Nosocomial infections in HIV-infected and HIV-uninfected children hospitalised for tuberculosis

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Abstract

Background

The interaction between tuberculosis and HIV-infected infection is well known and is responsible for the increase in the incidence of tuberculosis (TB) in sub-Saharan Africa over the last decade. This places a considerable extra burden on health services. The Brooklyn Hospital for Chest Diseases (BCH) is a non-acute TB hospital for the City of Cape Town, South Africa. The hospital has 60 children's beds and approximately 140 paediatric admissions annually. This study, undertaken before the availability of antiretroviral drugs in the public sector in South Africa, documents the occurrence of nosocomial infections in HIV-infected and HIV-uninfected children at BCH.

Method

This retrospective case-control study evaluated the occurrence of nosocomial infections in (HIV)-infected children and age- and time of admission-matched HIV-uninfected children admitted to the BCH, Cape Town, South Africa between July 1999 and December 2001 for the treatment of tuberculosis (TB).

Results

Forty-seven HIV-infected children (mean age 40 months) and 47 HIV-uninfected children (mean age 41 months) were studied. The HIV-infected children, who were not receiving antiretroviral therapy because it was not yet available in the public sector, experienced 109 episodes of nosocomial infections compared to 22 episodes amongst those not infected with HIV ($p = 0.001$). Twenty-five nosocomial infections (23%) among the HIV-infected children, but only two (9%) among the HIV-uninfected children, were serious enough to require transfer to a tertiary care hospital for management. Pneumonia was the commonest nosocomial infection and occurred in 26 (56%) HIV-infected patients, of whom three died, but in only four (9%) HIV-uninfected children, none of whom died. An outbreak of varicella affected 10 HIV-infected (21%) and 9 HIV-uninfected children (19%). One HIV-infected child died of varicella pneumonia. Other common nosocomial infections encountered in HIV-infected and HIV-uninfected children respectively were upper respiratory tract infections (pharyngitis, tonsillitis or rhinitis) affecting 21 and four, otitis media in five and one, oral candidiasis in seven and zero, urinary tract infection in four and one and acute gastroenteritis in five and zero children. Five HIV-infected children (11%) died and four of the deaths were known to be due to nosocomial infection; only one HIV-uninfected child died from severe miliary TB.

Conclusion

Nosocomial infections occurring in HIV-infected children are a serious cause of morbidity and mortality in children hospitalised for the treatment of tuberculosis. Their impact could be reduced by the earlier introduction of antiretroviral treatment and by immunisation against certain of the infecting agents. Post-exposure prophylaxis for varicella could prevent or alleviate disease.

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Introduction

The interaction between tuberculosis and human immunodeficiency virus (HIV) infection is well known and is responsible for the inordinate increase in the incidence of tuberculosis (TB) in sub-Saharan Africa over the last decade.[1] This epidemic affects both adult and childhood tuberculosis and places a considerable extra burden on health services. The Brooklyn Hospital for Chest Diseases (BCH) is a secondary level non-acute hospital that serves as the regional TB referral hospital for the Cape Town Metropole, as well as for complicated cases from further afield in the Western Cape Province. The hospital admits patients with severe or complicated disease, or whose social circumstances preclude community-based, directly-observed therapy, short course (DOTS). BCH has two paediatric wards; one for children aged zero to five years with 40 beds, and the other for children aged six to 12 years with 20 beds. There are approximately 140 paediatric admissions annually. This study, undertaken before the ready availability of antiretroviral drugs in the public sector in South Africa, documents the occurrence of nosocomial infections in HIV-infected and HIV-uninfected children at BCH.

Methods

This is a retrospective case-control study of children admitted to BCH from July 1999 to December 2001 who had their HIV status determined. Patient data were recovered from a prospectively-compiled patient register and hospital records. Each HIV-infected child was age-matched with an HIV-uninfected child admitted over the same period. In the case of infants aged zero to 12 months, controls were within two months of age of the HIV-infected child, for children aged one to two years, within three months, for children aged two to five years, within one year, and for children aged six to 12 years, within 18 months of the HIV-infected child. The negative controls were selected by choosing the closest age-matched patient admitted within four months of each HIV-infected patient.

The HIV status of the children was determined after pre-test counselling and with written informed consent from the child's legal guardian. Two HIV enzyme-linked immunosorbent assays (ELISAs) were performed in children older than 15 months, and a positive ELISA together with a positive polymerase chain reaction or detection of the p24 antigen was required in children younger than 15 months to confirm HIV infection.

