

Original Article

THE SPECTRUM OF OPPORTUNISTIC INFECTIONS AND ASSOCIATED FACTORS AMONG PEOPLE LIVING WITH HIV/AIDS ON HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY AT MERPATI CLINIC, BALI, INDONESIA: A RETROSPECTIVE STUDY

NOVIANA JOENPUTRI¹, KETUT SURYANA²

^{1,2}Department of Internal Medicine, Wangaya HIV Study Group, Merpati Clinic, Wangaya General Hospital in Denpasar, Bali, Indonesia
Email: noviana.joenputri@gmail.com

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ABSTRACT

Objective: Infections contributed to higher morbidity and mortality in people living with HIV/AIDS (PLWHA) in both developed and developing countries. This study aimed to describe the spectrum of opportunistic infections (OIs) and associated factors among PLWHA on highly active antiretroviral therapy (HAART) at Merpati Clinic, Wangaya Regional General Hospital in Denpasar, Bali.

Methods: This was a retrospective study. All of PLWHA, who still receiving HAART at Merpati Clinic from January 2018 to January 2020, who met inclusion and exclusion criteria, were included as subjects in this study. All data were collected through a review of the complete medical record of patients.

Results: The prevalence of OIs in this study was 43.4%. Most PLWHA who experienced OIs were male (68.8%), age ≤ 40 y old with a median of age 36 y old, educational status senior high school (57.7%), married (62.1%), employed (89.7%), CD4 cell count ≥ 200 cells/ μ l (67.6%) and transmission route of HIV non-Intravenous (IV) drug user (99.2%). Sex, age, marital status, and CD4 cell count were significantly associated with OIs, $p=0.000$, $p=0.005$, $p=0.005$, and $p=0.000$, respectively.

Conclusion: The commonest OI in this study was pulmonary tuberculosis. The presence of OIs was associated with sex, age of HIV diagnosis, marital status, and CD4 cell count. With the knowledge of OIs spectrum, clinicians are expected to be able to prevent, diagnose and treat OIs promptly to decrease the morbidity and mortality caused by OIs efficiently.

Keywords: HIV/AIDS, Opportunistic infection, Comorbidities

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INTRODUCTION

HIV/AIDS is still a global public health problem [1]. To increase the survival of PLWHA, access to HIV prevention, diagnosis, treatment, or OIs must be improved. OIs are infections that appear more frequently or more severe in immunocompromised people than in immunocompetent people. Although in the HAART era survival of PLWHA is prolonged, this is a challenge for clinicians in managing OIs that arise during the life of patients. Because of the immunosuppression experienced by PLWHA as a natural course of the disease, it can lead patients into life-threatening OIs [2]. Infections contributed to higher morbidity and mortality in PLWHA in both developed and developing countries [3-10]. CD4 cell count has been widely reported as a factor associated with the emergence of OIs [2, 11, 12].

Studies assessing socioeconomic factors related to the occurrence of OIs are still lacking. There were few studies that described the spectrum of opportunistic infections and associated factors in PLWHA in Bali. This study aims to describe the spectrum of opportunistic infections and associated factors among PLWHA on HAART at Wangaya Regional General Hospital in Denpasar, Bali, Indonesia.

MATERIALS AND METHODS

Research design

This retrospective study was conducted from January 2019 to January 2020 at Merpati Clinic, Wangaya Regional General Hospital in Denpasar, Bali, Indonesia. There were 253 patients who participated in this study. Ethical clearance was obtained No: 09/RSUDW/litbang/2019 by Ethical Committee of Wangaya Regional General Hospital in Denpasar Bali.

Population and subjects of the study

All of PLWHA, who still receiving HAART at Merpati Clinic from January 2018 to January 2020 who met inclusion and exclusion criteria were included as subjects in this study. Inclusion criteria including age more than 17 y old, experienced opportunistic infection during HIV infection, and had a complete medical record. Subjects were excluded if the medical record was not complete. We used a consecutive sampling technique to get the subjects.

Variables and data sources

All of the data were collected through a review of the complete medical record of patients. Study variables including demographic and socioeconomic data such as sex, age, educational status, marital status, occupation, transmission route of HIV, CD4 cell count, and the presence of OIs.

Statistical analysis

All the data was processed in the Microsoft excel datasheet. Univariate and bivariate analysis was done using IBM SPSS version 26.0 (IBM SPSS Inc) statistical software. Bivariate analysis was conducted using the Chi-square test. P-value of less than 0.05 was considered statistically significant for all tests.

RESULTS

Of the total 584 medical records analyzed, 253 (43.4%) patients experienced OIs. Most PLWHA with OIs were male (68.8%), aged ≤ 40 y (66.0%) with a median age of 36 y, senior high school (57.7%), married (62.1%), having a job (89.7%), CD4 cell count ≥ 200 cells/ μ l (67.6%), and non-IV drug users (99.2%). Complete demography and socioeconomic data can be seen in table 1.

