

# A study of prevalence of anemia by sociodemographic, clinical, and laboratory characteristics among HIV-positive patients

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## ABSTRACT

Anemia in 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. As anemia burden on morbidity and mortality among HIV patients increases, there is justified need to understand risk factors for the development of anemia. This study tends to establish risks for development of anemia among patients with HIV infection. The study was conducted at the department of medicine of a tertiary care teaching hospital in western Maharashtra from July 2015 to September 2016. A total of 316 HIV-infected patients were recruited. The overall prevalence of anemia in this study was 164 (51.9%). Severe anemia was seen in 10.4% of patients. The prevalence of anemia was comparable in both sexes. Low socioeconomic status was associated with higher prevalence of anemia than seen in medium- and high-income patients. The prevalence was significantly higher among indoor patients, among patients who reported the use of herbal medication, and among patients with moderate-to-severe malnutrition. Clinically, the presence of jaundice, blackening of nails, lymphadenopathy, skin changes, and fever was significantly associated with anemia. Body mass index assessment revealed underweight as well as normal weight patients who had anemia. On laboratory characteristics, leukopenia and leukocytosis were associated with anemia.

**Key words:** AIDS, anemia, blood indices, clinical features, HIV, sociodemographic

## INTRODUCTION

India has the third largest HIV epidemic in the world which is progressing toward the world leader. In 2016 statistics, HIV prevalence in India was an estimated 0.26%. Overall, India's HIV epidemic is slowing down, with a 32% decline in new HIV infections (86,000 in 2015), and a 54% decline in AIDS-related deaths (62,000) between 2007 and 2015. Despite this, 51% of HIV-related deaths in Asia are in India.<sup>[1,2]</sup>

The causes of anemia in HIV infection are multifactorial.<sup>[3]</sup> HIV, *per se*, causes a decrease in production of red blood cells (RBCs) and other bone marrow elements, as it has a direct effect on bone marrow stromal cells and causes cytokine secretion. The elevated level of cytokines and tumor necrosis factor further inhibit hematopoiesis in HIV. Treatment of HIV and reduction of virus load by the use of highly active antiretroviral therapy (HAART) may improve hematopoiesis.<sup>[4]</sup>

Patients with HIV may also acquire chronic Parvovirus B19 infection of bone marrow, resulting in profound decrease in the numbers of RBCs. In addition, anemia may result from the indirect effects of HIV infection, such as adverse reactions to medications such as zidovudine, opportunistic infections, neoplasms, and nutritional abnormalities arising from anorexia, malabsorption, or metabolic disorders. An inadequate supply of iron, folate, and

vitamin B12, defective bone marrow, and defect in the essential hematopoietic growth factor as well as erythropoietin, leads to alterations in the components of normal erythropoiesis, may produce anemia.<sup>[5,6]</sup>

In the anemia prevalence study Group, there was a 71% greater prevalence of anemia among women than among men when anemia was defined as a hemoglobin level of <12 g/dl in women and of <13 g/dl in men. This presumably reflects the overall higher prevalence of anemia in female persons, which may be largely attributed to menstrual blood loss, pregnancy and delivery.<sup>[7]</sup>

Anemia in HIV-infected patients can have serious implications, varying from functional and quality of life decrements to an association with disease progression and decreased survival.<sup>[7]</sup> There is an independent correlation between decreased survival in HIV-infected anemic patients regardless of cluster of differentiation (CD4<sup>+</sup>) T-lymphocyte count and plasma HIV ribonucleotide analog concentration. The HIV-infected patients who recover from anemia have better survival rates as compared to those who do not recover.<sup>[8]</sup>

The HIV prevalence among the low-risk general population in Ahmednagar district is moderate at 0.55% (PPTCT, 2008), while the trend has been constant over the past 6 years (HSS, ANC, 2003-08). The prevalence has been relatively higher in the high-

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risk men at 10.13% (CLINIC walk-in males, 2008) and female sex workers at 14.80% (HSS, FSWs, 2008). The district has a moderate epidemic potential among general population, but a high prevalence among the high-risk groups with a potential to further spread the infection into the low-risk population.<sup>[9]</sup>

As anemia burden on morbidity and mortality among HIV patients increases, there is justified need to understand risk factors for the development of anemia. This study has attempted to establish risks for development of anemia among patients with HIV infection.

### Aims and Objective

The aim of this study is to determine the prevalence of anemia by sociodemographic, clinical, and laboratory characteristics among HIV-positive patients attending the medicine department of a tertiary care teaching hospital.

## METHODOLOGY

The study was conducted between July 2015 and September 2016.

