

## HOSPITAL BASED SCREENING FOR HIV (HUMAN IMMUNODEFICIENCY VIRUS) IN CHILDREN IN A LOW RISK POPULATION - CROSS-SECTIONAL OBSERVATIONAL STUDY

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### ABSTRACT

#### BACKGROUND

Human Immunodeficiency Virus (HIV) infection is detected in a significant number of children globally. Since mass screening for detection of HIV infection in children is not feasible in a low risk and resource limited state, it is worthwhile to find out these cases among groups with high probability of the infection.

The aim of this study is to determine the probability of HIV infection, in a very low risk population, when a child is hospitalised with at least one of the selected manifestations that is known to be significantly associated with HIV infection.

#### MATERIALS AND METHODS

Hospitalised children aged between 19 months and 12 years admitted with predefined clinical pointers were screened for HIV infection by Micro-ELISA Kits. Positive micro-ELISA cases were subjected to Comb-Aid immune-blot test. Children positive for Immunoblot test as well were considered HIV positive cases.

#### RESULTS

Hundred patients were enrolled in the study. Four patients were detected of having HIV infection. Clinical pointers in these cases were fever (75%), hepatomegaly (75%), protein energy malnutrition (75%), cough (50%), recurrent bacterial infections (50%), generalised dermatitis (50%), diarrhoea (50%) and oral thrush (50%). Clinical pointers with significant positive correlation were recurrent bacterial infections, oral thrush and generalised dermatitis ( $p < 0.05$ ).

#### CONCLUSION

Hospital-based screening using specific clinical pointers is a useful tool to detect HIV Sero-positive cases in a low risk population.

#### KEYWORDS

Human Immunodeficiency Virus, Children, Selective Screening, Clinical Pointer.

**HOW TO CITE THIS ARTICLE:** Tali SH, Yousuf S, Kaul KA. Hospital based screening for HIV (Human immunodeficiency virus) in children in a low risk population - cross-sectional observational study. *J. Evolution Med. Dent. Sci.* 2017;6(7):550-553, DOI: 10.14260/Jemds/2017/117

#### BACKGROUND

An estimated 2.5 million children around the world are living with Human Immunodeficiency Virus (HIV)/Acquired Immunodeficiency Syndrome (AIDS) according to the 2010 report on the Global AIDS Epidemic released by Joint United Nations Program on HIV/AIDS. India has an estimated 220,000 children infected by HIV/AIDS. Women and children are increasingly becoming vulnerable to this disease. This alarming trend is being observed closely as more HIV positive mothers will unknowingly pass the virus on to their children. Children under 15 years of age account for 4.4% of all infections, while people aged 15 - 49 years account for 82.4% of all infections.<sup>(1)</sup>

Early diagnosis of HIV infection in a child is not only helpful in instituting prophylactic therapy, but also in

providing supportive care. However, undertaking diagnostic workup to screen all children for HIV infection in the low risk populations may not be that cost effective. When applied to the individuals with high probability of HIV infection in a low risk population, it is highly likely that cost effectiveness will be improved reasonably.<sup>(2,3)</sup> Although, several studies have been carried out in African countries<sup>(4-6)</sup> and many states of India<sup>(2,3,7)</sup> to determine the likelihood of HIV infection with a given clinical feature to the best of our knowledge. No such study has been carried out in the Kashmir division of Jammu and Kashmir state. As per NACO 2012 report, the state of Jammu and Kashmir falls among the states with the lowest HIV prevalence in India.<sup>(8)</sup> Hence, we conducted a prospective study to determine the probability of HIV infection in a very low risk population, when a child is hospitalised with at least one of the selected manifestations that is known to be significantly associated with HIV infection.

#### MATERIALS AND METHODS

This cross-sectional observational study was carried out at GB Pant Children's Hospital, Srinagar, which is a tertiary care hospital for children in the state of Jammu and Kashmir, India. The study was approved by Institutional Research Board (IRB) and Ethical Committee of the College. All children aged between 19 months and 12 years and admitted with predefined clinical pointers (Table 1) were included in

Financial or Other, Competing Interest: None.

Submission 14-12-2016, Peer Review 08-01-2017,

Acceptance 13-01-2017, Published 23-01-2017.

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DOI: 10.14260/jemds/2017/117



this study. Written informed consent from parent/guardian was taken prior to enrolment and screening. Pre-test counselling was provided to the parent or guardian of all patients regarding the nature of the study and implications thereof.

