

# Differences in Survival Rates of HIV Patients with Pulmonary TB and Extra Pulmonary TB at General Hospital Haji Adam Malik in 2015-2018

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## ABSTRACT

**Introduction:** The number of TB cases in Indonesia was increasing and it is estimated that one in five is extrapulmonary TB, is believed that there is a high mortality rate for extrapulmonary TB.

**Aim:** To assess difference in survival rates of HIV patients with pulmonary TB and extra pulmonary TB.

**Results:** Based on Fisher's Exact test, it was found that there was no statistical difference survival rates of HIV patients with pulmonary TB and extra-pulmonary TB at H. Adam Malik Hospital in 2015-2018 ( $p=0.303$ ). The mean survival of HIV patients with extrapulmonary TB was 4.3; and pulmonary TB patients was 3.5. Overall mean survival is 4.5 years. It was concluded that HIV patients with pulmonary TB was 1.21 times more likely to die than HIV patients with extrapulmonary TB (HR: 1.21; 95% CI 0.76-1.92).

**Conclusion:** HIV patients with pulmonary TB had a lower survival rate than HIV patients with extrapulmonary TB but it was not statistically significant. The 50% survival rate for HIV patients with extrapulmonary TB is 4.3 years and for pulmonary TB is 3.5 years

**Keywords:** HIV, co-infection, pulmonary TB, extrapulmonary TB, survival rates

## INTRODUCTION

Eighty percent of TB-HIV coinfection cases worldwide occur in sub-

Saharan Africa (SSA). Among TB patients, 53% were HIV-positive.<sup>[1]</sup> In 2019, an estimated 10 million TB cases occurred globally; of which 1.2 million deaths from TB occurred in HIV negative patients and 208,000 TB deaths occurred in HIV positive patients. As for gender, male (age>15 years) dominates with 56%; while women 32% and children (age<15 years) are 12%.<sup>[2]</sup>

The number of TB cases in Indonesia according to 2019 WHO report, it is estimated that there are 845,000 new TB cases per year with 92,000 deaths per year (per 100,000 population) of which there are 19,000 HIV positive TB cases (13 per 100,000 population).<sup>[2]</sup> It is estimated that prevalence of new TB cases by gender in Indonesia in 2017, was male 245,298 cases while female is 175,696 cases.

Although most TB programs focus on pulmonary TB infection, it is estimated that one in five worldwide TB infection cases is extrapulmonary TB, which is defined as TB infection occurring outside lung parenchyma. The incidence of extrapulmonary TB is more common in HIV patients up to 70% compared to general population. The severity itself is associated with patient's CD4 cell count. Mortality was high in HIV patients with extrapulmonary TB coinfection, compared with HIV patients with pulmonary TB. A study in Ukraine

divided TB-HIV co-infected patients into 2 groups, found that patients with extrapulmonary TB were 2.4 times (95% CI: 1.2-10.4) more likely to die. Pulmonary TB is caused by low CD4 count with more likely occurred opportunistic infections. [3] Although national statistics of treatment outcome for extrapulmonary TB are unknown, it is believed that there is a high mortality rate for extrapulmonary TB.

Therefore, researchers are interested in evaluate survival rates comparison of HIV patients with pulmonary or extrapulmonary TB and other factors related to HIV patients survival rates. This is expected to improved early detection, prevention, and can improve the survival rate of HIV patients.

## METHODS

This research is a retrospective cohort analytic study conducted at Haji Adam Malik General Hospital Medan from September 2020 - December 2020 based on medical record data. The sampling technique is total sampling in 3 years will be obtained. The inclusion criteria were: patient age  $\geq 18$  years, HIV positive, all HIV patients with pulmonary TB infection or extra pulmonary TB who came to outpatient installation of H. Adam Malik Hospital and never received treatment (new case). While exclusion criteria were incomplete patient data, namely examinations that supported diagnosis and CD4 examination, lost to follow-up and all HIV patients diagnosed with pulmonary TB or extra-pulmonary TB in other health care facilities and had received treatment.

Collected characteristics data of HIV patients with pulmonary TB and extrapulmonary TB which is age, gender,

risk factors through medical records in 2015. Then the patient data in 2015 will be re-evaluated in 2018 to assess survival rate.

## Statistical Methods

Data analysis using the SPSS-21 (Statistical Product and Science Service) application. The data will be analyzed descriptively to assessed frequency distribution of research subjects based on demographic characteristics. Statistical analysis used univariate and bivariate survival analysis. Survival analysis using Kaplan Meier.