Demographic details, clinical features, the results of diagnostic investigations and the outcome at the time of discharge for each child were noted.

A diagnosis of ***confirmed TB*** was accepted in the presence of a culture of *Mycobacterium tuberculosis* from gastric aspirate, sputum, cerebrospinal fluid (CSF) or any biopsy specimen or the finding of acid-fast bacilli on microscopy of any specimen if accompanied by a positive Mantoux tuberculin skin test (TST), or a chest radiograph compatible with childhood tuberculosis, or a history of recent close household contact with an adult with sputum microscopy smear-positive pulmonary TB.

Probable TB was diagnosed in children with two or more of the following:

- a positive TST (≥15 mm induration in HIV-uninfected; ≥5 mm in HIV-infected)
- an abnormal chest radiograph showing features of childhood TB (mediastinal adenopathy and/or a miliary picture responding to antituberculosis treatment)
- close contact with an adult with sputum microscopy smear-positive TB
- a CSF picture suggestive of TB meningitis (TBM) (elevated protein of >0.5 g/l, reduced glucose (<2.2 mmol/l) and a predominantly lymphocytic pleocytosis not exceeding 500 cells/mm^3)
- central nervous system imaging abnormalities suggesting TBM (basal meningitis, vasculitis, infarcts, hydrocephalus)

Treatment was in accordance with the recommendations of the South African TB Control Programme. Children with uncomplicated pulmonary TB received a six-month course of treatment consisting of an intensive phase of isoniazid, rifampicin and pyrazinamide for two months, with ethambutol added in cases of microscopy smear-positive sputum, cavitation or extensive opacification, followed by a continuation phase of isoniazid and rifampicin for four months. Patients with extra-pulmonary TB, including TBM and disseminated (miliary) TB, received isoniazid, rifampicin, pyrazinamide and ethionamide for six months. Patients with mono-resistant or multidrug-resistant TB received regimens appropriate to their respective drug susceptibility results.

At the time of the study, antiretroviral therapy was not yet available in the public sector in South Africa. All HIV-infected patients admitted to the study received trimethoprim/sulphamethoxazole as prophylaxis for *Pneumocystis jiroveci* pneumonia (PCP).

Nosocomial infection was diagnosed primarily on clinical grounds and defined as infection not present or incubating on admission to BCH and presenting 72 hours after hospitalisation in the case of bacterial infections, 96 hours in the case of viral respiratory tract infections, and 21 days in the case of varicella. Nosocomial infections acquired at the referring hospital were distinguished from those acquired at BCH; only the latter were considered for the study.

The effect of nosocomial infections was assessed in terms of the diagnostic evaluation required, the introduction of oral antibiotics at BCH (where no intravenous medication is administered), oral rehydration therapy, nasogastric feeds, need for transfer back to the referring or an appropriate hospital, and emergency treatment required before transfer to such hospitals (e.g. supplemental oxygen, intravenous antibiotics, or intensive care), prolongation of hospitalisation, or death.

Outcome definitions: Children were considered cured if repeat TB cultures were negative and/or all radiological and clinical signs had cleared. If residual changes were still evident either clinically (in the form of neurological deficits after TBM, or bony deformities after TB of bone, or clinical suggestion of bronchiectasis) or radiologically (chest radiograph not entirely clear, residual computed tomographic changes after TBM), they were classified as "cured with residual changes".

Children were considered improved if radiological and clinical improvement had occurred and they were discharged for further treatment elsewhere. Those with no radiological or clinical improvement upon discharge for treatment continuation were classified as unchanged.

Statistical analysis: Continuous variables are described as medians with lower and upper quartiles in parenthesis. Categorical variables were compared with the Chi squared test. The Wilcoxon Matched Pairs Test was used to

compare paired data. A p value of less than 0.05 was considered significant. Analysis was performed using Statistica® version 6.1 (Statsoft, Inc.)

The study was approved by the Institutional Review Board of the Faculty of Health Sciences, Stellenbosch University.

Results

During the 30 months of the study, 401 children were admitted to BCH; the HIV status of 156 (38.9%) was evaluated and 104 (66.7%) were HIV-uninfected and 52 (33.3%) were HIV-infected. Hospital records for three HIV-infected patients were lost and no suitable age-matched controls were found for two HIV-infected children. The final study population was therefore 47 age-matched pairs of HIV-infected and HIV-uninfected children. The demographic and diagnostic characteristics and the growth evaluation of the children are summarised in Table I. The major differences between the groups lie in the significantly poorer response to tuberculin testing in the HIV-infected children and their anthropometric findings. Height for age was significantly lower in HIV-infected children, as was weight for age. Weight for height, however, did not differ significantly. These anthropometric differences did not influence the TST results.

