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Incidence of Opportunistic Infections among Adult HIV Positive People Receiving Co-trimoxazole Prophylaxis

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ABSTRACT

In Ethiopia, Co-trimoxazole prophylaxis therapy (CPT) used to prevent opportunistic infections among people living with HIV is the standard of practice; however incidence of opportunistic infection and their predictors are rarely documented in the country. This was a retrospective follow up study to describe the incidence and predictors of opportunistic infections among 244 adults receiving CPT. Participants were followed for a median time of 72 weeks. During a study period a total of 53opportunistic infections were recorded; making the overall incidence rate 23.9/100 person-years. High incidence of opportunistic infections is likely to occur if: the clients were married (adjusted hazard ratio (AHR) 1.965;(95% CI: 1.109, 3.451), had history of tuberculosis treatment (AHR: 2.34(95% CI:1.05, 5.24)), patients who are indicated for CPT because of both clinical and WHO clinical staging criteria(AHR 2.418 (95% CI:1.02, 5.72),and had poor adherence to CPT (AHR, 2.11 (95% CI: 1.19-3.72)). Eventhough adherence is non-substitutable strategy to prevent opportunistic infection, the cohort of HIV patients failed to adhere to CPT, which in turn resulthigh incidence of opportunistic infections among them, therefore improving adherence as guideline should be a priority to prevent OIs among people living with HIV in the study region.

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1. INTRODUCTION

Human Immune Virus (HIV) is one of the world health and development challenges, and more than 34 million people are living with HIV and around million new infections occurred in the year 2011 [1],[2]. Regarding prevention and control of HIV/AIDS Ethiopia is showing remarkable results with 1.5 % of adult HIV prevalence [3]. However, opportunistic infections (OIs) continue to be a major cause of morbidity and mortality for people living with HIV in the country [4],[5]. Prophylaxis against common OIs is a recommended strategy to improve the quality of life of people infected with HIV through preventing early morbidity and mortality [4],[6].

Co-trimoxazole (a combination of sulfamethoxazole and trimethoprim) is a broad spectrum safe, well tolerated, low-cost, and widely available antimicrobial agent used as standard care for people living with HIV and also used in primary health care to treat various infections [6]-[10]. The Ethiopian national guideline recommends CPT for people living with HIV if one of the following conditions is fulfilled: 1. WHO clinical stage 2, 3 or 4 in the absence of CD4 count, 2. WHO clinical stage 3 or 4 irrespective of CD4

level, 3. CD4 count ≤ 350 cell/mm^3, 4. TB-HIV co-infected patient or 5. patient with a documented prior history of Pneumocystis Carini Pneumonia (PCP) [6],[7].

Studies confirmed that CPT significantly reduces morbidity and mortality in HIV positive people even in the area where the drug is highly resisted or malaria is endemic [9]-[17]. Nevertheless, the global implementation of CPT has been rated as sub-optimal [14],[18]. In Ethiopia CPT is taking place in 2006 but little has been known about the incidence of common OIs such as bacterial pneumonia, diarrhea disease, septicemia, enteritis, malaria or PCP among HIV positive people on CPT [4]. This study aimed to describe the incidence of common OIs among HIV positive people on CPT at Arba Minch Hospital since 2003 which provides care to cohorts of people with HIV.

2. RESEARCH METHOD

2.1. Study setting

This study was conducted at Arba Minch Hospital (AMH) which is located at Arba Minch town, Gamo Gofa Zone, South Ethiopia which is 500 km in south of Addis Ababa. The hospital provides comprehensive HIV care to all HIV positive people within Gamo Gofa zone or out. It is also one of few Ethiopian hospitals who started CPT to patients at the first time. The services are provided by multidisciplinary team which includes physicians, nurses, public health professionals, laboratory technologists, pharmacists, data clerks and volunteer who are adherence supporters. In case of illness, the hospital treats patients according to the national guideline for HIV management.

