Original Article

Sero-prevalence of Viral Co-infections in HIV Infected Children of Northern India

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ABSTRACT

Objective. To assess the prevalence of viral co-infections in HIV infected children.

Methods. Children born to HIV seropositive parents and those children who were suspected to be HIV infected based on clinical presentation by the pediatrician were screened for HIV –1 and 2 antibodies as per National Aids Control Organization (NACO) guidelines. Those found to be seropositive for HIV infection were further tested for Hepatitis B&C, Herpes simplex virus and Human cytomegalovirus infection.

Results. Among 803 children screened, 101 were found positive for HIVantibodies. Among the five viral markers tested, HCMV IgG was positive in 88 children (87.1%). HCMV IgM was positive in 35 cases (34.6%). HBsAg tested positive in 30 children, while anti-HCV IgM was reactive in 27 cases. IgM anti- HSV antibodies were observed positive in 59 (58.4%) cases. Both hepatitis virus coinfection (HBsAg and anti- HCV IgM antibodies) was observed in 10 HIV positive children, while both Herpesviridae family viruses (HCMV -IgM antibodies and HSV -IgM antibodies) were positive in 30 cases (29.7%).

Conclusion. Viral co-infections are significantly higher in HIV positive children, which adds to significant mortality and morbidity and should therefore be screened in all HIV positive children for timely treatment in order to improve the quality of life and better survival of HIV infected children. **[Indian J Pediatr 2009; 76 (9) : 917-919]** *E-mail:drsinghdk2@yahoo.com*

Key words : *HIV sero-prevalence; Viral co-infections*

The global impact of Human immunodeficiency virus (HIV) pandemic has been very dramatic and devastating and has been described as the 'epidemic of our country'.[1] In developed countries, acquired immunodeficiency syndrome (AIDS) in children constitutes only 2% of all HIV infections, while in Asia and Africa, it comprises 15-20% of all cases, due to greater affliction of women of child bearing age group.[2] Despite many efforts to prevent transmission of HIV-1 and 2 from mother to child, the transmission to infants has continued to increase globally, particularly in resource- poor settings.[3] Like adults, HIV positive children are also prone to develop various opportunistic infections and acquire other viral co-infections. These viral co- infections add to the morbidity, mortality and increase the treatment cost of these patients. There are very few studies documenting the sero-prevalence rates of viral co-infections among HIV infected children in the world and to the best of our knowledge, none from India.[4,5] The present study was thus undertaken to determine the prevalence of viral co-infections Hepatitis B virus (HBV), Hepatitis C virus (HCV), Human Cytomegalovirus (HCMV) and Herpes simplex virus (HSV) among HIV positive children.

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MATERIAL AND METHODS

Children of HIV positive parents or those referred by pediatrician suspecting HIV infection based on clinical presentation, were screened for HIV-1 and 2 infections by one enzyme linked immunosorbent assay (ELISA) and two rapid EIA tests using different HIV-1 and 2 antigen combinations, according to manufacturer's instructions, from April '05 to June '07. Informed consent from the parents was taken before testing and the study was approved by the Institutional Research Board (IRB). The interpretation of the result was done in accordance with the UNAIDS and World Health Organization (WHO) HIV testing strategies.[6] Children less than 18 mth were excluded from this study because facilities for diagnosing them for HIV-1 and 2 by HIV-RNA RT PCR, HIV-pro-virus DNA PCR and HIV P24

antigen detection assay, were not available in the department.

Serum samples of all HIV positive children, whether symptomatic or asymptomatic, were screened for detection of Hepatitis B surface antigen (HbsAg), microscreen ELISA (Span Diagnostic Ltd.), HCV-IgM antibodies (Innova HCV ELISA by Span Diagnostics Ltd.), HCMV-IgG and IgM antibodies (Radim, Italy) and HSV-IgM antibodies (Radim, Italy), as per manufacturer's instructions.

RESULTS

A total of 803 children, belonging to age group 18 mth to 18 yr were screened for HIV-1/2 infection, of which 101(12.6%) tested positive. Among them 99 were infected due to vertical transmission and two children acquired infection from infected blood transfusion. Both the parents in the latter two cases were HIV negative.The blood in these two cases were collected from their relatives (their HIV status was unknown) and was transfused to these children without HIV testing. Out of these 101 HIV positive children 22 were symptomatic and 79 were asymptomatic. Among the five viral markers tested, HCMV IgG was positive in 88 children (87.1%). HCMV IgM was positive in 35 cases (34.6%). HBsAg tested positive in 30 children, while anti-HCV IgM was reactive in 27 cases. IgM anti- HSV antibodies were observed positive in 59 (58.4%) cases. (Table 1)

