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Resistance of Commensal Intestinal *Escherichia Coli* and Other Enterics to Co-trimoxazole and Commonly Used Antibiotics in HIV/AIDS Patients

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Abstract

Trimethoprim-sulfamethoxazole (CTX) has been recommended by the World Health Organization as a prophylactic drug for HIV/AIDS-patients against opportunistic infections. However, daily use of CTX may reduce its efficacy to enteric *Escherichia coli*, thus increasing the burden of CTX-resistant pathogens. Resistance of enteric pathogens to CTX may affect empiric treatment approaches especially in HIV/AIDS patients. We prospectively investigated incidences of fecal *E. coli* resistance to CTX in 188 HIV-infected patients of 15-72 years of age, and determined changes in susceptibility patterns. The study was conducted in Dar es Salaam, Tanzania involving collection of stool specimens from HIV-patients prior and after initiation of CTX prophylaxis. Specimens were collected on 1st, 4th, and 24th weeks upon commencing CTX prophylaxis. Susceptibility profiling of *E. coli* and other enteric bacteria to CTX and other widely used antibiotics were done using Kirby-Bauer disk diffusion method. On the first visit, 143(76.1%) enteric bacteria were isolated. Of those, 123(86%) were *E. coli*. About 98.6% were resistant to CTX. On the second visit, 103(54.2%) bacteria were isolated; of those, 100(98.4%) of them exhibited resistance to CTX. On the third visit, 64(34%) out of 188 patients had significant enteric bacteria, and of those 63 (98.4%) were resistant to CTX. About 53.2% of bacterial isolates were resistant to ciprofloxacin and ampicillin. Majority (95.2%) of the patients had initiated CTX prophylaxis prior to testing at the care and treatment clinics. About 32% of the patients reported to have skipped some doses of CTX prophylaxis. Non-adherence to CTX prophylaxis and self-medication among patients may have attributed to the observed high prevalence rate of *E. coli* resistance to CTX and other commonly used antibiotics. For better understanding of the observed pattern of bacterial resistance to CTX, phenotypic and/or genotypic characterization of the isolated bacteria needs to be conducted.

Keywords: Antibacterial resistance; Enteric bacteria; HIV/AIDS patients; Co-trimoxazole prophylaxis

Introduction

Trimethoprim-sulfamethoxazole (CTX) is the most efficacious drug against non-typhoid Salmonella (NTS) bacteraemia particularly *Salmonella typhimurium* and *Salmonella enteritidis*, which are known to be the leading cause of morbidity and mortality in HIV infected patients in Africa [1,2]. Prophylaxis for opportunistic infections (OIs) with CTX has also been shown to reduce mortality and morbidity among HIV infected patients with sputum positive tuberculosis (TB) in several countries [3-5].

Antimicrobial resistance is a growing problem and a cause of great concern throughout the world [6-9]. Unlike higher organisms, bacteria can transfer DNA to other bacteria which are not their off-springs, and even to members of completely unrelated bacterial species. Hence, there is a general consensus on the existence of a high degree of rapid plasmid mediated transfer of CTX resistance between faecal *E. coli* and the *Salmonella* species as well as other Enterobacteria [10,11]. The level of faecal *E. coli* resistance to CTX would therefore cause similar resistance patterns in NTS and other bacteria. Antibiotic resistance carries a significant economic toll as well as a medical burden [12]. The WHO Office of Technology Assessment estimates that resistance in just six types of bacteria increased hospital treatment costs by billions of US dollars [13].

The growing health crisis of antibiotic resistance could render these important drugs ineffective in treating infections. The Centre for Disease Control (CDC) and Prevention has observed that "decreasing inappropriate antibiotic use is the best way to control resistance" [14]. Key steps in doing so include adoption of policies aimed at ending the inappropriate use of antibiotics in agriculture, as well as continued implementation of programs to educate patients and physicians about the need to use antibiotics more cautiously. Unless we act now, we face a future of untreatable bacterial infections. Immune-compromised patients such as people living with HIV/AIDS (PLHA) are the most likely to be affected by resistant bacterial and fungal infections.

