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Correlation of CD4 cell count with hematological abnormalities in HIV patients

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Abstract
Haematological abnormalities are well recognized in HIV disease and result from various influences on hemopoeitic tissue of the patients. Changes in Peripheral blood may reflect disease elsewhere in body. Hematological abnormalities, such as anemia, neutropenia and thrombocytopenia are commonly observed in patients infected with HIV. For this reason, the total leucocyte count, hematocrit, haemoglobin concentration and platelet count have been proposed as markers of the disease, especially resource limited countries. The present study was done to know various haematological abnormalities in patient and to demonstrate relationship of haematological profile and CD4 cell count of the HIV patient.
Keywords: *HIV, Haematological abnormalities, CD4 cell count.*

Introduction

AIDS (Acquired Immune Deficiency Syndrome) is the most serious of all infectious diseases known to man. Since its discovery in 1981, the disease has attracted attention from health care professionals around the globe[1]. Hematological abnormalities are well recognized in HIV disease and result from diverse influence on hemopoeitic tissue. Hematological abnormalities are multifactorial in etiology and may be due to direct effects of HIV, manifestations of secondary infections and neoplasm or side effects of therapy. Hematological parameters are important monitoring tools for assessing treatment and prognosis in HIV. Hence it is important to determine the exact and extent of Hematological changes in HIV patients which will lead to a holistic treatment and improve quality of life of these patients. Hematological abnormalities, such as anemia, neutropenia and thrombocytopenia are commonly observed in patients infected with HIV[2]. For this reason, the total leucocyte count, hematocrit and hemoglobin concentration have been proposed as alternative markers of the disease, especially for developing countries where financial resources are limited[3,4]. The present study demonstrates relationship of hematological profile and CD4 count of the HIV positive patient.

Aims and objectives

To study Hematological alterations in peripheral blood in HIV positive cases. To study correlation of hematological findings with CD4 cell count in HIV positive cases.

Material and Methods

The present study was undertaken in the Department of Pathology from January 2016 to December 2017. During this period 60 Known HIV positive patients who presented with hematological abnormalities were included in study. All the patients were studied prospectively with informed consent of the patient.

Complete blood counts (CBC) of all the patients were done on automated hematologyanalyzer (Mythic 18). Complete blood count (CBC) of patient includes the following parameters.

1. Hemoglobin (gm%)
2. Packed cell volume (PCV)
3. Total leucocyte count (/cumm)
4. Differential leucocyte count
5. Platelet count (lac/cumm.)

CD4 count of each p atient was done with the help of flow cytometer (TheBD FACSCalibur™ system) by Becton Dickinson. For determining percentages and absolute counts of Human total and helper lymphocytes in the erythrocytes lysed whole blood, BD TritestCD3FITC/CD4PE/CD45perCP reagents were used.BD Tritest CD3 fluorescein isothiocynate (FITC)/CD4 phycoerythrin (PE) /CD45 peridinin chlorophyll protein (per CP)s is a three colored direct immunofluorescence reagent for use to identify and determine percentages and absolute count of mature human T lymphocytes (CD3+) and helper (CD3+ CD4+) T lymphocyte subset in erythrocyte lysed whole blood.

Counts that were obtained from flowcytometer included

1. T lymphocytes (CD3 CD4 +) in percentage.
2. T Lymphocyte (CD3+) Absolute absolute count.
3. THelper lymphocytes (CD3+CD4+CD45+) percentage.
4. T Helper absolute count.
5. Lymphocyte absolute count.

Anemia was defined as hemoglobin<13 g/dl (men) and <12 g/dl (women)[2]. Leucopenia was defined as total WBC count less than 4000/ul[2]. Neutropenia was defined as absolute neutrophil count < 1000/ul. Lymphopenia was considered when absolute lymphocyte count <800/ul. Thrombocytopenia was considered when the total platelet count was below 150 x 10^3/ul [2,3]. Data were analyzed using standard statistical method (SPSS version 10.0) and correlation between absolute lymphocyte count and CD4 analysed. Statistical analysis was done using statistical software like SPSS (version 10.0). Values are presented as mean +SD and median + Q as appropriate. Percentages were used to describe the proportion of the discrete variables while the correlation in the continuous variables was also analyzed. A p value of < 0.05 was considered statistically significant.

