Bekele and Gebreanania, Prim Health Care 2019, 9:1
DOI: 10.4172/2167-1079.1000322

Primary Health Care: Open Access

Research Article Open Access

Drug Use Evaluation of Cotrimoxazole Prophylaxis and Contributing Factors among HIV Infected Patients in Northern Ethiopia

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Abstract

Background: Cotrimoxazole, an antibiotic that has been in use for many years, was found to be effective in reducing the occurrence of *Pneumocystis carinii* pneumonia in patients with HIV. It has been shown that cotrimoxazole is superior to other forms of prophylaxis in preventing toxoplasma encephalitis. The aim of the study was to evaluate the use of cotrimoxazole prophylaxis and its contributing factors among adult Human Immunodeficiency Virus (HIV) infected individuals attending Ayder referral hospital Antiretroviral (ART) clinic.

Methods: A cross-sectional quantitative study was carried out at Ayder referral hospital ART clinic, Mekelle special zone, North Ethiopia from January 3 to 15, 2012. Data regarding patients' clinical, laboratory findings, residential addresses and medications were abstracted from patients' records. All data were cleaned and entered into Statistical Package for Social Sciences (SPSS) software version 16.0 for analysis. Appropriateness of cotrimoxazole prophylaxis was presented descriptively. Bivariate and multivariate statistics using logistic regression were computed and *p* value of <0.05 was considered as significant.

Results: A total of 267 medical charts were identified and reviewed. The mean age of the patients was 35.19 years and 52.8% were females. The use of cotrimoxazole prophylaxis therapy was found to be appropriate in 255 (95.5%) of the patients. Sex of the patient, Cluster of Differentiation 4 (CD4) count of the patient and World Health Organization (WHO) clinical stage of the patient were found to be significantly associated with the appropriateness of cotrimoxazole prophylaxis therapy

Conclusions: The appropriateness of cotrimoxazole prophylaxis was good (95.5%) among patients living with HIV/AIDS in our study set up even though it was not to the full standard. Inappropriate uses of cotrimoxazole prophylaxis were more likely among female patients, patients with CD4 count >350 cells/mm^3 and patients not at WHO clinical stage IV.

Keywords: Cotrimoxazole; Prophylaxis; Drug use; HIV/AIDS; Contributing factors

List of Abbreviations: AIDS: Acquired Immunodeficiency Syndrome; ART: Antiretroviral Therapy; CBC: Complete Blood Count; CD4: Cluster of Differentiation 4; CI: Confidence Interval; CMV: Cytomegalovirus; COR: Crude Odds Ratio; CPT: Cotrimoxazole Preventive Therapy; CTX: cotrimoxazole; DUE: Drug Use Evaluation; HAART: Highly Active Antiretroviral Therapy; Hbg: Haemoglobin; HIV: Human Immunovirus; HIV: Human Immunodeficiency Virus; HRERC: Health Research Ethics Review Committee; MAC: Mycobacterium Avium Complex; OI: Opportunistic Infections; OR: Odds Ratio; PCP: *Pneumocystis carinii* Pneumonia; SPSS: Statistical Package for Social Sciences; TB: Tuberculosis; UNAIDS: United Nations Program on HIV/AIDS; WHO: World Health Organization

Introduction

AIDS-related illnesses remain one of the leading causes of death globally and are projected to continue as a significant global cause of premature mortality [1]. These are usually infections that develop as a result of damage to the immune system which are called Opportunistic Infections (OIs) [2]. They take advantage of the opportunity provided by a weakened immune system. Tuberculosis, Herpes zoster virus, bacterial pneumonia, lymphoma, *Pneumocystis jiroveci* (formerly *carinii*) pneumonia (PCP), esophageal candidiasis, Herpes simplex virus, cerebral toxoplasmosis, cryptococcosis, *cytomegalovirus* (CMV) and *mycobacterium avium* complex (MAC) are some of the common opportunistic infections [3].

According to the most recent data from the Joint United Nations Program on HIV/AIDS (UNAIDS), approximately 980,000 Ethiopians were living with HIV/AIDS in 2007 and 67,000 individuals have died as a result of infection with the virus. National projections estimate approximately 1.1 million Ethiopians are living with HIV and prevalence increased slightly to 2.3 percent by 2009 [4]. Ethiopia is the third highest with number of infections in Africa, according to UNAIDS [5].