As in many other developing countries, conditions that may foster antibiotic resistance in Tanzania differ from developed countries, and so resistance prevalence. Faecal pollution and other traits of overcrowded cities with poor sanitary conditions might create ideal settings for selecting, exchanging and maintaining resistance traits. In addition, medical abuse of antibiotics, along with low-quality drugs are also prevalent [13]. Self-medication, a common yet unmeasured practice among Tanzanian population, may also contribute to increased resistance rates [15]. Therefore, knowledge of antimicrobial resistance trends among bacterial isolates is essential in order to provide clinically appropriate and cost effective therapy.

Microbial infections such as NTS and *Salmonella* food-borne infections are particularly common problems for HIV/AIDS patients in Tanzania. HIV-infected patients are at greater risk of developing

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serious food-borne bacterial infections; therefore they have to take antibiotics daily to prevent recurrent infection of the bloodstream (septicaemia). CTX use had been implicated in development of CTX resistant *Streptococcus pneumonia* [16], but much less is known about development of resistance in gram-negative bacteria like *E. coli*, organisms for which CTX plays an important therapeutic role in HIV-infected patients.

Methodology

Study setting

The study was conducted in the three municipal hospitals in Dar es Salaam, which are Mwananyamala, Amana and Temeke hospitals. Apart from Muhimbili National Hospital which is a referral hospital, the three municipal hospitals are the major public hospitals providing care and treatment services for PLHA in Dar es Salaam, Tanzania. Patients over 18 years of age undergoing voluntary counselling and HIV testing with CD4 cell count of ≤350 cells/mm^3 are eligible to start CTX prophylaxis for opportunistic infections and were recruited in the study.

Pregnant women in their first trimester were excluded at each visit using a menstrual history and urine pregnancy test. Pregnant women in their second or third trimester were included in the study [17]. Patients below 18 year of age were also excluded from the study, unless parents' or guardians' verbal or written consent were obtained.

Study population and specimen collection

Stool specimens were collected immediately after registration and before starting CTX therapy. Information was sought to whether prior to registration at the CTC, any of the patients would have been using CTX for any particular disease condition. To compare and determine whether there would be changes in CTX resistance with time, three serial cross-sectional resistance studies were carried out using stool specimens collected from cohorts of newly registered patients selected randomly before commencement of CTX medication.

The CTX prophylaxis was given in form of 2 single-strength tablets, each containing 80 mg of trimethoprim and 400 mg of sulfamethoxazole, daily. Patients were categorized into two groups: patients who have been using CTX prior to registration at the CTC for over 3-6 months and those who were initiated CTX prophylaxis during the time of the study (naive). A structured questionnaire was used to gather information on the basic socio-demographic data.

Laboratory procedures

Whole stool was collected at the baseline visit and before administration of the first dose of CTX for all participants. Participants were then requested to return to the clinics on the 1st, 4th, and 24th weeks after the baseline visit. At each visit, whole stool was collected and the standardized clinical history and physical examination were repeated. Adherence to CTX prophylaxis was assessed at each follow-up visit by patient self-report.

Whole stool was inoculated onto MacConkey agar with CTX disk and incubated for 24 hours at 37°C. Plates were examined for the presence of flat, dry, lactose-utilizing colonies consistent with *E. coli*. The presence or absence of presumptive *E. coli* was recorded. If colonies consistent with *E. coli* (ATCC 25922, American Type Culture Collection, Rockville, MD) on regular basis were not observed within <16 mm of the CTX disk, the stool was classified as having susceptible *E. coli*. For colonies consistent with *E. coli* that appear within <16 mm of the CTX disk, the stool was classified as having non-susceptible *E. coli* as per recommendations [18,19]. Colonies nearest to the disk were picked and sub-cultured to blood agar. The inoculated blood agar or MacConkey plates were incubated for 24 hours at 37°C, and biochemical tests [oxidase and indole tests, sugars fermentation or/ and serological test (H&K antigens)] were performed on the resulting growth for confirmation of the isolates [20].

