ORIGINAL ARTICLES

HIV SEROPOSITIVITY IN HOSPITALIZED CHILDREN ON CLINICALLY DIRECTED SELECTIVE SCREENING: AN EXPERIENCE FROM CENTRAL INDIA

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Abstract

Background: Probability of HIV infection in a given clinical manifestation has been examined in a very few studies.
Aims: To assess the probability of HIV infection in children hospitalized with the selected manifestations included in either World Health Organization (WHO) or South African criteria.
Methods: Patients aged 18 months to 14 years hospitalized with at least two of the following clinical features: marasmus, prolonged pyrexia, persistent cough, chronic diarrhoea, repeated common infections, generalized lymphadenopathy, hepatosplenomegaly, generalized dermatosis, oral candidiasis were tested for HIV by ELISA test using WHO-UNAIDS strategy-II.
Results: Out of the recruited 110 cases, 9 cases were HIV positive with a seropositivity rate of 8.2%. In our study, only oral candidiasis was found to be an independent risk factor to predict HIV infection in children. However, probability of HIV infection increases with increase in the number of risk factors present concomitantly.
Conclusion: Number and nature of the clinical features present determine the probability of HIV infection in children, which increases with increase in number of risk factors.
Key Words: HIV, AIDS, Pediatrics, WHO clinical case definition

Introduction

HIV infection in children exhibits a variety of manifestations including prolonged fever, prolonged diarrhea, weight loss, recurrent or opportunistic infections, lymphadenopathy, and hepatosplenomegaly. (1,2) However, in developing countries like in India, there is high prevalence of malnutrition, poor hygiene and of infectious diseases like malaria and tuberculosis leading to childhood admissions without HIV infection but similar clinical features, thus to make a clinical diagnosis of HIV infection becomes very difficult. (3,4) As routine HIV testing is not a feasible option, especially in resource poor countries, clinically directed selective screening to diagnose HIV infection is the foremost way to detect maximum number of cases without wasting resources. (5)

For this purpose, first clinical case definition (CCD) was developed by World Health Organization (WHO), especially for use in countries where testing for HIV antibodies was not routinely available. (6) This has been evaluated in different settings in an attempt to determine the likelihood of HIV infection in a given clinical situation and to formulate their own screening criteria. (1,7-10) Of these, one study was conducted at Bloemfontein, South Africa (SA) and the proposed CCD was claimed to be easier to use, less subjective, and more sensitive (63.2% vs. 14.5%) than WHO-CCD. (1) However, as clinical profile of HIV in children vary greatly in different epidemiological settings, it is difficult to adopt one particular criteria for all the settings. Therefore, we conducted this prospective study to assess the probability of HIV infection in children hospitalized with at least two of the selected manifestations. We selected these clinical features as they were found to be associated with high probability of HIV infection in children and were included in either WHO or SA criteria for HIV screening.

Materials and Methods

This prospective study was conducted in pediatrics department of a tertiary care teaching institution of central India, over a period of 12 months. Clearance from the institutional ethics committee was obtained and written informed consent from the parents or legal guardians and assent from children above seven years of age was obtained before recruitment. Patients between 19 months and 14 years of age hospitalised with any two of the following clinical presentations were included in the study: prolonged fever for more than one month, prolonged diarrhoea for more than one month, marasmus (weight less than 60% or less than third percentile of the expected weight for age and sex), chronic cough persisting for more than one month, generalized dermatitis, repeated common infections (e.g. upper respiratory tract infections), oropharyngeal candidiasis, generalized lymphadenopathy, hepatosplenomegaly. We selected these clinical features as they were included in either WHO case definition or SA criteria. Children with other known causes of immunosuppression e.g. cancer, severe malnutrition, on long-term steroid or chemotherapy, children aged below 18 months and children whose parents refused to participate in the study were excluded. Pre-test counselling was provided including information on high risk behaviour in relation to HIV infection, technical aspects of screening and possible implications of result being found positive. After recruitment, demographic data including age, sex, weight, height, parents? education and occupation, socioeconomic status and any high risk behaviour in parents were noted in pre-designed patient data form. Present and past history along with physical examination finding was recorded.

