

CLINICAL PROFILE OF ANAEMIA AMONG HIV INFECTED PATIENTS AND ITS CORRELATION WITH CD4+ COUNT

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ABSTRACT: BACKGROUND: Various haematological manifestations are seen in HIV patients ranging from anaemia, thrombocytopenia, leucopenia, coagulation abnormalities and malignancies. Anaemia is recognized to be a significant clinical problem in patients with HIV infection and AIDS. Although anaemia can occur at any stage of HIV infection, its frequency and severity are positively correlated with progression of the disease. Anaemia appears to be independently associated with decreased survival in patients with HIV infection and AIDS. **AIMS AND OBJECTIVES:** to study the clinical profile of anaemia in HIV patients and to know its correlation with the CD4 count. **RESULTS:** Of the 43 patients studied, 34 were on HAART and 9 were treatment naïve subjects. Severe anaemia was detected in 23 subjects, moderate anaemia in 16 and mild anaemia was seen in 4 subjects. The mean haemoglobin of the study population was 7.57 gm%. 16 of the anaemic individuals had CD4+ count <200 cells/mm³. 21 patients (48.83%) had Zidovudine induced anaemia, 11 patients (25.58%) had anaemia of chronic disease, 8 patients (18.60%) had iron deficiency anaemia, 2 patients (4.65%) had both Zidovudine induced and iron deficiency anaemia and 1 patient (2.3%) had megaloblastic anaemia. **CONCLUSIONS:** Severity of anaemia significantly correlated with the CD4+ count in this study. Zidovudine induced anaemia was the most common type of anaemia, with a prevalence of 48.83%. Bone marrow was found to be normocellular in 67.5% of the study population and had no correlation with CD4+ count.

KEYWORDS: Anaemia, HIV/AIDS, CD4+count.

INTRODUCTION: Anaemia is recognized to be a significant clinical problem in patients with HIV infection and AIDS¹ Although anaemia can occur at any stage of HIV infection, its frequency and severity are positively correlated with progression of the disease.^(1,2) Various risk factors for HIV-related anaemia have been identified, including clinical AIDS, CD4+cell count <200 cells/mm³, high plasma viral load, female sex, African American ethnicity, and Zidovudine use³. Anaemia appears to be independently associated with decreased survival in patients with HIV infection and AIDS.^{3,4} This association has been consistent in many different types of studies, despite differences in patient populations, treatment regimens and definitions of anaemia.⁴

Research Questions:

1. What is the clinical profile of anaemia in HIV patients?
2. What is the correlation with their CD4+ count?

METHODOLOGY:

Type of study:	Case series.
No. of patients:	43.
Duration of study:	1 st January 2012 to 30 th December 2012.

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Data was entered in a pretested proforma consisting of 49 questions:

- The first 4 points related to particulars of the patient.
- Next 4 related to symptoms that the patient reported with to the Out- patient department.
- 2 related to general physical examination.
- 2 for per abdominal examination.
- The next 16 points were for complete blood count examination and peripheral smear.
- The next 6 questions related to bone marrow examination.
- 11 questions were for laboratory investigations.
- The next two points were related to Anti-Retroviral Treatment (ART).
- One point regarding transfusion of blood/ blood product.
- The last question related to improvement following institution of ART.

Inclusion Criteria:

1. Confirmed case of HIV infection.
2. Age between 18 years to 70 years.

Exclusion Criteria:

1. Patients diagnosed with tuberculosis, hepatitis B and hepatitis C.
2. Patients with gastrointestinal bleed.
3. Patients on drugs which may lead to bone marrow suppression:
 - a. Cytotoxic drugs in cancer chemotherapy, alkylating agents, anti-metabolites and antimetabolites.
 - b. Chloramphenicol.
 - c. Anti-protozoals: quinacrine, chloroquine and mepacrine.
 - d. Nonsteroidal anti-inflammatory agents: phenylbutazone, indomethacin, ibuprofen, sulindac and aspirin.
 - e. Anti convulsants: hydantoin, carbamazepine, felbamate.
 - f. Heavy metals: gold, arsenic, bismuth and mercury.

