Original Article

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Hematological Abnormalities in Early and Advanced HIV Infection Patients

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Abstract

Background: Hematological abnormalities in patients with HIV infection are common. These hematological abnormalities include anemia, leukopenia, thrombocytopenia, and sometimes pancytopenia with variable bone marrow abnormalities.

Methodology: A study was conducted from March 2008 to April 2010 in a tertiary care center-JSS Hospital, Mysore, Karnataka. The patients admitted to the Department of Medicine and Dermatology wards with the diagnosis of HIV infection as per standard WHO criteria were included in the study. A detailed history, physical examination, and relevant investigations were conducted. Data were collected using a pre-tested proforma to meet the objectives of the study.

Results: A total of 100 HIV-positive patients were included in the study and were assigned into either Groups A and B. Group A patients included HIV-positive patients with CD4 counts > 200 cells/cumm, and Group B included HIV-positive patients with CD4 counts < 200 cells/cumm. 50 patients were included in each group. Most of these patients (about 60%) were in the highly reproductive age group (21-40 years) and were predominantly males (78%). The common symptoms among these patients were fever (79%), weight loss (64%), and oral thrush (24%). Anemia was the most common laboratory abnormality seen in both the groups with 70% in Group A and 84% in Group B. Leukopenia was seen in 10% of patients in Group A and 60% of patients in Group B. Thrombocytopenia was seen in 32% cases among Group A and 78% cases among Group B.

Conclusion: In patients with HIV infection, the frequency and severity of hematological manifestations including hypocellular bone marrow increased with the decline in CD4 counts. This might lead to a significant impact on clinical outcome and patient's quality of life. Hence, all the HIV patients should also be investigated for hematological abnormalities and treated accordingly.

Key words: AIDS, CD4 counts, Hematological abnormalities, HIV

INTRODUCTION

HIV infection targets mainly the immune system and hence hematological abnormalities are among the most common clinicopathological features. These hematological abnormalities vary from anemia, leukopenia, and thrombocytopenia including bone marrow dysplasia. The pathophysiological basis for these hematological abnormalities may include impaired hematopoiesis, immune-mediated cytopenias, and/or coagulopathies especially in the advanced stage of the disease.[1,2]

HIV destroys the T-cell lymphocytes which in turn disables the immune system to defend the body against diseases and malignancies. This will also lead on to various devastating opportunistic infections paralleling the declining immunity. Peripheral blood picture findings are highly variable depending on the clinical severity of immunodeficient state.[3]

In general, hematological abnormalities progress in frequency and severity with the progression of the disease from the asymptomatic HIV carrier state to the advanced state of the disease.[4] About 15% of asymptomatic HIV

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carriers have mild anemia. The prevalence of anemia increases from 30% to 40% in those with the early disease to 75-90% in advanced patients. It may be still higher in HIV-infected infants and children.[5]

Granulocytopenia with or without lymphopenia occurs in approximately 8% of asymptomatic HIV carriers and as many as 70-75% of children and adults with AIDS. While anemia and granulocytopenia tend to occur concomitantly with a severity that parallels the course of the HIV infection, thrombocytopenia can occur independently of other cytopenias and at all stages of HIV infection. Isolated thrombocytopenia may be the first manifestation of HIV infection.[6,7]

The accurate measurement of CD4 cell counts is essential for the assessment of immune system of HIV-infected person as the pathogenesis of AIDS is largely attributable to the decrease in CD4 lymphocyte counts. CD4 counts help to categorize the HIV-infected patients from mild to severe form of the disease and in turn guide the treatment. It also depicts the patient's predisposition to various opportunistic infections.

Among the neoplastic complications, Kaposi's sarcoma is the most common neoplasm in patients with AIDS, occurring with a 700 fold increase in HIV-infected patients compared with age-matched, non-infected controls.[8] Other malignancies commonly seen in patients with AIDS are non-Hodgkin's lymphoma, seminoma, and non-melanoma skin cancer.[9]

The combined effect of the above alterations in hematological parameters will significantly compromise patient's quality of life who are already overburdened by the treatment of primary viral infection, secondary infections, and neoplastic complications. These hematopoietic abnormalities, in turn, lead to poor tolerance to therapies necessitating dose reductions, alteration of drug regimens, or interruption of therapies.

