

Hematological Parameters in HIV Patients: Association with CD4 Count

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ABSTRACT

Background: Around 2.1 million people are currently living with human immunodeficiency virus (HIV) infection in India. Hematological parameters have been proposed as alternative markers of HIV infection in areas with limited resources. This study aimed to describe hematological parameters in patients with HIV infection and to determine their association with CD4 cell counts. **Methods:** This cross-sectional study assessed 100 HIV patients on antiretroviral therapy (ART). Their blood samples were collected to measure complete blood count (CBC) and CD4 count. Patients with known hematological disorders, critically ill patients, and those not willing to give informed consent were excluded. The Chi-square test was used to find the association between hematological parameters and CD4 counts. **Results:** Most patients with HIV infection had anemia (85%), followed by thrombocytopenia (42%) and neutropenia (36%). There was a statistically significant association between the number of patients having anemia and CD4 cell counts. **Conclusion:** Hematological changes are common in HIV patients. Hematological parameters should be routinely monitored and managed to reduce morbidity. Also, patients with unexplained low blood counts should be screened for underlying HIV infection.

Keywords: HIV, anemia, CD4 count

Around 2.1 million people in India are estimated to have human immunodeficiency virus (HIV).¹ According to National AIDS Control Organization (NACO), the national prevalence is 0.22% (0.17-0.29%).² A higher prevalence of 7% has been reported in high-risk groups.¹

HIV attacks the immune system of the body. Opportunistic infections can take advantage of a weakened immune system and cause fatal health problems.³ The concentration of HIV RNA and CD4 count are important biomarkers of disease progression.⁴⁻⁶ Total lymphocyte count, white blood cell (WBC) count, and hemoglobin concentration have been proposed as alternative markers of HIV infection, especially in developing countries with limited financial resources.⁷

This study aimed to describe the hematological parameters in patients with HIV infection and to determine their association with CD4 cell counts.

METHODS

This cross-sectional study was conducted at a tertiary care teaching hospital in North India after approval from the Institutional Ethics Committee. Informed consent was obtained from all participants. One hundred patients coming to the ART Unit of Medicine OPD over 6 months were included in the study. Patients with known hematological disorders, critically ill patients, and those not willing to give informed consent were excluded. A semi-structured proforma was used to gather relevant information. Patient's blood samples were taken to measure their complete blood count (CBC) and CD4 counts. All patients were on ART at the time of taking their blood samples. Anemia, thrombocytopenia, leukopenia, neutropenia and lymphopenia were looked for in CBC. Their association with CD4 cell counts was determined.

Operational Definitions

Anemia was defined as hemoglobin <13 g/dL in males and <12 g/dL in females. Leukopenia was defined as WBC <4,000/ μ L. Thrombocytopenia was defined as a platelet count of <1,00,000/ μ L. Neutropenia was defined as an absolute neutrophil count of <1,500/ μ L. Lymphopenia was defined as a total lymphocyte count of <1,000/ μ L.⁸

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Sample Size Calculation

Open Epi software was used to calculate the sample size.⁹ Taking anticipated frequency as 0.22,² within 1% confidence limits and 95% confidence level, the sample size was calculated as 85.

Data Analysis

SPSS version 20.0 was used for statistical analysis. Descriptive statistics were used to analyze socio-demographic variables. The Chi-square test was used to determine the association between hematological parameters and CD4 counts. P value <0.05 was considered statistically significant.

RESULTS

We assessed 100 patients with HIV infection. There were 50 males and 50 females. They were in the age group 18 to 60 years with a mean age of 29.9 years. Most patients presented with fatigue (69 patients, 69%), fever (61 patients, 61%) and weight loss (44 patients, 44%). Other symptoms observed were cough (22 patients, 22%) and diarrhea (10 patients, 10%).

