

## Profile of Anaemia in HIV Positive Patients

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### ABSTRACT

**Background & Objectives:** This was a cross-sectional observational study designed to see the prevalence of anemia among HIV positive patients and its correlation with CD4 counts. **Materials & Methods:** Fifty five HIV/AIDS patients presented for the first time to Tribhuvan University Teaching Hospital [TUTH] were enrolled in the study. Patients' duration of HIV positivity, history regarding ART and duration, history of associated co morbid or opportunistic conditions were taken, CD4 counts, RFT, CBC test results were recorded. Patients' clinical and laboratory parameters were recorded. Anaemia was classified by WHO criteria for both men and women. **Results:** Out of 55 patients, 23 (42 %) had anemia, out of which 14 (60.87 %) had mild anemia (anemia but Hb not less than 9.5g/dl), four (17.39%) had moderate anemia (Hb 8 to 9.4 g/dL) and two (8.7%) had severe anemia (Hb 6.5 to 7.9 g/dL) and three (13.04%) had very severe or life threatening anemia (Hb less than 6.5 g/dL). Corresponding odds ratio from stage CD4 counts <200 to CD4 counts  $\geq$  200 for anemia was 4.55 times; which is statistically significant ( $p < 0.0001$ ). There was negative association between the prevalence of anemia and HIV stage (CD4 count). **Conclusion:** There was high prevalence of anemia and severity of immunodeficiency directly correlates with degree of anemia. Degree of anemia can be easily assessed even in rural clinical setting, hence degree of immunodeficiency can early be detected in all settings.

**Key words:** Anemia; CD4 counts; HIV positive

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### INTRODUCTION

World Health Organization (WHO) criteria for anemia in men and women are hemoglobin (Hb) concentration <13 and <12 g/dL, respectively.<sup>1,2</sup>

Anaemia may manifest as a mere laboratory abnormality in some individuals, other may experience typical symptoms (e.g. dyspnea, reduced exercise tolerance, diminished functional capacity) directly related to reduction in haemoglobin concentration.<sup>2</sup> The presence of anaemia is associated with increased morbidity and mortality in both children and adults with HIV infection.<sup>3-5</sup>

Despite the advent of Highly active antiretroviral therapy (HAART), HIV-related anaemia is still common, and independently associated with decreased survival.<sup>3,6,7</sup> Screening of anaemia, coupled with prevention and treatment efforts, should be included in HIV care initiatives.<sup>7</sup> CD4 measurements are the most important indicator of mortality and wider access to affordable tests is

needed in resource limited settings. In most cases, the cause of anaemia in HIV infected patients is multifactorial, reflecting the associated and often additive effects of infection, malignancy, malnutrition, and polypharmacy.<sup>2</sup> The finding of a low haemoglobin concentration warrants careful evaluation for treatable underlying illnesses, including a complete blood count with red cell indices and reticulocyte count, serum bilirubin and vitamin B12, red cell folate levels, iron studies, peripheral blood smear.<sup>8</sup> Mycobacterial, fungal, parasitic and viral infection cause mild to moderate anaemia in addition to HIV.<sup>9</sup> Malignancy and lymphoproliferative disorders being more common in HIV positive patients are also potential cause of anemia. Nutritional deficiencies are common in patients with advanced immunosuppression. There is paucity of data from Nepal on the haematological manifestations of HIV which prompted us to conduct this study. Moreover, in

the developing countries like Nepal, it is very difficult to assess the status in early stages of the disease because most people do not seek medical attention until they are very sick. By that time, the disease is already in the advanced stage. So this study was conducted to see anemia in HIV positive patients and the relation of anemia with CD4 counts in Nepalese context.

## MATERIALS AND METHODS

It was a Descriptive Analytical Cross-sectional study conducted in Tribhuvan University Teaching Hospital (TUTH) in Medical In-patient Department and the Medical Out Patient Department (OPD) from June 2010 to October 2011. Inclusion criteria for the study were HIV positive patients of age >15 years. Consent was taken from each individual for study. Exclusion criteria were follow-up cases, participants having any acute systemic illness, patients already having disease causing anemia co-occurring with HIV e.g. Rheumatoid arthritis (RA), Chronic Kidney disease (CKD) and Age <15 years. Participants were selected by these criteria. History of the patients (Ethnicity, Address, Area belonging to [mountains / terai], Blood Pressure, Pulse, Temperature, Respiratory rate, Weight /BMI and presenting complaints) were recorded in structured questionnaire and physical examination (general and systemic) was performed. Fifty five patients were incorporated in this study. Complete blood count (CBC), routine examination of urine, renal function test (RFT), sodium and potassium (Na/K), random blood sugar (RBS), HIV, Enzyme linked immunosorbent assay (ELISA)/Western blot, HBsAg, AntiHCV and CD4 count were done.

