Research Article

Prevalence and risk factors of opportunistic infections in HIV infected individual on anti-retroviral therapy

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Abstract

Introduction: The relationship between opportunistic infections (OIs) and Human Immunodeficiency Virus (HIV) infection is bi-directional. The immune-suppression caused by HIV allows the opportunistic pathogens to cause disease in HIV infected persons. OIs, as well as other co-infections that may be common in HIV-infected persons, such as sexually transmitted infections (STIs), can adversely affect the natural history of HIV infection by causing reversible increases in circulating viral load that could accelerate HIV progression and increase transmission of HIV. **Materials and Methods**: A cross-sectional study was carried out from 2010-2011 on HIV infected individuals who were receiving ART (anti-retroviral therapy) for 12 months. Data on socio-demographic and clinical variables along with risk factors and prevalence of OIs was analysed. **Results:** The prevalence of OIs in study population was 65%. Most of them were < 40 years of age. Most common OI was tuberculosis. Positive association for the presence of OIs was documented with marital status [odds ratio (OR) = 3.8, 95% confidence interval (CI) = .33–44.0; p = 0.58] and CD 4^+ count [odds ratio (OR) = 1.71, 95% confidence interval (CI) = .52–5.56; p = 0.55] on univariate analysis. **Conclusion**: The prevalence of OIs in HIV infected individuals on ART for 12 months was high in our study. A high index of suspicion should be maintained for OIs in HIV infected individuals despite the use of ART Early diagnosis and management of OIs in HIV infected individuals should be intensified.

Keywords: HIV, OIs, ART.

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INTRODUCTION

HIV pandemic is among the greatest health crises ever faced by humanity. Globally, 34.0 million people were living with HIV at the end of 2011[1]. Government of India launched the free ART (anti-retroviral therapy) programme on 1st April 2004, starting with eight tertiary-level government hospitals in the six high-prevalence states of Andhra Pradesh, Karnataka, Maharashtra, Tamil Nadu, Manipur, and Nagaland[2]. As on March 2013, there are around 18.13 lakhs People Living with HIV (PLHIV) registered at the 400 ART Centres functioning all around the country[2]. Currently near 6.5 lakhs are on first line ART. Along with this 840 Link ART Centres primarily established for dispensing ARV drugs, monitoring side effects and treating minor OIs[2]. India is estimated to have around 1.16 lakhs annual new HIV infections among adults and around 14,500 new HIV infections among children in 2011[2]. Morbidity and mortality in HIV disease result due to underlying immune suppression which leads to life threatening opportunistic infections (OIs) during the natural course of the disease[3]. The wide spread use of ART starting in the mid-1990s has had the most profound influence on reducing OI-related mortality in HIV infected persons in those countries in which these therapies are accessible and affordable[4,5]. Some patients do not have a sustained response to antiretroviral agents for multiple reasons including poor adherence, drug toxicities, drug interactions, or initial acquisition of a

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drug resistant strain of HIV-1. Therefore OIs continue to cause substantial morbidity and mortality in patients with HIV-1 infection despite use of ART[6]. This study was carried out to evaluate prevalence of OIs in HIV infected individuals on ART for 12 months and to investigate the socio-demographic and clinical risk factors associated with their occurrence.

MATERIAL AND METHODS

Study Participants. This was a descriptive cross-sectional study where in participants consisted of 100 HIV infected individuals attending the ART centre from 2010 to 2011 who were on first line ART for 12 months. Informed consent was taken from all the study participants. Inclusion criteria were HIV infected individuals who were on first line ART, patients of either sex, and patients who gave written informed consent. Exclusion criteria were patients with HIV infection who were not on ART.

Data Collection

Pro-forma contained patient identification data, personal history, family history, risk factor details, antiretroviral treatment history, and laboratory investigations. Essential laboratory investigations included hemoglobin, total leukocyte count, differential leukocyte count, erythrocyte sedimentation rate, serum creatinine, blood urea, serum bilirubin, SGOT, SGPT, blood sugar, VDRL, HBsAg, anti-HCV, and CD4 count. For each participant, detailed history and physical examination were carried out to identify features suggestive of ongoing OIs. Depending on the specific clinical diagnosis of OI made, appropriate investigations such as sputum acid fast bacilli (AFB); chest x-ray; stool microscopy; cerebrospinal fluid (CSF) analysis; blood, sputum, and urine cultures; and tissue histology were carried out to confirm the diagnosis where possible. Individuals diagnosed to have any OI were referred for appropriate treatment.

