International Journal of Contemporary Pediatrics
Sule A et al. Int J Contemp Pediatr. 2018 Sep;5(5):1962-1965
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20183540

Original Research Article

Anaemia in HIV infected HAART naïve and HAART exposed children

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Received: 13 July 2018
Accepted: 06 August 2018

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ABSTRACT

Background: The 2016 UNAIDS report estimates about 2.1 million people living with HIV in India, of whom about 7 per cent are children under the age of 15 year. The primary objective of this study was to analyze the prevalence of anaemia in HIV Infected HAART naïve and HAART exposed children. The secondary objectives were to analyze the type of anaemia and correlation of anaemia with dietary habits and associated opportunistic infections. Present study was a cross-sectional, observational study carried out in pediatric ART OPD and ward of a tertiary care teaching hospital, from June 2011 to May 2013.
Methods: Complete haemogram, peripheral smear and CD4 counts were done on 130 children with confirmed diagnosis of HIV infection. CDC staging was used to stratify children. We used Chi square test to determine the association between CDC staging, HAART therapy, diet and opportunistic infection with anaemia. P-value <0.05 was taken as significant.
Results: 80% (n = 27) of the children with no immunosuppression, 86% (n = 58) of the children with moderate immunosuppression and 84% (n = 24) children with severe immunosuppression were anemic. There was no statistically significant relation between worsening immunosuppression and prevalence of anaemia (p = 0.715). 88% of the children with no opportunistic infection (n = 72) were anemic, while 76% (n = 34) children with opportunistic infection were anemic. This difference was statistically significant (p = 0.016). 88% (n = 53) of the children on HAART were anemic while 74% (n = 51) of the children not on HAART were anemic. Children on HAART did not have significantly high prevalence of anaemia when compared to children not on HAART (p = 0.99). Anaemia was significantly more common in children consuming vegetarian diet (88%, n = 46) compared to children consuming mixed diet (74%, n = 58, p <0.01).
Conclusions: Prevalence of anaemia is similar in children on HAART compared to HAART naïve children and at all stages of immunosuppression. Anaemia was more common in the presence opportunistic infections and in children consuming vegetarian diet. Microcytic hypochromic anemia was most common type of anaemia followed by normocytic normochromic anaemia.

Keywords: Anaemia, Children, HIV infection, HAART, Opportunistic infections, Vegetarian

INTRODUCTION

The 2016 UNAIDS report estimates about 2.1 million people living with HIV in India, of whom about 7 per cent are children under the age of 15 year.[1] In 2005, the National AIDS Control Organization has dramatically increased access to antiretroviral therapy for children, and several thousands of children have been successfully initiated on specific anti-HIV therapy.[2] However, background co-morbidities compound the problem in

affected populations in India. Two such major co-morbidities include anaemia and poor nutrition, whose detrimental effects are magnified in the context of HIV infection. High prevalence of anaemia in children of all age group continues to be a major health problem in most parts of India. Anaemia is common in children with HIV infection. There is lack of literature about anaemia in pediatric patients with HIV infection in India. The causes of HIV-related anaemia are multifactorial and include direct and indirect effects of HIV infection.[3]

Few studies have shown correlation between immunosuppression, HAART drugs and anaemia. However, there is a lack of studies focused on correlation of anaemia in HIV infected children with their dietary habits, and opportunistic infections. Understanding nutritional co-morbidities will be beneficial in planning appropriate intervention strategies to reduce the overall burden of pediatric HIV in India.

The aim of this study was to determine prevalence of anaemia in HIV infected HAART naïve and HAART exposed children. We also aimed to study correlation of anaemia with their dietary habits, degree of immunosuppression and presence of opportunistic infections.

METHODS

One hundred thirty consecutive children from 6 months to 12 years of age with a confirmed diagnosis of HIV infection were enrolled from the pediatric ART OPD and ward over a two-year period.

Written informed consent was obtained from all parents/caregivers. Patients were excluded if parents/caregivers refused to become part of study or have any known hematological abnormality, like thalassemia, sickle cell anaemia, recent bleeding or bleeding disorder etc. Permission was obtained for conducting this study from Institutional Ethics Committee.