2.2. Patient selection

All adult patients who were registered from Sep 1, 2008 up to Aug 30, 2011 in chronic HIV care clinic plus who had both medical record chart and ART follow up chart were included in the study. This period was selected in order to have the recent possible 72 week (this period is considered the time period in which CPT is effective) follow up time [19]. Out of 768 patients registered within the given period, 244 patients become eligible and followed for maximum of 72 weeks (1.38 person years) based on the time when CPT was initiated as shown in Figure 1.

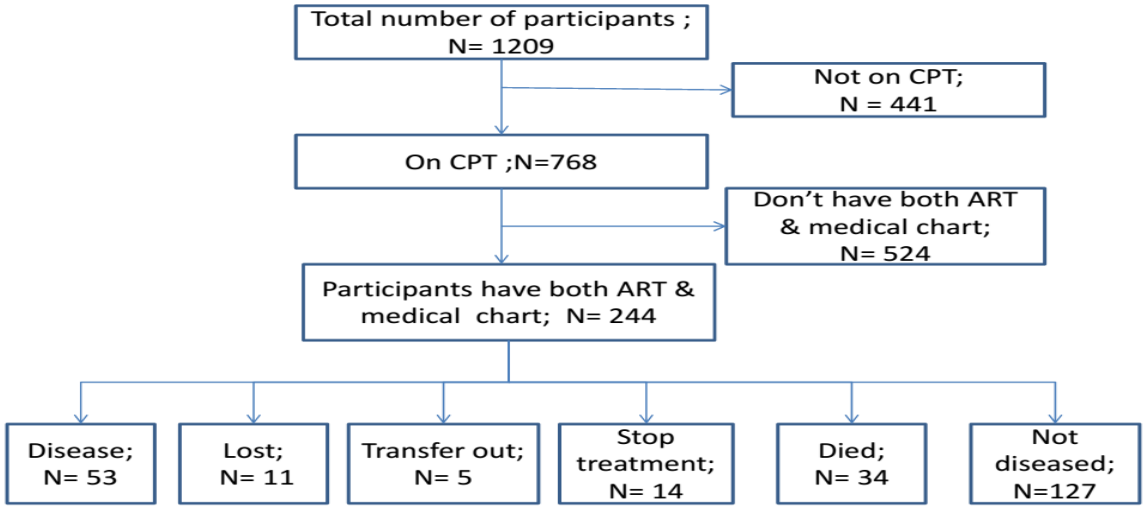

Figure 1. Participant inclusion flowchart, Arba Minch Hospital, Ethiopia

2.3. Study design and data collection

A retrospective follow up study was used. A structured and pretested data collection checklist was prepared and used to collect demographic, baseline clinical and hematological characteristics and follow up condition of the patients. Two health professionals who had bachelor degree with a special training for HIV care were selected to review records.

2.4. Statistical analysis

Data were entered in to Epinfo 7.1.0 and analyzed using the Statistical Package for the Social Science (SPSS) software package, version 20. The main outcome variables are morbidity (malaria, diarrhea, pneumonia, PCP and enteritis) and time to occurrence of morbidity within 72 weeks.

Survival time was calculated in weeks between the date of CPT initiation and (1) the date of event (morbidity), (2) the date transferred out (TO), (3) the date of the first missed appointment for lost cases, and (4) the date on which the patient completed the 72 weeks of follow up. The Kaplan Meier and Log rank test used to estimate survival probability and compare survival curves respectively. The Cox proportional hazard model was used to assess the relationship between baseline variables and morbidity after checking proportional hazard assumption using global goodness-of-fit test (Schoenfeld's method).

2.5. Ethical approval

Institutional ethical approval was obtained from the research and publication committee ethical review board of university of Gondar, Institute of Public Health. We obtained written permission from Gamo Gofa zone administration and AMH.

3. RESULTS AND ANALYSIS

3.1. Participant profile

Between September, 2008 and August 2011, 1209 patients were enrolled in chronic ART clinic, of them 768 patients were on CPT but only 244 patients who have both medical record and ART follow up chart were included in the study (Figure 1).

