disease progression rate and mortality. Majority of the females affected are in their reproductive age group. Untreated anemia may lead to multisystem disabling symptoms and fatigue, exhaustion, increased risk of HIV dementia and poor quality of life. On the other hand, endurance time in HIV-infected persons may be improved after recovery from anemia. There is significant association with reduced CD4 cell count and altered RBC parameters. Therefore it is important to evaluate the RBC parameters to improve the health and survival potential of HIV infected persons.

Key words: HIV, CD4 cells, Hemoglobin, RDW, MCV

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Introduction

The Hematologic changes in Human immunodeficiency virus (HIV) infection are well established as the most important complication of the disease. These abnormalities are clinically important in many patients. The pathogenesis of Human immunodeficiency virus-associated anemia are known to occur by three fundamental mechanisms namely, decreased Red Blood Cell production, increased Red Blood Cell destruction, and ineffective Red Blood Cell production⁽¹⁾. Hemoglobin levels reveal rapidity of disease development rates and independently predict prognosis^(2,3). The decrease in hemoglobin levels relate to the falling CD4 counts^(4,5). HIV infection affects hematological indices like MCV (Mean corpuscular

volume), MCH (Mean corpuscular haemoglobin) and MCHC (Mean corpuscular hemoglobin concentration) of patients regardless of age, sex and ART⁽⁶⁾. The Red cell distribution width (RDW) is an automated measurement of the heterogeneity of red blood cell sizes (e.g. anisocytosis) and is usually performed as component of a complete blood cell counts. Significance of Red cell distribution width lies in establishing the differential diagnosis of anemia. Red cell distribution width is now considered as a new marker of inflammatory activity⁽¹⁾.

Women represent 47% of all Acquired Immunodeficiency Syndrome (AIDS) cases globally. Presently, almost half of all new HIV infections are being reported in women. Of these less than 50% of them are aware of their infection and 84% are in the reproductive age group⁽⁷⁾. Chamarajanagar in Karnataka state is located in southern part. The population of Chamarajanagar is 10.20 Lakhs with a sex ratio of 989 females for every 1,000 males, and a female literacy rate of 54.32% with an overall literacy rate of 61.12% (Census 2011). The purpose of this study was to understand the relationship between RBC parameters and immune status in HIV patients. In view of this, the intention of this study was to explore red blood cell

parameters and immune status and to estimate the relationship between RBC indices and immune status.

Materials and Methods

This was a cross sectional study on secondary data maintained in the hematology laboratory for the period of 6 months from March 2015 to October 2015, in Chamarajanagar Institute of Medical Sciences, Chamarajanagar. Permission from the concerned authorities was obtained to collect the secondary data. The secrecy of patients was maintained by the hospital by not disclosing their names, as this data was the property of the hospital. Thus this secondary data don't require the consent of the patients. Subjects for the study were the reports of HIV patients above 21 years of completed age who were not on anti retroviral therapy, registered in the ART centre during the period mentioned above. According to 2012 ICTC (Integrated Counseling and Testing Centre) data for Chamarajanagar district, the HIV prevalence was female (1.70%) attendees. To detect the sample size "The confidence interval approach" was used. The inflated sample size for female was 27. The level of significance and absolute allowable error both were fixed at 5%. However all the available patients' reports (i.e. 52), above 21 completed years of age, in the ART centre during the period of the data collection were selected. The P value for age, i.e 0.057 suggests that the reports of patients have been randomly distributed across the age. Objectives were analyzed using the statistical techniques such as sample median, range, maximum, minimum, Mood median test, Spearman correlation, its test and SPLOM chart using standard statistical tool called R software.

Results

The CD4 count was significant and positively correlated with MCV, MCH, MCHC, Hemoglobin (HB) and hematocrit (PCV) values. However, insignificant but negative association could be seen between RDW and RBC (Table 1). Fig. 1 gives the pictorial representation of Table 2 in the form of SPLOM plot and supports Table 1. It also provides the 95% confidence parabola interval for each association. Wide parabolas for associated parameters indicate that there was a high spread among the values. Sample median CD4 was 495cells/cmm which seemed to be under observation. However, minimum was 20cells/cmm and maximum was 1300cells/cmm. These two extreme points had an influence on the median. Majority, i.e. 35 females had less than the median CD4 count. The range was 1280cells/cmm indicated that the variability was too high. The associated parameters were studied separately (Table 1). 33 of them had greater than 11.2 g% haemoglobin and 50% of them lie in inter quartile range of 1.6 g%, which seemed to be very safe. Median was less than the lower limit of the normal range of hematocrit. The individual 95% confidence plot suggested that the upper quartile was at 33%. Thus, only 25 % of females lie in the normal range, the rest of them had anemia. The 50th percentile was 86. The 95% confidence limit was larger and its upper limit was almost 100 indicating increased MCV. MCH median was well in normal range. MCHC median itself was more than the normal range; means more than 50% had high MCHC. Results were given in numbers as percentage has an issue of inflation of numbers. Therefore we comment based on numbers.