Anemia was the most common hematological abnormality seen in 85 patients (85%), followed by thrombocytopenia in 42 patients (42%) and leukopenia in 11 patients (11%). Neutropenia was seen in 36 patients (36%), whereas only 9 patients (9%) had lymphopenia. Sixty-eight out of 85 (80%) patients had normocytic normochromic anemia, whereas 7 (8%) had microcytic hypochromic anemia.

Sixty-four patients had CD4 cell count ranging from 201 to 500 cells/ μ L. Twenty-five patients had ≤ 200 CD4 cells/ μ L. Eleven patients had more than 500 CD4 cells/ μ L.

We found a statistically significant association between CD4 cell counts and the number of patients having anemia and neutropenia (Table 1). With a decrease in CD4 cell counts, more patients were found to have anemia and neutropenia.

DISCUSSION

This study was planned to describe hematological parameters in patients having HIV infection and to determine their association with CD4 cell counts.

We found anemia in 85% of HIV patients in our study. Our finding was similar to that reported by Parinitha et al. They assessed 250 HIV patients in Karnataka and found anemia in 210 of them (84%). Normocytic normochromic was the most common type of anemia,¹⁰ as was also the case in our study.

Anemia in HIV infection has varied causes. High viral load, opportunistic infections like *Mycobacterium avium* complex (MAC), inflammatory cytokines and malignancy play important roles. Also, zidovudine can cause myelosuppression and lead to macrocytic anemia. Defective iron metabolism, reutilization and vitamin B12 deficiency are other causes.^{10,11}

Hemoglobin concentration has been proposed as an alternative marker of HIV prognosis, especially in resource-poor developing countries.⁷ Durandt et al have discouraged this practice as few other causes like nutritional deficiencies, are independent causes for anemia and are unrelated to HIV infection.¹² But in the absence of better markers for disease progression in resource-poor areas, we the severity of anemia may be used as an indicator of disease progression.

We found neutropenia in 36% of patients. Also, there was a statistically significant association between CD4 cell counts and the number of patients having neutropenia. High viral load, low CD4 cell counts and use of drugs like sulfamethoxazole + trimethoprim are responsible for neutropenia in patients with HIV infection.¹²

High viral load directly affects hematopoiesis and leads to thrombocytopenia, leukopenia and lymphopenia, in addition to anemia and neutropenia.^{10,12} But we did not find a significant association of CD4 cell counts with the number of patients having thrombocytopenia,

Table 1. Association Between Hematological Parameters and CD4 Cell Counts

Parameter	CD4 cell count (per μ L) ≤ 200 (n = 25)	CD4 cell count (per μ L) 201-500 (n = 64)	CD4 cell count (per μ L) >500 (n = 11)	Chi-square statistic (P value)
Anemia (No. of cases)	23	51	11	26.063 (0.02)
Thrombocytopenia (No. of cases)	11	28	3	8.962 (0.06)
Leukopenia (No. of cases)	5	5	1	17.946 (0.22)
Neutropenia (No. of cases)	4	28	4	15.924 (0.04)
Lymphopenia (No. of cases)	6	3	0	13.965 (0.08)

leukopenia or lymphopenia. While for thrombocytopenia, statistical significance just missed the mark, p values were much higher for leukopenia and lymphopenia. The smaller sample size may have contributed to this statistical nonsignificance in our study. Future studies with larger sample sizes may give a better idea of the association between the two.

We propose regular monitoring and management of hematological changes in HIV patients to reduce morbidity. All patients who were identified to have hematological changes in our study, were requested to follow-up every 4 weeks for monitoring of CBC. As oral iron therapy takes 2 to 3 weeks to show its effects, we decided to monitor CBC at an interval of 4 weeks. But any further data was not collected as it was beyond the scope of this study.

Also, a progressive decline in all cell lines may indicate disease progression. Future longitudinal studies may be able to throw a better light on frequency of monitoring of these hematological parameters as a marker of disease progression.

