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RESEARCH ARTICLE

STUDY OF HAEMOGRAM IN HIV POSITIVE PATIENTSAND ITS CORRELATION WITH CD4 COUNT

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ABSTRACT

Introduction: HIV/AIDS is viewed as a pandemic affecting nearly all countries of the world. Haematologic abnormalities are among the most common complications of HIV infection.
Aims and Objectives: Present study was aimed at evaluating the haemogram in HIV positive patients and its correlation with CD4 count.
Materials and Methods: The present study was an observational study carried out in a tertiary care center during period of 12 months from January 2016 to December 2016 after the approval of Institutional Ethics Committee. All the pre ART HIV positive newly diagnosed patients without any gender preference attending ART center were included. However children below 15 years, patients with previously known haematologic disorders, pregnant and lactating women were excluded. A complete blood count on 3 part differential automated cell counter, peripheral smear examination and CD4 count on BD FACS flow cytometer was done.
Results: Females outnumbered males. Majority (84.54%) of the cases had anaemia. Leucopenia was found in 13.63% and thrombocytopenia in 8.18% of cases. Total leukocyte count was in correlation with CD4 count but the occurrence of anemia and thrombocytopenia was independent of the increase or decrease in the CD4 count.
Conclusion: Hematologic abnormalities like anemia and thrombocytopenia have also been reported to occur in early stages of HIV infection. Hence recognising these haematological alterations and treating them at the earliest is very important in order to reduce morbidity and mortality of patients.

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INTRODUCTION

HIV/AIDS is best viewed as a pandemic affecting nearly all countries of the world (Parinith *et al*., 2012). More than 95% HIV positive patients are in developing countries. In developing countries like India the disease is having a major impact on social and economic development. Increasing poverty and loss of one or more breadwinners to AIDS is further breaking down the building blocks of the nation. (WHO 2017) HIV attacks body's immune system (Joy *et al*., 2014). Infection with HIV-1 primarily involves a subgroup of T-lymphocytic cells, but other cell types are also invaded by the virus, including cell lines within the haematopoietic system (Mgogwe *et al*., 2012). Haematological changes are among the most common complications of HIV (Wankah *et al*., 2014). These changes are anemia, leucopenia and thrombocytopenia. Mechanisms of HIV induced myelosuppression is direct infection of haematopoietic stem cells by virus, inability of stromal cells to carry out normal functions, toxic effects of HIV proteins and changes in cytokine milieu (Joy *et al*., 2014). These haematologic changes can also be due to secondary infections, neoplasms or side effects of therapy (Parinith *et al*., 2012). Anemia and leucopenia are usually caused by inadequate production of RBCs and WBCs because of bone marrow suppression by HIV infection and abnormal cytokine production. Thrombocytopenia is caused by immune mediated destruction of platelets and inadequate platelet production. These act as morbidity in themselves by adversely altering the patient's quality of life such as from anaemia (fatigue and dyspnoea), leucopenia (infections) and thrombocytopenia (bleeding). They also hinder treatment of the primary viral infections, secondary infections and neoplasms (Suresh Venkata SatyaAttili *et al*., 2008). Abnormal haemogram is common manifestation and important predictive tool for morbidity in the human immunodeficiency virus (HIV) infection (Wankah *et al*., 2014). According to WHO patients having unexplained anemia, neutropenia and chronic thrombocytopenia are categorized into clinical stage 3. The measurement of CD4+ T-cell (CD4) counts is a strong predictor of progression to Human Immunodeficiency Syndrome (AIDS), as well as a means of monitoring antiretroviral therapy (ART) (Montarroyos *et al*., 2014). But in developing countries where sophisticated laboratory markers

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such as viral load or CD4 lymphocyte count (which requires an expensive technique like flowcytometry) are not available, baseline hemogram gives an idea not only about the current health status but also about clinical stage, disease progression. Some of the parameters like Hemoglobin, Total lymphocyte count are becoming surrogate markers for prediction of CD4 count, monitoring disease progression and to assess therapeutic reponse[7].Hence present study aims at evaluatinghemogram in HIV positive patients and its correlation with CD4 count.

