The clinical spectrum and cost implications of hospitalised HIV-infected children at Karl Bremer Hospital, Cape Town, South Africa

^a Schoeman CS, MBChB (Stell), MFamMed (Stell) ^b Pather MK, MBChB (UCT), MFamMed (Stell), BSc Hons Medical Sciences (Stell) ^a Intercare Walmer, Port Elizabeth ^b Division of Family Medicine and Primary Care, Faculty of Health Sciences, Stellenbosch University;
Correspondence to: Dr Michael Pather, e-mail: mpather@sun.ac.za

Keywords: clinical spectrum; cost implication; HIV-infected children; district hospital

Abstract

Background: HIV infection has become a common risk factor for hospital admission and a major contributor to childhood morbidity in South Africa. There remains a paucity of data describing the cost of hospitalisation of HIV-infected children in South Africa. The aim of this study was to describe basic demographics and clinical patterns as well as cost implications of the hospitalisation of HIV-infected children in the Karl Bremer Hospital, Cape Town, South Africa.

Methods: A prospective descriptive longitudinal study of HIV-positive paediatric admissions, matched with HIV-negative controls, was conducted. Patients were matched according to age, socio-demographic area and presenting symptoms. Questionnaires were used to elicit demographic and clinical information. Worksheets were used to record any costs incurred, which were calculated at rates applicable to 2001. This was done daily during admission. Data was statistically analysed in MS Excel and MS Access. Thirty HIV-positive children were identified, of which 23 could be matched with 23 HIV-negative children. HIV-positive children had a higher admission rate (2.09 versus 0.26 previous admissions, p = 0.000) and were also younger at the time of first admission to hospital (7.52 versus 13.78 months, p = 0.005). There is a statistically significant difference in duration of hospitalisation in the HIV-positive group when compared to the control group — duration of hospitalisation being longer in the HIV-positive group (7.91 versus 4.96 days, p = 0.005). Despite being treated for the same condition, there is a statistically significant difference in the cost incurred by children in the HIV-positive group (R6 203.16) when compared to the HIV-negative group (R3 901.96); p = 0.000.

Conclusion: This study shows a clear and statistically significant difference between the HIV-positive group and HIV-negative control group of children with regard to admission rate, age at first admission, duration of hospitalisation and cost incurred during hospitalisation. HIV-infected children in the pre-HAART (highly active anti-retroviral therapy) era were hospitalised more frequently and for longer periods than their HIV-uninfected counterparts. These findings seem to suggest that the cost of hospitalising HIV-positive children is significantly more than HIV-negative controls, which will increase the financial burden on already restricted health resources.

SA Fam Pract 2009;51(1):46-52

Introduction

In 1983, Rubinstein et al from the Albert Einstein College of Medicine in the Bronx, New York, first described a new syndrome of acquired immunodeficiency in seven children of sexually promiscuous and/or drug-addicted mothers. Since then HIV/AIDS has become a disease entity of pandemic proportions internationally.

In South Africa, 2002 figures put the prevalence of HIV infection at about 14% with over 6 million infections.² Again in 2004, the prevalence of HIV infection was estimated between 5.7 and 6.7 million infections.³ In the 2005 South African national household survey on *HIV Prevalence, Incidence, Behaviour and Communication,* both prevalence and incidence were measured.⁴ Therefore, the figures not only reflected the proportion of people in the population living with HIV at any given point in time (prevalence), but also the number of new infections that occur in non-infected individuals during a specific period of time, e.g. the annual incidence during one year. Incidence analysis confirms recent findings by Gray et al⁵ in Uganda that the highest incidence of new infections occurs during pregnancy. In the absence of mother-to-child transmission

(MTCT) prevention programmes (as is currently often the case in South Africa) this translates to HIV-infected newborns. Using a mathematical model, Ecker (San Francisco, 1996) found that routine HIV testing during pregnancy was cost-effective in populations where the prevalence of HIV exceeded 9 per 1 000.6 This is indeed the case in South Africa, and routine screening for HIV is offered at most antenatal clinics in South Africa.4 Immergluck et al found that universal screening is cost-saving no matter how low the HIV prevalence in a community.7

The 2005 South African national household survey on *HIV Prevalence, Incidence, Behaviour and Communication*⁴ estimated the national prevalence in the population of people two years and older at 10.8%, with a higher prevalence in women (13.3%) than men (8.2%). HIV prevalence increases with age from 3.3% in children of 2 to 14 years to 16.2% in adults of 15 to 49 years. The HIV prevalence in children is high, with 4.9% of boys and 5.3% of girls in the 2 to 4-year age group and 4.2% of boys and 4.8% of girls in the 4 to 9-year age group being HIV positive. *The Children's Report South African National HIV Survey* by Brookes, Shisana and Richter based on the 2002 household survey established



children to be at risk for contracting HIV through a number of sources other than MTCT during pregnancy and breast-feeding.⁴ These included sexual abuse, and the lower levels of care and protection afforded within the home, school and in communities equated to increased opportunities for offenders.