Fatigue has been reported as the most common symptom of HIV infection.^{13,14} It was also the most common presenting symptom in our study. Chronic ongoing inflammatory processes within the cardiovascular system and brain may be responsible for fatigue in HIV patients.¹⁵ Fever also occurs, mostly due to superimposed opportunistic infections like tuberculosis and MAC.¹⁶ Most opportunistic infections occur when CD4 cell count is <500 cells/mm³.¹⁷ Also, weight loss of even 5% has been associated with an increased risk of developing opportunistic infections in HIV patients.¹⁸

Eighty-nine of 100 patients in our study had CD4 cell count <500 cells/mm³. This may have contributed to the high prevalence of fever and weight loss in our study. The causes of these symptoms need to be looked for and managed effectively to give patients a better quality of life.

CONCLUSION

Anemia and neutropenia are most commonly associated with a decrease in CD4 counts in HIV patients.

Our study had a small sample size of 100 patients. This is a limitation of our study. Convenience sampling was used instead of random sampling. Also, this study had a cross-sectional design. All these factors may affect its generalizability.

Despite certain limitations, our study recommends that patients with unexplained low blood counts should

be screened for HIV infection, especially in high-risk populations and areas where the prevalence of HIV is higher.

It also invites the attention of researchers to explore this aspect further. Longitudinal studies with larger sample sizes will be beneficial in describing the course and progression of hematological changes in HIV patients. They can also guide in formulating recommendations related to the frequency of monitoring of hematological parameters.

REFERENCES

1. Paranjape RS, Challacombe SJ. HIV/AIDS in India: an overview of the Indian epidemic. *Oral Dis.* 2016;22 Suppl 1: 10-4.
2. HIV Facts & Figures. Available from: <http://naco.gov.in/hiv-facts-figures>.
3. Pasha I. To study the hematological parameters as predictors of morbidity in patients with HIV infection. *Global J Med Public Health.* 2004;3(1):1.
4. Anastos K, Kalish LA, Hessel N, Weiser B, Melnick S, Burns D, et al. The relative value of CD4 cell count and quantitative HIV-1 RNA in predicting survival in HIV-1-infected women: results of the women's interagency HIV study. *AIDS.* 1999;13(13):1717-26.
5. Kim S, Hughes MD, Hammer SM, Jackson JB, DeGruttola V, Katzenstein DA. Both serum HIV type 1 RNA levels and CD4+ lymphocyte counts predict clinical outcomes in HIV type 1-infected subjects with 200 to 500 CD4+ cells per cubic millimeter. *AIDS Clinical Trials Group Study 175 Virology Study Team. AIDS Res Hum Retroviruses.* 2000;16(7):645-53.
6. Hogg RS, Yip B, Chan KJ, Wood E, Craib KJ, O'Shaughnessy MV, et al. Rates of disease progression by baseline CD4 cell count and viral load after initiating triple-drug therapy. *JAMA.* 2001;286(20):2568-77.
7. Mofenson LM, Harris DR, Moya J, Bethel J, Korelitz J, Read JS, et al. Alternatives to HIV-1 RNA concentration and CD4 count to predict mortality in HIV-1-infected children in resource-poor settings. *Lancet.* 2003;362(9396): 1625-7.
8. Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J. *Harrison's Principles of Internal Medicine.* 19th Edition, New York, NY, USA: McGraw-Hill; 2015.
9. Menu OE. Sample size calculator. [Online][Cited 2017 November 1. Available from: URL: <http://www.openepi.com/SampleSize/SSPropor.htm>.
10. Parinitha S, Kulkarni M. Haematological changes in HIV infection with correlation to CD4 cell count. *Australas Med J.* 2012;5(3):157-62.
11. Marchionatti A, Parisi MM. Anemia and thrombocytopenia in people living with HIV/AIDS: a narrative literature review. *Int Health.* 2021;13(2):98-109.

