



## Hematological Profile Of People Living With HIV/AIDS Before Initiation Of Antiretroviral Therapy- A Cross Sectional Study

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### Abstract

**Background:** Hematological abnormalities are frequently reported in patients with HIV infection, in patients without antiretroviral therapy, and during the advanced stages of the disease. The present study was undertaken to analyse the hematological profile of people living with HIV/AIDS before initiation of antiretroviral therapy and to identify the possible correlation between WHO clinical stage and hematological abnormalities if any.

**Method:** Total 140 diagnosed HIV/AIDS inpatients and outpatients of either sex, aged >12 years who were not started antiretroviral therapy were included in the study. Patients were interviewed and investigated for hematological profile. CD4 count done by flow cytometric analysis. Patients were staged as per the WHO clinical staging given by the National AIDS control organization (NACO).

**Results:** The commonest hematological abnormalities in the study participants were anemia (78.57%) and leucopenia, especially lymphocytopenia (36 patients). The analysis of association between WHO staging and hematological abnormalities revealed statistical significance with anemia ( $p < 0.05$ ), thrombocytopenia ( $< 0.0001$ ), leucopenia, lymphocytopenia ( $p = 0.006$ ) and CD4 count ( $p = 0.02$ ). Anemia, leucopenia, thrombocytopenia, and lymphopenia were increased as CD4 count decreases and advanced WHO staging.

**Conclusion:** Anaemia is a very important and common presentation in HIV infection which increases with advanced clinical stages of disease. HIV patients are recommended to check up their CD4 counts regularly and to start HAART when it is appropriate in order to decrease the prevalence of anemia. However, patients with HIV infection should be investigated and treated for hematological abnormalities to reduce the morbidity of the patients.

**Keywords:** Hematological abnormalities; HIV infection; Antiretroviral therapy; WHO staging; Anemia; Lymphocytopenia

### Introduction:

The HIV epidemic is a convincing illustration of the balance between the power of science and the humanism of modern medicine. The epidemic is so serious that between 1981 and 2000, 21.8 million people had died of HIV/AIDS [1]. In India, 2.14 (1.59–2.84) million people are estimated to be living with HIV infection [2]. The national level HIV prevalence among adults in India, estimated to be 0.22% (0.16–0.30%) in year 2017, has shown a downward trend over the last few years. However,

this downward trend at the national level masks the variations at the regional, state and district levels in the country [2, 3].

Clinically significant hematologic abnormalities are common in HIV infection [4]. These abnormalities are due to impaired hematopoiesis, immune mediated cytopenias and altered coagulation mechanisms. These abnormalities may occur because of HIV infection itself, as sequelae of HIV related opportunistic infections or malignancies or because of

therapies used for HIV infection and associated conditions [5].

Disorders of the hematopoietic system including lymphadenopathy, anemia, leucopenia, and thrombocytopenia are common throughout the course of HIV infection and may be the direct result of HIV, manifestations of secondary infections and neoplasms, or side effects of therapy. Direct histologic examination and culture of lymph node or bone marrow tissue are often diagnostic. A significant percentage of bone marrow aspirates from patients with HIV infection have been reported to contain lymphoid aggregates, the precise significance of which is unknown. Initiation of HAART will lead to reversal of most hematologic complications that are the direct result of HIV infection [6].

Although, there is a lot of burden of HIV infection in our territory and tertiary care hospital. Despite this, so much less study done about HIV infection. The availability of various categories of diagnostic and monitoring techniques for HIV/AIDs, the costs of it are still unaffordable to several people in the resource poor settings. Early identification of the hematologic abnormalities would lead to appropriate planning of treatment strategies. Hence, the present study was conducted to know the pattern of these hematologic abnormalities among people living with HIV/AIDS (PLHA).