MATERIALS AND METHODS

The present observational study was carried out in a tertiary care center during the period of 12 months from January 2016 to December 2016 after the approval of Institutional Ethics Committee. All the pre ART HIV positive newly diagnosedpatients without any gender preference attending ART center were included. However children below 15 years, patients with previously known haematologic disorders, pregnant and lactating women were excluded. The clinical details of the patients were recorded. Blood sample for complete haemogram and CD4 count was collected in K3 EDTA bulb.A complete blood count on 3 part differential automated cell counter was done and correlated with detail peripheral smear examination. CD4 count was done on BD FACS flowcytometer. Various parameters of haemogram were correlated with CD4 count of patients. In the present study CD4 count was divided into 3 groups as ≥500, 200-499, ≤200 cells/mm^3 as per the CDC classification system for HIV positive adults. The results obtained were subjected to various statistical tests like mean, standard deviation, Chi-square test, Z test.

RESULTS

During the present study 110 cases were studied.There was female predominance 68 (61.81%), with a male to female ratio of 1:1.6.

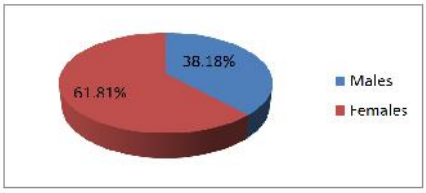

Figure 1. Gender distribution

Maximum number of cases {89 (80.90%)} were in the age group of 20 to 40 years. The overall mean age of patients was 32.06 years ± 9.08, with the minimum being 19 years and the maximum 61 years.

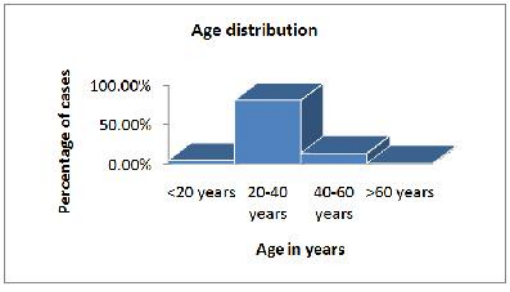

Figure 2. Age distribution

Table 1. Signs and symptoms of Patients (n=110 cases)

Sr. No.	Symptom / Sign	No. of Cases
1.	Fatigue	83 (75.45%)
2.	Dyspnoea	75 (68.18%)
3.	Weight Loss	12 (10.90%)
4	Fever	23 (20.90%)
5.	Pallor	19 (17.27%)
6.	Cough	15 (13.63%)
7.	Diarrhoea	20 (18.18%)
8.	Oral Thrush	8 (7.27%)
9.	Petechie, Purpura	--
10.	Jaundice	--
11.	Adenopathy	--

*(One patient showed more than one symptom/sign)

The commonest symptom was fatigue seen in 83 (75.45%) patients and 27 (24.54%) patients were asymptomatic. In the present study the commonest hematologic alteration was anemia observed in 93(84.54%) cases (Figure: 3), and predominant morphologic pattern of anemia found in present study was normocytic normochromic followed by microcytic hypochromia. (Figure : 4)

