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STUDY OF HEMATOLOGICAL PROFILE IN HIV INFECTED PATIENTS WITH CORRELATION TO CD4 CELL COUNT

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Conflicts of Interest: Nil

ABSTRACT:

Background: HIV infection is a multisystem disease, with haematological abnormalities among the most common clinicopathological manifestations involving all the lineages of blood cells. In the present study spectrum of hematological manifestations in patients with HIV/AIDS have been studied and correlated with the CD4 cell count. **Method:** The study was conducted on 100 HIV positive patients, which were divided in two groups according to their CD4 count, those having low CD4 (≤200/ul) (77% patients) and those having high CD4 (>200/ul), (23% patients). Complete hematologic profile was recorded. Relationship between CD4 counts and various hematologic parameters was analyzed. **Results:** The most common hematologic abnormality was anemia, seen in 89% (n=89) of the patients. Normocytic normochromic anemia was seen in 49 patients, which was the most common type. A strong association between anemia and CD4 counts was observed. Leucopenia was seen in 40 cases (40%) which had significant correlation with CD4 count while thrombocytopenia was seen in 31 cases (31%) and had no significant relationship with CD4 counts. The frequency and severity of these hematological manifestations increased with decline in CD4 count. **Conclusion:** Haematologic manifestations of HIV infection are common and more frequent with progression of disease. Therefore all HIV patients should be investigated for hematological abnormalities and treated accordingly to reduce morbidity and mortality.

Keywords: HIV, Haematological, CD4 count, Correlation, Anemia, Leucopenia, Thrombocytopenia

Introduction

Human immunodeficiency virus (HIV) infection is a global pandemic, with cases reported from virtually every country across the globe. Currently, in Asia, there are about 4.9 million people living with HIV, with an estimated 2.5 million in India alone [1]. HIV infection is often associated with a wide range of hematological abnormalities including impaired hematopoiesis, immune mediated cytopenias and coagulopathies, particularly in the later part of the disease [2-4]. Disorders of the haematopoietic system including anaemia, leucopenia and thrombocytopenia are common throughout the course of HIV infection [5]. The consequences of these hematological problems are twofold. First, they have major morbidity in themselves, adversely altering the patient's quality of life. Second, they hinder the treatment of the primary viral infection, secondary infections and neoplastic complications [6, 7].

The accurate measurement of CD4 cell counts is essential for assessment of immune system of HIV infected person as the pathogenesis of acquired immunodeficiency syndrome is largely attributable to the decrease in CD4 lymphocyte counts. In general, hematological abnormalities progress in frequency and severity with the progression of infection from the asymptomatic HIV carrier state to the later symptomatic stages of the disease [8]. HIV associated hematologic expressions seems to be dependent on the level of viral replication, as these abnormalities are severe

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in AIDS patients with high viremia and decreased CD4 counts [9]. There are few studies on haematological changes in HIV and very few have correlated results with CD4 count [5]. Hence, the present research was carried out with an objective to study the spectrum of hematological manifestations in patients with HIV/AIDS and also study the correlation between hematological manifestations and CD4 cell count.

Materials and Methods

This observational study was carried out in the ART clinic and Department of Pathology at Tertiary Care Hospital and Referral centre after obtaining permission from the Institutional Ethical Committee and NACO. Total 100 patients considered HIV positive as per WHO criteria having age >12 years of either sex irrespective of their antiretroviral treatment status were enrolled in the study. Patients with previously known hematological disorders and pregnant females were excluded from the study. The purpose of study was carefully explained to the selected patients and consent was taken.

All patients were interviewed, detailed history was taken with respect to risk factors and detailed physical examination was done. Appropriate investigations-a) complete hemogram including peripheral smear, b) bone marrow biopsy whenever indicated and c) CD4 lymphocyte counts by Flow Cytometry by standard technique using Becton-Dickinson FAC Scan were carried out.

The results were analyzed by calculating percentages, mean values, standard deviation, standard error, unpaired‘t’ test, Chi-square ‘t’ test and proportion test. Proportions were compared using Chi-square test of significance. A ‘P’ value of less than 0.05 was considered statistically significant.

