

# Hematological Manifestations in HIV Infected Patients and Correlation with CD4 Counts and Anti Retroviral Therapy

Swati Kathuria<sup>1</sup>, Permeet Kaur Bagga<sup>2</sup>, Sita Malhotra<sup>3</sup>

## ABSTRACT

**Introduction:** HIV infection is associated with a wide range of hematological abnormalities. Anemia, leucopenia and thrombocytopenia are the commonest hematological abnormalities associated with HIV. The use of antiretroviral drugs could positively or negatively affect these disorders. Thus a specific diagnosis and a determination of hematological parameters are required for initiating and monitoring early treatment to avert disease progression.

**Material and Methods:** The study was conducted on 100 HIV positive patients which were divided in two groups- 50 on ART and 50 not on treatment. Hematological parameters and CD4 counts were studied in both the groups.

**Results:** Anemia was the most common hematological abnormality detected in our study. The prevalence of anemia, leucopenia and thrombocytopenia was 46%, 25% and 24% respectively. The incidence of these abnormalities increased in patients having lower CD4 counts. Anemia was more common in untreated group whereas patients on ART had a higher incidence of leucopenia.

**Conclusion:** Patients should be investigated for hematological manifestations and appropriate steps should be taken to identify and treat these reversible factors.

**Keywords:** HIV, AIDS, Hematological, Anemia, Leucopenia, Thrombocytopenia, CD4, ART

## INTRODUCTION

HIV infection is accompanied by marked hematological changes that complicate health and treatment of patients. Hematological manifestations are diverse and may cause symptoms that are life threatening and impair the quality of life of these patients. These hematological abnormalities may also hinder therapy towards primary infection, opportunistic infections or associated neoplasm. 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. 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. Due to the lack of laboratory technologies in resource-limited countries, WHO guidelines suggest the use of simple tests such as hemoglobin (Hb) <12 g/dl and total lymphocyte counts (TLC) <1,200/cumm as indicators for initiation of antiretroviral therapy

(ART).<sup>1</sup> The use of antiretroviral drugs could positively or negatively affect these parameters, depending on the choice of combination used. The comparative studies between ART naive and on ART individuals is scarce in northern part of country. Thus the objective of this study was to study the hematologic profile of HIV-positive patients and its association with the clinicoimmunologic stage of the disease. This study also compared the hematological parameters between pre-ART and ART patients.

## MATERIAL AND METHODS

This study included 100 HIV positive patients attending ART centre. From each patient, 2 samples of blood, each of 2 millilitres were withdrawn carefully in a vacutainer using universal precautions, for CD4 count and for hematological parameters. The study population was divided in 2 groups: non treated and treated groups (group A and group B respectively). The study participants included all newly diagnosed patients, previously diagnosed asymptomatic patients not on any treatment, previously diagnosed patients who are on Anti Retroviral Therapy and patients giving consent for the study. Patients not giving consent for the study were excluded from the study. Complete confidentiality was observed throughout the procedure. All procedures done and methods used in this study were in accordance with the ethical standards of institutional research committee.

The investigations included CD4+ lymphocytes, complete hemogram with peripheral blood picture and bone marrow examination, only in cases where it was required. CD4+ T lymphocytes count were determined using the automated Becton Dickinson FACS count system using reagent 0.1% sodium azide. Hematological parameters were determined by 5 part automated blood analyser by Horiba (ABX Pentra 80) and peripheral blood picture. Cut-off values were defined to calculate the prevalence of different hematologic values. Anemia (Hb < 10 gm %), thrombocytopenia (platelets < 1.5 lakh/mm<sup>3</sup>), leucopenia (white blood cells (WBC) <4,000/mm<sup>3</sup>).

## STATISTICAL ANALYSIS

Descriptive statistics was expressed as mean  $\pm$  SD (Range). Comparisons between data were done by Student's t test and

<sup>1</sup>Junior Resident, <sup>2</sup>Associate Professor, Department of Pathology, <sup>3</sup>Associate Professor, Department of Microbiology, Government Medical College, Amritsar, India

**Corresponding author:** Dr. Permeet Kaur Bagga, MD Pathology, Associate Professor, Department of Pathology, Government Medical College, Amritsar, India

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chi-square test. A p value < 0.05 was taken as statistically significant

**RESULTS**

In the present study of 100 patients, 60% were males and 40% were females. Male patients were more in comparison to female patients. The age of the patients varied from 18 yrs to 64 yrs. The maximum numbers of patients (59%) were between 21-40 yrs. The mean age of the patients was 37.3 ±12.4 years.

**Hematological parameters**

Out of total 100 HIV positive patients, anemia, leucopenia and thrombocytopenia were the most common hematological abnormalities reported in HIV patients. Anemia was the most common presentation seen in 46 % patients followed by leucopenia in 25% and thrombocytopenia in 24% of patients. Table 1 summarises the mean values of various parameters in HIV infected patients.

CD4 count is considered to be the best marker for assessing immune function in HIV

patients. The CD4 counts were divided into 2 groups; <500 cells/μL and >500 cells/μL.