Co-trimoxazole is a synergistic fixed combination of sulfamethoxazole (an intermediate-acting antibacterial sulfonamide) and trimethoprim; both sulfamethoxazole and trimethoprim are synthetic folate-antagonist anti-infectives. It is an antibiotic that has been in use for many years, was found to be effective in reducing the occurrence of *Pneumocystis carinii* pneumonia in patients with HIV. It has been shown that cotrimoxazole is superior to other forms of prophylaxis in preventing toxoplasma encephalitis. Subsequently cotrimoxazole has become the standard primary and secondary chemoprophylaxis for *Pneumocystis carinii* pneumonia and toxoplasma encephalitis in HIV infected patients with significant immune system dysfunction [6].

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Received: November 22, 2018; **Accepted:** January 20, 2019; **Published:** January 27, 2019

Citation: Bekele ML, Gebreanania T (2019) Drug Use Evaluation of Cotrimoxazole Prophylaxis and Contributing Factors among HIV Infected Patients in Northern Ethiopia. Prim Health Care 9: 322. doi: 10.4172/2167-1079.1000322

At the dose of sulfamethoxazole 800 mg/trimethoprim 160 mg daily or three times weekly, cotrimoxazole has been demonstrated to be effective at reducing mortality due to *Pneumocystis pneumonia*, toxoplasmosis and other bacterial opportunistic infections. Adverse reactions are less frequent with this lower prophylactic dose of trimethoprim-sulfamethoxazole. The most common problems are rash, fever, leukopenia and hepatitis [7,8].

Even though the impact of cotrimoxazole use in the evolution of drug resistance is uncertain; there is concern that implementing wide and prolonged use of cotrimoxazole prophylaxis could be associated with the development of drug resistance in common pathogens, such as increased penicillin-resistant *Pneumococcus* [9]. Because Sulfadoxine-Pyrimethamine and cotrimoxazole exert their antimicrobial action by inhibiting the same enzyme in folic acid biosynthetic pathway the emergence of cross resistance to sulfadoxin-pyrimethamine by widespread use of cotrimoxazole is of great concern [10]. Therefore judicious use of this drug is warranted.

The Conference of Experts on the Rational Use of Drugs, convened by the World Health Organization (WHO) in Nairobi in 1985, defined rational drug use as: "*The rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost to them and their community*". Rational drug use implies an individual approach to patient treatment.

Aim of the Study

The aim of this study was to evaluate the use of cotrimoxazole prophylaxis and its contributing factors among Adult HIV infected individuals attending Ayder referral hospital ART clinic.

Methods

A retrospective cross sectional quantitative study was conducted during January, 2012 in Ayder Referral Hospital, Mekelle, Northern Ethiopia. It is a teaching hospital under Mekelle University, College of health sciences, which serves as a referral hospital for the society of Tigray regional state. Mekelle town is situated at about 783 km southwest of the capital Addis Ababa. The population of the Mekelle-special zone is estimated to be 215,546 [11].

The study was conducted after ethical clearance was granted from the Health Research Ethics Review Committee (HRERC) of the College of Health Sciences, Mekelle University (Ref. No.: CHS/720/DN-16). All patients living with HIV/AIDS and were on follow up in Ayder Referral Hospital ART clinic till October 15, 2011 were included in the study. The patients' addresses, socio demographic characteristics, CD4 count, WHO clinical stage, cotrimoxazole prophylaxis use and other pertinent clinical and laboratory parameters were abstracted from the patients' medical charts. A checklist designed in English language was used to collect data from respective medical charts. Data reviewing and abstraction was conducted by two pre-trained nurses on daily basis.

Checklists with incomplete data were excluded out. All data was cleaned and entered into Statistical Package for Social Sciences (SPSS) software version 16.0 for analysis. Demographic and clinical characteristics of the patients were analyzed and presented descriptively. Appropriateness of cotrimoxazole prophylaxis was also analyzed and presented descriptively using set criteria for initiation and discontinuation of cotrimoxazole prophylaxis therapy as a reference (Table 1). Bivariate and multivariate statistics using logistic regression were computed to assess the presence and degree of associations between appropriateness of cotrimoxazole prophylaxis therapy and its contributing factors and p value of <0.05 was considered as significant.

