ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

Study of prevalence of opportunistic infections among HIV/AIDS patients in Addis Ababa public hospitals

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THESIS SUBMITTED TO SCHOOL OF GRADUATE STUDIES OF ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF PUBLIC HEALTH.

MAY, 2011

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Acknowledgement

I would like to give a special thank to my advisor Dr. Negussie Deyessa for his unreserved and continuous constructive comments and valuable suggestions during the course of this research.

I am also indebted to the Addis Ababa university college of health sciences, school of public health and its staff for financing my research under taking.

I extend my thanks to the Addis Ababa health bureau, all ART clinics and their staff in the hospitals and the data collectors for their good cooperation and contribution and particularly the staffs of the Kebena Health Center for their material support.

Finally, I would like to express my Thanks to my family and particularly to my brother Tesfaye HaileSelasse and W/o Yeshimebet Liban for their encouragement and material support through out my work .

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List of Acronyms

AIDS	Acquired immunodeficiency syndrome
ART	Anti-retroviral therapy
CD4	Cell with CD-4 marker
CNS	Central nervous system
FMOH	Federal ministry of health
FHAPCO	Federal HIV/AIDS prevention and control office
HAART	Highly active anti retroviral therapy
HCT	HIV counseling and testing
HIV	Human immunodeficiency virus
IRIS	Immune reconstitution inflammatory syndrome
IRB	Institutional review board
OIs	Opportunistic infections
PCP	Pneumocystic carrini pneumonia
PLWHA	People living with HIV/AIDS
PMTCT	Prevention of mother to chilled transmission
SOFIS	Severe forms of opportunistic infections
STD	Sexually transmitted disease
TB	Tuberculosis
UNAIDS	United Nations Program on HIV/AIDS
WHO	World health organization

Abstract

Introduction: - The end result of HIV/ AIDS infection is the depletion of the immune system leading to a spectrum of various HIV/ AIDS associated opportunistic infections. Tuberculosis chronic and acute diarrhea of protozoal and bacterial infections, central nervous system infections with toxoplasma Gondi is the leading causes of morbidity and mortality in HIV/ AIDS infected patents.

Objective: To describe the prevalence of opportunistic infection among HIV/AIDS patients and to identify socio-demographic factors for the development of severe forms namely central nervous system toxoplasmosis, pneumocysitc carrini pneumonia in the antiretro viral therapy clinics of public hospitals in Addis Ababa.

Methods: A cross sectional study design on clinical records of HIV/AIDS patients in ART clinics. Systematic random sampling method was used to obtain the required sample. The total sample size was 566

Result: Oral candidacies 326(58. 0 %), Tuberculosis of all forms 260 (45.9%) and herpes zoster 198 (35%) had the highest prevalence. Therefore the prevalence of sever forms of the opportunistic infections made up 17.7% of the total sample. Using binary logistic regression model, WHO stage IV had an independent association with the distribution of the sever forms of the opportunistic infections. The odds of having the sever forms of the opportunistic infections was 40 times higher in the respondents who were in stage IV condition than stage III or II combined. The distribution of the sever form of opportunistic infections in St. Peter's hospital was lower by 85% as compared to the referent hospital. There was no difference in the distribution of the sever forms of the opportunistic infections in the other 7 hospitals. There was also no difference in the distribution of the sever forms of the opportunistic infections among the socio demographic group of the age, sex, marital status and education.

Conclusion: Oral candidacies, TB of all forms and herpes zoster were the predominant OIS. Only WHO stage IV condition and patients from St. Peters hospital were associated with the distribution of sever forms of the OIs.

Recommendation: Skilled professionals for the management of the OIs and the implementation of the TB and HIV collaborative activities are of critical importance.

1. INTRODUCTION

1.1 **Background Information**

It has now been three decades since the AIDS pandemic had been noticed. According to the UNAIDS report at the end of 2009 there were 33.2 million people living with HIV/AIDS globally .During the same year 2.5 million infections and 2.1 million deaths have also occurred. Of the global total 22.5 million living with AIDs 1.7 million new infections and 1.6 million deaths were in sub-Saharan Africa (1, 2).

Ethiopia is not spared from this epidemic .The country is one of the three Sub-Saharan countries that have the highest number of HIV infected persons The federal HIV/AIDS prevention and control office (HAPCO) in conjunction with international and local partners made single point estimate for adult HIV prevalence in Ethiopia. Accordingly the adult HIV infection prevalence was estimated at 2.1% and this figure is used in all planning exercises (3.4).

The country's response to the HIV epidemic was to establish first a task force in 1985 after the report of the first confirmed case of HIV infections and then a national AIDS council in April 2000. Finally the National council evolved into an office, the HIV/AIDS prevention and control office, HAPCO in 2002(3).

Since December 2007 HAPCO and its health program department have taken the responsibility to coordinate the health sector response against HIV/AIDS in Ethiopia. The major components of these responses include HIV testing and Counseling (HCT), prevention of mother to child transmission (PMTCT), infection prevention, Anti retroviral therapy (ART), Opportunistic infection Management (IP) (3).

ART was introduced in Ethiopia in 2003 in selected health facilities. The first adult guide line was issued in 2003(3). The Ethiopian free ART program was launched in 2005. As of October 2007 the total numbers of patients ever started on treatment were 109,552 out of 187,770 ever enrolled in 272 health facilities including 150 health centers. Nearly all 99% of the patients are on first line regimen (5).

1.2 Significance of the study /Statement of the problem /Rationale

After HIV Infection and the development of AIDS various kinds of opportunistic infections (OIs) develop in the patients that differ from country to country. Facilities required confirming the diagnoses of many OIs are not affordable in many of the countries with the highest burden of the disease. In Ethiopia chronic HIV/AIDS care and ART therapy is on better progress with relatively good intake of clients. This study was to provide information on the magnitude of the most frequent OIs observed in the ART clinics. Recommendations for prevention, control and effective treatment for the OIs had been presented to the concerned bodies. The null hypothesis of the research: There is no association between socio-demographic variables and the distribution of the sfois.

