Prevalence of Opportunistic Infections and Associated Factors among HIV Positive Patients taking Anti-Retroviral Therapy in DebreMarkos Referral Hospital, Northwest Ethiopia

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Abstract

Introduction: Opportunistic infections (OIs) are infections that are more frequent or more severe because of immune-suppression in HIV-infected persons, and they are the major clinical manifestation of HIV patients. They indirectly affect the natural history of HIV disease. Many studies concentrated on drug adherence, survival and other aspects of the diseases but limited studies are evident on OIs after Anti-Retroviral Therapy (ART) initiated. So this study was conducted to assess the prevalence of opportunistic infections and associated factors among HIV positive patients taking ART in DebreMarkos referral hospital, Northwest Ethiopia.

Methods: A cross sectional study design was conducted among HIV patients taking ART from 5 to 7 years. The study was conducted in DebreMarkos referral hospital among 423 patients. The data was entered in EPI data version 3.1 and analysis with done by using Statistical Package for Social Sciences (SPSS) version 16.0. Bivariate and multivariate analysis was performed to determine the association of each independent variable with occurrence of OIs. 95% CI and p-value less than 0.05 were considered as significant association.

Result: Majority, 241(57%) of the study participants were female patients. The mean age of the study participants was 35.17, with standard deviation of +/- 9.481 years. A total of 181 OIs were observed from the study participants during the study period. The commonest type of OIs were oral candidiasis 50(11.8%), followed by chronic diarrhea for greater than one month, 42(9.9%) and tuberculosis, 41(9.7%). The factors associated with OIs were: Age less than 40 years old was protective (AOR=0.47, 95%CI=0.25, 0.90); baseline WHO stages of III&IV was risk for development of OI by five times(AOR=4.759, 95%CI=2.163, 10.469); those who used to chew khat was at risk of developing OI almost five times more likely than those who did not chew (AOR=4.733, 95%CI=1.185, 18.915); patients with good ART adherence were less likely to develop OI compare to their counter parts (AOR=0.163, 95%CI=0.051, 0.522); current hemoglobin level of ≥ 10 g/dl was protective (AOR=0.313, 95%CI=0.162, 0.605); and recent weight of <60 kg (AOR=3.658, 95%CI=1.656, 8.078).

Conclusion and recommendation: The prevalence of OIs among HIV patients on ART is still high namely oral candidiasis, pathogens that cause chronic diarrhea and tuberculosis. Education on adherence of medications, and use of prophylactic medications for OIs should be given for HIV patients taking ART. Similar studies should be conducted to identify the relation between substance abuse and OIs in HIV patients taking ART.

Keywords: Opportunistic infections; HIV Patients; Anti-retroviral therapy; DebreMarkos Referral Hospital; Ethiopia

Introduction

Opportunistic infections (OIs) are defined as infections that are more frequent or more severe because of immune-suppression in HIV-infected persons, and they are the major clinical manifestation of HIV patients [1,2].

The natural history of HIV disease may be indirectly affected by the occurrence of opportunistic diseases, because HIV viral load increases in patients with acute opportunistic diseases. Survival in people infected with HIV has improved because of an increasingly powerful array of antiretroviral treatments, but neurological symptoms due to co morbidity conditions still remains public health important for HIV infected individuals [3-5].

Severely immune-compromised HIV patients may develop a variety of opportunistic infections that have a significant impact on their well-being, quality of life, health care costs, and their survival [6].

The most common opportunistic diseases in HIV patients are Candida esophagitis, Pneumocystis carinii pneumonia (PCP), disseminated Mycobacterium avium complex (MAC) infection, cytomegalovirus (CMV), Cryptococcus, kaposi sarcoma, herpes zoster, and tuberculosis [2].

The risk for the development of OI in HIV patients depends on exposure to potential pathogens, virulence of the pathogens, the degree of host immunity, and the use of antimicrobial prophylaxis [6]. And majority of these OI are associated with an increased hazard of death in HIV patients. Patients experiencing morbidity from opportunistic diseases may have interruptions in antiretroviral therapy causing more rapid progression of HIV disease. In addition studies found that opportunistic infections cause an up regulation in HIV replication and higher viral loads [2,7-11].

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Drug interactions may occur in patients who are taking antiretroviral therapy and other drugs for supportive care, treatment of opportunistic infections, and immunomodulation, as well as alternative drugs obtained from health care providers other than their primary provider [12].

OIs are one of the major causes of morbidity and mortality in patients with HIV infection throughout the world. Even if potent combination of antiretroviral therapy (ART) has reduced the incidence of OIs for certain patients with access to care, for those patients in the developed and developing world did not have access to care and have OIs [13,14].

