



POSITIVE EFFECT OF COTRIMOXAZOLE PROPHYLAXIS IN HIV-INFECTED CHILDREN IN KILIMANJARO, TANZANIA

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ABSTRACT

Introduction: Cotrimoxazole (CTX) has been used for the prophylaxis of *Pneumocystis jirovecii* (PCP) and other bacterial and protozoan infection in HIV infected individuals and was shown to reduce morbidity and mortality in people living with HIV/AIDS (PLHA).

Aim: To evaluate the effect of cotrimoxazole in HIV infected children enrolled into HIV care and treatment.

Methodology: We conducted a cross sectional, hospital-based study, between September 2005 and March 2006. Over this 6 month study period, 120 HIV-infected children between 5 months and 13 years of age were enrolled. The presence of diarrhoea, *Cryptosporidium*, use of CTX and nutritional status were assessed and if CD4% was available, the results were recorded. *Cryptosporidium* in stool was detected using modified acid fast staining and subsets of samples were also tested with PCR and/or ELISA methods.

Results: Of 120 children enrolled, the mean age was 79 months with a range of 6-165 months; 70 (58.3%) were male; 78 (65%) reported receiving CTX prophylaxis. Diarrhoea was reported in 37/120 (30.8%); however, only 9 (11.5%) of patients on CTX prophylaxis had diarrhoea. CTX use was significantly associated with diarrhoea reduction (p -value=0.001, CI=0.04-0.24). *Cryptosporidium* infection was detected in 13/120 (10.8%) patients, of whom 6 had diarrhoea. *Cryptosporidium* infection was detected in only 3/78 (3.9%) children on CTX prophylaxis compared to 10/42 (23.8%) not on CTX (p -value 0.001, CI=0.03-0.50). Of 100 patients with CD4% available, 59 (59.0%) had CD4% less than 15%, of whom, 10 (17.0%) had *Cryptosporidium*. Low CD4 percentage count was significantly associated with presence of *Cryptosporidium* in children not on CTX prophylaxis (p -value < 0.001). Death occurred in 13/120 children; 12 (92.3%) were not on CTX prophylaxis. CTX use was significantly associated with a reduced mortality (p < 0.001). Presence of diarrhoea ($p=0.16$), severe dehydration ($p=0.001$) and underweight ($p=0.031$) were predictors of death.

Conclusion: Cotrimoxazole prophylaxis is associated with a reduced risk of diarrhoea and mortality in HIV infected children. Apart from its prophylactic effect on PCP and Toxoplasmosis, CTX may also prevent other OIs including *Cryptosporidium* infection and diarrhoea.

Recommendations: All HIV infected children in resource limited settings should receive CTX prophylaxis in all disease stages.

INTRODUCTION

Cotrimoxazole (CTX) prophylaxis was found to prevent *Pneumocystis jirovecii* (PCP) and other bacterial and protozoan infection in HIV-infected individuals and was shown to reduce morbidity and mortality in people living with HIV/AIDS.

- The World Health Organization (WHO) recommendation for resource limited setting where the burden of morbidity and mortality is high due to other infection, is that cotrimoxazole prophylaxis may be offered to all children living with HIV.
- Tanzania National Guidelines recommend use of cotrimoxazole in exposed infants starting at 4-6wks of life until confirmed HIV-negative and symptomatic, HIV-infected children.

- In practice in northern-eastern Tanzania, cotrimoxazole prophylaxis is prescribed for all HIV infected children, irrespective of their CD4+ cell count.
- However, the outcome of this approach has not been studied.
- Therefore, the following study was conducted to describe outcome of children who receive cotrimoxazole as part of clinical care and children who have not received cotrimoxazole.

MATERIALS AND METHODS

- This study was conducted in 2 hospitals in the northern-eastern part of Tanzania: Kilimanjaro Christian Medical Center (KCMC); a referral, research, and teaching hospital and Mawenzi; a regional hospital.
- Children attending these hospitals in both the inpatient and outpatient setting were prospectively enrolled in this observational cohort study.
- The study was approved by the KCMC Ethical Committee.
- Parents or caretaker provided a written informed consent.