Paediatric HIV infection has become a common risk factor for hospital admission and a major contributor to childhood morbidity in South Africa. As early as August 1994 the US Public Health Service recommended zidovudine to reduce perinatal HIV transmission and, in July 1995, the use of routine HIV counselling and voluntary HIV testing. In industrialised countries, transmission rates in untreated non-breast-feeding populations range from 14% to 32% versus 25% to 48% among breast-feeding populations in resource-poor settings. Figures (reflecting midwife obstetric unit (MOU) antenatal statistics) released by the National Department of Health in 2005 indicate that 29.5 out of every 100 women attending antenatal clinics in South Africa are HIV infected. MTCT rates are around 30%, where (in the absence of breast-feeding) about 30% of MTCT occurs in utero and 70% occurs during labour and delivery.

In a study done in 2003, South African protocols recommended that infants be followed up for one year on co-trimoxazole prophylaxis from six weeks of age and then tested for HIV using Enzyme Linked Immunosorbent Assay (ELISA) testing at 15 months of age. The reality of this practice was illustrated by experience in Johannesburg, South Africa, where 60% of infants were lost to follow-up by six weeks and 85% by 12 months of age during a 24-month period. 12,13 Sherman et al estimated that a single HIV DNA polymerase chain reaction (PCR) test at six weeks of age will be more cost-effective to society than an HIV ELISA test at 12 months of age. 14

While neonatal HIV is being reduced to a transmission rate of approximately 1–2% by anti-retrovirals given to prevent MTCT in developed countries, ¹⁰ developing countries are still not offering these interventions routinely. The main reason for this is the perceived high cost of transmission prevention programmes rather than the lack of evidence of effectiveness. The AIDS Clinical Trial Group (ACTG) 076 study showed that zidovudine was associated with a reduction of perinatal transmission from 25% to 8%. ^{15,16,17} Since then, numerous observational studies have proven the efficacy and safety of MTCT regimens. ^{18–24} In 1999 a pilot study initiated in two Maternity Outpatients Units (MOUs) in Khayelitsha, Cape Town, South Africa, showed that voluntary counselling and testing was acceptable, and the use of short-course antenatal and intrapartum antiretroviral therapy (ART) was feasible in the South African setting. ²⁵ Dabis et al showed that short-course zidovudine to reduce vertical transmission to breastfed babies was well tolerated and acceptable. ²⁶

Breast-feeding has been a contentious issue, as confusion has often surrounded the risk of HIV transmission. An early meta-analysis estimated a 14% additional risk of postnatal infection for women with prevalent infection, and a 29% risk for women with incident infections while breast-feeding.²⁷ reflecting the increased infectiousness of primary HIV infection.²⁸ In more recent data by Miotti et al the reported cumulative transmission rate from breast-feeding in Malawi was estimated to be 3.5% at six months, 7% at 12 months and 10.3% at 24 months.²⁹ Results from a trial in Nairobi, Kenya, in which children born to HIV-infected mothers were randomised to breast-feeding or replacement feeding, show that more than 40% of infant HIV infections were acquired through breast-feeding, and that most infections were acquired in the first few months of life.³⁰ Guidelines on infant feeding and HIV have been published,

advocating assisting mothers in choosing how to feed their infants by receiving complete and accurate information. 31,32 Uninterrupted supply of safely prepared, nutritionally adequate breast milk substitutes would likely result in the lowest risk of disease and death. In industrialised countries these guidelines can safely and easily be implemented. In a developing country like South Africa, artificial feeding in unhygienic circumstances may be associated with increased risk of morbidity and mortality from infectious diseases and malnutrition.

Estimates of the costs involved in treating patients are scant. Costefficacy analyses have mainly concentrated on the overwhelming benefits of introducing an effective programme to reduce MTCT. The direct lifetime medical and social care costs of childhood HIV infection in Britain was estimated at £178 300 using 1995/6 prices.33 Wilkinson et al have calculated that a national programme preventing only 37% of expected paediatric infections would be cost-effective.34 During the second week of March 1999, a census study was conducted in the Cape Province Metropole with the aim of collecting data on all known HIV-positive paediatric in-patients and to establish cost. 35 They calculated that the cost per infant protected against vertical HIV transmission was between R8 326 and R10 806. The estimated lifetime cost of an infant diagnosed at 13 months (the median age for transmission in this study) surviving for 32 months from the time of diagnosis³⁶ would be R19 712. Leroy et al showed the cost of caring for an HIV-infected child in Abidjan to be 1.7 times more than caring for an HIV-exposed, uninfected child.37 Cotton et al, in a retrospective descriptive five-year analysis of 91 patients (with 189 admissions) admitted to a tertiary hospital, estimated that R1.4 million had been spent on these 91 children. They calculated that the percentage of hospitalisation days in HIV-infected children increased 3.4-fold during the study period.38 Soderland et al, using a Markov chain model simulation in a population of working class urban South Africans, showed that low-cost anti-retroviral regimens were almost as effective as high-cost regimens.¹⁶ Cost-effectiveness was improved when formula feeding interventions were added. However, with or without formula feeding, low-cost anti-retroviral interventions were likely to save lives and money.39

Cost estimates for paediatric HIV hospital services are just estimates. Beck et al showed that reliance on generic hospital prices to derive cost estimates for paediatric HIV services produced considerable underestimates of the cost of service provision compared to data derived through a research-based service-specific costing exercise. Differences increased with more intense use of services. The deficit ranged from ± 432 per patient-year for HIV-negative children to ± 574 per patient-year for asymptomatic HIV-infected children to as much as ± 7 418 per patient-year for children with AIDS.