Testing of antimicrobial susceptibility to commonly used antibiotics

Anti-microbial susceptibility testing was done on Mueller-Hinton agar plates. Susceptibility testing for ampicillin and ciprofloxacin were done using the Kirby-Bauer disk diffusion method [21]. For the isolated bacteria viz. *Staphylococcus aureus, Klebsiella spp* and *E. coli* interpretive criteria were used to evaluate zone sizes for ciprofloxacin and ampicillin based on the antibiograms for standardised control strains of *E. coli* (ATCC 25922) and *S. aureus* (ATCC 25923).

Data analysis

Statistical data analysis was done using a descriptive analysis of the subjects comparing changes in the proportion of *E. coli* non-susceptibility to CTX over time and assessment of the effect of CTX use on co-selection of non-susceptibility to other antimicrobial agents (ciprofloxacin and ampicillin). The Statistical Package for Social Sciences (SPSS, version 17.0) was used for descriptive analysis, independent-samples T-test for comparison of means of CD4 count, correlation and multinomial logistic regression among various dependent and predictor variables. Differences of assessed parameters among various sets of data were considered significant at $p<0.05$.

Ethical consideration

The study was granted ethical clearance by the Muhimbili University of Health and Allied Sciences Ethical Committee. Permission to conduct the study in the selected health facilities was sought from the Municipal Medical Officers in-charge. Following a written informed consent from the study participants, a standardized clinical history and physical examination were carried out. Patients were also informed that all the information gathered and laboratory results would be used for research purpose, but could be available for any participant who would wish to know the findings. In order to maintain confidentiality data were entered into the computer for analysis and interpretation by using code numbers.

Results

Demographic characteristics of the study participants

A total of 188 patients were recruited in this study. Out of those, 80(42.6%) were males and 108(57.4%) females, with age ranging from 15 to 72 years and median of 37 years of age. Majority (75.5%) of the participants had no formal education. A total of 60 (31.9%) patients were recruited at Amana, 63(33.5%) at Mwananyamala and 65(34.6%) at Temeke Municipal hospitals (Table 1).

Prevalence of opportunistic infections and correlation with CD4 cell count in patients

About half (51.1%) of patients were experiencing OIs. Of those OIs, 55% (n=53) were due to TB and 22(23%) were of fungal origins. The patients CD4 cell counts ranged from 4 to 1044 cells/µl, with median of 232 cells/µl. About 51.6% of the patients had 201-350 CD4 cell counts, while 74(39.4%) had CD4 cell count of <200. Nevertheless, 36 (43%) of the patients with CD4 cell count of <200 did not experience OIs during

Variables		Care and treatment centres			
		Amana	Mwananyamala	Temeke	Total (%)
Gender	Males	25	27	28	80(42.5)
	Females	35	36	37	108(57.5)
Age group	15-30	17	15	16	48(25.5)
	31-46	31	39	36	106(56.4)
	47-62	11	8	12	31(16.5)
	>62	1	1	1	3(1.6)
Education level	Informal	42	49	51	142(75.5)
	Primary	3	8	6	17(9.0)
	Secondary	2	1	2	5(2.7)
	College	13	5	6	24(12.8)

Table 1: Socio-demographic characteristics of patients who were recruited in the study.

OIs	CD cell counts (cells/µl)	Duration of CTX prophylaxis (months)					Total (%)
		>24	24	>6	< 6	< 3	
Present	1-200	19	10	5	2	2	38(20.2)
	201-350	24	6	7	2	8	47(25.0)
	351-500	3	-	3	1	-	7(3.7)
	>501	2	-	1	-	1	4(2.1)
None	1-200	17	5	6	2	6	36(19.1)
	201-350	34	5	3	3	5	50(26.6)
	351-500	2	1	1	2	-	6(3.2)

Table 2: Occurrence of opportunistic infections in relationship to the levels of CD4 cell count and duration of CTX prophylaxis in HIV infected patients (n=188).

the time of the study. It was also found that 4(2.1%) patients with CD4 cell count over 501 had OIs (Table 2).

