Cotrimoxazole Prophylaxis Impact On Cd4+ Cells & Infection Reduction In HAART Naïve HI V Infected Adults In our Urban Population, Kenya

Kirigi G[1], Juma R[1], Otieno P[1]. Omollo R[2], Sulleh A. J[3], Mutai B.C[3], Muiruri S[4].

1. *Kenya Medical Research Institute*
2. *DNDi*
3. *Mbagathi District Hospital*
4. *Kenyatta National Hospital, CCC*

corresponding author: Kirigi G: Principal Investigator, Centre for Clinical Research, Kenya Medical Research Institute: gkirigi@kemri.org

Summary

BACKGROUND

The study was undertaken to explore and generate information on the morbidity patterns in HAART Naïve HIV infected adults on oral Cotrimoxazole prophylaxis*(CTXp)* attending Mbagathi and Kenyatta National Hospitals, comprehensive care centres.

METHODS

A qualitative , retrospective study design of mixed methods was used which comprised; Clinical data extraction and Secondary data analysis of 450 personal medical records that existed and which met inclusion criteria based on age, baseline CD4+ cells ≥ 350 count, non-pregnant, absence of active TB and on *CTXp* for duration of six months at the time of enrollment.

RESULTS

The study showed that patients in both Mbagathi district and Kenyatta National hospitals comprehensive care centres (CCC) had at baseline CD4+ cells range; 350-600 and later at 12 months CD4+ cells range; 400-1500. Patients of younger age, when given *CTXp,* had a consistent high CD4+ cells count (above 1000 CD4+ cells count) while those of older age had CD4+ levels that were fluctuating. The median age was 31 years. In over 50% documentation, common infections were frequent and patients treated with essential antimicrobial drugs. We observed that *CTXp* prophylaxis may have reduced severity of infections and this could also have supported up to 60% of the resolved infections. The self-reported adherence to *CTXp* was observed as part of quality monitored care.

CONCLUSION

The findings of this study support work in a number of literature in other studies done outside Kenya on *CTXp* not associated with a worsened progression of HIV disease. Stockouts should be avoided due to public health implications. Further studies may be done to find out what potential *CTXp* has on HIV infected Kenyan patients with serious threat of bacterial infections in conjunction with the customized highly active antiretroviral therapy (HAART).

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Introduction

Cotrimoxazole (also known as fixed-dose trimethoprim-sulfamethoxazole) is commonly used in sub-Saharan Africa because of its low cost, wide availability, broad-spectrum antimicrobial activity and it is well-tolerated (James, 2015). CTXp is an important

part of HIV management and a care toolkit in resource-limited settings and where bacterial infections are highly prevalent and cause significant morbidity.

Recent research show heightened focus on the occurrence of resistance to ***CTXp.*** Nevertheless, prophylaxis with this drug combination before and in conjunction with antiretroviral therapy reduces mortality, morbidity, and rates of hospitalization among human immunodeficiency virus (HIV) infected adults, pregnant women, and children predominantly by reducing rates of pneumonia, diarrhea, and malaria, including those co-infected with tuberculosis (TB) and HIV

Clearly benefit from co-trimoxazole prophylaxis ***(Anna, 2013; Jonathan, 2004)***. Despite varied levels of resistance to ***CTXp,*** evidence in literature appear to suggest in favor of ***CTXp*** prophylaxis to continue after antiretroviral therapy is initiated until there is evidence of immune recovery or contraindication (Davidson, 2008).

In regard to ART naïve HIV infected patients receiving ***CTXp*** prophylaxis, little is known about the effects of ***CTXp*** in this population. This study is motivated by need to inform the practice and policy with evidence-based information.

Aim

The aim of this study is to gather information meet three specific objectives which should be able to estimate the proportion of HIV infected adults on ***CTXp*** who get infections and require other antimicrobial interventions including, Dapsone; determine the frequency and duration of such illnesses in HIV infected adults on ***CTXp*** and document the diagnoses, isolated pathogens (where possible) and outcomes.

Study

This study is undertaken to explore and generate knowledge on the morbidity patterns in antiretroviral therapy (HAART) naïve HIV infected adults on Cotrimoxazole prophylaxis alone attending Mbagathi and Kenyatta National hospitals CCCs. The assumption is to create primary data to help hypothesize for future controlled studies.