### Materials and Methods:

The present cross-sectional study was conducted in total 140 diagnosed HIV/AIDS inpatients and outpatients of either sex, aged >12 years who were not started antiretroviral therapy in the Department of Medicine, at rural tertiary care hospital in central India during a period of 24 months from 1st November 2018 to 31st October 2020. Institutional Ethical Committee approval was taken prior to the study. Patients with chronic infection like tuberculosis, chronic kidney disease, worm infestations, drug intake (phenytoin), chronic alcoholics, haemoglobinopathies and patients on anti-retroviral therapy were excluded from the study.

At the time of registration, the baseline information was taken especially with respect to sociodemographic factors, clinical findings, and other investigations. Written informed consent was taken in the language respondent/relatives understand i.e.,

Marathi/Hindi which was signed/thumb printed by the respondent/relatives. Data collection was done with help of detailed examination. Predesigned, pre-tested, structured questionnaire (proforma) was used for interview and examination purpose. Study subjects were interviewed and investigated for Hb%, packed cell volume (Hematocrit), MCV, MCHC, red cell distribution width (RDW), total count, differential count, ESR, platelet count and mean platelet volume. CD4 count done by flow cytometric analysis were obtained. They were staged as per the WHO clinical staging given by the National AIDS control organization (NACO).

- Stage I - Asymptomatic- Persistent generalized lymphadenopathy and - Performance scale 1: asymptomatic normal activity.
- Stage II - Wt. loss < 10% of body weight, Minor mucocutaneous manifestation (seborrheic dermatitis, fungal nail infection, recurrent oral ulcers, angular cheilitis), Herpes zoster (within last 5 years), Recurrent upper resp. infection (bacterial sinusitis) and Performance scale 2: Symptomatic, normal activity.
- State III - Wt. loss > 10% body weight unexplained chronic diarrhoea >1-month unexplained fever (intermittent/continuous) > 1-month, Oral Thrush, Oral hairy leukoplakia, Pulmonary TB within past 1-year, Severe bacterial infection (pneumonia, pyomyositis) and Performance Scale 3: bed ridden for <50% of day in last 1 month.
- Stage IV - HIV wasting syndrome (>10% BW loss + Unexplained, fever (or) Unexplained diarrhoea >1-month chronic weakness), Pneumocystis carinii pneumonia, Toxoplasmosis of brain, Cryptosporidiosis with diarrhoea >1 month, Cryptococcosis (extra pulmonary), Cytomegalo viral disease of organ other than liver, spleen and lymph node, Herpes simplex infection, Mucocutaneous, >1 month (or) visceral, Progressive multifocal leukoencephalopathy and Disseminated endemic mycosis, histoplasmosis, Coccidioidomycosis

### Data Analysis:

The quantitative data were expressed as mean, median, mean  $\pm$  SD, standard deviation. Qualitative type of data was expressed as percentage or

proportion. Data was analysed using SPSS (Statistical Programme for Social Sciences) software 21 version, OpenEpi Software Version 2.3. For quantitative type of data test of significance applied was student t test and for Qualitative data Chi square test was applied. P<0.05 was considered to be statistically significant.

**Observations And Results:**

A total of 140 patients were included in the study, of them 78 (55.71%) were males and 62 (44.29%) were females. Majority of patients (35.71%) belonged to 41 to 50 years age group with mean age of patients was 39.22±11.68 years, ranged from 14 to 72 years, (P=0.26). The maximum patients belonged to WHO stage II (35%), followed by stage III (34.28%) as shown in table 1.

**Table 1: Age and WHO staging distribution**

Parameters		Gender		Total
		Male	Female	
Age (In years)	13-20	06	01	07 (5%)
	21-30	12	14	26 (18.57%)
	31-40	20	18	38 (27.14%)
	41-50	26	24	50 (35.71%)
	51-60	09	03	12 (8.57%)
	>60	05	02	07 (5%)
WHO staging	I	20	10	30 (21.42%)
	II	25	24	49 (35%)
	III	27	21	48 (34.28%)
	IV	06	07	13 (9.28%)

Majority of cases showed generalised weakness (129), followed by weight loss (69), diarrhoea (56) and fever (55) as depicted in figure 1. One patient may have one or more than one clinical feature.

