

Prevalence of Hematological Changes in HIV/AIDS patients in a Tertiary care Hospital in Chhattisgarh

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Abstract:

Background: AIDS was first recognized in the United States in the summer of 1981. In 1983 HIV was isolated from a patient with lymphadenopathy and by 1984, it was demonstrated clearly to be the causative agent of AIDS. Clinically significant hematologic abnormalities are common in persons with HIV infection. Impaired hematopoiesis, immune-mediated cytopenias, and altered coagulation mechanisms have all been described in HIV-infected individuals. These abnormalities may occur as a result of HIV infection itself, as sequelae of HIV-related opportunistic infections or malignancies, or as a consequence of therapies used for HIV infection and associated conditions. Bone marrow abnormalities are found at all stages of HIV disease, increasing in frequency as the disease progresses. Anemia is a very common finding in patients with HIV infection, particularly in individuals with more advanced HIV disease. Thrombocytopenia is believed to be present in as many as 40% of HIV infected person. One of the most consistent laboratory abnormalities observed after HIV infection is CD4 lymphocytopenia.

Methods: The present study was conducted in the Department of Medicine, Pt J. N. M. Medical College, and Dr BRAM Hospital Raipur (C.G.) from July 2011 to June 2012. 30 HIV positive /AIDS patients of different age groups including 27 males and 3 females were included in the study attending outdoor or admitted in wards of Department of Medicine, in Dr. BRAM Hospital, Raipur. Diagnosis of HIV was done by rapid spot test reported reactive by VCTC, center in Department Of Microbiology of the institute.

Results: In this present study, 22(73.33%) were AIDS and 8 patients (26.67%) were HIV positive. Prevalence of AIDS and HIV positive cases both were more in males. 59.1% of the AIDS patients and 75% of HIV patients were in 30-40 years age group. Heterosexuality with high risk behavior was found to be the only mode of transmission. 87.28% of AIDS patients had anemia and 37.5% 8 HIV positive patients had anemia. Reticulocyte count was decreased in 18.18% and was increased in 4.54% of AIDS patients. In all AIDS patients and 62.5% of the HIV positive patients, ESR was increased. In 18.18% cases of AIDS there was leucopenia. 16.

Neutrophilia was present in 15.78% of AIDS cases and 12.5% of HIV cases.

Conclusion: Hematological changes are common due to impaired hematopoiesis, immune-mediated cytopenias, and altered coagulation mechanisms. These abnormalities may occur as a result of HIV infection itself, as sequelae of HIV-related opportunistic infections or malignancies or as a consequence of therapies used for HIV infection and associated conditions. Anemia is a very common finding in patients with HIV infection, particularly in individuals with more advanced HIV disease. HIV virus has tropism for CD4 cells having primary cellular receptor for HIV and also other cells. A direct cytopathic effect of CD4 lymphocyte is thought to be primary mechanism for CD4 depletion.

Keywords: HIV-Human Immunodeficiency virus; AIDS-Acquired Immunodeficiency Syndrome CD4-Cluster differentiation 4; CD8-Cluster differentiation 8

I. Introduction

Hematologic abnormalities are often encountered in patients with the acquired immunodeficiency syndrome (AIDS). The abnormalities vary but peripheral cytopenias are most commonly seen.[1]

Anemia and neutropenia are generally caused by inadequate production because of suppression of the bone marrow by the HIV infection through abnormal cytokine expression and alteration of the bone marrow microenvironment. Thrombocytopenia is caused by immune-mediated destruction of the platelets, in addition to inadequate platelet production. The incidence and severity of cytopenia are generally correlated to the stage of the HIV infection.[2]

Hematologic abnormalities can be attributed to direct and indirect effects of the HIV-1 infection, to opportunistic infections, and to toxicity of the therapeutic agents. In adults, during the primary infection stage, there may be symptoms of lymphopenia, followed by lymphocytosis and atypical lymphocytes, neutropenia, thrombocytopenia, and transient pancytopenia. During the asymptomatic stage, there is a gradual decrease in the CD(4+) T cell count, which initially may be masked by lymphocytosis due to an increased CD8(+) T cell count. Upon diagnosis of AIDS, patients present lymphopenia and, usually, pancytopenia.[3]