To date no prospective study describing the cost of the hospitalisation of HIV-infected children in South Africa has been done. This study therefore aimed to describe basic demographics and clinical patterns as well as cost implications of the hospitalisation of HIV-infected children at the Karl Bremer Hospital, Cape Town, South Africa.

Methods

Patient and clinical data

A prospective descriptive longitudinal study with controlled matching of study subjects was conducted. All children under the age of 12 admitted to a paediatric ward in a district hospital in the Cape Metropole (Karl Bremer Hospital, Bellville) were screened for inclusion in the study. The



sample obtained was 53 children (23 HIV-infected subjects were matched with 23 control subjects; 7 HIV-infected subjects could not be matched) (Table I). The duration of the study was six months, from September 2000 to February 2001, over which period a convenient sample of patients was obtained as they presented to the paediatric ward over the periods of observation. The study setting was the general paediatric unit in the hospital where patients were seen following referral from lower levels of care (primary care community health centres and general practice) as well as from the paediatric outpatient department.

All children over the age of 15 months who tested sero-positive for HIV and children under the age of 15 months where evidence of HIV was detected by either HIV-1 DNA PCR or p24 antigenaemia were included in the study. Children with the diagnosis of probable HIV were also included. In Karl Bremer Hospital the diagnosis of probable HIV infection was made when a child under the age of 15 months presented with clinical symptoms suggestive of HIV or AIDS and who tested sero-positive. Due to financial and logistical constraints at the time, DNA PCR could not be done on these patients to confirm HIV infection. Testing was conducted when there was a high index of suspicion. Children who had proven HIV infection (in previous admissions) were also included in the study. Data was collected for inpatients only.

Each study subject was matched with another inpatient (concurrent hospitalisation) of similar age and socio-demographic area and according to similar presenting symptoms (Table II). The control subject must have tested HIV negative. Informed consent was obtained for HIV testing from parents or guardians. If no suitable HIV-negative control could be found, the study subject was disregarded in the statistical analysis. Reasons for non-inclusion are clearly stated. Elimination of bias in matching was attempted by assigning a control in a blinded fashion when more than one possible match was available. On two occasions where similar subjects were admitted, the control was randomly selected.

A structured questionnaire (Questionnaire 1) was used to elicit sociodemographic and clinical information regarding the study subject. In order to calculate actual cost, information was gained on a daily basis using a second structured questionnaire (Questionnaire 2). The questionnaires were available in English and Afrikaans according to the preference of the interviewee. Consent forms and information sheets were available in Afrikaans, English and Xhosa. Where applicable, an interpreter was used to assist with communication.

Information was gathered throughout the inpatient stay of the patient, but became anonymous once the patient was discharged or transferred. Confidentiality and anonymity were therefore maintained once the patient was discharged or transferred. Therefore, Questionnaire 1 and Questionnaire 2 for each day as an inpatient were kept in the hospital folder of the study subject until discharge, at which time the completed data was removed from the patient records. The use of disposables was marked on a specially designed worksheet. The researcher and one other senior medical officer working in the Department of Paediatrics gathered information. The medical officer was trained in the exact nature of the study, its aims and objectives and was familiar with the questionnaires and their contents. Nursing staff were informed of the study and were requested to document any disposables that they had used on the worksheet. The persons collecting such data were not directly involved with the treatment protocols and management of the patients.

Laboratory investigations

Sera were screened for HIV1/HIV2 antibodies using the rapid test Determine (Abbott). All positive tests, as well as all sera of children under the age of 15 months, were sent to Groote Schuur Hospital for ELISA. Due to financial constraints, DNA PCR was not done routinely.

Cost involved and statistical analysis

The costs involved were obtained from the various departments in the hospital. Bottom-up costing was used and was obtained by capturing direct treatment cost, such as cost of medication, laboratory and radiological investigation. Medication cost was obtained from the pharmaceutical depot (Head Pharmacist) and was listed as accurately as possible. Box sizes were broken down into unit sizes, as well as tablet prices where suspensions had to be made up from tablets when suspensions were unavailable. The price of oxygen was obtained from records kept of prices from suppliers – price per litre of oxygen was calculated from the price per kilogram of oxygen. The financial department of Karl Bremer Hospital supplied the fee per patient per 12 hours of 2000/1. This fee did not include any disposables, tests or medication, but reflected the bed and meals only. The radiology department and laboratory financial staff supplied prices for the radiological and laboratory tests respectively. Disposable prices were obtained from stock list prices, and were broken down into unit prices where necessary.