### Inclusion Criteria

All consenting HIV-infected patients aged 18 years and older admitted at medicine wards and patients attending outpatient department at the time of study were included in the study.

### Exclusion Criteria

Pregnant and lactating women, patients under 18 years, as well as patients known to have chronic kidney disease, patients with known hemoglobinopathies, and patients who received blood transfusion within the previous 2 months were excluded from the study.

A structured questionnaire was used to collect sociodemographic information, medical, and past medical history including detailed drug use apart from ART. Information on ART types and duration was obtained from patients ICTC card number for patients on ART. Gynecological history was obtained for all enrolled women. Suspected pregnancy, i.e., last normal menstrual period longer than 1 month had urine pregnancy test UPT done. Patients' own statement of their monthly income was used to assess their economic status.

Patients were examined for pallor, jaundice, cyanosis, respiratory rate, pulse rate, body temperature, and blood pressure; mouth lesions, gum bleeding, lymphadenopathy, skin and nails changes, spleen, and liver size were recorded. Mid-upper arm circumference (MUAC) was measured to the nearest centimeter. MUAC of <18.5 was taken as acute severe malnutrition, 18.5-<22 acute moderate malnutrition, and  $\geq 22$  normal nutrition. Weight was recorded to the nearest 0.5 kg. Height was recorded to the nearest 0.5 centimeters. Body mass index (BMI) of <18.5 Kg/m<sup>2</sup> was taken as underweight, 18.5-24.9 kg/m<sup>2</sup> normal, 25-29.9 kg/m<sup>2</sup> overweight, and  $\geq 30$  kg/m<sup>2</sup> obesity. All patients were tested for complete blood count and CD4 count.

## RESULTS

From July 2015 to September 2016, a total of 1025 HIV-infected patients visited medicine department. 829 patients aged 18 years

and above attended outpatient clinic and 196 known HIV were admitted to the medicine wards. Out of these, 225 patients from the outpatient clinic and 91 admitted patients consented and met the inclusion criteria.

### Socio-demographic Characteristics

A total of 316 HIV-infected patients were recruited. Mean  $\pm$  standard deviation (SD) age was 44.1  $\pm$  10.1, median age was 44 years, and interquartile range 44 years. Majority of the patients 236 (75%) were in the age group of 25-49 years. Female patients comprised 232 (73%) of study population. 79% (251/315) of participants were employed, 160 (50.6%) were married, 199 (63%) attained primary education, and 215 (64.1%) had low income or lack source of income [Table 1].

### Prevalence of Anemia by Sociodemographic Characteristics

The mean  $\pm$  SD hemoglobin was 11.4g/dl  $\pm$  2.55. More than half of the patients 164 (51.9%) (female 121/232 [52.2%] and male 43/84 [51.2%]) had anemia, with 33/164 (20.1%) of anemic patients presenting with severe anemia. Anemia was common among the unemployed patients 41/65 (63.1%) than the employed ones 123/251 (49%) ( $P = 0.051$ ). Anemia was significantly more prevalent in participants with no income 41/65 (63.1%) than in those with low-, medium-, and high-income  $P = 0.047$ .

Admitted patients had significantly higher anemia prevalence 69 (75.8%) compared to 95 (42.2%) of patients who were recruited from the outpatient clinic,  $P = 0.001$  [Table 2]. Patients who reported the use of herbal medication in this study had a higher prevalence of anemia,  $P = 0.04$  [Table 3]. Of ART-naïve patients, 30 (68.2%) were anemic, while of those on ART irrespective of the regimen, 134 (49.7%) were anemic ( $P = 0.02$ ).

### Prevalence of Anemia by Clinical Characteristics

On physical examination, the presence of jaundice, blackening of nails, lymphadenopathy, skin changes and fever was significantly

**Table 1: Sociodemographic characteristics of the study population**

Characteristics	Categories	Frequency (%)
Age (years)	18-24	4 (1.3)
	25-49	236 (74.7)
	50+	76 (24.0)
Sex	Females	232 (73.4)
Marital status	Married	160 (50.6)
	Single	41 (13.0)
	Widow/widower	75 (23.7)
	Divorced	40 (12.7)
Level of education	No formal education	21 (6.6)
	Primary	199 (63.0)
	Secondary	76 (24.1)
	College/university	20 (6.3)
Occupation	Unemployed	65 (20.6)
	Employed	251 (79.4)
Approximate income	No income	65 (20.6)
	Low income	150 (47.6)
	Medium income	85 (26.9)
	High income	16 (5.0)