The reasons for inpatient treatment at BCH were not different between the two groups. In the HIV-infected and HIV-uninfected children, the reasons for admission were severity of disease in 27 (57.4%) and 34 (72.3%) cases, social reasons in seven (3.3%) and four (8.5%), and both severity of disease and social reasons in 13 (27.7%) and nine (19.1%) cases respectively.

Of the HIV-infected patients, there were two (4.3%) patients in Centers for Disease Control and Prevention (CDC) category N, five (10.6%) in category A, eight (17.0%) in category B, and 32 (68.1%) in category C.[2] In 25 of the patients assigned to category C, extrapulmonary or disseminated TB was the only category C defining criterion.

In 20 (42.6%) HIV-infected patients, the HIV status of the parents was documented, and in 18 they were also seropositive, implying vertical HIV transmission. The two children of sero-negative parents both had a history of sexual abuse.

The mean duration of hospitalisation for HIV-infected patients was 141 (106, 193) days, and that for HIV-uninfected patients 160 (115, 187) days (p = 0.58).

Nosocomial infections

Fifty-three of the 94 (56.4%) children experienced 131 episodes of nosocomial infection; 109 (83%) episodes occurred in 37 HIV-infected children and 22 in 16 HIV-uninfected children (p <0.001). HIV-infected children experienced a median of two (one, three) episodes of infection compared to a median of zero (zero, one) amongst HIV-uninfected children (p <0.001). Details of the infections experienced are summarised in Table II.

Twenty-five of 109 (22.9%) episodes of infection in HIV-infected children required transfer to a secondary or tertiary care hospital, but only 2/22 (9.1%) episodes affecting HIV-uninfected children (p=0.254) required transfer.

Pneumonia was the commonest nosocomial infection in both HIV-infected and HIV-uninfected children and accounted for 29 of 109 (26.6 %) episodes of infection amongst 26 HIV-infected patients. Thirteen of 26 (50.0%) of these patients required intravenous antibiotics and/or oxygen therapy and were transferred to secondary or tertiary hospitals. Three HIV-infected patients (11.5%) who developed pneumonia died: one with varicella pneumonia and two with suspected bacterial pneumonia. Four HIV-uninfected children had clinical and radiological signs of pneumonia. Two of these patients were transferred out, and the other two were managed at BCH with oral antibiotics. All four recovered.

Table I: Demographic and diagnostic features of HIV-infected and matched HIV-uninfected children

Demographic and diagnostic features	HIV-infected N = 47 (%)	HIV-uninfected N = 47 (%)	P value
Age (months)	39.9 (3.8–142.3)	40.55 (4.3–145.7)	NS
Sex (males)	24 (51.1)	34 (72.3)	NS
Culture of *M. tuberculosis*	27 (57.4)	32 (68.1)	NS
AFB seen in sputum, gastric aspirate or on histology	16 (34.0)	16 (34.0)	NS
Mantoux test (mm induration)	Median 0, range 0-26	Median 16, range 0-27	
≥15 mm	15 (31.9)	32 (68.1)	p<0,001
≥5 mm (HIV-infected)	21 (44.7)	-	
All positive Mantoux TST	21 (44.7)	32 (68.1)	p=0.022
Radiology compatible with TB	40 (85.1)	47 (100)	0.012
Close household TB contact	28 (59.6)	23 (48.9)	NS
Pulmonary TB	16 (34.0)	13 (27.7)	NS
Extra-pulmonary TB	28 (59.6)	28 (59.6)	NS
Pulmonary and extra-pulmonary TB	3 (6.4)	6 (12.8)	NS
Confirmed TB	27 (57.4)	32 (68.1)	NS
Probable TB	20 (42.6)	15 (31.9)	NS
Growth evaluation	Mean Z-score (SD)		
Height for age	-2.84 (1.60)	-2.09 (1.95)	0.018*
Weight for age	-1.89 (1.16)	-1.31 (1.40)	0.018*
Weight for height	-0.15 (1.67)	0.065 (1.59)	0.547*

NS = not significant, AFB = acid-fast bacilli, TB = tuberculosis

* = T-test for dependent samples

An outbreak of varicella (chickenpox) occurred in the period under review and 18 (19.1%) children experienced 19 episodes of varicella. This was the second commonest nosocomial infection experienced. Ten of the episodes occurred in nine HIV-infected children (including one CDC category C patient who had the illness twice, two months apart), and nine occurred in HIV-uninfected children. All 10 episodes in HIV-infected children were treated with acyclovir, as were four episodes in the HIV-uninfected children. Two children (both HIV-infected) developed varicella pneumonia, one of whom died. One of the HIV-infected children developed herpes zoster four months after varicella.