Observations and Results

A total 100 HIV positive patients attending ART clinic of Tertiary care hospital during the period of two years were studied, among them 80 were males and 20 were females with a sex ratio of 4:1. All the selected patients were divided in two groups according to their CD4 count, those having low CD4 (≤200/ul) (77% patients) and those having high CD4 count (>200/ul), (23% patients). Majority of patients were in the age group of 21-40 years (74%), with mean age of patients was 33.8 years, (Table 1).

Table 1: Age and sex distribution of HIV positive patients

Age in years	Males (n=80)	Females (n=20)	Total (n=100)
	No. (%)	No. (%)	No. (%)
<20	0 (0)	2 (10)	2 (2)
21-30	20 (25)	10 (50)	30 (30)
31-40	40 (50)	4 (20)	44 (44)
41-50	10 (12.5)	2 (10)	12 (12)
51-60	7 (8.75)	2 (10)	9 (9)
>60	3 (3.75)	0 (0)	3 (3)

Predominant symptoms were fatigue (86%), fever (80%) and predominant signs were pallor (75%) and oral candidiasis (48%). Other signs and symptoms were weight loss (78%), Anorexia (48%), Dyspnoea (46%), cough (44%), emaciation (40%), Lymphadenopathy (40%), Diarrhea (24%), Temperature (12%), edema (12%), Clubbing (8%), Petechiae/ Purpura (6%), Palpitation (5%), Jaundice (3%) and Cyanosis (3%).

The frequency of different haematological parameters is shown in table 2. Average Hb% was 10.02 gm%. All female patients were having Hb% below 13. Total leukocytes count was ranged from 1900 cell/mm^3-12300 cells/mm^3 and the prevalence of leucopenia was 40%. The neutrophil count was ranged from 38% to 89% of TLC with only 7% of the cases were having granulocytopenia. The lymphocyte count was ranged from 8.7% to 54% of TLC with prevalence of lymphopenia of about 38%. The

platelet count was ranged from 0.7- 4.5 lakh/mm^3 with prevalence of thrombocytopenia of about 31%. The CD4 cell count varied widely from 1.51 to 1041 and mean CD4 count was 135.14. CD8 count ranged 248 to 2140 and CD4/CD8 ratio ranged from 0.03 to 1.25.

Table 2: Frequency of haematological parameters

Haematological Parameters		Males (n=80)	Females (n=20)	Total (n=100)
		No. (%)	No. (%)	No. (%)
Hb gm%	≤6	10 (12.50)	2 (10)	12 (12)
	>6-≤9	28 (35)	7 (35)	35 (35)
	>9-≤13	35 (43.75)	11 (55)	46 (46)
	>13	7 (8.75)	0 (0)	7 (7)
TLC/ul	<4000	36 (45)	4 (20)	40 (40)
	>4000-11000	42 (57.5)	14 (70)	56 (56)
	>11000	2 (2.5)	2 (10)	4 (4)
Neutrophil count in %	≤50	4 (5)	3 (15)	7 (7)
	50-70	66 (82.5)	12 (60)	78 (78)
	>70	10 (12.5)	5 (25)	15 (15)
Lymphocyte count in %	≤20	34 (42.5)	4 (20)	38 (38)
	20-40	40 (50)	12 (60)	52 (52)
	>40	6 (7.5)	4 (20)	10 (10)
Platelet lakh/cumm	≤1.5	26 (32.5)	5 (25)	31 (31)
	1.5-4	52 (65)	12 (60)	64 (64)
	>4	2 (2.5)	3 (15)	5 (5)
CD4 count	≤200	66 (82.5)	16 (80)	82 (82)
	>200	14 (17.5)	4 (20)	18 (18)

The most common type of anemia was normocytic normochromic anemia seen in 49% cases, followed by microcytic hypochromic anemia (45%), (Figure 1). Bone marrow study was done in 8 cases out of which 4 cases were having normoblastic marrow, 2 cases were having hypercellular marrow and 2 were having hypoplastic bone marrow.