Table 1: Demographic and socioeconomic data of PLWHA on HAART with OIs

Variables	n (%)
Total	253 (100)
Sex	
• Male	174 (68.8)
• Female	79 (31.2)
Median of age (years)	36.0
Age of HIV diagnosis (years)	
• ≤40	167 (66.0)
• >40	86 (34.0)
Educational status	
• Elementary school	22 (8.7)
• Junior high school	46 (18.2)
• Senior high school	146 (57.7)
• Academy/University	39 (15.4)
Marital status	
• Single	60 (23.7)
• Married	157 (62.1)
• Divorced or widowed	36 (14.2)
Occupation	
• Yes	227 (89.7)
• No	26 (10.3)
CD4 cell count (cells/μl)	
• <200	82 (32.4)
• ≥200	171 (67.6)
Transmission routes of HIV	
• IV drug user	2 (0.8)
• Non-IV drug user	251 (99.2)

IV: intravenous

The three most common OIs were pulmonary tuberculosis (47.8%), followed by oral candidiasis (43.9%), and toxoplasmosis (10.3%). The distribution of OIs can be seen in table 2.

Table 2: The distribution of OIs among PLWHA on HAART

Variable	Yes n (%)	No n (%)
Pulmonary tuberculosis	121 (47.8)	132 (52.2)
Oral candidiasis	111 (43.9)	142 (56.1)
Toxoplasmosis	26 (10.3)	227 (89.7)
Community-acquired pneumonia	18 (7.1)	235 (92.9)
Pneumocystis pneumonia	11 (4.3)	242 (95.7)
Herpes zoster	11 (4.3)	242 (95.7)
Dermatitis seborrheic	5 (2.0)	248 (98.0)
Retinitis cytomegalovirus	3 (1.2)	250 (98.8)
Tuberculosis lymphadenitis	2 (0.7)	251 (99.3)

Patients also experienced comorbidities other than OIs such as hepatitis B (2.4%) and hepatitis C (0.3%) coinfection, sexually transmitted disease (STD) (7.1%), diabetes mellitus (DM) (1.2%), and hypertension (6.7%). (table 3) Among PLWHA with DM, all patients had pulmonary tuberculosis as OI.

Table 3: The distribution of other comorbidities among PLWHA on HAART

Variable	Yes n (%)	No n (%)
Sexually transmitted disease	18 (7.1)	235 (92.9)
Hepatitis B	6 (2.4)	247 (97.6)
Hepatitis C	1 (0.3)	252 (99.7)
Diabetes mellitus	3 (1.2)	250 (98.8)
Hypertension	17 (6.7)	236 (93.3)

Factors that significantly associated with the occurrence of OIs were sex, age of diagnosis, marital status, and CD4 cells count, $P < 0.05$. Whereas, factors such as educational status, occupation, and transmission routes of HIV were not significantly associated with OIs, $p > 0.05$. (table 4.)

Table 4: Factors associated with the occurrence of OIs among PLWHA on HAART

Variables	OIs	no-OIs	p-value
Total	253 (43.3)	331 (56.7)	
Sex			
• Male	174 (52.3)	159 (47.7)	0.000*
• Female	79 (31.5)	172 (68.5)	
Median of age (years)	36.0	32.0	
Age of HIV diagnosis (years)			
• ≤40	167 (39.8)	253 (60.2)	0.005*
• >40	86 (52.4)	78 (47.6)	
Educational status			
• Elementary school	22 (44.9)	27 (55.1)	0.514
• Junior high school	46 (45.1)	56 (54.9)	

• Senior high school	146 (41.1)	209 (58.9)	
• Academy/University	39 (50.0)	39 (50.0)	
Marital status			
• Single	60 (52.6)	54 (47.4)	0.005*
• Married	157 (38.9)	247 (61.1)	
• Divorced or widowed	36 (54.5)	30 (45.5)	
Occupation			
• Yes	227 (43.4)	296 (56.6)	0.907
• No	26 (42.6)	35 (57.4)	
CD4 cell count (cells/ μ l)			
• <200	82 (58.6)	58 (41.4)	0.000*
• \geq 200	171 (38.5)	273 (61.5)	
Transmission routes of HIV			
• IV drug user	2 (66.7)	1 (33.3)	0.413
• Non-IV drug user	251 (43.2)	330 (56.8)	

IV: intravenous; * $p < 0.05$ was statistically significance

DISCUSSION

The overall prevalence of OIs in this study was 43.3% ($n=253/584$). This was similar to Study Alemayehu *et al.* in Ethiopia (45.3%) [13]. Most PLWHA who experienced OIs were male and age ≤ 40 y old (66.0%). These findings were similar with the previous study, which reported male PLWHA experienced more OIs than females with age 29-35 group [14]. But, male to female ratio in this study seems lower than a similar study in India, 2.2:1 vs 3.09:1, respectively [14]. The median of age in this study was 36 y old, it is similar to previous studies [15-17].