Blood sample was drawn by venepuncture and sent to laboratory for HIV testing by ELISA using Pareekshak rapid membrane ELISA kits (a sandwich enzyme immunoassay) and Enzaids HIV 1&2 ELISA kits (an indirect heterogeneous enzyme immunoassay). Diagnosis of HIV infection was confirmed as per WHO-UNAIDS strategy II. (11) We could not confirm HIV positive cases by Western Blot or other confirmatory tests because of financial constraints. Parents of seropositive children were offered post-test counselling including information on antiretroviral therapy, providing support and exploring the possibility of achievable solutions to personal problems.

Table 1 - HIV serostatus in relation to each clinical feature

Clinical Manifestations	Total Cases	HIV +ve Cases	HIV-ve Cases	Sensitivity	Specificity	PPV	P Value
Repeated common infections	75	5	70	55.6%	30.7%	6.76	0.46
Prolonged pyrexia	66	3	63	33.3%	37.6%	4.55	0.15
Marasmus	64	6	58	66.7%	36.6%	8.57	1.00
Hepatosplenomegaly	61	4	57	44.4%	53.7%	7.84	0.50
Persistent Cough	49	2	47	22.2%	53.7%	0.50	0.29
Generalized Lymphadenopathy	37	3	34	33.3%	66.3%	8.11	1.00
Oro-pharyngeal Candidiasis	17	4	13	44.4%	87.1%	23.57	0.03
Chronic diarrhea	11	1	10	11.1%	90.1%	9.09	1.00
Generalized dermatosis	4	-	-	0	96.0%	0	1.00

PPV = Positive predictive value

Table 2 - HIV seropositivity and number of risk factors present

Number of risk factors present	Number of total cases	HIV positive Cases	HIV negative Cases	Seropositivity rate
Two	30	1	29	3.3%
Three	26	1	25	3.9%
Four	38	4	34	10.5%
Five	12	2	10	16.7%
Six	4	1	3	25%

Data were analyzed using SPSS version 16.0. Data were presented as percentage and compared by fisher?s exact test, whenever appropriate. P value < 0.05 was considered significant.

Results

Total 138 children were eligible for recruitment on the basis of clinical examination. Of these, 28 children were excluded from study due to various reasons (16 children were aged less than 18 months, 7 cases had other known causes of immunodeficiency and parents of 5 children refused to participate in the study). The mean age of the study population was 62.3 ± 26.7 months with a male: female ratio of 1.4: 1. Most of the cases (46, 41.8%) belonged to 18 months to 5 years age group.

On admission, the most common presentation was repeated common infections in 75 (68.2%) cases followed by prolonged pyrexia in 66 (60%) cases. On examination, 64 (58.2%) cases had marasmus while 61 (55.5%) cases had hepatosplenomegaly. Forty (36.4%) cases had different forms of tuberculosis including tubercular meningitis (TBM) in 14 (12.7%) cases. Generalized dermatosis was seen in only 4 (3.6%) cases (Table 1).

Out of the 110 cases, 9 cases (8.2%) were HIV positive on ELISA. HIV seropositivity rate for various clinical manifestations varies from 0% for generalized dermatosis to 23.6% for oral candidiasis. Seropositivity rate for common clinical manifestations like repeated infections and prolonged pyrexia were 6.7% and 4.6% respectively (Table 1). In our study, only oropharyngeal candidiasis was found to be an independent risk factor for predicting HIV infection (P=0.03).

The probability of HIV seropositivity increased significantly with increase in the number of risk factors present. As depicted in table 2, seropositivity rate increases from 3.3% for two risk factors to 25% when six risk factors were present.

Both the parents of 5 seropositive cases were HIV positive, parents of 3 cases were seronegative, while in 1 case parental status was undetermined as they didn?t present themselves for HIV testing. Thirty-two cases received blood transfusion in past for various reasons, of which 3 were HIV positive. Most common mode of transmission was vertical (55.6% cases), 3

cases (33.3%) got it through blood transfusion. In 1 case, exact mode of transmission was undetermined as parental status was unknown.