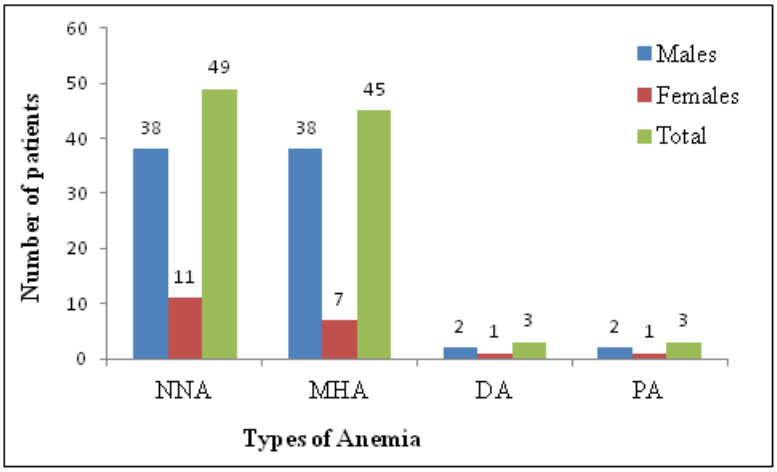

Figure 1: Frequency of type of anemia

Among the hematological manifestations, anemia (89%) was the commonest. The frequency and severity of anemia increased with declining CD4 count, which was not statistically significant, (p=0.119). Out of 80 cases, 36 (45%) were having total leucocyte count <4000, (p<0.041) while 6 cases (7.5%) had neutrophil count percentage <50, (p=0.618). Leucopenia was seen in 40 cases (40%) which had significant correlation with CD4 count, (p=0.019) whereas thrombocytopenia was seen in 31 cases (31%) and had no significant relationship with CD4 counts, (p=0.262), (Table 3).

Table 3: Correlations of different haematological parameters with CD4 count

Haematological Parameters		**≤200 (n=80)**	**>200 (n=20)**	**Total (n=100)**
		No. (%)	No. (%)	No. (%)
Hb gm%	≤6	5 (6.25)	3 (15)	8 (8)
	>6-≤9	30 (37.5)	3 (15)	33 (33)
	>9-≤13	38 (47.5)	10 (50)	48 (48)
	>13	7 (8.75)	4 (20)	11 (11)
TLC/ul	<4000	36 (45)	4 (20)	40 (40)
	>4000-11000	43 (53.75)	13 (65)	56 (56)
	>11000	2 (2.5)	3 (15)	4 (4)
Neutrophil count in %	≤50	6 (7.5)	1 (5)	7 (7)
	50-70	62 (77.5)	16 (80)	78 (78)
	>70	12 (15)	3 (15)	15 (15)
Lymphocyte count in %	≤20	40 (50)	3 (15)	43 (43)
	20-40	24 (30)	14 (80)	38 (38)
	>40	16 (20)	3 (15)	19 (19)
Platelet lakh/cumm	≤1.5	27 (33.75)	3 (15)	30 (30)
	1.5-4	50 (62.5)	16 (80)	66 (66)
	>4	3 (3.75)	1 (5)	4 (4)

Of the 80 cases having CD4 count <200, 44 (55%) cases were normocytic normochronic anemia which was statistically significant (p<0.0358). Normocytic normochromic and normocytic hypochromic anemia were seen commonly with the worsening of immune status and clinical stage. But there was no statistical significance of any particular anemia in relation to reduction in CD4 count, (Figure 2).