Criteria
Indications to start
☐ HIV–positive patient with active TB
☐ Symptomatic HIV disease (Stages 2, 3 or 4 of WHO HIV clinical staging)
☐ Asymptomatic patient, CD4 < 350 cells/mm^3
Indications to discontinue
☐ CD4>350 cells/mm^3
☐ Severe anemia (Hgb<7g/dL) at least for 3 months
☐ Severe thrombocytopenia (platelet < 50,000 cells/mL)
☐ Severe Neutropenia (Neutrophil <750 cells/mL)
☐ 1st trimester of pregnancy
Dose:
☐ 960 mg/day
Contraindications
• Sulfa allergy
• First trimester of pregnancy
• Breast feeding mothers during the 1st 6 weeks
• Renal insufficiency (Creatinine >1.5 mg/dL)
• Hepatic diseases (SGPT>115 UI/L for males, 90 UI/L for females)
• Bone marrow suppression
☐ Severe anemia (Hgb < 7g/dL)
☐ Severe Neutropenia (Neutrophil < 750 cells/mm^3)
☐ Severe thrombocytopenia (platelet < 50,000 cells/ mm^3)
Drug interactions
• Zidovudine
• Phenytoin
• Digoxin
Patient monitoring
♦ CD4 count every 3 months
♦ CBC every 3 months
♦ Creatinine every 3 months

Table 1: Drug use evaluation criteria for CPT for patients living with HIV/AIDS [12,13].

Results

A total of 267 medical charts of patients living with HIV/AIDS fulfilling all inclusion criteria were identified and reviewed. The mean age of the patients was 35.19 years ranging from 19 to 60 years. Male patients accounted 126 (47.2%) and females were 141 (52.8%). Five patients were in their first trimester of pregnancy and one patient was breast feeding in her first six weeks postpartum. Most (152, 56.9%) of the patients were from Mekelle town even though around one-fourth of the patients' residential address is not documented. Based on the documented values, most of the patients were orthodox in religion (166, 62.2%), married (83, 31.1%) and primary level in education (68, 25.5%) (Table 2).

Among the 267 patients whose charts were reviewed, ten patients were not taking cotrimoxazole prophylaxis and all these ten patients were taking ART; the total number of patients on ART being 256 (95.9%). Nearly one-third of the patients were with a CD4 count <100 cells/mm^3 (87, 32.6%) and nearly half of the patients were with a WHO clinical stage III (134, 50.2%). Five patients were taking zidovudine, phenytoin, or digoxin concomitantly with cotrimoxazole. Seven (2.6%) of the patients were documented to be allergic to sulfa drugs; but two of them were on cotrimoxazole prophylaxis. All patients on CPT were taking 960 mg daily. CD4 count was monitored every three months for most of the patients (257, 96.3%) (Table 3).

Among all of the patients whose charts were reviewed, the use of cotrimoxazole prophylaxis therapy was found to be appropriate in 255 (95.5%) and inappropriate in 12 (4.5%) of the patients (Figure 1). Among these 12 patients, 3 patients were candidates for CPT but not taking it. The rest 9 patients were on CPT but not candidates for CPT based on their clinical condition (Figure 2).

Demographic variables		Count	Percent
Sex of the patient	Male	126	47.2%
	Female	141	52.8%
	Total	267	100.0%
Address of the patient	Mekelle	152	56.9%
	Out of Mekelle	45	16.9%
	Not documented	70	26.2%
	Total	267	100.0%
Religion of the patient	Orthodox	166	62.2%
	Muslim	16	6.0%
	Protestant	5	1.9%
	Other	0	0.0%
	Not documented	80	30.0%
	Total	267	100.0%
Marital status of the patient	Married	83	31.1%
	Single	33	12.4%
	Separated/ divorced/widowed	60	22.5%
	Not documented	91	34.1%
	Total	267	100.0%
Educational status of the patient	Illiterate	41	15.4%
	Read and write	18	6.7%
	Primary	68	25.5%
	Secondary	30	11.2%
	Tertiary	19	7.1%
	Not documented	91	34.1%
	Total	267	100.0%
Occupation of the patient	Employed	26	9.7%
	Laborer	29	10.9%
	Student	2	.7%
	Merchant	20	7.5%
	Other	68	25.5%
	Not documented	122	45.7%
	Total	267	100.0%

Table 2: Demographic characteristics of patients living with HIV/AIDS in Ayder referral hospital ART clinic, January, 2012.