2. Literature Review

Opportunistic infections (OIS):- Opportunistic infections are late complications of HIV infection for the most part in patients with less than 200 CD4+ T-cells per micro liter. The causative agents are opportunistic organisms such as pneumocystiscarinnii, mycobacterium complex and cytomegalovirus (CMV) that cause illnesses in compromised immune systems. The common bacterial, fungal and protozoon parasites are also severe in HIV/ AIDS patients (6).

Severe opportunistic infections: - These are infections that occur in HIV/AIDS patients with a very weak immune system and advanced HIV disease. They are the WHO/AIDS defining conditions and the following are some of them

Pnemocystis carini Pneumonia (PCP): a frequent HIV associated opportunistic infection which occurs in 70 - 80% of the HIV/AIDS patients. The symptoms are Pneumonia with chest pain and dyspneoa (18, 19).

CNS Toxoplasmosis; - a severe opportunistic infection which is caused by a protozoa found in uncooked meat and cat faces (6, 18, 19). Overall it is seen approximately in 15% of patients with AIDS and is most common in the Caribbean countries and France.

Cryptococcosis:- Cryptococcus neoformans is the leading cause of meningitis in patients with AIDS, causing serious life-threatening infections in 6% to 12% of patients with AIDS (6). Before the AIDS epidemic the annual incidence of Cryptococcus infections in the USA was estimated to be one or two new cases per 1 million inhabitants. A study done in New York city using culture and cryptococcal latex agglutination test found out that the annual prevalence of Cryptococcus Infection among HIV/AIDS sero positive to be 6%-8.5%, far higher than in the general population (16).

Cryptosporidiosis with diarrhea:-The most common severe opportunistic infection that is spread by contaminated food or water which lead to prolonged episodes of diarrhea and interferes with the absorption of nutrients leading to serious weight loss.

Tuberculosis (TB): is a particularly important problem where in some countries up to 30% patients with TB are also HIV sero positive (6). In an individual infected with HIV the presence of TB affects the HIV/ AIDs progression in many ways. It increases HIV replication, which leads to increased viral load. This results in more rapid progression of HIV disease. It also increases occurrence of other Ols. In Ethiopia routine data from 44 sites in the year 2005/6 showed 41% of TB patients were HIV positive (7). Another routine data collected in 2006/7 showed that the co-infection was 31% (7,8). In a prospective cross- sectional study sought to assess the spectrum of HIV associated disease in Phnompenh, Cambodia, tuberculosis was the most common AIDs defining illness with a prevalence of 43% (9). The same study identified cryptosporidiosis (13%), severe bacterial infections (12%), crpotococcosis (12%) and PCP (10%). Another retrospective study conducted for a year in Bang Kog, Thailand found out that multi-drug resistance TB was also 26.6% in addition to the high prevalence of TB (10). Multi-drug resistance TB was significantly associated with past history of anti-TB treatment (P= O.0005; OR=2.5) (8, 10). A study that was done to screen for the presence of opportunistic infections in a tertiary hospital in India using both clinical, laboratory and radiological method was done in 80 patients (17). In this study 68.25% of the patients had evidence of Ols. Pulmonary tuberculosis was the most, occurring in 31% of the cases. Chronic diarrhea was the next common presentation occurring in 12.5% of the cases. Isoporabelli, cryptosporidiosis and Entamoeba histolitcia were the responsible organisms in the order given. Candida infections (7%), recurrent herpes zoster (3.5%), Cryptococcus meningitis (2.5%), PCP (1.5%), CNS toxoplasmosis (1.25%) were the other observed infections. The authors concluded that TB was the commonest OI in HIV patients in India, thus, early detection and prompt management of TB to prevent further immune deregulation as a necessary measure to be taken (17).

The most prevalent Ols that affect both children and adults in resources limiting settings in HIV/ AIDS patients were found out to be oropharyngial candidacies, bacterial pneumonia, crytococcosis , cryptosporidiosis , herpes simplex, herpes zoster, CMV, PCP and toxoplasmosis (18,19). Following these findings appropriate prophylaxis therapy for some of them was recommended to reduce the risk of HIV/AIDS progression particularly in those patients not taking ART due to various reasons (18, 19 and 20).

Protozoal diarrhea: - HIV/AIDs is manifested by a cluster of gastro –intestinal protozoal parasitic infectious Cryptosporidium, microsporidia and isosporabelli are the most common Ols that affect the gastro-intestinal tract. One study that was done to determine the prevalence of Ols in HIV-AIDS patients with and with out diarrhea in Gujarate , India showed that out of a total of 100 stool samples of HIV/AIDS seropositive patients 25% of the stool samples were positive for isosporablli (10%) for cryptosporidium parvum (9%) and microsporidia (2%) (11)

Bacterial infections. Bacterial infections are the leading cause of death in HIV/AIDS patients. HIV/AIDS patients in Ethiopia experience respiratory tract infections due to various bacteria The most common presentation is bacterial pneumonia where among hospitalized HIV/AIDS clients the prevalence was found out to be 13% (12).A similar study had showed the prevalence of pneumonia in HIV Sero positives to be 8% as compared to 2.4% for the general population. Streptococcus pneumonia was the most common offending pathogen in these patients (12).

Enteric bacterial infection: - Salmonella infections due to non- typhodial salmonella are more frequent among HIV- infected than HIV uninfected persons (12). The Prevalence of non-typhodial salmonella was 36.7% among HIV infected as compared to 20.4% in those who are not HIV infected (12). The prevalence of non salmonella typhi in the HIV infected patient is higher than the non HIV infected and the difference is statistically significant.