METHODOLOGY

A total of 100 patients detected to be HIV-positive as per the WHO criteria attending the Department of Medicine and Dermatology, JSS Hospital, Mysore during the period of March 2008-April 2010 were enrolled for the study. These patients were assigned into either Group A (HIV-positive patients with CD4 count > 200 cells/cumm) or Group B (HIV-positive patients with CD4 count < 200 cells/cumm).

Inclusion Criteria

HIV-positive patients as per the WHO criteria irrespective of their anti-retroviral treatment status, attending the Department of Medicine/Dermatology, JSS Hospital, Mysore.

Exclusion Criteria

1. Patients with previously known hematological disorders
2. Congenital hematological disorders
3. Age <18 years
4. Pregnant woman
5. Critically ill patients.

Data were collected using a pre-tested proforma to meet the objectives of the study. The purpose of the study was carefully explained. Informed and written consent was obtained from all the patients prior to the study.

Detailed history, general, and systemic examination was conducted with emphasis on signs suggesting hematological system involvement such as pallor, clubbing, jaundice, edema, glossitis, lymphadenopathy, koilonychias, angular stomatitis, petechiae, and hepatosplenomegaly.

The investigations included complete hemogram with peripheral blood picture, bone marrow cytology, and CD4 cells count by Flow cytometry by a standard technique using Becton-Dickinson FAC Scan.

Statistical Analysis

Descriptive statistics was expressed as mean ± SD (range). Results were compared using Chi-square test of significance. A $P < 0.05$ was considered statistically significant.

The study was carried out after obtaining permission from the Institutional Ethics Committee.

RESULTS

The patients were divided into two groups according to their CD4 counts: Group A (HIV-positive with CD4 counts >200 cells/cumm) and Group B (HIV-positive with CD4 counts <200 cells/cumm). Out of the 100 patients studied, 50 patients were included in each group.

Age and sex distribution: Most of the patients were males in the age group of 21-40 years (74%). The mean age of the patients in the present study was 33.8 years. In the Group A patients, males were predominant in the age group of 31-40 (50%), whereas females were predominantly in the age group of 21-30 (50%). In Group B patients, most of the patients were males and in the age group of 31-40 years (44.75%), whereas females were predominantly in the age group of 41-50 (66.67%) (Table 1).

Table 1: Age and sex distribution pattern in early and advanced HIV groups

Age in years	Group A (CD4 counts >200 cells/mm³) *n*=50			Group B (CD4 counts <200 cells/mm³) *n*=50		
	No. of males (%) *n*=40	No. of females (%) *n*=10	Total (%)	No. of males (%) *n*=38	No. of females (%) *n*=12	Total (%)
<20	0	1 (10)	1 (2)	0	0	0
20-30	10 (25)	5 (50)	15 (30)	3 (7.89)	1 (8.33)	4 (8)
31-40	20 (50)	2 (20)	22 (44)	17 (44.75)	2 (16.67)	19 (38)
41-50	5 (12.5)	1 (10)	6 (12)	15 (39.47)	8 (66.67)	23 (46)
51-60	4 (10)	1 (10)	5 (10)	2 (5.26)	1 (8.33)	3 (6)
>60	1 (2.5)	0	1 (2)	1 (2.63)	0	1 (2)
P value	Age and gender *P*=0.05 (S) overall *P*=0.000			Age and gender P=NS overall *P*=0.00		

Symptoms and Signs: Predominant symptoms in Groups A and B were fever (78% and 80%) and weight loss (62% and 66%). Predominant signs in Group A were pallor (70%) and adenopathy (8%), whereas in Group B was pallor (80%) and oral candidiasis (44%) (Table 2).

Peripheral blood picture: Anemia was the most common sign, about 77% of them had hemoglobin below 13 g% and about 6% had hemoglobin below 6 g%. Cytopenias of all peripheral blood cells have been observed in patients with HIV infection (Table 3).