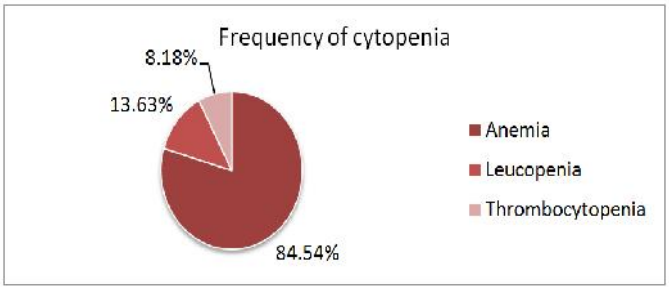

Figure 3. Frequency of cytopenia

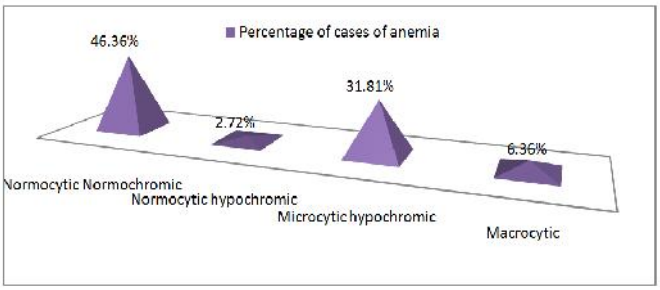

Figure 4. Morphologic Patterns of Anemia

Absolute lymphocyte count ranged from 884 to 7043 cells/mm3. In the present study 28 (25.45%) cases showed absolute lymphocyte count less than 1500 cells/mm3 (lymphopenia). Normal absolute lymphocyte count (1500-4000 cell/mm^3) was seen in 82 (75.54%) cases. More than 4000 cells/mm^3 was seen in 12 (10.9%) cases. Majority of patients 120 (92.72%) had absolute neutrophil count with normal range (2000-7000/mm^3). Neutropenia was seen in 3.63% cases and majority of them had a CD4 count <200cells/mm^3. Absolute neutrophil count above 7000/mm^{3}was seen in 4 (3.63%) cases. The absolute eosinophil count was within normal range in all cases. CD4 count ranged from minimum of 10 cells/mm^{3}to a maximum of 1743 cells/mm^3. Majority of cases 46(41.81%) had a CD4 count ≥500 cells/mm^3 followed by 42(38.18%) cases having CD4 count between 200-499 cells/mm3. Only 22 (20%) cases had a CD4 count ≤200 cells/mm^3. The below table shows the minimum, maximum values of all parameters along with their mean and standard deviation.

Table 2. Hemogram distribution according to reference ranges* (n=110 cases)

Sr.No.	Parameter	Below normal reference range	Within normal reference range	Above normal reference range
1.	Hemoglobin	93 (84.54%)	4 (3.63%)	13 (11.81%)
2.	RBC count	33(30%)	16(14.54%)	61(55.45%)
3.	Hematocrit	74(67.27%)	36(32.72%)	--
4.	Mean corpuscular volume (MCV)	35 (31.81%)	68(61.81%)	7(6.36%)
5.	Mean corpuscular hemoglobin (MCH)	59(53.63%)	41 (37.27%)	10(9.09%)
6.	Mean corpuscular hemoglobin concentration (MCHC)	38(34.54%)	72(65.45%)	--
7.	Red cell distribution width(RDW)	2 (10.81%)	56(50.90%)	52(47.27%)
8.	Total leukocyte count	14 (12.72%)	88 (80%)	8 (7.27%)
9.	Platelet count	11 (10%)	99 (90%)	--

(*Reference ranges are taken from Standard Textbook – Dacie and Lewis Practical Hematology, Eleventh Edition).

Table 3. Age, CD4 cell count and hematological parameter distribution

Parameter	Minimum	Maximum	Mean± SD
1.Age (years)	19	61	32.06±9.08
2.Hemoglobin (gm/dL)	5.7	15.6	10.63±1.94
3.RBC count (million/mm^3)	2.11	6.11	4.35±0.69
4.Hematocrit (%)	18.9	47.2	34.45±5.54
5.Mean corpuscular volume (MCV) (fl)	46	121	82.37±14.3
6.Mean corpuscular hemoglobin (MCH) (pg)	13	39.4	25.6±5.24
7.Mean corpuscular hemoglobin concentration (MCHC) (gm/dL)	26.5	34.2	31.61±1.77
8. Red cell distribution width(RDW) (%)	11.2	22	14.34±1.9
9.Total leucocyte count(TLC) ($x10^3$ /uL)	1.5	15.3	6.55±2.5
10.Platelet count ($x10^3$ /uL)	70	593	244.83±75.7
11.CD4 count (cells/mm^3)	10	1743	476.34±330.4

Table 4. Comparison of hematologic parameters with CD4 count (n=110 cases)