Other serious nosocomial infections that required transfer to secondary or tertiary hospitals were:

- empyaema – in an HIV-infected child
- laryngotracheobronchitis/croup in an HIV-infected child
- persistent diarrhoea in an HIV-infected child who had more than three loose stools a day for 17 days before developing signs of dehydration, despite oral rehydration therapy and nasogastric nutrition
- pyelonephritis in two HIV-infected children requiring intravenous antibiotics
- primary peritonitis in an HIV-infected child
- meningitis in two HIV-infected children, one with pneumococcal meningitis and one with aseptic meningitis

The clinical impact of nosocomial infection is summarised in Table III. Nosocomial infections led to transfers to other hospitals, special investigations or additional treatment, but in no child was hospital stay in BCH prolonged.

The outcome of the TB treatment is summarised in Table IV. Six (6.4%) children died; five of these were infected with HIV, four had category C disease and one had category A disease. The age at death ranged from four to 67 months. Of the five HIV-infected children, three died of pneumonia (one varicella pneumonia), one of septicaemia with an unknown primary focus and one child (category C disease) died unexpectedly on weekend home leave and the cause of death was unknown. A five-month-old HIV-uninfected infant died from severe miliary TB. In four of the five HIV-infected children who died, the deaths were caused by nosocomial infections.

Table II: Nosocomial infections diagnosed in HIV-infected and matched HIV-uninfected children

Diagnosis*	HIV-infected N = 47	HIV-uninfected N = 47
Lower respiratory tract infections		
Pneumonia	29	4
Respiratory tract infection with lower airways obstruction	3	1
Exacerbation of bronchiectasis	2	0
Empyaema	1	0
Laryngotracheobronchitis	1	0
Upper respiratory tract		
Pharyngitis/tonsillitis/rhinitis	21	4
Otorrhoea	3	3
Acute otitis media	5	1
Oral cavity		
Candidiasis	9	0
Herpes stomatitis	7	1
Miscellaneous		
Conjunctivitis	4	1
Skin infections	7	0
Varicella zoster (shingles)	1	0
Urinary tract infection	4	1
Central nervous system		
Bacterial meningitis	2	0
Aseptic meningitis	1	0
Gastrointestinal tract		
Acute gastroenteritis	5	0
Protracted diarrhoea	1	0
Spontaneous peritonitis	1	0
Fever without focus		
Suspected bacterial septicaemia	1	0
Suspected viraemia	1	0
Varicella (chickenpox)	10	9

* Some diagnoses occurred more than once in the same child

Table III: The impact that nosocomial infections had on the children *

Effect of nosocomial infection	HIV-infected	HIV-uninfected
Death	4	0
Transfer to secondary or tertiary hospital	25	2
Laboratory or radiological investigation at BCH	35	6
Introduction of oral antibiotics/acyclovir	71	11
Oral rehydration	8	1
Nasogastric feeds	9	1
Oxygen therapy**	13	2
Intravenous fluids or antibiotics†	18	3
Topical therapy	21	5
Prolongation of hospitalisation	0	0
No effect	0	0

* some nosocomial infections had more than one effect
† these patients were transferred out after being stabilised

Table IV: Outcome of children hospitalised for tuberculosis at Brooklyn Chest Hospital

Outcome of tuberculosis after hospitalisation	HIV-infected N = 47 (%)	HIV-uninfected N = 47 (%)	P value
Cured	10 (21.3)	21 (44.7)	0.028
Cured with residual changes	11 (23.4)	14 (29.8)	NS
Improved, transferred out to complete treatment elsewhere	17 (36.2)	11 (23.4)	NS
Condition unchanged, discharged to complete treatment elsewhere	4 (8.5)	0	NS
Died	5 (10.64%)	1 (2.13%)	NS

Discussion

TB is a major public health problem in South Africa, especially in the Western Cape, and the HIV pandemic has led to an escalation of this problem. In 1997/1998, TB prevalence in the Western Cape was 614/100 000 (all ages), while the national figure was 419/100 000.[3] The HIV prevalence at Western Cape public health antenatal clinics in October 2000 was 8.7% compared with 24.5% nationally, although 16.8% of TB cases in the Western Cape were co-infected with HIV compared to 32.8% nationally.[4]