The most common type of anemia in Group A (CD4 counts > 200 cells/cumm) was normocytic normochromic anemia and normocytic hypochromic anemia, while in Group B (CD4 counts <200 cells/cumm) it was normocytic normochromic anemia and pancytopenia.

Leukopenia was seen in 10% cases of Group A and 60% cases of Group B patients. Thrombocytopenia was seen in 32% and 78% cases of Groups A and B, respectively.

Bone marrow cellularity: Bone marrow picture was hypercellular in 64% and 68%; normocellular in 36% and 20% of Groups A and B patients, respectively, while it was hypocellular in 12% of Group B patients. In addition, megakaryocytic dysplasia was seen 2 cases of Group A and 7 cases of Group B patients. Marrow eosinophilia was seen in 2 cases (4%) of Group A and 4 cases (8%) cases of Group B (Table 4).

Table 2: Symptoms and Signs in early and advanced HIV groups

Symptoms and signs	No. (%)		
	Group A (CD4 counts >200 cells/mm³) (*n*=50)	Group B (CD4 counts <200 cells/mm³) (*n*=50)	Total (*n*=100)
Fatigue	17 (34)	24 (48)	41 (40)
Fever	39 (78)	40 (80)	79 (79)
Weight loss	31 (62)	33 (66)	64 (64)
Jaundice	03 (06)	05 (10)	08 (08)
Dyspnea	04 (08)	10 (20)	14 (14)
Anorexia	08 (16)	20 (40)	28 (28)
Cough	06 (12)	18 (36)	24 (24)
Diarrhea	02 (04)	03 (06)	05 (05)
Palpitation	06 (12)	05 (10)	11 (11)
Pallor	35 (70)	40 (80)	75 (75)
Clubbing	01 (02)	11 (22)	12 (12)
Icterus	03 (06)	05 (10)	08 (08)
Oral thrush	02 (04)	22 (44)	24 (24)
Adenopathy	04 (08)	18 (36)	22 (22)
Edema	01 (02)	03 (06)	04 (04)
Petechiae	01 (02)	02 (04)	03 (03)

DISCUSSION

Hematological abnormalities and impaired immune status represent one of the common causes of mortality in HIV-infected patients. This hematological status worsens with the progression of the disease.

In the present study, the age of the patients ranged from 19 to 62 years. 60% of these patients were in the highly productive age group of 21-40 years. There was an overall male predominance (78%) which is in accordance with a study done by Sharma *et al.* (79.7%).[10] Females were much younger with 54% of them in the age group of 21-30 years.

The most common symptoms were fever (79%), weight loss (64%) followed by fatigue (41%). The most common signs were pallor (75%) and oral thrush (24%). The increased frequency of these symptoms and signs could possibly be due to the severity of the illness, and the majority of patients were in WHO clinical Stages III and IV.

The anemia was the most common hematological finding, about 77% of them had hemoglobin below 13 g% and about 6% were having hemoglobin below 6 g%. This incidence was in accordance with previous studies of Rajeev *et al.* (75%).[11] When hemoglobin (Hb)% is correlated to CD4 counts, in the Group A patients, about 70% of cases had Hb% <13 g%, whereas in Group B, 84% of cases had Hb% <13 g%. Morphologically the most common type of anemia was normocytic normochromic

Table 3: Hb, TLC, neutrophils, lymphocyte, and platelets counts in relation to CD4 counts in early and advanced HIV groups