Table 1. Sero-prevalence of Various Viral Markers in 803 Children Tested

Viral markers	Total	Number positive	Frequency (%)
HIV-1&2 antibodies	803	101	12.6
HBsAg	101	30	29.7
HCV (IgM antibodies)	101	27	26.7
HCMV (IgG antibodies)	101	88	87.1
HCMV (IgM antibodies)	101	35	34.6
HSV (IgM antibodies)	101	59	58.4
HBsAg & HCV-IgM	101	10	9.9
HCMV-IgM & HSV-IgM	101	30	29.7
HBsAg, HCMV & HSV	101	04	3.9
HBsAg, HCV, HCMV & HSV	101	01	0.9

Analyzing the multiple infections, it was observed that both HBsAg and anti- HCV IgM antibodies were positive in 10 HIV positive children, while both Herpesviridae family viruses HCMV (IgM antibodies) and HSV (IgM antibodies) were positive in 30 cases (29.7%). The DNA viruses (HBV, HCMV and HSV) co-infection together was observed in only 3 HIV positive children. Only one child had all the four virus co-infection and during this study period this child died.

DISCUSSION

Pre or post-natal acquisition of viral co-infections in HIV infected children may influence HIV disease progression. Biological determinants that contribute to accelerated disease progression may include relative immunologic immaturity, thymic HIV- mediated destruction during active thymopoiesis and sharing of human leucocyte antigen (HLA) class 1 between mother and infant.[7] HIV-1 infected infants who acquire HCMV infection within the first 18 mth of life have a significantly higher rate of HIV-1 disease progression and central nervous system disease than those who are infected with HIV -1 alone.[8]

In a study by Chakraborty *et al*[4] in Africa, it was found that all 71 HIV positive children were seropositive for HCMV-IgG antibodies. They found HBsAg positivity in only 4% of children, while HCV was not detected in any case. HCMV viruria was detected in 15% cases, which suggest the presence of primary or re-activated HCMV infection. In the present study HCMV-IgM sero-positivity was seen in 34.6% cases.

Grando *et al*[5] conducted a study to compare various viral co-infections by doing polymerase chain reaction (PCR) of oral swabs of HIV positive children regardless of the presence of oral lesions in Brazil and USA. They found an overall CMV positivity of 15.2%,19% in Brazilian children and 8% in American children. They also found 48 % positivity for HSV infection. In the present study also HSV was the commonest viral co-infection amounting to 58%. HSV infection is considered the most frequent viral infection in HIV infected patients.[5] Early HSV infection and its high frequency in HIV infected children correlate with a rapid evolution of the disease suggesting a worsening prognosis for the patient.

Ray and Mahajan reported HCMV (IgM) sero-prevalence of 8.5% in normal pregnant women.[9] In the present study in HIV positive children, we found a sero-prevalence of HCMV (IgG) and HCMV (IgM) to be 87.1% and 34.6% respectively. This is significantly higher as compared to HIV negative individuals. HCMV infection causes a lot of morbidity and mortality especially in immuno-compromised individuals. CMV retinitis is one of the common complications especially in children. Thus it is essential to periodically examine the HIV-HCMV coinfected children for this serious complication. Moreover, those children who have tested positive for HCMV-IgM should also be subjected to either HCMV-PCR in urine or blood or to HCMV antigen detection for confirmation of diagnosis of acute infection with the virus.

A study conducted by Hussain T *et al*[10] showed sero-prevalence of HIV, HBV, HCV and syphilis to be 2.4%, 2.9%, 1% and 5.4% respectively among patients attending

sexually transmitted diseases (STD) and ante-natal clinics (n= 863). HIV-HBV co-infection was seen in 0.2%, HBV-HCV in 0.1% and HIV-HCV in no case. In the present study we found HBV, HCV, HCMV and HSV sero-prevalence of 29.7%, 26.7 %, 34.6% and 58.4% among HIV positive children respectively, which is significantly higher as compared to other age groups.

There are scattered reports from various parts of India which reveal the prevalence of HBV in common population in India. One such study from Tamil Nadu states the prevalence of HBsAg as 5.7% in the general population and community sero-prevalence (HBsAg and anti-HBs antibody) of 27.4%.[11]

Clinically most of the HIV positive children had hepato-splenomegaly, which may be partly attributed to high prevalence of HBV and HCV infection in these patients. HCV- RNA concentration has been found to be independently associated with disease progression.[12] Clinical or biochemical jaundice was present in very few of these children. This may be because of short duration of illness, since most of the children belonged to 2-5 yr age group, while both HBV and HCV cause chronic liver disease.

CONCLUSION

The observed frequencies of viral co-infections in the present study population may reflect the transmission biology of these different viruses and their prevalence in the maternal population. It is therefore, strongly recommended that all HIV positive children should be screened for these viral co-infections as many of these viral co-infections require specific antiviral treatment. Timely and targeted management of these viral co-infections can decrease mortality and morbidity in HIV infected children.

Contributions: AB and DKS conducted the study and collected the data. RR critically reviewed and revised the manuscript.

Conflict of Interest: None

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