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Human immunodeficiency virus sero-positivity in malnourished children with chronic diarrhoea

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Abstract

Diarrhoea is a major cause of morbidity and mortality among infants and children worldwide. Diarrhoeal disease occurs more commonly in Human Immunodeficiency Virus (HIV) infected than in uninfected children and their outcomes are worse. Case management of HIV-infected infants and children is complicated by immunodeficiency, malnutrition and other opportunistic infections. Present hospital based prospective study was undertaken to determine HIV sero-positivity in children with chronic diarrhea. The subjects in the present study were of age group of more than one month up to 12 years old. The detailed clinical and personal history of the subject was recorded, which included demographic data, socio-economical conditions and HIV status. Random collection of stool sample was done and was subjected for macroscopic and microscopic examination along with saline and iodine wet mount. Total 21% HIV positive children were detected in the study group, while in control group none of the children showed HIV positivity. Out of 94 bacterial isolates obtained from study group, *Escherichia coli* (*E. coli*) were the predominant isolate. Out of 44 *E. coli* isolates from HIV negative cases, 7 were typed as Enteropathogenic *E. coli* (EPEC) by specific antisera. Mixed infections were observed in all HIV positive patients. Common isolate was *E. coli*, which was associated with *Klebsiella pneumoniae*, *Candida albicans*, *Rota virus* and *Isospora belli*. None of the *E. coli* was serotyped as Enterohaemorrhagic *E. coli* (EHEC) and EPEC from this group. All HIV sero-positive cases, with less than 1 year of age, from study group were found to be associated with Grade III malnutrition. Such malnutrition conditions were most commonly observed in early age of life and maximum association of these conditions were seen with AIDS or HIV positive conditions. Keeping in view, the small subgroup, there is need for further studies with larger sample size to establish the above correlation.

Keywords: Human immunodeficiency virus, malnourished children, chronic diarrhoea

1. Introduction

Diarrhoea is a major cause of morbidity and mortality among infants and children worldwide. Diarrhoea is a condition, usually related with poor hygiene, consumption of contaminated water and food, as well as patient's immune status. Immune status is commonly associated with malnutrition, which enhances the severity and integrity of diarrhoea in patient. In India, malnutrition in children is very common observation, often associated with poverty and illiteracy. Hence, chronic diarrhoea is one of the major problems associated in health management. In developing countries, diarrhoeal disease accounts for an estimated 17.5–21% of all deaths in children under the age 5 years, equivalent to 1.5 million deaths per year [1]. Of all the child deaths from diarrhoea, 78% occur in the African and South-East Asian regions, which are also disproportionately burdened with infant and childhood HIV infections. Diarrhoeal disease occurs more commonly in HIV-infected than in uninfected children, and their outcomes are worse [2-4] Persistent diarrhoea in particular is associated with a high risk for death in HIV-infected children. Case management of HIV-infected infants and children is complicated by immunodeficiency, malnutrition, other infections that increase susceptibility, gastrointestinal manifestations of primary HIV disease and gastrointestinal symptoms associated with antiretroviral drugs for those being treated [5-7] The severity of acute diarrhoeal episodes can range from mild to moderate to severe cases that can lead to hospitalization or death. Severity is influenced by many factors, including the agent and its pathogenicity and host characteristics, such as immunodeficiency and age. Little information is available on the etiology of diarrhoea in HIV-infected or -exposed

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children, partially because of issues of feasibility and the costs associated with integrating HIV programmes into etiological studies. In general, studies on diarrhoea are limited by a lack of control specimens and testing of a reduced spectrum of enteric pathogens due to cost and lack of the necessary training, advanced laboratory skills, commodities and equipment. As a result, some of the studies of HIV-infected children were conducted in areas with a known high HIV prevalence or among HIV-infected children tested for a limited spectrum of enteric pathogens.

Pediatric HIV is rampant in India due to the increasing prevalence of HIV infection in women and ineffective measures for prevention of perinatal transmission. Sexual route and infected needles account for most infections in the adolescent period. Diarrhea occurs in almost 90% of patients with HIV, in developing countries, at sometime during the clinical course [8]. Hence in the light of currently available information, the present hospital based prospective study was undertaken to determine HIV sero-positivity in children with chronic diarrhea.