So this study was conducted to assess the prevalence of OI and the associated factors for the development of OIs in HIV Positive Patients taking antiretroviral therapy (ART) in DebreMarkos Referral Hospital, Northwest Ethiopia from 2005 to 2013.

Methods

Study area and period

The study was conducted in DebreMarkos Referral Hospital among ART followers in DebreMarkos town, Northwest Ethiopia. DebreMarkos is the capital city of East Gojjam Zone. It is located 300 km away from Addis Ababa, the capital city of Ethiopia, and 265 km from Bahir Dar capital city of Amhara regional state. The study was conducted from patients enrolled to treatment from September, 2005 to January, 2013 from registrations card.

Study design

Cross sectional study design was conducted.

Study population

All adult HIV positive individuals’ record on care and support follow up who had started ART at DebreMarkos Referral Hospital ART clinic from September, 2005 to February, 2008 were traced to the year 2013 in the study.

Sample size determination

Since there was no similar study conducted in the study area, the prevalence of OIs among HIV patient on ART was considered to be 50%-95% confidence interval (CI) and 10% for patients with incomplete data was considered given a final sample size of 423 using single population proportion formula.

Sampling technique

A total 8412 patients were enrolled in ART starting from 2005 to 2013 but about3290 of the patients started ART after 2008 and they were excluded from the study. The main reason patients excluded after 2008 entrance was to follow OI prevalence from patients with a minimum of 5 years and a maximum of 7 years. In addition, transfer out, lost, drops; children’s <15 years old were also excluded since we did not have further information from these patients regarding their OI status and children were excluded because of the interest of the study was for adults only. Patients with initial OIs were not recorded as case for this study. Finally there were 1646 patients that fulfill the inclusion criteria from that a total of 423 were selected by using simple random sampling technique through computer generation number method using their identification number as sampling unit.

Operational definition (taken from ART registration card)

Lost to follow up: Not seen since >/= 1 month < 3 months.

Drop: Lost to follow up for >3 months.

Transfer out: A patient is referred to another health facility for care as evidenced by his/her document.

Adherence

Adherence is defined as good if adherence is >95% (<2 doses of 30 doses or <3 dose of 60 dose is missed) as documented by ART physician; poor if adherence is between 85%-94% (3-5 doses of 30 doses or 3-9 dose of 60 dose is missed) as documented by ART physician; as documented by ART physician.

Opportunistic infections

- Oesophageal candidiasis
- Kaposi’s sarcoma
- Cryptococcal meningitis
- Oral recurrent candida
- Unexplained chronic diarrhoea>1 month
- Unexplained persistent fever >1 month
- Unexplained presumed weight loss >10%
- Pneumocystis jiroveci pneumonia
- Recurrent severe bacterial pneumonia
- Active TB
- Severe bacterial infection (pneumonia, empyema, pyomyositis, meningitis, suspected bacteraemia/septicemia, bone or joint infection)
- Others (anaemia, skin conditions, herpessimplex, toxoplasmosis)

Data processing and analysis

The data was entered in EPI data version 3.1 and analysis was done by using Statistical Package for Social Sciences (SPSS) version 16.0. Prior to the analysis, the whole data was cleaned, coded and entered. The completeness of the data was checked. Bivariate analysis was performed to determine the association of each independent variable with the dependent variable (occurrence of OIs). Variables with P-value less than 0.25 and known associated factors from different literature were included for further analysis using the multivariate analysis. 95% CI and p-value less than 0.05 considered as significant association.

Ethical consideration

Ethical clearance was obtained from Institutional Research Ethics Review Committee (IRERC) of DebreMarkos University, College of Medicine and Health science (Ref. No: HSC/1210/21/05).Then officials at different levels in the study area were communicated through letters from department of public health. Permission was obtained from DebreMarkos Referral Hospital and ART clinic. Confidentiality of the information was assured and privacy of the information was also maintained.

Results

This study assessed the prevalence of and associated factors for OIs. The study included 423 patients HIV Positive Patients who were in ART from 5 to 7 years in DebreMarkos Referral Hospital.
Prevalence of opportunistic infections