Results and Observations

The present study was undertaken in the Department of Pathology from January 2017 to December 2018. During this period 60 Known HIV positive patients presented with haematological abnormalities on peripheral blood were studied.

Table No. 1: Age wise distribution of cases

Age group	No. of patients	% of patients
<20	1	1.61
21-30	12	19.35
31-40	33	54.83
>40	14	24.19
Total	60	100

Out of 60 patients 45(72.58%) had anemia. Out of the 45 patients having anemia, 35 patients had CD4 count above 200 cells/cumm.and remaining 15 patients had CD4 count below 200cells/cumm. The median CD4 count for anemicpatients was 478 cells /cumm.

Table No 3 The Hematological Parameters Studied In Study Population

Hematological parameters	Values	No of patients	%
Hemoglobin	<12 gm%	45	72.58
	>12 gm%	15	27.42
White blood cell count	<4000/mm3	14	23.3
	>4000/mm3	46	76.7
Absolute lymphocyte count	<800/mm3	17	28.3
	>800/mm3	43	71.7
CD4 count	<200/mm3	28	46.7
	>200/mm3	32	53.3
Neutrophil count	<1000/cumm	27	45.0
	>100/cumm	33	55.0
Platelet count	<1.5	28	46.7

13 (20.96%) patients were found to have leucopenia. while 46(76.7%) of the patients were found to have WBC count above 4000/cumm. Out of 13 patients 9 patients had CD4 count above 200 cells/cumm and remaining 4 patients had CD4 count below 200 cells/cummm. Neutrophil count was below 1000/cumm of the total count in 27(45%) of the patients as 33(55%) of the patients found to have more than1000/cumm. Out of these 27 patients 18 patients had CD4 count above 200 cells/cumm. And 9 patients had CD4 count below 200 cells/cumm. Thrombocytopenia was seen in 30(50%) of the patients out of total 60 patients. Out of total 30 patients of thrombocytopenia 21 patients had CD4 count above 200 cells/cumm and remaining 9 cases had CD4 count below 200 cells/cumm. Absolute lymphocyte count (ALC) shows lymphopenia in 20 (32.25%) of the patients. Out of total 9 cases had CD4 count above 200 cells /cumm. Absolute CD4 count was below 200cells/ cumm in 28(46.7%) of the patients. while in 32(46.7%) patients has CD4 count above 200 cells /cumm.

Table No 4 Hematological Parameters in Study Population

Parameter	No. of patients	% of patients
Anemia	**45**	**72.58**
Leucopenia	**13**	**20.96**
Neutropenia	**27**	**45**
lymphopenia	**20**	**32.25**
Thrombocytopenia	**30**	**50**

Out of the total 60 patients studied 43 (71.7%) patients had packed cell volume value between 31 to 40%.while 13 patients had PCV value between 21- 30%. Pearson's correlation coefficient is the method of measuring the correlation. Pearson's correlation coefficient is known as the best method of measuring the correlation, because it is based on the method of covariance.

Table No 5 Hematology Parameter And Correlation With CD4 Count

Hematology parameter	No. of patients	CD4 count above 200cells/cumm	CD4 count below 200 cells/cumm	Median CD4 count
Anemia	**45**	**35(77.7%)**	**10(22.3%)**	**478**
Leucopenia	**13**	**9(69.23%)**	**4(30.7%)**	**321**
Neutropenia	**27**	**18(66.6%)**	**933.3%)**	**378**
Thrombocytopenia	**30**	**21(70%)**	**9(30%)**	**423**
Lymphopenia	**20**	**13(65%)**	**7(35%)**	**278**

Table No 6 Correlation between Hematologic Parameters and CD4 Counts in 60 Patients