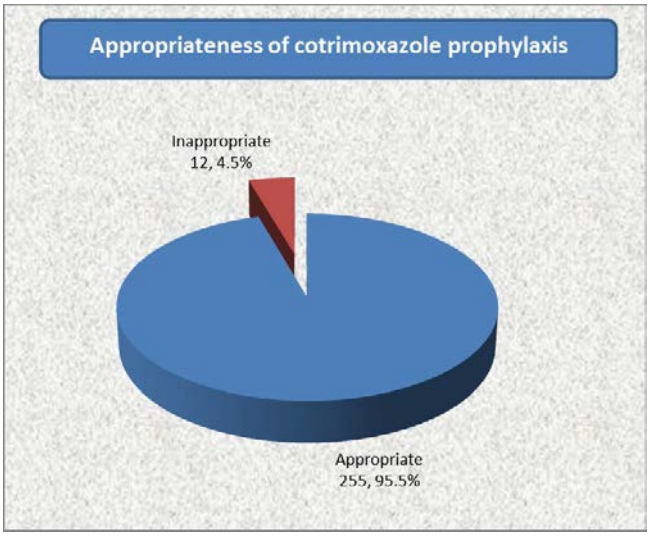

Figure 1: Appropriateness of cotrimoxazole prophylaxis therapy among patients living with HIV/AIDS in Ayder referral hospital ART clinic, January, 2012.

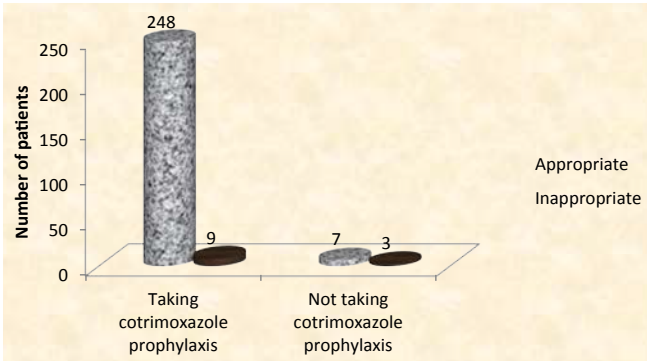

Figure 2: Use of cotrimoxazole prophylaxis therapy and its appropriateness among patients living with HIV/AIDS in Ayder referral hospital ART clinic, January, 2012.

Among variables tested for association using binary logistic regression, sex of the patient, CD4 count of the patient and WHO clinical stage of the patient were found significantly associated with the appropriateness of cotrimoxazole prophylaxis therapy. Female patients were 4.733 times (95% C.I=1.017-22.031) more likely to take inappropriate cotrimoxazole prophylaxis than male patients. Similarly, patients with CD4 count of 350-500 cells/mm^3 and >500 cells/mm^3 were 28.667 (95% C.I=2.263-363.162) and 43.000 (95% C.I=1.925-960.423) times more likely to receive inappropriate cotrimoxazole prophylaxis respectively. On the contrary, the odds of receiving inappropriate cotrimoxazole prophylaxis therapy was 87.1% times (COR=0.129, 95% C.I=0.026-0.646) lesser in patients who were WHO clinical stage IV as those who were stage I (Table 4). But, in multivariate analysis, none of the variables were found to be significantly associated with the use of cotrimoxazole prophylaxis therapy.

Discussion

Drug therapy is considered to be a major component of patient management in health care setting including primary health care. Although the benefits acquired by patients from pharmacological interventions are valuable, the risk of drugs and consequences of inappropriate use cannot be overlooked [10]. Therefore, it is clear that Patients who are candidates for Cotrimoxazole Prophylaxis Therapy (CPT) should be initiated and monitored appropriately in order to assess their progresses as a result of prophylaxis to look clinical outcomes and ADRs and initiate appropriate management. Monitoring of patients on CPT also enables practitioners to assess patients' adherence to their medication and discontinue the drug when the CD4 count is restored to the recommended level.