Impact of HIV/AIDS on conventional sexually transmitted diseases (STI)

Sexually transmitted infections are the major health problems in all countries but especially so in developing countries. There is little information on the incidence and prevalence of STIS in Ethiopia but the Integrated Disease Surveillance team of the FMOH compiled 58623 and 27947 STI cases from all the regions in 2002 and 2003 respectively using routine quarterly reports. (13). Except for the adult prevalence of HIV (2.1%) and syphilis (1.8%) there was no national estimate on the prevalence of other STIS (13). According to EDHS 2005 men and women with a history of sexually transmitted infections (STI) or STI symptoms had higher rate of HIV infection than those with no history of STI symptoms (24). Among 137 STI cases of men and women observed for STIs 3% were positive for HIV as compared to 2% of 7181 men and

women with no history of STI or symptoms of STI (24). The number of reported STIs has increased since the beginning of the HIV epidemic (25). A study of female sex workers in Addis Ababa had found high prevalent rates of syphilis (37.4%) gonorrhea (30%), trichomoniasis (24%). In 1997 a study in 2 factory workers found that 25% of males and females tested positive for syphilis. More than 50% of these factory workers were positive for herpes simplex 2 antibodies (25). These data are significant because many studies have established a positive correlation between the presence of ulcerative STI and HIV infection. The clinical features of various STIS are influenced by co-infection with HIV. This is seen in the following example: Syphilis can have an atypical presentation with tendencies to rapidly progress to neurosyphills. Atypical lesions of chancroid are common and tend to be less purulent often with indurations mimicking primary syphilis (13).recurrent or persistent genital ulcers caused by herpes simplex are common in patient with HIV and they are often multiple and extensive. There is a high risk of treatment failure when there is STI and HIV co-infection (13).

A survey conducted to determine the prevalence of OIs from patients attending 5 major hospitals in one of the states of Nigeria (Kebbi state) found that out of 1950 patients attending the hospitals 606 (31%), were HIV seropositive and 374(61%) were infected with one or more of the following infections; these were; STD/Gonorrhea (22%) ascaris (15%), Giardiasis (13%), Trichomoniasis (10%), candidacies (8.6%), tuberculosis (TB) (6.7%) (14). The study concluded that these findings in the state were in line with reports from other areas especially Sub-Saharan Africa and concluded that the state government should enforce control strategies against the spread of HIV/AIDS, enhance improved hygiene/environmental sanitation to reduce the level of OI parasitic disease transmission, and enforce mass health education against HIV/AIDS as well as OIS (14)

The spectrum of HIV/AIDS related diseases is not well described in the African continent as in industrialized countries but a review made in 4 African countries, Cótediviore, South Africa, Kenya and Ethiopia listed Tuberculosis, bactereimia (sepsis), Isosporiasis, bacterial pneumonia, cerebral toxoplasmosis and esophageal candidacies as the major illnesses in the order given and concluded that some of the diseases were preventable by OI prophylaxis even in the absence of ART (15).

In the Ethiopian context a one year prospective study of consecutive patients admitted to the medical wards of Tikur Anbessa teaching hospital had shown the morbidity and mortality patterns of patients with HIV/AIDS with the following findings (12,21). Oropharyngeal candidacies 136 (57.4%), tuberculosis 131 (55%), CNS mass Lesions 74 (31.2.%), sepsis 56 (24.9 %), herpes zoster 40 (16.9%), PCP 34 (14.3%), bacterial pneumonia 22(9.3%) ,cryptococcal meningitis 14(5.9%) and others 82 (34.6%). The authors concluded that OIS were the major causes of morbidity and morality among HIV patients and many of the common OIS were both preventable and treatable (21).

In another study that was done at Zewditu memorial hospital in Addis Ababa to determine the proportion of patients that developed the immune reconstitution inflammatory syndrome (IRIS) among HIV/ AIDS patients , the patterns of Ols prior to the start of HAART were the following, herpes zoster 43%, tuberculosis 31.14%, oral candidacies 16.4%, tuberculosis & toxoplasmosis 22.3%, PCP 2.3%, and toxoplasmosis. 15% (22). The study concluded that the proportion of IRIS in the hospital was 17.2% out of 186 patients on HAART (22). The most prevalent Ols were TB, herpes zoster rush and Cryptococcus. The study emphasized the need to be aware of IRIS by clinicians and all health workers and to have adequate provisions of anti-microbial and other medications for proper management of the patients (22).

The conclusion at the end the literature review is “the prevalence of P.C.P, cryptococcal meningitis is lower and the prevalence TB of all forms is higher in the ART clinics of public hospitals of Addis Ababa.

The null hypothesis of the research: There is no association between socio-demographic variables and the distribution of the SOFIS.

Many studies have come up with the answer to my null hypothesis. Those studies were done in the past (temporal difference). Our study was done to see if there is a change in trend from the previous studies in the distribution of the sofis.

3. Objective of the study

General objective

To describe the magnitude of opportunistic infections among patients and determinants of OIs.

Specific objectives

1. To determine the types and frequencies of the OIs in among patients the ART clinics of the public hospitals.
2. To assess the distribution of HIV/AIDS related OIs among patients in the ART clinics of the public hospitals.
3. To determine possible socio-demographic factors associated with severe forms of OIs in the ART clinic patients.

To describe the magnitude OIS among patients and determinants of OIs.
Only socio demographic variables were used because this study was

1. a retrospective study
2. there was a shortage of time (only 2 month)

This was a retrospective study.

Clinical, immunological, pharmacological, virological factors were not studied because this study was a retrospective study and there was a shortage of time. (Only 2month). The study was done on clinical records of patients who had been on follow up on HIV/AIDS chronic care ART clinics.

4. Methodology

4.1 Study setting

The study was conducted in Addis Ababa public hospitals ART clinics. Addis Ababa is the capital city of Ethiopia. It has an area of 450 sq. kilometers with an estimated population of over 3 million. As of date chronic HIV care and ART therapy is being given at 48 sites (9 public, 11 private and 3 uniformed forces hospitals plus 26 health centers) in the city. Data from Addis Ababa health bureau as of June 2010 shows a total of 108,033 cases of HIV follow up and treatment for ART in the public hospitals, health centers and private hospitals. Out of these, 50,213 have their follow up in 9 government hospitals (23). Of these sites all the public hospitals providing free ART service to the general public were selected for the study.

4.2 Study design

Facility based cross-sectional study to describe the prevalence of OIs and socio demographic factors associated for occurrence of severe form of OIS in Addis Ababa pubic hospital from January to end of February 2011. A prospective study design was not considered.

4.3 Source population

All public hospitals in Addis Ababa providing chronic HIV/AIDS care and ART service and all clients that were to be enrolled for the service were the source population.

4.4 Study population

The clients enrolled in the public hospital for chronic HIV/AIDS care and ART follow up were the study population. It was the clinical records of HIV/AIDS enrolled clients who were adults and above 18 years that were included in the study. All people less than 18 years old are excluded.