This study examined the contribution of nosocomial infections to in-hospital morbidity and mortality in HIV-infected and HIV-uninfected children hospitalised for TB in a Western Cape TB referral hospital. The most striking finding is the significantly larger number of HIV-infected children who developed nosocomial infections (37; 78.7% vs. 16; 34.0%), and the significantly larger number of infectious episodes per HIV-infected child. The nosocomial infections in HIV-infected children were often severe, with 25 (23%) episodes resulting in transfer of the children to secondary or tertiary hospitals, compared with only two (9%) in the HIV-uninfected children. The CDC category did not influence the number of nosocomial infections.

Pneumonia was the commonest nosocomial infection in HIV-infected children and contributed significantly to morbidity and mortality in this group; 13 (50%) of the HIV-infected patients who developed pneumonia required intravenous antibiotics and/or oxygen therapy and transfer to other hospitals, and three died. Other South African studies also found pneumonia to be the commonest nosocomial infection in HIV-infected children with TB,[5] and the commonest cause of illness and mortality in HIV-infected children in general.[6]

Because diagnoses at BCH were primarily clinical and radiological, the aetiological agents in most of the cases of pneumonia are unfortunately unknown. All HIV-infected patients received trimethoprim/sulphamethoxazole as prophylaxis against PCP. The conjugate vaccine against *Haemophilus influenzae* type b became part of the national immunisation program for South African children in 1998, but children older than one year during this study period were probably not immunised against *Haemophilus influenzae* type b.

Streptococcus pneumoniae, *Haemophilus influenzae* and other gram-negative bacteria are known to be frequent causes of bacterial pneumonia in HIV-infected children.[6] Empirical therapy for children with pneumonia in hospitals in Cape Town includes cover against Gram-positive and Gram-negative organisms, with intravenous trimethoprim/sulphamethoxazole being added in the case of infants younger than one year old with positive or unknown HIV status and clinical suspicion of PCP.

Varicella was the most common nosocomial infection in HIV-uninfected children and the third most common in HIV-infected children. All HIV-infected children who developed varicella were treated with oral acyclovir. Of the nine HIV-infected children who developed varicella, four (44.4%) developed complications during the period of hospitalisation, compared with none of the HIV-uninfected children. Pneumonia occurred in two patients, one of whom died, recurrence of varicella occurred in one child and varicella zoster occurred in another. No episodes of bacterial super-infection of skin lesions were recorded in either the HIV-infected or the HIV-uninfected patients and no persistence of varicella lesions beyond one month after onset was recorded in the HIV-infected group. At least one of the episodes of varicella developed by an HIV-infected child in BCH was a recurrence, since the child was known to be varicella IgG positive at admission.

Other studies have shown very high incidences of recurrence (either recurrent varicella or of zoster) in HIV-infected children who developed varicella before the era of antiretroviral therapy. A study from Romania showed that, in the case of HIV-infected children who were followed from their primary episodes, 45% had a recurrence within 24 months.[7] Factors determining whether a recurrent episode will be varicella or zoster are not known. Recurrences may be due to reactivation, although re-infection often cannot be excluded.

The Romanian study also reported high rates of complications from varicella zoster virus (VZV) infections in HIV-infected children not receiving antiretroviral therapy. Of 38 cases of varicella, 40% developed complications, including skin super-infection, pneumonia and thrombocytopaenia, and two (5%) children died from respiratory failure. Most of these children had not received acyclovir.[7]

The overall low incidence of gastroenteritis in our study population is striking; only five children (5.3%) developed acute gastroenteritis (five out of 131 nosocomial infection episodes).

HIV-infected children not only suffered many more severe infections than their uninfected counterparts, but they also suffered many more minor illnesses, such as skin infections and upper respiratory tract infections, which may affect the children's quality of life and place a considerable extra burden on both staff and resources, as detailed in Table IV.

As is well described, a significantly lower percentage of HIV-infected children had a reactive Mantoux test compared to HIV-uninfected children. The numbers of positive cultures for *M. tuberculosis* and/or acid-fast bacilli seen in sputum, gastric washings, CSF or tissue on direct microscopy, and history of household TB contact, however, did not differ significantly between the groups.

