Opportunistic infection manifestation of HIV-AIDS patients in Airlangga university hospital Surabaya

T P Asmarawati1,2*, A Putranti2, B E Rachman1, U Hadi1 and Nasronudin1,3

1Tropical and Infectious Diseases Division, Department of Internal Medicine, Faculty of Medicine, Dr. Soetomo General Hospital, Jl. Mayjen Prof dr Moestopo 6-8, Surabaya 60131, Indonesia
2Airlangga University Hospital, Kampus C Mulyorejo, Surabaya, East Java, Indonesia
3Director of Airlangga University Hospital, Kampus C Mulyorejo, Surabaya, East Java, Indonesia

*Corresponding author: tripudyasmarawati@gmail.com

Abstract. Opportunistic infections are common in HIV-infected patients especially those who progress to acquired immunodeficiency syndrome. There are many factors involved in the prevalence of opportunistic infections. We investigated the patterns of opportunistic infection in HIV-infected patients admitted to Airlangga University Hospital Surabaya. This study was an observational study, conducted in adults patients with HIV infection from January 2016 to September 2017. Data collected from the medical records of the patients. The number of samples in this study was 58. The mean age was 42.9 years, mostly male. Most patients admitted were in clinical stadium III or IV. Heterosexual transmission is a common risk factor in patients. The most prevalent opportunistic infections found in patients were oral candidiasis (58.6%), followed by pulmonary tuberculosis (41.4%) and pneumonia/PCP (41.4%). Other infections found were toxoplasmosis, chronic diarrhea, cytomegalovirus, meningitis TB, hepatitis C, amoebiasis, and cerebritis. Opportunistic infections occurred more often in age ≥40 years and increased as clinical stadium get worse. From the results, we conclude that oral candidiasis and pulmonary tuberculosis were the most common opportunistic infections found in Airlangga University Hospital. The pattern of opportunistic infections in this study could help the hospital to set priorities related to the management of patients.

1. Introduction
Human immunodeficiency syndrome (HIV) infection is an important public health problem in worldwide population. It affected 35 million people globally in 2012, with 97% of people infected with HIV live in low or middle-income countries. There is an increase in the number of people living with HIV in Indonesia, with the mean prevalence in most regions about 0.4%. Approximately, in the year 2012, there were 591,823 people living with HIV which distributed in all province in Indonesia. Meanwhile, prevalence in Papua region has already included in widespread epidemic (2.3%).

People living with HIV are vulnerable to have opportunistic infections (OI). This infection can be caused by bacterial, fungal, viral and parasitic agents. Opportunistic infections are common in HIV-infected patients especially those who progress to acquired immune deficiency syndrome (AIDS). The progressive destruction of the immune system by chronic HIV infection leads to decrease of CD4 cell level. These infections are the leading cause of morbidity and mortality in HIV-infected patients and
affect the quality of life. The use of highly active antiretroviral therapy (HAART) has significantly reduced the incidence of opportunistic infections and progression to AIDS.\(^2\)

Many studies have shown that CD4 highly correlates with opportunistic infections, however, the pattern of which may vary according to geographical region. For example, frequent infections in America and Europe are pneumocystis carinii pneumonia (PCP), cryptococcal meningitis, cytomegalovirus, and toxoplasmosis. But in developing countries where tuberculosis is endemic, Mycobacterium tuberculosis infection may be the most common opportunistic infection in HIV-infected patients. The differences in hospital facilities setting may also contribute to the different patterns of opportunistic infection.\(^3\)\(^6\)

Study about the spectrum of opportunistic infection manifestation in HIV-infected patients is necessary to provide a database in every health facilities. It’s also essential to determine local priorities in HIV care and targeted expenditure on prophylaxis and treatment of opportunistic infection in HIV. Therefore this study is conducted in Airlangga University Hospital, which is secondary referral hospital in Surabaya, to assess the types of opportunistic manifestation in HIV-infected patients.

2. Methods
This study was a descriptive observational study in patients diagnosed with HIV/AIDS-infection who admitted to Airlangga University Hospital. All patients with HIV/AIDS infection who admitted from January 2016 until September 2017 were studied. This study uses a secondary data which collected from medical records. Data patients characteristic and prevalence of opportunistic infections shown as a frequency distribution. Data were computed with SPSS version 17.0. Analysis of comparison between opportunistic infections and age, gender, and clinical stadium uses chi-square test, with \(p<0.05\) considered as significant.