Pulmonary tuberculosis (47.8%) followed by oral candidiasis (43.9%), and toxoplasmosis (10.3%) were the most frequently observed OIs. Previous studies also reported the most prevalent OIs were pulmonary tuberculosis followed by oral candidiasis [2, 12, 17-21]. Oral candidiasis was previously reported as the most prevalent OI fungal in PLWHA due to severe suppression of the immune system [22].

One of the important complications in PLWHA patients treated by HAART is the immune reconstitution inflammatory syndrome (IRIS) phenomenon [23, 24]. Around 30% of PLWHA with tuberculosis coinfection have a risk of tuberculosis-associated IRIS (TB-IRIS) [25]. TB-IRIS can appear as paradoxical tuberculosis or unmasking tuberculosis-associated IRIS [26]. A study reported patients with TB-IRIS had characteristics such as a mean of age 35.87 (± 8.54) years, a mean of CD4 cell count 200 (± 263), a form of tuberculosis lymphadenitis (75%), and IRIS mostly occurred about 1-4 w after HAART initiation [27]. In this study, there were no patients who met the paradoxical or unmasking tuberculosis-associated IRIS criteria.

The prevalence of pneumocystis pneumonia (PCP) in this study was 4.3%, it was lower than reported by Kumar *et al.* [18]. It may be caused by the lack of facilities for PCP diagnosis in our hospital. The prevalence of herpes zoster in this study also lower from the previous study, 4.3% vs 11.2%, respectively [15].

Patients also experienced comorbidities other than OIs such as hepatitis B (2.4%) and hepatitis C (0.3%) coinfection, STD (7.1%), diabetes mellitus (1.2%), and hypertension (6.7%). (table 3) STD in this study was more prevalent than reported by Bhaumik *et al.* [16]. It might be caused by most HIV transmission routes in this study was non-IV drug users or sexually. HIV/AIDS and DM are known as the disease that suppressed cell-mediated immunity, thus causing patients more susceptible to OIs. Among PLWHA with DM in this study, all the patients had pulmonary tuberculosis as OI. Indira *et al.* reported, there was no profile difference of OIs between PLWHA with or without DM [28].

Factors that significantly associated with the occurrence of OIs in this study were sex ($p=0.000$), age ($p=0.005$), marital status ($p=0.005$), and CD4 cell count ($p=0.000$). Iroezidu *et al.* also reported that age and CD4 cell count were significantly associated with OIs but not with sex and marital status [29]. Patients with age ≤ 40 y old experienced OIs 1.89 times higher ($p=0.02$) [29]. Some similar studies reported that CD4 cell count significantly associated with the occurrence of OIs [2, 11, 12]. The risk of OIs was significantly higher

in patients with current CD4 cell count < 200 cells/ μ l (OR= 6.11, 95% CI= 3.46-10.78, $p < 0.0001$) [29].

Fungal OIs that most commonly appeared on CD4 cell count < 200 cells/ μ l were oral candidiasis, cryptococcal meningitis, and PCP [22]. Patients with CD4 cell count < 200 cells/ μ l had higher risk to pulmonary tuberculosis (9.4 times, $p < 0.001$), oral candidiasis (27.2 times, $p < 0.001$), and pneumonia (11.1 times, $p = 0.008$) [2]. OIs that most commonly appeared on CD4 cell count > 200 cells/ μ l were tuberculosis and candidiasis [14]. This may cause the most OIs in this study were pulmonary tuberculosis and oral candidiasis. Therefore, patients with CD4 cell count < 200 cells/ μ l (32.4%) in this study need more attention to the occurrence of life-threatening OIs.

The strengths of this study are a large number of samples and most of the medical record data are complete. The lack of several diagnostic support for OIs in PLWHA become the limitation of this study. It might cause some OIs to be undiagnosed.

CONCLUSION

Although all of the patients have received HAART, the prevalence of OIs is still high. The commonest OIs in this study were pulmonary tuberculosis, followed by oral candidiasis and toxoplasmosis. The presence of OIs was associated with sex, age of HIV diagnosis, marital status, and CD4 cell count. There were no patients occurred with IRIS. With the knowledge of the OIs spectrum, clinicians are expected to be able to give more education to PLWHA on HAART about personal hygiene and medication compliance. Regular and systematic medical examination, early diagnosis, and prompt treatment of OIs are needed to decrease the morbidity and mortality caused by OIs efficiently.

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AUTHORS CONTRIBUTIONS

All authors contributed to the concept of study. All authors also had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

CONFLICTS OF INTERESTS

All authors have disclosed no conflicts of interest.

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