Anemia, leucopenia and thrombocytopenia were more commonly found in patients having lower CD4 counts. In patients with CD4 count <200 cells/ μL, the incidence of anemia, leucopenia and thrombocytopenia was 22/46( 47.8%), 14/25(56%) and 13/24( 54.1%) respectively whereas the incidence of anemia, leucopenia and thrombocytopenia in patients with CD4 count >500 cells/ μL was only 5/46( 10.8%), 1/25 (4%) and 2/24 (8.3%) respectively. Table 2 summarises the correlation of different hematological parameters with CD4 counts.

The hematological parameters were compared between both the groups i.e. patients not on any treatment (pre-ART) and patients taking treatment (ART). The incidence and comparison of different hematological parameters between both the groups is shown in Tables 3 and 4

Bone marrow aspiration was carried out in 18 patients with indications of anemia, leucopenia, thrombocytopenia and

		N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
Age (years)	Group A	50	36.88	12.244	1.731	20	60
	Group B	50	37.72	12.722	1.799	18	64
	Total	100	37.3	12.429	1.243	18	64
CD4 (cells/micro Litre)	Group A	50	433.5	306.029	43.279	26	1205
	Group B	50	463.72	341.596	48.309	34	1948
	Total	100	448.61	323.016	32.302	26	1948
Hb(gm%)	Group A	50	9.7	2.393699	0.33852	4.5	13.7
	Group B	50	10.426	2.696771	0.381381	4.5	14.8
	Total	100	10.063	2.562931	0.256293	4.5	14.8
RBC (millions/ Cumm)	Group A	50	3.5034	1.01187	0.1431	1.2	5.4
	Group B	50	3.6792	0.807543	0.114204	1.1	4.96
	Total	100	3.5913	0.915064	0.091506	1.1	5.4
PCV (%)	Group A	50	39.63	7.223128	1.021505	16	54
	Group B	50	40.12	7.057692	0.998108	28	58
	Total	100	39.875	7.108998	0.7109	16	58
MCV (fl)	Group A	50	86.88	11.94826	1.689739	68	128
	Group B	50	96.968	15.36715	2.173243	66.4	128
	Total	100	91.924	14.60275	1.460275	66.4	128
MCH (pg)	Group A	50	28.86	4.73226	0.669243	20.5	42.4
	Group B	50	39.7302	43.88409	6.206148	13.7	341
	Total	100	34.2951	31.5294	3.15294	13.7	341
MCHC (gm/dl)	Group A	50	31.9162	3.701492	0.52347	20.5	42.4
	Group B	50	33.978	2.666595	0.377114	20.7	40
	Total	100	32.9471	3.372576	0.337258	20.5	42.4
RDW	Group A	50	13.08	1.731108	0.244816	9.5	17.5
	Group B	50	12.556	1.690207	0.239031	9.6	16
	Total	100	12.818	1.722365	0.172237	9.5	17.5
TLC (/cumm)	Group A	50	6252	2321.614	328.326	2200	10300
	Group B	50	5906	2800.54	396.056	2100	14700

**Table-1:** Mean values of different parameters

		CD4 (cell/ cmm)	Hb (gm%)	RBC (million/ cm)	PCV (%)	MCV (fl)	MCH (pg)	MCHC (g/dl)	RDW	TLC (/cmm)	PC (/cmm)
CD4 ( cell/cmm)	Pearson Correlation	1	.621**	.597**	0.046	0.011	0.083	0.102	-0.166	.326**	.276**
	Sig. (2-tailed)		0	0	0.65	0.915	0.409	0.311	0.099	0.001	0.005
	N		100	100	100	100	100	100	100	100	100

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

**Table-2:** Correlations of different parameters with CD4 count

Parameters	Group A (Pre ART)		Group B (ART)		Total	
	No. of cases	%age	No. of cases	%age	No. of cases	%age
Anemia (Hb <10 gm %)	25	54.34	21	45.66	46	100.00
Leucopenia (TLC <4000/cumm)	10	40.00	15	60.00	25	100.00
Thrombocytopenia (<1.5lakhs/cumm)	12	50.00	12	50.00	24	100.00

Table-3: Distribution of parameters in both groups

Parameter	Group A (PRE-ART)		Group B (ART)	
	No. of cases	%age	No. of cases	%age
Anemia (Hb <10 gm %)	25	50.00	21	42.00
Non-Anemia (Hb >10 gm %)	25	50.00	29	58.00
<b>Total</b>	<b>50</b>	<b>100.00</b>	<b>50</b>	<b>100.00</b>
X <sup>2</sup> = 0.64 (p >0.05)				
Leucopenia (TLC <4000/cumm)	10	20.00	15	30.00
Non-Leucopenia (TLC >4000/cumm)	40	80.00	35	70.00
<b>Total</b>	<b>50</b>	<b>100.00</b>	<b>50</b>	<b>100.00</b>
X <sup>2</sup> = 1.33 (p >0.05)				
Thrombocytopenia (Platelet Count <1.5 Lakhs/cumm)	12	24.00	12	24.00
Non-Thrombocytopenia (Platelet Count >1.5 Lakhs/cumm)	38	76.00	38	76.00
<b>Total</b>	<b>50</b>	<b>100.00</b>	<b>50</b>	<b>100.00</b>
X <sup>2</sup> = 0.00 (p >0.05)				

Table-4: Comparison of parameters in both the groups

pancytopenia. Bone marrow was normocellular in 9 patients, hypercellular in 5 patients and hypocellular in 4 patients. The bone marrow was megaloblastic in majority of patients (6/18) followed by dimorphic reaction (4/18).

