Research Article

Anemia in human immunodeficiency virus-infected children and its relation to disease stages

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Abstract

Background: Anemia in human immunodeficiency virus (HIV)-infected children is associated with more rapid disease progression and a poorer prognosis if not treated appropriately.

Objective: This study aimed at determining the severity of anemia among HIV-infected children and its relation with the World Health Organization (WHO) clinical and immunological HIV infection staging among HIV-infected children.

Materials and Methods: The children who were HIV positive (confirmed by enzyme-linked immunosorbent assay for HIV-1 and HIV-2), and attending the outpatient department of ART Centre and SN Children Hospital, Allahabad, Uttar Pradesh, India, during period of 1 year. The study population consisted of 47 patients, belonged to both sexes and age of 18 months to 18 years. Written and informed consent was taken from parents/guardian. Detailed history was taken and full clinical examination was done in all cases. Blood sample for complete blood count and CD4 was collected.

Result: Of 47 studied children, anemia (Hb < 11.5 g/dL) was present in 39 (82.98%) cases. Mild anemia was present in 25 (53.19%). Severe anemia was only found in the WHO clinical and immunological stages 3 and 4.

Conclusion: Most of the HIV-infected children usually present with mild anemia. Mild and moderate anemia had no correlation with disease stages but severe anemia was present mostly in stages 3 and 4.

KEY WORDS: HIV, anemia, pallor, the WHO stage, immunological stage

Introduction

Human immunodeficiency virus (HIV) infection is a worldwide problem but more so in developing countries. In India, the estimated number of children living with HIV increased from 1.42 lakhs in 2007 to 1.45 lakhs in 2011. Combination antiretroviral therapy access among children remains limited with only 15% of clinically eligible individuals received treatment in the year 2006.[1] Ever since, the report of first pediatric case in 1983, there has been an alarming increase in the rate of disease. Combination antiretroviral therapy access among children remains limited with only 15% of clinically eligible individuals received treatment in the year 2006.[2] With more data becoming available, the gravity of the problem is being better understood and HIV infection in children and adolescent is being recognized as a major issue.

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The most common, and well-studied, hematopoietic abnormality associated with HIV infection is anemia. Although anemia occurs less after in the era of highly active antiretroviral therapy than in past, it remains a significant clinical problem. The degree of anemia correlates with stage of HIV infection. The severity of anemia appears to increase with deteriorating immune status and in children it is a strong predictor of disease progression.[3,4]

The most frequent form of anemia in children with mild HIV disease has the feature of deficiency anemia whereas anemia in patient with advanced immunodeficiency has the

characteristic of anemia of chronic diseases.[5] The causes of HIV-related anemia are multifactorial and include direct and indirect effects of HIV infection.

In this study, we studied the prevalence of anemia in HIV-infected children and its relation to staging of HIV infection irrespective of multifactorial etiology of anemia in HIV-infected children.

Materials and Methods

A total of 47 ambulatory and clinically stable HIV-infected children (confirmed by enzyme-linked immunosorbent assay for HIV-1 and HIV-2) aged 18 months to 18 years attending the outpatient department of anti-retroviral therapy center at tertiary care setting, were included in the study. Written consent was taken from parents/guardian prior to investigation and for being part of the study. Parents' and sibling's HIV infection status were also enquired. Detailed history was taken, and complete physical examination of all the patients was done. Accordingly, patients were allocated in different stages of the World Health Organization (WHO) clinical HIV/AIDS (acquired immune deficiency syndrome) staging.[6] Blood samples were collected in ethylenediaminetetraacetic acid vial and mixed for 5–10 min. Absolute CD4 count of each patient was carried out with Partec CyFlow® counter flow cytometer to assess the WHO immunological HIV/AIDS stage of the HIV-infected child. Complete blood count was done on automated cell counter.