Data Analysis

Data analysis was carried out using the SPSS software, version 17, and Epi Info, version 7.1.4 statistical software. Prevalence of HIV-related OIs was described in percentage. For univariate statistical analysis, the X^2 test where appropriate was used to determine significance of association between OIs and various socio-demographic and clinical variables. P-values < 0.05 were considered statistically significant.

RESULTS

Socio-demographic variables of the study population

Of the 100 HIV infected study participants enrolled in the study 66 of them were below 40 years of age and most of the study participants were male, literate and married. Alcoholic intake was found in majority of them as shown in Table 1.

Table 1: Socio-demographic variables in study population

Variables	OI present n=65(%)	OI absent n=35(%)	Total
Age			
<20	0	0	0
21-40	35	21	56
41-60	25	14	39
>61	5	0	5
Gender			
Female	14	8	22
Male	51	27	78
Marital status			
Married	64	33	97
Single	1	2	3
Literacy			
Illiterate	4	0	4
Primary school	9	10	19
Secondary school	46	23	69
Graduate	6	2	8
Alcohol intake			
No	20	9	29
Yes	45	26	71

Prevalence of opportunistic infections of the study population

The prevalence and type of OIs is shown in table 2 and table 3 respectively. Of the 100 HIV infected study participants the prevalence rate of OIs was 65%.

Table 2: Prevalence of OIs in study population

OIs	Frequency
Number with single OIs	41

Number with dual OIs	20
Number with triple OIs	2
Number with > 3 OIs	2

Table 3: Type of OIs in study population

OIs	Frequency n=65
Tuberculosis	21
Tuberculosis + Herpes zoster	3
Tuberculosis + candida	3
Tuberculosis + chronic diarrhea	3
Tuberculosis + toxoplasmosis	1
Tuberculosis + kala azar	1
Tuberculosis + Herpes zoster + toxoplasmosis	1
Tuberculosis + candida + chronic diarrhea	1
Herpes zoster	7
Herpes zoster + chronic diarrhea	2
Herpes zoster + cytomegalovirus	2
Herpes zoster candida	1
Candida	6
Candida + chronic diarrhea	3
Candida + *Pneumocystis jirovecii*	1
Candida +chronic diarrhea + cytomegalovirus + C*ryptococcus neoformans*	2
Chronic diarrhea	4
Cytomegalovirus	2
Toxoplasmosis	1

Risk factors for opportunistic Infections

As shown in Table 4, the socio-demographic and clinical variables that had positive association with the presence of OIs on univariate analysis includes marital status [odds ratio (OR) = 3.8, 95% confidence interval (CI) = .33–44.0; p = 0.58] and CD 4^+ count [odds ratio (OR) = 1.71, 95% confidence interval (CI) = .52–5.56; p = 0.55]. Although the risk of having OIs was higher in individuals who were not married and CD 4^+ count <200, the difference did not attain statistical significance. The risk of OIs did not significantly differ according to age (OR = 0.77, 95% CI = .33-1.7; p = 0.7), gender (OR = 1.07, 95%CI = 0.4–2.8; p = 0.91), literacy (OR = 0.0, 95%CI = 0.4–1.0; p = 0.33), alcohol intake (OR = .77, 95% CI = 0.30–1.96; p = 0.76).

Table 4: Risk factors for OIs in study population

Variables	OI present n=65(%)	OI absent n=35(%)	Odds ratio	95%CI	p-value
Age					
<40	35	21			
>40	30	14	0.77	0.33-1.7	0.7
Gender					
Female	14	8			
Male	51	27	1.07	0.4-2.8	0.91
Marital status					
Married	64	33			
Single	1	2	3.8	0.33-44	0.58
Literacy					
Illiterate	4	0			
Literate	61	35	0	0.4-1.0	0.33
Alcohol intake					
No	20	9			
Yes	45	26	0.77	0.30-1.96	0.76
CD 4^+ count					
<200	58	29			
>200	7	6	1.71	0.52-5.56	0.55