## RESULTS

### Research Sample Characteristic

In this research, it was found that HIV patients with TB infection mostly are men with 98 HIV patients with pulmonary TB (62.8%) and 58 patients with Extra Pulmonary TB (37.2%).

Table 1: Frequency distribution of HIV patients with pulmonary TB and extra pulmonary TB based on gender

Gender	TB type			
	Pulmonary TB		Extra pulmonary TB	
	N	%	N	%
Male	98	62,8	58	37,2
Female	14	36,8	24	63,2

Mean age of HIV patients with pulmonary TB was 32.5 years, while mean age of HIV patients with extrapulmonary TB was 33.5 years. For CD4 levels, Median 47 was found in HIV patients with pulmonary TB and median 39.5 in HIV patients with extrapulmonary TB as shown in table 2.

Table 2: Frequency distribution of HIV patients with pulmonary TB and extrapulmonary TB based on age and CD4 cell count

Variable	Pulmonary TB	Extrapulmonary TB
Age (years old)	32,50 (22-61)	33,5 (20-63)
CD4	47 (2-928)	39,5 (1-514)

Table 3: Proportion survival rates of HIV patients with pulmonary TB and extra pulmonary TB at H. Adam Malik Hospital in 2015-2018

TB type	Outcomes						P value
	Survived		Not Survived		Total		
	n	%	N	%	n	%	
Pulmonary TB	64	57.1	48	42.9	112	100	0,303
Extrapulmonary TB	53	64.6	29	35.4	82	100	

\*Fisher's Exact test

Based on Fisher's Exact test, it was found that there were no statistical

difference survival rates of HIV patients with pulmonary TB and extra-pulmonary

TB at H. Adam Malik Hospital in 2015-2018 ( $p=0.303$ ). The mean survival of HIV patients with extrapulmonary TB was 4.3; meaning that 50% of extrapulmonary TB patients died within 4.3 years and the mean survival of pulmonary TB patients was 3.5, where as many as 50% of pulmonary TB

patients died within 3.5 years. Overall mean survival is 4.5 years. It was concluded that HIV patients with pulmonary TB was 1.21 times more likely to die than HIV patients with extrapulmonary TB (HR: 1.21; 95% CI 0.76-1.92).

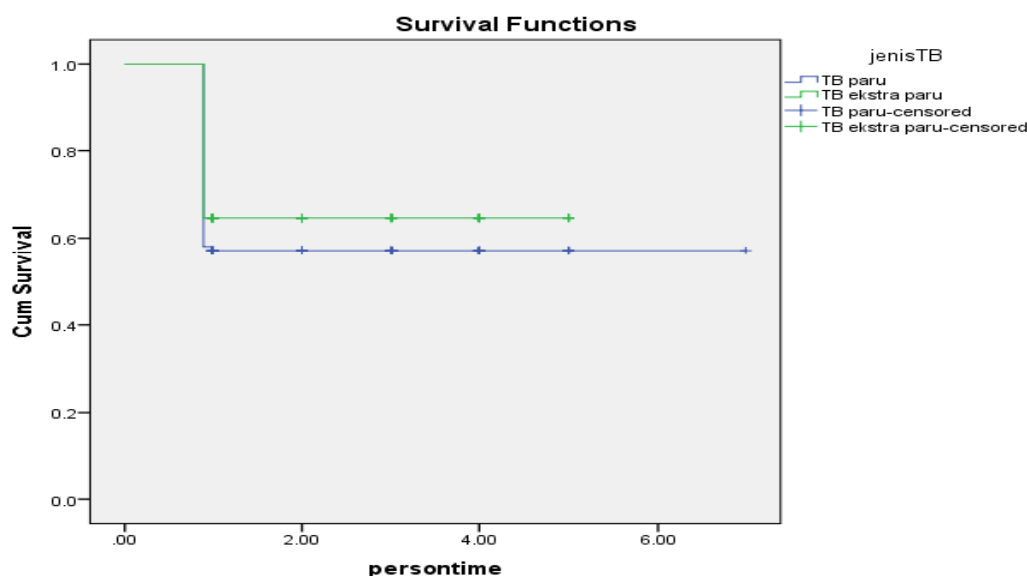


Figure 1: Kaplan Meier curve of HIV patients with pulmonary TB survival rates at H. Adam Malik Hospital in 2015-2018.

