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Review Article

A STUDY OF BONE MARROW ABNORMALITIES IN HIV POSITIVE PATIENTS WITH PERIPHERAL HEMATOLOGICAL ABNORMALITIES AND ITS CORRELATION WITH CD4 COUNT

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A R T I C L E I N F O

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A B S T R A C T

Background: We are beginning to learn various clinical manifestations and abnormalities in patients with HIV disease in India. There is a possibility that the manifestations in Indian patients may not be the same as reported from other countries like USA and Africa. Hence, it is imperative to methodically observe and follow clinical and laboratory aberrations in such patients in order to improve our diagnostic and therapeutic skills pertinent to HIV/AIDS. Here, we aimed at studying the bone marrow abnormalities in patients with HIV disease and to investigate their association with peripheral blood abnormalities and CD4 count. ***Aim of the Study:*** To correlate the association of Bone marrow abnormalities and CD4 count. ***Material & Methods:*** This study was conducted in Department of General Medicine, Osmania General Hospital, Hyderabad, by applying the inclusion and exclusion criteria, we selected 50 patients for our study among them. ***Results:*** Out of 59 patients 14(28%) were grouped as non AIDS and 36(72%) as AIDS(NACO criteria). Peripheral blood and bone marrow examination was done in 50 patients with either anemia, leucopenia or thrombocytopenia or in their combination. ***Conclusion:*** Peripheral and bone marrow abnormalities are common in HIV related disease and has got significant impact on clinical outcomes and quality of life (QOL). HIV infection affected the highly productive a 21-40 years of age (74%) and predominantly males (80%) in the present study.

INTRODUCTION

HIV is the abbreviation used for the Human Immunodeficiency Virus[1]. HIV attacks the body's immune system. Normally, the immune system produces white blood cells and antibodies that attack viruses and bacteria[2]. The infection fighting cells are called T-cell lymphocytes. Months to years after a person is infected with HIV, the virus destroys all the T-cell lymphocytes[3]. This disables the immune system to defend the body against diseases and tumors. Various infections will be able to develop in the face of decreased immune response. These opportunistic infections take advantage of the body's weakened immune system. These infections, which in normal individual won't cause severe or fatal health problems, will eventually cause the death of the HIV patient.

HIV infection is a multisystem disease, hematological abnormalities are among the most common clinicopathological manifestations of HIV infection[4]. HIV infection is associated often with a wide range of hematological abnormalities, including impaired haematopoiesis, immune mediated cytopenias and coagulopathies, particularly in the advanced stages of the disease[5].

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An Indian study (Patwardhan MS *et al*)[6] revealed anemia as most common hematological abnormality which was normocytic, normochromic type in 61% of patients. Thrombocytopenia was seen in 13% of patients.

Bone marrow abnormalities are found at all stages of HIV disease, increasing in frequency as the disease progresses. Bone marrow findings are highly variable depending on the clinical severity of the immunodeficient state. Bone marrow examination in HIV infected patients is usually performed to evaluate peripheral cytopenias or when systemic infections or malignancies are suspected.

Aim of the Study

To study bone marrow abnormalities in HIV positive patients with peripheral hematological abnormalities and to correlate the association of Bone marrow abnormalities and CD4 count.

MATERIAL & METHODS

A total of 50 patients, study subjects include those who are HIV positive according to NACO guidelines from March 2018 to February 2020 at Osmania General Hospital, Afzalgunj, Hyderabad Telangana State.

Data was collected by using pre-tested proforma meeting the

objectives of the study. Purpose of the study was carefully explained to the patients and consent was taken.

The study population included 50 HIV positive symptomatic or asymptomatic patients. HIV was diagnosed by ELISA method as per NACO guidelines.

Inclusion Criteria

HIV positive patients who has anemia, leukopenia, thrombocytopenia.

Exclusion Criteria

- Patients who has chronic liver disease, chronic kidney disease other than explained by HIV.
- Patients with diagnosed malignancy
- Patient receiving chemotherapy not related to HIV.
- Patient with diagnosed chronic infections or inflammations (TB, SLE etc..)