The Research Question Is To Address

What data exist in large personal medical records that quantify morbidity patterns in ART naïve HIV infected adults on ***CTXp*** alone?

Methods

This study adopted a qualitative survey design of mixed methods. They comprised of clinical data extraction questionnaire of secondary data from 450 personal medical records in the hospital.

This files existed in the two identified sites which met inclusion criteria based on age, baseline CD4+ cells ≥ 350 count, non-pregnant, absence of active TB and on ***CTXp*** for a duration of six months at the time of enrollment.

The duration taken to observe morbidity characteristics of patients was one year between 2012 -2013.

Two sites were identified for their large volumes of a documented follow up of patients living with HIV but HAART naïve HIV infected adults.

Personal medical records were available and approvals obtained from each hospital manager. At Mbagathi District Hospital (MDH), the target was 150 records of ART naïve patients on ***CTXp***.

At MDH, 8132 files of HIV positive patients were open for content and extract of data. At Kenyatta National Hospital (KNH), the target was 300 records of HAART naïve patients on ***CTXp***. At KNH, 1424 files of HIV positive patients were open for content and extract of data.

Data was harmonized and cleaned for analysis. Continuous data was analysed using mean (SD) and median (IQR) where appropriate while categorical or binary data using proportions (n[%]).

Summerised data was visualised in tables and figures. Confidentiality was maintained. Data analysis was done using STATA version 11.2

RESULTS

Gathering of information was to meet three specific objectives:

1 To estimate the proportion of HIV infected adults on ***CTXp*** who got infections and required other antimicrobial interventions including Dapsone.

2 To determine the frequency and duration of such illnesses in HIV infected adults on ***CTXp***

3 To document the diagnosis, isolated pathogens (where possible) and outcomes.

Table 1: *Baseline demographic and body temperature characteristics*

		OVERALL	MDH	KNH
Age (years)	Mean (SD)	32.4 (9.0)	34.4 (9.4)	29.7 (7.7)
	Median (IQR)	31 (26 to 38)	33 (28 to 40)	29 (25 to 34)
Temp (˚c)	Mean (SD)	36.3 (0.5)	36.3 (0.5)	-
	Median (IQR)	36.4 (36.0 to 36.6)	36.4 (36.0 to 36.6)	-
Gender	Male: n (%)	119 (24.7)	40 (24.7)	79 (24.8)
	Female: n (%)	363 (75.3)	122 (75.3)	240 (75.2)

KNH = Kenyatta National Hospital
MDH = Mbagathi District Hospital
Median age of study population = 31 years

Table 2: *Baseline group clinical haematology characteristics*

		OVERALL	MDH	KNH
CD4 count (cells/mm3)	Mean (SD)	638.6 (248.9)	651.1 (301.1)	630.1 (215.2)
	Median (IQR)	577.5 (455 to 749)	553 (439 to 780)	582 (473 to 732)
WBC (x103/µL)	Mean (SD)	5.9 (1.8)	6.1 (1.8)	5.9 (1.8)
	Median (IQR)	5.6 (4.7 to 7.0)	5.3 (4.7 to 7.9)	5.6 (4.7 to 6.9)
Neutrophils (%)	Mean (SD)	39.2 (16.3)	38.7 (-)	39.2 (16.3)
	Median (IQR)	41.4 (30.6 to 49.8)	38.7 (-)	41.5 (30.6 to 49.8)
Lymphocytes (%)	Mean (SD)	46.3 (13.3)	36.1 (17.1)	46.6 (13.1)
	Median (IQR)	46.1 (39.5 to 54.5)	40.7 (34.0 to 48.1)	46.1 (39.7 to 54.9)
Monocytes (%)	Mean (SD)	7.5 (5.4)	7.5 (5.5)	8.0 (3.5)
	Median (IQR)	7.1 (3.8 to 10.0)	7.0 (3.7 to 9.9)	7.5 (6.2 to 11.4)
Basophils (%)	Mean (SD)	0.9 (0.8)	2.8 (-)	0.9 (0.8)
	Median (IQR)	0.8 (0.6 to 1.1)	2.8 (-)	0.8 (0.6 to 1.0)
Haemoglobin (g/dL)	Mean (SD)	13.3 (2.3)	12.4 (2.4)	13.3 (2.3)
	Median (IQR)	13.3 (12.3 to 14.5)	13.0 (11.9 to 13.5)	13.4 (12.3 to 14.5)