METHODOLOGY: A total of 50 HIV-infected subjects were included in the study. Data on age, gender, weight, height, duration of HIV infection, receipt of HAART including treatment regimen and duration of HAART, any h/o blood transfusion was collected in a pretested proforma meeting the objectives of the study. A detailed history, clinical examination and necessary investigations were recorded. Body mass index (BMI) was calculated as weight in kg /m.²

Detection of HIV infection and confirmation: For the detection and confirmation of HIV infection we employed the following three tests. The diagnosis of HIV infection was made when all the three tests were positive:

1. HIV 1/2 Triline card test: Immuno-chromatographic based assay for detection of antibodies to HIV-1 and HIV-2 in human serum or plasma. It demonstrates a sensitivity and specificity of 100%.
2. SD Bioline HIV 1/2 3.0: It is an immuno-chromatographic (rapid) test for the qualitative detection of antibodies to HIV-1 and HIV-2. It demonstrates a sensitivity of 100 % and specificity of 99.8%.

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3. HIV 1/2 rapid test kit (TRISPOT): It is an immuno-concentration based assay which employs r-proteins for the detection of antibodies to HIV-1 and HIV-2 in human serum or plasma. These proteins correspond to the highly antigenic structural and non-structural proteins of HIV and offer the advantage of high degree of sensitivity and specificity due to multiple epitopes. It demonstrates a sensitivity and specificity of 100%.
- The patients diagnosed to have HIV were divided into 4 clinical stages using the 'WHO clinical staging for HIV/AIDS for adults and adolescents (2006)⁵ according to the NACO guidelines. For the clinical staging of HIV infection, screening of opportunistic infections and recognizing HIV related clinical events, presumptive and definitive criteria recommended by WHO were employed.
 - Duration of HIV infection was defined from the first positive HIV-test result.
 - HAART was defined as a regimen containing at least three antiretroviral drugs in accordance with the NACO guidelines. Antiretroviral treatment analysis included the type of drugs used and the duration of antiretroviral treatment. The antiretroviral drugs evaluated in our study included zidovudine, stavudine, lamivudine, nevirapine and efavirenz. None of the participants in our study were on second-line antiretroviral therapy regimens.
 - Receipt of HAART refers to patients who were receiving HAART at the time of study or who had received HAART previously.

Estimation of CD4+ Count: CD4+ cell count was done using the Becton and Dickinson FACS count system which works on the principle of flow cytometry. The CD4+ cell count was measured in cells per cubic millimetre.

Anaemia: Anaemia was defined as haemoglobin (Hb) <12gm% for both males and females. Severity of anaemia was grouped as mild, moderate and severe. Mild with Hb 10–12 gm%, moderate with Hb 8–10 gm% and severe with Hb <8gm%:

- a. Anaemia was labelled as zidovudine-induced (ZIDO) if there were no other identifiable causes after the work-up, if a temporal relation was determined with the introduction of the drug, and if recovery was obtained following cessation of the drug.
- b. Iron deficiency anaemia (IDA) was diagnosed based on the serum iron levels.
- c. Anemia of chronic disease (ACD) was when patient had a decreased serum iron levels with decreased TIBC and increased in marrow iron stores.

The study population was divided into three groups depending on CD4 count with CD4 count <200 cells/mm³, CD4 count 200 cells/mm³–500 cells/mm³ and CD4 count >500 cells/mm³. The prevalence of various haematological manifestations were compared between these groups.

Statistical analysis was performed using SPSS software 14.0 version (USA). Data with normal distribution were expressed as mean±standard deviation. For statistical analysis Pearson correlation test, Chi Square test, Student's t-test and Mann-Whitney U test were used wherever appropriate. Pearson correlation test was applied to determine correlation between CD4 cell counts and haematological manifestations. p value <0.05 was considered to be statistically significant.