Statistical Analysis

The data were analyzed using mean, standard deviation, Pearson's chi-square test, student 't' test, Kruskal-Wallis test, fischer exact test. Proportions were compared using chi-square test of significance. A 'p' value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 Hematological Manifestations

Parameters	Non AIDS(n)	AIDS(n)	P-value
Anemia	8	32	0.05
Leucopenia	1	4	0.41
Thrombocytopenia	2	1	0.11
Lymphopenia	3	9	0.05

Table 2 Bone Marrow Findings

Bone Narrow Cellularity	Non - AIDS(n)	AIDS(n)
Normocellular	10	27
Hypocellular	1	3
Hypercellular	3	6

Table 3 Myelodysplasia in non AIDS and AIDS groups

Myelodysplasia in B.M in HIV patients	Non AIDS(n)	AIDS(n)	TOTAL
No dysplasia	11	23	34
Granulocytic	2	11	13
Erythroid	1	1	2
Megakaryocytic	0	1	1

Table 4 Prevalence of anemia among HIV Patients with various Myelodysplastic changes

Hemoglobin	Granulocytic(n)	Erythroid(n)	Megakaryocytic(n)	P-value
Normal	2	1	0	0.04
Decreased	12	2	0	

Table 5 CD4 count among HIV patients with various myelodysplastic changes

CD4 Count	Granulocytic (n)	Erythroid (n)	Megakaryocytic(n)	P-value
<200	1	0	0	
200 - 350	6	0	1	0.01
351 - 500	1	1	0	

Table – 6 TLC among HIV Patients with Various Myelodysplastic Changes

Total Leucoyte Count	Granulocytic(n)	Erythroid(n)	Megakaryocytic(n)	P-value
Normal	10	2	0	<0.01
Decreased	5	0	0	

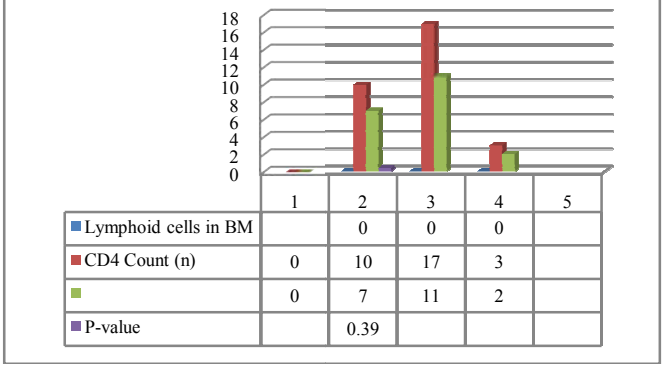
Table 7 Various hematological and bone marrow parameters among non aids and aids groups

Parameters	non Aids(n=14)	Aids(n=36)	P-value
Hemoglobin (gm/dl)	11.2±1.52	10.42±1.83	0.05
Packed Cell Volume(ml%)	22.01±16.01	27.32±12.36	
Total RBC count (mill/mm^3)	4.40±0.35	3.08±0.92	
MCV(fL)	80.52±5.46	81.90±5.62	
MCH(pg)	27.35±2.72	27.61±1.82	
Reticulocyte count(%)	0.82±0.25	0.95±0.23	
TLC count(cells/mm^3)	7586.02±1520.52	7452.21±1990.11	0.04
Lymphocyte count (%)	26.35±11.52	24.32±10.25	0.54
Neutrophil(%)	66.52±11.52	69.75±11.82	
Eosinophil(%)	4.65±7.36	2.95±3.42	
Monocyte(%)	1.77±2.25	2.04±2.36	
Basophil(%)	0.6±0.2	0.5±0.12	
Absolute Neutrophil count X 10^9/L	5.11±1.42	5.04±1.76	
Absolute lymphocytic count X 10^9/L	2.08±9.26	1.78±8.32	
Absolute eosinophil count X 10^9/L	3.86±5.68	2.21±2.65	
Platelets (lacs/ mm^3)	1.92±0.62	1.93±0.48	0.95
CD4 count/pl	264.21±98.42	176.52±110.92	0.01
Plasma cells(%) in bone marrow	3.88±2.22	5.02±2.83	0.18
Lymphoid cells(%) in bone marrow	14.52±8.32	11.20±11.01	0.31

Table 8 Myelodysplasia and Its Correlation WITH CD4+ T-Lymphocyte Count

Dysplasia	CD4 Count <200/l	CD4 Count >200 ml	P-Value
No	21	11	0.05
Yes	9	7	

Graph - 1 : Lymphoid Cells In Bone Marrow And Its Correlation With Cd4 Count



DISCUSSION

Clinical presentation in patients with HIV/AIDS is diverse and it may arise from involvement of almost any body system. Hematological abnormalities are not uncommon in HIV/AIDS. Large percentage of patients with HIV has anemia, leucopenia and thrombocytopenia during the course of disease.

According to Paradela A *et al*[7], 90 % of patients are reported to have bone marrow abnormalities during the course of disease in the form of increased cellularity, dysplasia or granulomatous involvement. 'invitro' studies have shown that HIV can directly infect the hematopoietic and mesenchymal cells and can influence their activity. The exact mechanism of HIV induced bone marrow and peripheral blood changes are not known, however, these are possibly due to either direct effect of HIV, nutritional deficiencies, opportunistic infections or bone marrow suppression by antiretroviral therapy, and other drugs used in the treatment of HIV infection.