Data regarding each patient was analysed using Microsoft Access as well as Microsoft Excel worksheets. The Department of Statistics at the University of Port Elizabeth assisted in analysing the data. Where relevant, the chi-square test was used to look at differences in proportions between the two groups.

Ethics approval

This research has the approval of the Ethics Committee of Stellenbosch University. Guidelines by the Medical Research Council on research in children were adhered to.41

Results

A total of 30 HIV-positive inpatient children were identified. Twenty-three children were matched with control subjects of similar age and sociodemographic area according to presenting symptoms.

Unmatched HIV-positive children

Seven children could not be matched. These children were mainly older children (mean age 31.14 months). Important socio-demographic and basic descriptive information regarding admission and outcomes of the seven HIV positive unmatched children is provided in Table I. In addition the presenting symptoms in this group were coughing (100%), fever (57.1%), vomiting (28.6%), abdominal pain (14.3%), diarrhoea (14.3%), skin rashes (14.3%) and chest pain (14.3%). Diagnoses were pneumonia (71.4%), oral candidiasis (71.4%), gastro-enteritis (14.3%), anaemia (14.3%), lung abscess (14.3%), tinea corporis (14.3%), foetal alcohol syndrome (14.3%) and nappy rash (14.3%).

Matching

Forty-six children (23 HIV-positive and 23 matched HIV-negative children) were included in the study for analysis. Matching was done according to age, socio-economic background and presenting symptoms (see Table II).

Table I: Demographics, admissions and outcomes of seven HIV-positive unmatched children

Number of patients	7
Mean age	31.14 months (1–75*)
Mean number of previous admissions	2.83 (0-9*)
Mean age at first admission	17.83 months (2–53*)
Male: female	6:1
Patients from squatter communities	4 (57.1%)
Patients living in flat/house	3 (42.9%)
Mean duration of admission (days)	5.83 (3–14)
Transfer to chronic care facility	1
Discharged to home	6

*upper and lower limits given = range

Table II: Baseline characteristics and presenting symptoms of patients in the HIV positive and matched control groups.

	HIV positive	Controls	
Mean age in months (SD*)	14.52 (18.22)	14.35 (17.92)	
Gender (M:F)	13:10	14:9	
Ro	esidence		
Informal settlement	9 (39%)	12 (52%)	
Farm	1 (4%)	0 (0%)	
Flat	2 (9%)	0 (0%)	
House	8 (35%)	9 (39%)	
Wendy house	3 (13%)	2 (9%)	
Presenting complaint			
Cough	11 (48%)	13 (57%)	
Diarrhoea	10 (43%)	10 (43%)	
Nausea/vomiting	9 (39%)	9 (39%)	
Fever	7 (30%)	7 (30%)	
Dyspnoea	6 (26%)	6 (26%)	
Feeding difficulties	2 (9%)	2 (9%)	
Oral thrush	1 (4%)	0 (0%)	
Malnutrition	1 (4%)	1 (4%)	
Mouth ulcers	1 (4%)	1 (4%)	
Epistaxis	1 (4%)	0 (0%)	
Skin rash	1 (4%)	0 (0%)	
Abnormal weight loss	1 (4%)	0. (0%)	
Abdominal pain	0 (0%)	1 (4%)	

*SD = standard deviation

Clinical signs and diagnoses

The majority of children presented with symptoms of respiratory or diarrhoeal disease. Diagnoses were most often made on clinical grounds, with very little microbiological investigations to isolate organisms (Table III). Some patients included in the study had multiple complaints, which explains the different percentages. Although there was a statistically significant difference in the presenting clinical signs, differences in diagnoses were not statistically significant (see Table III).

Table III: Clinical signs and diagnoses in HIV-positive and control group

	HIV positive	Controls
Clinical signs		
Lymphadenopathy	20 (87%)	9 (39%)
Hepatomegaly	15 (65%)	8 (35%)
Candidiasis	11 (48%)	3 (13%)
Splenomegaly	9 (39%)	3 (13%)
Seborrhoeic dermatitis	4 (17%)	0
Dehydration	5 (22%)	6 (26%)
Respiratory distress	4 (17%)	9 (39%)
Chronic suppurative otitis media	2 (9%)	1 (4%)
Dental carries (pulpitis)	2 (9%)	0
Conjunctivitis	1 (4%)	0
Sinusitis	1 (4%)	0
Mouth ulcers	1 (4%)	0
Abdominal mass	1 (4%)	0
Ecchymosis	1 (4%)	0
Abdominal distention	0	1 (4%)
Skin rash	0	1 (4%)
Localised oedema (legs)	0	1 (4%)
Diagnosis		
Gastro-enteritis/diarrhoea	10 (43%)	9 (39%)
Malnutrition	8 (34%)	7 (30%)
Marasmus	1 (4%)	0
Pneumonia	9 (39%)	8 (34%)
Oral thrush	5 (22%)	2 (9%)
Pulmonary tuberculosis confirmed	4 (17%)	1 (4%)
Nappy rash	4 (17%)	0
Iron deficiency anaemia	3 (13%)	0
PCP pneumonia	2 (9%)	0
Chronic suppurative otitis media	2 (9%)	1 (4%)
Abdominal tuberculosis	1 (4%)	1 (4%)
Acute meningococcaemia	1 (4%)	0
Congenital syphilis	0	2 (9%)
Candidiasis	1 (4%)	0
Scabies	1 (4%)	0
Conjunctivitis	1 (4%)	0
Tonsillitis	1 (4%)	0
Croup	0	1 (4%)
Acute bronchiolitis/bronchitis	1 (4%)	3 (13%)
Paralytic ileus	0	1 (4%)
•		, ,