The study also revealed that all patients had been on CTX prophylaxis for different period of time. There was a positive association between the duration of CTX use and CD4 cell count among patients (r=0.0.17; p=0.817). About 54% (n=101) of patients were on CTX prophylaxis for more than a year. Out of these, 53 (52.5%) were not experiencing OIs, despite the fact that 17 (17%) of them had CD4 cell count below 200 (Table 2).

Regarding the level of CD4 cell counts, no significant differences were observed between patients with OIs and those without OIs (p=0.538; df=187; F=5.597). Comparison of the number of OIs per patient between CTX users and non-users, revealed no significant differences (p=0.512; df=176; F=2.655). However, CTX users were 1.2 times less likely to acquire OIs than non-users (p<0.05).

A negative correlation between CD4 cell counts and number of OIs was observed (r=-0.021; p=0.391). Though not statistically significant, this observation was complemented by the regression coefficient (Standardized Beta=-0.029; p>0.05). A slight correlation though not statistically significant was also evident between the period of exposure to CTX prophylaxis and CD4 cell counts (r=0.017; p=0.409). Figure 1 shows some of the common OIs among the study participants in relationship to CD4 cell count and sex of patients.

Adherence patients to CTX prophylaxis for opportunistic infections

Of 188 patients, majority (95.2%; n=179) of them had been on CTX prophylaxis prior to registration at the CTC. Of 179 patients on CTX prophylaxis, 57(32.0%) had skipped some CTX prophylaxis regimens due to various reasons. Twenty two (12.3%) of patients who admitted to have had skipped doses of CTX prophylaxis had CD4 cell count of 1-200 as compared to 40(22.3%) patients with the same amount of CD4 cell count who reported to be adherent. Among patients with CD4 cell count of 201-350, 17.3% of them had skipped doses of CTX on several occasions, while 45(25%) patients mentioned that they had never skipped the dose of medication. Ten patients (5.3%) in the category of CD4 cell count of 1-200 and 17 with CD4 cell count of 201-350 could not recall if they ever had skipped doses of CTX prophylaxis.

The most cited reasons for non-adherence were unavailability of CTX at the hospitals (35%) and CTX induced side effects (27%). Other reasons for non-adherence were forgetting to take the medication at the pre-determined time and frequency (18%), travelling and therefore not able to visit CTCs for prescription refill (12%) and burden of pills due to concomitant use of CTX with other medications including ARVs and other drugs for OIs (4%).

Ten (5.3%) out of 188 patients who admitted to have had altered the dose and frequency of use of the medication, only 3 of said it was due to CTX side effects. However, out of 161 (85.6%) patients who claimed not to have had changed the use of medication, 23(14.3%) of them had experienced several side effects as indicated in Figure 2.

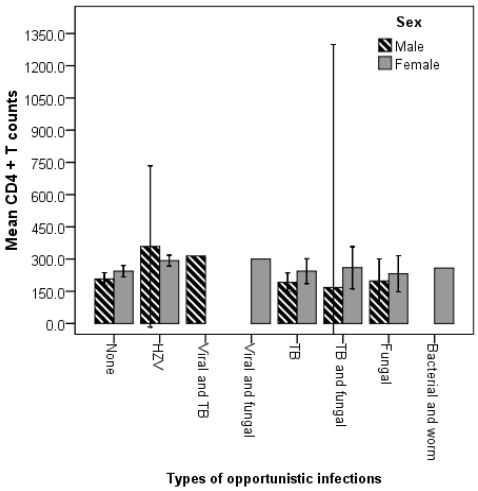

Figure 1: Common opportunistic infections experienced by HIV-infected patients in relationship to CD4 cell count levels (Error bars: 95% confidence of interval).

