CHAPTER 1

1. **INTRODUCTION**

   1.1. **Background**

Tuberculosis (TB) is still a global public health threat and it is one of the world's leading opportunistic disease and cause of death in patients with HIV infection (Kementerian Kesehatan RI, 2016; World Health Organization, 2018b). As early as 1993, the World Health organization (WHO) declared TB a global emergency and it is estimated that between years 2009-2025 nearly one billion people will be newly infected, 200 million people will get TB and 40 million are likely to die from it if control programs do not improve (World Health Organization, 2014b, 2018c). The HIV/AIDS pandemic has substantially altered the epidemiology of tuberculosis. Many persons with *Mycobacterium tuberculosis* and HIV have a 5-10% annual risk of developing active Tuberculosis (UNAIDS, 2018a). The double impact of TB and HIV co-infection is keeping large number of people trapped in poverty with these diseases that reinforce each other (Kementerian Kesehatan RI, 2015).

HIV is a high-risk factor for developing Tuberculosis (TB) disease in those with latent or new *Mycobacterium tuberculosis* infection and cause of death in patients with HIV infection. The risk of developing TB is between 20 and 37 times (World Health Organization, 2011a), 16 and 27 times (UNAIDS, 2018a) greater in people living with HIV than among those who do not have HIV infection. Tuberculosis is responsible for

more than a quarter of deaths in people living with HIV (World Health Organization, 2011a). In 2017, approximately 300,000 people died from AIDS related Tuberculosis (UNAIDS, 2018b; World Health Organization, 2018d).

Globally, UNAIDS reported 10.4 million TB cases in 2015 of which 1.2 million were living with HIV, 10 million TB cases in 2017 of which 1.6 million died from the Tuberculosis (UNAIDS, 2018a, 2018b). Tuberculosis (TB) is a leading killer among people living with Human Immune deficiency Virus (HIV) (WHO, 2017). At least one in four deaths among people living with HIV can be attributed to TB, and many of these deaths occur in resource-limited settings (World Health Organization, 2010c). Collaborative Tuberculosis and HIV activities are essential to prevent, diagnose and treat Tuberculosis among people with HIV and HIV among TB patients, and to ensure that HIV-positive Tuberculosis patients are identified and treated appropriately (World Health Organization, 2010c). According to World Health Organisation , about a third of the 40 million people with HIV/AIDS are co-infected with *Mycobacterium tuberculosis* (World Health Organization, 2011a).

In 2015, 57% of Tuberculosis cases among people living with HIV were not diagnosed or treated, resulting in 390,000 tuberculosis-related deaths among people living with HIV. In 2016, 57% of notified Tuberculosis patients had a documented HIV test result, up from 55% in 2015 (UNAIDS, 2018a). Documentation of HIV status averaged 66% of Tuberculosis patients in the 30 high TB/ HIV burden countries, but varied considerably, from 14% in Indonesia to above 80% in 18 high TB/HIV burden

countries in the WHO African Region (World Health Organization, 2017a, 2017d, 2018b). Indonesia is one of the 30 countries with a high Tuberculosis burden, TB-HIV and MDR-TB burden across the world (World Health Organization, 2018b). In recent years, the implementation of collaborative TB/HIV activities has been rising globally. This has created the need for additional research into how to deliver quality and integrated services for TB and HIV prevention, treatment and care, and thus prevent unnecessary deaths (World Health Organization, 2010c). In 2013, there were 1.1 million new TB/HIV co-infected cases globally, accounting for 12% of incident TB cases and 360 000 deaths rates (World Health Organization, 2017d).

The Asia-Pacific region which contributes more than a half of all Tuberculosis cases worldwide but traditionally reports low TB/HIV co-infection rates (World Health Organization, 2017d). In 2014, the estimated number of HIV-TB cases in the South East Asia region were 210,000 corresponding to 11 per 100 000 and 5% of all estimated TB-incident cases (World Health Organization SEARO, 2016a). In 2018, the total HIV-TB cases drastically increased to 477,461 cases of which 86% were on antiretroviral therapy (World Health Organization, 2019a).