2.1. Opportunistic infection diagnostic criteria
The diagnosis of OI was made according to standard guidelines where possible and facilities available. Candidiasis was detected by clinical examination followed by isolation of the yeasts from oropharyngeal or vaginal swabs. Pulmonary TB defined by the presence of a cough with or without fever, weight loss, night sweats or hemoptysis and demonstration of acid-fast bacilli (AFB) in two or more sputum samples and chest X-ray features compatible with TB, and/or detection of Mycobacterium TB by gene Xpert/Rif TB. Extra-pulmonary TB defined as clinical evidence suggestive of TB without characteristic of pulmonary involvement followed by histology of lymph node biopsy (for TB lymphadenitis) or followed by radiologic findings suggestive of TB process (for TB meningitis). Chronic diarrhea was initially diagnosed based on a history of diarrhea more than three weeks. Pneumonia and PCP were diagnosed based on clinical features (fever, cough, and dyspnea) with supportive chest X-ray infiltrates and positive sputum bacteriological smear. Toxoplasmosis defined as seropositive of IgG and/or Ig M toxoplasma. CMV infection defines as seropositive result fo IgG and/or IgM CMV.

3. Results and Discussion
The number of patients in this study was 58. A general characteristic of patients was shown in table 1. The mean age was 42.9 years, range from 19-74 years, mostly male. The CD4 ranged from 2-487 cells/\(\mu l\). Most patients admitted were in clinical stadium III or IV. Heterosexual transmission is the main risk factor in patients. These data are similar to the pattern from the Ministry of Health information data in 2016.\(^7\)

| Characteristic   | n=58 | %  |
|------------------|------|----|
| Age (years)      |      |    |
| Mean±SD          | 42.9±13.3 |    |
The most prevalent opportunistic infections found in patients were oral candidiasis, followed by pulmonary tuberculosis and pneumonia/PCP, as shown in table 2. There were no differences in the distribution of opportunistic infections according to gender, except in toxoplasmosis which is found more often in male samples (table 3). Research conducted at seven provinces in Indonesia (North Sumatera, West Sumatera, Riau Islands, South Sulawesi, North Sulawesi, Maluku, and Papua) in 379 HIV-infected patients with opportunistic infections showed that tuberculosis, candidiasis, and diarrhea were the most common OI with tuberculosis as the leading cause OI. These results quite different with our results because of the small sample size in our study and also the data collected was a local data from our hospital. Another research conducted in Bali on 2016 showed a similar pattern with our study, which showed that oral candidiasis was the most common opportunistic infection, followed by pulmonary tuberculosis.

Table 2. Prevalence of opportunistic infections.

| Opportunistic infections | n (%) |
|--------------------------|-------|
| Oral candidiasis         | 34 (58.6) |
| Pulmonary tuberculosis   | 24 (41.4) |
| Pneumonia/PCP            | 24 (41.4) |
| Toxoplasmosis            | 19 (32.8) |
| Chronic diarrhea         | 12 (20.7) |
| CMV                      | 7 (12.1) |
| Meningitis TB            | 3 (5.2%) |
| Hepatitis C              | 2 (3.4) |
| Amoebiasis               | 1 (1.7) |
| Cerebritis               | 1 (1.7) |

Table 3. Distribution of opportunistic infections according to gender.

| Opportunistic Infections | Male n (%) | Female n (%) | p    |
|--------------------------|------------|--------------|------|
| Oral Candidiasis         | 27 (79.4)  | 7 (20.6)     | 0.275|
| Pulmonary TB             | 19 (79.2)  | 5 (20.8)     | 0.462|
| Pneumonia/PCP            | 20 (83.3)  | 4 (16.7)     | 0.179|
| Toxoplasmosis            | 18 (94.7)  | 1 (5.3)      | 0.012|
| Chronic diarrhea         | 10 (83.3)  | 2 (16.7)     | 0.414|
| CMV                      | 7 (100)    | 0 (0)        | 0.096|
| Meningitis TB            | 3 (100)    | 0 (0)        | 0.293|
Hepatitis C 2 (100) 0 (0) 0.395
Amoebiasis 1 (100) 0 (0) 0.551
Cerebritis 0 (0) 1 (100) 0.088

Oppportunistic infections arise more often in age ≥40 years, except cerebritis which occurs in patient <40 years (table 4). This tendency might be due to the decrease of the immune response in older age and also caused by comorbidity of the patients, such as diabetes mellitus, hypertension, coronary heart disease, or chronic renal failure.

**Table 4.** Distribution of opportunistic infections according to age.

| Opportunistic Infections | Age <40 years | Age ≥40 years | p  |
|--------------------------|---------------|--------------|----|
| Oral Candidiasis         | 14 (41.2)     | 20 (58.8)    | 0.239 |
| Pulmonary TB             | 9 (37.5)      | 15 (62.5)    | 0.246 |
| Pneumonia/PCP            | 9 (37.5)      | 15 (62.5)    | 0.246 |
| Toxoplasmosis            | 6 (31.6)      | 13 (68.4)    | 0.111 |
| Chronic diarrhea         | 6 (50)        | 6 (50)       | 0.788 |
| CMV                      | 3 (42.9)      | 4 (57.1)     | 0.834 |
| Meningitis TB            | 2 (66.7)      | 1 (33.3)     | 0.473 |
| Hepatitis C              | 0 (0)         | 2 (100)      | 0.179 |
| Amoebiasis               | 0 (0)         | 1 (100)      | 0.346 |
| Cerebritis               | 1 (100)       | 0 (0)        | 0.280 |

