Short Communication

Prevalence of thrombocytopenia and its relation with WHO clinical and immunological staging among human immunodeficiency virus-infected children

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Abstract

Objective: The aim was to study the thrombocytopenia in human immunodeficiency virus (HIV) infected children and its relation with WHO clinical and immunological HIV/AIDS staging. **Study Design:** Observational analytic cross-sectional study. **Materials and Methods:** 47 ambulatory and clinically stable HIV-infected children (confirmed by enzyme-linked immunosorbent assay for HIV-1 and HIV-2) aged 18 months-18 years attending the out-patient Department of anti-retroviral therapy center at tertiary care setting, were included in this study. Detailed history was taken, and thorough clinical examination was done in all cases. Blood sample for complete blood count and CD4 count was taken. **Primary Outcome:** Thrombocytopenia in HIV-infected children. **Secondary Outcome:** WHO clinical and immunological HIV/AIDS staging in HIV-infected children and its relation to thrombocytopenia. **Results:** Of 47 studied children, thrombocytopenia was found in 14 (29.78%) cases. Patients with thrombocytopenia were found in all stages of the disease; however, it was strongly associated with increasing immunological stages (correlation coefficient, r = 0.948). **Conclusion:** Thrombocytopenia commonly occurs in children with HIV and its occurrence increases with an increase in WHO clinical and immunological HIV/AIDS staging.

Key words: *Human immunodeficiency virus, Immunological human immunodeficiency virus/AIDS staging, Thrombocytopenia, WHO clinical human immunodeficiency virus/AIDS staging*

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 year 2006 [1]. Disorders of the hematopoietic system including anemia, leukopenia and/or thrombocytopenia are common throughout the course of HIV infection. Possible causes of cytopenias were inadequate production of the cells due to suppression of the bone marrow by the HIV infection through abnormal cytokine expression and alteration of the bone marrow microenvironment. The incidence and severity of cytopenia are generally correlated to the stage of the HIV infection [2]. Recent data suggest that impaired platelet production may be an important pathogenic mechanism responsible for the occurrence of thrombocytopenia in HIV-infected patients. The findings of megakaryocytic dysplasia in the bone marrow of thrombocytopenic patients together with evidence that HIV can infect megakaryocyte support this contention [3]. Thrombocytopenia may represent the first manifestation of HIV infection, and it may progress over time and lead to severe bleeding [4]. Therefore, we planned this study to observe the occurrence of thrombocytopenia in HIV-infected children and its relation with WHO clinical and immunological HIV/AIDS staging.

MATERIAL AND METHODS

47 ambulatory and clinically stable HIV-infected children (confirmed by enzyme-linked immunosorbent assay for HIV-1 and HIV-2) aged 18 months-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 WHO clinical HIV/AIDS staging [5]. Absolute CD4 czount of each patient was done 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. Blood was collected in ethylenediamine tetraacetic

acid vial and mix for 5-10 min. Thrombocytopenia was defined as a reduction in platelet count to $<150 \times 10^9$/L [6]. The platelet count was compared with pre-established mean values in children.

Sample Size

In our study, the primary outcome was thrombocytopenia in HIV-infected children. In previous studies, observed a prevalence of thrombocytopenia was 5-15% [7-12]. We have taken prevalence as a positive factor for sample size calculation, and the average prevalence of thrombocytopenia is 7.5%. Sample size calculation for qualitative data = $4.P.q/E^2$, where P is the positive factor (prevalence or incidence), which is taken 7.5, q is 100−P = 100-7.5 = 92.5 and E is the allowable error, which vary from 10% to 20%, we kept it minimum as 10%. So, calculated sample size will be 28. Our sample size of 47 is more than the calculated sample size for valid and precise results.

Data Analysis

Data were analyzed using SPSS software (SPSS Inc., IBM, UK). To describe nominal data, simple percentages were used. Mean and standard deviations were used to describe normally distributed data from the subjects. The Spearman rank correlation test was used to determine the relationship between different continuous variables.

RESULTS

47 patients were enrolled in the study, out 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).

Table 1: Distribution of cases by age and sex

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

On clinical staging on the basis of WHO clinical staging criteria, 6 (12.76%) out 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 WHO immunological staging, 24 (51.06%) out of 47 cases were found in Stage 1, 9 (19.15%) cases each in Stage 2 and Stage 3 and 5 (10.63%) cases were in Stage 4. Thrombocytopenia was found in 14 (29.78%) cases. On studying its relation with WHO clinical stages, we find that thrombocytopenia had weak relation with increasing WHO clinical stages (correlation coefficient, r = 0.609). On the other hand, cases with thrombocytopenia were found in all the immunological stages of the disease and it was strongly associated with increasing immunological stages of the disease (correlation coefficient, r = 0.948) (Table 2).

DISCUSSION

Thrombocytopenia is a common hematologic finding in patients infected with the HIV. Multiple mechanisms may contribute to the development of thrombocytopenia as immune-mediated platelet destruction, enhanced platelet splenic sequestration, and impaired platelet production.

In our study, 14 (29.78%) patients had thrombocytopenia while Suarez et al. [13] noted thrombocytopenia in 27% cases and Silva et al. [14] in 25% cases. Many authors have reported lower prevalence of thrombocytopenia (5-15%) in HIV seropositive patients [7-12]. We noted high prevalence of thrombocytopenia in our study when compared to other studies of western countries. This may be due to the better immune status of children in western countries when compared to children in Indian scenario.

The highest incidence of thrombocytopenia (100%) was seen in WHO clinical Stage 4. Mir et al. [15] reported thrombocytopenia in 61% cases in the advanced stage. The progression of thrombocytopenia was more strongly associated (correlation coefficient, r = 0.948) with immunological advancement of the disease as compared to clinical progression of the disease (correlation coefficient, r = 0.609). In the present study, with decreasing CD4 counts, prevalence of thrombocytopenia was increasing. It means the prevalence of thrombocytopenia was proportionally high among patients who had low CD4 lymphocyte count and vice-versa. Similar findings have been reported by Wondimeneh et al. [16].

Table 2: Distribution of cases with thrombocytopenia in relation to WHO clinical staging and immunological staging

WHO clinical stages	Thrombocytopenia n (%)	WHO immunological stages	Thrombocytopenia n (%)
Stage 1 (n=6)	2 (33.33)	Stage 1 (n=24)	6 (25.0)
Stage 2 (n=26)	7 (26.92)	Stage 2 (n=9)	3 (33.33)
Stage 3 (n=13)	3 (23.07)	Stage 3 (n=9)	3 (33.33)
Stage 4 (n=2)	2 (100)	Stage 4 (n=5)	2 (40.0)
Total (n=47)	14 (29.79)	Total (n=47)	14 (29.79)

CONCLUSION

This study has provided additional information with regard to the occurrence of thrombocytopenia in HIV-infected children. As CD4 counts of HIV patients decreasing, they have more likely to have thrombocytopenia. Therefore, early diagnosis and treatment of thrombocytopenia is necessary to prevent the bleeding problems associated with the thrombocytopenia in HIV-infected children.

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