Detailed history, general and systemic examination was carried out. Patients were categorized as per CDC guidelines. Relevant investigations results (e.g. sputum and chest X-ray for tuberculosis, endoscopy for esophageal candidiasis) where necessary were carried out. Detailed dietary history was taken (24-hour recall) and specific enquiry was made whether the child consumes non-vegetarian food. Children who consumed non-vegetarian food (chicken, mutton, beef, eggs) at least once a week were classified as taking mixed diet and others were labeled vegetarian. Presence or absence of pallor was noted on general examination.

Blood samples were collected using universal precaution. Samples were tested immediately after collection. The investigations included complete hemogram and RBC indices using auto (PCE 120 by ERMA Inc) as well as peripheral blood smear examination. Absolute CD4 cell count analysis was carried out by flowcytometry (Fax caliber machine, Manufacturer- Biological Diagnostics).

Age related normal hematological values (reference ranges) were obtained from Nelson's text book of Pediatrics. Anaemia was defined as values that deviate from reference ranges. CD4 percentage was obtained by absolute CD4 count and total lymphocyte count. Values were categorized according to CDC guideline as no immunosuppression, moderate immunosuppression and severe immunosuppression.

Data was analyzed using Microsoft office excel 2007 data sheet and SPSS version 20, STATA. Presence/absence of anaemia, opportunistic infections, HAART status, dietary habits (vegetarian/mixed) were analyzed in the study group as a whole and also in different stages of the disease. Chi Square test was used for determining the association between CDC staging and abnormal hemoglobin. P-value <0.05 was taken as significant.

RESULTS

Children in the study group were resident of Pune or surrounding districts of Maharashtra. The mean age of the study population was 7.35 years, among them 61% (n = 79) were males and 39% (n = 51) were females. Most of the study population belonged to lower socio-economic status. All of them acquired infection by vertical transmission from the mother. Out of 130 children, 34 children had no immunosuppression, whereas 68 and 28 had moderate and severe immunosuppression respectively as per CDC staging. Fifty two percent (n = 69,53%) children in the study population were not on ART and 48% (n = 61,47%) were on ART. Anaemia in different stages of immunosuppression in study population is shown in Table 1.

Eighty three percent of this study population was anaemic. The mean hemoglobin concentration in this study population was 8.38±1.90 gm%. The maximum and minimum values of hemoglobin were 13.1 gm% and 4.8 gm% respectively. Commonest type of anaemia found in this study group was microcytic hypochromic anaemia, seen in 52 (40%) cases followed by normocytic normochromic anaemia seen in 46 (35%) cases.

In this study, 80% (n = 27) of the children with no immunosuppression were anemic, 86% (n = 58) of the children with moderate immunosuppression were anemic and 84% (n = 24) children with severe immunosuppression were anemic. There was no statistically significant relation between worsening immunosuppression and prevalence of anaemia (p = 0.715).

Microcytic hypochromic anaemia was found almost equally in all stages. This blood picture was seen in 39%

(n = 13) in no immunosupression,40% in moderate(n=27) and 42% in severe immunosuppression (n = 12). Normocytic normochromic blood picture was most commonly found in severe immunosuppression (n = 16,57%) compared to children in no immunosuppression (n = 8,24%) and children with moderate immunosuppression (n = 22,32%). Thus, normocytic normochromic anaemia was more common as the disease progressed. This difference was statistically significant (p<0.01).

Table 1: Prevalence of anaemia and type of anaemia stratified according to the level of immunosuppression.

Parameter	Qualitative classification	No IS	Moderate IS	Severe IS	Total	P value
Haemoglobin	Low	27	58	24	109	<0.715
	Normal	7	10	4	21	
Type of anaemia as per RBC indices and peripheral smear	MHA	13	27	12	52	<0.01
	NCNA	8	22	16	46	
	MNA	11	15	0	26	
	MA	0	4	2	6	

IS: Immunosuppression; MHA: Microcytic hypochromic anaemia; NCNA: Normocytic Normochromic anaemia; MA: anaemia Macrocytic

88% of the children with no opportunistic infection (n = 72) were anaemic, 80% of children suffering from tuberculosis (n = 18), 74% (n = 13) of the children suffering from candidiasis and 75% (n = 3) of children having *P. jiroveci pneumonia* were anaemic. This difference was statistically significant (p = 0.016). 88% (n = 53) of the children on HAART were anaemic while 74% (n = 51) of the children not on HAART were anaemic. Children on HAART did not have statistically significant high prevalence of anaemia when compared to children not on HAART (p = 0.999). Of the 53 anaemic children on HAART, 36 were on Zidovudine (AZT). Once anaemia was diagnosed these children were shifted to non-AZT based therapy.