A study by UNICEF Indonesia found out that one person in Indonesia is infected with HIV in every 25 minutes (UNICEF INDONESIA, 2012). In 2016, there were 620,000 people living with HIV of which 13% were accessing antiretroviral therapy, 48,000 new HIV infections and 38,000 AIDS-related deaths (UNAIDS, 2018b). According to Indonesia Ministry of Health, the incidence rate of HIV is 24 cases per 100,000 people

with a target rate of 18 cases per 100,000 people (Kementerian Kesehatan RI, 2017, 2018). Since 2010, new HIV infections have decreased by 22% though AIDS-related deaths have increased by 68% and these deaths could be due to coinfections with Tuberculosis (Kementerian Kesehatan RI, 2014; Pusat Data Dan Informasi Kementerian Kesehatan RI, 2018a). According to World Health Organization in 2018, Indonesia had a total Tuberculosis incidence of 845,000 cases (319 per 100,000 population), HIV-TB incidence of 21,000 cases (7.9 per 100,000 population) (World Health Organization, 2018e). The number of new TB cases in Indonesia were 420,994 cases in 2017 (Pusat Data Dan Informasi Kementerian Kesehatan RI, 2018b). Based on gender, the number of new cases of TB in 2017 in men was 1.4 times greater than in women. Even based on the Indonesia prevalence survey of Tuberculosis, the prevalence in men was 3 times higher than in women and this was possibly because men are more exposed to TB risk factors such as smoking and non-compliance with taking medication. (Pusat Data Dan Informasi Kementerian Kesehatan RI, 2018b). According to World Health Organization, the incidence rate of Tuberculosis cases in Indonesia in 2018 was 319 having Tuberculosis per 100,000 people with a target of 190 Tuberculosis cases by 100,000 people in 2020 (World Health Organization, 2017d).

The prevalence and incidence of TB infection in people with HIV, or routine testing of Tuberculosis patients for HIV infection was not nationally implemented in Indonesia had not been routinely reported by 2011. In 2011, Indonesia was estimated that the TB-HIV rate was 3% nationally though in some provinces the reported TB/HIV co infection rate is reported to be much higher, for example Papua (14%) and Bali (3.9%)

(Departemen Kesehatan Republik Indonesia, 2011; Rachman BE, 2018). However the estimated prevalence of HIV in new TB cases increased to 6.3% in 2013 (World Health Organization, 2017d). By 2017, a substantial number of TB patients were coinfected with HIV, with over 10% of TB patients testing positive. However, HIV testing coverage is still low (<20%) and true burden of TB-HIV coinfection is not yet known. Indonesia has reported the lowest coverage (10%) of the provision of Tuberculosis preventative treatment to PLHIV newly enrolled in HIV care in 2018 among the 38 high TB and 41 TB-HIV burden countries (World Health Organization, 2019a). Improving access to HIV testing for all TB patients should be a priority and the urgency of providing immediate ART to all TB-HIV coinfected patients (World Health Organization, 2017b).

East Java (Jawa Timur) Province has been designated as a region with HIV prevalence concentrated along with five other provinces, namely DKI Jakarta, Papua, Bali, Riau and West Java (Kementerian Kesehatan RI, 2010; Dinas Kesehatan Jawa Timur, 2017, 2018; World Health Organization, 2017c). East Java Province in 2017 and 2018 ranked second in Indonesia in the number of patients with smear TB discovery + new cases (Dinas Kesehatan Jawa Timur, 2017, 2018). In East Java, out of the 47,223 Tuberculosis cases (as at 28th November 2019) in East Java, 34,230 of them knew their HIV status before Tuberculosis diagnosis of which 1,235 TB-HIV coinfections in East Java of which 12% (highest) are from Surabaya, 681 started ART treatment, 628 started PPK treatment (Data from Dinas Kesehatan East Java as at November 2019). In 2018,

the total number of all Tuberculosis (TB) cases treated until cured in East Java was 20,797, cases out of an estimated number of 229,961 cases (Dinas Kesehatan Jawa Timur, 2018).

