

## A Study Of Factors Associated With Anaemia In HIV Infected Individuals

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**Abstract:** Background: Anaemia is the most common hematologic manifestation seen in HIV infection. The etiologies of anaemia may be different from the general population. Objectives: to study the etiology of anaemia in HIV positive individuals. Material & Methods: A cross-sectional study will be carried out on 100 consecutive HIV patients in different stages of disease attending the Department of Medicine, Vijayanagara Institute of Medical Sciences Bellary, Karnataka during the period of 18 months from October 2014 to May 2016 applying following inclusion and exclusion criteria. Results: Mean age of the patients was 39 years and 72% of the subject were male. CD4 count was lesser than 200/ $\mu$ l in 61% of patients and was greater than 200 in 39% of the patients. 42% patient had moderate grade anaemia and 58% had severe grade anaemia patient mild grade anaemia was excluded. 54% of patient had anaemia due to chronic disease, 12% had iron deficiency anaemia, 11% had anaemia due to vitamin B12 deficiency, 22% had anaemia due to zidovudine induced anaemia and 1 patient had anaemia due Hemolysis. There was significant difference in hemoglobin values among patients who had CD4 count less than 200/ $\mu$ l (mean Hb 6.387gm/dl) and CD4 count greater than 200/ $\mu$ l (mean Hb 7.469gm/dl) ( $p=0.001$ ). There was positive correlation between CD4 count and hemoglobin ( $r=0.2637$ ,  $p=0.001$ ) There was positive correlation between Vitamin B12 levels and CD4 count ( $r=0.2748$ ) or ( $r=0.271$ ) but relationship is weak. Conclusion: It was concluded that mean age of the patients was 39 years. the patients included in this study had advanced disease. Most of the patient had anaemia of chronic disease when compared to other etiology. [Naik K Natl J Integr Res Med, 2019; 10(2):48-51]

**Key Words:** anaemia, CD4 count, Hemolysis, iron deficiency anaemia

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**Introduction:** The human immunodeficiency virus (HIV) is a lentivirus (a subgroup of retrovirus) that causes and over time acquires immunodeficiency syndrome (AIDS).<sup>1,2</sup> AIDS is a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancer to thrive. Without treatment, average survival time after infection with HIV is estimated to be 9 to 11 years, depending on the HIV subtype.<sup>3</sup>

AIDS was first clinically observed in 1981 in the United States. The initial cases were a cluster of injection drug users and gay men with no known cause of impaired immunity who showed symptoms of pneumocystis carinii pneumonia (PCP), a rare opportunistic infection that was known to occur in people with very compromised immune systems. Soon thereafter, additional gay men developed a previously rare skin cancer called Kaposi's sarcoma (KS). Many more cases of PCP and KS emerged, alerting U.S. Center for Disease Control and Prevention (CDC) and a CDC task force was formed to monitor the outbreak. The earliest retrospectively described case of AIDS is believed to have been in Norway beginning in 1966.

Anaemia in human immunodeficiency virus (HIV)-infected patients can have serious

implications, which vary from functional and quality-of-life decrements to an association with disease progression and decreased survival. In 2002, 16 members of the Anaemia in HIV Working Group, an expert panel of physicians involved in the care of HIV-infected patients that met first in 1998, reconvened to assess new data and to translate these data into evidence-based treatment guidelines.

The group reached consensus on the prevalence of anaemia in the highly active antiretroviral therapy era; the risk factors that are independently associated with the development of anaemia; the impact of anaemia on quality of life, physical functioning, and survival; the impact of the treatment of hepatitis C virus co-infection on anaemia in HIV-infected patients; evidence-based guidelines for treatment of anaemia in HIV-infected patients, including the therapeutic role of Epoetin Alfa; and directions for future research.<sup>4</sup> The overall incidence of anaemia among HIV positive patients ranges from 10% in asymptomatic patients up to 92% in individuals with full-blown AIDS.<sup>5</sup>

In HIV positive patient's anaemia is a prognostic marker of future disease progression or death, independent of CD4 and viral load.<sup>5</sup> Anaemia impacts a range of dimensions of quality of life.

The common causes of anaemia in HIV and non HIV patients are varied so treatment will differ. Understanding the association between anaemia and HIV infection is important because treatments for anaemia are available including recombinant human erythropoietin, blood transfusion, and in drug-induced anaemia, cessation of myelosuppressive therapies. Hence knowledge of the pathophysiological mechanisms and the prevalence of various causes of anaemia will help us in treatment of anaemia in HIV positive patients. Very few studies have examined factors associated with anaemia in the setting of a developing country.