Weight

Weight distribution between the HIV-positive and HIV-negative (control) group clearly shows that the HIV-positive group had a statistically and clinically significant lower weight. Both the p-value and Cohen's d are significant. Given that children were matched for age and the mean age is almost equal, this is significant (see Table IV).



Table IV: Weight differences, age at first admission and duration of hospitalisation in HIV-positive and HIV-negative controls

Weight (kg)		HIV positive	HIV-negative controls
Quartile 1	< 4.825	35%	17%
Quartile 2 and 3		52%	43%
Quartile 4	> 8.1175	13%	39%
Mean		6.06	7.85
Differences based on sample means		Mean	-1.79
		t-stat	-3.99
		p-value	0.000
		Cohen's d	-0.59
Age at first admis	ssion (months)	HIV positive	HIV-negative controls
Quartile 1	< 2	43%	13%
Quartile 2 and 3		35%	57%
Quartile 4	> 11.75	22%	30%
Mean		7.52	13.78
Differences based on sample means		Mean	-6.26
		t-stat	-2.99
		p-value	0.005
		Cohen's d	-0.44
Duration of hospi	talisation (days)	HIV positive	HIV-negative controls
Quartile 1	< 4	17%	30%
Quartile 2 and 3		43%	61%
Quartile 4	>7	19%	9%
Mean		7.91	4.96
Differences based on sample means		Mean	2.96
		t-stat	4.68
		p-value	0.000
		Cohen's d	0.69

Admissions

HIV-positive children clearly had a higher previous admission rate and were also younger at the time of first admission. Again the p-value showed a statistically significant difference between the HIV-positive and the HIV-negative groups. When groups were analysed based on sample frequencies the Chi²-test and Cramer's V were significant in admission rate and age at first admission. See Table V for a comparison in previous admission rate and cost of hospitalisation between the two groups.

Outcome

In the HIV-positive group, 19 children (83%) were discharged, 1 (4%) was transferred to a tertiary hospital (for an abdominal mass suggestive of abdominal tuberculosis), 1 (4%) was transferred to a TB hospital and 2 (9%) died.

In the control group, 22 children (96%) were discharged and 1 (4%) was transferred to a tertiary hospital for bronchoscopy and the management of probable pulmonary tuberculosis.

Table V: Admission rates and cost of hospitalisation of HIV-positive and HIV-negative controls

Previous admission rate	HIV positive	HIV-negative controls
• Mean	2.09	0.26
Differences based on sample means	Mean	1.83
	t-stat	7.84
	p-value	0.000
	Cohen's d	1.16
Cost of hospitalisation in HIV-positive and HIV-negative control group	HIV positive	HIV-negative controls
Mean cost in rand (SD*)	6 203.16 (4 598.08)	3 901.96 (2 373.07)
Mean cost per day in rand	784.22	786.69
Differences based on sample means	Mean (rand)	2 301.17
	t-stat	4.48
	p-value	0.000
	Cohen's d	0.66

^{*}SD = standard deviation

Duration of hospitalisation

The duration of hospitalisation was significantly longer in the HIV-positive group when compared to the HIV-negative control group. This was both statistically and clinically significant when analysed for differences in mean and sample frequencies (see Table V).

Cost of hospitalisation

HIV-positive children were more expensive to hospitalise despite being treated according to the same protocols as HIV-negative children. This difference was statistically significant. This meant not having any access to medication such as anti-retrovirals or additional micro bacteriological testing. Cost drivers were mainly due to the fact that HIV-infected children required longer hospitalisation periods (see Table V).

Discussion

Clinical indications for admission in this study are comparable with earlier South African studies. 35,33,42,43 The main indications for admission were gastroenteritis, pneumonia, gastroenteritis and pneumonia, and tuberculosis.

The most important finding of this study is the difference in the cost of hospitalisation of HIV-positive and HIV-negative children. The average cost of hospitalisation for an HIV-positive child is R784.22 per day, as opposed to R786.69 per day for an HIV-negative child. However, the total cost per hospital admission was R6 203.16 for HIV-positive children and R3 901.96 for HIV-negative children. (The average cost for each HIV-positive inpatient in a South African tertiary hospital in 2004 was estimated as R18 765.76 in a retrospective study. ⁴³) HIV-positive children were not treated with any special protocols, extra microbacteriological testing or antiretroviral medication at the time of this study. Therefore the management does not cost significantly more than that of HIV-negative children per day. However, HIV patients required admissions for longer periods than HIV-negative controls — often due to the dependence on



oxygen and the presence of multiple diagnoses. This results in a higher total cost. HIV-negative children would receive the same investigations and similar medication, but seem to respond much more rapidly to treatment offered. Similar costs for investigations and medication would then be concentrated in shorter hospital stays, resulting in slightly more expensive per-day cost.