Parameter	Pearson correlation
Age	0.126
Hb(gm/dl)	0.151
PCV %	0.081
TLC (cells/ul)	0.221
ALC (Cells/ul)	0.665**
Platelets (x103)	-0.56

**. Correlation is significant at the 0.01 level (2-tailed)

ALC :Absolute lymphocyte count

Pearson's correlation coefficient gives information about the degree of correlation as well as the direction of the correlation. If Pearson's correlation coefficient value is near ± 1, then it said to be a perfect correlation. Out of all the hematology parameters hemoglobin, packed cell volume, total leucocyte count, platelets count do not show significant correlation with CD4 count. However absolute lymphocyte count shows a statistically significant correlation withCD4 count where correlation is significant at the 0.01 level (2- tailed)

Discussion

Hematological abnormalities are among the most common complications of HIV. These involve all lineages of blood cells. HIV associated hematological abnormalities seem to be dependent on the level of virus replication, as these abnormalities are severe in late-stage AIDS patients with high viremia[2, 4]. The mechanism underlying these abnormalities is still obscure. A specific diagnosis of the cause and mechanism must be sought because specific treatment may be needed for its correction[2].

Out of 60 patients 45(72.58%) had anemia. Out of the 45 patients having anemia 35 patients had CD4 count above 200 cells/cumm.and remaining 15 patients had CD4 count below 200cells/cumm. The median CD4 count for anemicpatients was478 cells /cumm.

13 (20.96%) patients were found to have leucopenia. while 46(76.7%) of the patients were found to have WBC count above 4000/cumm. Out of 13 patients 9 patients had CD4 count above 200 cells/cumm and remaining 4 patients had CD4 count below 200

cells/cummm. Neutrophil count was below 1000/cumm of the total count in 27(45%) of the patients as 33(55%) of the patients found to have more than 1000/cumm neutrophil count. Out of these 27 patients 18 patients had CD4 count above 200 cells/cumm. And 9 patients had CD4 count below 200 cells/cumm. Thrombocytopenia was seen in 30(50%) of the patients out of total 60 patients. Out of total 30 patients of thrombocytopenia 21 patients had CD4 count above 200 cells/cumm and remaining 9 cases had CD4 count below 200 cells/cumm.

Absolute lymphocyte count (ALC) shows lymphopenia in 20 (32.25%) of the patients. Out of total 9 cases had CD4 count above200 cells /cumm. Absolute CD4 count was below 200cells/ cumm in 28(46.7%) of the patients. while in 32(46.7%) patients has CD4 count above 200 cells /cumm. Anemia is the most common hematological abnormality in HIV seropositive patients and its incidence is strongly associated with the progression of the disease. In our study we found anemia in 45 (72.58%) out of 60 patients.

Neutropenia is common in the advanced stages of AIDS and often caused or exacerbated by concomitant myelosuppressive drugs[4]. Adverse drug reactions and their complications can cause neutropenia in patients with HIV/AIDS. Throm-bocytopenia is correlated with low CD4 cell count and older age there is paucity of data from India on the hematological manifestations of HIV[4, 10].

Leucopenia is common in patients with HIV infection and seems to correlate with the severity of the disease. Of interest is the contribution of lymphopenia, neutropenia, and granulocytopenia to the reduction of total number of white cells. Care must be taken when interpreting the ratio of T helper to T suppressor cells. Only when there is lymphopenia does a decreased ratio indicate depletion of T helper cells. In patients with a normal lymphocyte count a decreased ratio might result either from T helper cell depletion or from T suppressor cell increase[10,11]. Mir[5] found a 79% incidence of lymphopenia in 40 patients with AIDS and in a series of 925 HIV antibody positive patients studied during 1987, 305 (33%) were lymphopenic; most of these patients had AIDS or ARC. In our study we found lymphopenia in 20 (33.3%) out of 60 patients.