Table 1: Spearman Rho association table

	PCV	RDW	RBC	MCV	MCH	MCHC	HB
PCV	-0.537 0.000						
RBC	0.214 0.128	0.299 0.031					
MCV	0.515 0.000	-0.683 0.000	-0.655 0.000				
MCH	0.348 0.013	-0.880 0.000	-0.682 0.000	0.881 0.000			
MCHC	-0.159 0.261	-0.031 0.928	-0.148 0.294	0.669 0.628	0.457 0.001		
HB	0.781 0.000	-0.488 0.001	0.119 0.400	0.442 0.001	0.632 0.000	0.402 0.003	
CD4	0.363 0.008*	-0.262 0.060	-0.007 0.940	0.409 0.003	0.425 0.002	0.274 0.049	0.409 0.003

Cell Contents: Spearman rho
E-Value

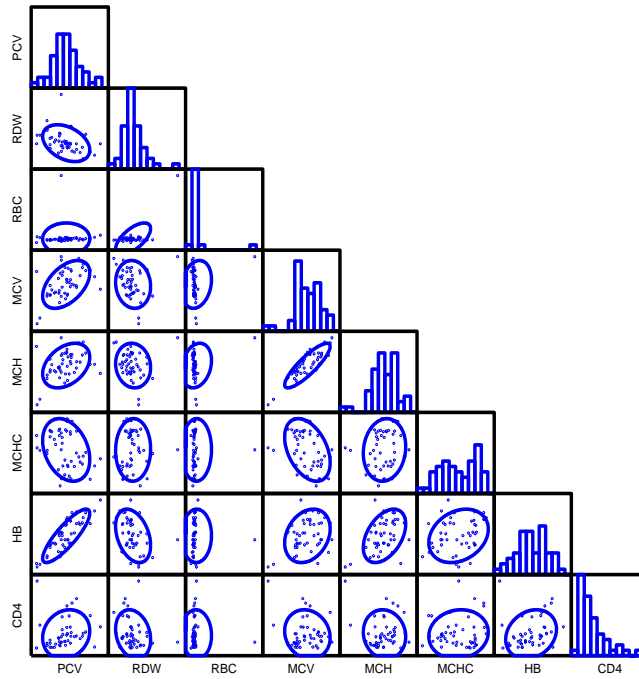


Fig. 1: SPLOM PLOT

Table 3: Frequency table for parameters

PCV
Individual 95.0% CIs
Sex N≤ N> Median Q3-Q1 -----+-----+-----+-----
F 36 16 31.25 6.23 (----*-----)
-----+-----+-----+-----
32.0 34.0 36.0
RDW
Individual 95.0% CIs
Sex N≤ N> Median Q3-Q1 -----+-----+-----+-----
F 28 24 15.80 2.27 (-----*-----)
-----+-----+-----+-----
15.60 15.90 16.20
RBC
Individual 95.0% CIs
Sex N≤ N> Median Q3-Q1 --+-----+-----+-----+-----
F 34 18 3.570 1.018 (-----*-----)
--+-----+-----+-----+-----
3.30 3.60 3.90 4.20
MCV
Individual 95.0% CIs
Sex N≤ N> Median Q3-Q1 -----+-----+-----+-----+-----
F 30 22 86.0 27.3 (-----*-----)
-----+-----+-----+-----+-----
85.0 90.0 95.0 100.0

MCH	
Individual 95.0% CIs	
Sex	N ≤ N> Median Q3-Q1
F	29 23 29.05 11.15 (-----*-----)
-----+-----+-----+-----+-----	
28.0 30.0 32.0 34.0	
MCHC	
Individual 95.0% CIs	
Sex	N ≤ N> Median Q3-Q1
F	25 27 35.35 4.75 (-----*-----)
-----+-----+-----+-----+-----	
34.0 35.0 36.0	
HB	
Individual 95.0% CIs	
Sex	N ≤ N> Median Q3-Q1
F	33 19 11.20 1.60 (-----*--)
-----+-----+-----+-----+-----	
11.20 12.00 12.80 13.60	
CD4	
Individual 95.0% CIs	
Sex	N ≤ N> Median Q3-Q1
F	17 35 495 453 (-----*-----)
-----+-----+-----+-----+-----	
240 360 480 600	