KNH = Kenyatta National Hospital
MDH = Mbagathi District Hospital
Median CD4 = 577
Hb = 13.3g/dl

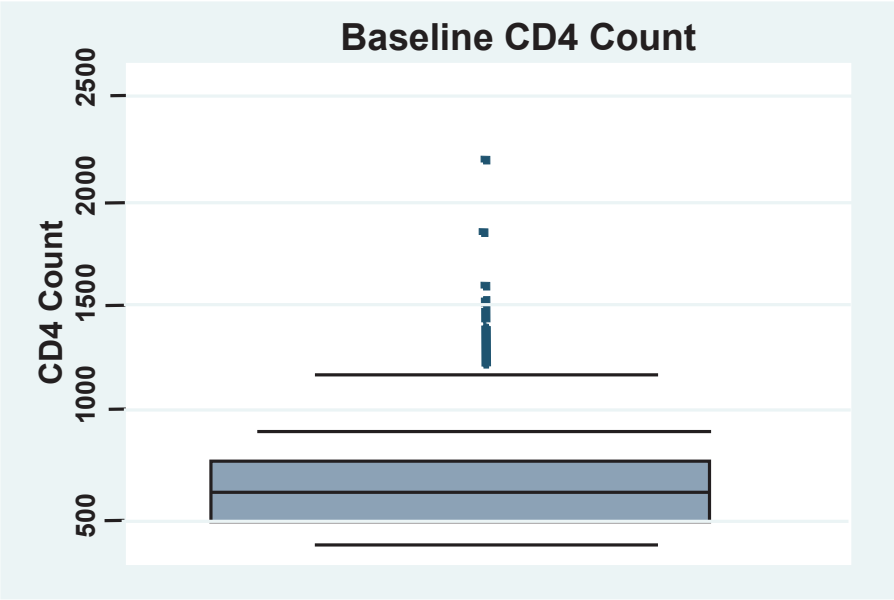

Figure 2: *CD4 + cells at Baseline and at 6 months*

- CD4+ skewed.
- Requisite for inclusion ≥ 350 CD4+cells/mm3
- Baseline CD4+ range 350 – 600

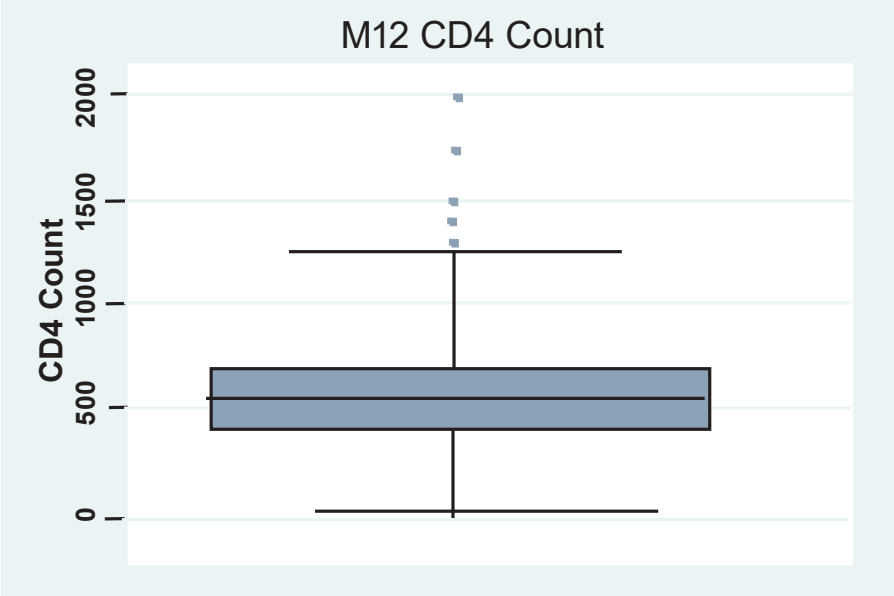

Figure 2: *CD4+ cells at month 12*

- CD4 skewed
- CD4 range 400-1500

Table 3*: Treatment Outcomes*

	OVERALL	MDH	KNH
Cure: n (%)	289 (60.0)	133 (82.1)	155 (48.6)
Missing: n (%)	174 (36.1)	19 (11.7)	155 (48.6)
Death: n (%)	-	-	-
*** Resistant to antimicrobials: n (%)**	-	-	-