A total of 181 OIs were observed from the study participants during the study period. The overall prevalence of OIs among the study participants were 42.8%. From these; 86(61%) of patients had only 1 opportunistic infection during study period, while the prevalence of 2, 3, and 4 OIs per one patient during the study period were 49(34.8%), 5(3.5%), and 1(0.7%) respectively (Table 2). The commonest type of OIs among HIV patients in ART in the current study area were oral candidiasis 50(11.8%), followed by chronic diarrhea for greater than 1 month 42(9.9%) and tuberculosis 41(9.7%). The prevalence

| Characteristics | Frequency | Percentage |
|-----------------|-----------|------------|
| Sex             |           |            |
| Male            | 182       | 43         |
| Female          | 241       | 57         |
| Age             |           |            |
| < 40 years old  | 325       | 76.8       |
| ≥ 40 years old  | 98        | 23.2       |
| Religion        |           |            |
| Orthodox        | 392       | 92.7       |
| Protestant      | 6         | 1.4        |
| Muslim          | 24        | 5.7        |
| Others          | 1         | 0.2        |
| Occupation      |           |            |
| Employed        | 184       | 43.5       |
| Not employed    | 239       | 56.5       |
| Marital status  |           |            |
| Married         | 172       | 40.7       |
| Widowed         | 88        | 20.8       |
| Never married   | 43        | 10.2       |
| Divorced        | 101       | 23.9       |
| Separated       | 19        | 4.5        |
| Educational status |        |            |
| No education    | 122       | 28.8       |
| Primary         | 148       | 35.0       |
| Secondary       | 105       | 24.8       |
| Tertiary        | 48        | 11.3       |
| Place of residence |        |            |
| Rural           | 126       | 29.8       |
| Urban           | 287       | 70.2       |

Variables with a p-value of less than 0.25 from the bivariate analysis and variables with p>0.25 but found to have association with occurrence of OIs among HIV patient taking ART from similar study, were entered to multivariate analysis to identify the significant associated factors for OIs. Accordingly, as described in Table 5, the associated factors for OIs among HIV patient taking ART at p-value less than 0.05 were: Age less than 40 years old were 0.47 times less likely to acquire OI than patients at older ages (COR=0.47, 95%CI=0.29, 0.74), educational status of primary education was preventive compared to non-educated patients (COR=0.590, 95%CI=0.356, 0.978), patients at baseline WHO stages III&IV were at high risk of OI development after ART initiation too, (COR=3.343, 95%CI=3.183, 12.64), patients who used to chew Khat was found to be at risk for OI occurrence (COR=2.30, 95%CI=1.12, 8.06), patients with recent weight of <60 kg were at higher risk of OI (AOR=0.31, 95%CI=0.05, 0.52); patients with recent hemoglobin level of≥10 g/dl were 0.16 times less likely to develop OI after ART started (AOR=0.16, 95%CI=0.05, 0.52); patients with recent weight of <60 kg were at higher risk of OI development than their counter parts (COR=0.31, 95%CI=0.162, 0.61); and patients at older ages were 0.47 times less likely to acquire OI than patients at younger ages (COR=0.47, 95%CI=0.29, 0.74).

Factors associated with OIs among HIV patients taking ART

Bivariate and multivariate analysis was conducted to identify the associated factors for occurrence of OIs among HIV patient taking ART. As described in Table 4; the independent variables were found to have association with occurrence of OIs in bivariate analysis were age less than 40 years old were 0.47 times less likely to acquire OI than patients at older ages (COR=0.47, 95%CI=0.29, 0.74), educational status of primary education was preventive compared to non-educated patients (COR=0.590, 95%CI=0.356, 0.978), patients at baseline WHO stages III&IV were at high risk of OI development after ART initiation too, (COR=3.343, 95%CI=3.183, 12.64), patients who used to chew Khat was found to be at risk for OI occurrence (COR=2.30, 95%CI=1.12, 8.06), good ART adherence was preventive for OI occurrence (COR=0.20, 95%CI=0.09, 0.45), and patients with a base line CD4 count of less than 200 cells/μl were almost double risk of OI development than their counter parts with higher CD4 count at base line (COR=1.91, 95%CI=1.16, 3.14).

Discussion

The current study assessed the prevalence and associated factors of opportunistic infections among HIV Positive Patients. The study found that 141 (33.3%) of HIV patients taking ART had got at least one OI during the study period and overall OIs prevalence of 42.8% with repeated infection. When compared with other similar studies, the prevalence of OIs in the current study area is comparable with a prevalence of 30% [15].