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RESULTS: Anaemia was graded as mild, moderate and severe. Among the 43 study subjects, 34 patients were on HAART and 9 were treatment naïve. 6 patients had mild anaemia, 14 had moderate and 23 patients had severe anaemia.

16(37.2%) subjects had a CD4+count of < 200 cells/mm³ of which 11 had severe anaemia, 17 (39.53%) had a CD4+count between 200-500cells/mm³ of which 7 had severe anaemia and the remaining 10(23.25%) patients had a CD4+count of > 500 cells/mm³ of which 5 had severe anaemia.

14 of the test subjects had hypocellular marrow and the remaining had normocellular marrows. 12 subjects had decreased iron staining grade. 3 subjects were also seen to have increased iron staining on bone marrow studies.

Of the 43 patients with anaemia, 21 patients(48.83%) had zidovudine induced anaemia, 11 patients (25.56%) had anaemia of chronic disease, 8 patients (18.60%) had iron deficiency anaemia, 2 patients (4.65%) had both zidovudine induced and iron deficiency anaemia and 1 patient (2.3%) had megaloblastic anaemia.

11 patients had associated neutropenia and only one of the subjects had thrombocytopenia.

DISCUSSION: The clinical spectrum of HIV infection in India is different from that in the rest of the world. There is also great variability within India as well. Haematological disorders like anaemia are the second commonest cause of morbidity and one of the common causes of mortality in HIV patients. (2) The mean haemoglobin of the study population was 7.57gm%.

Of the patients with anaemia, 53.48% had severe anaemia and 23.25% of the anaemic patients needed blood transfusion. Attili SVS et al in the Varanasi study⁶ found severe anaemia in 35.5% of the patients. The high prevalence of severe anaemia in this study could be due to the background anaemia in normal population and their referral to the Medicine department of a tertiary hospital.

Of the patients who were anaemic, 14 patients (32.58%) were symptomatic. 8 patients (18.6%) presented with dyspnoea and 6 patients (13.95%) presented with both dyspnoea and palpitation. No patient had hepatosplenomegaly. The rest were detected incidentally and referred to the Medicine out-patient department.

Of the 16 patients with CD4 count < 200cells/mm,³ 68.75% (11 patients) had severe anaemia, of the 17 patients with CD4 count 200–500cells/mm,³ 35% (7 patients) had severe anaemia and of the 10 patients with CD4count > 500cells/mm³ 30% (5 patients) had severe anaemia. The severity of anaemia increases with fall in CD4 count. Similar trend was noted in other studies as in Dikshit B et al,⁷ Attili SVS et al,⁶ Akinbami A et al,⁸ Spivak et al.⁹

Among the patients with anaemia (43 patients), majority (21 patients; 48.83%) of the patients had Zidovudine induced anaemia, followed by anaemia of chronic disease seen in 11 patients (25.58%), followed by iron deficiency anaemia in 8 patients (18.60%), 2 patients (4.65%) had both Zidovudine induced and iron deficiency anaemia both and 1 patient (2.3%) had megaloblastic anaemia. Similar result was found in a study conducted by, Suresh Venkata Satya Attili et al,⁶ were as study conducted by Byomakesh Dikshit et al⁷ found anaemia of chronic disease as the most common subtype followed by iron deficiency anaemia.

Among the 21 patients with Zidovudine induced anaemia, majority (13 patients) were females; majority of the patients (16 patients) developed anaemia within 6 months of starting Zidovudine based regimen and the mean duration of development of anaemia was 3.94 months.

These results were comparable to study conducted by Agarwal D et al.¹⁰

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The mean CD4+count in patients with Zidovudine induced anaemia was 255.6cells/mm³ and their mean BMI was 18.99kg/m.² The mean CD4+ count and the mean BMI in patients with Zidovudine induced anaemia was lower than the study population.