DISCUSSION

AIDS a fatal disease few decades ago now has become a chronic manageable disease due to availability of ART. The identification of pathogens responsible for OIs is very important in managing the HIV infected individual. To prevent these infections by adequate prophylaxis, the spectrum of OIs of a particular locality should be known. At present the initiation of prophylactic therapies against

opportunistic pathogens is mainly based on the absolute CD 4^+ count, as it is generally accepted as the best indicator of the immediate state of immunologic competence of the patient with HIV infection.[7] The relative frequencies of specific OIs may vary in different countries and even in different areas within the same country.[8-10] Knowledge of the most common OIs of that geographical area will help in implementing the preventive measures against that pathogen. In our study, the prevalence of OIs was 65%. The higher prevalence of OI in our study could be due to poor compliance to ART, upon that initial period of ART, that is, within few days of initiation of ART, there is high risk of immune reconstitution inflammatory syndrome and OIs and all the study participants were on ART for less than a year. All these together could have lead to increased prevalence. The study done by Moges *et al*.[12] in North West Ethiopia showed overall prevalence of OIs to be 42.8% with repeated infection. Other similar studies revealed a prevalence of 47.6% both in Taiwan[13] and South Africa.[14] Conversely, Iroezindu *et al*.[15] showed only 22.4% of OI prevalence In our study, most common OIs were pulmonary tuberculosis (TB) 34%, *Herpes zoster 7%*, oral candidiasis 6%, chronic diarrhea 4%. Remaining OIs were contributed by cytomegalovirus, kala azar, *Cryptococcus neoformans, Pneumocystits jirovecii.* The study by Damtie *et al*.[16] showed that TB followed by oral candidiasis and diarrhea were the major OIs encountered by HIV-infected patients. The study by Goud and Ramesh[17] also showed TB as the commonest OIs. Moges *et al*.[12] in their study found that oral candidiasis, chronic diarrhea, and TB as common types of OIs. The study by Ghate *et al*.[18] showed TB was the most common OI, followed by oral candidiasis, herpes zoster, and cryptococcal meningitis. In contrast, Gautam *et al*.[19] showed that herpes zoster was the most common OI followed by TB, skin infection, and chronic diarrhea. Saha *et al*.[20] showed that the common co-infections/OIs were oral candidiasis followed by chronic diarrhea, HSV-2, TB, CMV, HBV, and HCV, while Elizabeth *et al*.[21] showed that the most common OIs were oropharyngeal candidiasis followed by TB. In the study by Shahapur and Bidri,[22] pulmonary TB was the most common OI, followed by candidiasis, cryptosporidial diarrhea, herpes zoster, cryptococcal meningitis, and pneumocystis pneumonia.

Type of OIs

There were a total of 94 opportunistic infections diagnosed in the 65 study participants. Forty one (41%) patients had single OI, 20 (20%) had dual OIs while 2 (2%) had triple OIs and 2 (2%) had more than three OIs. The study by Iroezindu *et al*.[15] in Nigeria showed a total of 96 opportunistic infections diagnosed in the 76 patients. Fifty five (16.2%) patients had single OI, 20 (5.9%) had dual OIs while 1 (0.3%) had triple OIs. In our study, the risk of OIs did not significantly differ according to gender, age, literacy, marital status. Moges *et al*.[12] in their study assessed the factors associated with occurrence of OIs among HIV-infected patients taking ART. Accordingly, younger age, advanced baseline WHO stage, khat use, ART adherence, recent hemoglobin status, and recent weight were found to be associated factors for OIs occurrence. In our study, neither age nor gender had a significant relationship with occurrence of OIs. Palella *et al*.[23] also found no signification association between age and OIs in a cohort of US patients. In contrast Lawn *et al*.[24] demonstrated increased risk of TB in younger patients (<33 years), while Ghate *et al*.[18] in a predominantly ART-naive population in India reported that older age was a strong determinant of OIs. Contrarily, male gender was found to be strongly associated with the occurrence of OIs in other reports.[25,26] Large prospective cohort studies are needed to further investigate the relationship between socio-demographic variables and HIV-related OIs in developing countries. In our study, occurrence of OIs had a positive association with CD 4^+ count (OR = 1.71, 95% CI = 0.52–5.56; p = 0.55), which was similar to the study conducted by Damtie *et al*.[16] and Iroezindu *et al*.[15]. So, early initiation of ART could prevent OIs.

CONCLUSION

The findings of this study suggest that OIs remain a challenge in HIV infected individuals receiving ART. In India access to healthcare and facilities in rural areas are limited. To build infrastructure, diagnostic facilities, and clinical expertise to manage OIs significant effort and investment will have to be made for the effective management of AIDS patients. A high index of suspicion should be maintained for OIs in PLHIV despite the use of ART. Individuals who continue to have low CD 4^+ cell count while on ART should be aggressively evaluated for OIs. Prophylaxis for candidiasis should be widely implemented in the routine management. Proper management of OIs in HIV infected individuals on ART is most important for compliance related issues and hence prevention of HIV drug resistance.

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