In our current study, all of the patients who were on CPT were taking cotrimoxazole 960 mg daily. This result was found to be consistent with the study result of other studies in Ethiopia [12-15]. In contrast, our study finding was much higher than a study result from Hawassa referral hospital in which only 87% of the patients were taking the appropriate cotrimoxazole regimen [10].

It was also noted from the present study that almost half (50.2%) of the patients were patients under the category of WHO clinical stage III and stage II accounted the least (12.0%) (Table 3). In comparison, it was noted that there were no patients at WHO clinical stage I in a study conducted at Hawassa [10].

In our current study five patients (1.95%) were taking cotrimoxazole

Clinical variables		Taking cotrimoxazole prophylaxis					
		Yes		No		Total	
		Count	Percent	Count	Percent	Count	Percent
CD4 count of the patient	<100	86	33.5%	1	10.0%	87	32.6%
	100-150	58	22.6%	3	30.0%	61	22.8%
	150-200	50	19.5%	2	20.0%	52	19.5%
	200-350	52	20.2%	4	40.0%	56	21.0%
	350-500	8	3.1%	0	0.0%	8	3.0%
	>500	3	1.2%	0	0.0%	3	1.1%
WHO stage of the patient	I	33	12.8%	6	60.0%	39	14.6%
	II	30	11.7%	2	20.0%	32	12.0%
	III	133	51.8%	1	10.0%	134	50.2%
	IV	61	23.7%	1	10.0%	62	23.2%
Taking ART	Yes	246	95.7%	10	100.0%	256	95.9%
	No	11	4.3%	0	0.0%	11	4.1%
Taking zidovudine	Yes	2	0.8%	0	0.0%	2	0.7%
	No	255	99.2%	10	100.0%	265	99.3%
Taking phenytoin	Yes	2	0.8%	0	0.0%	2	0.7%
	No	255	99.2%	10	100.0%	265	99.3%
Taking digoxin	Yes	1	0.4%	0	0.0%	1	0.4%
	No	256	99.6%	10	100.0%	266	99.6%
Severe anemia (Hgb<7g/dl)	Yes	4	1.6%	0	0.0%	4	1.5%
	No	122	47.5%	5	50.0%	127	47.6%
	Not documented	131	51.0%	5	50.0%	136	50.9%
Severe neutropenia (<750 cells/mm^3)	Yes	0	0.0%	0	0.0%	0	0.0%
	No	1	0.4%	0	0.0%	1	0.4%
	Not documented	256	99.6%	10	100.0%	266	99.6%
Severe thrombocytopenia (<50000 cells/mm^3)	Yes	1	0.4%	0	0.0%	1	0.4%
	No	1	0.4%	0	0.0%	1	0.4%
	Not documented	255	99.2%	10	100.0%	265	99.3%
Renal insufficiency (Cr> 1.5mg/dl)	Yes	0	0.0%	0	0.0%	0	0.0%
	No	49	19.1%	3	30.0%	52	19.5%
	Not documented	208	80.9%	7	70.0%	215	80.5%
Hepatic disease (SGPT>115UI/L for males, 90UI/L for females)	Yes	2	0.8%	0	0.0%	2	0.7%
	No	99	38.5%	4	40.0%	103	38.6%
	Not documented	156	60.7%	6	60.0%	162	60.7%
Sulfa allergy	Yes	2	0.8%	5	50.0%	7	2.6%
	No	242	94.2%	2	20.0%	244	91.4%
	Not documented	13	5.1%	3	30.0%	16	6.0%
First trimester of pregnancy	Yes	4	1.6%	1	10.0%	5	1.9%
	No	128	49.8%	6	60.0%	134	50.2%
	Not documented	2	0.8%	0	0.0%	2	0.7%
	Male	123	47.9%	3	30.0%	126	47.2%
Breast feeding mother during the first 6th weeks	Yes	1	0.4%	0	0.0%	1	0.4%
	No	129	50.2%	7	70.0%	136	50.9%
	Not documented	4	1.6%	0	0.0%	4	1.5%
	Male	123	47.9%	3	30.0%	126	47.2%
CD4 count every 3 months	Yes	248	96.5%	9	90.0%	257	96.3%
	No	4	1.6%	0	0.0%	4	1.5%
	Not documented	5	1.9%	1	10.0%	6	2.2%
CBC every 3 months	Yes	1	0.4%	0	0.0%	1	0.4%
	No	1	0.4%	0	0.0%	1	0.4%
	Not documented	255	99.2%	10	100.0%	265	99.3%
Creatinine every 3 months	Yes	0	0.0%	0	0.0%	0	0.0%
	No	1	0.4%	0	0.0%	1	0.4%
	Not documented	256	99.6%	10	100.0%	266	99.6%