Bone marrow aspiration and biopsy is generally needed in

patients presenting with hematological abnormalities where the cause could not be discerned. The present study involved 50 patients of HIV / AIDS who had anemia, leucopenia, and thrombocytopenia. Clinico- epidemiological features are presented and are similar to the data reported from India and other countries. Three fourths (72%) of our patients had clinical AIDS while the rest (28%) were either asymptomatic or symptomatic but did not fit into criteria of AIDS[8].

The common age group of patients was 20-42years with a range of 20-65 years. Male to female ratio was 4:1.

Eighty percent of patients had anemia and its prevalence was significantly higher in patients with AIDS than in non AIDS (p=0.05). The most common type of anemia was normocytic normochromic, Six percent (3 Patients) in our study had macrocytic anemia and all were on ART.

Leucopenia was observed in 11.11% of AIDS and 7.14% of non AIDS and all patients showed granulocytic dysplasia, emphasizing that the latter was a major cause for leucopenia. Lymphopenia was seen in 21.1% of Non AIDS and 27.27% of AIDS patients. Prevalence of thrombocytopenia in patients with HIV/AIDS has been variably reported in 13 % to 61% cases. Our study revealed a prevalence of 6% and it was significantly different in AIDS and non AIDS group.

Bone marrow was particularly examined for cellularity, fibrosis, dysplasia and for the evidence of granuloma. Previous reports indicate that most of the cases with HIV have hypercellular bone marrow.

However present study revealed bone marrow to be normocellular in 74%, hypocellular in 8% and hypercellular in 18% patients. The difference is difficult to explain but it is likely to be due to different cohort of patients included in various studies. This is in accordance with reports by Treacy *et al*[9]. Myelodysplastic changes due to HIV can explain normocytic or macrocytic anemia which is common in patients with AIDS.

Myelodysplastic changes in bone marrow were found in 32.0% cases as compared to 50- 90 % reported in literature. Myelodysplasia was significantly more common in AIDS (36.1%) than in non-AIDS (21.14%), (p = 0.05). Cells most commonly showing dysplasia in our study were granulocytes (26%) followed by erythroid in 4.0% and megakaryocytes in 2%. Dysplastic changes observed in granulocytic series were cytoplasmic vacuolations (60%), nuclear dysmorphism (30%), monocytoid cells (1%) and others (1%); in erythroid series were irregular nuclear outline and basophilic stippling (66.67%), megaloblastoid changes (33.33%) and in megakaryocytic series were hypolobulation (100%).

Various studies have reported that plasma cells in bone marrow are increased in all patients with HIV infection. We observed increased number of plasma cells in the marrow of 57.0% of Non AIDS and 69.0% of AIDS patients. Mean percent of plasma cells in bone marrow sample of Non AIDS was 3.88 ± 2.22 and 5.02 ± 2.83 in AIDS, however, this difference was not statistically significant.

Lymphoid cells were found to be decreased in the marrow in 35% of non AIDS and 54% of AIDS patients. Mean count of lymphoid cells was 14.52 ± 8.32 percent in Non AIDS and 11.20 ± 11.01 percent in AIDS patients. However, it is interesting to note that decreased lymphoid cells in bone marrow was more common in AIDS patients compared to non-AIDS. Further studies are needed to define the diagnostic and prognostic significance of decreased lymphoid cells in bone marrow of non-AIDS and AIDS patients. However, we hypothesize that decrease in marrow lymphoid cell pool is consequent upon the destruction of lymphoid cells by HIV.

CONCLUSION

1. Peripheral and bone marrow abnormalities are common in HIV related disease and have got significant impact on clinical outcomes and quality of life (QOL).
2. HIV infection affected the highly productive a 21-40 years of age (74%) and predominantly males (80%) in the present study.
3. The most common symptom was fatigue (86%) and fever (80%), and among the signs pallor (75%) and oral thrush (48%) were common. This may be due to the advanced clinical disease status and worsening immunity (88% of cases were in clinical stages III or IV). But there was no statistical significance in relation to CD4 count.
4. Leucopenia was seen in 40 cases (40%) which had significant correlation with CD4 count (p = 0.019).
5. Thrombocytopenia was seen in 30 cases (30%) in correlation with CD4 count. But there was no statistical significance (p = 0.262).
6. Bone marrow study showed normocytic 37 cases, and hypercellular in 4 cases and hypocellular in 9 cases.
7. Myelodysplasia was more common in AIDS more than in NONAIDS group and frequently associated with anemia and with advanced disease (CD4 count <200/microL.

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