ORIGINAL ARTICLE

The Prevalence of Pulmonary Tuberculosis Among Newly Diagnosed HIV/AIDS Individuals Admitted in Gresik, Indonesia

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ABSTRACT

Introduction: HIV is a major problem that threatens Indonesia and across the world. Since HIV attacks the immune system, people with HIV are susceptible to opportunistic infections due to low immunity such as tuberculosis. This study aims to determine the prevalence and risk factors that contribute to pulmonary tuberculosis among HIV/AIDS patients admitted to Ibnu Sina Gresik Hospital from the 2018-2019. **Methods:** This research uses the Observational Analytical, Cross-Sectional method. We collected data from new diagnosed HIV patients with pulmonary tuberculosis. HIV diagnosis was obtained with a rapid test method and CD4 levels. At the same time, a pulmonary tuberculosis diagnosis was obtained with Xpert MTB/RIF. **Results:** We found that 58 individuals were HIV positive, and eight among them were also positive for TB (13.79%). The majority of individuals were male (68.97%), in the age group of 26-45 years (70.69%). The majority of those positive with HIV-TB had CD4 number < 200 cell/μL. No significant difference was found in the prevalence of TB among HIV patients based on gender, age, and number of CD4. **Conclusion:** We found TB co-infection among new diagnosed HIV individuals with a low level of CD4. Initial screening of individuals at risk of HIV infection is important to avoid co-infection with other diseases that can worsen the individual's condition. So, in the end, the severity and mortality rate in HIV patients can be reduced.

Keywords: HIV/AIDS, Tuberculosis, CD4 level, Xpert MTB/RIF

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INTRODUCTION

Nowadays, a major problem that threatens Indonesia and other countries around the world is the Human Immunodeficiency Virus (HIV). HIV infection can progress for a worse condition named Acquired Immune Deficiency Syndrome (AIDS). Around 36.9 million people in 2017 are living with HIV around the world. New HIV infections in 2017 reached 1.8 million worldwide. In Indonesia, from 2005 to March 2019, the number of HIV cases reaches 338,363 people. The case of AIDS in Indonesia until December 2018 has already reached 114.065 people. From January-March 2019, the documented HIV transmission reached 11,081 people, while the reported AIDS transmission reached 1,536 people (1).

Globally, although the number of cases of HIV decreases, many people are still susceptible to HIV infection, especially for populations with a high risk of HIV-infected or known as the key population of HIV. The key population of HIV is a population group that determines the success of preventive and treatment; thus, this group needs to be actively involved in the prevention of HIV/AIDS for both themselves and others (2). The Ministry of Health has implemented a strategy to reduce HIV transmission in key populations by educating them on how to reduce new HIV transmission rates, mortality rates due to HIV/AIDS, negative stigma, and discrimination against people with HIV (3,4).

The final stage of HIV infection is marked by decreased immunity which further leads to AIDS. An individual living with HIV/AIDS (or ODHA in Indonesia) begins to reveal symptoms due to opportunistic infections. This opportunistic infection can be caused by microorganisms which in general may not cause serious illness in healthy people. However, for ODHA, it can jeopardize their life (5). At the beginning of the AIDS epidemic, the main target for various infections and tumors was the lung of people living with HIV (6). Opportunistic infections that arise in people living with HIV depend on the HIV stage, history of infection, virulence from

infected organisms, and host-related factors. The infection can be observed in various body systems such as the digestive system, the central nervous system or peripheral systems, and various other organs that can be caused by bacteria, viruses, fungi, parasites, or other metabolic diseases (5).

Approximately 10.4 million people were diagnosed with tuberculosis (TB) in 2015. This number also includes 1.2 million people co-infected with HIV. Since almost 60% of TB-HIV co-infection was not detected, it led to 390.000 death related to TB in people living with HIV (32%). Meanwhile, in 2017, 10.0 million people were infected with TB, and 900.000 among them were also infected with HIV. The number of deaths caused by TB-HIV was also reduced to 300.000 cases. Most TB cases occur in Asia (60%) and Africa (7% from Nigeria and South Africa) (7). The person living with HIV has a high risk for TB infection caused by reactivation of latent TB, and co-infection with TB could trigger to more rapid progression of the disease. In the initial phase, active pulmonary TB was observed non-symptomatic. At the same time, another type of TB (extrapulmonary) is commonly found. In patients who have immunosuppression (CD4 cells lower than 200cells mm-3, the clinical course can be vastly progressed and can lead to a high mortality rate (8).