Zidovudine (AZT) therapy is probably the most common cause of anemia in HIV-infected patients. Marrow erythroid hypoplasia, aplasia, and megaloblastic maturation have developed as a result of AZT therapy.[4]

Granulocytopenia with or without lymphopenia occurs in approximately 8% of asymptomatic HIV carriers, and in as many as 70 to 75% of children and adults with AIDS. The pathogenesis of Granulocytopenia often is multifactorial but commonly associated with antiviral and other drugs suppressive of myelopoiesis.[5] The etiology of neutropenia includes bone marrow infection or infiltration, myelosuppressive therapies, the presence of antibodies to HIV, and accelerated apoptosis.[6] One of the earliest and most consistent abnormality observed after HIV infection is CD4+ lymphocytopenia. The decrease in CD4 is progressive with the risk of acquiring opportunistic infections. A direct cytopathic effect of HIV on CD4 lymphocyte is thought to be primary mechanism. Both function and number of CD4 lymphocytes are affected.[5]

II. Material and Methods

Study Population-All patients, who were having HIV/AIDS whether symptomatic or asymptomatic, attending outdoor of Medicine department or admitted in indoor of department of Medicine of Dr. B.R.A.M. Hospital, Raipur (C.G.) during the study period and gave oral informed consent after understanding the purpose of study, constituted the study populations.

Study Period -The present study was conducted in the Department Of Medicine; Pt J. N. M. Medical College, Raipur (C.G.) from July 2011 to June 2012.

Study Size -30 HIV/AIDS patients of different age groups including 27 males and 03 females were qualified to be enrolled in the study attending outdoor or admitted in wards of Department of Medicine, in Dr. Bhim Rao Ambedkar Memorial Hospital, Raipur from July 2011 to June 2012.

History and physical examination was done and recorded on a pre-designed proforma. Enrolled patients were evaluated for complete blood counts, ESR, CD4/CD8 count, and Bone marrow aspiration was done and analysed.

Inclusion Criteria-

HIV Positive or AIDS Patients divided into 2 groups

Exclusion Criteria-

- i. All HIV negative individuals
- ii. Known case of Malignancy and Patients on prolonged steroids, taking immunosuppressive drugs.
- iii. Patients who doesn't gave consent for the study

III. Results

A total of 30 patients were studied which included both males and females. The age of patients ranged from 20 years to 68 years. Out of these Thirty, 27 were males and 3 were females with male:female ratio 9:1. The patients were subdivided in two groups –

- A. AIDS
- B. HIV- positive

Table – 1 Showing distribution of AIDS and HIV positive among 30 cases

Group	Numbers	Percentage
AIDS	22	73.33
HIV Positive	8	26.67
Total	30	100

Among 30 cases, 22 (73.33%) were AIDS and 8 patients (26.67%) were HIV positive. Full blown AIDS was more prevalent as compared to only HIV positive cases.

Table – 2 Showing sex prevalence among 30 cases

Group	AIDS		HIV Positive		Total	
	No	%	No	%		
Male	20	90.9	7	87.5	27	90
Female	2	9.1	1	12.5	3	10

Among 22 AIDS patients 20 (90.9%) were males and 2 (9.1%) were females whereas in 8 HIV positive patients 7 (87.5%) were males and 1 (12.5%) were female in this table. Both AIDS and HIV positive cases were more prevalent in males.

Table -3 Showing mean age of males and females in AIDS and HIV positive patients among 30 cases

	Age in years	
	AIDS	HIV Positive
Male	36.15±1.41	32.57
Female	27±7.77	30±5.58

Above table shows that mean age of males in AIDS and HIV positive was 36.15 years and 32.57 years respectively. Mean age of females in AIDS and HIV positive was 27±7.77 years and 30±5.58 years. Mean age of males in both the groups was higher as compared to females.