Surabaya city ranks with the highest number of TB and HIV-TB patients amongst all the other cities and districts in East Java (Data from Dinas Kesehatan East Java Province as at November 2019). There are 5,533 Tuberculosis patients in Surabaya of which 3,691 know their HIV status (Data from Dinas Kesehatan East Java Province as at November 2019). The number of TB-HIV confections in Surabaya are still very high; 183 patients in 2017, 162 patients in 2019 and 172 patients in 2019 (Data from Dinas Kesehatan Kota Surabaya as at 28th February 2020). There has been a steadily increasing number of Tuberculosis patients in Surabaya from 2015 to 2019 though the case detection rate is still below the target number as shown in Figure 1.1 below.
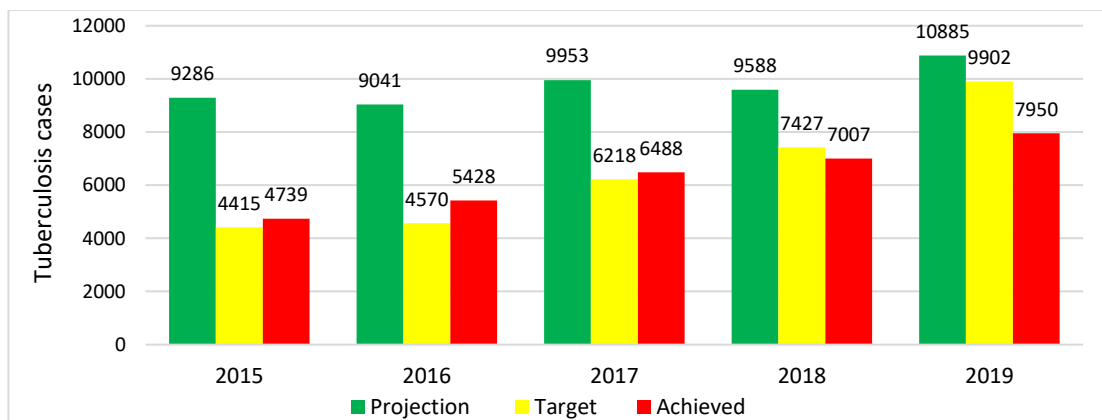
Source: Data from Dinas Kesehatan Kota Surabaya
Figure 1.1 Trend of Tuberculosis cases versus the Projections and Targets in Surabaya city: 2015-2019

The Tuberculosis Prevention Program is carried out in addition to conducting promotional and preventive activities, as well as conducting early detection activities

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where active tuberculosis sufferers are found that also involve the community, as well as providing treatment until recovery. Countermeasure program tuberculosis must also be supported by commitment from stakeholders (Dinas Kesehatan Jawa Timur, 2018). The National policy for TB/HIV collaboration activities is in place, guidelines, and training materials have been developed. National Tuberculosis Programme (NTP) has revised the recording and reporting system to include information on TB/HIV with its top priority as to provide quality DOTS services at all ART facilities.

1.2. Problem statement

There is little population-based epidemiology data about an association between HIV infection and TB, either transmitted or acquired, and the data that are available are inconsistent. The latest treatment outcome data for new cases of Tuberculosis show a global treatment success rate of 85% in 2017, an increase from 81% in 2016. The improvement was mainly due to progress in India (World Health Organization, 2019a). The latest treatment outcome data for people with MDR/RR-TB show a global treatment success rate of 56%. Unfortunately, Indonesia is not yet among high MDR-TB burden countries (Bangladesh, Ethiopia, Kazakhstan and Myanmar) with better treatment success rates that are more than 70% (World Health Organization, 2019a). In the 2016 cohort, Indonesia was among the 30 high MDR-TB burden countries with a TB treatment success rate that were lower than 50% with reasons attached to high rates of death (17%) and loss to follow-up (26%) (World Health Organization, 2019a).