## DISCUSSION

In this research it was found that proportion of HIV patients with pulmonary TB at H. Adam Malik Hospital in 2015-2018 were 64 people (57.10%) while HIV patients with extrapulmonary TB were 53 people (64.60%). Based on Fisher's Exact test, it was found that there was no statistical difference in survival rates of HIV patients with pulmonary TB and extrapulmonary TB at H. Adam Malik Hospital in 2015-2018. This research contradicts Zenner et al study where HIV patients with extrapulmonary TB are at greater risk of death than HIV patients with pulmonary TB.<sup>4</sup> In Ohene et al study, the treatment success rate for extrapulmonary TB was 70.1% and for pulmonary TB was 84.2%. Meanwhile, mortality rate for pulmonary TB was 12.6% and 28.7% in extrapulmonary TB patients.<sup>[5]</sup>

Using Kaplan Meier test showed that survival rate of HIV patients with extrapulmonary TB was better than HIV with pulmonary TB, where as many as 50%

of extrapulmonary TB patients died within 4.3 years while 50% of pulmonary TB patients died. Within 3.5 years. In addition, it was found that group of HIV patients with pulmonary TB was 1.21 times more likely to die than HIV patients with extrapulmonary TB (HR: 1.21; 95% CI 0.76-1.92).

The Zenner et al in 2015 study reported, as many as 18% of deaths within 6 months occurred in HIV patients with pulmonary TB. The mortality rate found 51.7% were men and 48.3% were women. Mortality rate in pulmonary TB is 11.9% and extra pulmonary TB is 16.1% while HIV patients with extra pulmonary TB have greater risk of death than HIV patients with pulmonary TB. It was found that survival rate of HIV patients with TB is determined by number of patients with undiagnosed HIV, the availability of ARVs and ability to detect and treat TB promptly. A European cohort study showed lower survival rates in TB coinfecting HIV patients in East than in West, related to poor access to ARVs.

Better outcomes through ART initiation and TB treatment are well documented in HIV and TB endemic areas. [4]

In Mabunda et al study, Limpopo Province recorded TB mortality rate 12.4% during the year observed, with majority of deaths recorded among economically active age group (25-54 years). Death was significantly associated with older age, location of extrapulmonary disease, HIV coinfection; negative pulmonary TB smear and previous history of TB. These findings are consistent with previous reports of death higher risk associated with negative sputum smears, coinfection with HIV and other co-morbidities, and older age. The association between HIV infection and TB death was evident in this research: HIV-positive patients were more likely to have extrapulmonary TB and have negative smear results, and mortality was higher among those who were HIV-positive. [6]

Research conducted by Diwakar et al, using a prospective cohort study, found that of 9 deaths that occurred, 5 were due to pulmonary TB while 4 were due to extrapulmonary TB with overall survival rate found to be 92% in 6 months after taking ARVs and 91% after one year on ARVs. From this research, it was also found that early ART can be beneficial in clinical and immunological improvement by increasing CD4 cells and reducing opportunistic infections that occur in HIV patients. [7]

The risk factors that influence HIV patients with pulmonary TB mortality in combined ARV administration have been studied by Yong-Ji et al. In this study, it was found that of 4914 HIV patients, 359 of them had pulmonary TB, 90.53% were male patients with median age 39 years. At the time pulmonary TB was diagnosed, the median CD4 T-cell count was 51/mm<sup>3</sup> and 27.3% of patients were taking ARVs. During follow-up period, 53 patients died with an overall mortality rate 15.92%, and most deaths occurred 6 months after diagnosis pulmonary TB. Demographic profiles were compared between case

fatality and survival, with older age, lower CD4 cell count, lower antiretroviral therapy, late diagnosis, and more severe clinical manifestations such as shortness of breath, more extensive lesions and pulmonary atelectasis. Among patients who had not received antiretroviral drugs before administration of TB drugs, administration of ARVs for 8 weeks after administration of TB drugs increased mortality rate, whereas administration of ARVs for 4-8 weeks after initiation of TB drugs was associated with fewer deaths. [8]

In contrast to this research which was conducted on outpatients, Van der et al study was conducted on HIV patients with tuberculosis who received ARV therapy in inpatient prospective cohorts. The aim of this study was to document clinical decline in HIV patients with tuberculosis receiving ARVs in hospitalization. There was a total of 112 patients of which 60% were women with median age 32 years. In this study, incidence of TB-IRIS, nosocomial infections and drug poisoning were found to be complicated HIV patients with TB who were hospitalized receiving ARV therapy. Despite high morbidity, the mortality rate tends to be low where 89% of participants live 3 months after ARV administration, which can be concluded that adequate clinical and diagnostic care and supportive treatment resources are needed. [9]

## CONCLUSION

HIV patients with pulmonary TB had a lower survival rate than HIV patients with extrapulmonary TB but it was not statistically significant. The 50% survival rate for HIV patients with pulmonary TB is 3.5 years is 4.3 years and for extrapulmonary TB.

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