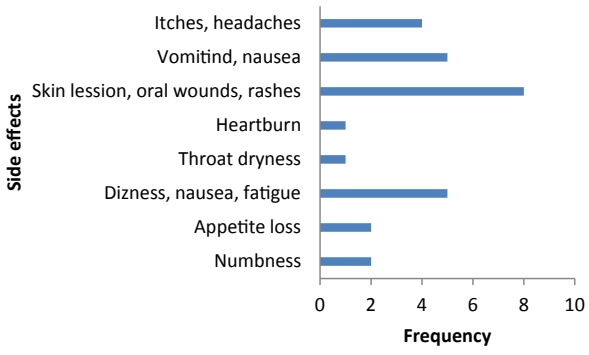

Figure 2: CTX-induced side effects as reported by HIV-infected patients using CTX prophylaxis for opportunistic infections (n=26).

Visits	Remarks	CD4+ T cell counts				Total (%)
		1-200	201-350	351-500	501-1200	
Start	NA	-	-	2	-	2(1.1)
	S	15	14	3	4	36(19.1)
	R	59	83	8	0	150(79.8)
						R(80.6)
1st week	NA	20	23	2	-	45(23.9)
	S	1	0	0	1	2(1.1)
	R	53	74	11	3	141(75.0)
						R(98.6)
4th week	NA	32	42	8	3	85(45.2)
	S	1	2	0	0	3(1.6)
	R	41	53	5	1	100(53.2)
						R(97.1)
24th week	NA	50	61	10	3	124(66.0)
	S	0	1	0	0	1(0.5)
	R	24	35	3	1	63(33.5)
						R(98.4)
Total		**74**	**97**	**13**	**4**	**188(100.0)**

Key: NA-no isolate; R-resistant to CTX; Sensitive to CTX.

Table 3: Susceptibility of the *E. coli* isolates to CTX in relation to patient's CD4 cell count (n=188).

Antibiotics	Isolated microbes								
	1st Week			4th week			24th week		Total
	Eco	Sta	Kle	Eco	Sta	Kle	Eco	Sta	N=188
Cipro (S)	45	-	1	1	-	-	-	-	47(25.0)
Cipro, Amp (S)	2	-	-	1	-	1	1	-	5(2.7)
Cipro (S), Amp (R)	37	3	1	22	7	2	7	-	79(42.0)
Amp (S), Cipro (R)	1	-	-	1	-	-	5	2	9(4.8)
Cipro, Amp (R)	30	3	-	14	5	2	-	3	60(31.9)

Key: S-sensitive; R-resistant; Eco-*E. coli*, Sta-*S. aureus*; Kle-*Klebsilla* spp; Amp-ampicillin; Cipro-ciprofloxacin.

Table 4: Susceptibility patterns of two commonly used antibiotics on the isolated bacteria from stool of HIV infected patients (n=188).

Susceptibility profiling of isolated microbes

A total of 186 bacteria were isolated from patients prior to commencing the CTX prophylaxis study. The bacteria were comprised of 121(65%) *E. coli*, 28 (15%) *S. aureus* and 20% were other enterics. Of these bacteria, 150(80.6) were resistant to CTX (Table 3). During the first week of visit: a total of 143(76%) isolates (*E. coli, S. aureus, Klebsiella*) were obtained from 188 patients. Of those, majority were *E. coli*. Significant number of the isolates (98.6; n=141) were resistant to CTX. In the second visit (4th week); a total of 103 bacteria were isolated and identified, of those 76(74%) were *E. coli* while 63(97%) of the isolates were resistant to CTX. Of 103 tested isolates, 100(97.1) were resistant to CTX. In the last visit (24th week); only 64(34%) bacteria were isolated from 188 patients. Of those, *E. coli* constituted 61% of the isolates. About 98.4% (n=63) of the isolates were resistant to CTX. The antibiotic susceptibility profiles for ciprofloxacin (Cipro) and ampicillin (Amp) are summarized in Table 4.