Surabaya ranks with the highest number of TB and HIV-TB patients amongst all the other cities and districts in East Java (Data from Dinas Kesehatan Jawa Timur as at November 2019) and also a persistent increase in the percentage of HIV-TB coinfection among the notified TB cases in Indonesia from 2009 to 2017 as shown in Figure 1.2 below. This creates a research interest to analyze the factors that influence Tuberculosis treatment outcomes among HIV positive and HIV negative patients.
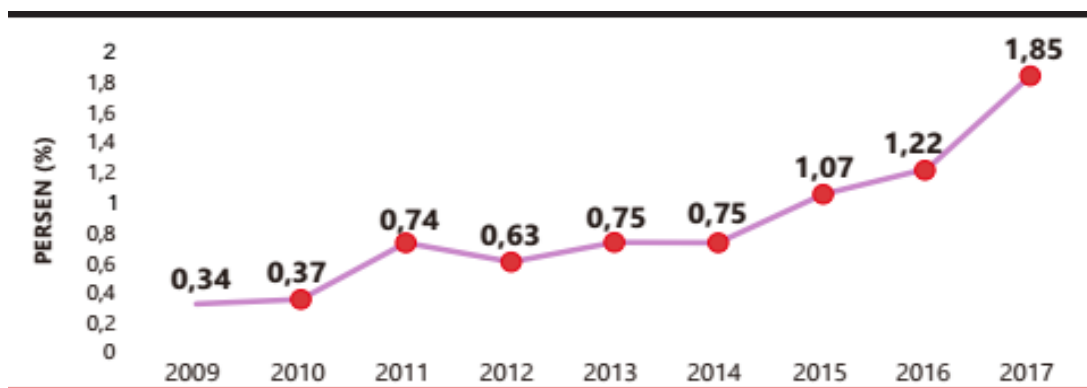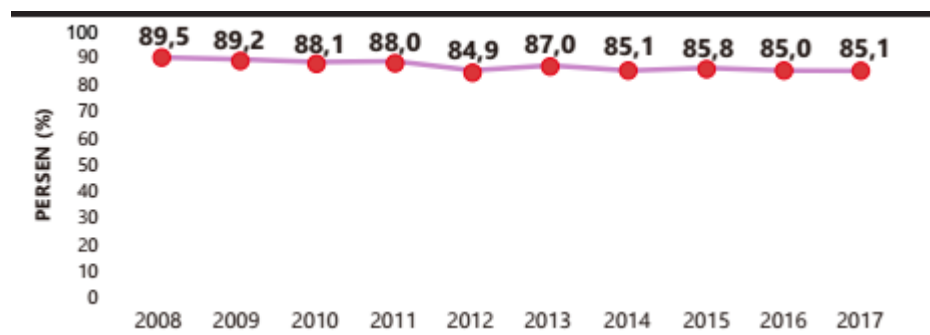

Source: Tuberkulosis Infodatin, Pusat data dan Informasi Kementerian Kasehatan RI, 2017
Figure 1.2 Percentage of HIV Positive TB coinfected Patients among Annual-Notified TB Patients in Indonesia, 2009 - 2017

Tuberculosis treatment success rate in Indonesia in 2015 was at 87.8% slightly better than the 2015 global TB treatment success rate of 83% and the 2015 global set target of 85% (Ministry of Health Republic of Indonesia, 2015; World Health Organization, 2017d, 2019a; Pusat Data Dan Informasi Kementerian Kesehatan RI, 2018b). In 2017, TB treatment success rates in Indonesia among the new and relapse cases was at 85%, among previously treated cases excluding relapse registered was at 73%, among HIV-positive TB cases registered was at 69% far below the target of 90% (World Health Organization, 2018e). In many high TB burden countries, TB treatment success rates

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remain below the national and global targets with very high lost to follow up and death rates. The high lost to follow up rates results in increasing numbers of drug-resistant TB (Ministry of Health Uganda, 2019). The trend of the Tuberculosis success rate in Indonesia from 2008 to 2017 is also shown in Figure 1.3 below and has been below the national target of 90%.