Table – 4 Showing distribution of 30 cases according to symptoms and signs

Symptoms	AIDS		HIV Positive	
	No	%	No	%
Fever	21	95.45	8	100
Weight loss	18	81.81	5	62.5
Diarrhoea	9	40.90	2	25
Cough	18	81.81	3	37.5
Oral Thrush	11	50	0	0
Pallor	22	100	7	87.5
Icterus	2	9.9	0	0
Lymphnodes	4	18.18	1	12.5
Hepatitis	0	0	0	0

This table showed that among 22 AIDS patients pallor was present in 22(100%) and fever was present in 21 (95.45%) patients followed by weight loss and cough each in 18 patients (81.81%). Followed by oral thrush in 11 (50%), diarrhoea in 9 (40.90%) patients were the main symptoms. In 8 HIV positive cases fever was present in all 8 (100%) patients followed by weight loss in 5 (62.5%) cases and pallor and cough each in 3 (37.5%) cases. Pallor present in 100% of AIDS patients and 87.5% of HIV patients.

Table 5 Showing Variations in ESR in 30 HIV patients

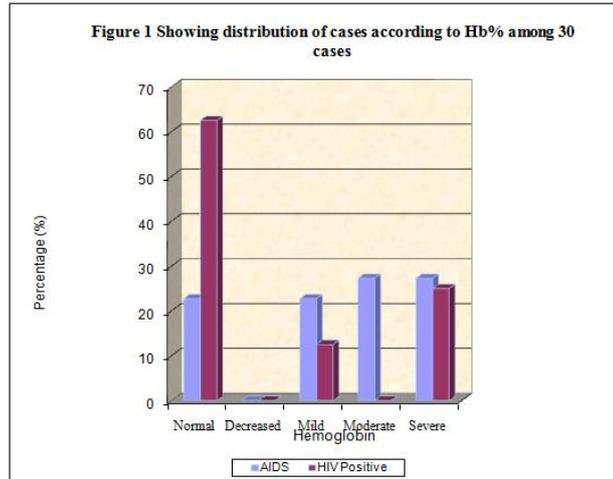
	Value		AIDS		HIV Positive	
	Male	Female	No.	%	No.	%
Normal	0-17mm/h	1-25mm/h	0	0	3	37.5
Increased	>17	>25	22	100	5	62.5

ESR was increased in 100% AIDS patients and 62.5% of the HIV positive patients in this table.

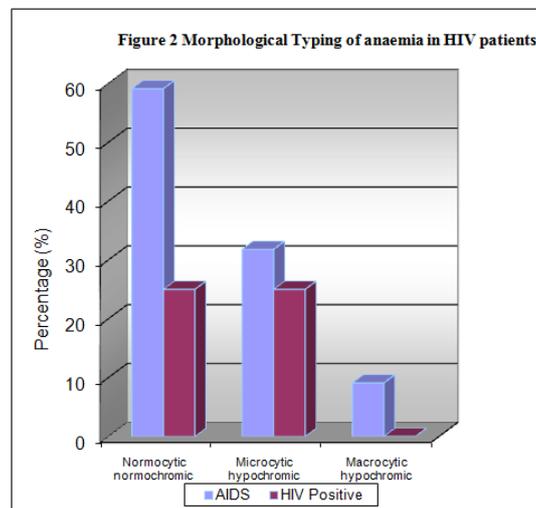
Table – 6 Variations in TLC in HIV patients

	Value in thousand	AIDS		HIV Positive	
		No.	%	No.	%
Normal	4.0-11.0	17	77.27	7	87.5
Increase	>11.0	1	4.54	1	12.5
Decrease	<4.0	4	18.18	0	0