Table 1: Socio demographic characteristics of HIV patients taking Anti-Retroviral Therapy in Debre Markos Referral Hospital, Northwest Ethiopia; 2013 (n=423).

| S.No. | Opportunistic infection | Frequency | Percentage |
|-------|-------------------------|-----------|------------|
| 1.    | 1 opportunistic infection| 86        | 61         |
| 2.    | 2 opportunistic infections| 49        | 34.8       |
| 3.    | 3 opportunistic infections| 5         | 3.5        |
| 4.    | 4 Opportunistic Infections| 1         | 0.7        |
| Total |                         | 141       | 100        |
A study conducted in Taiwan showed that the prevalence of OIs to be 47.6%, which is greater than the current study area [16]. The reason for such difference could be due to the difference in the duration of follow up. The current study followed the study participant for 5 to 7 years while the earlier was for shorter period that may give less chance for observation of OIs. Other study conducted in Nigeria also showed that OI prevalence to be 22.4%, which is below the result for the current study. The reason for such difference could be due to the difference in the socio demographic characteristics, most of study participants in this study were at advanced HIV stage and sample size difference. The current study used a sample of 423, while the study in Nigeria used 354 [17].

From different OIs in HIV patients, the common types of OIs among HIV patients on ART in the current study area were oral candidacies, chronic diarrhea for more than 1 month and tuberculosis. Similar findings were also observed in other studies [16-18]. This might be because of their diagnosis is relatively easy to identify from patients than other OIs.

Factors associated with occurrence of OIs among HIV patients taking ART were also assessed. Accordingly younger age, advanced baseline WHO stage, khat use, ART adherence, recent hemoglobin status, and recent weight were found to be associated factor for OIs occurrence.

**Table 4:** Bivariate analysis variables with occurrence of opportunistic Infections among HIV Positive Patients taking Anti-Retroviral Therapy in Debre Markos Referral Hospital, Northwest Ethiopia; 2013.

A significant association at 95% CI, ** Single includes: Widowed, Never married, Divorced and Separated *** OI prophylaxis include: Cotrimoxazole and/or INH and/or Fluconazole
Patients with age less than 40 year were less likely to develop OIs than their counterparts. A study conducted in India also found that being old people as a predominant factor for OIs [19]. This could be explained by older patients immune get decreased while the viral load gets increased that predispose for opportunistic infections which is not otherwise cause for younger patients in normal condition.

In addition, patients with advanced baseline WHO stages of III & IV were more likely to develop OIs by a factor of 4.8, than those with a base line WHO stage of I & II. Similar finding were also observed in a study conducted in Nigeria showing that advanced WHO clinical stage at baseline to be an independent clinical risk factors for the occurrence of OIs [17]. Similar findings were also observed in studies [15,20-23]. This could be because of lower immunity as WHO staging is higher that further predispose for OIs. Majority of Patients also start treatment at their advanced stage of AIDS that will be difficult to reverse the stage easily with treatment.

Peoples who use khat along with ART medications are at risk to develop OIs by 4.733 than those who don't use Khat. Alcohol use and

| S.No | Variables                        | Opportunistic Infection | COR      | 95% CI    | P-value |
|------|----------------------------------|-------------------------|----------|-----------|---------|
| 1.   | Sex                              |                         |          |           |         |
|      | Male                             | 127(69.8%)              | 0.814    | 0.442     | 1.498   | 0.508   |
|      | Female                           | 155(64.3%)              |          |           |         |
| 2.   | Age                              |                         |          |           |         |
|      | <40 years old                    | 230(70.8%)              | 0.471    | 0.247     | 0.896   | 0.022*  |
|      | ≥ 40 years old                   | 52(63.1%)               |           |           |         |
| 3.   | Educational status               |                         |          |           |         |
|      | No education                     | 72(59.0%)               | 0.809    | 1.000     | 1.630   | 0.553   |
|      | Primary                          | 105(70.9%)              |           |           |         |
|      | Secondary                        | 73(69.9%)               |           |           |         |
|      | Tertiary                         | 32(66.7%)               |           |           |         |
| 4.   | Place of residence               |                         |          |           |         |
|      | Rural                            | 199(67.0%)              | 0.956    | 0.513     | 1.782   | 0.888   |
|      | Urban                            | 83(65.9%)               |           |           |         |
| 5.   | Baseline WHO stage               |                         |          |           |         |
|      | Stage I-II                       | 92(90.2%)               | 4.759    | 1.185     | 18.915  | 0.028** |
|      | Stage III-IV                     | 190(59.2%)              |           |           |         |
| 6.   | Alcohol use                      |                         |          |           |         |
|      | Yes                              | 107(62.9%)              | 1.436    | 1.185     | 2.517   | 0.207   |
|      | No                               | 175(69.2%)              |           |           |         |
| 7.   | Cigarette smoking                |                         |          |           |         |
|      | Yes                              | 10(55.6%)               | 1.109    | 1.304     | 4.045   | 0.675   |
|      | No                               | 272(67.2%)              |           |           |         |
| 8.   | Khat use                         |                         |          |           |         |
|      | Yes                              | 7(41.2%)                | 4.733    | 1.185     | 18.915  | 0.028*  |
|      | No                               | 275(67.7%)              |           |           |         |
| 9.   | ART adherence                    |                         |          |           |         |
|      | Good                             | 273(69.3%)              | 0.163    | 0.0511    | 0.522   | 0.002*  |
|      | Poor                             | 9(31.0%)                |           |           |         |
| 10.  | Occupation                       |                         |          |           |         |
|      | Employed                         | 127(69.0%)              | 0.974    | 0.521     | 1.820   | 0.934   |
|      | Not employed                      | 155(64.9%)              |           |           |         |
| 11.  | Baseline CD4 count               |                         |          |           |         |
|      | <200                              | 43(54.4%)               | 1.340    | 0.678     | 2.649   | 0.400   |
|      | ≥ 200                             | 239(69.5%)              |           |           |         |
| 12.  | Current Hemoglobin level         |                         |          |           |         |
|      | <10                               | 23(36.5%)               | 0.313    | 1.062     | 0.605   | 0.001*  |
|      | >10                               | 201(71.8%)              |           |           |         |
| 13.  | Marital status                   |                         |          |           |         |
|      | Single**                          | 159(63.3%)              | 0.700    | 0.398     | 1.230   | 0.215   |
|      | Married                           | 123(71.5%)              |           |           |         |
| 14.  | OI prophylaxis given***          |                         |          |           |         |
|      | Yes                               | 25(56.6%)               | 2.186    | 0.937     | 5.102   | 0.070   |
|      | No                               | 257(68.0%)              |           |           |         |
| 15.  | Condom use                       |                         |          |           |         |
|      | Yes                               | 238(66.3%)              | 1.449    | 0.676     | 3.102   | 0.340   |
|      | No                               | 44(68.8%)               |           |           |         |
| 16.  | Recent weight                    |                         |          |           |         |
|      | <60kg                             | 208(61.9%)              | 3.658    | 1.656     | 8.078   | 0.001*  |
|      | >60kg                             | 74(85.1%)               |           |           |         |