Table 3: Clinical characteristics of patients living with HIV/AIDS in Ayder referral hospital ART clinic, January, 2012.

with digoxin, phenytoin or zidovudine which can potentially put the patients on severe harm. This is in line with the national drug use evaluation for CPT threshold, which is 95%. But only zidovudine was found to be administered concomitantly with cotrimoxazole in a study conducted at Jimma University specialized hospital in which 18 patients (5.6%) were taking them together. Four (1.6%), 1 (0.4%), 2 (0.8%) and 2

		Appropriateness of cotrimoxazole prophylaxis		COR[§] (95% CI[¥])
		Appropriate	Inappropriate	
Sex of the patient	Male	124	2	1.00
	Female	131	10	4.733 (1.017-22.031)*
Address of the patient	Mekelle	147	5	1.00
	Out of Mekelle	44	1	0.668 (0.076-5.871)
	Not documented	64	6	2.756 (0.812-9.360)
Religion of the patient	Orthodox	160	6	1.00
	Muslim	16	0	0.00
	Protestant	4	1	6.667 (0.643-69.067)
	Not documented	75	5	1.778 (0.526-6.010)
Marital status of the patient	Married	79	4	1.00
	Single	33	0	0.00
	Separated/divorced/widowed	59	1	0.335 (0.036-3.073)
	Not documented	84	7	1.646 (0.464-5.839)
Educational status of the patient	Illiterate	40	1	1.00
	Read and write	17	1	2.353 (0.139-39.844)
	Primary	68	0	0.00
	Secondary	29	1	1.379 (0.083-22.973)
	Tertiary	17	2	4.706 (0.399-55.447)
	Not documented	84	7	3.333 (0.397-28.017)
Occupation of the patient	Employed	25	1	1.00
	Laborer	29	0	0.00
	Student	2	0	0.00
	Merchant	20	0	0.00
	Other	64	4	1.563 (0.166-14.670)
	Not documented	115	7	1.522 (0.179-12.927)
CD4 count of the patient	<100	86	1	1.00
	100-150	57	4	6.035 (0.658-55.386)
	150-200	50	2	3.440 (0.304-38.904)
	200-350	54	2	3.185 (0.282-35.980)
	350-500	6	2	28.667 (2.263-363.162)*
	>500	2	1	43.000 (1.925-960.423)*
WHO stage of the patient	I	31	8	1.00
	II	30	2	0.258 (0.051-1.317)
	III	134	0	0.00
	IV	60	2	0.129 (0.026-0.646)*
Taking ART	Yes	244	12	1.00
	No	11	0	0.00
CD4 count every 3 months	Yes	246	11	1.00
	No	4	0	0.00
	Not documented	5	1	4.473 (0.481-41.612)

Table 4: Association of factors affecting use of cotrimoxazole prophylaxis among patients living with HIV/AIDS in Ayder referral hospital ART clinic, January, 2012.

(0.8%) patients with severe anemia, severe thrombocytopenia, hepatic disease and sulfa allergy were taking cotrimoxazole (Table 3).

It was revealed that, among parameters used for follow up evaluation, CD4 count was checked every three months for 257 (96.3%) of the patients; only 6 (2.2%) were found to be not documented. In comparison, only 28 (46.7%) of the patients had CD4 count for follow up evaluation in Jimma University specialized hospital [12]. On the other hand, 265 (99.3%) and 266 (99.6%) of the patients were found to be without any documentation about the status of CBC and creatinine respectively (Table 3). This was in line with a study result of Jimma in which monitoring for adverse reactions during follow-up visits was not consistently done for all patients [12]. This indicates that, the usual parameter for monitoring cotrimoxazole prophylaxis was CD4 count of the patient. This could be due to the fact that our practitioners more acquainted with effectiveness of the drug therapy and left the issue of drug therapy safety behind because the other parameters left not documented were parameters aiming at the safety of cotrimoxazole.