Effect of CTX prophylaxis on the prevalence of OIs in HIV-infected patients

For every one unit decrease in CD4 cell count there was likelihood of 0.03 increase for occurrence of OIs (p=0.702). For patients who did not use CTX the possibility of getting OIs was 0.14 times higher than those who were on CTX prophylaxis. Those who were non-adherent to CTX prophylaxis regimens had 0.16 higher chances of developing OIs, which is 1.17 times than those who did not skip any of the prescribed doses (p=0.718). Similarly, a negative association was observed between the quantity of medication taken and occurrence of OIs in patients (r=-0.060; p=0.216). This is an indication that more drugs apart from CTX were needed to manage OIs in patients as time progressed.

Comparative analysis of the association between the number of OIs and CD4 cell counts with respect to patients` sex revealed that males were 1.36 times (p=0.309) less likely to have OIs as compared to females; though the differences were statistically not significant.

Discussion

CTX contains two main antimicrobial active ingredients, i.e. sulfamethoxazole and trimethoprim. Given together, these antimicrobial agents provide good coverage against a wide range of bacteria such as *Streptococcus pneumoniae*, *Escherichia coli* and non-typhoid Salmonella, protozoa (*Isospora belli*, *Toxoplasma gondii* and *Plasmodium falciparum)* as well as fungi especially *Pneumocystis jirovecii* [22]. According to the results of earlier studies, CTX may decrease both mortality and morbidity in adults with HIV infection, regardless of the use of ART [23-25].

The results of this study show an overall high (93.7%) resistance rate to CTX among the isolated enteric *E. coli.* These findings are similar to those reported by other researchers [26,27]. Many factors may be the reasons for the high prevalence of *E. coli* resistance to CTX. In Tanzania, CTX tablets and syrups are readily available in the retail pharmacies and health facilities. Although easy availability improves access to the drug, this also may contribute to irrational use of the medicine through self-medication. This is most likely to happen in PLHA who may be using the drug for management of OIs without proper guidance from qualified health care workers. Another reason for high resistance of *E. coli* to CTX and other commonly used antibiotics could be due to poor adherence of patients to the prescribed medication as reported by some patients in this study.

The efficacy of CTX in areas of high bacterial resistance, its relative usefulness among individuals with differing CD4 cell counts, and the mechanisms through which it exerts its effects are unclear [9,11]. In this study, we could not establish the direct benefit of CTX prophylaxis in individuals with different levels of CD4 cell counts. To a greater extent this observation could have been contributed by the fact that majority of patients who were recruited in the study had already been initiated CTX prophylaxis before registration to the CTCs. Since these patients did not follow normal procedures for initiation of CTX prophylaxis at the CTCs, it is not known whether the patients were eligible to start prophylaxis based on the CD4 cell count. In addition, adherence to CTX prophylaxis during that time could not be ascertained. Another co-founding factor in this aspect could be due to non-adherence of patients to CTX prophylaxis even after enrolment at the CTCs as reported by one third of patients who admitted to have had skipped doses of CTX prophylaxis.

CTX prophylaxis might be a particularly useful intervention for people with no access to antiretroviral drugs and for those who are not yet eligible to start using antiretroviral drugs based on CD4 cell count. A recent randomised controlled trial in Senegal found no beneficial effect of CTX prophylaxis on mortality [28]. On the other hand, another study revealed that daily CTX prophylaxis was associated with

reduced morbidity and mortality and had beneficial effects on CD4-cell count and viral load [29]. In the present study, the occurrence of OIs was not in correlation with CD4 cell count levels among patients. However, CTX users were less likely to develop OIs as compared to non-users. These findings indicate the need to monitor the use of CTX for prophylaxis of OIs. In order to ensure rational use of CTX prophylaxis, factors such as adherence, availability of CTX in the health facilities, self-medication and proper management of OIs should be part of HIV/AIDS management program.

By preventing some OIs, CTX reduces the frequency of episodes of increased HIV viral load associated with acute illness, resulting in improved long-term CD4 cell response [30,31]. Increases in cytokine activity have been associated with a long-term decrease in CD4 cell count and increase in HIV viral load [32]. This is due to reactivation of the immune system by the presence of microbial and parasitic infections [33]. It has been reported that CTX prophylaxis exerts its effect partly through the reduction of transient increases in viral load and associated with CD4-cell count declines [34].

