

# A Study on Etiopathological Evaluation of Anaemia in Newly Diagnosed HIV-Infected Adults at a Tertiary Health Care Centre of Eastern India.

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## ABSTRACT

**Background:** Anaemia is a common feature among HIV infected people and has been uniformly demonstrated that the severity of anaemia increase the morbidity and mortality in PLWH independent of CD4 count. There are wide variations in the prevalence of anaemia from different countries all over the world and gender specific variation observed in different studies. **Aims and Objectives:** Aims of our study were to study the different types and the various etiologies of anaemia in newly diagnosed HIV infected adults. Also to find out the relation between absolute CD4 counts and severity of anaemia. **Methods:** Fifty newly diagnosed HIV infected adults with anaemia were included in the study. Study conducted from July 2014 to June 2015 at a tertiary care hospital and medical teaching institute in eastern India. Detailed medical history was taken, thorough physical examination was done and relevant routine laboratory investigations were done in all patients. Few special investigations were done in selected patients. **Results:** In this study 70 % of the patients belonged to the lower socio economic group and 58% of the cases were addicted to alcohol which is also a significant associated risk factor. The mean CD4 count was 170.1 with a standard deviation of 123.16. The mean Hb% of the population was 7.13 with a standard deviation of 1.27031492. The most common etiology found was anaemia of chronic disease (34%) and other etiologies were HIV induced myelodysplasia (32%), iron deficiency anaemia (16%), helminth infection (14%) and vitamin B<sub>12</sub> deficiency leading to megaloblastic anaemia was seen in 4% cases. **Conclusion:** Anaemia of chronic disease is the most common etiology, which has correlation with disease activity.

**Keywords:** HIV/AIDS, Anaemia, people living with HIV/AIDS (PLWH).

## INTRODUCTION

The Human Immune-deficiency Virus (HIV) is a retrovirus that infects cells of the immune system, destroying or impairing their function. It involves almost all the systems in the human body.<sup>[1]</sup> Anaemia is the commonest hematological ailment affecting HIV infected individuals at various CD4 counts and due to various etiologies.<sup>[2-3]</sup> World Health Organization defines anaemia as hemoglobin levels less than 13 g/dl for males and less than 12 g/dl for females.<sup>[4]</sup> But this definition is a generalization for all the countries, for the purposes of this study the hemoglobin cutoff values for adults are.

Although anaemia can occur at any stage of HIV infection, its frequency and severity are positively correlated with faster progression of the disease and mortality.<sup>[5-6]</sup>

Severity of anaemia	Hb in g/dl
Mild	10–11.9
Moderate	9.9–7
Severe	6.9–4
Very severe	<4

The etiology of anaemia in HIV infection is multifactorial and typically the anaemia may result from low production of red blood cells, increased RBC destruction or ineffective RBC production<sup>[8]</sup> and frequently the laboratory features are compatible with anaemia of chronic disease with a low reticulocyte count, normocytic and normochromic red blood cells with normal iron stores and cytokine mediated poor erythropoietin response.<sup>[7, 8]</sup> Anaemia of chronic disease, nutritional deficiency anaemias,

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infections leading to anaemia and HIV induced myelodysplasia are some of the many causes of anaemia. The presentation of a patient of HIV infected individual is almost always different. Considering the seriousness of other opportunistic infections in HIV infected individuals anaemia is often not given proper attention, its cause is left undiagnosed and untreated while only hemoglobin levels are corrected.

There is a relative lack of data regarding the etiopathological evaluation of anaemia in newly diagnosed HIV-infected adults, particularly from the eastern part of India in the 1st decade of the 21st century. This study might give us an insight at the prevalence of the various etiologies of anaemia in newly diagnosed HIV-infected adults giving the clinician a chance to focus his resources on the most prevalent causes of anaemia and lead to a decrease in morbidity associated with it eventually benefiting the quality of life of the patient.

