JMSCR Vol||06||Issue||01||Page 31943-31949||January 2018

www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 71.58
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v6i1.87

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

Anaemia in HIV-Positive Patients in Relation to Immune Status of the Disease - A Hospital Based Study

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Abstract

Introduction: *Disorders of hematopoietic system including anemia, leucopenia and thrombocytopenia are common throughout the course of HIV infection. Anemia is common in patients with HIV infection, particularly those with advanced disease. Anemia is associated with quality of life decrements, decreased survival and increased disease progression in adults with HIV infection. It has adversely changing patient's quality of life and hamper treatment of both the primary viral infection and the secondary infections.*

Material and Methods: *This is a prospective cross sectional study of 500 HIV positive patients, conducted in the Department of Pathology of Government Medical College and Hospital between the period two years. The hematological parameters were obtained by processing whole blood on Electronic Cell counter. Demographical and clinical data of the patient was also obtained. Data obtained from Electronic counter, peripheral smear examination and BD FACScan flow cytometer was put together and analyzed.*

Results: *Anaemia was the most common haematological abnormality observed. The overall prevalence of anaemia, neutropenia, thrombocytopenia, lymphopenia, leucopenia, pancytopenia and eosinophilia was 70%, 3.4%, 3.4%, 7.6%, 5.6%, 4.0% and 9.8% respectively. The prevalence of anemia and other hematological abnormalities were higher in patients with advanced disease, CD4 count <200/ µl. ART was associated with lower prevalence of anemia*

Conclusion: *Prevalence of haematological abnormalities in HIV positive patients is significantly high even in this HAART era. Anemia is the most common hematological abnormality in HIV seropositive patients and its incidence is strongly associated with the progression of the disease. ART is associated with reduced prevalence of Anaemia and has therapeutic and preventive implications.*

Keywords: *Anaemia, ART, HIV, AIDS, HAART.*

Introduction

The emergence of pandemic of Acquired Immunodeficiency Syndrome (AIDS), have posed the greatest challenge to public health in modern times. AIDS has evolved from a mysterious illness to a global pandemic which has infected tens of millions in less than 30 years. Clinically significant hematological abnormalities are

common in persons with human immunodeficiency virus (HIV) infection. The consequences of these haematologic findings are double. First, they have major morbidity in themselves, adversely altering patient's quality of life. Second, they hinder treatment of both the primary viral infection and the secondary infections and neoplastic complications. The poor hematological tolerance of therapies often necessitates alteration of drug regimens, dose reductions, or interruption of therapies.[1,2]

Anemia is the most common hematological abnormality in HIV seropositive patients and its incidence is strongly associated with the progression of the disease. Anaemia is common in HIV-infected individuals, occurring in approximately 10 to 20 percent at initial presentation and diagnosed in approximately 70 to 80 percent of patients over the course of disease In patients not receiving effective antiretroviral therapy (ART), anemia is associated with increased mortality, independently of CD4+ T-cell count and viral load.[3] There are few studies from India describing hematological manifestations particularly Anemia in patients with HIV/AIDS.[4,5,6] Hence, we decided to study Anemia profile of HIV positive patients in relation to immune status and stage of the disease.

Material and Methods

This is a prospective cross sectional study of 500 HIV positive patients, conducted in the Department of Pathology at Government Medical College and Hospital between the periods of two years. All the patients included in this study were serologically diagnosed cases of HIV infection and were registered with ART center.

Demographical and clinical data of the recruited patients was obtained. 2ml of peripheral venous blood was collected in bulb containing 5.4mg K2 EDTA. The blood was analyzed within four hours of collection with storage at 4˚C wherever required. The hematological parameters were obtained by processing whole blood on Electronic Cell counter which yields 18 parameters and 3 histograms. Peripheral smears stained with Leishman stain were also studied. CD4 count, CD4% and absolute lymphocyte count were obtained by running the samples on BD FACScan flow cytometer. Bone Marrow examination was not done. Data obtained from Electronic counter, peripheral smear examination and BD FACScan flow cytometer was put together and analyzed. Patients were divided into 3 categories A, B, C as suggested by Sullivan et al.[7] Category A: Patient infected with HIV but never suffered from clinical or immunological AIDS, Category B: Patient either suffered from or were suffering from immunological AIDS but not clinical AIDS and Category C: Patient either suffered from or were suffering with clinical AIDS irrespective of past and present immunological status. To correlate the haematological abnormalities with present immunological status the patients were divided into three groups as follows: Group 1: CD4 count >500/ cells/µl, Group 2: CD4 count 200-500 cells/µl and Group 3: CD4 count <200 cells/µl. Anaemia was defined as hemoglobin concentration < 13 gm% for males, <12 gm% for females. Severe anaemia was defined as hemoglobin concentration <7.5 gm%.[8,9] Anaemia was classified as microcytic, normocytic, macrocytic and dimorphic after correlating RBC indices, RBC histogram and findings of peripheral smear.