Type of test	Unit no. of cells	No. (%)		
		Group A (CD4 counts >200 cells/mm^3) (*n*=50)	Group B (CD4 counts <200 cells/mm^3) (*n*=50)	Total (*n*=100)
Hb in g%	<6	03 (06)	03 (06)	06
	6-9	12 (24)	18 (36)	30
	9-13	20 (40)	21 (42)	41
	>13	15 (30)	08 (16)	23
P value		Hb and CD4 count *P*=0.34, overall *P*=0.000		
TLC (×1000 cells/mm^3)	≤4	05 (10)	30 (60)	35
	4-11	39 (78)	18 (36)	57
	>11	06 (12)	02 (04)	08
P value		TLC and CD4 count *P*=0.00, overall *P*=0.00		
Neutrophils (%)	≤50	03 (06)	04 (08)	07
	50-70	40 (80)	39 (78)	79 (14)
	>70	07 (14)	07 (14)	
P value		Neutrophils and CD4 count *P*=0.925, overall *P*=0.00		
Lymphocyte (%)	≤ 20	13 (26)	25 (50)	38
	20-40	30 (60)	15 (30)	45
	>40	07 (14)	10 (20)	17
P value		Lymphocytes and CD4 count *P*=0.009, overall *P*=0.002		
Platelets (in lakhs/mm^3)	<1	04 (08)	20 (40)	24
	1-1.5	12 (24)	19 (36)	31
	>1.5	34 (68)	11 (22)	45
P value		Platelets and CD4 count *P*=0.00 (S), overall *P*=0.032		

Hb: Hemoglobin, TLC: Total leukocyte count

Table 4: Bone marrow picture in relation to CD4 counts in early and advanced HIV groups

Bone marrow cellularity	No. (%)		
	Group A (CD4 counts >200 cells/mm^3) (*n*=50)	Group B (CD4 counts <200 cells/mm^3) (*n*=50)	Total (%) (*n*=100)
Hypocellular	0 (0)	06 (12)	06
Normal	18 (36)	10 (20)	28
Hypercellular	32 (64)	34 (68)	66
P value	Bone marrow and CD4 count *P*=0.015, overall *P*=0.00		

type followed by normocytic microcytic and the least being pancytopenia.[11]

Leukopenia was prevalent in 35% of the patients. Leukopenia was seen in 10% cases of Group A and 60% cases of Group B. Lymphocytopenia was seen in 26% cases of Group A and 50% cases of Group B. Neutropenia was seen in 6% of cases of Group A patients and 8% cases of Group B. According to Zon *et al.*, the incidence of leukopenia range from 57% to 85% in patients with fully developed AIDS, whereas it was <5% in asymptomatic seropositive patients presenting with leukopenia.[12] However, according to Castella *et al.,* the incidence of granulocytopenia was around 75% probably because of influence from anti-retroviral therapy along with the disease itself.[13]

The prevalence of thrombocytopenia (platelet count below 1.5 lakhs/mm^3) was 24%. This is in accordance with studies of Murphy *et al.* (30%) and Zon *et al.* (40%). In a multi-centric AIDS cohort study of 1500 HIV-positive individuals, 6.7% had platelet counts <1.5 lakhs/mm^3 on at least one semiannual visit. In the present study, thrombocytopenia was seen in 36% cases of Group A patients and 78% cases of Group B patients.[14,15]

Bone marrow study in Group A cases showed hypercellularity in 64% and was normocellular in 36%. Whereas in Group B, 68% were hypercellular, 20% normocellular, and 12% were hypocellular. In number of earlier studies bone marrow is hypercellular in early stages of the disease and hypocellular later on as disease advance. In addition, there were 2 cases of megakaryocytic dysplasia in Group A and 7 cases in Group B. Megakaryocytic dysplasia has become increasingly recognized in patients with fully developed AIDS patients and also in isolated thrombocytopenia according to van der Lelie *et al.*[16] Furthermore, in the present study, marrow eosinophilia was seen in 4% cases of Group A patients and 22% cases of Group B patients. However, according to Zon *et al.* and Delacrétaz F *et al.*, marrow eosinophilia is common and has been reported in 9% and 61% of patients with AIDS.[17,18]

CONCLUSION

In the present study, the most common hematological manifestations found were anemia, leukopenia, and thrombocytopenia. The frequency and severity of these hematological manifestations increased with the decline in CD4 counts and have got a significant impact on clinical outcomes and patients quality of life. Hence, all patients should be investigated for hematological abnormalities and treated accordingly to reduce the morbidity and mortality.

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