## MATERIALS AND METHODS

It was an institutional based cross sectional study done by 50 consecutive newly diagnosed HIV-infected adults with anaemia who were attending outpatient department or were admitted at the Carmichael Hospital for Tropical Disease, School of Tropical Medicine, Kolkata. The exclusion criteria were those patients or parent of the patients (in case of a minor) unwilling to give consent, infants & children <18 years, pregnancy, known hemoglobinopathies like thalassemia, sickle cell anaemia and Patient suffering from medical condition known to cause anaemia like chronic kidney disease, hypothyroidism etc. Thorough history was taken and systemic examination was done. Routine laboratory investigations- complete blood counts, urine examination, stool examination and serum urea, creatinine and CD4 count were done in all patients. Few other investigations like Iron profiles (in microcytic/dimorphic type of anaemia), Vitamin B12 and folic acid assay (in macrocytosis), Direct Coombs test, bone marrow aspiration cytology studies, Chest X-Ray, USG whole abdomen etc were done in selected cases. The data's were recorded in a predesigned case data sheet. After data collection, it was analysed by appropriate statistical software (medcalcr version 9).

## RESULTS

Out of 50 patients, 68% were males and 32% were females with male: female (1.21: 1). The mean age of the population was 34 with a standard deviation of 9.94. Among male the mean age was 33.97 years with a standard deviation of 8.77 years. It was slightly higher in females (mean = 35.12 years, standard deviation = 12.02 years). However, this

difference was not statistically significant ( $p = 0.7033$  by unpaired t test).

The baseline population was mainly consisted of lower socio-economic group (70 %), followed by middle class as depicted in the Figure 1. Total 29 (58%) subjects were having addicted to either alcohol or tobacco or both as shown in the table below [Figure 2].

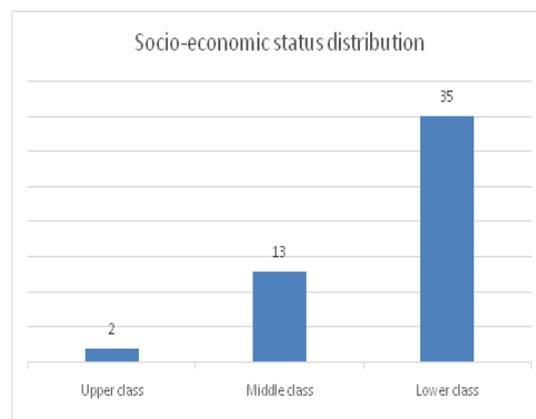


Figure 1: Distribution of subjects according to socio-economic status.

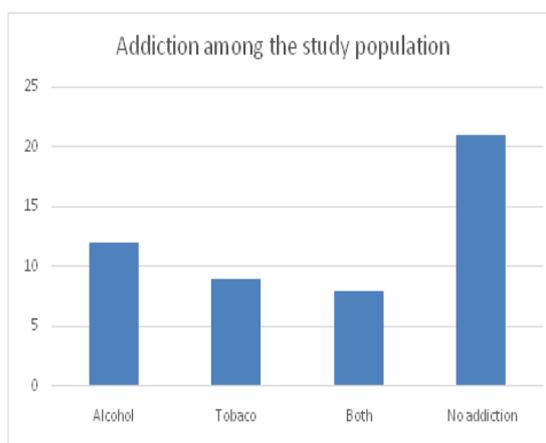


Figure 2: Prevalence of addiction among the study population.

Regarding the educational status, 33 patients (66%) were literate. Fatigue was the most common symptom ( $n=41$ , 82%) followed by fever ( $n=29$ , 58%), weight loss ( $n=27$ , 54%), shortness of breath ( $n=11$ , 22%) etc. Pallor ( $n=29$ ; 58%) was the most common sign followed by hepatomegaly ( $n=21$ ; 42%), lymphadenopathy ( $n=8$ ; 16%), splenomegaly ( $n=7$ ; 14%).

The mean CD4 count was 170.1 with a standard deviation of 123.16. The mean Hb% of the population was 7.13 with a standard deviation of 1.27031492. All the cell lines in peripheral blood were affected which gave the following picture of different cell lines [Figure 3].

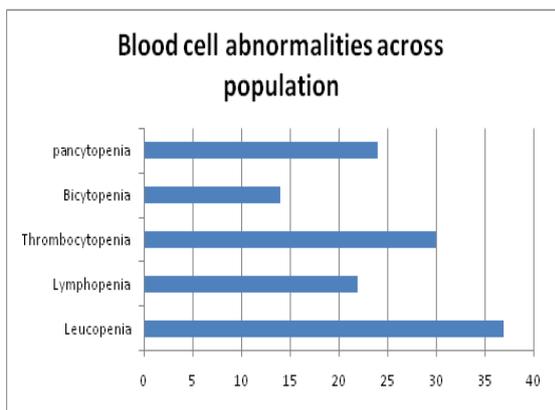


Figure 3: A view of blood cell abnormalities across the population.