Of the 43 HIV patients, 29 patients (67.44%) had normocellular bone marrow and 14 patients (32.56%) had hypocellular marrow. Comparable results were found in other studies. A study conducted by Tripathi AK et al in KGMU Lucknow¹¹ found that bone marrow was normocellular in 74.55% and hypocellular in 7.27% of patients. Another study conducted by Agarwal D et al¹⁰ found normocellular in 66.6% of the patients.

CONCLUSIONS: Severity of anaemia significantly correlated with the CD4 count in this study and severity of anaemia increased with fall in CD4+ count.

Zidovudine induced anaemia was the most common type of anaemia, with a prevalence of 48.83%.

Bone marrow was found to be normocellular in 67.5% of the study population and had no correlation with CD4 count.

LIMITATIONS:

1. All subjects selected were from a tertiary care centre.
2. Small study group and without matched controls.

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TREATMENT GROUPS	NUMBER OF PATIENTS WITH ANAEMIA
HAART	34
TREATMENT NAÏVE	9
TOTAL	43

Table 1: Distribution patients based on whether on treatment or naïve to treatment

SEVERITY OF ANAEMIA	NUMBER OF PATIENTS
MILD (10-12gm %)	6
MODERATE (8-10gm %)	14
SEVERE (< 8gm %)	23
TOTAL	43

Table 2: Distribution of patients based on grade of anaemia

CD4+ COUNT (cells/mm ³)	ANAEMIA
< 200	16
200 -500	17
>500	10
TOTAL	43

Table 3: Distribution of patients based on CD4+ count

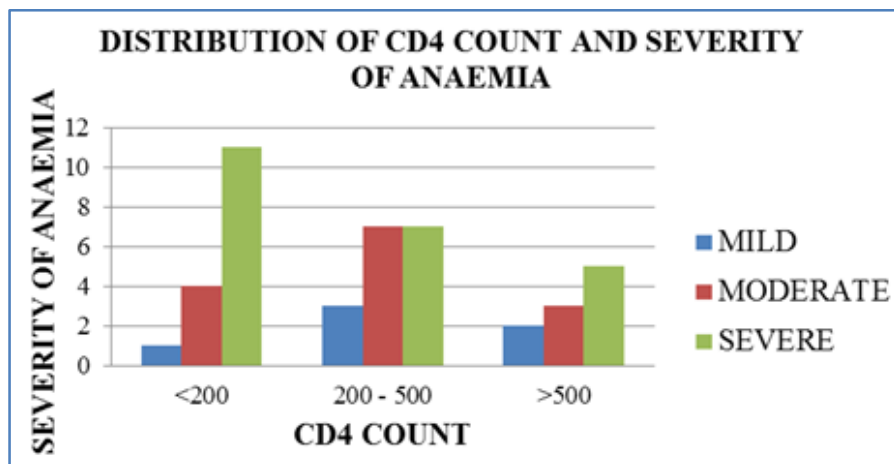
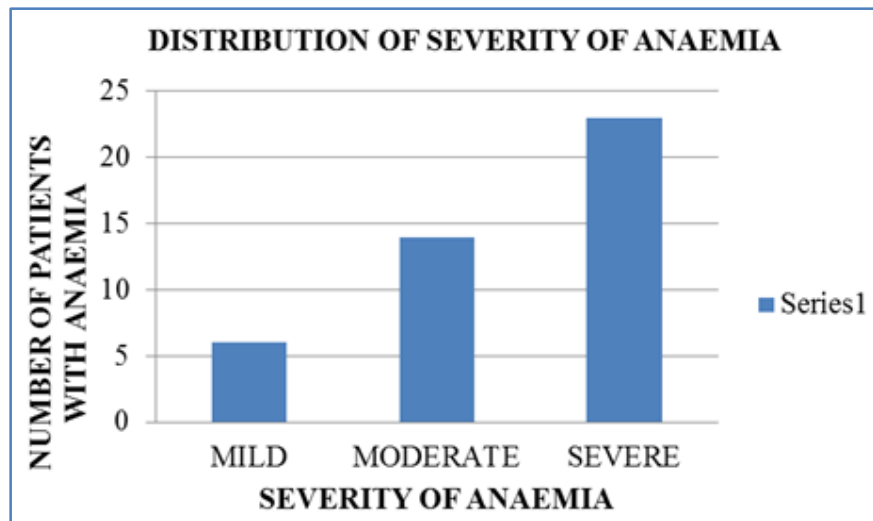
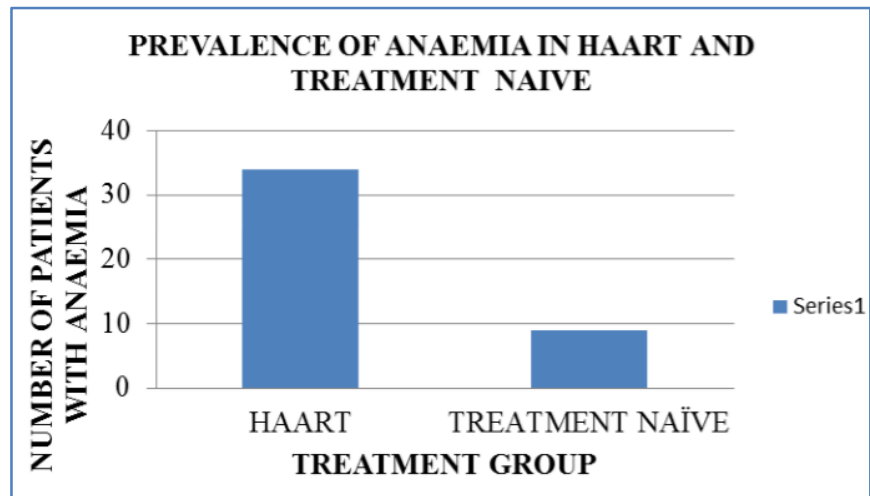
CD4+ COUNT(cells/mm ³)	SEVERITY OF ANAEMIA			TOTAL
	Mild	Moderate	severe	
< 200	1	4	11	16
200 -500	3	7	7	17
>500	2	3	5	10
TOTAL	6	14	23	43