As per our current study, 12 (4.5%) of the patients were either taking cotrimoxazole prophylaxis without indication and/or not taking it even though they were with right indication to be put on CPT. Among these patients, 3 patients were candidates for CPT but not taking it. The rest 9 patients were on CPT but not candidates for CPT based on their clinical condition (Figures 1 and 2). This might put the health care system to incur extra costs for those patients who were not indicated to use but actually the drug on top of the unwanted side effects of the drug that might occur on the patient without any clinical relevance. In addition, such types of practices might lead to the development of resistant strains as cotrimoxazole is a broad spectrum drug that is

used widely for other disease states. In contrast, only 108 (45.9%) of patients eligible for Cotrimoxazole Prophylactic Therapy (CPT) and were actually taking cotrimoxazole prophylactic therapy in a study conducted to evaluate HIV/AIDS clinical care quality in North West Ethiopia [16]. This could be due to the low patient load in our study set up paving a way for the practitioners to get ample time to evaluate and provide standardized care for the patients as our referral hospital was inaugurated only around four years back. On top of that, it could also be due to increased awareness and communication of both national and WHO guidelines.

In the present study, sex of the patient, CD4 count of the patient and WHO clinical stage of the patient were found to be significantly associated with the appropriateness of cotrimoxazole prophylaxis therapy. Female patients and patients with CD4 count of 350-500 cells/mm^3 and >500 cells/mm^3 (compared with a CD4 cell count <100 cells/mm^3) were more likely to receive inappropriate cotrimoxazole prophylaxis respectively. On the contrary, the odds of receiving inappropriate cotrimoxazole prophylaxis therapy was lesser in patients who were WHO clinical stage IV as those who were stage I (Table 3). One possible reason for vulnerability of female patients to take inappropriate CPT might be the limited participation and infrequent follow ups because of cultural and psychosocial stigmas which usually undermines the roles and responsibilities of females in the study area. The probable rationale beyond why patients with severe disease stage and low CD4 count were taking appropriate CPT might be due to the fact that the practitioners give due attention to these patients because of the severity of clinical state.

Other studies have also demonstrated female sex and a CD4 cell count that was 100-149 cells/mm^3 or 150-199 cells/mm^3 (compared with a CD4 cell count <100 cells/mm^3) was associated with not receiving appropriate cotrimoxazole prophylaxis in United States [17]. Male gender (Odds Ratio (OR) =1.47) was also found to be significantly associated with increased likelihood of cotrimoxazole prophylaxis from data collected from ten United states HIV primary care sites in the HIV Research Network [18]. But, in study conducted in Africa, predictors of co-trimoxazole use were current CD4 cell count, haemoglobin concentration, BMI and previous WHO stage 3 or 4 events on ART [18,19].

Conclusion

From this study it can be concluded that appropriateness of cotrimoxazole prophylaxis was good (95.5%) among patients living with HIV/AIDS in our study set up even though it was not to the full standard. Some patients were not even taking cotrimoxazole prophylaxis; nearly one-third of the patients were with a CD4 count <100 cells/mm^3; and some few patients were taking potentially interacting drugs concomitantly with cotrimoxazole. All patients on CPT were taking 960 mg daily and CD4 count was monitored every three months for most of the patients. Most of the data relevant for follow up and monitoring were not documented. Inappropriate uses of cotrimoxazole prophylaxis were more likely among female patients, patients with CD4 count >350 cells/mm^3 and patients not at WHO clinical stage IV.

Strengths and Limitations of the Study

The strength of the study was the use of standardized drug use evaluation protocol validated by the Federal Ministry of Health of Ethiopia particularly designed for cotrimoxazole prophylaxis. The limitation of the study could be the cross-sectional design used which might not define the cause- effect relationship of the factors happened to be associated with the use of cotrimoxazole prophylaxis and the use of only quantitative data without triangulating with qualitative due to resource shortage.