Thirty-two (68%) of the HIV-infected children fell into CDC clinical category C. However, in 25 of these patients (78%), extra-pulmonary or disseminated TB was the only CDC category C-defining condition present. Since HIV-uninfected patients in this sample had a similar incidence of extra-pulmonary TB, it is debatable whether this *per se* denotes category C HIV disease in all these patients. The lack of supporting data on CD4 cell counts is a limitation of the study.

TB accelerates HIV disease progression,[8] and it is not surprising that other South African studies have also documented a poorer treatment-response and a higher mortality rate due to non-TB causes amongst HIV-infected children with TB.[5,9,10] In this study, the cure rate was significantly lower amongst the HIV-infected patients than the uninfected patients, but although more deaths occurred in the HIV-infected children, this difference was not statistically significant.

With the recent introduction of antiretroviral therapy in the public sector in South Africa, it may be expected that the mortality and morbidity of HIV-infected children on TB treatment will be reduced. The advent of highly active antiretroviral therapy has significantly reduced the incidence of and mortality from pneumonia and other opportunistic infections in the developed world.[6] In many children, however, it is the diag-

nosis of TB that precipitates testing for HIV-infection and several months will usually pass before antiretroviral treatment is started and becomes fully effective, leaving the children susceptible to nosocomial infections, as described in this paper.

The administration of the conjugate pneumococcal vaccine could be considered for those HIV-infected children being treated for tuberculosis. The vaccine is not as immunogenic in HIV-infected children as in their HIV-uninfected counterparts, but given their burden of pneumococcal disease it might still make a significant difference.[6]

Hospital outbreaks of varicella are common. Vaccination against VZV has been shown to be safe and immunogenic in asymptomatic or minimally symptomatic HIV-infected children (CDC clinical categories N1 and A1) and is recommended for such children.[11,12] A recent study has also shown that it may be immunogenic in HIV-infected children who have developed symptoms or have a CD4 cell percentage of more than 15% at the time of immunisation.[13] Vaccination at this stage also significantly reduces the chances of reactivation compared to allowing the child to develop chickenpox at a later stage, when immunity has further deteriorated. The varicella vaccine is contraindicated in T-cell immunocompromised children, including those on steroid treatment (≥2 mg/kg prednisone), as is given to children with TBM. Most of our HIV-infected patients were CDC category C at admission with unknown CD4 cell counts, which means that the efficacy of varicella-zoster vaccination at admission would be debatable. However, a recent study showed the vaccine to be safe and immunogenic in HIV-infected patients at any stage of disease who are on antiretroviral therapy and have a CD4 count of >700 cells/µl.[14] Passive immunisation against VZV at admission may not be effective, as it has been shown that breakthrough disease can occur due to a longer incubation period of VZV in HIV-infected children.[15] Cost is a constraint to the general immunisation of HIV-infected children against VZV at the time of HIV diagnosis.

For post-exposure prophylaxis, vaccination should be given within 72 hours of exposure, and this could prevent or alleviate illness in the majority of children.[16] For children at risk of severe disease, including HIV-infected children, other T-cell immunocompromised children and premature neonates, varicella zoster immunoglobulin (VZIG) can be given within 96 hours post exposure at a dose of 1.25 ml (one vial)/10 kg body weight (minimum dose) to a maximum of 6.25 ml (five vials).[12] Some trials in healthy children have shown acyclovir (30–40 mg/kg/day in three to four divided doses orally), given at time five to seven days post exposure for five to seven days' duration, to be effective in preventing or modifying varicella. Studies on the effectiveness of acyclovir in post-exposure prophylaxis in immunocompromised children are sparse, but it has been shown to prevent the development of disease in premature babies[17] and, as an adjunct to VZIG, in children with renal disease receiving steroids.[18] High-dose acyclovir could therefore be useful in preventing or alleviating varicella disease in HIV-infected or other immunocompromised patients, especially if the vaccine is contraindicated.[16]

This study has several limitations, of which the retrospective nature of the study is the most important. CD4 counts were not available and thus the exact CDC category of HIV disease was difficult to determine. BCH is also a non-acute hospital and few special investigations can be done, which means that the identification of the etiologic agents of nosocomial infections was not possible in most infections.

In summary, HIV-infected children admitted to hospital for the management of TB experienced considerably more morbidity and mortality due to nosocomial infection than HIV-uninfected children. The most common nosocomial infection and cause of death in HIV-infected children was pneumonia, probably due to other organisms and not due to TB. Varicella occurred very commonly during this period and caused serious illness, a high rate of complications and one death. Such outbreaks can be largely prevented. HIV-infected children also suffered significantly more minor illnesses.

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