The main cost driver was the length of hospitalisation — based on the day fee (R372.00 per 12 hours), which is by far the most expensive daily cost involved. Cotton et al showed a 3.4-fold increase in days spent in hospital in HIV-positive children versus HIV-negative children in a study conducted over five years. ⁴⁰ This study showed only a 1.6-fold increase. However, this was enough to show the statistically significant difference in cost between these two groups. The difference in comparative stay could be explained by the much shorter study period, as well as the exclusion of the mainly older (and often sicker) HIV-infected children who could not be matched. Cotton et al also conducted their study in a tertiary hospital where more aggressive or resistant pathology is expected.

Cost calculated only dealt with the hospitalisation of these children (direct cost) and no attempt was made to calculate intangible or indirect costs. These would include, among others, the cost in primary care clinics, transport to medical facilities, tertiary hospitals and the financial burden on the parents of HIV-positive children. The burden on parents would include travel costs and reduced family income due to absence from work

Meyer et al concluded that paediatric HIV infection accounts for almost one-third of childhood hospital admissions in a tertiary hospital in Soweto, South Africa, in 2000.⁴² Yeung et al found that HIV infection accounted for 26% of paediatric hospital admissions in a rural hospital in South Africa.⁴⁴ Both concluded that paediatric HIV disease poses a substantial burden and challenge for the health service and its resources.

In a retrospective study conducted at the Red Cross Children's Hospital, a tertiary hospital in the Cape Town Metropole, South Africa, found that 4% of their admissions were HIV positive. 43 The length of stay was nine days for HIV-positive children, compared to four days for HIV-negative children. However, HIV-positive children consumed 12%, 61% and 9% of the total budgets allocated for antibiotics, antifungals and analgesics respectively. This reflected 9% of the total budget for medication. HIV-positive patients, who formed 4% of the total admissions, consumed 26% of the total budget for direct treatment costs! This clearly showed that the current admission policies regarding HIV-positive patients to the Red Cross Children's Hospital was unsustainable in the face of this increasing paediatric epidemic, non-availability of ART and MTCT programmes.

In a retrospective study, Havens et al used patient records to calculate the mean lifetime charges for hospital-based care of children living with HIV in Wisconsin, Milwaukee, USA. They concluded that the care of children with HIV is expensive, and that the information should be used for analysing the economic impact of universal counselling, HIV testing and transmission preventative programmes in pregnant women.⁴⁵

If one looks at national prevention programmes, it has been estimated that a small component (0.94%) of the national health budget would be required to prevent 37% of paediatric HIV infections. This would amount to approximately R155.9 million in 1997 rand costs.³⁴

Despite HIV being a very expensive treatable condition in high-income countries, cost-effectiveness analyses show that anti-retroviral therapeutic regimens offer good value for resources spent on many other

accepted healthcare interventions.⁴⁶ Interestingly, a study reviewing multistate HIV-related health service utilisation in the USA concluded that inpatient and outpatient costs for patients on HAART were not significantly lower than for patients not on HAART.⁴⁷ Hospitalisation rates remained relatively high among minority or disadvantaged groups, suggesting disparities in care. Social circumstances were not measured.⁴⁷

In low-income countries such as South Africa, barriers to treatment are partly social and logistic, but overwhelmingly capacity and cost related. On the basis of limited data available, Creese et al argued that HIV-prevention programmes are likely to be more cost-effective than HAART therapy alone.⁴⁸ This was reiterated by a sub-Saharan study by Marseille et al.⁴⁹ At \$10 000 per patient year, HAART was clearly unaffordable.⁴⁶ Recent international efforts to expand access to ART in low-income countries such as South Africa have resulted in an increased number of people seeking HIV testing and care. This expanding awareness provides opportunities for directing novel prevention strategies to those at risk of transmitting the disease.⁵⁰

Evaluating interventions in terms of impact and cost-effectiveness will form an important role in aiding health planners and policy makers to allocate resources. The cost of strengthening the infrastructure to levels capable of providing interventions also needs to be assessed.⁵¹ Factors such as fairness and justice, benefits and costs outside the health sector, acceptability, affordability and feasibility also need to be considered.³⁶ In South Africa there remains a need to initiate, sustain and support programmes that are cost-effective, acceptable and feasible.

Conclusion

This study shows a clear and statistically significant difference between the HIV-positive group and the HIV-negative control group of children with regard to admission rate, age at first admission, duration of hospitalisation and cost incurred during hospitalisation. These findings seem to suggest that HIV-positive children in the pre-HAART era were hospitalised more frequently and for longer periods than their HIV-uninfected counterparts, and this may add to the financial burden on already restricted health resources in South Africa.

Declaration

We declare that we have no financial or personal relationship(s) which may have inappropriately influenced us in writing this paper.