Granulocytopenia is a less well recognised feature of HIV disease but was seen in 185 (20%) of 925 HIV antibody positive patients in a study by Costello c. n Treacy's[6] series two thirds of the patients with AIDS or ARC having bone marrow examinations were granulocytopenic' and this figure was similar in a larger series of 60 patients at St Stephen's Hospital undergoing bone marrow examinations (Proceedings of meeting on prospective indications for intravenous immunoglobulin, 1988). A left shift in the granulocytic series is a common finding' and may reflect the clinical condition of the patient. Murphy et al[2] studied 105 HIV antibody positive patients and found neutropenia in 20% of patients with AIDS, 25% of patients with persistent generalised lymphadenopathy (PGL), but none of 26 asymptomatic HIV antibody positive subjects. Thus in at least some patients with neutropenia an autoimmune mechanism might be implicated. In our study we found 27 (45%) of the patients had neutropenia.

Of the 925 HIV antibody positive patients studied by Costello[6] Anaemia is commonly seen in patients with AIDS. Thrombocytopenia is a well-recognised occurrence in patients infected with the HIV virus. It may be immune in aetiology, related to drugs, or part of the pancytopenia often seen in ill patients with opportunistic infections. They also found a 13% incidence of thrombocytopenia (121 of 925patients studied over 12 months) in patients who were at risk for HIV disease. In our study we found thrombocytopenia in 31 (50%) out of 60 patients. Out of all the haematology parameters hemoglobin, packed cell volume, total leucocyte count, platelet count do not show significant correlation with CD4 count. However, Absolute lymphocyte count shows a statistically significant correlation withCD4 count where correlation is significant at the 0.01 level (2-tailed).

Among the Indian reports study at PGI Chandigarh by Byomakesh Dikshit et al[4] (2009) studied two hundred HIV infected individual were screened for hematological abnormalities from March 2007–March 2008. The most common hematological abnormality was anemia, seen in 65.5% (131/200) patients. Iron deficiency anemia was seen in 49.2% (/200) cases while anemia of chronic disease occurred in 50.7% (/200) cases. There was a strong negative correlation between anemia and CD4 counts in this study. Thrombocytopenia was seen in 7% (14/200) cases and had no significant correlation with CD4 counts. Our results on prevalence of anemia showed comparable results with other studies from India[10-16].

A study by Mir et al[5] on a cohort of 60 HIV infected individuals reported anemia, thrombocytopenia, leucopenia and various permutations of these in majority of individuals[12]. The highest rate of anemia occurs in patients with advanced HIV disease. Severe anemia (defined as hemoglobin less than 7.5 gm/dl) was observed in 18.5% (n = 37) patients as compared to 7% in a study by Kasthuri et al[7].The cumulative incidence of anemia was highest among patients who had CD4 lymphocyte count < 200 cells/µL and was lowest with CD4 lymphocyte count > 500 cells/µl, showing an inverse correlation between anemia andCD4 cell count ($p < 0.001$).The hemoglobin, PCV, MCV, MCH, and MCHC showed statistically significant correlation with CD4 counts ($p < 0.001$) in both males and females. Thrombocytopenia is known to be a frequent complication of HIV infection. The mean platelet count in their cohort was 239.8 ± 101.3 × 103/µl (range 13.6–685 ×103/µl). It had no significant correlation with CD4 counts confirming to the data with the previous study.

Conclusion

The study concluded the fact that there is a positive correlation between absolute lymphocyte count and CD4 count in this re-emphasizes the usefulness of these two parameters in the clinical staging of HIV/AIDS. A reduction in absolute lymphocyte count and depletion of CD4 cells are typical of HIV/.AIDS. Unexplained anemia and leucopenia are suspicious laboratory features. The positive correlation between absolute lymphocyte count and CD4 count in this re-emphasizes the usefulness of these two parameters in the clinical staging of HIV/AIDS. A reduction in absolute lymphocyte count and depletion of CD4 cells are typical of HIV/.AIDS. Unexplained anaemia and leukopenia are suspicious laboratory features. The positive correlation between absolute lymphocyte count and CD4 count in this re-emphasizes the usefulness of these two parameters in the clinical staging of HIV/AIDS. A reduction in absolute lymphocyte count and depletion of CD4 cells are typical of HIV/.AIDS.

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