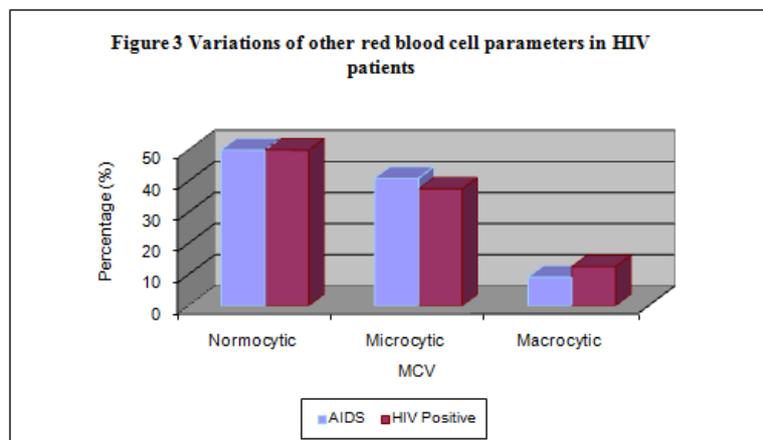
This table shows that 17(77.27%) of AIDS and 7(87.5%)of HIV positive patients had normal Total leucocyte count whereas 1(4.54%)of AIDS and 1(12.5%) of HIV had increased TLC and in 4(18.18%) of AIDS cases had decreased TLC.



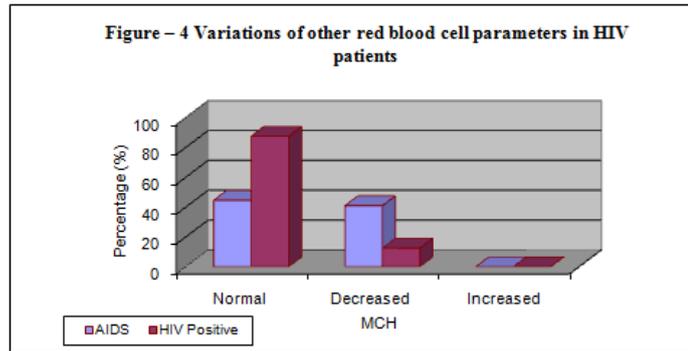
This figure shows that severity and prevalence of anemia was higher in AIDS patients as compared to HIV positive.



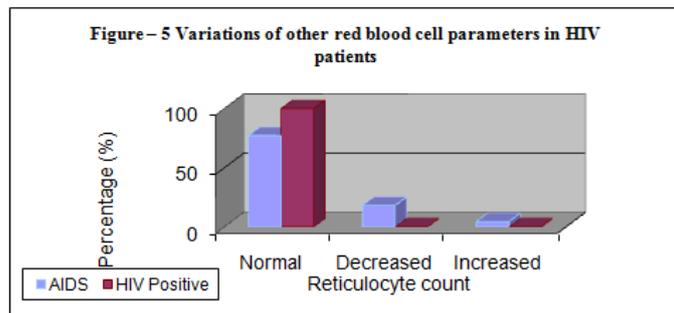
Most of the patients are having normocytic normochromic type of anemia in both AIDS and HIV positive patients as shown in this figure.



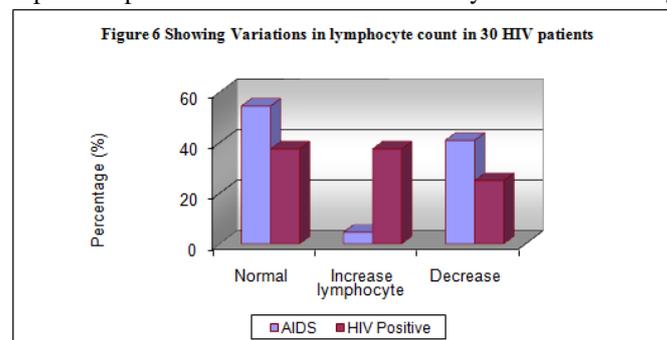
This figure shows that out of 22 AIDS patients MCV of 11(50%) AIDS patients and 4(50%) of HIV patients were Normocytic. MCV of 9(40.9%) AIDS patient and 3(37.5%) HIV patients were microcytic. 2 (9.09%) of AIDS patients were macrocytic.