References

- Rubinstein A, Sicklick M, Gupta A, et al. Acquired immunodeficiency with reversed T4/T8 ratios in infants born to promiscuous and drug-addicted mothers. JAMA 1983;249(17):2350–6.
- HIV/AIDS profile in the province of South Africa, Indicators for 2002. Available from: www.mrc.ac.za/bod/ AIDSindicators2002.pdf (Accessed 06/2006).
- Department of Health, 2005. National HIV and Syphilis Antenatal Sero-prevalence Survey in South Africa 2004. Available at: www.doh.gov.za/docs/reports/2004/hiv-syphilis.pdf (Accessed 06/2006).
- Human Sciences Research Council. South African National Prevalence, HIV Incidence, Behaviour and Communication Survey 2005.
 Gray R, Wawer M, Brookmeyer R, et al. Probability of HIV-1 transmission per coital act in monogamous,
- heterosexual, HIV-1 discordant couples in Rakai, Úganda. Lancet 2001;357:1149-53.

 6. Ecker JL. The cost-effectiveness of HIV screening in pregnancy. Am J Obstet Gynecol Feb
- 1996;174(2):716–21.

 7. Immergluck LC, Cull WL, Schwartz A, et al. Cost-effectiveness of universal compared with voluntary
- screening for HIV among pregnant women in Chicago. Pediatrics April 2000;105(4):E54.

 8. Centers for Disease Control and Prevention. Recommendations of the US Public Health Service Task Force on the use of zidovudine to reduce perinatal transmission of HIV. MMWR Morb Mortal Wkly Rep 1994;43(RR-11):1–20.
- Centers for Disease Control and Prevention. US Public Health Service recommendations for HIV counselling and voluntary testing for pregnant women. MMWR Morb Mortal Wkly Rep 1995; 44(RR-7):
- De Cock KM, Fowler MG, Mercier E, et al. Prevention of mother-to-child HIV transmission in resource-poor countries. JAMA March 2000;283(9):1175–82.
- 11. Mock PA, Schaffer N, Bhadrakom C, et al. Maternal viral load and timing of mother-to-child HIV

- - transmission, Bangkok, Thailand. AIDS 1999;13:407-14.
- 12. Jones SA, Sherman GG, Varga CA. Exploring socio-economic conditions and poor follow-up rates of HIVexposed infants in Johannesburg, South Africa. AIDS Care 2005;17(4):466-70.
- 13. Sherman GG, Jones SA, Coovadia AH, et al. PMTCT from research to reality results from a routine service. S Afr Med J 2004;94:289-92.
- 14. Sherman GG, Matseula TC, Jones SA. Is early HIV testing of infants in poorly resourced prevention of mother to child transmission programmes unaffordable? Trop Med Int Health 2005;10:1108-13
- Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of HIV-1 with zidovudine treatment. N Engl J Med 1994;331:1173–80.
- 16. Soderland N, Zwi K, Kinghorn A, et al. Prevention of vertical transmission of HIV: analysis of cost effectiveness of options available in South Africa. BMJ 1999;18:1650-6.
- 17. Wilfert CM. Prevention of perinatal transmission of human immunodeficiency virus: a progress report 2 years after completion of AIDS Clinical Trial Group trial 076. Clinical Infectious Diseases 1996:23:438-41.
- 18. Cooper ER, Nugent RP, Diaz C, et al. After AIDS Clinical Trial 076: the changing patterns of zidovudine use during pregnancy, and the subsequent reduction in vertical transmission of HIV in a cohort of infected women and their infants. J Infect Dis 1996;174:1207-11.
- Culnane SL, Fowler M, Lee SS, et al for the Pediatric AIDS Clinical Trials Group Proto. Lack of long-term
 effects of in utero exposure to Zidovudine among uninfected children born to HIV-infected women. JAMA 1999;281:151-7.
- Fiscus SA, Adimora AA, Schoenbak VJ, et al. Perinatal HIV infection and the effect of zidovudine therapy on transmission in rural and urban countries. JAMA 1996;275:1483