Source: Tuberkulosis Infodatin, Pusat data dan Informasi Kementerian Kasehatan RI, 2017
Figure 1.3 Tuberculosis treatment success for Tuberculosis Patients (All Cases) in Indonesia, 2008 - 2017

Cure rates tend to have a gap with treatment success rates, so the contribution of patients who recover to treatment success rates decreased. In an effort to control the disease, the phenomenon of declining cure rates needs to receive great attention because it affects the transmission of TB disease (Pusat Data Dan Informasi Kementerian Kesehatan RI, 2018b).
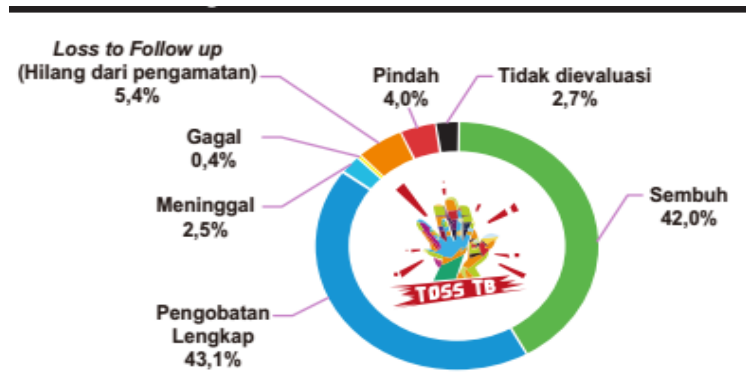
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Source: Tuberkulosis Infodatin, Pusat data dan Informasi Kementerian Kasehatan RI, 2017
Figure 1.4 Tuberculosis treatment outcomes (ALL cases), 2017

Tuberculosis treatment success in Indonesia and East Java of 70% and 84% respectively are still below the target line of 90% as shown in Figure 1.5 below. A study was chosen in Surabaya because it has the highest number of Tuberculosis and HIV-TB cases in East Java.
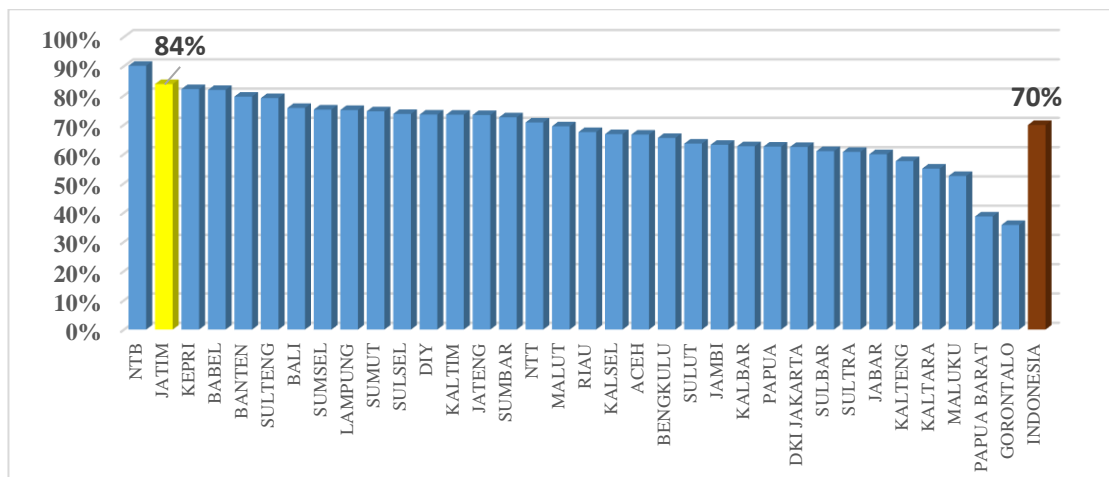
Source: Dinas Kesehatan Jawa Timur, November 2019
Figure 1.5 Tuberculosis treatment Success Rate of all Cases per Province in Indonesia, 2018 *(Update: As at 16-10-2019)*

The treatment success rates of TB patients in Surabaya for the last three years are almost close to the set target of 90%; 87.1% in 2016, 90.0% in 2017 and 90.1% in 2018

(Data from Dinas Kesehatan Kota Surabaya as at 28th February 2020). It is also important to note that the percentage of those that cured from Tuberculosis was decreasing from 2016 to 2018 (37.5%, 36.7%, 34.3%) while the percentage of those that completed treatment was increasing from 2016 to 2018 (49.6%, 53.3%, 55.9%) (Data from Dinas Kesehatan Kota Surabaya as at 28th February 2020).