Results

Hematological profile of 500 seropositive (HIV-positive) patients was studied between the periods of two years. 300/500(60%) patients were females while 200 (40%) patients were males. 380/500 (76%) patients were in the age group 15-40 years. Heterosexual transmission was the most common risk factor for transmission of HIV infection which was identified in 480(96%) patients. The overall prevalence of various haematological abnormalities and their relation with present immunologic status of the patients are shown in Table 1.

Anemia was the most common abnormality observed in our study with an overall prevalence of (70%). The prevalence of anemia increased from 60% in Group 1 to 73% in Group 2 and to 76% in Group 3 showing progressive increase in prevalence of anemia with decreasing CD4 count (Table 2). Anemia was most prevalent in Category A followed by Category B and Category C .In Category A, the prevalence of anemia in patients without ART was 65 % while that in patients on ART for >12 months was 30%. In Category B, anemia was prevalent in 79% patients who were not on ART as compared to only 59% patients who were on ART. We also observed that the prevalence of anemia gradually decreased in patients on ART as the duration of ART increased from 94% in patients on ART for <6months to 60% in patients on ART for 6-12 months to 54% in patients on ART for >12 months. In Category C, anemia was prevalent in 100% patients who were not on ART as compared to only 74% in patients who were on ART. We also observed that the prevalence of anemia decreased in patients on ART as the duration of ART increased from 80% in patients on ART for <6months to 24 % in patients on ART for >12 months (Table3). Although, overall prevalence of anemia in Category A and Category C was lower than in Category B, after removing ART as confounding factor, i.e. when comparing patients not on ART, significantly higher prevalence of anemia was noted in Categories B and C as compared to Category A. The overall prevalence of severe anemia was 3.4%. Except 2.0% prevalence of severe anemia in Category B, none of the patient in Category A or Category C who were on ART had severe anemia. We also observed that, the prevalence of severe anemia increased from 1.3% in Group 1 to 2% in Group 2 and to 10% in Group 3 showing progressive increase in prevalence of severe anemia with decreasing CD4 count. Microcytic anemia (60%) was the most common type of anemia followed by Macrocytic anemia (24%). Normocytic anemia was present in 11% of anemic patients, while dimorphic anemia was seen in 6 % anemic patients. Microcytic anaemia decreased from 88% in Category A to 35% in Category C. Macrocytic and Dimorphic anaemia were more frequently seen in Category B and Category C, especially in patients on ART. We also observed that patients on ART though not anaemic, had normal or slightly raised Hb, low RBC Count, raised MCV, MCH and MCHC.

Tables 1: Correlation between hematological abnormalities and immunological Status and overall prevalence of all hematological abnormalities Observed in different groups

Group	Group 1	Group 2	Group 3	Total
	n = 150	n= 260	n = 90	n = 500
Anaemia	89	185	59	333
Severe anaemia	2	6	9	17
Neutropenia	3	8	6	17
Thrombocytopenia	6	12	20	38
Lymphopenia	0	2	21	23
Leucopenia	0	5	14	19
Pancytopenia	0	0	4	4
Eosinophilia	12	20	17	49

Table 2: Prevalence of anaemia in different categories

Group	Group 1	Group 2	Group 3	Total
	n = 150	N = 260	n = 90	n = 500
Anaemia	89	185	59	333
Severe anaemia	2	6	9	17
Total	91 (60%)	191 (73%)	68 (76%)	350 (70%)

n: Number of patients in each group

Table 3: Correlation between Anaemia and duration of ART in various Categories

Category	Category A		Category B		Category C	
	Total	Anaemia	Total	Anaemia	Total	Anaemia
ART <6 months	0	0	16	15	5	4
ART 6-12 months	0	0	22	12	8	6
ART>12 months	20	6	170	93	72	53
Total on ART	20	6	204	150	85	63
Total not on ART	130	85	56	44	5	5
Total	150	91	260	194	90	68