Oppportunistic infections tend to occur more often as the clinical stadium get worsen (table 5). The differences between clinical stadium were significant in oral candidiasis, pulmonary tuberculosis, toxoplasmosis, and amoebiasis. While the differences in pneumonia/PCP, chronic diarrhea, cytomegalovirus (CMV), meningitis TB, hepatitis C, and cerebritis were nonsignificant. The risk of opportunistic infections has known to increased along with the degree of immune deficiency. However, several case reports and retrospective studies suggested that minority with HIV-infected develop opportunistic infection earlier than expected. Some infection such as tuberculosis can occur in all clinical stadium and a patient without any signs of immunodeficiency. Environmental and genetic factors possibly play a role in the risk of developing opportunistic infections at relatively high CD4 level or early clinical stadium.10,11

**Table 5.** Distribution of opportunistic infections according to the clinical stadium.

| Opportunistic infections | Clinical Stadium II | Clinical Stadium III | Clinical stadium IV | p  |
|--------------------------|---------------------|----------------------|---------------------|----|
| Oral Candidiasis         | 2 (5.9)             | 11 (32.4)            | 21 (61.8)           | 0.024 |
| Pulmonary TB             | 0 (0)               | 9 (37.5)             | 15 (62.5)           | 0.025 |
| Pneumonia/PCP            | 2 (8.3)             | 8 (33.3)             | 14 (58.3)           | 0.373 |
| Toxoplasmosis            | 0 (0)               | 2 (10.5)             | 17 (89.5)           | 0.000 |
| Chronic diarrhea         | 0 (0)               | 5 (41.7)             | 7 (58.3)            | 0.292 |
| CMV                      | 0 (0)               | 2 (28.6)             | 5 (71.4)            | 0.339 |
| Meningitis TB            | 0 (0)               | 1 (33.3)             | 2 (66.7)            | 0.713 |
| Hepatitis C              | 0 (0)               | 0 (0)                | 2 (100)             | 0.330 |
| Amoebiasis               | 0 (0)               | 0 (0)                | 1 (100)             | 0.042 |
| Cerebritis               | 0 (0)               | 0 (0)                | 1 (100)             | 0.580 |

4. Conclusion
Oral candidiasis and pulmonary tuberculosis were the most common opportunistic infections found in Airlangga University Hospital. These infections occurred more often in age >40 years and advanced
clinical stadium. There were no differences in the prevalence of opportunistic infections according to gender.

The pattern of opportunistic infections found in this study can help the hospital to be able to set priorities related to the management of patients ranging from prevention, early detection, and appropriate treatment to improve survival of the patients.

References
[1] Peraturan Menteri Kesehatan Republik Indonesia no. 87 Tahun 2014 Pedoman pengobatan antiretroviral
[2] Kaplan J E, Benson C, Holmes K K, Brooks J T, Pau A and Masur H 2009 Guidelines for prevention and treatment of opportunistic infection in HIV-infected adults and adolescents: Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America MMWR Recomm. Rep. 58 1-207
[3] Agarwal S G, Powar R M, Tankhiwale S and Rukadikar A 2015 Study of opportunistic infection in HIV-AIDS patients and their co-relation with CD4+ cell count Int. J. Curr. Microbiol. App. Sci. 4(6) 848-61
[4] Sonowal R and Goswami A 2015 Opportunistic infection in HIV seropositive patients: A study in a tertiary hospital in Assam, Northeast India Sch. J. App. Med. Sci. 3(1C) 206-8
[5] Dabla V, Gupta A K and Singh I 2015 Spectrum of opportunistic infection among HIV-seropositive patients in Delhi region-a study by Delhi state AIDS control society J. Med. Dis. 3(1)
[6] Iroezindu M O, Ofondu E O, Hausler H and VanWyk B 2013 Prevalence and risk factors for opportunistic infections in HIV patients receiving antiretroviral therapy in a resource-limited setting in Nigeria J. AIDS Clinic. Res. S3
[7] Pusat Informasi dan Data Kementerian Kesehatan RI Studi dan analisis HIV-AIDS 2016
[8] Rusli R dan Setiawati V 2014 The cases with opportunistic infections among HIV patients in Indonesia 2011 BMC Infect. Dis. 14(2) 45
[9] Utama M S dan Merati T P 2016 Association of opportunistic infections with HIV-RNA and CD4 cell count in pre-ARV and ARV failure at the care support treatment clinic of Sanglah hospital, Bali J. Epid. Res. 2(2)
[10] Podlekareva D, et al. 2006 Factors associated with the development of opportunistic infections in HIV-1–infected adults with high CD4+ cell counts: A Euro SIDA study J. Infect. Dis. 194 633–41
[11] Lama J and Planelles V 2007 Host factors influencing susceptibility to HIV infection and AIDS progression Retrovirol. 4 52