KNH = Kenyatta National Hospital
MDH = Mbagathi District Hospital

- 60% documentation of the infections that was resolved
- 36% had missing documentation on treated infection outcomes
- *data on isolates and susceptibility testing documentation missing except microscopy results of urine in some cases

***Table 5**: Adverse Events*

SYSTEM ORGAN CLASS TERM	MEDDRA PREFERRED TERM	COUNT (N)
Blood And Lymphatic System Disorders (2)	Lymphadenopathy	2
Eye Disorders (3)	Conjunctivitis allergic	3
Gastrointestinal Disorders (19)	Abdominal pain	4
	Abdominal pain upper	2
	Dental caries	1
	Diarrhoea	2
	Dyspepsia	4
	Enteritis	2
	Gastro esophageal reflux disease	1
	Peptic ulcer	1
	Stomatitis	1
	Vomiting	1
General Disorders & Administration Site Conditions(4)	Chest pain	2
	Oedema peripheral	1
	Pain	1
Infections And Infestations(117)	Eye infection	1
	Fungal skin infection	5
	Helminthic infection	1
	Herpes zoster	10
	Hiv peripheral neuropathy	2
	Influenza	2
	Lower respiratory tract infection	6
	Malaria	1
	Onychomycosis	1
System Organ Class Term	**MedDRA Preferred Term**	**Count (n)**

***Table 5**: Adverse Events*

INFECTIONS AND INFESTATIONS(117)	**ORAL CANDIDIASIS**	**2**
	Parotitis	1
	Pelvic inflammatory disease	2
	Peptic ulcer	2
	Pharyngitis	1
	Pneumonia	6
	Respiratory tract infection	13
	Rhinitis	9
	Sinusitis	2
	Subcutaneous abscess	3
	Tinea capitis	2
	Tinea infection	1
	Tinea versicolour	1
	Tonsillitis	7
	Upper respiratory tract infection	13
	Urinary tract infection	2
	Vaginal infection	10
	Vulvovaginal candidiasis	10
	Vulvovaginitis	1
Uraemia (1)	Blood creatinine increased	1
	Blood urea increased	1
	Weight decreased	1
Metabolism And Nutrition Disorders(4)	Decreased appetite	3
	Diabetes mellitus	1
System Organ Class Term	**MedDRA Preferred Term**	**Count (n)**
Musculoskeletal And Connective Tissue Disorders(14)	ARTHRALGIA	2

***Table 5**: Adverse Events*

	Back Pain	5
	Muscle Spasms	1
	Myalgia	5
	Pain In Extremity	1
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)(1)	Uterine Leiomyoma	1
Nervous System Disorders(23)	Dementia	1
	Headache	14
	Neuropathy Peripheral	3
	Post Herpetic Neuralgia	4
	Somnolence	1
Pregnancy, Puerperium And Perinatal Conditions(6)	Eclampsia	6
Renal And Urinary Disorders(2)	Dysuria	2
Reproductive System And Breast Disorders(4)	Pruritus Genital	2
	Vaginal Discharge	2
Respiratory, Thoracic And Mediastinal Disorders(18)	Asthma	4
	Cough	9
	Oropharyngeal Pain	3
	Rhinorrhoea	2
Skin And Subcutaneous Tissue Disorders(21)	Dermatitis	2
	Penile Ulceration	1
	Pruritus	11
	Rash	7
Vasculardisorders(2)	Hypertension	2

Table 6: *summary of diagnoses*

Diagnoses	Total Count (n)
Infections and infestations	117
Nervous system disorders	23
Skin and subcutaneous tissue disorders	21
Gastrointestinal disorders	19
Respiratory, thoracic and mediastinal disorders	18
Musculoskeletal and connective tissue disorders	14
Pregnancy, puerperium and perinatal conditions	6
Metabolism and nutrition disorders(4)	4
Eye disorders	3
Hypertension	2
Renal and urinary disorders	2
Neoplasms benign, malignant and unspecified (Incl uding cysts and polyps)	1
Uraemia	1