*Significant association at 95% CI, ** Single includes: Widowed, Never married, Divorced and Separated *** OI prophylaxis include: Cotrimoxazole and/or INH and/or Fluconazole

Table 5: Multivariate analysis for selected variables with occurrence of opportunistic Infections among HIV Positive Patients taking Anti-Retroviral Therapy in Debre Markos Referral Hospital, Northwest Ethiopia; 2013
cigarette smoking were not found to be associated with occurrence of OIs among HIV patients taking ART. Similar study conducted in resource limited setting in Nigeria also found alcohol consumption and smoking to have no association with occurrence of OIs among HIV patients taking ART [17]. Due to inadequate studies conducted on a relationship between substance abuse and OIs among HIV patients taking ART medication, further study is recommended to determine the effect of substance abuse on clinical and immunologic status of peoples living with HIV (PLWH).

ART drug adherence was also found to have a significant association with occurrence of OIs. Peoples with good ART adherence were less likely to develop OIs on the course of HIV infection, while HIV patients with poor ART adherence were 74% time more likely to get OIs. This finding was also similar with other studies [17,24,25]. This might be because of the current study also found that 93.1% of PLWH have good adherence to ART medications. This is higher when compared with adherence of 78% in a study conducted in Nigeria [17]. Another explaining reason could be good adherence for ART will suppress viral replication and would increase CD4 cells that intern decrease risk of new opportunistic infection.

HIV Patients with a recent weight of less than 60 kg were 3.7 times more likely to develop OIs than their counter parts. In addition, current hemoglobin status of patients was also another factor found to be associated with occurrence of OIs. Patients with a current hemoglobin level of greater than 10 mg/dl were less likely to develop OIs while, patients with hemoglobin level of less than 10 mg/dl were 84% times more likely to develop OIs. Similar studies conducted in Nigeria also support this idea [17].

Limitations of the study

Using secondary data in which some important variables were not documented well and many opportunistic infections was presumed diagnosis may be mentioned as the possible limitations of this study.

Concluding Remarks

This study showed the prevalence of OIs among HIV patients on ART is still high, which requires several activities from the ministry of health (MOH), hospitals, health professionals and patients. The common types of OIs among HIV patients taking ART are oral candidiasis, chronic diarrhea and tuberculosis.factors associated with OIs occurrence were age less than 40 years, advanced base line WHO stage, khat use, ART adherence, current hemoglobin status, and recent weight. For PLWH who are on HAART, health professional should give necessary education on adherence of medications, and use of prophylactic medications to prevent OIs. Studies should also be conducted to identify the relation between substance abuse and OIs in HIV patients taking ART and further follow up study will help to identify OIs occurrence.

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