4.5 Inclusion and Exclusion Criteria

4.5.1 Inclusion Criteria

Clinical records of clients who were adults and 18 years and above were included.

4.5.2 Exclusion Criteria

Clinical records that did not have complete information relevant for the study were excluded.

4.6 Sample size determination

Sample size was computed using the formula for single population proportion. The assumption of prevalence of TB in HIV/AIDS patients was 31% which was obtained from FMOH (7,8). A 95% confidence level and 4% precision was taken.

The following formula was used

$$n = \frac{(Z\alpha/_2)^2 \times P\,(1-p)}{d^2}$$

n = sample size

$\underline{Z\,\alpha}/_2$ = 95% CI two tailed (1.96)

d= desired precisions = 4%

P= prevalence of OIS = 31% in HIV/AID patients

Accordingly the total sample size for this study was 566.

4.7 Sampling procedure

A systematic random sampling was used to select the clinical records from the master register of each hospital as a sampling frame. Sample size for each hospital was obtained in proportion to the number of HIV AIDS patients registered in each hospital. Sampling interval ($k^{th)}$ was determined by dividing the total HIV patients in each hospital by the allocated sample size. From the total cases in sample the first clinical record was selected by simple random sampling and every ($k^{th)}$ record was selected for gathering information until the required sample was obtained.

4.8 Data collection procedure

Data collection format was prepared to extract the necessary data for the study based on the patient registration form for HIV care and ART clinic intake of the FMOH.A structured log book was then prepared for each hospital and the necessary data for the study taken and registered on it. The structured log book was pretested in one health institution which was not part of the study hospitals, and amendments were made accordingly.

Eight clinical nurses and one health officer who were working in the ART clinics were recruited for data collection and for supervision respectively. The clinical nurses did the data collection and the health officer did the supervision. Training for the data collectors and the supervisor on sampling methods, ethical issues and on the use of the log book was given for one day. One data entry personnel were employed for data entry and cleaning. During the data collection period it was not possible to do the data collection in one of the 9 hospitals. There were many principal investigators from many fields in the Alert hospital. It was not possible for the institutional review board (IRB) to accommodate and give permission with in the period of the data collection time and due to lack of time the sample size from Alert Hospital was proportionally redistributed to other 8 hospitals.

Study Variables

Dependent variable: - Occurrence of sever form of the opportunistic infections.

Independent Variables: Socio-demographic variables (including age, sex, religion, marital status, education level, occupation, income

4.9 Data quality assurance

Training of data collectors and the supervisor and pretesting of the data collecting format and log book was made to ensure the quality of the data. The principal investigator and the supervisor made spot-checking and reviewing the completed log books from each hospital. The investigator and supervisor checked about 10% of the records and entered about 10% of the data in to the computer and cleaned the data that were entered.

4.10 Data Analysis /Data quality management

Collected data were entered and cleaned into a computer using EPI info 3.3.1 and analyzed using SPSS version 16 statistical package. Frequency distribution and percentage calculation was made to describe socio-demographic characteristics and to determine the magnitude of the relative burden of OIS in the ART clinics. Crude and adjusted odds ratio was done to determine whether any association existed with a 95% confidence interval Binary logistic regression analysis was made to see the relative effect of independent variable (socio-demographic variable) on the dependent variable (severe forms of OIS).

Operational definitions

Opportunistic Infections:- They are a category of infections that occur in immune compromised hosts and considered to be a complication of HIV infection :- PCP, CNS toxoplasmosis, TB of all forms.

Severe forms of opportunistic infections: - AIDS defining opportunistic infections that are life threatening; some of them are CNS Toxoplasmosis, PCP, Cryptcoccal meningitis and cryptosporidiosis with diarrhea.

4.11 Ethical consideration

This study was carried out after getting ethical clearance and formal letter of cooperation was obtained from the school of public health, college of health science Addis Ababa University to conduct the study. The letter was taken to Addis Ababa health bureau and the 3 federal hospitals. Permission was then obtained from each hospital's ethical intuitional review board /IRB/. The purpose of the study was then explained to each ART clinic's head and all research ethical issues to keep the privacy, confidentiality, beneficence and justice to make the study under the legal frame work of the institutional board review was strictly adhered to. All the necessary precautions were taken to keep all documents in a safe and secure place. Names and other identification of the study subjects were omitted during data collection.

4.12 Dissemination of results

After the completion of the study the result will be presented during thesis defenses in the school of public health as a partial fulfillment of the master of public health. The findings of this study will be circulated to AAU, college of health sciences, school of public health, and Addis Ababa Health bureau. At the end it will be disseminated to national or international conferences and the Ethiopian public health association for possible publication.

5. Results

5.1 Socio-demographic characteristics of participants

Majority of the study participants 315 (55.7%) were females. The mean age of the study respondents was 37 ± 8.99 (SD).one hundred twenty seven (22.4%) of the respondents were in the age group of 35-39 years followed by the age group of 30-34 years and less than 30 years which were 120 (21.2%),. The rest were above the age of 44. 503 (88.9%) of the respondents were followers of the Christian religion and the reaming follow the Muslim faith. Two hundred thirty one (40.8%) of the respondents were married and 192 (33.9%) were the divorced /separated/ widowed. The rest were singles. 301 (52.2%) had completed secondary school and above and the rest had a primary or bellow level of education. 330 (58.3%) were self-employed while government employees were 178 (31.4%). The remaining had unspecified employment status. At intake into the respective hospitals the majority of the study subjects 310 (54.8%) were in WHO stage III condition while 210 (38.2%) were in WHO stage IV condition. The remaining was in stage II condition (Table 1).

5. Results

The general impression about the result:

The ART clinics in the public hospitals are doing the job very fine.

Why Saint Peters' hospitals have lower proportion of the sofis was well explained.

It is highly recommended that modifiable SD factors like religion, marital status, occupation, residence could be modified to reduce the SOFIS.

Table I: Socio demographic, WHO stage and hospital source of respondents in Addis Ababa public hospitals HIV/AIDS/ART clinics, Jan-February 2011(n =566), Addis Ababa Ethiopia.