## DISCUSSION

Anemia was the most common hematologic abnormality detected in our study. Among 100 patients, 46(46%) were found to be anemic out of which 25(54%) belonged to pre-ART group and 21(45%) belonged to ART group. The prevalence of anemia reported is in agreement with studies done by Mathews et al (40.1%)<sup>2</sup>, Patwardhan et al (30.8%)<sup>3</sup>. However, the prevalence of anemia found in some of the other studies was 65.5% by Dikshit et al<sup>4</sup>, 61% by Kasthuri et al<sup>5</sup>, 74.6% by Attili et al.<sup>6</sup> This may be due to the difference in study population, socio-demographic characteristics of study subjects and study design methods. The incidence of anemia in the setting of HIV infection also depends on the level of hemoglobin used in defining anemia.

There was relatively higher prevalence of anemia in patients not receiving ART (54%) as compared to that in those receiving antiretroviral therapy (ART) (45%). This finding is in agreement with a study conducted by Mathews et al<sup>2</sup> and Enawgaw et al.<sup>7</sup> Thus, the use of ART results in decrease in the prevalence of anemia.

In the present study, normocytic normochromic anemia was the most common morphologic type of anemia (57%), followed by macrocytic (26%) and microcytic hypochromic (17%) anemia. In this study majority of pre-ART patients (66%) have normocytic-normochromic anemia while about 42% patients on ART developed macrocytic anemia. This is probably due to the effect of ART which is responsible for the development of macrocytosis. In our study, anemic patients on Zidovudine therapy had mostly a macrocytic type of anemia. This finding is consistent with the study conducted by Mathews et al.<sup>2</sup>

In the present study, the incidence of anemia was highest among patients who had CD4 lymphocyte count < 500 cells/ $\mu$ L (41/46)

and was lowest with CD4 lymphocyte count > 500 cells/ $\mu$ L (5/46), showing an inverse correlation between anemia and CD4 cell count which was statistically significant ( $p < 0.05$ ). This is consistent with studies done by Dikshit et al<sup>4</sup> and Enawgaw et al.<sup>7</sup>

In the present study, majority of the patients had a normal leucocyte count (70%). Leucopenia in the present study was seen in 25% of patients. This is in accordance with study done by Enawgaw et al<sup>7</sup> which reported leucopenia in 20.8% cases and 26.6% cases respectively. However, Mathews et al<sup>2</sup> observed a lower number of leucopenia cases in only 5.88% cases. This difference may be due to variation in study populations, clinical conditions and study design methods. Leucopenia was slightly more prevalent in patients on ART (15/25=60%) as compared to patients not on ART (10/25=40%). This is in similarity to studies done by Wanjari et al<sup>8</sup> and Enawgaw et al.<sup>7</sup>

In the present study, out of 25 leucopenic patients, 24 had their CD4 counts < 500 cells/ $\mu$ L and only 1 had CD4 count > 500 cells /cu mm; thus indicating when patient's CD4 count decreases prevalence of leucopenia increases. This difference was found to be statistically significant ( $p < 0.05$ ). This may be due to suppression of bone marrow and direct infection of T cells. This finding is in accordance with studies done by Atilli et al<sup>6</sup>, Wanjari et al<sup>8</sup> and Enawgaw et al.<sup>7</sup>

Most of the patients in our study had normal platelet counts. Thrombocytopenia was seen in 24% patients; with equal incidence in both the groups. This was similar to the finding of Patwardhan et al (13%)<sup>3</sup> and Pande et al (23.33%)<sup>9</sup>. However studies by Enawgaw et al (6.6%)<sup>7</sup> reported lower incidence of thrombocytopenia. This difference may be due to variation in study populations, clinical conditions and study design methods. However, there was no significant difference in the prevalence of thrombocytopenia between study participants on ART and pre-ART.

Thrombocytopenia was recorded in 22 patients with CD4 counts <500 cells/ $\mu$ L and only 2 patients with CD4 counts >500

cells/ $\mu$ L reported thrombocytopenia, thus thrombocytopenia increased as CD4 decreased. This correlation was found to be statistically significant ( $p < 0.05$ ). This finding is in accordance with study done by Enawgaw et al.<sup>7</sup>

## CONCLUSION

HIV Infection is accompanied by marked hematological changes that complicate health and treatment of patients. The hematologic abnormalities are prevalent through all stages of the disease, and some of these may serve as indicators of clinical progression and thus they can be used to assess the stage of the disease in resource poor places where CD4 count evaluation is not available. At the same time patients with HIV infection should be investigated and treated for hematological abnormalities to reduce the morbidity of the patients.

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