Most of the patients (41.42%) had oral ulcers, 40% had diarrhoea, 35.71% had respiratory infection, 3.57% had oral candida and 2.86% had herpes

infection. As one patient may have one or more than one opportunistic infection, hence the total is exceeding sample size. However, on general examination 75.71% had raised pulse rate, 7.85% had lymphadenopathy, 3.57% icterus, 2.14% each had hepatomegaly and splenomegaly respectively.

**Figure 1: Clinical features distribution**

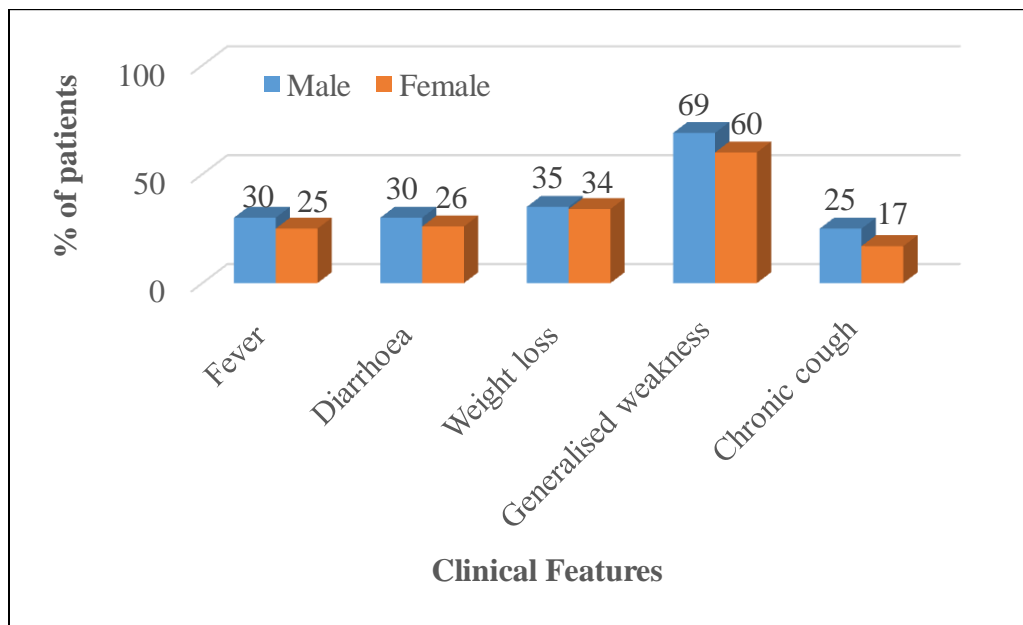


Table 2 show the mean values and ranges of various hematological parameters among people living with HIV/AIDS (PLHA).