S. No.	Parameter		CD4≥500 cells/mm^3 (n=46)	CD4 200-499 cells/mm^3 (n=42)	CD4≤200 cells/mm^3 (n=22)
1.	Hemoglobin				
	Males	>13gm/dL	6 (13.04%)	4 (9.57%)	-
		<13gm/dL	11 (23.91%)	13 (30.95%)	9 (40.90%)
	Females	>12gm/dL	3 (6.52%)	-	-
		<12gm/dL	26 (56.52%)	25 (59.52%)	13 (50.09%)
2.	Total WBC count	<4000/mm^3	-	2 (4.76%)	13 (50.09%)
		4000-11000/mm^3	39 (84.78%)	39 (92.85%)	9 (40.90%)
		>11000/mm^3	7 (15.21%)	1 (2.38%)	-
3.	Platelet count	<150x10^3/mm^3	-	4 (9.57%)	5 (22.72%)
		150-450x10^3/mm^3	45(97.82%)	37 (88.09%)	17 (77.27%)
		>450x10^3/mm^3	1 (2.17%)	1 (2.38%)	-

Table 5. Comparison of Anemia, Leucopenia and Thrombocytopenia with different CD4 counts

Parameter	CD4≥500 cells/mm^3 (n=46)	CD4 200-500 cells/mm^3 (n=42)	CD4≤200 cells/mm^3 (n=22)	Statistical test*	Remarks
Anemia (no. of cases)	38 (82.60%)	35 (83.33%)	20 (90.90%)	6	p>0.05
Leucopenia (no. of cases)	-	2 (4.76%)	12 (54.54%)	Z=4.57	p<0.01
Thrombocytopenia (no. of cases)	-	5 (11.90%)	6 (27.27%)	Z=1.54	p>0.05

*Statistical test : Chi-square test, Z-test.

Table 6. Comparison of mean hemoglobin (Hb) values

Name of Author	Treacy *et al* 1987 (n=20)	Kaloutsi *et al* 1994 (n=40)	Dhamangaonkar *et al* 2014 (n=203)	Present study 2017(n=110)
Mean Hb values (g/dL)	11.34	10.8	9.78	10.63

Table 7. Comparison of Frequency of Anemia

Name of Author	Percentage
Karcher *et al*1991(n=197)	89%
Kaloutsi *et al* 1994(n=40)	85%
Tripathi *et al* 2005(n=74)	82.4%
Parinitha *et al* 2012(n=250)	84%
Present study 2017 (n=110)	84.5%

Table 8. Comparison of Red cell indices

Parameter (Mean and SD)	Pornprasert et al. 2009	Present study 2017
MCV	87.62 ± 7.15	80.39 ± 13.4
MCH	29.26 ± 2.39	25.06 ± 5.24
MCHC	33.36 ± 0.937	31.57 ± 1.77
RDW	14.18 ± 2.94	14.34 ± 1.90

Table 9. Comparison of frequency of Leucopenia and Thrombocytopenia

	Patwardhan *et al* 2002 (n=500)	A Akinbami *et al* 2010 (n=205)	Parinitha *et al* 2012 (n=250)	Present Study 2017 (n=110)
Leucopenia	24.4%	26.8%	29.6%	13.6%
Thrombocytopenia	13%	16.1%	18%	8.18%

Table 10. Comparison of CD4 cell count distribution with other studies

	A Akinbami *et al* 2010 (n=205)	Parinitha *et al* 2012 (n=250)	Present Study 2017 (n=110)
CD4≥500 cells/mm^3	19.51%	8.4%	41.81%
CD4 200-500 cells/mm^3	37.21%	21.6%	38.18%
CD4≤200 cells/mm^3	53.17%	70%	20%

The above table shows that in patients having CD4 count >500 cells/mm^3, most common finding was anemia, but leucopenia and thrombocytopenia was not observed in this group. Majority of the patients with CD4 count ≤200 cells/mm^3 presented with cytopenias and none of them had a normal hemoglobin value neither did they show leukocytosis or thrombocytosis. The frequency of leucopenia increased with a drop in the CD4 cell count and highest frequency was seen in cases with CD4 count ≤200 cells/mm^3. Statistical test used for cases of leukopenia (showed a significant difference, p value<0.01) Thus the number of cases with leucopenia increased with reducing CD4 cell counts .This indicates a higher occurrence of leucopenia with progression of disease. In the present study the occurrence of anemia and thrombocytopenia was not dependent on increase or decrease in CD4 count and these parameters did not show a significant difference (p value>0.05) between three groups with differing CD4 cell counts.