Discussion

Hematologic changes have been accepted as powerful determining predictors of morbidity and mortality in HIV-infected patients⁽⁸⁾. It has been demonstrated that severe anemia is linked with faster rate of HIV disease progression⁽⁹⁾. The present study observed a significant correlation with CD4 cell count for RBC parameters - MCV, MCH, MCHC, PCV, and haemoglobin as well as insignificant for parameters - RDW and RBC count. The reason for HIV-associated anemia is acknowledged to be multi-factorial. These includes the indirect effects of HIV infection, adverse reactions to therapy, opportunistic infections or malignancies, anorexia or mal-absorption and metabolic disorders related to HIV⁽¹⁰⁾. HIV firmly affects a bone marrow stromal cell which leads to reduced synthesis of red blood cells and other bone marrow elements⁽¹¹⁾. However the present study did not involve patients on antiretroviral therapy. Previous study has showed that soluble factors like HIV proteins and cytokines may inhibit the growth of hematopoietic cells in the bone marrow⁽¹²⁾.

Earlier studies have shown that HIV-positive patients (on ART and non-ART) had a reduced haematocrit and were significantly lower in HIV-positive female subjects not on ART than their male

counterpart⁽¹³⁾. This finding correlated with our study and confirms the prevalence of anemia in HIV patients

It is well known that CD4 cell count serves as the chief clinical marker of immune-competence in patients with HIV infection. HIV attacks and destroys cells with the CD4 antigen. MCV was significantly higher in HIV in the present study signifying the possibility of developing macrocytic anemia. Similar findings were noted in earlier studies that reported low levels of vitamin B12 and folate deficiency in HIV infected patients⁽¹³⁾.

RDW was observed to be significantly higher in prior studies on HIV-positive patients. Previous studies ascribed these high values of RDW to an underlying inflammatory state leading to impaired erythrocyte maturation and anisocytosis. This aggravates oxidative and inflammatory stress, which is a potential mechanism for the increased cardiovascular risk in this condition⁽¹³⁾. However in the present study RDW did not show significant association. Median RDW-CV was 15.8 indicating mild anisocytosis. Mean RDW-CV reported in earlier study was 15⁽¹⁴⁾. RDW is also commonly affected haematological parameter in HIV positive cases in a previous study⁽¹⁵⁾

Earlier studies showed haemoglobin ranged from 2.3g/dl to 19.3g/dl and 3.8 to 17.3g/dl respectively⁽¹⁴⁾.

In the present study, haemoglobin ranged from 4.6g/dl to 14g/dl with a median of 9.4. Earlier studies reported mean values of 3.66 million/mm³ and 3.09 million/mm³ with a standard deviation of 0.84 and 0.36 respectively⁽¹⁴⁾. Median RBC count was 3.57million/mm³ in the present study. Median MCV was 86 in the present study. Past studies reported mean value of 87.3and 81.8 correspondingly⁽¹⁴⁾. In the present study median MCHC was 35.35g/dl. Earlier study had mean value of 32.5 and standard deviation of 1.74⁽¹⁴⁾. Median hematocrit in the present study was 31.25. Earlier studies showed mean hematocrit of 31.33 and 27.36 respectively⁽¹⁴⁾. In recognized HIV infection, lower hemoglobin levels have been shown to have a relationship with decreasing CD4+ cell counts and many studies have found an association between anemia during established infection and a quicker evolution to AIDS and death⁽¹³⁾.

Anemia is also one of the strongest predictors of HIV mortality and poor responses to ART⁽⁴⁾. Decline of anemia is thus one of the means to improve medical care for HIV-infected patients. In diverse study settings, the prevalence of anemia in people with AIDS has been estimated at 63% to 95%, making it more frequent than thrombocytopenia or leucopenia in patients with AIDS⁽¹⁶⁾. Therefore measurement of RBC parameters may have an impact on the treatment and care of newly diagnosed HIV-infected patients.