Characteristics	Frequency	Percentages
Age (years)		
<30	120	21.2
30-34	120	21.2
35-39	127	22.4
40-44	82	14.5
>-44	117	20.7
Mean ±SD	37.03±8.991	
Sex		
Male	251	44.3
Female	315	55.7
Marital status		
Single	143	25.3
Married	231	40.8
Divo/wido/sepa	192	33.9
Religion		
Christian	503	88.9
Muslim	63	11.1
Educational level		
Primary or below	265	46.8
Sec. school and above	301	52.2
Occupational status		
Government employee	178	31.4
Private employee	330	58.3
Other	58	10.2
WHO staging		
II	40	7.1
III	310	54.8
IV	216	38.2
Hospital ID		
Zewditu	213	37.6
St. Paul	77	13.6
Petros	67	11.8
Black lion	66	11.7
Yekatit	56	9.9
Menilik II	47	8.3

Characteristics	Frequency	Percentages
Ras Desta	30	5.3
Gandi	10	1.8

5.2. The Types and frequencies of the opportunistic infections

Out of the 566 clinical records assessed for the presence of the OIs 17.7% (95% CI: 14.7, 21), oral candidacies 329 (58.1%, 95% CI: (54, 62.2), herpes zoster 198(35%, 95% CI 31.38.9) and pulmonary TB 166 (29.3%, 95% CI: 25.6, 33.1) were found out to be the predominant OIs observed in the order given. When the frequencies for both pulmonary and extra pulmonary TB 94(16.6%) were combined the prevalence for TB of all forms was 260 (45.9%) making it the second predominant OI in the study subjects. OIs like toxoplasmosis of the CNS 40(7.1%), PCP 28(4.9%) cryptoccocal meningitis 21(3.7%) and cryptosporidiosis with diarrhea 20(3.5%), made up 100 (17.7 %) of the total cases of the OIs observed These OIs are stage IV AIDS defining conditions in the WHO classification criteria and has been taken as the severe forms of the OIsand used as the out come variable in the bivariate analysis (table 3).

Table 2. Types and frequencies of opportunistic infections at chronic HIV/AIDS care /ART clinics in public hospitals, Addis Ababa Ethiopia, 2011 (n =566**),**

Opportunistic infection	**N**	**%**	**(95% CI)**
Oral candidacies	329	58.1	(54.1, 62.2)
Herpes zoster	198	35.0	(31.1, 38.9)
Pulmonary TB	166	29.3	(25.6,33.1)
Recurrent bacterial pneumonia	117	20.7	(17.3, 24.00)
Extra pulmonary TB	94	16.6	(13.5, 19.70)
Esophageal candidacies	58	10.2	(7.7, 12.7)
CNS Toxoplasmosis	40	7.1	(5.00, 9.20)
Pneumocystis cariniipneumonia	28	4.9	(3.20, 6.70)
Crypto cocal meningitis	21	3.7	(2.20, 5.30)
Crypotosporidiosis with diarrhea	20	3.5	(2.00, 5.1)
Mycosis , recurrent	4	0.7	(00, 1.4)
Sever opportunistic infections	100	17.7%	(14.7,21.0)

5.3. Sociodemographic characteristics and severe forms of the Opportunistic infections.

A bivariate and multivaret logistic regression model was used to seethe association between severe forms of the opportunistic infection with socio-demographic variables, the WHO stage of the respondents and hospitals. The WHO stage and clients of St. Peter's hospital were associated with the distribution of the severe forms of OIs among the study population. The WHO stage had an independent association with the distribution of the severe forms of the OIs. The Odds of having the severe forms of the OIs was 37 times higher in the respondents who were in stage IV condition than stage III or II condition. [AOR 40.2; 95% CI: (17.6., 92.21) p = 0.000], the chi square test also done to verify the association that existed between the WHO staging and the distribution of the sever forms OI.

The distribution of the OIs in St. Peter's Hospital was lower by 85% as compared to the referent hospital [AOR 0.15; 95% CI: (0.04, 0.53); P=0.003]. There were no statistically significant differences in the distribution of the severe forms of the OIS in the other 7 hospitals.

There was also no statistically significant difference in the distribution of the severe forms of the OIs among the socio-demographic groups of age, sex, marital status, religion, education level or occupation. Soci demographic variables don't have any effect on the distribution of the OIs.

Table 3. Socio demographic and WHO stage as possible determinants for sever Opportunistic infections in public HIV/AIDS/ ART clinics. Addis Ababa, Ethiopia. 2011 (n =566)

Variables	Sever opportunistic infections		Crude OR (95% CI)	X^2(df)	p-value
	Yes N (%)	No N (%)			
Age (years)					
<30	13(10.8)	107(89.2)	1.00	6.36(4)	0.17
30-34	23(19.2)	97()80.8)	1.95(0.89,4.33)		
35-39	27(21.3)	100(78.7)	2.22(1.03,4.84)		
40-44	18(22.0)	64(78.0)	2.31(1.00,5.41)		
>44	19(16.2)	98(83.8)	1.60(0.71,3.64)		
Sex					
Male	52(20.7)	199(79.3)	1.00	2.9(1)	0.90
Female	48(15.2)	267(84.8)	0.69(0.44,1.08)		
Marital status					
Single	30(21.0)	113(79.0)	1.00	5.40(2)	0.07
Married	46(19.9)	185(80.1)	0.94(0.54,1.62)		
Divo/wido/sep	24(12.5)	168(87.5)	0.54(0.29,1.01)		
Religion					
Christian	84(16.7)	419(83.3)	1.00	2.9(1)	0.09
Muslim	16(25.4)	47(74.6)	1.70(0.88,3.26)		
Educational level					
Primary or below	43(16.2)	222(83.8)	1.00	0.71(1)	0.39
Sec. school and above	57(18.9)	244(81.1)	1.21(0.76,1.91)		
Occupational status					
Government employee	33(18.5)	145(81.5)	1.00	2.40(2)	0.30
Private employee	61(18.5)	269(81.5)	1.00(0.61,1.64)		
Other	6(10.3)	52(89.7)	0.51(0.18,1.36)		
WHO staging					
II/III	7(2.0)	343(98.0)	1.00	151(1)	0.00
IV	96(43.1)	123(56.9)	**37.05(16.73,82.07)***		
Hospital Id					
Zewditu	50(23.5)	163(76.5)	1.00	18.39(7)	0.01
Ras Desta	7(23.3)	23(76.7)	0.99(0.40,2.45)		
Gandi	2(20.0)	8(80.0)	0.82(0.17,3.96)		
St. Paul	10(13.0)	67(87.0)	2.04(0.61,6.73)		
Black lion	14(21.2)	52(78.8)	1.13(0.36,3.53)		
Petros	3(4.5)	64(95.5)	**0.15(0.04, 0.53)***		