Fig.2. Kilimanjaro Christian Medical Centre



Fig.1 Tanzania and Kilimanjaro map

PROCEDURES

Inclusion Criteria

- HIV infected children not started on antiretroviral treatment

Clinical data collected

- Height and weight, presence of cough or diarrhoea, temperature, general physical examination and use of cotrimoxazole

Investigations

- Full blood count, CD4+ cell count, stool for microscopy examination and *Cryptosporidium* (modified acid fast, ELISA or PCR), slide for malaria parasites and chest x-ray

Data entry and analysis

- Data was entered into computer using the SPSS version 12, relationships were tested using the Chi square test at 5% tolerable error and the OR at 95% CI

RESULT

TABLE 1: COHORT DISTRIBUTION

Variables	N=120	%
Mean age (Range)	79 months (6-159)ms	
Males	70	58.3
Female	50	41.7
KCMC	105	87.5
Mawenzi	15	12.5
Disease stage I	2	1.7
stage 2	37	30.8
stage 3	48	40
stage 4	33	27.5
Mother HIV-positive	91	75.6
HIV-negative	1	0.8
unknown status	28	23.3
Father HIV-positive	57	47.5
HIV-negative	6	5
unknown status	57	47.5
Diarrhoea present	37	30.8
<i>Cryptosporidium</i> positive	13	10.8
Cotrimoxazole prophylaxis	78	65

TABLE 2: BIVARIANT ANALYSIS OF CONDITIONS ASSOCIATED WITH NO COTRIMOXAZOLE PROPHYLAXIS

Variables	OR	95% CI	p-value
Presence of <i>Cryptosporidium</i>	2.57	1.7 3.9	0.001
Presence of diarrhoea	4.49	2.7 7.49	<0.001
Fever prior 48hrs	2.9	1.73 4.84	<0.001
Cough prior 48hrs	1.01	0.54 1.88	0.981
Other antibiotics prior 48hrs	3.55	1.86 6.75	<0.001
Antimalaria prior 48hrs	3.25	2.25 4.69	<0.001
Persistence diarrhoea	0.78	0.57 1.08	0.216
Mortality	0.3	0.22 0.43	<0.001

MORTALITY

- Death occurred more often in children not on CTZ; 12/13 deaths occurred in children not receiving CTZ. Low CD4% was not associated with increased risk of death ($p=0.756$). Of death, 10/12 disease stage IV, 2/12 stage III and 1 stage II.

TABLE 3: MORTALITY

Variables	OR	95%CI	P-value
No cotrimoxazole prophylaxis	0.05	0.01 0.33	<0.001
Presence of diarrhoea	3.59	1.29 10.23	<0.016
Presence of <i>Cryptosporidium</i>	3.66	1.31 10.22	<0.035
Persistence diarrhoea	1.11	0.27 4.63	0.633
Severe dehydration	0.16	0.07 0.35	<0.001
Underweight	0.42	0.23 0.77	<0.038
CD4+ percentage <15%	1.09	0.62 1.92	0.756

LIMITATIONS

- This study did not enroll subjects who received cotrimoxazole for different intervals, so could not explore duration of the patients being on cotrimoxazole prophylaxis.
- Patients included were of different age groups which also may determine the outcome due different disease progression.

CONCLUSIONS AND RECOMMENDATIONS

- Cotrimoxazole prophylaxis was significantly associated with reduction in diarrhoea occurrence, less occurrence of *Cryptosporidium* infection and also reduction in mortality rate compare to children who were not on cotrimoxazole prophylaxis.
- Diarrhoea, underweight and severe dehydration were associated high mortality rate.
- In resource limited settings where the burden of morbidity and mortality is high due to infections, cotrimoxazole prophylaxis should be offered to all children living with HIV at all disease stages.

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Fig. 3 KCMC with view of Mt. Kilimanjaro



Fig. 4 View Mt. Kilimanjaro