**Table 2: Hematological profile of patients**

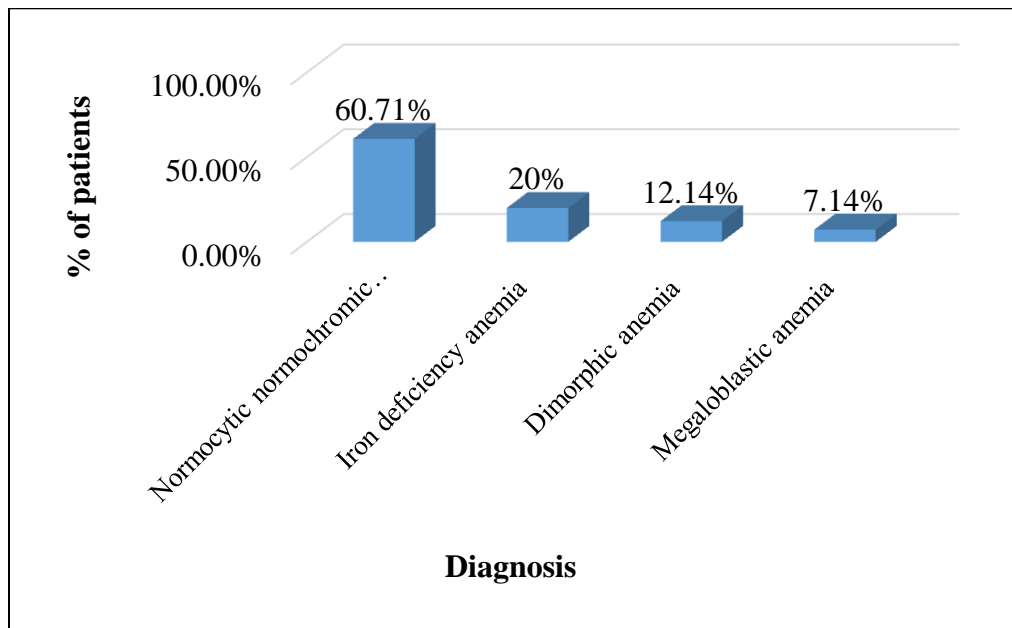
Hematological parameters	Mean ± SD	Ranged
Total leucocyte count (cells/mm <sup>3</sup> )	6813.57±2755.17	1600 to 17400
Neutrophil count (%)	60.95±12.47	-
Lymphocyte count (%)	29.45±11.64	-
Monocyte count (%)	5.34±2.5	-
Eosinophil count (%)	4.12±3.23	-
Platelet count (Lakh/mm <sup>3</sup> )	2.52±1.03	0.29 to 6.6
Platelet volume in (fL)	9.18±1.05	3.6 to 12.6
CD4 count (cells/microliter)	259.39±216.38	4 to 953
Hemoglobin value (g/dl)	10.75±2.92	1.4 to 21.7
PCV (Hematocrit)	34.37±8.42	12.7 to 65.9

MCV (fL)	85.81±11.11	51.8 to 128.7
MCHC (g/dl)	32.38±1.89	24.9 to 35.4
RDW (%)	15.02±2.35	11.5 to 24.3

Mean corpuscular volume (MCV); Mean corpuscular haemoglobin concentration (MCHC); Red Cell Distribution Width (RDW)

Majority 60.71% had normocytic normochromic appearance on peripheral smear examination, followed by 20% showed Microscopic Hypochromic with anisopoikilocytosis, pencil cell, as depicted in figure 2. ESR at 1hr was >15 (mm/h) in majority (69.23%) of males while ESR was >20 (mm/h) in majority (72.48%) of females.

**Figure 2: Peripheral smear distribution**



The analysis of association between WHO staging and hematological abnormalities revealed statistical significance with anemia ( $p < 0.05$ ), thrombocytopenia ( $< 0.0001$ ), leucopenia, lymphocytopenia ( $p = 0.006$ ) and CD4 count ( $p = 0.02$ ) as shown in table 3.

**Table 3: Correlation of WHO clinical stage with hematological abnormalities and anemia subjects**

Hematological parameters		WHO staging				P value
		I	II	III	IV	
leucocyte (WBC)	Leucocytopenia	05	07	08	04	0.46
	Neutropenia	03	07	02	00	0.23

Abnormalities	Lymphocytopenia	06	09	13	08	0.006*
	Monocytopenia	13	12	21	05	0.1
	Eosinophilia	07	12	12	05	0.53
Platelet count (Lakh/mm <sup>3</sup> )	≤1.65	02	09	14	12	<0.0001*
	1.66-4.15	25	37	27	01	
	>4.15	03	03	07	00	
Mean Platelet Volume (fL)	<9	14	19	23	04	0.61
	9-12.95	16	30	25	09	
CD4 Count (cells/microliter)	<200	08	23	31	11	0.02*
	201-500	17	16	11	02	
	>500	05	10	06	00	
Packed cell volume (%) (Male)	<38.8	08	15	20	06	0.1
	38.8-46.4	09	08	04	00	
	>46.4	03	02	03	00	
Packed cell volume (%) (Female)	<35.4	09	14	19	06	0.19
	35.4-44.4	01	09	02	01	
	>44.4	00	01	00	00	
MCV (fL)	≤79	07	06	13	04	0.52
	79.1-98.3	19	37	32	08	
	>98.3	04	06	03	01	
MCHC (g/dl)	≤32.3	11	15	15	05	0.9
	32.4-35.9	19	34	33	08	