Discussion

Clinically directed selective screening to diagnose HIV infection in children requires awareness among pediatricians about the spectrum of clinical manifestations of HIV infection in a particular area or community. Therefore, constant work is necessary in this field so as to determine clinical manifestations of HIV in different geographical regions, as these manifestations differ from community to community. Although actual prevalence of pediatric HIV infection in India is unknown, seroprevalence in hospitalized children was estimated to be 2.3% by Shah I et al. (12) In our study, overall HIV seropositivity rate was 8.18% in clinically directed selective screening, which is lesser than that of high prevalence areas e.g. 15% - 20% in Mumbai. (13,14)

Many studies have demonstrated the role of clinically directed selective screening to detect HIV infection (14-16) and WHO-CCD was proposed for the same purpose but its sensitivity varied greatly in different studies, e.g. 69% in Zambian study (17) to 19% in Ivory Coast study (18). Also, WHO-CCD contains 9 items, divided into major and minor signs and 6 of 9 signs require medical history, which can not be objectively verified. So that sometimes it becomes difficult to use it in outpatient department with a heavy patient load. Additionally, accompanying person's inability to recollect the history and duration of symptoms also creates situation more difficult. Therefore in our study, we tried to include more objective signs which be obtained by simple physical examination without dividing them into minor or major criterion.

We have replaced the sign 'weight loss or abnormally slow growth' included in WHO-CCD, which depends on the subjective observation of caretaker, with an objective finding i.e. marasmus as included in SA criteria. On applying this weight criterion in our study, only 58.2% cases had marasmus compared to history of weight loss in 88.2% cases. Other Indian studies also reported a high incidence of severe malnutrition in these children, ranging from 44.56% by Merchant et al (19) to 81.9% by Lahiri et al. (20) Seropositivity rate for severe malnutrition was reported to be 26% by Bavdekar et al (14) as against the seropositivity rate of 9.38% for marasmus in our study.

In this study, seropositivity rates of chronic diarrhoea, marasmus and oropharyngeal candidiasis were higher than overall seropositivity rate of 8.18%. However, only oropharyngeal candidiasis was an independent predictor of HIV infection (P=0.03).

Oropharyngeal candidiasis is one of the most consistently identified risk factor for predicting HIV infection. (14, 21-23) Many different independent risk factors for pediatric HIV infection were identified in other studies including generalized dermatitis (14) lymphadenopathy (14,21), malnutrition (21), chronic diarrhea (22,23), and pneumonia. (24) However, in our study we did not find chronic diarrhea, dermatitis, marasmus or lymphadenopathy as significant risk factor for HIV infection. This indicates the variability of significant risk factors from one community to other and making it imperative to conduct studies in different population groups to determine significant risk factors for that particular group.

In our study, repeated common infections, chronic fever, marasmus, and hepatosplenomegaly were the common clinical manifestations of HIV infection, which are same as seen in other studies from India (25-29) as well as other tropical countries. (21-24) However, none of these was significantly associated with HIV seropositivity, which could be explained by the fact, that in developing countries other common causes of childhood admissions e.g. malaria and tuberculosis present with the similar clinical presentations. The probability of HIV infection increased progressively with increase in number of risk factors concomitantly present, which can be explained by the presence of more manifestations in children with advanced stage of the disease or greater immunosuppression.

In our study, most common mode of transmission was vertical followed by transfusion related (33.3%), which is collaborating to results of other Indian studies. (25-29) It indicates towards a worrisome fact that despite regulations requiring screening of donors, transfusion-associated HIV continues to occur in India, which can be either due to poor adherence to screening procedures or due to unsafe injection practices. In the present study, of the 40 tubercular patients, one patient was HIV positive (2.5%). Merchant et al reported seropositivity 24% and 18% in children with chronic diarrhea and disseminated tuberculosis respectively (19), while Karande S et al reported 6.5% seropositivity in TBM patients. (30)

Few study limitations were that we could not confirm positive ELISA tests by PCR or other confirmatory tests because of financial constraints. Secondly, present study was conducted on relatively small number of hospitalized children so it may not present true picture of HIV prevalence in community.

In conclusion, probability of HIV infection increases with increase in the number of risk factors and these risk factors differ from community to community. Therefore, further large scale community trials are needed to determine these risk factors for that particular population group, especially for use by paramedical workers to screen suspected HIV cases on outpatient basis.

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