**Table 2: Prevalence of anemia by sociodemographic characteristics**

Characteristics	Attribute	Total patients n=316	Anemic patients n=164 (51.9)	P
Age (years)	18-24	4 (100)	1 (25)	0.431
	25-49	236 (100%)	126 (53.4)	
	50+	76 (100%)	37 (48.7)	
Sex	Female	232 (100%)	121 (52.2)	0.490
Marital status	Married	160 (100)	89 (55.6)	0.263
	Single	41 (100)	16 (39)	
	Widow/widower	75 (100)	40 (53.3)	
	Divorced	40 (100)	19 (47.5)	
Education	No formal education	21 (100)	10 (47.6)	0.234
	Primary	199 (100)	111 (55.8)	
	Secondary	76 (100)	36 (47.4)	
	College/university	20 (100)	7 (35)	
Occupation	Unemployed	65 (100)	41 (63.1)	0.051
	Employed	251 (100)	123 (49)	
Approximate income	No income	65 (100)	41 (63.1)	0.047
	Low income	150 (100)	81 (54)	
	Medium income	85 (100)	36 (42.4)	
	High income	16 (100)	6 (37.5)	

**Table 3: Prevalence of anemia by clinical characteristics**

Characteristics	Total patients (%)	Patients with anemia n=164 (51.9%)	P
History of blood transfusion since HIV diagnosis	28 (100)	21 (75)	0.01
Co-trimoxazole chemoprophylaxis	234 (100)	127 (54.3)	0.15
Herbal medication use	17 (100)	13 (76.5)	0.04
Patients on ART	272 (100)	134 (49.7)	0.02
Presence of jaundice	3 (100)	3 (100)	0.09
Nail changes	35 (100)	22 (62.9)	0.17
Presence of lymphadenopathy	7 (100)	6 (85.7)	0.07
Presence of tachypnea (breath per minutes)	12 (100)	11 (91.7)	0.01
MUAC (cm)			
Severe acute malnutrition	3 (100)	3 (100)	0.01
Moderate acute malnutrition	19 (100)	15 (78.9)	
Normal nutrition status	294 (100)	146 (49.7)	
BMI (kg/m <sup>2</sup> )			
Underweight	40 (100)	30 (75)	0.001
Normal weight	153 (100)	85 (55.6)	
Overweight and obese	123 (100)	49 (39.8)	

MUAC: Mid-upper arm circumference, BMI: Body mass index

associated with anemia [Table 3]. MUAC assessment revealed anemia in all patients with severe acute malnutrition and 78.9% of patients with moderate acute malnutrition ( $P = 0.01$ ). BMI

assessment revealed 30 (75%) patients with underweight had anemia while those with normal weight 85 (55.6%) had anemia ( $P = 0.001$ ).

### Prevalence of Anemia by Laboratory Characteristics

On laboratory characteristics, leukopenia and leukocytosis were associated with anemia as it was seen in 53 (60.2%) and 53 (60.2%), respectively,  $P = 0.04$ . Lymphopenia, erythropenia, thrombocytopenia, and thrombocytosis were significantly associated with anemia,  $P = 0.001$  [Table 4]. Microcytic anemia was observed in 40 (90.9%), normocytic in 68 (52.3%), and macrocytosis in 56 (39.4%).

### DISCUSSION

The overall prevalence of anemia in this study was 164 (51.9%). Severe anemia was seen in 10.4% of patients. Anemia prevalence was comparable to both sexes, being slightly more than 50% for each sex. These results were similar to the study by Akanmu *et al.* which reported anemia in 52.8% of HIV-positive subjects.<sup>[10]</sup> Higher prevalence has been reported up to 84% of cases in the study by Parinitha and Kulkarni.<sup>[11]</sup> Higher prevalence in this study could be explained by the fact that majority of participants (70%) were the WHO stage IV HIV, and the advanced stage is associated with anemia.<sup>[12]</sup>

### Sociodemographic Characteristics

The study population in this study had a mean age of 44 years. The majority of study subjects in the present study were females (73.0). As per HIV surveillance in 2014 report, women were overall more likely to be HIV positive. In the present study, most participants had received primary education only, the finding similar to the latest population-based HIV survey which showed that HIV prevalence was lower among educated than uneducated or persons with lower education.<sup>[13]</sup> Majority of study participants were employed, and only a few participants had no income at all.

Married group comprised 50.6% this is similar to other reports which show HIV prevalence is highest among those who are currently or formerly married.<sup>[13]</sup> AIDS case reporting confirms the observation that more HIV prevalence is among married than unmarried persons (UNAIDS, 2016).