Normocytic normochromic anaemia was the predominant morphology amongst all the cases, the distribution of which is shown in the Figure 4.

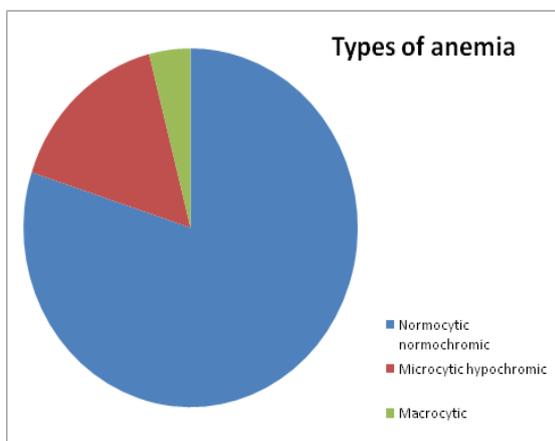


Figure 4: Morphological types of anemia.

The most common etiology found was anemia of chronic disease (34%) and other etiologies were HIV induced myelodysplasia (32%), iron deficiency anaemia (16%), helminth infection (14%) and vitamin B<sub>12</sub> deficiency leading to megaloblastic anaemia was seen in 4% cases [Figure 5].

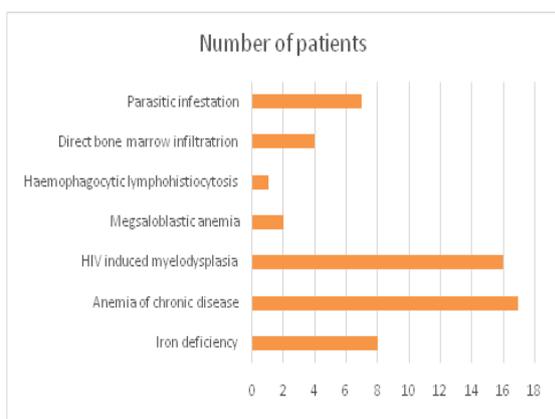


Figure 5: Number of patients in each etiological category of anemia.

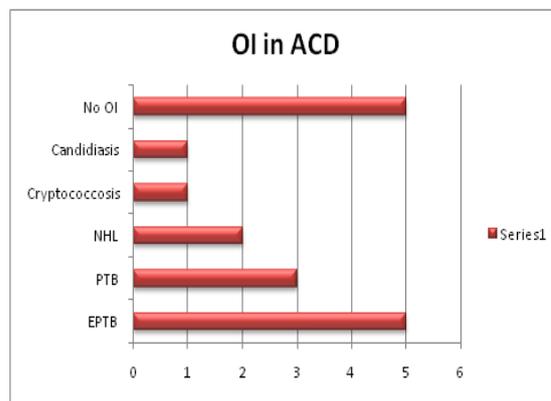


Figure 6: Opportunistic infections in patients with Anaemia of chronic disease.

### DISCUSSION

The primary aim of this study was to study the different types and the various etiologies of anemia in newly diagnosed HIV infected adults. In our study the most common etiology found was Anaemia of chronic disease seen in 34% cases. Out of all the cases of anaemia of chronic disease no significant OI could be detected in 10% of the total cases i.e; 29.41% cases of anaemia of chronic disease [Figure 6]. The anaemia in these cases may be due to HIV itself, but this cannot be said with certainty. The next most significant etiology was HIV induced myelodysplasia seen in 32% cases. These were the patients presenting with pancytopenias and bicytopenia in peripheral blood associated with dysplastic changes in bone marrow involving all cell lines. The literature suggests the facts that MDS caused by HIV is different from primary MDS and chances of conversion to leukaemia in HIV induced MDS are very low. It is also shown that HIV induced MDS respond well to HAART. The next involved etiologies as per number of cases are Iron deficiency anaemia and helminth infection causing 16% and 14% cases each. This shows that iron deficiency anaemia is not the most common etiology as is popular belief and that stress must be given on trying to identify the proper etiology of anaemia in each individual case irrespective of the severity of anaemia. The incidence of Helminth infection seen here in HIV positive individuals is comparable to that in literature.<sup>[9]</sup> But 57% of the cases of helminth infections were actually co infections along with IDA, which points out the fact that chronic blood loss due to helminth infection might have eventually led to the development of IDA.