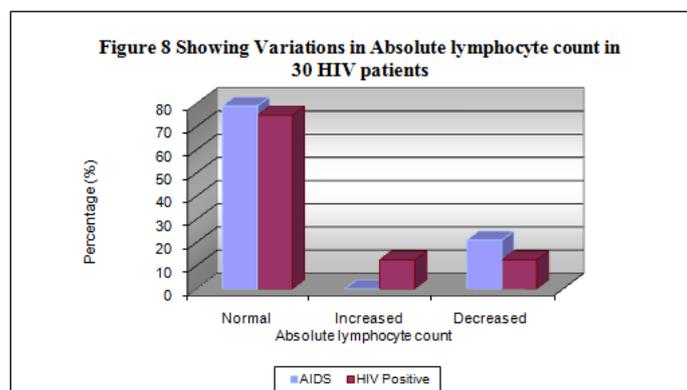
MCH was normal in 12(54.55%) AIDS patients and 7 (87.5%) HIV positive patients, whereas 9(40.91%) AIDS and 1(12.5%) HIV patients had decreased MCH in this figure



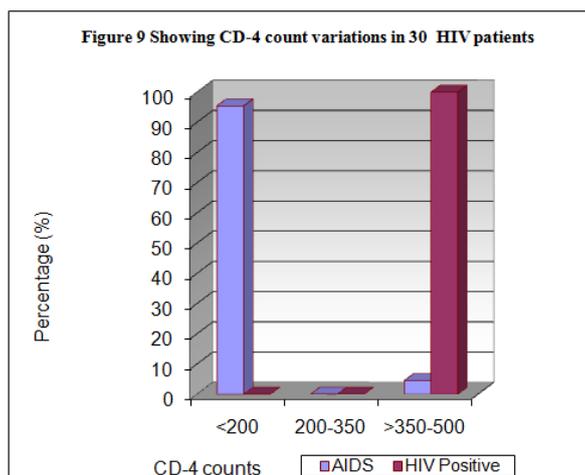
Reticulocyte count was decreased in 4 (18.18%) AIDS patients and increased in only 1(4.54%) of AIDS case and in 8 (100%) HIV positive patients all had normal reticulocyte count in this figure.



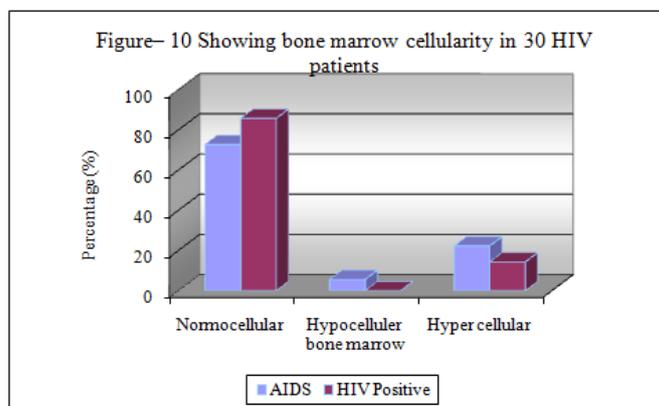
This figure shows that 12(54.54%) AIDS cases and 3(37.5%) HIV positive cases had normal lymphocyte count. 1(4.54%) AIDS case and 3(37.5%) HIV positive cases had increase lymphocyte count, whereas 9(40.9%) AIDS cases and 2 (25%) HIV positive cases had decreased lymphocyte count.



This figure shows that Absolute lymphocyte count was normal in 15(78.94%) AIDS cases and 6(75%) HIV cases. Absolute lymphocyte count was decreased in 4(21.05%) AIDS cases and 1(12.5%) HIV patient. One(12.5%) HIV patients had increased Absolute lymphocyte count.



This figure shows that CD4 count was <200 in 21(95.45%) of AIDS patients and only 1(4.54%) AIDS patient had CD4 count >350-500. Whereas all HIV positive patients had CD4 count >350. CD4 count was <200 in nearly all AIDS patients



This figure shows that out of 25 AIDS patient 13(72.72%) had normocellular and 4(22.22%) had hypercellular marrow and only 1 (5.55%) had hypocellular marrow. Whereas in 7 HIV patients 6(85.71%) had normocellular and 1(14.28%) had hypercellular marrow. In both AIDS and HIV group normocellular and hypercellular marrow were more common.