Sl. No.	Clinical Pointer	Description
1	Fever	Documented Fever (Axillary Temperature > 37.8°C) ≥ 1 Month
2	Diarrhoea	≥ 2 loose Stools per Day ≥ 1 Month
3	Persistent Cough	Cough ≥ 1 Month
4	Malnutrition	≥ Grade 3 PEM as Defined by Indian Academy of Paediatrician's Classification
5	Oral Thrush	Presence of Whitish Plaques in Oral Cavity which could not be easily Removed without Leaving an Erythematous Base
6	Generalised Lymphadenopathy	Enlarged Lymph Nodes (> 1 cm in Axilla and >1.5 cm in Inguinal Region) in ≥ 2 Non-Contagious Sites for > 2 Months
7	Hepatomegaly	Liver below Costal Margin > 4 - 7 cm (As per age) as Detected Clinically
8	Generalised Dermatitis	Including Eczema and Maculopapular Dermatitis
9	Chronic Parotid Swelling	Swelling of at least 1 Parotid Gland for a Minimum Period of 3 Months
10	Recurrent Bacterial Infection	Occurrence of > 2 Episodes of Serious Bacterial Infections such as Pyogenic Meningitis or Pneumonia in Past 2 Years
11	Disseminated Tuberculosis	Miliary Tuberculosis or CNS Tuberculosis or Pulmonary Tuberculosis in Conjunction with Abdominal Tuberculosis
12	Pneumocystis Carinii pneumoniae	Diagnosed on the Basis of Clinical Features, Arterial Blood Gas Analysis, Chest Radiography and Microbiological Studies

**Table 1. Definition of Predetermined Clinical Risk Factors**

After recruitment, details of demographic data, history and physical examination findings were recorded in a predesigned proforma. Five millilitres (5 mL) of venous blood were collected and were sent to laboratory for HIV screening by Micro-ELISA Kits. Micro-ELISA positive cases were subject to Comb-Aid immunoblot testing in sequence. When both the tests were positive, HIV was confirmed as per National AIDS Control Organisation (NACO) guidelines. CD4 count was done in every patient who was confirmed HIV positive. As a secondary end point of the study, the parents of children (children who eventually were HIV positive) were screened for HIV infection after offering pre-test counselling.

**Statistical Analysis**

The data was analysed using the SPSS software programme version 18. Chi-square test was used with Yates correction. Relative Risk and Odds Ratio were determined wherever applicable.

**RESULTS**

A total of 100 patients were enrolled in the study. Four were sero-positive for HIV infection. Baseline characteristics of the study population are depicted in Table 2.

Sl. No.	Age (Months)	No. of Patients
1	19 - 32	6 (6%)
2	33 - 46	4 (4%)
3	47 - 60	9 (9%)
4	61 - 74	5 (5%)
5	75 - 88	7 (7%)
6	89 - 102	10 (10%)
7	103 - 116	17 (17%)
8	117 - 130	14 (14%)
9	131 - 144	28 (28%)
<b>Total</b>		<b>100 (100%)</b>
<b>Gender</b>		
1	Male	58 (58%)
2	Female	42 (42%)
<b>Total</b>		<b>100 (100%)</b>

**Table 2. Age and Gender of the Study Population (n = 100)**

No. of subjects (total and sero-positive) with a predefined clinical pointer are in shown in Table 3. Statistical analysis is shown in Table 4. Correlation of no. of risk factors with sero-positivity is shown in Table 5. Demographic and other characteristics of HIV sero-positive cases are in Table 6.

Sl. No.	Clinical Pointers	Total No. of Subjects (Percentage); N=100	No. of HIV Sero-positive Cases (Percentage); N=4
1	Fever (> 1 month)	48 (48%)	3 (75%)
2	Diarrhoea (> 1 month)	12 (12%)	2 (50%)
3	Cough (> 1 month)	27 (27%)	2 (50%)
4	Malnutrition (Grade III or more)	33 (33%)	3 (75%)
5	Oral Thrush	4 (4%)	2 (50%)
6	Generalised Lymphadenopathy	8 (8%)	2 (50%)
7	Hepatomegaly	46 (46%)	3 (75%)
8	Generalised Dermatitis	3 (3%)	2 (50%)
9	Chronic Parotid Swelling	0 (0%)	0 (0%)
10	Recurrent Bacterial Infection	8 (8%)	0 (0%)
11	Disseminated Tuberculosis	18 (18%)	0 (0%)
12	Pneumocystis Carinii Pneumoniae	0 (0%)	0 (0%)

**Table 3. Total No. of Subjects with a Specific Clinical Pointer and No. of HIV Sero-Positive Subjects having that Clinical Pointer**

**DISCUSSION**

In our study, there was a statistically significant correlation between presence of recurrent bacterial infection, oral thrush and generalised dermatitis and the prediction of HIV infection sero-positivity (p < 0.05). Although fever, severe malnutrition and hepatomegaly were the most common findings in HIV positive patients, they did not predict HIV sero-positivity.