This study was conducted with the objective: to study the etiology of anaemia in HIV positive individuals and to study the relationship between anaemia and immunological status as indicated by the CD4 count.

**Materials and Methods:** A cross-sectional study will be carried out on 100 consecutive HIV patients in different stages of disease attending the Department of Medicine, Vijayanagara Institute of Medical Sciences Bellary, Karnataka during the period of 18 months from October 2014 to may 2016 applying following inclusion and exclusion criteria. All respondents were adults, aged more than 18 yrs. Permission for the study was obtained from the College authorities prior to commencement. Informed consent was taken prior to inclusion in the study.

**Inclusion Criteria:** HIV patients above 18 years of age and Anaemia with hemoglobin less than 10 gm/dl

**Exclusion Criteria:** HIV patients below 18 years of age and HIV patients who do not give consent for the study

**Method of collection of data:** The study will be undertaken in 100 HIV positive patients who will be attending the Department of Medicine, Vijayanagara Institute of Medical Sciences, Bellary during the study period of October 2014 to may 2016. A detailed and careful history will be taken regarding the duration and symptoms of the disease. A thorough systemic examination will be done.

**Test:** HIV was confirmed by the ELISA test. CD4 counts were analyzed using the Flowcytometry method. Hemoglobin, total count and differential

count were performed in the laboratory using automated counting chambers. Further work up for anaemia including peripheral smear examination, mean corpuscular volume estimation, serum ferritin and B12 levels were done. Bone marrow aspiration and biopsy was done for few of the patients as part of anaemia evaluation. Other tests were done as per the needs of the patient.

**Statistical methods:** Once data was collected and tabulated using MS Office Excel, the tabulated data was then analyzed. Descriptive Analysis was done using Percentages, Proportions, Mean and Standard Deviations and inferential Analysis was done using unpaired T-tests, chi-square.

**Results:** In our study 12 patients were between 18-30 years, 39 patients were between 31-40 years of age, 43 patients were 41-50 years of age and 6 patients were >50 years. 100 patients with HIV infection and anaemia were included in the study. Minimum age was 18 years and maximum age was 55 years (Mean age was 39). Out of 100 HIV patients 72 were male and 28 were female. Among 72 male patients 47 patients having CD4 count of <200 and 25 were having CD4 >200. Among 28 female patients 15 patients having CD4 count of <200 and 13 were having CD4 >200. (Table 1). Out of 100 HIV patients 72 were male and 28 were female. Among 72 patients 8 having CD4 count of <200 and 10 were having CD4 >200 with disease duration >1 month. Among 44 male patients 28 having CD4 count of <200 and 16 were having CD4 >200 with disease duration 1-12 months. Among 38 female patients 25 having CD4 count of <200 and 13 were having CD4 >200 with disease duration >12 months.

**Table 1: Distribution of CD4 counts**

CD COUNT	Number of patients	%
<200/ $\mu$ l	61	61%
>200/ $\mu$ l	39	39%
Total	100	100%

Out of 100 HIV patients 61 were having cd-4 counts of <200/ $\mu$ l, mean haemoglobin was 6.210 39 were having cd-4 counts of >200/ $\mu$ l, Mean haemoglobin was 6.767. only patient below Hb 10mg/dl was included in the study, out of which 58 had severe anaemia and 42 had moderate anaemia. Out of 100 patient, 69 had normocytic anaemia, 14 had megaloblastic and 17 had microcytic anaemia. (Table 2).

**Table 2: Etiology of anaemia**

Etiology	No of patients	%
Anaemia chronic disease (inflammation)	55	55
Iron deficiency anaemia	12	12
B12/Folate deficiency anaemia	11	11
Zidovudine Induced anaemia	22	22
Anaemia secondary to hemolysis	1	1
TOTAL	100	100

There was significant difference in hemoglobin values among patients who had CD4 count less than 200/ $\mu$ l (mean Hb 6.210) and CD4 count greater than 200/ $\mu$ l (mean Hb 6.767gm/dl) ( $p=0.0449$ ). There was positive correlation between CD4 count and hemoglobin ( $r=0.2637$ )

**Table 3:CD4 count and haemoglobin**

CD4 count	Anaemia	Mean $\pm$ SD
<200	61	6.210 $\pm$ 1.252
>200	39	6.767 $\pm$ 1.461
total	100	

**Discussion:** Mean age in males was 40 years and in females was 40 years. These demographic data are similar to those documented in other studies done in India.<sup>6</sup> Eighty one of patient in this study are married and 9 of patient are unmarried. 8 out of 9 married patient are male and 1 was female. Through Premarital and extramarital sexual contact, most male have acquired the disease, whereas females have mostly acquired the disease from their spouses. Females have generally been diagnosed as HIV positive when their husbands came with opportunistic infections.