IV. Discussion

Hematologic abnormalities can be attributed to direct and indirect effects of the HIV-1 infection, to opportunistic infections, and to toxicity of the therapeutic agents. In adults, during the primary infection stage, there may be symptoms of lymphopenia, followed by lymphocytosis and atypical lymphocytes, neutropenia, thrombocytopenia, and transient pancytopenia. During the asymptomatic stage, there is a gradual decrease in the CD(4+) T cell count, which initially may be masked by lymphocytosis due to an increased CD8(+) T cell count. Upon diagnosis of AIDS, patients present lymphopenia and, usually, pancytopenia.[3]

The 1-year incidence of anemia was 36.9% for persons with one or more acquired immunodeficiency syndrome (AIDS)-defining opportunistic illnesses (clinical AIDS), 12.1% for patients with a CD4 count of less than 200 cells/ μ m or CD4 percentage of <14 but not clinical AIDS (immunologic AIDS), and 3.2% for persons without clinical or immunologic AIDS.

The increased risk of death associated with anemia differed by first CD4 count: for patients with a CD4 count of 200 cells/ μ L the risk of death was 148% greater for those who developed anemia; for patients whose first CD4 count was <200 cells/ μ L, the risk of death was 56% greater for those in whom anemia developed.[7]

Anemia is multifactorial. HIV infection itself causes anemia, probably as a consequence of HIV infection of stromal cells rather than HIV infection of hematopoietic stem cells. Other common causes of anemia in AIDS are anemia of chronic disease consequent on opportunistic infections, bone marrow suppression by antiretroviral therapy, and hemolytic anemia induced by oxidant drugs.[8]

The central feature of HIV disease is opportunistic infection and malignancy resulting from CD4 cell depletion. When working with cells such as erythrocytes or platelets, is that CD4 and CD8 lymphocytes are a

remarkably complex and heterogeneous mixture of subpopulations, each with the prospect of different turnover rates and tissue distributions, not to mention differential susceptibility to HIV infection. Studies to date indicate that CD4 cell depletion is associated with increased T-cell turnover in HIV infection, strictly parallel to hemolytic anemia or idiopathic thrombocytopenic purpura, conditions that induce dramatic rises in both cell production and elimination.

After HIV infection, the half-life of CD4 T lymphocytes drops, but the production rate does not respond with a compensatory increase. With the suppression of virus replication by antiretroviral therapy, production rates of both CD4 and CD8 cells increase significantly. [9]

HIV-related thrombocytopenia (Tr-HIV) is the most common hemostatic disorder with a high morbidity and affects patients from every risk group independently of age, sex, or stage of infection. Two mechanisms are responsible for the Tr-HIV: bone marrow failure and immunological disorders, namely, circulating immune complex deposited on the platelet membrane and the production of autoantibodies directed against platelets.[10]

Immune thrombocytopenic purpura (ITP) occurs in as many as 40% of patients infected with the human immunodeficiency virus (HIV).HAART seems to be effective in improving platelet counts in the setting of HIV-associated ITP, enhancing CD4+ cell counts, and reducing HIV viral loads.[11]

Among the most common bone marrow findings were hypercellularity (53% of specimens), myelodysplasia (69%), evidence of reticuloendothelial (RE) iron blockade (65%), megaloblastic hematopoiesis (38%), fibrosis (20%), plasmacytosis (25%), lymphocytic aggregates (36%), and granulomas (13%). Most of the bone marrow abnormalities associated with HIV infection appear to be related directly to the infection or its complications and not to therapeutic intervention.[12]

V. Conclusion

Anaemia and thrombocytopenia are the most common hematologic abnormalities associated with HIV infection and found in majority of AIDS patients. Decrease in the CD4 cell count occurs with earliest burst of virus replication. Neutropenia is found in approximately half of the patients during the course of illness and can put the patients at the risk of bacterial infection.

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