Diagnosis of HIV positive status was done through positive ELISA for HIV confirmed by Western Blot. Anaemia was classified by WHO criteria for both men and women: grade 1 or mild (9.5-10.9 g/dL), grade 2 or moderate (8-9.4 g/dL), grade 3 or severe (6.5-7.9 g/dL), and grade 4 or life-threatening (<6.5 g/dL).

Data were analyzed by using the SPSS Statistical

**Table 1:** Distribution of anemic patients according to severity

Grading of anemia	Male	Female
Grade I	13	3
Grade II	1	3
Grade III	0	2
Grade IV	1	2

Software (Version 16.0 for windows). variables are presented as means ( $\pm$  standard deviation), Frequencies and percentages were calculated for all the categorical variables. Students t-test was used to compare the mean hemoglobin of the various CD4 cell count strata. Chi-squared for trend was used to determine significant trends in the percent of patients with a given grade of anemia at different CD4 cell count strata. Univariate logistic regression was performed to understand the associations between age, sex, HIV-associated co-morbidities, CD4 cell counts for anemic versus non anemic patient.  $p < 0.05$  was considered statistically significant.

## RESULTS

A total of 55 patients were enrolled in the study. The mean age of enrolled patients was 35.85 years  $\pm$  9.56 years. The number of patients in different age group; 30.91% patients were of age 16-30 years, 52.73% patients were of age 31-45 years and 16.36% patients were of age 46-60 years.

The study population consisted of 69% males and 31% females. Eighty two percent were from Mountainous region and 18% from Plains. A total of 41.82% of study population was Brahmin/Chhetri, and 18.18% were Newars and 40% from other castes.

Out of 55 enrolled patients, 26 (47%) patients were found to have additional disease/opportunistic infections. Eleven (20%) patients had pulmonary or extrapulmonary forms of tuberculosis. One (1.8%) patient was seropositive for both Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV), whereas 7(12.72%) patients were seropositive for HCV. One (1.8%) patient was co-infected each with Pneumocystis carini pneumonia (PCP), syphilis, oesophageal candidiasis and molluscum contagiosum. Three (5.5%) patients had herpes infections and two (3.6%) patients had toxoplasmosis (Table 3).

In this study, 22 (40%) patients had malnutrition/underweight Body Mass Index (BMI<18.5). Twenty (36%) of the study patients were taking

**Table 2:** Correlation between different parameters with hemoglobin level

Variables	Yes (Hb level gm%)	No (Hb level gm%)	P value
ART use	11.58	12.02	0.60
Malnutrition	10.93	11.86	0.39
Opportunistic infections	11.81	11.9	0.91

Antiretroviral therapy (ART) (HAART, most regime containing zidovudine), 35 (64 %) were not taking ART.

Out of 55 patients, 23 (42 %) had anemia, out of which 14 (60.87%) had mild anemia (anemia but Hb more than 9.5 gram percent), four (17.39 %) had moderate anemia (Hb 8-9.4 gram percent) and two (8.7 %) had severe anemia (Hb 6.5-7.9 gram%) and three (13.04 %) had very severe or life threatening anemia (Hb less than 6.5 gram percent) ( Table 1).

Overall, 47.4% of males and 29.4% of females had anemia. No association between anemia and either age or sex was noted.

A total of 47% of patients in the study had a medical history/diagnosis of HIV associated condition/opportunistic infections. Those having HIV-associated condition had mean Hb of 11.81 gram% compared to 11.90 gram % in those without such condition. If an underweight BMI was present, the mean Hb was 10.93 gram % compared to 11.86 gram percent in those not having underweight BMI. If there was a use of ART, the mean Hb 11.58 gram % compared to 12.02 gram percent in those not taking ART ( Table 2 ).