CD4 count is used to assess the immunological status of the HIV-infected child. CD4% varies less than CD4 counts hence considered more valuable in children less than 5 years of age. Percentage of CD4 cells were calculated on the basis of absolute CD4 counts using following formula:[6]

$$\% \text{ CD4 counts} = \frac{\text{Absolute CD4 counts}}{\text{Total lymphocyte counts}} \times 100$$

Anemia

Anemia was defined and graded according to age-appropriate reference standards published by the WHO.[7]

Sample Size

In our study, primary outcome is the anemia in HIV-infected children. In previous studies, prevalence of anemia has been observed 66–92%.[8–10] We have taken prevalence as a positive factor for sample size calculation and average prevalence of anemia is 79%. Sample size calculation for qualitative data is $4Pq/E2$, where P is the positive factor (prevalence or incidence) that is taken 79; q is $100 - P = 100 - 79 = 21$; and E is the allowable error that varies from 10% to 20%, we kept it on average as 15% and the calculated sample size will be 47. So, our sample size of 47 is appropriate for valid and precise results.

Data were analyzed using SPSS software version 13. To describe nominal data, simple percentages were used. Mean and standard deviations were used to describe normally distributed data from the subjects. Spearman's rank-order correlation test was used to determine the relationship between different continuous variables.

Result

Study Population

Forty-seven patients were enrolled in the study, of which, 37 (78.7%) were male, and 10 (21.3%) were female with male-to-female ratio of 3.7:1. The mean age of patients was 6.64±3.59 years (range 1.5–14 years). The most commonly involved age group was 1.5–5 years and almost half (46.81%) of the cases belong to this group. There was no case in the age group of 15–18 years (Table 1).

Anemia

Of the 47 studied children, anemia (Hb <11.5 g/dL) was present in 39 (82.98%) cases. Mild anemia was present in 25 (53.19%), and moderate in 11 (23.40%) cases whereas severe anemia was present only in 3 (6.38%) cases (Table 2).

On clinical staging on the basis of the WHO clinical staging criteria, 6 (12.76%) of 47 cases were in stage 1, 26 (55.31%) cases in stage 2, 13 (27.66%) in stage 3, and 2 (4.26%) cases were in stage 4. On the WHO immunological staging, 24 (51.06%) of 47 cases were found in stage 1, 9 (19.15%) cases each in stages 2 and 3, and 5 (10.63%) cases were in stage 4.

On studying the correlation between severity of anemia and the WHO clinical stages, we found that mild anemia cases were almost equally distributed in all stages (r = 0.242) whereas severe anemia cases were mostly found in stages 2 and 4 (r=0.765) (Table 3).

When we studied the correlation between severity of anemia and immunological stages, we found in mild anemia, there was no correlation with stage of the disease whereas in cases of severe anemia, the percentage of cases increases with immunological stage (r = 0.948) (Table 4).

Table 1: Distribution of cases by age and sex

Age group (years)	Male (%)	Female (%)	Total (%)
1.5–5	18 (38.30)	4 (8.51)	22 (46.81)
5–10	13 (27.66)	4 (8.51)	17 (36.17)
10–15	6 (12.77)	2 (4.25)	8 (17.02)
Total	37 (78.73)	10 (21.27)	47 (100)

Table 2: Anemia in cases

Severity of anemia	Number (n = 47)	Percentage
No anemia	8	17.02
Mild (Hb 11.5–9.0 g/dL)	25	53.19
Moderate (Hb 9.0–7.0 g/dL)	11	23.40
Severe (<7.0 g/dL)	3	6.38
Total	47	100

Table 3: Distribution of cases with anemia in relation to the WHO clinical staging

Severity of anemia	The WHO clinical staging				Total
	Stage 1 (*n* = 6)	Stage 2 (*n* = 26)	Stage 3 (*n* = 13)	Stage 4 (*n* = 2)	(*n* = 47)
Mild (Hb 11.5–9.0 g/dL)	3 (50.00%)	12 (46.15%)	9 (69.23%)	1 (50.00%)	25 (53.19%)
Moderate (Hb 9.0–7.0 g/dL)	2 (33.33%)	8 (30.77%)	1 (7.69%)	0 (0.00%)	11 (23.40%)
Severe (<7.0 g/dL)	0 (0.00%)	2 (7.69%)	0 (0.00%)	1 (50.00%)	3 (6.38%)
Total (%)	5 (83.33%)	22 (84.61%)	10 (76.92%)	2 (100%)	39 (82.98%)