Indonesia is known as the country with a high burden of TB. Currently, Indonesia is placed second as the country with a high number of TB in the world. In 2017, there were 420.994 TB reported cases, with 1.85% among them were also infected with HIV(9). Tuberculosis can be categorized as number two opportunistic infection observed in Indonesia, and it is also the highest cause of death in HIV patients (10). However, early detection of TB infection in HIV patients can be helpful for effective treatment; thus, it can prevent the mortality rate in HIV patients caused by co-infection with TB.

In Indonesia, areas that have a high number of TB cases include West Java and East Java province (11). The number of new cases of tuberculosis in East Java province in 2018 reached 20.535 (9). It is a great of interest for us to study the prevalence of TB in HIV infected patients in East Java province, one of which is in Gresik. Several reasons were considered so that patients were reluctant to visit health care centers and chose to wait for opportunistic infections to develop. One reason is that they are afraid to receive negative stigma from their place. So they chose to hide the fact that they were infected with HIV (12). Based on the epidemiology results, the number of HIV cases in Gresik were increased by 29% since 2015 (13). Thus, early screening is favorable to control HIV transmission in the Gresik area.

MATERIALS AND METHODS

A cross-sectional was conducted at RSUD Ibnu Sina, Gresik, between January 2018 to December 2019. All patients were newly diagnosed as HIV positive. Inclusion criteria were set; patients with all gender and all age, positive TB which were confirmed by rapid diagnostic tests such as Xpert MTB/RIF only, and new diagnosed HIV patients with known CD4 levels.

Xpert MTB/RIF assay
The Xpert MTB/RIF assay in this study referred to previous studies (13–15). In the specimen (sputum) container, sample reagent was added with a 3:1 ratio. Then it was agitated gently twice in room temperature for 15 minutes incubation. Then 2 ml of these mixtures were placed on the testing cartridge. Place the cartridge to Xpert MTB/Riff assay machine after closing its lid.

CD4 count
Then, the HIV CD4 examination is carried out by the PIMATM CD4 analyzer (Abbott, Illinois, USA) as it is described in another study (14). Twenty-five microliter (25 µl) blood venous sample was drawn from patients or sample obtained from a finger prick, then immediately placed to the cartridge. After the low and normal value control cartridge gave acceptable value, the sample then could be proceeded. Antibodies (anti CD4 and CD3) were added to samples. Visualization was done by observation of fluorescent omitted from labeled antibodies. The image of CD3 and CD4 then were presented as the number of cells/mm3 within 20 minutes incubation time.

Statistical analysis
Age, gender, and CD4 value were presented with n (%). Statistical analysis was calculated with Microsoft Excel for Mac version 16.25. Correlation analysis was performed with the Chi-Square test with p <0.005.

RESULTS

The Occurrence of pulmonary TB and HIV co-infection
Our results showed that there were 58 new HIV-positive patients in the period of 2018-2019. Among 58 HIV-positive patients, eight of them were also infected with TB (13.79%). All positive TB cases were pulmonary. Tuberculosis diagnosis was performed using Xpert MTB/RIFF with all TB positive were showing sensitivity toward rifampicin.

The majority of new diagnosed HIV-patient were male (68.97) while those who were positive with TB were also majority male (6 patients from 8 HIV-TB patients, Table I). The susceptibility of TB among HIV patients was not correlated with different gender

($\chi 2 = 0.16$; p=0.69).

Table I : Distribution of HIV-TB and HIV cases as regards gender

Gender	HIV (n %)	HIV (n %)	Total (n %)	Chi Square	#p
Female	2 (3.45)	16 (27.59)	18 (31.03)	0.16	0.69
Male	6 (10.34)	34 (58.62)	40 (68.97)		
Total	8 (13.79)	50 (86.21)	58 (100)		

Meanwhile, according to the Ministry of Health, Republic of Indonesia, we can categorize a range of age groups to 12-25 years old (teenager), 26-45 years old (adult), and 46-65 years old (adult). The majority of HIV patients were in the group of adults (70.69%). However, the difference in a group of age also did not correlate with the susceptibility of TB infections among people living with HIV ($\chi 2 = 0.33$; p=0.85, Table II).