DISCUSSION

Complete haemogram is a reflection of the health status of an individual. Haematological alterations encountered in HIV-infected individuals are anemia, leucopenia, thrombocytopenia. Although in the majority of cases, hematologic abnormalities are detected in middle or advanced stages of HIV infection, some of these like anemia and thrombocytopenia have been reported to occur in early stages of HIV infection (Parinitha and Kulkarni, 2012). Hence recognising these haematological alterations and treating them accordingly is very important in reducing the morbidity and mortality of patients. In the present study the majority of the patients (89 (80.90%)) were in the age group of 20 to 40 years. There was female predominance (61.81%), with a male to female ratio of 1:1.6. Female preponderance was also observed by Akinbami *et al*. (2010) (68.3%) and Saha *et al*. (2015) (57.33%). This may be because of lack of health awareness among women and nutritional negligence. In the present study haemoglobin ranged from 5.7g/dl to 15.6g/dl and the values for mean Hb were in concordance with other studies. Majority (84.54%) of the cases in present study had anemia. Similar observations were made by Kaloutsi *et al*. (1994), Karcher *et al*. (1991), Tripathi *et al*. (2005) and Parinitha *et al*. (2012). In the present study mean RBC count was 4.35± 0.69 million/mm^3. Whereas Tripathi *et al*. (2005) (3.09± 0.36 million/mm^3) and Parinitha *et al*. (2012) (3.66± 0.84million/ mm^3) observed a lower mean RBC count. The commonest morphologic pattern observed on peripheral smear in the present study was normocytic normochromic. Similar observation was made by Tripathi *et al*. (2005) and Parinitha *et al*. (2012). The second most common pattern was microcytic hypochromic. Saha *et al*. (2015) showed a preponderance of microcytic hypochromic anemia. This may be due to pre-existing iron deficiency anemia, poor socioeconomic status, poor hygiene. This emphasizes the need to evaluate these patients for coexistent nutritional deficiency. Present study showed macrocytic anemia in 6.36% cases which may be attributed to Vitamin B12 deficiency. The mean values of MCV, MCH, MCHC, RDW in present study are lower as compared to other studies. This may be due todifference in the study design. Pornprasert *et al*. (2009) had evaluated these parameters in HIV positive thalassemia trait patients. The table above depicts that number of cases of leucopenia and thrombocytopenia in the present study were less as compared to other studies. This may be due to difference in the sample size.

The table above depicts that in the present study maximum number of cases had CD4 count ≥500 cells/mm^3 whereas Akinbami *et al*. (2010) and Parinitha *et al*. (2012) found maximum number of cases in patients with CD4 count ≤200 cells/mm^3. This may be due to variation in sample size. Haematologic manifestations are common in HIV-infected patients. Anemia is the most common manifestation and the most frequent form is normocytic and normochromic type. Anemia, if persistent is associated with substantially decreased survival. Hemoglobin levels reflect rapidity of disease progression and improvement in levels are predictive of treatment success. (Obirikorang and Yeboah, 2009) Thus in developing countries where sophisticated laboratory markers such as viral load or CD4 lymphocyte count (which requires an expensive technique like flowcytometry) are not available, baseline hemogram gives an idea not only about the current health status but also about clinical stage, disease progression. Some of the parameters like Hb, TLC are becoming surrogate markers for prediction of CD4 count, montoring disease progression and assess therapeutic reponse. (19) As per revised guidelines of NACO dated 05th May 2017 it has been decided to "TREAT ALL PLHIV (Patients Living with HIV/AIDS) with Antiretro viral Therapy regardless of CD4 count, clinical stage, age or population." So now a days baseline hemogram is becoming a valuable tool in HIV positive patient.