Yekatit	5(8.9)	51(91.1)	**0.32(0.12, 0.84)***
Menilik II	9(19.1)	38(80.9)	1.29(0.37-4.47)

* indicates statistically significant associations at p<0.05

Table IV: - Socio demographic, and WHO stag as possible determinants for sever opportunistic infections in public HIV/AIDS/ chronic care and ART clinics, 2011, Addis Ababa Ethiopia. (n =566)

Characteristics	Crude OR (95% CI)	Adjusted OR (95% CI)
Age (years)		
<30	1.00	1.00
30-34	1.95(0.89,4.33)	0.89(0.34,7.27)
35-39	**2.22(1.03,4.84)***	0.98(0.42,2.26)
40-44	2.31(1.00,5.41)	1.04(0.46,2.30)
>44	1.60(0.71,3.64)	1.34(0.54,3.28)
Sex		
Male	1.00	1.00
Female	0.69(0.44,1.08)	1.05(0.60,1.827)
WHO staging		
II/III	1.00	1.00
IV	**37.05(16.73,82.07)***	**40.2(17.6,92.21)***
Hospital		
Zewditu	1.00	1.00
Ras Desta	0.99(0.40,2.45)	2.98(0.70,12.58)
Gandi	0.82(0.17,3.96)	1.48(0.57,3.81)
St. Paul	2.04(0.61,6.73)	3.99(0.41,38.35)
Black lion	1.13(0.36,3.53)	0.95(0.30,3.04)
St.Peter's	**0.15(0.04,0.53)***	**0.15(0.04, 0.53)***
Yekatit	**0.32(0.12, 0.84)***	0.51(0.17, 1.6)
Menilik II	1.29(0.37,4.47)	0.76(0.19,3.01)

Adjusted for age, sex, WHO staging and hospitals

6. Discussion

Determining the types and relative frequencies of the major OIs and possible determinant factors is important for proper management and prevention strategy of the common OIs. The overall OI prevalence at intake in the ART clinics in the public hospitals is high. The types of the OIs were various ranging from the common oral candidacies to the life threatening CNS toxoplasmosis and the fungal cryptococcal meningitis. The results of this study compared more or less in a similar manner to studies done in Ethiopia previously and other countries.

A one year prospective study of consecutive patients admitted to the medical wards of Tikur Anbass a hospital had shown the morbidity and mortality patterns of patients with HIV/AIDS and the common OIs observed were, oropharyngeal candidacies 136(57.4), tuberculosis 131(55.6), sepsis 56 (24.9%), herpes zoster 40 (16.9) and cryptoccocal meningitis 14(5.9%) (12,21).

A different study that was done at Zewiditu Memorial hospital in 2005 on 186 HIV/AIDS patients to determine the proportion of patients who developed the immune reconstitution inflammatory syndrome (IRIS) found out that prior to the start of HAA RT the patients had the following OIS (22). Herpes zoster was present in 43% of the cases; tuberculosis in 31.4% of the cases; Oral candidacies in 16.4% of the case, toxoplasmosis of the CNS in 2.3% of the cases and PCP in 2.1% of the cases.
The relative distribution of the OIs in the present study is similar to the above two studies except the slight difference in the order of the OIs.

A retrospective clinical record analysis was done at the Ministry of health from 1986 to 1990 (26). The study was a nationwide retrospective review of 636 HIV/AIDS cases and the findings were, tuberculosis in 239 (25%) of cases; Herpes zoaster in 203(21.6%) of cases and oral candidacies in 200 (21.6%) of cases and PCP in 6(0.6%) of cases.

Around the same time in 1990, 100 HIV positive patients were followed prospectively at Tikur Anbasa Teaching Hospital and the demographic, social and clinical presentations were reviewed

(27). Pulmonary tuberculosis was present in 26 (25%) of cases, extra pulmonary TB in 29% of the cases and cryptosporidiosis and herpes zoster in 3% the case respectively.

A retrospective cross-sectional study was done in Jimma referal hospital, south west Ethiopia on 925 HIV/AIDS patients from July 1993 – June 1997 (32). The patients were in the hospitals AIDS control program and review of the clinical profiles of the patients were; tuberculosis 239 (25%). herpes zoster 203 (21.9%), orophargngeal candidacies 200 (21.6%), herpes simplex 16(1.7%) and PCP 6 (0.6%).

In the above 3 studies TB both pulmonary and extra-pulmonary, herpes zoster and oral candidacies were the main presentations in the HIV/AIDS patients. In the present study also TB of all forms was 45% of the total cases and is second in rank after oral candidacies which are similar to the above studies.

In this study oral candidacies was the predominant presentation with 329 (58%) having the condition. This is similar with the findings of a consecutive crossectional study at the adult ART clinic at Tikur Anbassa University Hospital (28). From a total of 384 patients examined 169 (44%) had dental caries and 123 (32%) had different forms of oral candidacies. The oral lesions seen were significantly high among age groups 40 years and above (P=0.016, CI: 1.06-2.05). The distribution of the oral lesions was similar between male and female subjects. Risk factors found to be associated in this study were frequency of cleaning the teeth, cigarette smoking, having advanced clinical stage of HIV disease and CD4 level below 200.

A similar study done in Brazil at the infections disease control division in a general hospital in the School of medicine at Saô Palo, Brazil showed that oral candidacies was present in 113 (33.2%) participants of the 340 HIV infected individuals (29). The study showed that oral lesions were associated with age, smoking habits, level of CD4 lymphocytes, HIV load and use of HAART.