Table II : Distribution of HIV-TB and HIV cases as regards age

Age	HIV-TB (n %)	HIV (n %)	Total (n %)	Chi Square	#p
12-25	1 (1.72)	4 (6.89)	5 (8.62)	0.33	0.85
26-45	5 (8.62)	36 (62.07)	41 (70.69)		
46-65	2 (3.45)	10 (17.24)	12 (20.69)		
Total	8 (13.79)	50 (86.21)	58 (100)		

HIV infection has damaged the patients' immune system Later, we asked whether the number of CD4 contributed to TB infection among individuals with HIV. Based on the CDC, there are three classification system for HIV infection. The first category for CD4 number was below 200 cells/uL; the second category for CD4 number was between 200-499 cells/ul, and third category for CD4 number was above 500 cells/ul (17). These patients were admitted to the hospital with a low number of CD4 (below 200 cells/ uL, Table 3), and none of them had a CD4 number above 500 cells/uL. Due to several reasons, most of the patients try to avoid the negative stigma for being HIV-positive. Thus, they tend to visit healthcare center once their immune system is really bad or once an opportunistic infection showing its symptoms. Since the majority of patients showed a low number of CD4, we could not conclude that a low number of CD4 could make these patients prone to TB infections. The correlation between the number of CD4 and the prevalence of TB infection in patients with HIV were not statistically significant ($\chi^2 = 0.18$; p=0.67, Table III).

Table III : Distribution of HIV-TB and HIV cases as regards CD4 number

CD4 count	HIV-TB (n %)	HIV (n %)	Total (n %)	Chi Square	#p
<200	7 (14.89)	39 (82.98)	46 (97.87)	0.18	0.67
>200	0 (0)	1 (2.13)	1 (2.13)		
Total	7 (14.89)	40 (85.11)	47(100)		

DISCUSSION

The occurrence of TB among new diagnosed HIV-patients was 13.79%. Since almost all patients (97.87%) showed a low level of CD4, this indicates that HIV infection has progressed to AIDS. The manifestation of immunosuppression in AIDS patients reduced the number of CD4+ T cells which contributed to increase the risk of developing active TB (15). Even before the reduce number of CD4+, it is known that individuals with HIV infection can be susceptible to TB infection (16).

Since the number of male patients with positive HIV was larger than the number of female patients, the comparison from which gender is prone to TB infection could not be answered in this study. Previous studies observed that males are twice as susceptible to HIV-TB than women (11). Meanwhile, other studies showed that although responses to tuberculosis could be different between male and female, the outcomes after tuberculosis treatment were similar (17). Thus, differences in gender could not lead to a difference in the prevalence of TB among individuals with HIV-positive. This question should be addressed in a future study with more data of HIV-TB (greater area than Gresik) to give a definite conclusion.

Our result showed that the majority of HIV positive cases were in adult age (12-25). The prevalence of TB in HIV patients was also high in this range of age (8.62%). Although the majority of individuals with HIV are in the productive age range, this does not affect the incidence of TB co-infection (18). On the other hand, other studies suggested that this phenomenon is related to socio-economic issues and responsibility for individuals and families (19).

Several studies suggested that patients with lower CD cell count were prone to a higher risk of TB infection (20,21). However, TB infection can also lower the CD4 count. Since all HIV-TB patient in this study visited healthcare center after TB symptoms appear, it was not clear whether the reducing number of CD4 was caused by HIV infection only or HIV-TB co-infection (22–24).

Finally, our results showed that it is necessary to screen HIV infected individuals, especially in areas which have a high risk of HIV transmission (among a key population of HIV). With early detection of HIV, we can reduce the occurrence of opportunistic infections. It has been mandatory from the Ministry Health to educate people about HIV infection and transmission to reduce negative stigma and improve the quality of life of people with HIV. However, based on our observation, people are still reluctant to check their risk for HIV infection, especially those who live with a key population group.

CONCLUSION

We can conclude that the prevalence of TB in HIV positive patients admitted Ibn Sina Gresik Hospital from 2018-2019 was 13.79%. We did not observe the significant difference in gender, age and number of CD4 that makes HIV patients easily infected with TB in this study.

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