 –8.
- 21. Lallemant M, Jourdain G, Le Coeur S, et al. The perinatal HIV prevention trial (Thailand) Single-dose perinatal Niverapine plus standard Zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand, N Eng J Med 2004:351:217-42.
- 22. Mofenson LM. McIntyre JA. Advances and research directions in the prevention of mother to child HIV-1 transmission. Lancet 2000;355:2237-44.
- Scott GB. Perinatal exposure to antiretroviral agents: risks and benefits. Am J Neuroradiol 2005;26:689–92.
- 24. Simonds R.J. Steketee R. Nesheim S. et al. Impact of zidovudine use on risk and risk factors for perinatal transmission of HIV: Perinatal HIV Collaborative Transmission Studies. AIDS 1998;12:301–8
- 25. Abdullah MF, Young T, Bitalo L, et al. Public health lessons from a pilot programme to reduce Mothe child transmission of HIV-1 in Khavelitsha, S Afr Med J Jul 2001:91(7):579-82.
- 26. Dabis F, Msellati P, Meda N, et al. Six-month efficacy, tolerance, and acceptability of a short regimen of oral zidovudine to reduce vertical transmission of HIV in breastfed children in Cote d'Ivoire and Burkina Faso: a double-blind placebo-controlled multicentre trial. Lancet 1999;353:786-92
- 27. Dunn DT, Newell ML, Ades AE, et al. Risk of HIV type 1 transmission through breastfeeding. Lancet 1992;340:585-8
- 28. Van de Perre P, Simonon A, Msellati P, et al. Postnatal transmission of HIV type 1 from mother to infant: a prospective cohort study in Kigali, Rwanda, N Eng J M 1991;325;593-8.
- 29. Miotti PG, Taha TE, Kumwenda NI, et al. HIV transmission through breastfeeding: a study in Malawi. JAMA
- 30. Nduati R, John G, Mbori-Ngacha D, et al. Effect of breastfeeding and formula feeding on transmission of HIV-1: a randomised clinical trial. JAMA 2000;283:1167-74.
- 31. Joint United Nations Programme on HIV/AIDS (UNAIDS). HIV and infant feeding: a policy statement developed collaboratively by UNAIDS, WHO and UNICEF. Geneva, Switzerland, UNAIDS May 1997; No.
- 32. Joint United Nations Programme on HIV/AIDS (UNAIDS). Prevention of HIV infection in infants and young children: strategic options. Geneva, Switzerland. UNAIDS April 1999.
- 33. Postma MJ, Beck EJ, Mandalia S. Universal HIV screening of pregnant women in England: cost effectiveness analysis. BMJ 1999;318:1656-60.
- 34. Wilkinson D, Floyd K, Gilks CF. National and provincial estimated costs and cost effectiveness of a programme to reduce mother-to-child HIV transmission in South Africa. S Afr Med J 2000 Aug;90(8):794-8.
- 35. Roux P, Henley L, Cotton M, et al. Burden and cost of inpatient care for HIV-positive paediatric patients status in the Cape Town Metropole during the second week of March 1999. S Afr Med J 2000;90(10):1008-11.
- 36. Hussey GD, Reijnhart RM, Sebens AM, et al. Survival of children in Cape Town known to be vertically infected with HIV-1. S Afr Med J 1998;88:554–8.
- 37. Leroy V, Giraudon I, Viho, I et al. Medical care costs of children born to HIV-infected mothers in Abidjan, Cote Ivoire 1996-1997. AIDS 2000;14:1076-8.
- 38. Cotton M, Schaaf HS, Willemsen E, et al. The burden of mother-to-child transmission of HIV-1 disease in a low prevalence region a five year study of hospitalised children. SA J Epid and Infect 1998;13(2):46-9.
- Coutsoudis A, Pillay K, Spooner E, et al. Influence of infant-feeding patterns on early mother-to-child transmission of HIV-1 in Durban, South Africa: a prospective cohort study. Lancet 1999;354:471–6.
- 40. Beck EJ, Beecham J, Mandalia S, et al. What is the cost of getting it wrong? J Public Health Med Sept
- 41. A guide to Ethical Considerations in Medical Research. South African Medical Research Council. December 1979, 28,
- 42. Meyer TM, Pettifor JM, Gray GE, et al. Paediatric admissions with human immunodeficiency virus infection at a regional hospital in Soweto, South Africa. J Trop Pediatr. 2000 Aug;46(4):224-30.
- 43. Yengopal V, Naidoo S. Cost of inpatient care for HIV positive patients at Red Cross Children's Hospital, Cape Town. SA J of HIV Med Nov 2004;17:32–40.
- 44. Yeung S, Wilkinson D, Escott S, et al. Paediatric HIV infection in a rural South African District hospital. J Trop Paediatr 2000 April;46(2):107-10.
- 45. Havens PL, Cuene BE, Holtgrave DR. Lifetime cost of care for children with HIV infection. Pediatr Infect Dis J Jun 1997;16(6):607-10.
- 46. Yazdanpanah Y. Costs associated with combination antiretroviral therapy in HIV-infected patients. J Antimicr Chemo 2004;53(4):558-61.
- 47. Fleishman JA, Gebo KA, Reilly ED, et al. Hospital and outpatient health service utilization among HIVinfected adults in care 2000-2002, Med Care Sept 2005;43(9 Suppl); III40-52.
- 48. Creese A, Floyd K, Alban A, et al. Cost-effectiveness of HIV/AIDS interventions in Africa: a systematic review of the evidence. Lancet 2002;359:1635–43.
- 49. Marseille E, Hofmann PB, Kahn JG. HIV prevention before HAART in sub-Saharan Africa. Lancet 2002:359:1851-6.
- 50. McClelland RS. Baeten JM. Reducing HIV-1 transmission through prevention strategies targeting HIV-1 seropositive individuals. J of Antimicr Chemo 2006;57(2):163–6.
- 51. Scotland GS, Van Teijlingen ER, Van der Pol M, et al. A review of studies assessing the costs and insequences of interventions to reduce mother-to-child HIV transmission in sub-Saharan Africa, AIDS May 2003;17(7):1045-52.