2. Material and Methods

This prospective longitudinal study was undertaken at the Department of Microbiology, T.N. Medical College and B.Y.L. Nair Charitable Hospital, Mumbai. The study was reviewed and approved by the Institutional Ethics Committee. Selection of subjects for the study and control group was done on the basis of standard classification of malnourished and chronic diarrhea [9]. The subjects in the present study were of age group of more than one month up to 12 years old. Study group and Control group included 100 patients each. Study group included all types of infective chronic diarrhoea, except, anaerobic infection in pediatric group, while acute diarrhoea cases in pediatric group were taken as control group. The detailed clinical and personal history of the subject was recorded which included demographic data, socio-economical conditions and HIV status. Patients recruited were either hospitalized or outdoor patients at B.Y.L. Nair Charitable Hospital. HIV status of these patients was confirmed by the pediatrics department. The samples were considered as HIV positive when found reactive by all three different methods. HIV (1 and 2) antibody testing using rapid kits were done and declared reactive as per National AIDS control organization (NACO) guidelines strategy [10].

Random collection of stool sample was done before starting any empirical treatment from clinically diagnosed malnourished children with infective chronic diarrhoea. Each stool sample was immediately transported to the Microbiology laboratory [11] and was subjected for macroscopic [12] and microscopic examination [13-14]. Also saline [15, 16] and iodine wet mount of each stool sample was carried [17]. A loopful of stool sample was inoculated on culture media like MacConkeys, Blood, *Campylobacter*, Sabourauds dextrose and *E. coli* Hichrome agar and these media were incubated at appropriate temperatures. The minimum battery of tests was performed for identification of isolates obtained [18] *E. coli* serotyping of EPEC was carried out by using antisera kit of Denka Seiken UK, Ltd.

3. Results

Table 1: HIV status in Cases and controls $n_1 = 100$; $n_2 = 100$

HIV status	Groups		Total
	Cases (%)	Controls (%)	
Positive	21	0	21
Negative	79	100	179
Total	100	100	200

* p value > 0.001

Key: n_1 = number of Cases, n_2 = number of controls

Total 21% HIV positive children were detected in cases (study group), while in control group none of the children showed HIV positivity.

Table 2: HIV status and malnutrition grades in Cases $n = 100$

HIV status	Malnutrition grades		Total
	Grade II (%)	Grade III (%)	
Positive	0	21	21
Negative	47	32	79
Total	47	53	100

* p value > 0.001

Key: n = number of Cases

In all HIV positive cases from cases (study group), Grade III malnutrition was observed.

Table 3: Bacterial isolates from study group patients with HIV status $n_1 = 21$; $n_2 = 73$

Name of the organisms	No of bacterial isolates		Total
	n_1	n_2	
<i>E. coli</i>	0 (0.00%)	44 (60.30%)	44 (46.80%)
<i>E. + Klebsiella pneumoniae</i>	14 (66.70%)	0 (0.00%)	14 (14.90%)
<i>E. coli</i> + other organisms	7 (33.33%)	0 (0.00%)	7 (7.45%)
<i>Klebsiella pneumoniae</i>	0 (0.00%)	18 (24.70%)	18 (19.15%)
<i>Proteus vulgaris</i>	0 (0.00%)	1 (1.40%)	1 (1.06%)
<i>Shigella flexneri</i>	0 (0.00%)	4 (5.50%)	4 (4.25%)
<i>Salmonella paratyphi A</i>	0 (0.00%)	3 (4.10%)	3 (3.20%)
<i>Salmonella typhi</i>	0 (0.00%)	3 (4.10%)	3 (3.20%)
Total	21 (100.00%)	73 (100.00%)	94 (100.00%)

* p value > 0.001

Key: n_1 = number of bacterial isolates from HIV positive cases

n_2 = number of bacterial isolates from HIV negative cases

Out of 94 bacterial isolates obtained from study group, *E. coli* was the predominant isolate. Out of 44 *E. coli* isolates from HIV negative cases, 7 were typed as EPEC by specific antisera.

Table 4: Mixed infection from HIV positive cases. n = 21

Organisms	No of cases
<i>E. coli</i> + <i>Klebsiella pneumoniae</i>	66.66%
<i>E. coli</i> + <i>Candida albicans</i>	9.50%
<i>E. coli</i> + <i>Rotavirus antigen</i>	19.00%
<i>E. coli</i> + <i>Isospora belli</i>	4.80%
Total	100.00%

Mixed infections were observed in all HIV positive patients. Common isolate was *E. coli*, which was associated with *Klebsiella pneumoniae*, *Candida albicans*, *Rota virus* and *Isospora belli*. None of the *E. coli* was serotyped as EHEC and EPEC from this group.