3.2. Description of study subject and incidence of OIs

Out of 244 patients 159 (57%) were female with mean age of 34.1years (SD: 10.1) and most of them were unemployed and urban dweller as shown in Table 1.

Table 1. Demographic characteristic of participants at Arba Minch Hospital

Character		Number	Percent
Sex	Male	105	43
	Female	139	57
Occupation	Employed	52	21.3
	Self-employed	61	25
	Unemployed	131	53.7
Education level	No formal education	54	22.1
	Primary	90	36.9
	Secondary	76	31.1
	Tertiary	24	9.8
Residence	Urban	207	84.8
	Rural	37	15.2
Family size	1 -3	114	46.7
	>3	130	53.3
Age group	< or = 23	27	11.1
	24 – 33	105	43
	34 – 43	76	31.1
	>or = 44	36	14.8
Marital status	Married	142	58.2
	Other	102	41.8

Participants contributed for 221.327 person-years (PY) of follow up and average period of follow-up was 47.17 (SD± 28.7) weeks. The median CD4 count was 157 (IQR: 79 - 241) cells/ mm^3. Of the 244 participants 161 (66%) had CD4 < 200 cells/mm^3, 226 (92.6%) were on ART and 63 (25.8%) had poor adherence to drugs, of which 22(34.9%) developed OI.

During the follow up period, 53 cases were recorded as having OIs, 11 were lost to follow up, 5 transferred out, 14 stopped treatment, 34 died and 127 did not develop event during follow up. Fifty three cases make the overall incidence rate 23.9/100 PY (95% CI; 18.3, 29.5) of them 37% were malaria, 24.5% were pneumonia, 16.9% were enteritis, 13.2% were diarrhea and 3.8% were PCP. Two or more disease episodes were reported in 2 (3.8%) clients and only 3 (5.7%) patients were admitted to hospital.

3.3. Association of OIs with baseline and follow up characteristics

Overall cumulative probability of survival beyond 72 weeks was 0.74 and the median survival time was 59.7 (95% CI: 56.2, 62.5).Compare patients with TB treatment history, adherence to CPT, criteria to initiate CPT and marital status, had significant association with survival time (Figure 2-5 below respectively). Baseline CD4 count [CHR 0.831 (95% CI: 0.47, 1.48)] and WHO clinical stages [CHR 1.49 (95% CI: 0.85, 2.62)] had no association with survival time.

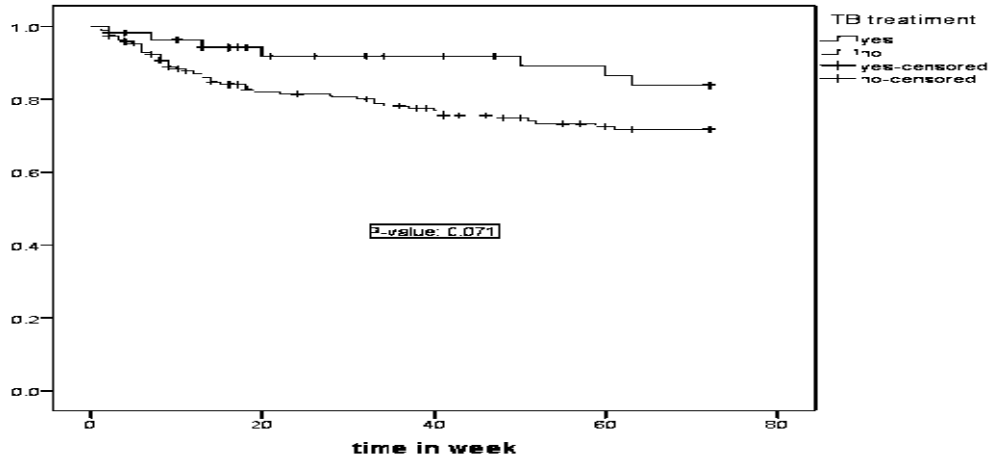

Figure 2. Kaplan–Meier curve of probability of remaining free from OIs over time, by TB treatment history