Table 2: Correlation of diet, OI and HAART with anaemia.

Parameter	Anaemia present	P value
Vegetarian diet	n = 46 (88%)	<0.01
Mixed diet	n = 58 (74%)	
OI present (n = 48)	n = 34 (76%)	0.016
No OI (n = 82)	n = 72(88%)	
On HAART (n = 61)	n = 53 (88%)	0.99
Not on HAART (n = 69)	n = 51 (74%)	

OI: Opportunistic infection; HAART: Highly Active Anti-Retroviral Therapy

Anaemia was significantly more common in children consuming vegetarian diet (88%, n = 46) compared to children consuming mixed diet (74%, n = 58, p<0.01). This may be due to less bioavailability and absorption of iron from vegetarian food sources compared to non-vegetarian food sources.

DISCUSSION

Present study reports high prevalence of anaemia in HIV infected children. Significantly, present study shows that anaemia is more common in HIV infected children consuming vegetarian diet compared to children who had mixed diet and in children with Opportunistic infections compared to those who did not.

Anaemia may occur as a result of HIV infection itself, as sequelae of HIV-related opportunistic infections or malignancies or as a consequence of therapies used for HIV infection and associated conditions.[4]

In the present study, anaemia was found to be common in children with HIV/AIDS. 109 out of 130 children (83%) were anemic. Prevalence of anaemia in the study by Shet et al was 66% and in that Adetifa et al was 77.9%.[5,6] Microcytic hypochromic anaemia was the commonest type (40%) of hematological abnormality in the study. Its frequency remained almost same irrespective of the degree of immunosupression. Normocytic normochromic anaemia was seen in 35% of our patients, however, occurred more frequently as immunosupression increased. This may be the result of anaemia of chronic disease, probably due to direct effect of HIV/AIDS.

Erhabor et al in their studies also found that the prevalence of normocytic normochromic anaemia was more in the children with advanced and severe immune suppression than those with mild and no immune suppression.[7] Microcytic hypochromic anaemia on the other hand was probably due to iron deficiency and not related to HIV status as iron deficiency was very common in India.[8] Studies have clearly demonstrated that anaemia is associated with decreased survival and increased disease progression in adults with HIV infection.[9,10] A study of serum immunoreactive erythropoietin, in HIV-infected patients, in various stages of illness, showed that levels of the hormone failed to rise commensurate with increasing anaemia, suggesting that insufficient amounts of erythropoietin may be one cause of anaemia in this setting.[11] Other studies have suggested that soluble factors in the serum of HIV-infected patients may inhibit hematopoiesis, or that direct HIV infection of

marrow progenitor cells may play a role in producing anaemia and other hematological abnormalities associated with HIV infection.[12]

Zidovudine (AZT) therapy can cause macrocytic anaemia in children on Zidovudine based ART.[13] Dapsone used for treatment or prevention of Pneumocystis Carinii Pneumonia (PCP) may cause hemolytic anaemia or generalized myelosuppression.[14] None of the children in our study received Dapsone. Infection with Mycobacterium Avium Complex (MAC) and parvovirus B19 are other common cause of anaemia in advanced HIV disease.[15,16] Anti- erythrocyte anti-bodies produce a positive direct anti-globulin test in approximately 20% of HIV-infected patients with hypergammaglobulinemia.[17]

Opportunistic infections were found to be significantly associated with anaemia in our series.Recent studies in adults have found higher prevalence of anaemia in adults with TB coinfection.[18]

The strengths of the present study include number of children studied and assessment of diet of the children. The limitations include lack of studies for the exact etiology of anaemia (serum ferritin, B12 levels etc.) due to lack of resources.