12. Durandt C, Potgieter JC, Mellet J, Herd C, Khoosal R, Nel JG, et al. HIV and haematopoiesis. *S Afr Med J*. 2019;109(8b):40-5.
13. Schnall R, Siegel K, Jia H, Olender S, Hirshfield S. Racial and socioeconomic disparities in the symptom reporting of persons living with HIV. *AIDS Care*. 2018;30(6):774-83.
14. Xiao X, Reynolds NR, Saligan L, Lei Y, Wang M, Wang H. Effectiveness of non-pharmacological interventions to decrease fatigue in people living with HIV/AIDS: a protocol of systematic review and meta-analysis. *BMJ Open*. 2020;10:e040996.
15. Zuñiga JA, Harrison ML, Henneghan A, García AA, Kesler S. Biomarkers panels can predict fatigue, depression and pain in persons living with HIV: a pilot study. *Appl Nurs Res*. 2020;52:151224.
16. Hot A, Schmulewitz L, Viard JP, Lortholary O. Fever of unknown origin in HIV/AIDS patients. *Infect Dis Clin North Am*. 2007;21(4):1013-32, ix.
17. Sullivan M, Feinberg J, Bartlett JG. Fever in patients with HIV infection. *Infect Dis Clin North Am*. 1996;10(1):149-65.
18. Wheeler DA, Gibert CL, Launer CA, Muurahainen N, Elion RA, Abrams DI, et al. Weight loss as a predictor of survival and disease progression in HIV infection. Terry Bein Community Programs for Clinical Research on AIDS. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1998;18(1):80-5.



Women are More Prone to Develop Hypertension after 50

A study by the Public Health Foundation of India (PHFI) showed that Indian women in their 50s are more likely than men in the same age group to have hypertension.

The researchers evaluated the data gathered from three large national surveys which included the Longitudinal Ageing Study of India wave-1, the Study of Ageing and Health wave-2, and the National Family Health Survey-4. Each comprised of a representative sample of Indian adults from all the states and Union territories, with a sample size ranging up to 3,00,000 people.

According to Prof Parimala Mohanty, the study's author, the findings showed that Indian women had a higher risk of having hypertension after turning 50, which was consistent with findings from earlier studies conducted in several Western countries. The experts also noted that age-related BP increase was more pronounced among women than those among males. One of the main reasons behind the rise in women's hypertension cases after 50 years of age was the bio-hormonal changes postmenopausal. (Source: *Livemint*, August 17, 2022)

UNICEF: World's First Malaria Vaccine to Benefit Millions of Children

The United Nations Children's Fund (UNICEF) has given the pharmaceutical company GSK a contract for the first ever supply of a malaria vaccine with a potential value of USD 170 million. If fulfilled, the agreement would result in the availability of 18 million doses of RTS,S over the following 3 years, potentially saving thousands of lives each year.

Etleva Kadilli, Director of UNICEF's Supply Division, said that the introduction of the vaccine is a significant step in saving children's lives and lowering the burden of malaria as part of the malaria preventive and control program. The vaccine could offer additional protection against malaria to approximately 25 million children each year in areas of more than 30 nations with moderate to high malaria transmission when the availability increases. It took 35 years of research and development to develop the RTS,S malaria vaccine, the first-ever vaccine against *Plasmodium falciparum*, the most dangerous malaria parasite in the world and most common in Africa.

As part of the WHO-led Malaria Vaccine Implementation Program, the pilot usage of the regular vaccine was started in Ghana, Kenya and Malawi in 2019. In October 2021, the WHO recommended the broad use of the first malaria vaccine in nations with moderate to high *P. falciparum* malaria transmission. This recommendation was based on the pilots' experiences and the data they produced. The door for a wider rollout of the vaccine was soon opened by Gavi, the Vaccine Alliance's decision to support the malaria vaccine program in qualifying nations in December 2021.

The afflicted nations are anticipated to have a high demand for the malaria vaccine. The initial supply will be limited; however, as manufacturing capacity rises to the required level, the supply will gradually enhance. (Source: *ETHealthWorld*, August 17, 2022)