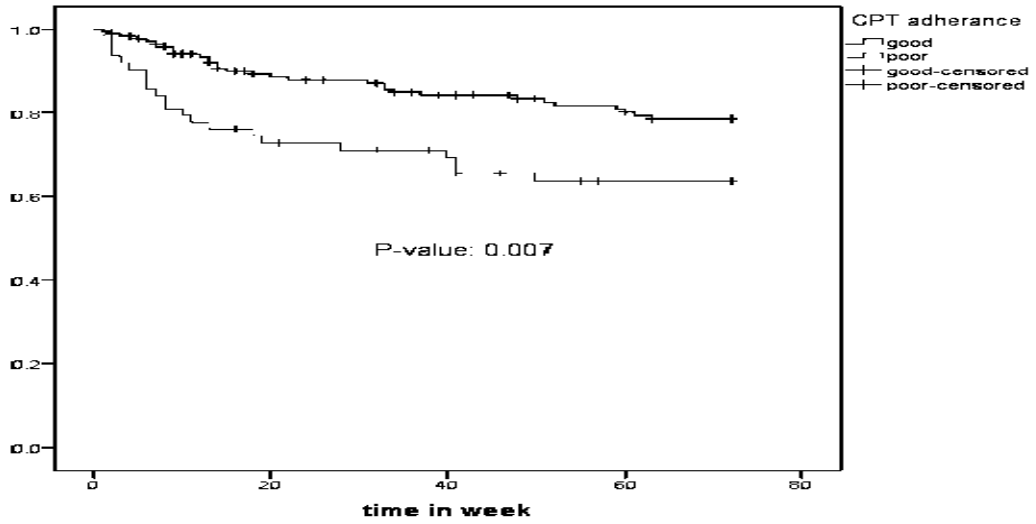

Figure 3. Kaplan–Meier curve of probability of remaining free from OIs over time, by level of adherence to Co-trimoxazole prophylaxis

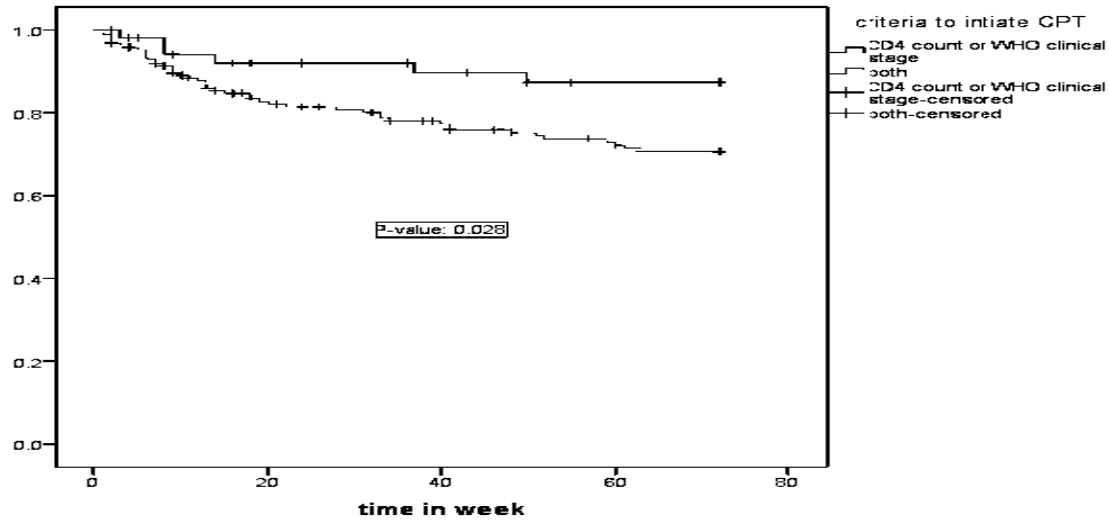

Figure 4. Kaplan–Meier curve of probability of remaining free from OIs over time, by criteria to initiate Co-trimoxazole prophylaxis