Table 4: Type of Anaemia in different Categories

Type	Category A	Category B	Category C	Total
Microcytic	80	104	24	208
Normocytic	7	26	4	37
Macrocytic	3	48	32	83
Dimorphic	1	12	8	21
Hemolytic	0	1	0	1
Total	91	191	68	350

Discussion

Anaemia was the most common haematological abnormality observed in 70% patients, severe anaemia being present in 3.4% of patients. Both anaemia and severe anaemia were more prevalent in patients belonging to Group 3. After removing ART as a confounding factor anaemia and severe anaemia were more prevalent in patients belonging to Category B (Immunological AIDS) and Category C (Clinical AIDS) as compared to patients belonging to Category A. ART was found to be associated with lower prevalence of anaemia and severe anaemia in all Categories. These findings are consistent with the findings of other studies conducted by Sullivan et al[7], Berhane et al[10], Mocroft et al[11], Amegor et al[12] and Huang et al[13] who found that anaemia was more prevalent in patients with advanced disease, CD4 count<200/µl and ART reduces the prevalence of anaemia in patients with HIV/AIDS especially when taken for more than 12 months. Earlier studies mention normocytic anaemia to be the most common type of Anaemia in patients with HIV-related diseases. Manisha et al[4] observed that anaemia was normocytic, normochromic in 61%, microcytic in 33% and macrocytic in 6% patients. Dikshit et al [5] who performed iron studies in all anaemic patients found that Iron deficiency anemia was seen in 49.2% (/200) cases while anemia of chronic disease occurred in 50.7% (/200) cases indicating higher prevalence of microcytic anaemia in Indian population. Microcytic anaemia was the most common type of anaemia observed in our study. Prevalence of normocytic, macrocytic and Dimorphic anaemia increased remarkably in Category B and Category C probably due to interplay of various factors like advanced disease, opportunistic infections, antiretroviral and anti infectious drug therapy.

Several biological mechanisms may account for the improvement of anemia after initiation of HAART. The anemia of chronic disease accounts for a large proportion of the anemia that occurs during HIV infection, given the burden of chronic disease and opportunistic infections.[14,15] Inflammatory cytokines such as tumor necrosis factor (TNF)-α have been implicated in the suppression of erythropoiesis[16,17], and HAART appears to reduce the expression of TNF-α by monocytes.[18] HAART has been shown to reduce diarrheal disease and enteric infections such as microsporidiosis and cryptosporidiosis.[19,20] Diarrheal disease and HIV enteropathy are associated with steatorrhea and impaired

absorption of micronutrients[21], and it is a reasonable assumption that reduction of diarrheal disease and gut abnormalities would improve the absorption and metabolism of micronutrients that are involved in erythropoiesis such as vitamin A, vitamin B12, folate, and iron. Recent studies suggest that potent antiretroviral therapy improves antioxidant micronutrient status.[22] Parvovirus B19 infection, another infectious cause of anemia, has been eliminated by HAART, presumably through immune reconstitution.[23,24] Another mechanism by which HAART could improve nutritional status and anemia is through the reduction of neurologic disease and anorexia.[25,26]

Although antiretroviral therapy has been associated with impairment of erythropoiesis through drug-related bone marrow toxicity, overall, HAART is associated with an improvement in hemoglobin concentrations rather than exacerbation of anemia. A recent in vitro study shows that protease inhibitors may actually stimulate hematopoiesis.[26]

Conclusion

Prevalence of anaemia and other hematological abnormalities in HIV positive patients increases as the stage of the disease advances and correlates best with the present immunological status of the patient independent of the stage of the disease. Prevalence of hematological abnormalities in HIV positive patients is significantly high even in this HAART era. ART is associated with reduced prevalence of all haematological abnormalities and has therapeutic and preventive implications.

Source(s) of support: Nil
Conflicting Interest (If present, give more details): Nil
Acknowledgement: Nil

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