CD4 measurements indicate a strong association between the prevalence of anemia and the severity of HIV disease. Table 4 demonstrates the negative association between the prevalence of anemia and CD4 counts, indicating that the percentage of patients with anemia increased as CD4 counts decreased. Corresponding odds of having anemia for CD4 counts < 200/cmm is 4.522 times the odds of having anemia for CD4 counts >200/cmm (  $p < 0.001$  .CI 95% )

## DISCUSSION

This hospital based cross-sectional study, conducted at Tribhuvan University Teaching

Table 3: HIV associated conditions in study population

Parameters	Frequency	Percent
HBV/HCV	1	1.8
HCV	6	10.9
Herpes infection	3	5.5
Mollus contagiosum	1	1.8
Oesophageal candidiasis	1	1.8
PCP	1	1.8
Syphilis	1	1.8
Tuberculosis	11	20.0
Toxoplasmosis	2	3.6

Table 4: CD4 count-wise patient distribution & their mean Hb

CD4 count	No. of patient	Mean Hb
0-99	6	10.88
100-149	6	8.75
150-199	5	9.22
200-249	5	13.02
250-299	9	12.54
300-349	5	12.24
>=350	19	13.12

hospital, Kathmandu, Nepal evaluated the hematological abnormalities in HIV positive patients. This study included the patients with HIV positive status, some taking ART, some not. Anemia (defined as hemoglobin <12 and 13 g/dL for female and male respectively) was present in 42% of the 55 patients with HIV/AIDS evaluated in a clinical practice setting.

This study highlights a high (42%) prevalence of anemia among HIV-infected individuals according to the WHO definition for anemia (hemoglobin <12 g/dL for females and <13 g/dL for males). This is similar to the 40 % prevalence reported in a study done in south India and 20 to 60% in studies done in America and Europe.<sup>10</sup> Most developing country studies have focused specifically on groups at higher risk for anemia, such as pregnant or TB coinfecting patients. Since this study has patients of both genders distributed across all CD4 count strata, it may more accurately reflect the prevalence of anemia in the general HIV infected population. Further analysis of our data revealed an association between anemia and decreasing CD4 counts consistent with previous similar study.<sup>11-13</sup> The mean haemoglobin of the patients dropped proportionately according to the fall of CD4 counts except mean Hb in the CD4 range of 0 to 99; which may be due to use of ART (and iron and folic acid along with) in all patient of this CD4 range. Corresponding odds ratios for CD4 count <200 with CD4 counts >200 for anemia (hemoglobin <12 for female/<13 for male) was 4.522 times; which is statistically significant (  $p < 0.001$ , 95% CI). This demonstrates the negative association between the prevalence of anemia and CD4 counts, indicating that the proportion of patients with anemia increased as severity of HIV increased, suggesting decreasing immune function have direct impact on Hb synthesis. Degree of anemia can be easily assessed in any rural clinical setting. This provides an opportunity for earlier assessment of immune status, so earlier and more effective management and improved outcomes in HIV positive population.

This study also notes the presence of additional diseases in HIV positive patients in about half of patient numbers (47%). Among these tuberculosis is the most common, pulmonary or extrapulmonary forms of tuberculosis being present in 20%. Other opportunistic infections besides tuberculosis were also noted in the study-1.8% patients were co-infected with PCP, 1.8% with oesophageal candidiasis, 1.8% with molluscum contagiosum, 5.5% patients with herpes infections and 3.6 percent with toxoplasmosis.

Because of common routes of transmission some patients (12.72%) were seropositive for HCV and other few (1.8%) were seropositive for both HBV and HCV; and other few (1.8%) were coinfecting with syphilis.

The main limitation of the analysis of factors associated with anemia in this study is its cross sectional design, which precludes definite determination of the temporal and causal relationships between anemia and significantly associated factors. Patients could not afford for and could not undergo additional investigations like vitamin B12, folic acid level, iron profile and bone marrow examination which are needed to find the additional causes of anemia. All of the investigations could not be incorporated in the study.

So it is recommended that every patient with anemia be asked for high risk behavior for acquiring HIV and they should be tested for HIV. Every HIV positive patients should be frequently tested for anemia. Such anemic patients should be offered full range of investigation for anemia like RBC indices, reticulocyte, iron profile, serum folate and vitamin B12 level to find out the cause and effect of anemia. Early correction of anemia by addressing the contributing causes, supplementing the deficient substrates should be done to improve treatment outcome in HIV positive patients. Vitamin B12, folic acid level tests should also be made available in government hospitals so that the cost will be low to the patients.

## CONCLUSION

This study provides an understanding of anemia in HIV positive patients and early identification of severity of immunodeficiency. The severity of immunodeficiency correlates with degree of anemia as found in this study. This study highlights a high prevalence of anemia among HIV-infected individuals.

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