CONCLUSION

Anaemia is very common in HIV infected children. Children on HAART had similar prevalence of anaemia when compared to children not on HAART. Anaemia was significantly more common in children consuming vegetarian diet compared to children consuming mixed diet and in children who had opportunistic infections. Microcytic hypochromic anaemia was the commonest type followed by normocytic normochromic type. Frequency of normocytic normochromic anaemia increased in advanced stage of the disease.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. UNAIDS. Global AIDS update. 2016. Available at http://www.unaids.org/sites/default/files/media_asset/global-AIDS-update-2016_en.pdf
2. National AIDS Control Organization. Guideline for HIV care and treatment in infant and children. 2006. Available at http://apps.who.int/medicinedocs/documents/s18022en/s 18022en.pdf
3. Claster S. Biology of anemia, differential diagnosis, and treatment options in HIV infection. J Infect Dis. 2002;185(2):S105-9.
4. Coyle TE. Hematologic complications of human immunodeficiency virus infection and the acquired immunodeficiency syndrome. J Med Clin North Am. 1997;81(2):449-70.
5. Shet A, Mehta S, Rajagopalan N. Anaemia and growth failure among HIV-infected children in India: A retrospective analysis. BMC Pediatr. 2009;9:37.
6. Adetifa IM, Temiye EO, Akinsulie AO. Haematological abnormalities associated with pediatric HIV/AIDS in Lagos. Ann Trop Paediatr. 2006;26:121-5.
7. Erhabor O, Ejele OA, Nwauche CA. Some hematological parameters in Human Immunodeficiency Virus (HIV) infected Africans. the Nigerian perspective. Niger J Med. 2005;14:33-8.
8. Chellan RR, Lopamudra P. Prevalence of iron-deficiency anaemia in india: results from a large nationwide survey. J Population Soc Studies. 2010;19:59-80.
9. Mocroft A, Kirk O, Barton SE, Dietrich M, Proenca R, Colebunders R, et al. Anaemia is an independent predictive marker for clinical prognosis in HIV-infected patients from across Europe. Euro SIDA study group. AIDS. 1999;13:943-50.
10. Sullivan PS, Hanson DL, Chu SY, Jones JL, Ward JW. Epidemiology of Anaemia in Human Immunodeficiency virus (HIV)-infected persons: results from the multistate adult and adolescent spectrum of HIV disease surveillance project. Blood. 1998;91:301-8.
11. Spivak JC, Barnes DC, Fuchs E. Serum immunoreactive erythropoietin in HIV-infected patients. JAMA. 1989;261:3104-7.
12. Folks TM, Kessler A, Orenstein JM. Infection and replication of HIV-1 in purified progenitor cells of normal human bone marrow. Sci. 1988;242:919-22.
13. McKinney RE, Maha MA, Connor EM. A multicentric trial of oral zidovudine in children with advanced human immuno-deficiency virus disease. N Engl J Med. 1991;324:1018-25.
14. Medina I, Mills J, Leoung G. Oral therapy for pneumocystis carinii pneumonia in the acquired immune deficiency syndrome. A controlled trial of trimethoprim-sulfamethoxazole versus trimethoprim-dapsone. N Engl J Med. 1990;323:776-82.
15. Hawkins CC, Gold JW, Whimbey E. Mycobacterium avium complex infections in patients with acquired immunodeficiency syndrome. Ann Intern Med. 1986;105:184-8.
16. Mitchell SA, Welch JM, Smith WS. Persistent B 19 parvovirus infection in a patient with AIDS: case report. Genitourin Med. 1990;66:95-6.
17. McGinniss M, Macher AA, Rook A. Red cell autoantibodies in patients with acquired immunodeficiency syndrome. Transfusion. 1986;26:405-9.
18. Assefa M, Abegaz W, Belay M. Prevalence and correlates of anaemia among HIV infected patients on HAART at Zewditu Memorial Hospital,Ethiopia. BMC Hematol. 2015;15:6.

Cite this article as: Sule A, Kulkarni RK, Kinikar A, Valvi C, Rajput U, Dawre R. Anaemia in HIV infected HAART naïve and HAART exposed children. Int J Contemp Pediatr 2018;5:1962-5.