Clinical Pointers	HIV Sero-Positive	HIV Sero-Negative	X <sup>2</sup>	p Valve	Odds Ratio	Specificity	Sensitivity
Fever (> 1 Month) (n = 27)	3 (6.25%)	45 (93.75%)	0.35	> 0.05	4.05	53	75
Cough (> 1 Month) (n = 27)	2 (7.4%)	25 (92.59%)	0.233	> 0.05	1.35	74	50
Severe Malnutrition	3 (9.09%)	30 (90.90%)	1.64	> 0.05	3.45	69	75
Recurrent Bacterial Infection (n = 9)	2 (25%)	6 (75%)	5.38	< 0.05π	1.04	94	50
Generalised Dermatitis (n = 3)	2 (66.66%)	1 (33.33%)	17.04	< 0.05π	1.010	99	50
Hepatomegaly (n = 46)	3 (6.97%)	43 (93.4%)	0.456	> 0.05	3.81	55	75
Chronic Diarrhoea (n = 12)	2 (16.66%)	10 (83.33%)	2.56	> 0.05	1.16	89	50
Oral Thrush	2 (50%)	2 (50%)	12.17	< 0.05π	1.02	98	50

**Table 4. Statistical Assessment**

π = P value Statistically Significant

The strength of our study is that it has shown the feasibility of applying clinical pointer based screening tool in a very low risk population for HIV infection detection. However, the results of our study would not be applicable to screening of asymptomatic children as our target population were symptomatic in hospitalised children. Furthermore, children aged 18 months and younger were not enrolled as diagnosing HIV infection in them would need performance of HIV, DNA, PCR which was not possible because of economical constraints.

Common clinical manifestations in HIV positive patients were fever (75%), severe malnutrition (75%), hepatomegaly (75%), cough for more than one month (50%), chronic diarrhoea (50%), recurrent bacterial infection (50%), oral thrush (50%) generalised dermatitis (50%). These findings are consistent with other published studies.<sup>[9,10]</sup> Although, generalised lymphadenopathy is a common presenting risk factor for HIV in hospitalised children,<sup>[2,7]</sup> our observation did not reveal any such finding. Also, no case of disseminated tuberculosis was reported in our study, which is also a common clinical pointer<sup>[11]</sup> for detecting HIV sero-conversion in this population. This may be due to the fact that less number of subjects was enrolled in our study.

In this study, generalised dermatitis, oral thrush and recurrent bacterial infections were significant predictors for detection of HIV positivity rate (p < 0.05), which is consistent with other studies.<sup>[12,13,3]</sup> Patients with single clinical risk factor had a sero-positivity rate of 3.7%, patients with 5 clinical risk factors had sero-positivity rate of 50% and those with 6 or 7 such factors predicted a rate of 100%. This study shows that as the number of predefined clinical risk factors increases, the probability of sero-conversion to HIV also increases. This finding correlates well with the findings of other studies.<sup>(3)</sup>

No. of Risk Factors Present	HIV Positive Cases (n = 4)/ Percent of Total	HIV Negative Cases (n = 96)	Total No. of Subjects with the Clinical Pointer (n = 100)
1	1 (3.7%)	27	(28)
2	0 (0%)	41	(41)
3	0 (0%)	22	(22)
4	0 (0%)	5	(05)
5	1 (50%)	1	(02)
6	1 (100%)	0	(01)
7	1 (100%)	0	(01)

**Table 5. Risk Factor Correlation (HIV Positive Vs HIV Negative)**

In our study, all HIV sero-positive cases were from rural areas. This may be related to low education level and lack of healthcare awareness in such populations.

At the time of admission in the hospital, there was no family history of HIV infection or AIDS in any of the studied 100 patients including HIV positive cases. On contact tracing, first patient had both mother and father positive for HIV infection. The other two patients (siblings) provided history of prolonged maternal illness (pulmonary tuberculosis) and death, although no HIV testing was performed on her. The fourth patient's mother had died of recurrent pneumonias, but was never screened for HIV infection. None of the affected patients had received any blood transfusion. There was no history of sexual abuse or repeated syringe use in any of the affected patients (Table 5). So most probably the transmission of the disease was vertical, which is consistent with other studies.<sup>(14)</sup>

Case No.	Mother Sero-Positive	Father Sero-Positive	Blood Transfusion/Sexual Abuse/Exposure to Injections	Male (M)/ Female (F)	Rural (R)/ Urban (U)	CD4 Count/ mm <sup>3</sup>
1	Yes	Yes	No	F	R	1340
2Ω	¥	No	No	M	R	560
3Ω	¥	No	No	M	R	720
4	€	Yes	No	F	R	350

**Table 6. Demographic and other Characteristics of HIV Sero-Positive Cases**

¥ = Mother had died of pulmonary tuberculosis, but never tested for HIV. € = Mother had died of recurrent chest infections, but never tested for HIV. Ω = Siblings.

**CONCLUSION**

Our study suggests that the hospital-based, clinically-directed screening has a practical role in diagnosis of HIV infection in a

resource limited settings even in low prevalence population. Moreover, contact tracing may be an effective tool in searching for hidden HIV infected cases.

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