Therefore, there is urgency to scale up interventions such as isoniazid TB preventive therapy, TB treatment, TB infection control, as well as HIV testing and improved access to antiretroviral treatment. Increased awareness and concerted action is required to reduce TB/HIV coinfection rates in the Asia-Pacific region and to improve the outcomes of people living with HIV (World Health Organization, 2017d). A number of considerations are made before and during TB treatment which greatly influence the Tuberculosis treatment outcomes. Among these include classification of TB patient by previous history, HIV status, and drug susceptibility status, Identifying TB Regimen, Dosing (adjusted for weight), Identification of treatment adherence system (treatment supporter), Patient health education and counselling (disease, treatment and its duration, side effects, monitoring, frequency of clinic visits), Identification of HIV status and TB-HIV co-management, Identification of other co-morbidities like diabetes, malnutrition, Treatment monitoring (clinically and laboratory), Linkage to TB support services e.g. management of malnutrition, Adjunct therapy, Determination of TB treatment outcome (interim e.g. Sputum conversion, and Final outcomes among others (Ministry of Health Uganda, 2019).

1.3. Formulation of the problem

The main research question of this study is "What factors influence Tuberculosis treatment outcomes among HIV positive and HIV negative patients in Surabaya"?

1.4. Research Objectives

1.4.1. General objective

To analyze the factors that influence Tuberculosis treatment outcomes among HIV positive and HIV negative patients in Surabaya.

1.4.2. Specific objectives

1. To calculate the percentage of Tuberculosis patients that had treatment success and treatment failure in HIV positive and HIV negative patients in Surabaya.

2. To analyze the time taken to have a treatment success or treatment failure in HIV positive and HIV negative patients in Surabaya.

3. To analyze the factors (Gender, Age, Diabetes history, Patient category, History of TB contact, TB Clinical form) influencing Tuberculosis treatment outcomes in HIV positive and HIV negative patients in Surabaya.

1.5. Benefits of research

1.5.1. Theoretical benefit

The results of this study will be an epidemiological baseline to mitigate these risk factors through application of various interventions as depicted in a number of health care theories that have a disease control approach. It is noteworthy to study the impact of HIV on Tuberculosis treatment outcome among Tuberculosis patients in Surabaya and will be used as a comparison and reference for future researchers.

1.5.2. Practical benefit

It is necessary to implement strategies and the given recommendations at the end of the study that will promote shared actions against risk factors between Tuberculosis and HIV/AIDS infections to strengthen the health care network, aimed at producing an individualized care, comprehensive and responsive performance in Surabaya.

1.5.3. Benefit to the community.

The author hopes that the study findings will influence decision making and prioritization in Surabaya, thereby contributing to a better treatment outcome and quality of life of HIV positive and HIV negative patients in Surabaya. Recommendations from the study can adopted by the government of the Republic of Indonesia (Ministry of Health) to create a way forward for new health policies about the treatment of Tuberculosis in HIV positive and HIV negative patients.

1.5.4. Benefit to the Faculty of Public Health, Airlangga University

It is one way in the Faculty and University to engage in Community Social responsibility to give back to the community since these research results can be a baseline in the development of new health policies in the study region and the whole country at large.

1.5.5. Benefit to the researcher

The researcher is a Masters of Epidemiology student at Airlangga University and therefore this research and dissemination of its findings is a requirement to attain his academic qualification of a Master's degree from Airlangga University. It is vital and noteworthy as reference of the author's research skills, critical thinking abilities and ability to identify research problems in quest for a public health related job and further studies.