Vitamin B<sub>12</sub> deficiency leading to megaloblastic anaemia was seen in 4% cases with a classical macrocytic picture in peripheral blood smear. There was only one case of Hemophagocytic lymphohistiocytosis proven by the diagnostic criteria as per the present literature.<sup>[10-12]</sup> Direct infiltration of bone marrow by infections was seen in 8% cases two of

them showing granulomas in bone marrow exam associated with culture showing AFB proven to be MTB, one showed budding yeast cells along with macrophages, which was proven to be a case Histoplasma and one case showed LD bodies in the bone marrow proving it to be a case of visceral leishmaniasis. All of these are documented causes of anaemia in HIV.<sup>[13,14]</sup>

In this study, 70 % of the patients belonged to the lower socioeconomic group while only 4% of the cases belonged to the upper socioeconomic group. The illiterate population comprised 34% of the cases. Illiteracy directly leads to a fall in the socio economic status of an individual as it is one of the important criteria of the modified Kuppuswamy scale. A significant reason behind the increased prevalence in a low socioeconomic group is under the utilization of health care facilities as compared to the other groups.<sup>[15]</sup> The increased prevalence of anaemia in a low socioeconomic group is well documented in multiple studies.<sup>[16]</sup>

Alcohol and its addiction have been known to cause an increase in incidence of megaloblastic anaemia while also showing increases in iron stores of the patient.<sup>[17,18]</sup> In the present study, 58% of the cases were addicted to alcohol, which is also a significant associated risk factor present in these cases.

The mean CD4 count was 170.1 with a standard deviation of 123.16. This low value of mean CD4 is probably an indicator of the fact that the time of presentation to a health care facility for patients in India is during the late course of the disease. The mean Hb% of the population was 7.13 with a standard deviation of 1.27031492. In a simple regression analysis between Hb% and CD4 a weakly positive relationship was found with a 'r' value of 0.2085. Though in most series the correlation of Hb% and CD4 count is linear<sup>[19-21]</sup>, there are studies in which a weak correlation was observed between CD4 cell count and Hb% (S.M. Alavi et al -  $r = 0.451$ ,  $p = 0.056$ ).<sup>[22]</sup> In a study done in northwest Ethiopia on 400 ART naive HIV patients findings showed that one-third of HAART naive HIV positive patients in Northwest Ethiopia are anaemic and the increase in the prevalence of anaemia with decreased CD4 cell count was statistically significant.<sup>[23]</sup>

Bicytopenia was present in 14 (28%) cases, while pancytopenia was present in 24 (48%) cases. This is much higher as compared to patients not suffering from HIV. The majority of the cases belong to normocytic normochromic morphology (80%), in tune with the data available worldwide.<sup>[24]</sup>

## CONCLUSION

- Anaemia in HIV is also associated with demographic factors like socio economic status, literacy rates and addiction in the population so

impetus must be given to the improvement of these parameters in the general populace.

- The most prevalent morphological variety of anaemia in HIV infected adults not on HAART is Normocytic Normochromic.
- Pancytopenia is also present along with anaemia in a significant number of cases.
- Haemoglobin levels are related to the CD4 status of the patient and are indicative of worsening of the disease.
- Anaemia of chronic disease is the most common etiology closely followed by HIV induced myelodysplasia.