4. Discussion

AIDS is rapidly expanding and is loaded with a high fatality ratio, due to the combined effects of malnutrition and opportunistic infections. Diarrhea is a common manifestation in all groups of AIDS patients. The digestive tract is a target of the disease in both settings. Opportunistic infections play a major role in children with severe immune impairment, with *Cryptosporidium parvum* being the leading agent of severe diarrhoea. Several therapeutic approaches are effective in reducing fecal output, but the eradication of the parasite is rarely obtained. Other opportunistic infections may induce severe and protracted diarrhoea, including atypical *Mycobacteria* and *Cytomegalovirus*. Diagnosis of diarrhoea should be individually tailored based on presenting symptoms and risk factors. Aggressive treatment of infectious diarrhoea is required in severely immune-compromised children. However, antiretroviral therapy prevents the development of severe Cryptosporidiosis. Intestinal dysfunction contributes to growth failure and further immune derangement, leading to wasting, the terminal stage of AIDS. Nutritional management is crucial in HIV-infected children and is based on aggressive nutritional rehabilitation through enteral or parenteral routes and micronutrient supplementation. HIV may play a direct enteropathogenic role and is implicated in both diarrhoea and intestinal dysfunction. Thus, severe enteric infections and intestinal dysfunction characterize the intestinal involvement of HIV infection. Diagnostic approaches include microbiological and morphological examinations and assessment of digestive processes, but immunological and virological data should be also carefully considered [19]

In this study, 21% of HIV positivity was reported in malnourished children with chronic diarrhoea. These figures were well correlated with finding of Beau *et al* study in 1999, [20] which stated a combination of chronic diarrhoea and malnutrition, frequently occurred in HIV sero-positive children and constituted a bad prognosis factor. In present study the *Candida albicans* was isolated from HIV positive children in 2% of the cases which was similar with Lee *et al.* study in Washington, who had found yeast and fungal infections usually occurred in immune-compromised patients with chronic diarrhoea. Copious yeast was present in their stool sample. *Candida* species could be pathogen in some conditions [21] Study also reported detection of *Isospora belli* in 1% of the HIV positive children with chronic diarrhoea. Smith *et al* had documented that *Isospora belli* was seen rarely in individuals with normal immune system but in immune-compromised patients, which leads to chronic high volume watery diarrhoea, persistent for months *Isospora belli* was seen [22].

In HIV cases due to malnutrition and opportunistic infections, more than one etiology was usually seen in chronic diarrhoea cases which indicated a poor outcome in disease progression. Present study reported mixed infection in all HIV positive patients. All 21 cases reported mixed infection with *E. coli* organisms. In 14 cases, *E. coli* was associated with *Klebsiella pneumoniae*, 4 cases with *Rotavirus*, 2 cases with *Candida albicans*, and 1 case with *Isospora belli*. Amdekar *et al* also reported that infection with one or more enteric pathogens was the predominant cause of persistent diarrhoea in children when present with malnutrition and could be very severe in HIV positive children [23]. *E. coli* was known to cause multiple episodes of diarrhoea lasting for several weeks. Other infectious agents include, EPEC, *Cryptosporidium*, *Giardia*, *Salmonella*, *Shigella*, and *Clostridium*. Infectious diarrhoea can be caused by multiple pathogens which was commonly observed in HIV positive patients. This infectious diarrhoea usually remains persistent for long time due to immunodeficiency along with infection.

There are several body mechanisms, which protect body from the bacteria causing gastritis. Bacteria have to overcome these defense mechanisms in order to produce disease in a host; certain conditions can act as predisposing factor or risk factors with diarrhea [24] Pre-existing malnutrition is associated with decreased turnover of epithelial cells resulting in delayed recovery, which may prolong episodes of infectious diarrhoea by itself as well as by promoting tissue invasion by other pathogens. Persistent diarrhoea are at higher risk when associated with malnutrition as they have decreased host immunity, delayed repair of intestinal damage and reduced food intake etc [25].

The highest HIV prevalence that is 84% was reported by Colebunders *et al* in Zaire in a study done in persistent diarrhea cases [26]. Various workers from African subcontinent reported seropositivity of HIV infection in diarrhea ranging between 26 – 39%. [27, 28]

In Mumbai, HIV seropositivity was seen in 24%, 18.2% and 48.8% of the cases of chronic diarrhea studies [29, 30, 31] Chronic diarrhea was not a significant independent risk factor for predicting HIV infection [31]. In present study, 11.6% of cases had oral candidiasis and one of them turned out to be HIV seropositive. The positive predictive value of HIV infection increases with the presence of other risk factors along with chronic diarrhea.

5. Conclusion

All HIV sero-positive cases, with less than one year of age, from study group were found to be associated with Grade III malnutrition. Such malnutrition conditions were most commonly observed in early age of life and maximum association of these conditions were seen with AIDS or HIV positive conditions. Keeping in view the small subgroup, there is need for further studies with larger sample size to establish the above correlation.

6. Recommendations

There were significant gaps in the available information on the prevention and treatment of diarrhoea in HIV-infected and exposed children. Appropriately large prevention and intervention trials were needed. Additional studies were required to determine the etiology of acute, bloody, persistent and chronic diarrhoea among HIV-infected and

exposed children; patterns of resistance of etiological agents and the prevalence of various pathogens.

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