In our study 72% had established diagnosed greater than 1 year and 38% has diagnosed within 1 years, this was much similar to many studies<sup>6</sup>. The mean CD4 count was 237/ $\mu$ l. Mean CD4 count in males was 233/ $\mu$ l and in females was 229/ $\mu$ l. 62% of patients had CD4 count lesser than 200/ $\mu$ l in and 39% of the patients had greater than 200/ $\mu$ l. These features were similar to the other studies done in South India.<sup>6</sup> Thus the patients included in this study had advanced disease. Severity of anaemia was classified according WHO grading<sup>7</sup>. 58% percent had severe grade anaemia, 42% had moderate grade. This was in contrast to a study done by mohsnmeidani et al in which majority of patients were found

to have mild to moderate grade anaemia occurring in 67% of patients<sup>8</sup>. This is probably because our study was done in a tertiary care hospital and majority of the patients had advanced disease and severe grades of anaemia. In our study most of patients had anaemia of chronic disease in comparison to other etiologies. 54% had anaemia of chronic disease, 22 % had anaemia secondary to use of zidovudine, 12% had iron deficiency anaemia, 11% had B12/folate deficiency and 1 % had anaemia due to hemolysis. Levin AM et al Shown that low CD4 cell counts (<200 cells/ $\mu$ l) and higher HIV-1 RNA level in plasma have been independently associated with anaemia.<sup>9,10,11</sup> However various factors not related to disease progression may interfere in the direct relationship between CD4 count and hemoglobin including antiretroviral therapy, blood loss etc. and need to be excluded as in the above study.

There may be no correlation between CD4 and anaemia if all the etiologies of anaemia are included as in our study. In our study there was significant difference in hemoglobin values among patients who had CD4 count less than 200/ $\mu$ l (mean Hb 6.387 gm/dl and CD4 count greater than 200/ $\mu$ l (mean Hb 7.469gm/dl) ( $p=0.001$ ). There was positive correlation between CD4 count and hemoglobin ( $r=0.2637$ ,  $p=0.001$ ) in our study.

Among patients with low immunological status as expressed by CD4 count less than 200/ $\mu$ l, the etiologies of anaemia were ,anaemia of chronic disease (67%), zidovudine induced anaemia (15%), B12/folate deficiency (11.5%), iron deficiency (6.5%) Among patients with CD4 count greater than 200/ $\mu$ l , the most common etiologies of anaemia were Anaemia of chronic disease (33.5%), zidovudine induced anaemia (33.5) Iron deficiency (20%), B12/folate deficiency (10%), anaemia secondary to hemolysis (2.5%) In patients who had anaemia of chronic disease mean Hb (6.554gm/dl) in patient with CD4 >200/ $\mu$ l and disease mean Hb (7.785gm/dl) in patient with CD4 <200/ $\mu$ l which was significant with p value of 0.0023.

**Conclusion:** Mean age of the patients was 39 years. 72% of the subject were male. CD4 count was lesser than 200/ $\mu$ l in 61% of patients and was greater than 200 in 39% of the patients. Thus the patients included in this study had advanced disease. Out of 100 patients 42% patient had

moderate grade anaemia and 58% had severe grade anaemia patient with Mild grade anaemia was not included in the study. Most of the patient had anaemia of chronic disease when compared to other etiology.

54% of patient had anaemia due to chronic disease, 12% had iron deficiency anaemia, 11% had anaemia due to vitamin B12 deficiency, 22 % had anaemia due to zidovudine induced anaemia and 1patient had anaemia due Hemolysis. There was significant difference in hemoglobin values among patients who had CD4 count less than 200/ $\mu$ l (mean Hb 6.387gm/dl) and CD4 count greater than 200/ $\mu$ l (mean Hb 7.469gm/dl) (p=0.001

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