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## REFERENCES

1. Dr. Mukund B. Kulkarni, Dr. Muktpal M. Bhalerao, Dr. S.U.Mungal, Dr. S. P. Dube. Anemia in People Living With HIV/AIDS: A Cross Sectional Study from India. IOSR Journal of Dental and Medical Sciences. 2015;14(2): PP 04-08
2. Scientific Research and Essay. 2007; 2(8): 315-318.
3. Coyle TE. Hematologic complications of human immunodeficiency virus infection and the acquired immunodeficiency syndrome. Med Clin North Am. 1997; 81:449-70.
4. World Health Organization. Worldwide prevalence of anaemia 1993-2005. Geneva: World Health Organization. 2008.
5. Hambleton J. Hematologic complications of HIV infection. Oncology 1996.
6. Kreuzer KA, Rockstroh JK. Pathogenesis and pathophysiology of anaemia in HIV infection. Ann Hematol. 2011;23:45-9.
7. Spivak JL. The blood in systemic disorders. Lancet. 2000.
8. Kreuzer KA, Rockstroh JK, Jelkmann W, Theisen A, Spengler U, Sauerbruch T, et al. Inadequate erythropoietin response to anaemia in HIV patients: relationship to serum levels of tumor necrosis factor-alpha, interleukin-6 and their soluble receptors. Br J Haematol. 1997;11:69-75.
9. Walson JL, Stewart BT, Sangare L, Mbogo LW, Otieno PA, Piper BKS, et al. PLOS Negl Trop Dis. 2009; 4(3): e644.
10. Janka GE. Hemophagocytic syndromes. Blood Rev. 2007; 21(5):245-253.
11. Chen TL, Wong WW, Chiou TJ. Hematophagocytic syndrome: an unusual manifestation of acute human immunodeficiency virus infection. Int J Hematol. 2003;78: 450-2.
12. Grateau G, Bachmeyer C, Blanche P, et al. Hemophagocytic syndrome in patients infected with the human immunodeficiency virus: nine cases and a review. J Infect. 1997; 34:219-25.
13. Hillman RS. Anaemia. In: Fauci AS, Martin JB, Braunwald E, et al., eds. Harrison's principles of internal medicine. 14th ed. New York City: McGraw-Hill. 1998;334-9.

14. NACO, UNGASS India report: progress report on the declaration of commitment on HIV/AIDS; 2006.
15. Mutchler JE, Burr JA. Racial differences in health and health care utilization in later life: The Effect of Socioeconomic status. *Journal of Health and Social Behavior* .1991; 32: 342-356.
16. Betsy Lozoff, MD. Elias Jimenez, MD. Julia B. Smith, EdD. *Arch PediatrAdolesc Med*. 2006;160(11):1108-1113. doi:10.1001/archpedi.160.11.1108.
17. Iwama H, Iwase O, Hayashi S, Nakano M, Toyama K. Macrocytic anaemia with anisocytosis due to alcohol abuse and vitamin B6 deficiency. *The Japanese Journal of Clinical Hematology*. 1998; 34(11): 1127-1130
18. Ioannou G, Dominitz J, Weiss N, Heagerty P, Kowdley K. The effect of alcohol consumption on the prevalence of iron overload, iron deficiency and iron deficiency anaemia. *Gastroenterology*. 2012; 126(5): 1293-1301.
19. Creagh T, Mildvan D. Greater prevalence of anaemia in women and African Americans with HIV/AIDS in the HAART era: a study of 10,000 patients [abstract 475]. The Anaemia Prevalence Study Group. In: Program and abstracts of the 40th Annual Meeting of the Infectious Diseases Society of America (Chicago). Alexandria, VA: Infectious Diseases Society of America. 2002;127.
20. Levine AM, Berhane K, Masri-Lavine L, et al. Prevalence and correlates of anaemia in a large cohort of HIV-infected women: Women's Interagency HIV Study. *J Acquir Immune Defic Syndr*. 2001; 26:28-35.
21. Semba RD, Shah N, Klein RS, et al. Prevalence and cumulative incidence of and risk factors for anaemia in a multicenter cohort study of human immunodeficiency virus-infected and -uninfected women. *Clin Infect Dis*. 2002; 34: 260-6.
22. S.M. Alavi, F. Ahmadi and M. Farhadi. Correlation between Total Lymphocyte Count, Hemoglobin, Hematocrit and CD4 Count in HIV/AIDS Patients. *Acta Medica Iranica* 2009; 47(1): 1-4.
23. Ferede G and Wondimeneh Y. Prevalence and related factors of anaemia in HAART-naive HIV positive patients at Gondar University Hospital, Northwest Ethiopia. *BMC Haematology*. 2013.
24. Coyle TE. Hematologic complications of human immunodeficiency virus infection and the acquired immunodeficiency syndrome. *Med Clin North Am*. 1997;81: 449-70.

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