RDW (%)	11-14	17	28	19	05	
	>14	13	21	29	08	
Anemia subjects	Male	11	16	24	06	0.01*
	Female	10	17	19	07	0.05*

The association between CD4 count and leucocyte (WBC) abnormalities revealed statistical significance with leukocytopenia (p=0.02) and lymphocytopenia (p=0.03) as shown in table 4.

**Table 4: CD4 count wise distribution of leucocyte (WBC) abnormalities**

Leucocyte (WBC) abnormalities		CD4 count			P value
		<200	201-500	>500	
Leucocyte (WBC) Abnormalities	Leucocytopenia	18	06	00	0.02*
	Neutropenia	08	03	01	0.55
	Lymphocytopenia	25	09	02	0.03*
	Monocytopenia	26	17	08	0.97
	Eosinophilia	20	11	03	0.46

**Discussion:**

In the present study hematological abnormalities were analysed in 140 HIV positive patients before initiation of antiretroviral therapy. Most of the patients (35.71%) belonged to 41 to 50 years age group with mean age of patients was 39.22±11.68 years which is comparable with the previous studies [7-10]. Majority (55.71%) were males and 44.29% were females. On WHO staging majority 34.28% were in stage II, 30% were in III, 26.42% were in I and only 9.30% were in stage IV which showed no significance (P=0.49). This finding is correlated with the other studies [8, 11]. The most common presenting complaints were generalised weakness found in 92.14% of cases whereas most common opportunistic infection seen was oral ulcers

(41.42%). On general examination most of the patients (75.71%) had raised pulse rate.

Mean total leucocyte count (TLC) in cells/mm<sup>3</sup> was 6813.57±2755.17, ranging from 1600 to 17400 cells/mm<sup>3</sup>. Majority (75%) were in normal range, 17.15% had <4000 and 7.85% had >11000 cells/mm<sup>3</sup> TLC. On differential leucocyte count, neutropenia was seen in 12 patients, lymphocytopenia was seen in 36 patients, monocytopenia was seen in 51 patients, eosinophilia was seen in 36 patients. Mean neutrophil count was 60.95±12.47%, lymphocyte count was 29.45±11.64%, monocyte count was 5.34±2.5%, eosinophil count was 4.12±3.23%. Mean platelets count in lakh per mm<sup>3</sup> was 2.52±1.03, ranging from 0.29 to 6.6 lakh per mm<sup>3</sup>. Majority were in normal range (65%), 25.71% had <1.65 lakh per mm<sup>3</sup> and 9.29% had >4.15 lakh per mm<sup>3</sup>, (P=0.88). Mean