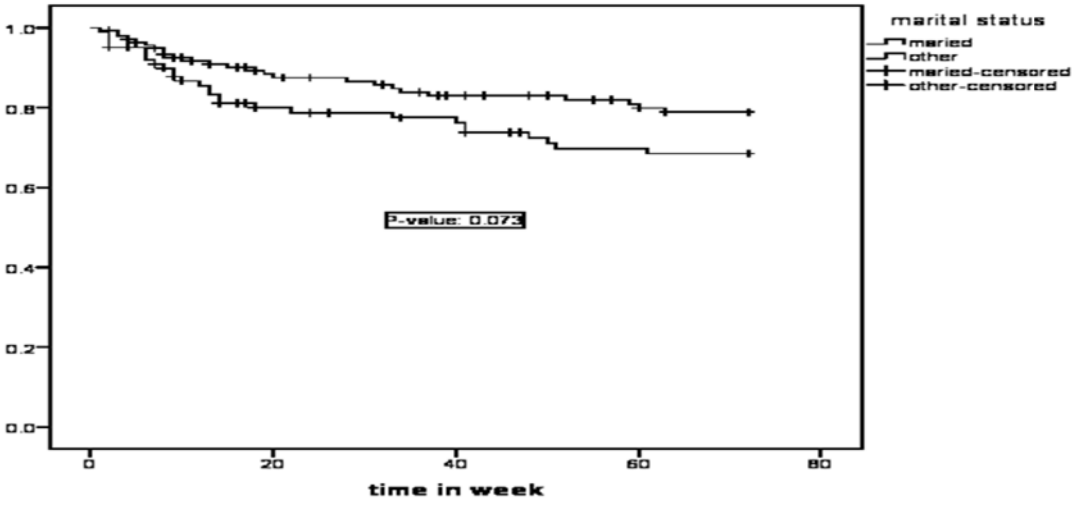

Figure 5. Kaplan–Meier curve of probability of remaining free from OIs over time, by marital status

Multiple variable cox regression analysis revile that adherence to CPT was an important predictor of risk for opportunistic infection, CHR was 2.087 (95% CI: 1.208, 3.604) for patients with poor adherence to CPT and AHR was 2.108 (95% CI1.194-3.72) as shown in Table 2.

Table 2. Predictors of opportunistic infections among HIV positive patient

Characteristics	Number	PY	Event	CHR (95% CI)	AHR (95% CI)
Education					
No formal education	54	44.44	16	1	1
Primary	90	87.21	19	0.64 (.33-1.24)	0.647 (0.329, 1.271)
Secondary	76	67.54	16	0.67 (.33-1.34)	0.677 (0.335, 1.368)
Tertiary	24	22.13	2	0.26 (.06-1.13)	0.252 (0.057, 1.113)
Marital status					
Married	142	131.88	25	1	1
Not married	102	89.44	28	1.63 (.95-2.79)	1.965 (1.109, 3.451)
Residence					
Urban	207	186.23	41	1	1
Rural	37	35.10	12	2.09 (1.21-3.60)	1.244 (0.635, 2.436)
Family size					
1-3	114	106.88	21	1	1
4-12	130	114.44	32	1.42 (0.81-2.45)	1.74 (0.96, 3.16)
Weight	244	221.33	53	0 .99 (.95-1.00)	0.992 (0.963, 1.020)
WHO stage					
I & II	104	102.13	19	1	1
III & IV	140	119.19	34	1.49 (0.85, 2.62)	1.35 (0.69, 2.66)
CD4 count					
< 200	161	139.33	36	1	1
≥ 200	83	82	17	.831 (.47, 1.48)	0.678 (.36, 1.26)
TB treatment					
Yes	55	53.08	7	1	1
NO	189	168.25	46	2.04 (0.92, 4.53)	2.34(1.05, 5.24)
Functional status					
Working	159	149.67	40	1	1
Ambulatory & bedridden	85	71.65	13	0.66 (0.35, 1.24)	0.645 (0.337, 1.236)
Criteria to indication CPT					
CD4 count/ WHO stage	51	55.5	6	1	1
Both	193	165.83	47	2.6 (1.07, 5.84)	2.418 (1.02, 5.72)
Adherence					
Good	181	165.63	31	1	1
Poor	63	55.69	22	2.09 (1.21-3.60)	2.108 (1.19-3.72)