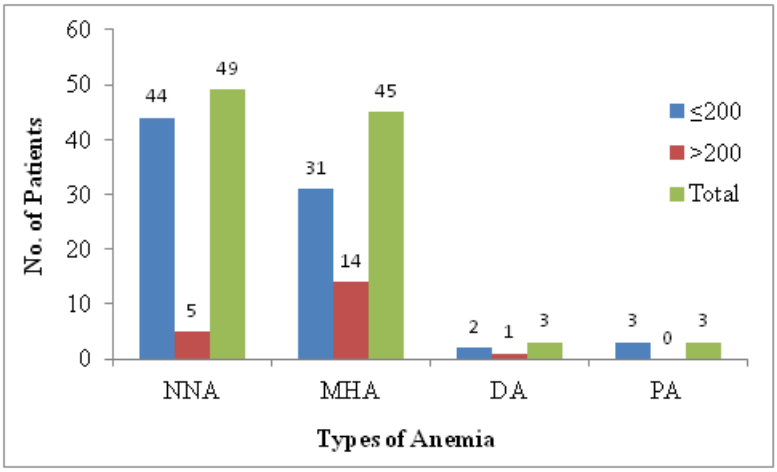

Figure 2: Type of Anemia in relation to CD4 cell count

Discussion

In present study, total 100 HIV positive patients were analyzed with respect to their haemoglobin levels, TLC, Neutrophil, Lymphocyte, platelet and CD4 counts and inference was drawn. The mean age of patients was 33.8 years, majority (74%) were in the age group of 21 to 40 years. Male patients outnumbered the female patients. High risk behavior and migration opportunities may be attributed to high prevalence of HIV among male patients. This demographic data is in concordance with the previous studies [5, 10-12]. Out of 100 patients 23% patients had CD4 cell count >200 cells/mm^3 while 77% had CD4 cell count of less than 200 cells/mm^3. Thus, in this study the incidence of patients with low CD4 count (<200/ul) was high. This higher incidence can be explained on the basis that most of the study population comprised of uneducated, rural population who had little or no knowledge of their illness and hence presented late in the course of their disease.

Among the various symptoms noted in the patients, the most common symptom was fatigue (86%) and fever (80%) followed by weight loss (78%), this increase prevalence could be possibly due to severity of the illness as majority of them were in the WHO clinical stage III and IV. Among the signs, pallor was the most common present in 75% of the patients followed by oral thrush (48%). These findings were compared with the study done by Devi et al [10] and Dhal et al [11].

In current study, anemia defined according to WHO criteria as hemoglobin levels of <13 gm% in males and <12 gm% in females. Out of 80 males, 81.25% (65/80) had anemia while out of 20 females, 90% (18/20) had anemia. Overall prevalence of anemia was 89% in the study population with severe anemia being present in 12% of the subject, this is higher as compared with earlier studies [4,13 ,14]. The higher incidence of anemia in existing study can be explained on the basis of fact that most of the patients comprised of rural population and many of these subjects had pre-existing nutritional anemia. This led to an increased proportion of subjects who were found to be anemic. On comparing CD4 counts with hemoglobin percentage, 89% of cases having Hb% less than 13 gm% had CD4 counts ≤200 cells/mm^3 and only 11 cases were having CD4 counts more than 200 cells/mm^3. The commonest type of anemia noted was normocytic normochromic anemia (49%) which was in accordance to studies done by Patwardhan et al [15] and Kasthuri et al [16]. Normocytic hypochromic anemia was found in 38% of the cases. Seven (7%) cases of macrocytic hypochromic anemia and 3 cases each of dimorphic anemia and pancytopenia were seen. Both the cases of macrocytic anemia were on anti retroviral therapy. In correlation of different type of anemias with respect to clinical stage there was increased possibility of normocytic hypochromic anemia and normocytic normochromic anemia as clinical stage worsened which was also statistically significant.

40% of the patients had total leukocyte counts of less than 4000 cells/ul while 4% had total leukocyte counts of more than 11000 cells/ul, this is less as compared to other studies [14,17]. Of the 40 cases of leucopenia 36 cases had CD4 counts less than 200 cells/mm^3, thus there is a positive correlation between the total leukocyte count levels and the CD4 cell counts. This implies that as the CD4 levels increased, the total leukocyte count also followed a similar trend and showed a rise in the count. Surprisingly granulocytopenia was seen only in 7% of the cases. Out of 100 cases, 30 were having platelet counts below 1.5 lakhs/mm^3 and one case had thrombocytosis. When compared with CD4 count 33.75% (27/80) of the cases had CD4 count below 200 cells/mm^3. Again single case of thrombocytosis had CD4 counts less than 200 cells/mm ^{3}, this is in accordance with studies done by Zon et al [14] and Murphy et al [17]. So, the current study able to establish a positive correlation between the absolute platelet count levels and CD4 cell counts but this correlation was not significant.

Conclusion

The commonest haematological manifestations found were anemia, leucopenia and thrombocytopenia. The frequency and severity of these haematological manifestations increased with decline in CD4 count and had got significant impact on clinical outcomes and quality of life.

The incidence of anemia and lymphopenia were correlates with disease progression. Thrombocytopenia was independent of disease progression. Hence, all HIV patients should be investigated for hematological manifestations and treated accordingly to reduce morbidity and mortality.

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