### Prevalence of Anemia by Sociodemographic Characteristics

53.4% of the patients between 25 and 49 years of age were anemic. Many studies have found significantly high prevalence of anemia in female HIV-infected patients than in males.<sup>[7,14,15]</sup> However, in our study, anemia prevalence was comparable in both males and females probably because there was no statistically significant difference in employment status and level of income among males and females. Unemployment and none or low income was associated with significantly higher prevalence of anemia than in medium- and high-income patients. Unemployment and none or low income may be associated with dietary insufficiencies and thus anemia.

### Prevalence of Anemia by Clinical Characteristics

Admitted patients had significantly higher anemia prevalence 75.8% compared to 42.2% of patients who were recruited from

**Table 4: Prevalence of anemia by laboratory characteristics**

Characteristics	Total patients (%)	Patients with anemia n=164 (51.9)	P
Leukocytes			
Leukopenia	88 (100)	53 (60.2)	0.04
Normal count	219 (100)	104 (47.8)	
Leukocytosis	9 (100)	7 (77.8)	
Lymphocyte			
Lymphopenia	16 (100)	15 (93.8)	0.001
Normal count	285 (100)	143 (50.2)	
Lymphocytosis	15 (100)	6 (40)	
RBCs			
Erythropenia	190 (100)	116 (61.1)	0.001
Normal level	126 (100)	48 (38.1)	
MCV (fL)			
Microcytosis	44 (100)	40 (90.9)	0.001
Normocytosis	130 (100)	68 (52.3)	
Macrocytosis	142 (100)	56 (39.4)	
MCH (pg)			
Hypochromasia	40 (100)	40 (88.9)	0.001
Normochromasia	117 (100)	65 (55.6)	
Hyperchromasia	154 (100)	59 (38.3)	
Platelets			
Thrombocytopenia	22 (100)	16 (72.7)	0.001
Normal count	279 (100)	134 (48)	
Thrombocytosis	15 (100)	14 (93.3)	

MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin

the outpatient clinic ( $P = 0.001$ ). This higher prevalence among admitted patients on HAART was also reported on one other study on HIV patients.<sup>[7]</sup> This could be explained by the fact that admitted patients are likely to have low CD4 and advanced stage of HIV, and these have been associated with anemia.<sup>[16]</sup>

Among patients with a history of blood transfusion 75% were anemic, this could be due to the effect of autoantibodies from a previous transfusion or autoimmune effect caused by HIV itself.<sup>[7,14,15]</sup> Co-trimoxazole use was associated with higher prevalence of anemia 54.3% compared to 45.1% in patients not taking cotrimoxazole, and this could be due to the effect of cotrimoxazole on folate metabolism.

68.2% of naïve-naïve patients were anemic compared to 49.7% of those on ART. This could be due to the effect of HIV on bone marrow suppression, having an advanced stage of HIV and low CD4 count which are likely to occur in the absence of ART.<sup>[16,17]</sup>

Anemia was more prevalent in patients with black nails 62.9% compared to patients with normal colored nails; other nail changes were not statistically significant. This blackening of nails could be a side effect of zidovudine use or due to fungal infection of the nail. Six patients (85.7%) among those with lymphadenopathy were anemic.

MUAC assessment revealed anemia in all patients with severe acute malnutrition and 78.9% of patients with moderate acute malnutrition ( $P = 0.01$ ). These findings may offer an explanation to the association of deficiency of iron and folate and anemia

that was observed in this study. Underweight as assessed by BMI and low waist circumference were also associated with anemia.

## Prevalence of Anemia by Laboratory Characteristics

On laboratory characteristics, leukopenia, lymphopenia, and thrombocytopenia were associated with anemia, together with a low RBC, could indicate ineffective hematopoiesis. Similar findings were reported by Parinitha and Kulkarni,<sup>[11]</sup> this could be due to the direct effect of HIV on the hematopoietic system causing bone marrow suppression, secondary infections, neoplasms, or side effects of therapy. On the other hand, thrombocytosis in HIV could be reactive. Macrocytosis was prevalent in the absence of anemia as it was seen in 60.6% of patients. This observation could be due to side effect of medication such as co-trimoxazole and ART (zidovudine and stavudine are implicated drugs).<sup>[18,19]</sup>

## CONCLUSION

This study showed that risk factors for anemia among HIV patients are multifactorial and they include low income, low socioeconomic status, unemployment, undernourishment, malnourishment, and ART naïve status. Anemia is a common problem among HIV patients and admitted patients had a higher prevalence of severe anemia compared to patients seen at outpatient clinic. This would mean that anemia contributes to burden of HIV care as it is associated with increased morbidity among these patients.

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