Table 4: Distribution of cases with anemia in relation to the WHO immunological staging

Severity of anemia	Immunological staging				Total
	Stage 1 (*n* = 24)	Stage 2 (*n* = 9)	Stage 3 (*n* = 9)	Stage 4 (*n* = 5)	(*n* = 47)
Mild (Hb 11.5–9.0 g/dL)	13 (54.17%)	6 (66.67%)	5 (55.55%)	1 (20.00%)	25 (53.19%)
Moderate (Hb 9.0–7.0 g/dL)	5 (20.83%)	2 (22.22%)	2 (22.22%)	2 (40.00%)	11 (23.40%)
Severe (<7.0 g/dL)	0 (0.00%)	0 (0.00%)	1 (11.11%)	2 (40.00%)	3 (6.38%)
Total (%)	18 (75.00%)	8 (88.89%)	8 (88.89%)	5 (100%)	39 (82.98%)

Discussion

Our study found a high prevalence of anemia among HIV-infected children, majority of them were with mild anemia. The frequency as well as severity of anemia were correlated with clinical and immunological HIV disease stages and found a significant association between the presence of anemia and disease staging.

The overall prevalence of anemia was 82.98%, and 6.38% had severe anemia (Hb < 7 g/dL). The mean hemoglobin was 9.99 g/dL (SD 1.78) in our study. Almost similar results were reported by Adetifa et al.[8] where overall prevalence of anemia was 77.9%, mild anemia in 39.7%, and severe anemia in 5.9%. The prevalence of anemia in the study of Shet et al.[9] was 66%, and 8% had severe anemia (Hb < 7 g/dL). In a group of HIV-infected children in a rural Ugandan clinic, high prevalence of anemia was reported.[10] In a 60-case study, 92% prevalence of anemia was reported by Mir et al.[11] The difference in prevalence of anemia in various studies may be due to variation in nutritional status of the cases enrolled in the studies.

Our data indicate that anemia was more severe among those with advanced disease stage and a higher degree of immunosuppression. The prevalence of anemia in the WHO clinical stages 1, 2, 3, and 4 was 83%, 85%, 77%, and 100%, respectively. Hemoglobin level was significantly lower among those with advanced and severe clinical stages, compared to those in stages 1 and 2. With respect to immunological stage, anemia was present in 100% of those with stage 4 whereas only 75% of children with stage 1 were anemic ($r = 0.948$).

Shet et al.[9] demonstrated a higher anemia prevalence among those with more advanced disease. Similarly, Belperio et al.[4] stated that as HIV disease progresses, the prevalence and severity of anemia increase and anemia has been shown to be a statistically significant predictor of progression to the HIV-related diseases. The mean hemoglobin concentration decreased as disease progressed in the study of Adetifa et al.[8] Silva et al.[12] found anemia in 100% patients up to 12 months of age.

HIV-related anemia generally is due to reduced red blood cell (RBC) production, secondary to a variety of causes, but it may also involve nutritional deficiencies, increased RBC destruction, or a combination of these problems.[13] Other common causes of anemia in HIV infection are anemia of chronic disease consequent of opportunistic infections and bone marrow suppression by antiretroviral therapy.[14]

Results of this study need to be interpreted cautiously in light of some important limitations. First, the exact causes of anemia in these patients were not determined. Second, the lack of data on anemia in a comparable group of HIV-negative children in the same setting limits our ability to interpret the prevalence results.

Conclusion

Most of the HIV-infected children usually present with mild anemia. Mild and moderate anemia had no correlation with disease stages but severe anemia was present mostly in advanced stages of the disease.

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