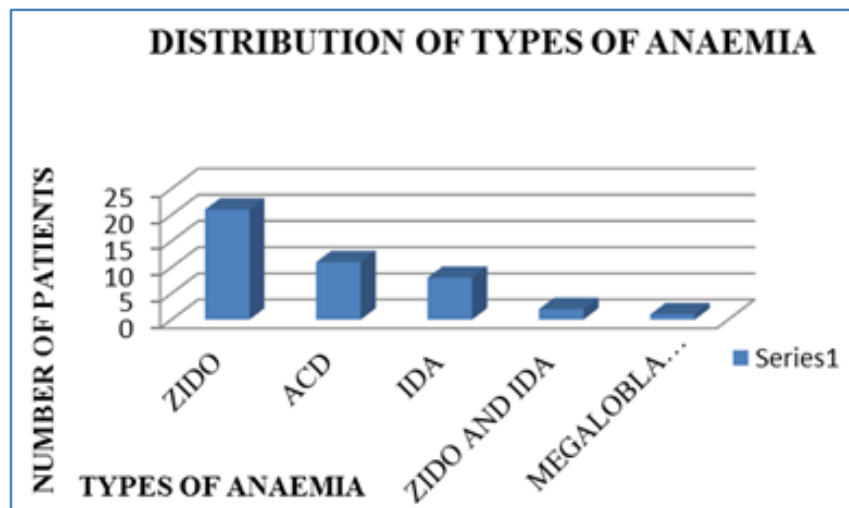
Table 4: CD4+ count and grade of anaemia

TYPES OF ANAEMIA	NUMBER OF PATIENTS
Zidovudine induced anaemia	21
Anemia of chronic disease	11
Iron deficiency anaemia	8
Zidovudine induced anaemia and iron deficiency anaemia	2
Megaloblastic anaemia	1
TOTAL	43

Table 5: Distribution of patients according to the aetiology of anaemia

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