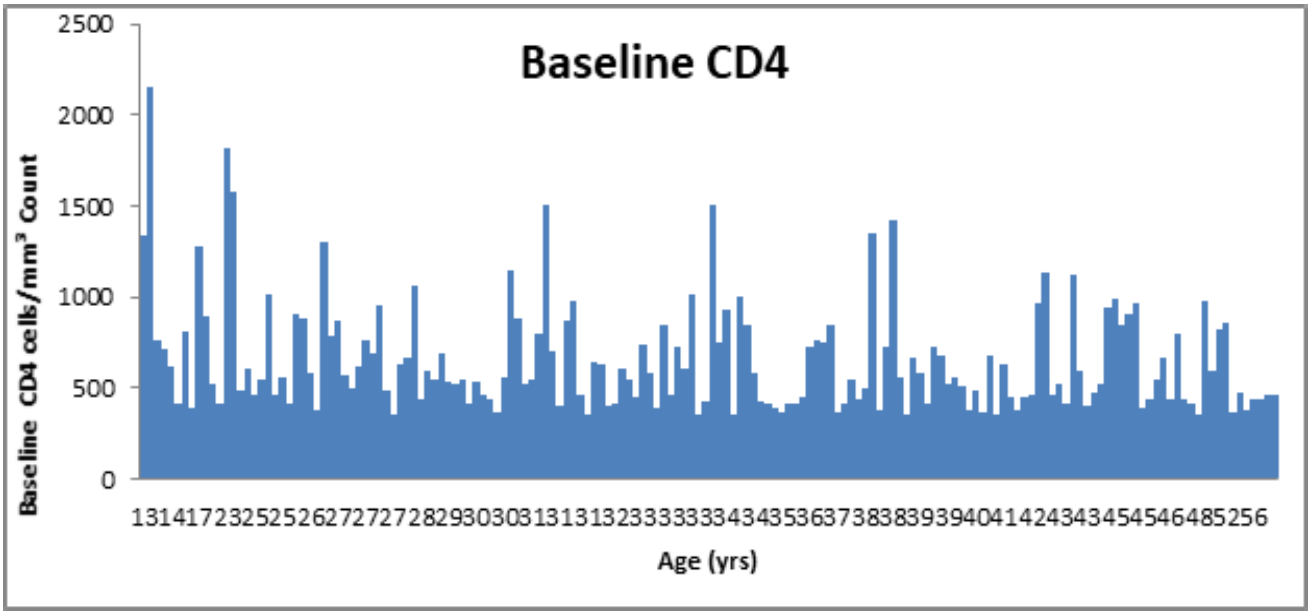

Fig 3: *CD4 count versus age*

DISCUSSION

The discussion of the results of the study and findings relate to the three specific objectives stated in the introduction section:

Objective

1: is achieved by analyses of treatments provided other than Cotrimoxazole prophylaxis information (table 2, 3, 4).

Objective 2:

Achieved by analysis of frequency of adverse events (documentation of treatments plans and drug adherence in Mbagathi & KNH sites ***(table 5)***

Objective 3:

Achieved by a summary description of diagnoses ***(tables 6)***

Patients of younger age, when given ***CTXp,*** had a consistent high CD4+ cells usually above 1000 CD4 count while those of older age had CD4 levels that were fluctuating.

Large volumes of secondary data in MDH and KN was processed for information on morbidity patterns and treatment outcomes.

CONCLUSION

To conclude, continued ***CTXp*** is likely to be beneficial to all ART naïve HIV infected adults with baseline CD4 ≥ 350cells/mm3 where ART is not practicable or a patient is yet to decide on starting ART.

It is clear that continued *CTXp* was not associated with drug induced severity of HIV disease and this was supported by documentation of adherence to ***CTXp*** as quality of monitored care.

Evidently, continued intake of Cotrimoxazole prophylaxis can prevent severe secondary infections in ages 30yrs or below. In Kenya, this age group is within the most affected and vulnerable to HIV transmission

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