4. DISCUSSION

Here we describe incidence of OIs by demographic, baseline clinical condition and follow up result of 244 HIV patients receiving Co-trimoxazole prophylaxis and followed up for median 59.7 weeks in Arba Minch hospital. In these patients diagnosis and treatment heeled according to the national standard of treatment but some diagnosis were conducted syndromeically may exaggerate incidence rate.

This study indicated that, the overall incidence rate of OIs in patients on CPT was 23.9/100 PY (95% CI; 18.3, 29.5), which usually occurred within the first 22 weeks primarily due to malaria and pneumonia, it is higher compared to observational study from South Africa has reported incidence rate 0.48/100 person month [20] but lower than finding from Coˆ te d'Ivoire [21]. Low incidence rate observed in present study might be due to considering only major Co-trimoxazole preventable infections. In our study malaria was major type of OIs which is greater than findings from Coˆ te d'Ivoire (3.9/100 PY) and Uganda (3.7/100PY) [21],[22], this greater rate of malaria probably because of two things, the first one is the place is very endemic area for malaria and the second reason is by the time of follow up any febrile case was treated as malaria using syndromic approach. But the finding is consistent with finding from Malawi [23]. The rate of pneumonia is higher compared to the result from Coˆ te d'Ivoire 2.7/100 PY [21] but lower compared with finding from Malawi [23].Incidence rate of diarrhea was higher in Uganda and Malawi 10.2/100 PY and 37/100 PY respectively [22],[23].

In this study, patients having poor adherence had a significantly high risk of developing OIs than patients having good adherence (AHR was 2.108 95% CI1.194-3.72); this high rate of infection in poorly adhere patients is might be inconsistence or inappropriate use of drug reduce the efficacy. In this study, marital status of patients significantly affect incidence of OIs; unmarred patients are nearly two times at risk of developing Co-trimoxazole preventable OIs; less support for adherence for unmarried patients might increase risk of developing OIs. Patients initiated CPT if they meet both WHO clinical staging and CD4 count more like develop OIs than patients initiated by ether of the criteria; this might be patients started if they meet both criteria were in advanced stage of disease status.

In this study patients categorized in to two baseline CD4 count (CD4 count < 200 cell/mm^3 and CD4 ≥ 200 cell/mm^3) were equal likely affected by morbidity; this finding is consistent with findings from other studies [10],[14],[17],[24],[25]. This finding reveal that patients by baseline WHO clinical stage (WHO stage

1 or 2 and WHO stage 3 or 4) equally at risk of developing OIs; this finding is consistent with results from other studies [9],[17],[24].

Limitation of the study

Because of the retrospective nature of the data collection, we relied on the available information for the number and types of diseases reported during follow up. Some of the diagnoses were presumptive as there was limited capacity to make definite diagnosis.

5. CONCLUSION

Incidence rate of OIs among HIV positive people treated at Arba Minch Hospital ART clinic was high. More importantly, patient poor adherence to CPT was associated with high risk of incidence rate of OIs. The need to strengthen the strategies to enhance adherence to CPT is strongly recommended. Future research should be done using prospectively design to identify another cause for high incidence rate of OIs and proper time for initiation of CPT.

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AUTHORS' CONTRIBUTIONS

YT designed the study, supervised data collection, analyzed the data and drafts the manuscript. DJ established the HIV cohort at the hospital. YY participated in design of the study and interpretation of the data. AT, critically reviews the paper and re-structured the manuscript. All authors read and approved the final manuscript.

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