Conclusion

It is well known that HIV infection is frequently associated with hematologic manifestations, thus affecting the RBC parameters. Anemia influences the natural history of HIV by increasing the disease progression rate and mortality. Majority of the females affected are in their reproductive age group. Untreated anemia may lead to multisystem disabling symptoms and fatigue, exhaustion, increased risk of HIV dementia and poor quality of life. On the other hand, endurance time in HIV-infected persons may be improved after recovery from anemia. There is significant association with reduced CD4 cell count and altered RBC parameters. Therefore it is important to evaluate the RBC parameters to improve the health and survival potential of HIV infected persons.

References

1. Puerta S, Gallego M, Palacios R, Ruiz J, Nuño E, Márquez M, Santos J. Higher red blood cell distribution width is associated with a worse virologic and clinical situation in HIV-infected patients. *Biomed Central* 2010;13:69.
2. Paton NI, Sangeetha S, Earnest A, Bellamy R. The impact of malnutrition on survival and the CD4 count response in HIV infected patients starting antiretroviral therapy. *HIV Medicine*. 2006;7(5):323–330.
3. Mocroft A, Kirk O, Barton SE, Dietrich M, Proenca R, Colebunders R, Pradier C, D'Arminio Monforte A, Ledergerber B, Lundgren JD. group ESIDA. Anaemia is an independent predictive marker for clinical prognosis in

- HIV-infected patients from across Europe. *AIDS*. 1999;13(8):943–950.
4. Anastos K, Shi Q, French AL, Levine A, Greenblatt RM, Williams C, DeHovitz J, Delapenha R, Hoover DR. 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. *Journal of Acquired Immune Deficiency Syndromes: JAIDS*. 2004;35(4):383–392.
5. Costello C, Nelson KE, Suriyanon V, Sennun S, Tovanabutra S, Heilig CM, Shiboski S, Jamieson DJ, Robison V, Rungruenthanakit K, Duerr A. HIV-1 subtype E progression among northern Thai couples: traditional and non-traditional predictors of survival. *Int J Epidemiol*. 2005;34(3):577–584.
6. Obirikorang C, Yeboah FA. Blood haemoglobin measurement as a predictive indicator for the progression of HIV/AIDS in resource-limited setting. *Journal of Biomedical Science* 2009;16:102-109.
7. Marfatia YS, Archana Sharma, Divyesh Mistry, A clinico- Epidemiological study of HIV in Females, *Indian J Sex Transm Dis*, 2004; VOL. 25 NO. 2,74.
8. Doukas MA: Human immunodeficiency virus associated anemia. *Med Clin North Am* 1992;76:699.
9. Mocroft A, Kirk O, Barton SE, Dietrich M, Proenca R, Colebunders R, Pradier C, D'Arminio Monforte A, Ledergerber B, Lundgren JD: Anaemia is an independent predictive marker for clinical prognosis in HIV-infected patients from across Europe. *EuroSIDA study group. AIDS* 1999,13:943–950.
10. Akinbami A, Oshinaike O, Adeyemo T, Adediran A, Dosunmu O, Dada M, Durojaiye I, Adebola A, Vincent O. Haematologic Abnormalities in Treatment-Naïve HIV Patients. *Infectious Diseases: Research and Treatment* 2010;3:45–49.
11. Tripathi AK, Misra R, Kalra P, Gupta N, Ahmad R. Bone Marrow Abnormalities in HIV Disease. *Journal of the Association of Physicians of India* 2005;53:705-711.
12. Alem M, Kena T, Baye N, Ahmed R, Tilahun S. 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 Scientific Reports* 2013;2:6-11.
13. Ifeanyiichukwu Martin Ositadinma, Osakue Stanley Ikponmwo, Okeke Chizoba Okechukwu Haemmorheology and red cell indices in HIV positive individuals on anti-retroviral therapy in Delta state, *Int J Cur Res Rev | Vol 7 • Issue 12 • June 2 015*
14. SS Parinitha and MH Kulkarni, Haematological changes in HIV infection with correlation to CD4 cell count. *Australasian Medical Journal* 2012,5,3,157-162.
15. Sachin Sharma, Ashok Yadav Raised red cell distribution width is a common hematological finding of HIV infection *International Journal of Medical Science and Public Health | 2014 | Vol 3 | Issue 12*.
16. Sullivan PS, Hanson DL, Chu SY, Jones JL, Ward JW (1998) Epidemiology of anemia in human immunodeficiency virus (HIV)-infected persons: results from the multistate adult and adolescent spectrum of HIV disease surveillance project. *Blood*.91:301–308.