REFERENCES

AkinsegunAkinbami, OlajumokeOshinaike, TitilopeAdeyemo, AdewunmiAdediran, OwolabiDosunmu, Mobolaji Dada, Idris Durojaiye, AlabaAdebola and Oshunkalu Vincent. 2010. Hematologic Abnormalities in Treatment-naïve HIV patients. Infectious Diseases: *Research and Treatment*, 3: 45-49.

Col JyotiKotwal a, MajVikram Singh b, AnupamKotwal c, Brig VibhaDutta, Maj Gen Velu Nair, AVSM, 2013. VSMe *Medical Journal Armed Forces India*, 69; 319-25 journal homepage: www.elsevier.com/locate/mjafi

Dhamangaonkar A.C, Mathew A, Pazare A.R. 2014. Total Lymphocyte Count and Haemoglobin Concentration Combined as a Surrogate Marker for Initiating Highly Active Antiretroviral Therapy in a Resource Limited Setting as against CD4 cell count. *West Indian Med J*., 63(5): 460.

Joy S, Mehrotra A, Kejriwal A. 2014. Hematologic manifestation of HIV in a tertiary center. *Transworld Medical Journal*, 2(1):10-13.

Kaloutsi V, Kohlmeyer U, Maschek H, Nafe R, Choritz H, Amor A, and others. 1994. Comparison of bone marrow and hematologic findings in patients with human immunodeficiency virus infection and those with myelodysplastic syndromes and infectious diseases. *Am J Clin Pathol*., 101(2):123-9.

Karcher DS, Frost AR. 1991. Bone marrow in human immunodeficiency virus (HIV)-related disease morphology and clinical correlation. *Am J ClinPathol*., 95(1):63-71

Mgogwe J1,Semvua H3, Msangi R5, Mataro C2,4, Kajeguka D2,3, Chilongola J2, 2012. The evolution of haematological and biochemical indices in HIV patients during a six-month treatment period. *African Health Sciences*, 12(1): 2 – 7.

Montarroyos UR, Miranda-Filho DB, Cesar CC, Souza WV, Lacerda HR, *et al*. 2014. Factors Related to Changes in CD4+ T-Cell Counts over Time in Patients Living with HIV/AIDS: A Multilevel Analysis PLoS ONE 9(2): e84276. doi:10.1371/journal.pone.0084276.

Obirikorang C. and Yeboah, F A. 2009. Blood hemoglobin measurement as a predictiveindicator for the progression of HIV/AIDS in resource limited setting. *J Biomed Sci*., 16(1):102

Parinitha SS, Kulkarni MH. 2012. Haematological changes in HIV with correlation to CD4count. *AMJ*, 5,3,157-162. http//dx.doi.org/10.4066/AMJ.2012.1008.

Patwardhan MS, Gowlikar AS, Abhyankar JR, Atre MC. 2002. Hematologic profile of HIV positive patients. *Ind J Pathol Microbiol*., 45(2):147-50.

Pornprasert *et al*. 2009. Evolution of Hematological Parameters in HIV-1 Infected Patients with and without Thalassemia Carriages During Highly Active Antiretroviral Therapy. *HIV Clin Trials*, 10(2):88–93

Saha, D., Jyoti R, Kini, R Subramaniam. 2015. A Study of the Hematological Profile of Human Immunodeficiency Virus Positive Patients in Coastal South Indian Region. *J Med Sci*., 35(5):190-193.

Suresh VenkataSatyaAttili, V. P. Singh, MadhukarRai, Datla Vivekananda Varma, A. K. Gulati, ShyamSundar. 2008. *Turk J Hematol*., 25:13-19.

Treacy M, Lai L, Costello C, Clark A. 1987. Peripheral blood and bone marrow abnormalities in patients with HIV related disease. *Br J Haematol*., 65:289-94.

Tripathi AK, Kalra P, Misra R, Kumar A, Gupta N. 2005. Study of bone marrow abnormalities in patients with HIV disease. *JAPI*, 53:105-10.

Wankah *et al*. 2014. Profile of blood cell abnormalities among antiretroviral therapy naïve HIV patients attending the Yaounde University Teaching Hospital, Cameroon. *BMC Hematology*, 14:15.

WHO- Immunisation, Vaccines and Biologicals; WHO 2017

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