platelet volume in fL was  $9.18 \pm 1.05$ , ranging from 3.6 to 12.6 fL Mean CD4 count cells per microliter was  $259.39 \pm 216.38$ , ranging from 4 to 953 cells per microliter,  $P = 0.49$ . Moreover, the prevalence of anemia was significantly higher (34.5%,  $P = 0.011$ ) in patients with CD4 count  $< 200/\mu\text{l}$ , this is consistent with different studies [10, 12, 13]. Mean hemoglobin value of all respondents was  $10.75 \pm 2.92$  g/dl, ranging from 1.4 to 21.7 g/dl. Anemia seen in males, 73.09% had  $\text{Hb} < 13.3$  g/dl and in females 85.48% had  $\text{Hb} < 12$  g/dl. Majority 71 cases (50.71%) had Hb in 10.1 to 15 g/dl, among them 47 were males and 24 were females, ( $P = 0.008$ ). However, majority of patients were anemic 110 (78.57%), among them 57 were males and 53 were females, ( $P$  value = 0.03). Mean PCV of all respondents was  $34.37 \pm 8.42\%$ , ranging from 12.7 to 65.9%. Majority 106 had abnormal PCV findings, among them 57 were males and 49 were females,  $p = 0.2$ . Mean MCV was  $85.81 \pm 11.11$  fL ranging from 51.8 to 128.7 fL. Majority 96 had MCV findings between 79.1 to 98.3 fL. i.e., within normal limit, among them 57 were males and 39 were females,  $P = 0.008^*$ . Mean MCHC was  $32.38 \pm 1.89$  g/dl, ranging from 24.9 to 35.4%. Majority 94 had MCHC findings between 32.4 to 35.9 g/dl. I.e., within normal limit, among them 56 were males and 38 were females. Mean RDW was  $15.02 \pm 2.35\%$ , ranging from 11.5 to 24.3%. majority 71 had RDW findings  $> 14\%$ , among them 36 were males and 35 were females. These findings of hematological parameters are correlated with the previous studies done by Ofori DN *et al* [7], Enawgaw B *et al* [9] and Patil S *et al* [10].

Maximum number of patients (60.71%) had normocytic normochromic appearance on peripheral smear examination which is comparable with the study conducted by Enawgaw B *et al* [9]. 20% showed microscopic Hypochromic with anisopoikilocytosis, pencil cell. 12.14% showed microcytic hypochromic and macro-ovalocytes and 7.14% showed macrocytes, hyper segmented neutrophils, poikilocytes, Howell jolly body, Cabot ring appearance. Mean ESR ( $n = 140$ ) of all respondents was  $33.21 \pm 16.22$  mm/h, ranging from 6 to 68 mm/h. ESR findings showed that in males 69.23% had raised ESR and among females 72.48% had raised ESR, this is comparable with the Shruti *et al* study [14]. ESR is neither sensitive nor specific when used as a general screening test, it is usually

elevated in the presence of infectious disease and chronic illness [15].

The analysis of association between WHO staging and hematological abnormalities revealed statistical significance with anemia ( $p < 0.05$ ), thrombocytopenia ( $< 0.0001$ ), leucopenia, lymphocytopenia ( $p = 0.006$ ) and CD4 count ( $p = 0.02$ ). However, the association between CD4 count and leucocyte (WBC) abnormalities revealed statistical significance with leukocytopenia ( $p = 0.02$ ) and lymphocytopenia ( $p = 0.03$ ). These findings are correlated with the earlier studies [7, 9, 16-18].

Based on the present study results, the hematological disorders are very common in HIV patients. Anaemia is a very important and common presentation. Incidence of anemia increases with advanced clinical stages of disease in HIV infection. HAART produces a definitive improvement of hematological parameters and CD4 cell count. There was significant association between increase in hemoglobin level and CD4 cell count while there was significant association between low hemoglobin level and advanced WHO staging, both can be used for clinical evaluation. HIV Infection is accompanied by marked hematological changes that complicate health and treatment of patients. The hematologic abnormalities are prevalent through all stages of the disease, and some of these may serve as indicators of clinical progression and thus they can be used to assess the stage of the disease in resource poor places where CD4 count evaluation is not available. At the same time patients with HIV infection should be investigated and treated for hematological abnormalities to reduce the morbidity of the patients.

### Conclusion:

The commonest hematological abnormalities in the study participants were anemia and leucopenia, especially lymphocytopenia. Anemia, leucopenia, thrombocytopenia, and lymphopenia were increased as CD4 count decreases and advanced WHO staging. Based on the present finding, HIV patients are recommended to check up their CD4 counts regularly and also to enforce that hematological parameter should be performed for every patient and to start HAART when it is appropriate in order to reduce the prevalence of anaemia and lymphocytopenia. We also recommend that work should be done on newly diagnosed patients since most work done by other



researchers shows a correlation between CD4 count and lymphocyte count.

### Limitations:

This study does not address iron status of study participants, hemoglobinopathies, inherited

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