In this study, patients on CTX prophylaxis had relatively less likelihood of harbouring opportunistic pathogens as compared to those who were not on prophylaxis. Non-adherent patients were 1.17 times more likely to develop OIs as compare to adherent patients. In addition, the occurrence of OIs was associated with relatively higher rate of decrease in CD4 cell count over time. The pattern of occurrence of OIs in relationship with declining immunity in HIV/AIDS patients has also been reported by other researchers [35,36]. Our study could not establish an association between CTX prophylaxis and CD4 cell count due to the fact that majority of the patients were on CTX prophylaxis prior to enrolling into the CTX prophylaxis programme. Contrary to two previous reports which found that compliance with CTX prophylaxis regimens among HIV patients was excellent, our study shows about a third of the patients reported to have been non-adherent [37,38].

CTX can cause several side-effects, especially in the intravenous formulation. The most common reactions are rash, fever, nausea, low white blood cells and liver inflammation. Skin rashes due to CTX are common among HIV-positive people [17,39,40]. Some of these were also reported by the interviewed patients in this study. These should be taken seriously and the drug withdrawn or the dose reduced because some people can develop Stevens-Johnson syndrome which is a potentially fatal allergic reaction [41]. However in this study, the treatment was very well tolerated, with only 14% of the patients reporting some mild side effects which were much less than those reported in other studies [42]. Moreover, these side effects could not be entirely correlated to CTX since some patients were also using anti-TB and antifungal drugs.

Analysis of CD4 cell counts and a number of OIs or their occurrence mong the patients showed no statistically significant differences in benefit of CTX prophylaxis. Because of limited data on level of immunosuppression other than CD4 counts, such as viral load or viremia, development of malignancies, and the observed problem of self-medication among PLHA; our study could not clearly suggest when to commence CTX prophylaxis. The privation of statistical association between CTX prophylaxis and mortality among individuals with higher CD cell counts has been reported elsewhere [24,37]. This could be due to variability of morbidity and/or mortality rates among individual patients; presumably as result of differences in HIV status and severity and number of OIs. In the present study, an association between CD4 cell count and the effect of CTX prophylaxis on mortality could not be determined due to limited time of study, patient follow up and small sample size.

Questions remain about the efficacy of CTX in areas of high bacterial resistance, its relative usefulness among individuals with differing CD4 cell counts, and the mechanisms through which it exerts its effect. CTX seems to significantly increase survival in HIV-infected patients on ART. Further research is needed to determine the optimum duration of CTX treatment in these patients. The observed high resistance of *E. coli* and other enterics to CTX and other commonly used antibiotics is of greater concern. This calls for immediate intervention in order to re-assess the use of CTX for prophylaxis of OIs in Tanzania.

Conclusions and Recommendations

Majority (95.2%) of the patients had initiated CTX prophylaxis prior to testing at the CTCs. This could have led to the high prevalence rate of *E. coli* resistance to CTX and other commonly used antibiotics. Resistance of *E. coli* to CTX was very high. In addition, resistance of *E. coli* to the commonly used antibiotics ciprofloxacin and ampicillin was also relatively high (53.2%). Patients who were not on CTX prophylaxis had relatively higher possibility of contracting OIs. As shown in this study, TB is still the leading cause of morbidity in HIV patients in Tanzania. Therefore the use of CTX prophylaxis in HIV/AIDS-patients (in Tanzania) should be re-visited because of high antibacterial resistance revealed in this study.

Self-medication of CTX among HIV patients should be discouraged through counseling of the patients during their visits to the CTCs. HIV/AIDS care providers in CTCs, should put in place adherence strategies to ensure that CTX is used rationally to maximize its benefits for prevention of OIs. For better understanding of the pattern of *E. coli* resistance to CTX and other commonly used antibiotics, phenotypic and/or genotypic characterization of the isolated bacteria needs to be carried out.

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