A cross-sectional study conducted among 100 HIV positive patients in Phnompen, Cambodia at 2 general hospitals revealed the following findings (9);- Oral candidacies 80%, Esophageal candidacies (39%), pulmonary TB 25%, extra – pulmonary TB 28%, cryptosporidiosis 13%, and PCP 10%. No statistical significant difference was found between gender, age, occupation or residence in the Cambodian study. The findings from this study were similar to the Cambodian one except that herpes zoster was not present in the Cambodian case.

The prevalence of OIS in patients that attended 5 General hospitals in Kebbi-State, Nigeria was different from this study, as show below. The study was a screening test which was performed among 600 HIV-seropositive OPD attendants and the results were STD/gonorrhea 22.6%, trichomoniasis 10%, TB 6.5%, and candidacies 8.6% (14). The major AIDS defining conditions like PCP, toxoplasmosis and cryptococcal meningitis were not observed in the Nigerian study. The difference from this study might be due to the presentation of the patients in the general hospital before the full-blown AIDS defining illness they began to express themselves in the Nigerian study.

On the other hand a screening test for the presence of opportunistic infections on 80 confirmed HIV positive patients in a tertiary care hospital in New Delhi, India showed (31), pulmonary Tuberculosis in 31% of cases, chronic diarrhea in 12% of cases, oral candidacies in 7% of cases, herpes zoster in 7% of cases, cryptococcal meningitis in 2.5% of cases, PCP in 1.5% of cases and CNS toxoplasmosis in 1.5% of cases (31). The current study has a similar pattern in the presentation of the OIs.

A review of the medical records of 342 HIV infected patients was made before the beginning of HAART to assess the relative frequencies of specific OIS in a Brazilian university hospital (30). The findings were, oropharynpeal candidiaces 108 (43.7%), PCP 31 (12.6%), herpes zoster 30 (23.1%), sepsis 25 (10.1%), tuberculosis 23 (9.3%), cryptococcal meningitis 16 (6.9%) and toxoplasma encephalitis 11(4.4%). The sever forms of the OIS like PCP (12.6%) and sepsis (10.1%) were found to be higher in the Brazilian study as comparel to the current study. This difference could be due to a difference in the geographical spread of the parasite. It could as well

be that the study was done prior to ART therapy and temporal difference as the study was done in 2003.

In a study to assess central nervous system opportunistic infections a retrospective study was done on the clinical records of 126 HIV infected patients in a Thailand out patient and inpatient university hospital. Cryptococcal meningitis was present in 94 (75%) of the patients followed by tuberculosis meningitis 9(7%) (33). The explanation given of the high prevalence of cryptococcalmeningitis by the authors was that cryptococcal meningitis was highly endemic in Thailand even prior to the HIV epidemic.

Another prevalence study on cryptococcal meningitis was don in New York city where the annual prevalence of the disease rose to 6% - 8.5% from a low prevalence rate of 1 case per million prior to the AIDS epidemic. (16)

A study done to find out the occurrence of cryptococcal meningistis patients from Tikur Anbasa hospoital Addis Ababa, Ethiopia over a 2 year period from October 1998 – April 2000 showed the following (34). Out of 1088 cerebrospinalfluid / CSF/ lab investigations the disease was found in 19 (7%) of the cases.The findings of cryptococcalmeningitis in this study were 21 (3.7%) which is lower than the above findings.

In contrast to the studies that we have mentioned above and to this study as well a prospective study on the development of OIs in HIV infected patients in the USA showed PCP as the predominant OI (16) followed by esophageal candidacies, mycobacterium avium complex, CMV retinitis, Bacterial pneumonia, cryptococcosis and TB (16). In the USA study there was a difference in the prevalence by sex and HIV exposure mode. Esophageal candidacies, tuberculosis, herpes simplex were significantly higher among women. Kaposis sarcoma was frequent among men.

Esophagi Candidacies and toxoplasmosis were more frequent among injection drug users.
Some alternative explanation for variation of the distribution of the OIs had been mentioned to be due to the differential spread of the microbial agents in the different ecological setups and the differences in the endemicity of certain infections diseases like the high prevalence of TB in developing countries and PCP in north America (17,36). Geographical factors had been mentioned to play a role for the differences in the prevalence of the OIs. PCP is less frequent in Africa when compared to the 85% prevalence in reports from USA and Europe (36). Prevalence rates of 3% to 10% had been reported in Cote'd'ivore. In contrast 37% and 24% of prevalence had been observered in African AIDS patients in the USA and Europe suggesting a difference in the distribution of the parasite in the environment.

Modes of HIV exposure in the case of Kaposi's sarcoma where the prevalence is high in men who make sex with men has been given as an explanation for the variation of OIs in different groups (15,16). But to get a conclusive and definitive answer for the variation of the occurrence of OIs further analytical studies either case- control or cohort study will be of critical importance.

In summary the types and frequencies of the different OIs in this study were similar to the various studies done previously in this country and many studies done in Brazil, Cambodia, India and Thailand. Oral candidacies 329 (58%) is the leading OI in the study and when pulmonary TB 166 (29.3%) and extra pulmonary TB 94 (16.6%) are combined together TB of all forms comprises of 266 (45.9%) making TB the second leading OI in the study . Herpes zoster is third in rank of presentation 198 (35%) in the list. The stage IV AIDS defining illnesses like toxoplasmosis of the CNS 40 (7%), PCP 28 (4.9%) cryptococcal meningitis 21 (3.7%) and cryptosporidiosis with diarrhea 20 (3.5%) made up 100 (17.7%) of the OI cases in the study.
These stage IV conditions which are life threatening were considered as the sever forms of the OIS and in combination were used as the out come variable for the analysis of the determinant factors.
The WHO stage had an independent association for the distribution of the severe forms OIS. The odds of having the severe form of the OIS was 37 times higher in the respondents who were in stage IV condition than in stage III or stage II condition. This finding is in agreement with the WHO classification symptomatology as explained in the medical literature,(6, 36).