Implications of the Study Findings

Based on the study findings, the health care providers should record all patients' medical charts containing appropriate follow up and monitoring parameters, patients with mild disease state should not be overlooked, standard guidelines for cotrimoxazole prophylaxis should be used. The health facility and other stakeholders at large should give due attention to devise a better data documentation and storing system and feedback systems, train professionals on updates of cotrimoxazole prophylaxis therapy, train and/or recruit clinical pharmacists or drug experts in the medical team, integrate pharmacy systems with the clinical service and establish objective drug information service as much as possible. On its top, continued awareness creation and communication of the appropriate use of cotrimoxazole prophylaxis is also required for all health practitioners.

Acknowledgement

The authors would like to thank Ayder Referral hospital ART clinic staffs for giving us the background information of the set up.

Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Anderson PL, Kakuda TN, Fletcher CV (2008) Human Immunodeficiency Virus Infection. In: Pharmacotherapy: A Pathophysiologic Approach. USA: McGraw-Hill Companies Inc.
2. WHO (2009) AIDS epidemic update 2009.
3. Hoffmann C (2006) Opportunistic Infections (OIs). In: HIV Medicine. Flying Publisher.
4. USAID (2010) HIV/AIDS profile in Ethiopia.
5. http://www.africanservices.org/index.php/African-Services-in-Ethiopia/Background-HIV/AIDS-in-Ethiopia
6. American Society of Health System Pharmacists (2008) AHFS drug information 2008.
7. William A, Petri J (2006) Sulfonamides, Trimethoprim-Sulfamethoxazole, Quinolones and Agents for Urinary Tract Infections. In: Goodman & Gilman's the Pharmacological Basis of Therapeutics.
8. Drug Administration and Control Authority of Ethiopia (2010) Standard treatment guideline for general hospitals.
9. World Health Organization (2006) Guidelines on co-trimoxazole prophylaxis for HIV-related infections among children, adolescents and adults: Recommendations for a public health approach.
10. Deresse D, Alemayehu T (2009) Evaluation of the use of cotrimoxazole prophylaxis in people living with HIV/AIDS in Hawassa referral hospital: A retrospective evaluation. Asian J Med Sci 1: 88-90.
11. Central Statistics Agency (2008) Summary and statistical report of the 2007 population and census: Population size by age and sex.
12. Diriba L, Worku F, Girma T (2008) Evaluation of prophylactic use of cotrimoxazole for people living with HIV/AIDS in Jimma university specialized hospital, Southwest Ethiopia. Ethiop J Health Sci 18: 59-64.
13. Federal Ministry of Health (2006) Guideline for cotrimoxazole prophylaxis in HIV/AIDS care and treatment.
14. Geresu B, Misganaw D, Beyene Y (2014) Retrospective evaluation of cotrimoxazole use as preventive therapy in people living with HIV/AIDS in Boru Meda hospital. BMC Pharmacol Toxicol 15: 4.
15. Sisay M, Bute D, Edessa D, Mengistu G, Amare F, et al. (2018) Appropriateness of cotrimoxazole prophylactic therapy among HIV/AIDS patients in public hospitals in Eastern Ethiopia: A retrospective evaluation of clinical practice. Front Pharmacol 9: 727.

16. Alemayehu YK, Bushen O, Muluneh AT (2009) Evaluation of HIV/AIDS clinical care quality: The case of a referral hospital in North West Ethiopia. Int J Qual Health Care 21: 356-362.

17. Teshale EH, Hanson DL, Wolfe MI, Brooks JT, Kaplan JE (2007) Reasons for lack of appropriate receipt of primary pneumocystis jiroveci pneumonia prophylaxis among HIV-infected persons receiving treatment in the United States: 1994-2003. Clin Infect Dis 44: 879-883.

18. Gebo KA, Fleishman JA, Reilly ED, Moore RD; HIV Research Network (2005) High rates of primary mycobacterium avium complex and pneumocystis jiroveci prophylaxis in the United States. Med Care 43: III-23-III-30.

19. Walker AS, Ford D, Gilks CF, Munderi P, Ssali F, et al. (2010) Daily co-trimoxazole prophylaxis in severely immunosuppressed HIV-infected adults in Africa started on combination antiretroviral therapy: an observational analysis of the DART cohort. Lancet 375: 1278-1286.