The finding in the study that the respondents in St. Peter's hospital had a lower distribution of the severe forms of the OIS can not be well explained. The study was done on diagnoses made during intake to the ART clinics. Final diagnoses after intervention therapy had been taken were not used. There was no known prophylaxis or therapeutic management differences between the hospitals. All HIV/AIDS care and ART management protocols are standardized and differences due to the quality of care between the health facilities can not be given as an explanation. But when we see St. Peter's Hospital it is significantly associated with lower distribution of the sever forms of OI (Adjusted OR=0.15; 95% CI: (0.04, 0.53)); p= 0.003. One possible explanation for this difference in the distribution the sever forms of OIs could be that St. Peter's hospital is a TB specialized hospital that takes care of a different category of clients as compared to the other hospitals. TB could be the earlier manifestation as an OI before other sever OIs could manifest themselves in the respondents from the other hospitals.

Regarding the association between socio-demographic characteristics and distribution of sever forms of OI. There is no statistically significant difference in the distribution of the OIS with age groups, sex, religion, education level or occupation .

7. Strength and limitation of the study

7.1 Strength of the study

- It has provided the relative distribution of the opportunistic infections which will be useful for planning of the health services and medical programs in the ART clinics of the hospitals.
- It can serve as a base line for further OI incidence studies for the future.

7.2 Limitations of the study

- Some of the studies that were reviewed for comparisons were prospective studies. The other studies were screening studies. Some others were retrospective clinical record reviews which makes direct comparison with the current study difficult.
- The study was done on a secondary data which makes the result obtained less informative than that done using a primary data using a prospective study.
- Being a cross sectional study; it cannot show cause-effect relation ship between the variables studied. A prospective study was not done because prospective studies take very long time, costly and need more resources.

8. Conclusions and Recommendations

8.1 Conclusions

- Out of the clinical records assessed for the presence of OIs, oral candidacies 329, (58.1%), TB of all forms 260 (45.9%) and herpes zoster 198 (28.9%) were found out to be the predominant OIS observed.
- The severe forms of OIs, toxoplasmosis of the CNS 40 (7.1%), PCP 28 (4.9%) Cryptococcus meningitis 21 (3.7%), and cryptosporidiosis with diarrhea 20 (3.5%) made up 100 (17. %) of the total case of OIs.

- The WHO stage of the respondents was found out to be the variable that was associated with the distribution of the sever forms of the OIs. The odds of having the sever forms of the OIS was 37 times higher in the respondents who were in stage IV condition .than stage III or II conditions.

- The distribution of the OIs in St. Peters hospital was lower by 85% as compared to referent hospital.

- There was no statistically significant difference in the distribution of the sever forms of the OIs in the other 7 hospitals.
- There was no statistically significant difference in the distribution of the sever forms of the OIs among the socio-demographic groups of age, sex, marital status, religion, educational level or occupation.

8.2 Recommendations

1. The ART clinics need to have skilled health professionals of all categories for proper diagnosis and management of the prevalent OIs in the population
2. Provision of adequate and sustainable antimicrobials and other medications needed for prophylaxis and treatment of the prevalent OI is of critical importance.
3. TB of all forms has high contribution to the disease burden and it is the second leading OI presenting in 45% the cases. Strengthening of the implementation of the TB/HIV collaboration activity is of vital importance.
4. Enforcing mass health education against HIV/AIDS/STD as well as the most common OIs like TB which are transmissible to the general population is highly recommended particularly starting INH(IPT) is very important.

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Annex 1

Data collection format

Unique ART ID number

Unique patient ID number

Data collection format for school of public health Addis Ababa university MPH research project on prevalence of OIS among patients on HIV/ AID care / ART therapy in governmental hospitals in Addis Ababa, 2011.GC.

No	Variable	Descriptive categories
	Part 1. socio Demographic characteristic	
1	Age incomplete years	
2	Sex	Male Female
3	Marital status	Single Married Divorced Widowed Separated
4	Level of education completed	No education Primary education Secondary education Tertiary education
5	Religion	Orthodox Muslim Protestant Catholic
6	Occupation	Government employee private employee Daily laborer House wife Merchant Factory worker Other specify
7	Residence	Region Kifle Ketema Woreda
8	Part II;WHO staging of the client	Stage 1 condition Stage II condition Stage III condition Stage IV condition

	Part III. Diagnosed opportunistic infections	
3.1	Ora candidacies	1.yes 2. No
3.2	Esophageal candidacies	Yes No
3.3	Herpes zoster	Yes No
3.4	Recurrent bacterial pneumonia	Yes No
3.5	Pulmonary TB	Yes No
3.6	Extra pulmonary TB	Yes No
3.7	Mycosis, recurrent	Yes No
3.8	Crptosporidiosis with diarrhea	Yes No
39	Pneumocystis cariniipneumonia (pcp)	Yes No
3.10	Toxoplasmosis of the CNS	Yes No
3.11	Crypto coca meningitis	Yes No
	Others (specify)	----------

Annex 2: English patient information sheet

Description of the study

Title of the study

Assessment of prevalence of OIS in HIV-AIDS patients in government hospitals of Addis Ababa ART clinics.

Conduct of the Research

It is the third decade since the AIDS pandemic caused major human death of the century. The AIDS epidemic had more severely affected sub Saharan Africa and Ethiopia is not speared form this tragedy. HIV-AIDS is manifested by various types of diseases known as OIS. Knowing the prevalence of OIS and their predisposing factors is of paramount importance. This study is planned for this effect and the proposal or the study is approved by the institutional review board of Addis Ababa University ethics review committee.

Information which is necessary for the study will be taken from your chart. Since information will be collected from your medical chart, it will not do you any harm and the information will be taken only when you give permission. The participation is totally voluntary. You will not face any problem if you do not allow the information to be taken from your cart. There will also be no negative consequences on your treatment. Your name or any other identifying information will not be recorded on the questionnaire.

All information taken from your cart will be kept strictly confidential and will be put in a safe place. In addition, it will be used only for the study purpose.

Address

Dr. Gedlu Beshah

Tel: 0922 34 66 53 C/O Abiye Gebre

Annex 3

Amharic patient information sheet

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DECLARATION

I, the under signed, declared that this thesis is my original work, and has not been presented for a degree in any other university and that all source of material used for this thesis and all people and institution that gave support for this have been duly acknowledge.

Name: Gedlu Beshah Signature_____

Place: Addis Ababa

Date of submission:

This Thesis work has been submitted with my approval as University Advisor.

Advisor's Name Signature

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